CLINICAL APPLICATIONS OF OTOACOUSTIC EMISSIONS IN ASSESSMENT OF OLIVOCOCHLEAR DYSFUNCTION

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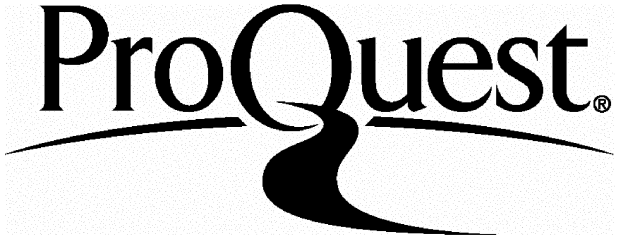

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ABSTRACT

The efferent olivocochlear system provides feedback to the sensory receptors and afferent nerves of the cochlea. This study examined efferent auditory effects in humans by measurement of otoacoustic emissions during contralateral acoustic stimulation. Results were analyzed with a view to optimizing protocols for non-invasive clinical assessment of olivocochlear dysfunction.

An experimental paradigm for assessing the loss of olivocochlear innervation was applied to vestibular nerve section patients whose olivocochlear bundle had been severed for treatment of peripheral labyrinthine disorders. Control patients were studied, who had undergone a similar surgical procedure for vascular decompression of the vestibular nerve, but without section of the olivocochlear fibres. The role of middle ear reflexes was investigated in patients with unilateral section of the middle ear muscle tendons for treatment of myoclonus. Patients with pathological lesions along the olivocochlear pathway from cochlea to cortex were also investigated.

Normal subjects demonstrated significant and repeatable inhibition of otoacoustic emission amplitude during contralateral white noise at least 25dB above sensation level in normal subjects. The test was sensitive to olivocochlear disruption via vestibular nerve section, lesions of the olivary nuclei, or cerebello-pontine angle. Cases with a history of noise exposure also showed a loss of inhibitory effects. Control cases with lesions not affecting the olivocochlear pathway maintained normal levels of inhibition.

The findings support the conclusion that otoacoustic emissions provide a means of evaluating efferent function, and that surgical or pathological disruption of the olivocochlear system results in a significant loss of efferent auditory effects.

CHAPTER I

INTRODUCTION

INTRODUCTION

The mammalian auditory system comprises both an ascending and descending neural pathway between the cochlear hair cells, auditory nuclei of the brainstem, midbrain and cortex. Rasmussen (1942, 1946) first described the "efferent cochlear bundle", which is the ultimate portion of the descending pathway. These efferent fibers travel from the superior olivary complex (SOC) via the olivocochlear bundle (OCB) in crossed and uncrossed paths innervating each ear where they form synaptic connections with the hair cells and the cochlear afferent nerve fibers respectively (Warr 1992). Two anatomically distinct olivocochlear pathways have been documented; the medical olivary complex (MOC) which primarily innervates the outer hair cells (OHC), and the lateral olivary complex (LOC) which predominantly forms axo-dendritic synapses with the afferent fibres of the inner hair cells (IHC) (Warr & Guinan 1979).

The physiology of lower order mammalian olivocochlear systems has been extensively explored. Studies demonstrated that activation of the olivocochlear fibers via electrical and acoustic stimulation was associated with the modulation of cochlear hair cell and afferent nerve fibre responses (Guinan 1996: review). Efferent auditory effects (EAE) were observed in intracellular hair cell responses (Brown et al. 1983, Brown and Nuttall 1984), extracellular cochlear responses (Fex 1959, 1962) and auditory nerve compound and single unit responses (Galambos 1956, Desmedt 1962, Wiederhold and Kiang 1970, Buno 1978, Guinan 1986, Warren and Liberman 1989).

However, the advent of otoacoustic emissions (OAE) offered a non-invasive means of observing the micro-mechanical responses of the cochlea to efferent activation (Kemp 1978, Kemp 1997). Otoacoustic emissions are pressure oscillations, recordable in the ear canal via a microphone. OAE are generated by the interaction between the micro-mechanical contractile responses of the outer hair cells, supporting structures of the organ of Corti and the basilar membrane (Brownell et al. 1985, Ashmore 1987, Ashmore 1994). The result is a sensitive and frequency specific "cochlear amplification" of movement that travels through the cochlea and also back through the middle ear structures and into the ear canal (Davis 1983). OAE can be observed in the majority of human subjects with normal pure tone audiometry (Robinette and Glattke 1997, Gorga et al. 1999, Probst and Harris 1997).

Outer hair cells are a key element in the production of OAE, providing a cycle by cycle enhancement of organ of Corti movement (Ashmore 1994). In addition, outer hair cells receive direct innervation from the olivocochlear system, and can be considered both sensory and motor units. The exact mechano-electrical changes that result from efferent innervation of the cochlea remain open to

conjecture. However, it follows that excitation of the efferent system could alter the nature of cochlear responses as measured by otoacoustic emissions.

The study considered whether olivocochlear disruption was associated with loss of otoacoustic emission inhibition. The clinical utility of the test procedures was considered as part of a neuro-otological test battery, examining the impact of lesions along the efferent pathway. The findings from pathological and surgical cases were compared to the results from normal and control subjects.

The role of the efferent olivocochlear system was measured by examining changes in the amplitude of otoacoustic emissions associated with activation of the crossed efferent system by means of presentation of contralateral acoustic stimuli. The test protocol was designed with knowledge of the effective procedures for mammalian efferent systems, and adapted to form clinically viable protocols. Efferent auditory effects were quantified in subjects with normal hearing and audiological histories, and the results guided the development of the protocols used for the clinical evaluation of efferent dysfunction in the neuro-otological patients studied. The consultant Neuro-otologist established the diagnosis for the patients studied.

An experimental paradigm was applied, appropriate for non-invasive testing of loss of efferent auditory effects in humans. Direct evidence of the impact of "de-efferentation" was observed in vestibular nerve section patients in whom the olivocochlear bundle was sectioned as a consequence of treatment of peripheral labyrinthine dysfunction. The nerve section procedure results in section of both medial and lateral olivocochlear fibres, but without damage to the cochlea or disruption of afferent auditory innervation. Even in specialized Neuro-otological centres, vestibular nerve section patients are relatively uncommon. Long-term study allowed for comparison of cochlear responses in the presence and absence of olivocochlear feedback in vestibular nerve section patients before and after section of the olivocochlear and vestibular fibres.

Control experimental information was gathered by studying patients before and after neural or otological surgery that did not interrupt the olivo-cochlear efferents. The effects of the surgical procedures on efferent auditory effects were provided by examining patients who underwent retrolabyrinthine surgery for vascular decompression of the VIII cranial nerves, but without nerve section. In order to differentiate the role of middle ear muscle reflexes versus olivocochlear reflexes, patients with absent middle ear reflexes were studied following unilateral section of the tensor tympani and stapedial tendons for the treatment of myoclonus causing audible, objectively intense tinnitus.

The study examined the relation of olivocochlear disruption to loss of otoacoustic emission inhibition. In order to gain information regarding the clinical utility of the procedures, the study included patients with neuro-otological lesions along the efferent pathway, from outer hair cells to cortex. The effect of ototoxic drugs, lesions of the olivary nuclei and cerebello-pontine were investigated.

The findings were analyzed and the optimal clinical procedures for olivocochlear testing were discussed, including the potential of these procedures for examining the role of the olivocochlear efferent system in humans.

CHAPTER II

BACKGROUND

ANATOMY & PHYSIOLOGY

BACKGROUND

Anatomy of the Auditory System

Cochlear Anatomy

The cochlea is divided into 3 fluid filled vestibulae (scalae), with the sensory structure (the organ of Corti), situated within the scala media. The organ of Corti is comprised of inner and outer hair cells held at the apex by the reticular lamina, and at the base within a complex mechanical structure of supporting cells arising from the basilar membrane. The outer stereocilia of the outer hair cells are embedded in the tectorial membrane and Hardestry's membrane (Lim 1980). The majority of studies indicate that the stereocilia of the inner hair cells are not attached to the tectorial membrane, though Hensen's stripe is situated directly above the IHC (Lim 1980, Hunter-Duvar 1978). The body of each inner hair cell is surrounded by the rigid supporting cells. In contrast, the cell body of outer hair cells are unrestrained, with their apical surfaces rigidly held in the reticular lamina formed from the processes of the supporting Dieter cells, and their bases held in a chalyx of the supporting cell. The outer hair cells possess a cytoskeletal lattice associated with the lateral plasma membrane that reinforces the cell circumference whilst allowing changes in cell length and diameter (Brownell 1990, Holley and Ashmore 1990a).

Afferent Auditory Anatomy

The inner hair cells may be considered to be the primary sensory receptors on the basis of that they receive the great majority of afferent cochlear nerve fibres (95% of the 50,000 afferent fibers in cats (Spoendlin 1969, Liberman 1980a, 1982a, Liberman et al. 1990), whereas the outer hair cells communicate with a relatively small number of thin unmyelinated afferent fibres (Spoendlin 1969, Kiang et al. 1982). The afferent auditory nerves terminate within the ipsilateral cochlear nuclei of the brainstem. Afferent impulses ascend through the central nervous system via the superior olives, trapezoid body, inferior colliculi, medial geniculate bodies, and primary and associated auditory cortexes. The auditory pathway decussates to the contralateral side at several levels from the olivary complex and above, ensuring that a unilaterally presented stimulus will be represented bilaterally at many sites in a tonotopic orientation from brainstem to cortex.

Efferent Auditory Anatomy

The descending auditory system roughly parallels the afferent pathway, with the primary auditory cortex communicating with the superior olivary complex via a multi-synaptic path. The major projections descend from the cortical pyramidal cells (layer V) of the primary auditory, secondary auditory and anterior auditory fields. Cortical projections descend in a tonotopic arrangement to

terminate predominantly on the ipsilateral dorsal cortex of the inferior colliculus (Sahley et al. 1997). Descending axons from inferior colliculus modulate the excitability of uncrossed and crossed medial efferents (Rajan 1990, Vetter et al. 1993). Collicular projections also go to many brainstem nuclei, suggesting that the olivocochlear nuclei may not be the major target of the inferior collicular projection (Thompson and Thompson 1993). An efferent reticular bundle also innervates the cochlea from the ipsilateral caudal pontine reticular formation (Rossi and Cortesina 1963, Adams and Warr 1976).

Innervation patterns from the superior olivary complex to the cochlea appear similar across human and mammalian species (cat, guinea pig, chinchilla) (Rasmussen 1946, Arnesen 1984, Warr 1992). Approximately 1,500 OC fibres (ipsilateral and contralateral) innervate each inner ear (Warr and Guinan 1979). In general, each ear receives twice as many ipsilateral as contralateral fibres, and each ear receives about 60% from the lateral versus the medial OC (Warr and Guinan 1979, Sahley et al. 1997, review). Approximately 70% of MOC fibres innervate the contralateral ear, whilst 30% innervate the ipsilateral ear (Liberman et al. 1990, Sahley et al. 1997). Approximately 90% of the LOC neurons travel ipsilaterally, versus 10% to the contralateral ear (depending on the species) (Reviews: Warr 1992, Sahley et al. 1997, Guinan 1996).

The crossed fibres travel across the brainstem at the floor of the IV ventricle, and join the ipsilateral OC fibres in the vestibular nerve root to exit the brainstem. The OC bundle (OCB) travels within the inferior vestibular nerve, until crossing via an anastomosis to the cochlea at the bundle of Oort (Schuknecht 1974).

The LOC fibres innervate the IHC region, primarily targeting the dendrites of the radial afferent fibres (Liberman et al. 1990). Liberman et al. (1990) found that every IHC examined received vesicle-filled terminals, with most innervation on the modiolar side of each inner hair cell (corresponding to high-threshold afferents). There were roughly the same number of efferent synapses at all cochlear locations. Hashimoto et al. (1990) report observation of direct contact with IHC by the LOC fibres. Both efferent fibre types are highly branched (Brown 1987).

The MOC efferents predominately form direct axosomatic terminals on the outer hair cells (Liberman and Brown 1986), with the number of terminals decreasing from first to third row of OHCs (Liberman et al. 1990). Benson et al. (1996) note that the MOC efferents give off branches to the cochlear nucleus which synapse with the same targets as the type II afferent fibres, both of which contact the outer hair cells.

Figure II.1

Anatomy of the Auditory System

The principle neural pathways responding to stimuli from each cochlea provide bilateral innervation ascending to the auditory cortex, and descending to both cochleae. The scale is altered to illustrate both gross neural pathways, and neural connections. Ascending pathways and nuclei from the cochlea to auditory cortex are drawn with open circles and descending pathways and nuclei with filled circles. Olivocochlear pathways are drawn in color.
(Adapted from Baloh 1998.)

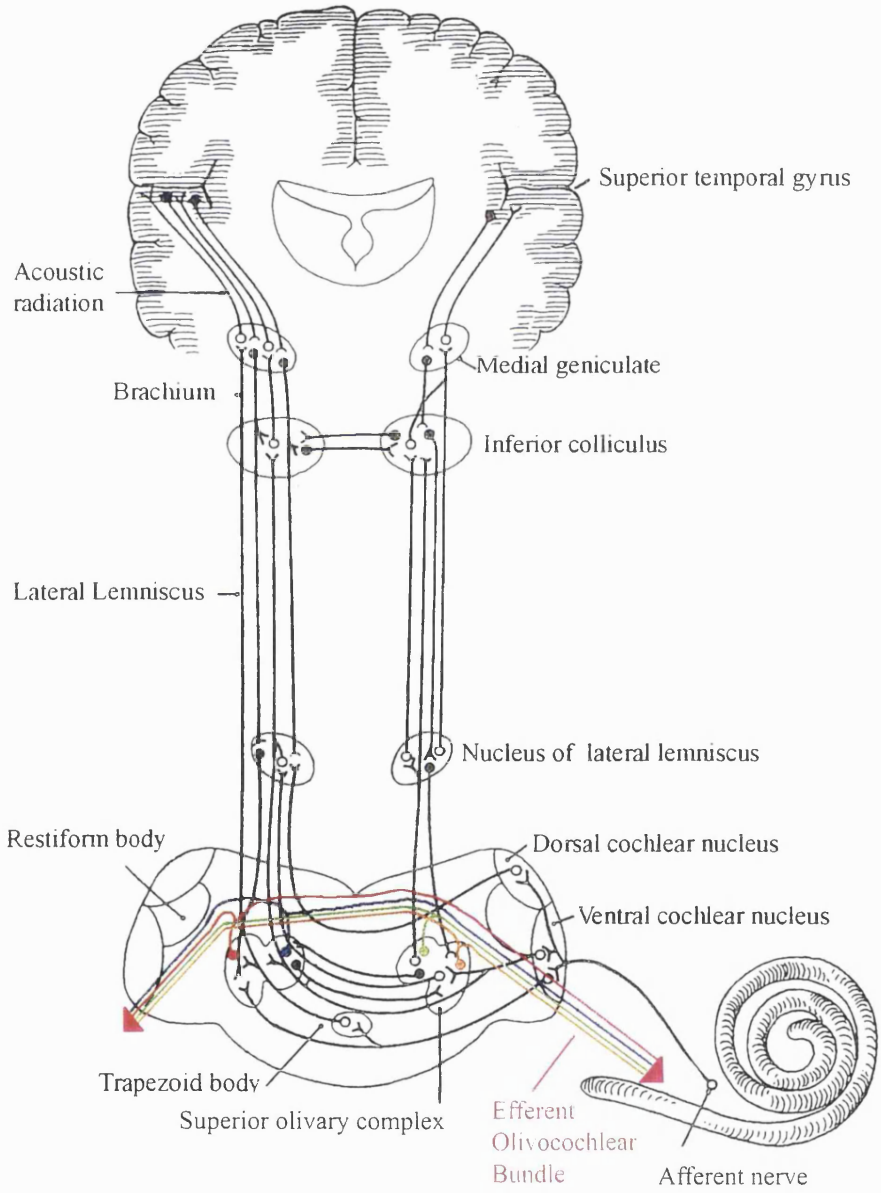
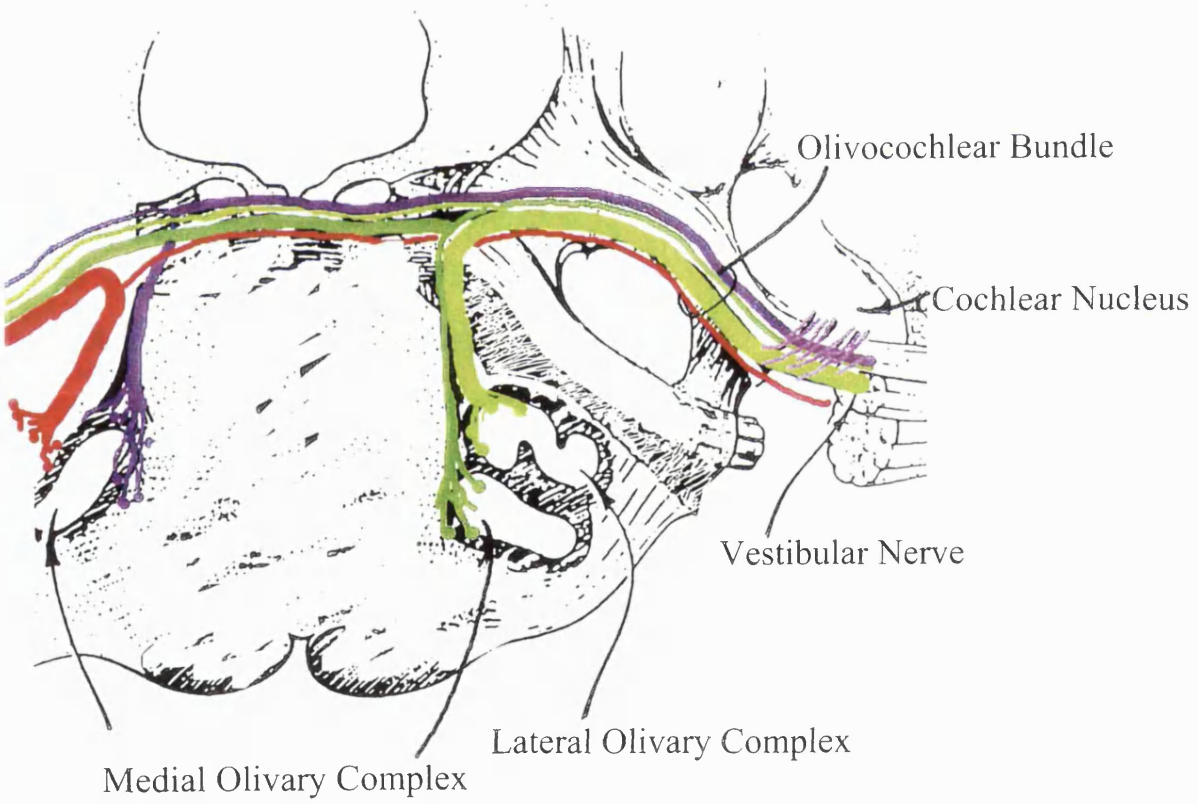


Figure II. 2

Anatomy of the Olivocochlear System

Both cochleae receive bilateral innervation from the Lateral and Medial Olivary Systems. Line thickness indicates the proportion of the total Olivocochlear Bundle innervating each ear (see text). Dark purple and dark green show the Medial Olivary pathways with the majority of fibres innervating the contralateral ear. Red and light green show the Lateral Olivary pathways with the majority of fibres innervating the ipsilateral ear. (Adapted from Guinan 1996 and Schuknecht 1974.)



Physiology of the Auditory System

Cochlear Physiology and Mechanics

The cochlear partition oscillates in response to sound, causing a relative shift between the apical surface of the hair cells at the reticular lamina, and the tectorial membrane. This creates a shearing motion of the outer hair cell stereocilia by direct mechanical displacement between the tectorial membrane, and the surface of the outer hair cells. It is thought that the effective stimulus to the inner hair cells arises from movement of the endolymphatic fluid and Hensen's stripe above inner hair cell stereocilia (Lim 1980). Studies reveal that the shearing of the stereocilia mechanically opens membrane channels in the cilia which allows the flow of extracellular ions along their potential gradients between the fluid medium inside and the apical surface outside of the cell (Pickles et al. 1984, Hudspeth 1989, Pickles and Corey, 1992). The metabolic activity of the spiral vascularis of the cochlea, creates differing ionic compositions within the scalae, generating a large potential difference across the apical surface of the hair cell membranes. If the resultant change in internal receptor potential of the hair cell is sufficient, neuro-transmitter will be released from the hair cell which leads to generation of an impulse along the afferent cochlear nerve.

Russell and Sellick (1977) first demonstrated that the inner hair cells are sharply tuned, using intracellular microelectrodes in vivo in guinea pigs. This contrasted with the relatively broad tuning curves indicated by Békésy's early measurements in cadavers using relatively loud stimuli (Békésy 1960). However, these findings were in agreement the sharp VIII nerve tuning observed by Kiang et al. (1965), and with subsequent mechanical and physiological studies revealing sharp tuning of the basilar membrane (Rhode, 1971, Rhode 1978, Sellick et al. 1982, Khanna and Leonard, 1982, Robles, et al. 1986, Nuttall et al. 1990, Cooper and Rhodes 1992, Mammano and Ashmore 1992, Xue et al. 1993), reticular lamina (Mammano and Ashmore 1992), inner and outer hair cells (Russell and Sellick 1977, 1978, 1983, Russell et al. 1986, Dallos et al. 1982). Studies showing that tuning was lost with anoxia or cochlear insults lead to the conclusion that the narrow mechanical tuning was dependent on an active, physiologically vulnerable mechanism. (Rhode 1971, Sellick et al. 1982.)

Observations of outer hair cell motility by Brownell et al. (1985), Ashmore and Brownell (1986) and Ashmore (1987, 1994) demonstrated that outer hair cells are active motor units that produce sufficient force to influence movement of the cochlear partition in such a highly tuned manner (Brundin, Flock, Khanna and Ulfendalh, 1991, Reuter, Giter, Thurm and Zenner 1992). The lattice structure of the OHC generates micro-mechanical responses to acoustic stimuli and high-frequency forces up to 25kHz in response to electrical stimulation (Holley and Ashmore, 1990b). Mammano and Ashmore (1993) studied displacement of the cochlear partition using Michelson interferometry to observe in situ, movement during local current stimulation. They found that current passed from the scala

tympany to scala media, which shortens the outer hair cells, caused the reticular lamina to move down, and the basilar membrane to move up. The converse was observed when current polarity was reversed. Of particular interest, is that the basilar membrane moved by about 5 times less than reticular lamina movement. This would result in an even greater relative shift between the apical surface of the hair cells, and thus greater shear or effective stimulus to the inner hair cells. It is interesting to speculate that a highly tuned reticular lamina is a focus of the cyto-architecture of the organ of Corti.

Thus, outer hair cells can be considered sensory and motor cells which transduce the motion of the basilar membrane and generate motile forces to cancel the viscous damping of the cochlear partition, creating a tight positive feedback loop to control and amplify the movement of the cochlear partition on a cycle by cycle basis (up to about 25kHz in mammals) (Gale and Ashmore 1997). It is thought that this amplification process provides the fine frequency tuning that enhances the sensitivity and frequency selectivity of the auditory system (Davis 1983).

In addition to amplifying the movement of the basilar membrane, the amplified oscillations are reflected back along the cochlear partition towards the tympanum (Shera and Guinan 1999). The presence of an impedance mismatch between the fluid filled cochlea and the air filled middle ear, assists in the reflection of a delayed transmission of these oscillations into the middle ear, and through the middle ear ossicles and tympanum, and are recordable as otoacoustic emissions. Indeed, outer hair cells have been shown to be integral to the generation of otoacoustic emissions and for cochlear and afferent nerve thresholds below approximately 40dB sensation level (SL) (Ryan and Dallos 1975, Dallos and Wang 1974).

Physiology of the Olivocochlear System in Mammals

Animal studies have shown that electrical stimulation of the efferent fibers at the floor of the IV ventricle results in inhibition of intracellular hair cell responses (Williams and Russell unpublished observations, Brown et al.1983, Dallos et al. 1982), auditory nerve responses (Weiderhold and Kiang 1970), and compound action potentials (Galambos 1956) with a concomitant increase in cochlear microphonics (Fex 1962, Sridhar et al. 1997). Gifford and Guinan (1987) suggest that electrical stimulation is conducted by the large myelinated MOC system, and is unlikely to activate the smaller unmyelinated fibers of the LOC system. Recently Guinan and Stankovic (1996) demonstrated that electrical stimulation was associated with potent inhibitory effects on auditory nerve fibres (6-50% fractional decrease), the magnitude of which depended on the spontaneous rate and intensity of the ipsilateral stimuli, as well as on the protocol which circumvented the effects of adaptation. They suggested that the potency of the inhibitory effect would not be due solely to alteration of basilar membrane movement.

Further evidence for efferent control of cochlear responses was provided by numerous studies that demonstrated efferent neuro-transmitter acetylcholine blockers reversibly diminish inhibitory effects whether activated by electrical stimulation of the OC fibres in the brainstem (Bobbin and Konishi 1971a,b, 1974, Fex and Adams 1978). Efferent control is also exerted by the release of adenosine triphosphate (ATP) from efferent fibres which may act to regulate the polarization of the OHC (Housley et al. 1992), and GABA which may allow chloride to enter and hyperpolarize the OHC (Gitter and Zenner 1992, Eyblin 1993: review).

It has also been demonstrated that electrical stimulation of the olivocochlear fibres alters the micro-mechanical responses of the organ of Corti, resulting in changes in the amplitude and phase of otoacoustic emissions (tone evoked emissions (Guinan 1986), click evoked (Kemp and Souter 1988) and distortion product otoacoustic emissions (Mountain 1980, Siegel and Kim 1982). Consistent with afferent nerve studies, loss of suppression was associated with perfusion of the cochlea with d-tubocurarine, an efferent blocker (Siegel and Kim 1982).

Electrical excitation at the fourth ventricle may over-stimulate the efferent and surrounding fibers (Kemp and Souter 1988) and provide non-physiologic stimulation, although similar inhibitory effects have been observed during presentation of sound to the contralateral cochlea. Liberman and Brown (1986) demonstrated that MOC neurons respond to sound, thus physiological stimulation of the crossed pathway could be readily achieved by presenting acoustic stimulation to the contralateral ear. Several animal studies have demonstrated that the presentation of moderate levels of contralateral sound is associated with inhibition of auditory nerve fiber responses (Warren and Liberman 1989, Bonfils 1986a, Buno 1978), compound nerve responses (Liberman 1989) and otoacoustic emission distortion products (Brown and Kemp 1984, Puel and Rebillard 1990). Warren and Liberman (1989) reported that in cats, contralateral acoustic stimulation produced a relative decrease in afferent nerve activity from 10 - 55% of the response rate recorded under quiet conditions (compared to inhibition "effectively" produced by reducing the stimuli level by said amount. Puria et al. (1996) report greater effective inhibition in afferent nerve and distortion product emissions. Efferent neuro-transmitter blockers have been shown to reverse sound induced changes in otoacoustic emissions during efferent activation via acoustic stimulation (Kujawa et al. 1994, 1993, Sridhar et al. 1995, Bobbin 1996: review)

In order to determine if the changes ascribed to efferent function are dependent on olivocochlear innervation, several studies investigated the effect of sectioning the OCB (de-efferentation). Some studies failed to observe loss of suppression with section of only the crossed component of the OCB at the floor of the IVth ventricle (Littman et al. 1992, Kakigi et al. 1997, reviews). However, the entire ipsilateral OCB (MOC and LOC) can be sectioned as it runs within the vestibular nerve (Puel and Rebillard 1990, Warren and Liberman 1989). Warren and Liberman (1989) found that inhibition of

auditory nerve fibres, due to contralateral sound, "completely disappeared immediately after severing the entire OCB", whereas most of the suppressive effect remained after lesioning only the COCB. With complete unilateral de-efferentation, no change in sensitivity or tuning of afferent nerves was observed, but this is consistent low spontaneous activity of OC neurons which do not respond until sound pressure exceeds the threshold of the least sensitive auditory nerve (Liberman 1988, Warren and Liberman 1989, Liberman 1990). Walsh et al. (1998a) found that chronic de-efferentation in kittens altered afferent nerve and DPOAE thresholds. Afferent nerves showed elevation of the tuning curve tip, decrease in tip-to-tail ratio, and decrease in sharpness of tuning. Such pathophysiology is consistent with damage to the OHC as seen in adult animals with ototoxic insult (Kiang et al. 1970, Dallos and Harris 1978) or acoustic trauma (Liberman and Kiang 1978).

The role of middle ear reflexes in the observed efferent effects has been considered in several studies which have shown that inhibitory effects remain demonstrable in animal preparations with sectioned middle ear muscles or following administration of paralytic agents rendering the middle ear reflex inactive (Puel and Rebillard 1990, Brown and Nuttall 1983), DP emissions (Puel & Rebillard, 1990), and auditory nerve responses (Pang and Guinan 1997a, b). Pang and Guinan (1997b) suggest the stapedial and olivocochlear systems provide a complimentary, but different system for reducing masking of a signal. The stapedius provides a low frequency attenuation regardless of the frequency of the stimulus, whereas the medial olivocochlear efferents can attenuate select cochlear and thus select frequency regions in response to low level sounds, reducing auditory nerve fibre adaptation and enhancing detection of transients (Winslow and Sachs 1987, Kawase et al. 1993 a,b).

Physiology of the Human Efferent Olivocochlear System

Clinical reports demonstrate inhibition of human cochlear responses during contralateral acoustic stimulation, affecting the amplitude of N1 (Prasher and Gibson 1984, Folsom and Owsley 1987) and compound action potentials (Kawase and Takasaka 1995), indicating the effect of OCB stimulation on afferent cochlear output. The development of otoacoustic emissions technology offered an opportunity to investigate non-invasively efferent auditory effects on outer hair cells, the effector units of the olivocochlear bundle. The majority of humans with normal hearing have measurable otoacoustic emissions (Glattke and Robinette 1997, Harris and Probst 1997, Gorga et al. 1993, 1999). Suppressive effects on of all types of otoacoustic emissions have been demonstrated in humans. Several studies demonstrated that efferent auditory effects could be reliably assessed using transient click evoked emissions during alternating quiet and noise contralateral stimulation. Suppression was measured in terms of the total pressure of the response over 500-6000 Hz in a 2.5-20.5 msec window. The protocols described allow for effective and immediate analysis of the inhibitory effects in a clinical setting (Collet et al. 1990, Ryan et al. 1991, Collet et al. 1993, Collet et al. 1994, Veuillet et al. 1991, 1992, Williams 1992, Williams et al. 1993, 1994, Berlin et al. 1993, 1994, Hood 1999,).

Frequency specific information about the inhibitory effects has been reported using narrow band stimuli to evoke the emissions and narrow band masking to define the specificity of the inhibitory effects. Several studies have found inhibition in humans to be maximal within the mid-frequency range for transient emissions (Veuillet et al., 1991). Using distortion product emissions to measure cochlear responses, several studies have also demonstrated frequency specific suppression (Brown et al. 1983). Moulin et al. 1993 showed that contralateral broad band noise suppressed DPs recorded from 0.5-5 kHz, with greatest effect in the mid frequencies. Chery-Croze et al. 1993 also demonstrated frequency specific inhibition of 2f1-f2 distortion product, especially when the DP = 1kHz with narrow band noise centered around 1kHz, and when the DP = 2 kHz with narrow band noise centred around 2 kHz and lower frequencies. Using spontaneous emissions, Mott et al. (1989), and Harrison and Burns (1993) found suppression to be associated with a positive frequency shift, and variable changes in spontaneous emission amplitude. Long et al. (1994) and Souter (1995) found suppression of stimulus frequency emissions to be most effective with low level contralateral noise which was centered on the ipsilateral stimulus used to evoke the emission. With higher intensity noise, the most effective contralateral noise was centered at frequencies above the ipsilateral emission stimulus. Micheyl et al. (1999) demonstrated greater suppression of TEOAE using harmonic complex contralateral stimuli, with maximal effect related to rate of temporal fluctuation of the stimulus envelope.

Williams et al. (1993) reported a phase advance during contralateral acoustic stimulation consistent with Guinan's observations in animals (Guinan 1986). Giraud et al. (1996) confirmed a phase lead with maximal effect at 1.5 kHz with lower click intensities, with the magnitude of phase shift inversely proportional to the intensity of click level (57 - 69 dBSPL).

The frequency dispersion of the click evoked otoacoustic emission waveforms is inversely related to time, so that the mid-frequencies tend to occur in the middle portion of the 20 msec window, with high frequencies occurring earlier, and lower frequencies occurring later (Kemp et al. 1990). Using a system that analyzes inhibition within short time segments, Hood et al. (1993) and Berlin et al. (1993) demonstrated that maximal inhibitory effects occur in the middle to latter portion of this post-stimulus time period (10-20 msec) (corresponding to frequencies above 1kHz).

Efferent auditory effects have been used to examine "auditory neuropathy" patients who present with difficulty in hearing, but without vestibular dysfunction (Starr et al. 1996) These subjects presented with abnormal audiometric thresholds, absent acoustic reflexes and abnormal auditory brainstem responses. However, they have normal OAE, but abnormal efferent inhibition.

Human studies have confirmed animal experiments which suggest that inhibition concurrent with contralateral noise is unlikely to be related to cross masking, providing that the noise intensity is kept

below levels know to result in transcranial transmission or an elevation in the recording noise floor of the otoacoustic emissions (Collet et al., 1990; Veuillet et al., 1991). Moulin et al. (1993) rejected the influence of cross masking via air and bone conduction by testing subjects with the contralateral ear sealed with a plastic ear plug, or who were unilaterally deaf. They found that the noise floor of the recording did not increase with increasing levels of contralateral stimulation.

Further, several studies of humans with pathologically absent middle ear reflex function due to Bell's palsy suggest that inhibition of emissions is unrelated to middle ear acoustic reflexes. (Collet et al. 1994, review, Moulin et al. 1993).

Based on findings from earlier physiological investigations in animals and human findings, this investigation utilized otoacoustic emissions to develop tests that offered repeatable efferent auditory effects in normal hearing subjects. Clinically viable protocols were developed that enabled assessment of olivocochlear dysfunction in a clinical setting.

CHAPTER III

METHODS

METHODS

Ethical approval was obtained for this study in accordance with hospital and international standards (ISO), and non-consenting patients were not tested. All audiometric tests were conducted in sound-isolation chambers with sound levels referenced to ISO standards. The protocols for patients and for normal subjects are described below. In addition to audiometric tests conducted for each subject, patients also underwent vestibular tests, central imaging and additional investigations prescribed by the consultant, as part of their clinical diagnostic test battery. The diagnostic opinions were established by the consultant neuro-otologist.

Test Battery

The initial battery for all subjects comprised history, otoscopy, pure tone threshold audiometry, tympanometry, and then acoustic reflex thresholds. Thresholds to white noise and middle ear reflex thresholds were measured, and used to set sound levels of contralateral and ipsilateral stimuli least likely to stimulate middle ear reflexes or result in trans-cranial transmission of sound. Otoacoustic emissions, and efferent tests were then conducted. As medically indicated patients thereafter performed electrophysiological recordings of auditory evoked responses followed by vestibular tests including electronystamography, opto-kinetic reflex and vestibulo-ocular reflex testing, and finally bithermal caloric irrigation. Central imagining was not conducted on the same day as neuro-otological tests. Normal subjects did not perform auditory evoked response, vestibular tests or central imaging.

The entire neuro-otological battery for patients, including efferent OAE tests, but excluding imaging, was conducted over approximately 2 hours per patient. OAE and efferent OAE tests for three different intensities of contralateral acoustic stimuli took approximately 15 minutes per subject per ear.

The order of testing was designed to minimize loud stimuli immediately before OAE. However, clinical demands, patient compliance, and time constraints on occasion dictated a different order to testing. Nonetheless, OAE testing was preceded by approximately 5 minutes between tests. Caloric testing was always completed after OAE and other audiometric tests were complete. Due to time constraints and clinical demands, bilateral efferent tests were not completed on all subjects.

Protocols

The consultant conducted a complete history of each patient. Due to clinical constraints, the author conducted a verbal history with patients and normal subjects noting current and previous auditory and vestibular complaints (including the patients' subjective impression of hearing loss, hearing asymmetry, tinnitus, hyperacusis, noise exposure, occurrence of vestibular complaints, and difficulties with speech discrimination in noise).

Otoscopy was conducted on all patients and normal subjects. If cerumen was found to be blocking the view of the tympanum, it was cleared (without syringing) by the consultant.

Pure tone audiometric (PTA) thresholds from 250 - 8000 Hz and to white noise were recorded relative to dBHL ISO using a GSI 16 or Madsen OB802 Audiometer with TDH 39 headphones. In some subjects 3000 Hz and 6000 Hz were also tested. ANSI S3.21-1978 (R1986) threshold search technique was used, but with initial presentation at 40dBHL followed by the standard 10 dB down - 5 dB up procedure. Threshold was considered the lowest hearing level at which responses occur in at least one half of a series of ascending trials, with a minimum of two responses out of three required at a single level. Normal threshold levels were considered as < 25 dBHL re. ISO at 500 Hz, 1000 Hz, 2000 Hz, 4000 Hz, 8000 Hz. A mild loss is considered as >25 dBHL to 40dBHL; a moderate loss is >40dBHL to 60dBHL; a moderately severe loss is >60dBHL to 80dBHL; a severe loss is >80dBHL to 95dBHL; a profound loss is >95dBHL.

Tympanometry and acoustic reflex thresholds (ART) to ipsilateral and contralateral tones at 1000 Hz and 2000 Hz, and to clicks and contralateral WN were tested on a GSI 33 Middle Ear Analyzer. Normal tympanometry was considered to be 0.3 - 1.4 ml compliance and +/- 100 daPa pressure. ART thresholds for pure tones at 1 and 2 kHz was considered to be a repeatable 0.2 ml deflection from baseline, which showed an increase in magnitude at higher stimulation levels. The detection threshold to WN was chosen to be more sensitive, at a deflection of 0.1 ml, which is the minimum sensitivity of the device. The normal range for ART responses was 75 - 100 dB HL, with inter-aural differences of 15 dB or less (Prasher and Cohen 1993).

Auditory brainstem responses were recorded with 90 to 100 dB nHL alternating polarity clicks presented via TDH 39 headphones at a rate of 9.1 or 11.1 clicks per second on a Medelec ST10 or Bio-Logic Traveler respectively. The high pass filters was set at 30 Hz, and low pass filter at 3000 Hz. The electrode montage was set for one channel recording, with silver chloride disks electrodes on the vertex (Cz) and both mastoids. For ipsilateral responses, the vertex electrode was inverting (-), the ipsilateral mastoid electrode non-inverting (+), and contralateral mastoid connected to ground.

Contralateral responses were recorded with contralateral mastoid electrode non-inverting, and ipsilateral to ground. Averaged waveforms for 1024 click responses within the artifact rejection threshold were displayed over 10 msec. Two separate averages of 1024 click responses were recorded for each ipsilateral and contralateral recording, for right and left sides. Normative values established on the equipment used for absolute wave latency (Waves I, III, V), inter-wave intervals (Waves I-III, III-V, I-V), and inter-aural differences are listed in Appendix A.3 (Prasher et al 1994, Hine et al 1997).

Bithermal caloric responses were directly observed using water stimulation at 44°C and 30°C for 40 seconds at each temperature level, as described by Fitzgerald and Hallpike (1942) and Luxon (1995). Cold irrigation (30°C) was first applied to the left ear and response was determined by direct observation of ocular movements during optic fixation, and then without fixation in the dark, using Frenzle glasses. The angle of movement was noted, in addition to the end point of movement. Following a rest period the right ear was irrigated with cold water, with ocular responses observed according to the procedure described above. Testing continued with hot irrigation in the left ear followed by a rest, and then the right ear (Dix and Hood 1984). Significantly reduced function was considered to be canal paresis greater than 15%.

Vestibulo-ocular observations and recordings were conducted to establish abnormality, asymmetry or lack of suppression that might indicate central involvement (Luxon 1996, 1997, Baloh and Honrubia 1989). Observation of spontaneous and gaze evoked nystagmus were made during and without fixation. Saccades and smooth pursuit function were recorded (at 0.2 - 0.4 Hz target velocities). Opto-kinetic nystagmus (OKN) stimuli at $40s^{-1}$ (full field and drum) were examined. Sinusoidal and full rotational vestibulo-ocular reflex stimulation at 0.2 Hz was conducted, and examined for asymmetry and duration of nystagmus (Luxon 1996, 1997).

Central electrophysiological tests were conducted for a subset of patients. Middle and late latency auditory evoked potentials were recorded using an electrode montage for two channel recording with bilateral mastoid silver chloride disc electrodes linked together connected to the inverting terminal. Cz was connected to the non-inverting (+) terminal, and Fpz to ground. Middle latency responses (MLR) were averaged in response to 1024 alternating 100 μsec clicks presented at 7.1/sec at 80dBnHL via insert earphones. Filters were set at 5-1500 Hz, and the window from 5-100 msec. Normal responses were considered to be Pa 1.0uV (0.5-2.0uV) with peak latency at 25-35msec. Late latency responses (LLR) were averaged in response to clicks presented at 1.1/sec at 80dBnHL via insert earphones. Filters were set at 1-100 Hz, and the window from 10-600 msec. Normal responses were considered to be peak latencies as follows: N1: 90-100msec; P2: 180-200 msec; N2: 260-290 msec; P3: 290-310 msec (Kraus 1994).

Central auditory processing evaluation utilized the SCAN-A testing behavioral function to assess ability discriminating low-pass filtered words, auditory figure-ground, and competing words, using norms established by Keith (1986).

Central nervous system radiography comprising MRI, CT or air CT meatography were performed as requested by the Consultant. Neuro-otological examination, medical diagnosis, surgery and management were conducted by the consulting surgeon. Vestibular nerve section patients and vascular decompression patients underwent a retro-labyrinthine surgical approach to the cerebello-pontine angle, as described by Silverstein and Norell (1990).

Otoacoustic Emission Test Protocols

OAE recordings were made for all subjects using an ILO88 or ILO92 as described by Kemp et al. (1990). The stimulus was a non-filtered 80 us click, presented at a rate of 50/sec. Care was taken to adjust the probe position so that the amplitude of the stimulus frequencies varied as little as possible across the recordable frequency range. Bilateral presence of otoacoustic emissions was confirmed by using the standard "non-linear clicks" (at 80+/-5 dB) procedure with 260 averages.

The "non-linear click" protocol provided improved signal detection utilizing knowledge of the non-linear intensity function of cochlear responses. It has been shown that otoacoustic emission amplitude saturates at higher intensities (Kemp 1990). For each data record, the ILO non-linear protocol presents 4 clicks, 3 of which are at a constant intensity and polarity. The fourth click is three times greater and of reverse polarity. The average response to the 3 similar clicks is compared with the response to the larger reversed polarity click and used to extract the signal, noise and linear components. Those components of the response that have not saturated are presumed to be linear, non-cochlear responses and are rejected. The summation of the three averaged clicks and the opposite polarity large click response represents the noise of the response, and the difference represents the signal (Kemp et al. 1990). The linear click protocol (4 clicks of equal amplitude and polarity) was used for efferent testing to avoid averaging together efferent responses evoked during different click intensities or opposite polarities.

The cross-correlated otoacoustic emission response amplitude was calculated in terms of dB SPL by the ILO system. This gave a measure of the total pressure of the response over a 500 - 6000 Hz frequency band of the response spectrum. The standard clinical protocol uses a window from 2.5 msec to 20.5 msec (2.56 msec cosine ramped onset and offset). Emission amplitude was calculated using this window and with a window beginning at 4.5 (+/-0.5) msec (2.56 msec cosine ramped onset) in order to remove ear canal stimulus artifacts that may remain when using "linear" averaging techniques.

Efferent Auditory Effect (EAE) Protocols

The ipsilateral ILO probe and contralateral stimulation headphone were positioned comfortably, with the first test ear being varied, right or left, from subject to subject. The initial click stimulus level from the ILO probe was set to 67 +/- 7 dBpeSPL using the "linear" click procedure. Separate tests were conducted at several click intensities ranging from 55-85 (+/-2) dBpeSPL, providing that subject compliance and recording stability were acceptable.

Contralateral white noise acoustic stimulation was provided by a Madsen OB802 or GSI 16 audiometer via TDH 39 headphone calibrated re. dBHLISO. The confounding effects of middle ear muscle responses were minimized by keeping the white noise and click levels at least 10dB below the acoustic reflex detection level.

The standard efferent auditory effect protocol utilized the ILO to record a series of click evoked responses (each comprising the average of 60 click responses within the rejection threshold). One or more recordings were made in "quiet" conditions, (with the noise generator turned off) to set the appropriate click level, and to establish a baseline otoacoustic emission amplitude in quiet conditions. Contralateral noise was thereafter manually turned on ("noise" condition) for every alternate recording. Noise onset began during the interval whilst the system saved the previous record to disk. The noise was then turned off ("quiet" condition) during the following disk-save interval. The key sequence used to save the data and reset the contralateral stimulation was standardized in order to minimize the variability of the onset of the contralateral noise relative to the onset of the emission evoking clicks. The contralateral noise always began before the onset of the clicks, preceding them by approximately 1-3 seconds, and was continuous until after the end of the emission recording session. Using the standard protocol, each average of 60 click evoked responses took approximately 11-15 seconds to collect.

If subject compliance, or environmental noise interfered with the recording, the "quiet/noise" alternating sequence would be changed in order to capture the condition missed, and then the repetition of alternating conditions would continue. This procedure enabled the re-establishment of the quiet baseline at regular intervals so that comparison of quiet / noise pairs could be made to assess "fast efferent effects" between responses from adjacent stimuli pairs.

After a series of paired recordings were complete, contralateral noise was increased or decreased. Additional series were thereafter completed with contralateral levels ranging from 0 - 55dBSL provided that the subject compliance and recording stability remained high, and taking into consideration the need to avoid stimulus intensities sufficient to cause activation of middle ear responses.

The effect of contralateral stimulation on otoacoustic emissions was calculated by comparing the difference in response amplitude between the paired responses in quiet and noise conditions. The averaged response to the click stimuli were expressed as the response in dB SPL by the ILO system, representing the total average pressure within the recordable frequency spectrum of the ILO system (frequency bandwidth roll-off knees at 500 and 5000Hz). The time window was set to 4.5 (+/-0.5) msec (with a 2.56 msec cosine rise time) in order to minimize the effect of middle ear oscillations. Signal to noise ratio was improved if necessary, by averaging two or more recordings made in the same contralateral conditions. In order to control for trans-cranial transmission effects, a recording was rejected if the noise floor was noticeably elevated during contralateral noise conditions (>2dB increase relative to the previous acceptable recordings).

Efferent Auditory Effect Analysis

The CEOAE response amplitude was converted mathematically from dB SPL into micro Pascal units before any mathematical or statistical comparisons were made (0 dB SPL referenced to 20 micro Pascal).

The "fast" efferent effect was measured by calculating the change in OAE response amplitude in the quiet versus noise conditions of each stimulus pair, and expressed as percentage inhibition relative to the quiet recording. Positive % values represent a decrease in emission amplitude during noise relative to the response amplitude in quiet, and negative % inhibition represents responses that were larger during noise than the response in quiet. This provided a measure of the fractional change in emission amplitude per individual, that is, the decrease in emission amplitude as a fraction of the emission amplitude in quiet conditions, expressed as percentage change.

Inhibition was also calculated in terms of dB ratio for the alternating stimuli conditions (Formula 2: e.g. dB quiet - dB noise). Formula 1 was utilized, and provided that all dB values were converted into linear Pascal units before arithmetic or statistical operations were performed.

Formula 1. Fast Efferent Effect

$$\% \text{ inhibition} = (1-(\text{CEOAE noise}/\ \text{CEOAE quiet})) \times 100.$$

Formula 2. Ratio dB

$$\text{dB inhibition} = (\text{CEOAE dB SPL}_{\text{quiet}} - \text{CEOAE dB SPL}_{\text{noise}}).$$

Inclusion Criteria

The minimum inclusion criteria for all subject groups required: external meati with a clear view of the tympanic membrane, absence of external meati abnormalities, measurable click evoked otoacoustic emissions, tympanometric pressure between +/-200daPa with compliance between 0.3-1.4ml, and pure tone thresholds equal to or better than 35 dB HL between 1000 and 2000 Hz.

Normal Subjects

The criteria for normal subjects included absence of otological symptoms reported in the history, normal otoscopy, and audiometric pure tone thresholds >25dBHL. Adult volunteers (8 males, 14 females, age 19-43) were either hospital non-medical staff, or external non-health professionals. A verbal history excluded those with complaints of hearing or balance difficulties, tinnitus, or noise exposure. (Clinical time constraints prohibited questionnaires.) Tympanometry required middle ear pressure between +/-50 daPa, and compliance between 0.3 – 1.4ml, with A type tympanograms necessary for inclusion in the study. (See Appendix Table A2.)

A total of 22 volunteers were tested. Due to clinical and time constraints, only eight of the above subjects were able to complete full efferent auditory evaluations in both ears. Thus, a total of 30 ears were tested, with sixteen ears providing data for analysis of intra-individual bilateral efferent effects.

Vestibular Nerve Section Patients

Vestibular neuritis, which has also been termed vestibular neuronitis, is a sudden unilateral loss of vestibular function without associated auditory symptoms or central nervous system involvement in an otherwise healthy subject. It is believed to have a viral aetiology. Unlike Meniere's disease the vertigo is typically prolonged and subsides gradually over days or weeks rather than hours. Further compensation then usually ensues. In the majority of patients, vestibular neuritis is a benign self-limiting condition without any significant long term vestibular problems. A few patients however continue to experience recurrent attacks of vertigo, invariably lasting for several days. Although the episodes are not usually as prolonged as the initial attack the severity of vestibular symptoms is of similar magnitude and very distressing. This condition is termed recurrent vestibulopathy. When the attacks occur frequently they can be effectively abolished by vestibular nerve surgery. Typically the auditory function is not adversely affected in this condition. (Jackler and Brackmann 1994, review). This contrasts with the clinical features of patients with perilymph fistula (PLF). The onset of inner ear symptoms with PLF invariably occurs following head trauma, physical straining or baro-trauma and almost always results in sensorineural hearing loss that is often fluctuant in character. Because of their normal hearing, patients with recurrent vestibulopathies may therefore be excellent subjects for measuring efferent function by otoacoustic emissions, which requires a mean auditory thresholds of $\leq$30 decibels over the speech range for consistent results.

Like other peripheral vestibular disorders, radiographic imaging studies are normal. Vestibular investigations carried out between episodes will typically show a unilateral canal paresis with normal central vestibular function and normal posturography.

18 vestibular nerve section patients were assessed for vestibular, audiometric, electrophysiologic and neurologic function. Whilst vestibular nerve section patients are uncommon even at specialist neuro-otological centres, many of the patients were necessarily excluded from the study as they displayed significant hearing impairment as well as vestibular symptoms. Five patients were excluded from the study on the basis of pure tone thresholds greater than 35 dB HL, and absence of recordable otoacoustic emissions. Five patients were excluded for additional pathologies including facial nerve involvement or traumatic injury.

Eight patients (2 male, 6 female, age 30-46) were diagnosed as having recurrent vestibulopathy. A complete history was taken by the consultant, and verbal questions the investigator at the time of efferent testing (clinical constraints on time prohibited written questionnaires). Patients presented with disabling vestibular symptoms of at least 3 years duration. Bouts of vertigo, nausea and disequilibrium were reported to occur repeatedly with increasing severity. Pure tone thresholds were normal for 5 of 8 patients. Three patients showed slight to mild sensorineural hearing loss above 3000 Hz. Tinnitus was reported in 3 of the 8 cases.

Vestibular tests of these patients using bithermal caloric stimulation showed canal paresis of >15%, with suppression evident during visual fixation. Central involvement was excluded by neuro-otological examination, auditory and vestibular tests and by central imaging. Radiography (CAT, MRI, CT-Air meatography) confirmed absence of lesions. Auditory brainstem responses and acoustic reflexes did not indicate central abnormalities. Central involvement in vestibular function was examined by observation and electro-nystamographic recordings of pursuit, saccades, OKN, VOR responses, with and without fixation. Recordable otoacoustic emissions were required to be present bilaterally in order to complete efferent testing. (See Appendix A.1, A.3.)

Whenever possible, efferent otoacoustic emission tests were conducted before and after vestibular nerve section to allow for direct analysis of the effect of de-efferentation. Post-surgical patients who underwent nerve section before the onset of this study were also examined to assess cochlear activity in the absence of efferent feedback. Clinical time constraints and patient compliance often required that the complete efferent stimulation intensity series could not be collected, especially given the disabling effects of vestibular dysfunction. Eight patients completed post-operative studies. Five completed pre-operative tests, although 1 did not attended follow-up studies, and 3 had some hearing loss which was taken into consideration in this study.

Vascular Decompression Patients

Vascular compression syndrome is the term used to classify conditions thought to be caused by compression of a cranial nerve by a blood vessel (Schwaber and Hall 1992, Lovely et al. 1999). These conditions include hemi-facial spasm and trigeminal neuralgia. The cochleo-vestibular nerve compression syndrome is a more recently recognized clinical entity, which has been popularized by Jennetta and colleagues (Lovely et al. 1999). Both small arterial and venous blood vessels are observed to be in close association with the cochlear and vestibular nerves, and can unusually be demonstrated by radiological imaging. Air meatography was once the investigation of choice, but due to its invasive nature and the more widespread availability of magnetic resonance imaging; this latter modality has become the scanning investigation of choice. It is undertaken both to exclude acoustic nerve tumours whilst local blood vessels in close association with the VIII nerve can usually be demonstrated. The most widespread theory of patho-physiology proposed by Schwaber (in Jackler & Brackmann 1994), suggests that the syndrome begins with an episode of vestibular neuritis which causes axonal loss and nerve swelling. An adjacent blood vessel then adheres to the cochlear and / or vestibular nerve and then causes chronic ectopic excitation. As a result of this chronic excitation the VIIIth nerve nuclei undergo re-organisation or neuroplastic change, which results in hyperfunctioning of the nerve.

Ryu et al (1999) found that symptoms of neuro-vascular compression syndrome of the VIII nerve were clearly related to the part of the nerve that was compressed, with vertigo and tinnitus related to compression of the rostro-ventral and caudal surfaces of the VIII nerve. However, Lempert (1998) notes that it is a matter of debate if compression of the vestibular nerve by a pulsating arterial loop is a common cause of vertigo. Spontaneous resolution of symptoms are reported. Brunstein and Ferreri (1990) note frequent asymptomatic neurovascular contacts. Imaging has been found to be misleading in some cases, with no consistent relationship between the MRI and the laterality of the cochlear or vestibular abnormalities (De Carpentier et al 1996). However, Schwaber and Hall (1992) found that of their 13 patients with CNCS who underwent decompression surgery, 11 had vessels in contact with the VIII nerve. Schwaber and Hall (1992) found that 81% of the group (51 of 63 patients) had some hearing loss, and 75% (42 of 56 patients) had ABR abnormalities. ENG abnormalities were observed in 93% of these cases (57 of 61 patients). Bergsneider et al (1995) conclude that vascular compressive vestibular neuropathy may exist, but that diagnostic criteria should be improved.

Treatment by microvascular decompression should relieve clinical symptoms in the majority of patients. Jannetta and colleagues found microvascular decompression to yield excellent long-term relief of symptoms with low morbidity and mortality in 4400 operations (McLaughlin et al. 1999, Jannetta et al 1984, Moller 1991, Moller et al 1993a, Moller et al 1993b). Lovely et al (1999) found that 98% of their decompression patients (n=320) returned to normal activities postoperatively. (Lovely et al. 1999).

The consultant established diagnosis of patients included in this study, based on their history and lack of response to treatment with conventional vestibular sedatives and Cawthorne-Cooksey vestibular rehabilitation exercises, and the marked severity of their symptoms. Patients in this study typically demonstrated marked movement disequilibrium and sometimes atypical positional vertigo. Before undergoing surgery, these patients were unable to go out on their own, unable to drive and unable to work. Whilst air CT meatography or MRI scanning may well show a close association between vessels and nerves, true neuro-vascular conflict can only be reliably identified at surgery

The patients reported in this study were selected as controls because treatment involved surgery in very close proximity to the vestibular nerve in the CP angle which would invariably result in some degree of local scarring but does not cause complete de-afferentation of the vestibular nerve as with a section procedure.

In the vascular decompression cases studied here, presence of a vascular loop compressing the cochleo-vestibular nerve of each patient was observed upon imaging, and confirmed during surgery. These cases showed no central signs of abnormality upon vestibular or auditory electrophysiological evaluations. On this basis, it was presumed that peripheral vestibular symptoms were associated with the vascular loops. All cases were tested for efferent effects during improvement of vestibular symptoms. Despite the possibility that vascular compression was not the sole cause of their disorder, and despite recurrence of disequilibrium subsequent to efferent testing, these cases provided useful information about the impact of retrolabyrinthine surgery on efferent auditory effects.

The audiometric and vestibular profiles of 3 vascular decompression patients (2 male, 1 female, age 28-41) were assessed. A slight hearing loss was present in one case at frequencies above 4000 Hz, and tinnitus was reported in all cases.

Central involvement was assessed by neuro-otological examination, auditory and vestibular tests and by central imaging. Radiography (CAT, MRI, CT-Air meatography) confirmed absence of lesions, with observation of a vascular loop using meatography. Observation during surgery confirmed the presence of vascular loops on the cochleo-vestibular nerve. Auditory brainstem responses and acoustic reflexes did not indicate central abnormalities. Central abnormalities in vestibular function were not observed in caloric or vestibulo-ocular observations of pursuit, saccades, OKN, VOR responses, with and without fixation. Recordable otoacoustic emissions were required to be present bilaterally in order to complete efferent testing. (See Appendix A.2, A.3.)

Middle Ear Section Patients

Two subjects with unilateral audible middle ear myoclonus (1 male age 35 years, and 1 female age 32 years) were studied following unilateral section of the tendons to the stapedial and tensor tympani muscles. Palatal myoclonus was not observed. Audible clicking sounds were detected from the ear canal. Neither patient reported balance or hearing dysfunction, nor signs of central vestibulo-auditory disorders. Pre-surgical pure tone thresholds were normal bilaterally (<25dBHL), as were tympanometry (-15 to 10daPa), and auditory brainstem responses). Recordable otoacoustic emissions were required to be present bilaterally in order to complete efferent testing. (See Appendix A.2, A.3.)

Pathological Patients

Five patients (4 male, 1 female, age 23- 43) with lesions or disorders thought to impact the efferent auditory system as it courses from the brainstem to the hair cells and organ of Corti were examined. In two patients, MRI confirmed central lesions (olivo-ponto-cerebellar degeneration, cerebellar pontine angle meningioma). The patients' history included exposure to noise, with electrophysiological results excluding central effects. One patient underwent high-dose quinine therapy, suggesting ototoxic damage.

In pathological cases, a single site of lesion or precise aetiology cannot be precisely defined. Whilst MRI images confirmed the location of the central lesions, dysfunction resulting from abnormalities of additional lesions may also have been involved, including effects from additional degeneration, compression or ischaemia. Whilst the history and dysfunction indicated noise or ototoxic effects, it remains possible that other disorders were involved. Vestibulo-ocular tests (caloric, ENG, VOR, OKN) confirmed central involvement in patients with lesions of the brainstem or CPA. Vestibular dysfunction was not observed in the patients with ototoxic exposure, noise exposure or difficulty with discriminating speech in noise. In addition to the above, inclusion criteria required bilateral recordable otoacoustic emissions. (Appendix A. 2, A.3).

Statistical Analysis

Multi-way analysis of variance with multiple comparisons was used to compare sample means for three groups (normal ears, control ears without disruption of OCB system, and "experimental" ears, or those ear with surgical or pathological disturbance to the OCB system. Multi-way comparisons utilized ANOVA and the multi-way comparisons using Scheffe's test (alpha = 0.05).

Sample distributions and normality was analysed by Kolmogorov-Smirnov (KS) testing (which compared a normal distribution with a mean and standard deviation equivalent to the distribution of the sample groups (Riffenburgh 1993). P values gave the probability of incorrectly rejecting the null hypothesis, that the samples were normally distributed.

Means of a subset of patients (with unilateral section of the OCB following vestibular nerve section) was compared with those of the normal group using the Student's t-test and F test.

Sample Statistics

The sample distributions from the normal, experimental and control groups had a normal distribution, verified by Kolmogorov-Smirnov (KS) testing, when considering the data from each group at three levels of contralateral acoustic stimulation. (See Table III.1.)

Table III. 1.

Kolmogorov-Smirnov Test of Normality

P values	0dBSL	35dBSL	45dBSL
Normal	0.983	0.199	0.995
Control	0.077	0.847	0.983
Experimental	0.878	0.886	0.929

CHAPTER IV

NORMAL RESULTS

Efferent Auditory Effects in Normal Hearing Subjects

NORMAL RESULTS

Efferent Auditory Effects in Normal Subjects

Robust and repeatable inhibition of otoacoustic emission amplitude was observed upon presentation of white noise to the contralateral ear. A number of tests were conducted per individual to explore the nature of the inhibitory effect and to explore the salient stimuli and recording parameters, providing information for definition of the optimal clinical protocol for efferent testing.

The figure below shows that superimposition of the otoacoustic emission waveforms is demonstrates the difference in peak to peak amplitude of the emissions recorded in quiet and in noise. By filtering the waveforms in narrow frequency bands, the peak to peak difference is more readily discernible. A phase shift of the otoacoustic emission waveforms can also be observed upon superimposition of the waveforms. Given good recording conditions, it is possible to determine if efferent suppression has occurred by making a recording in quiet (12 sec) and a recording in noise (12 sec), and comparing the difference in peak to peak amplitude, and the total response amplitude in dBSPL. (See Figure IV.1.)

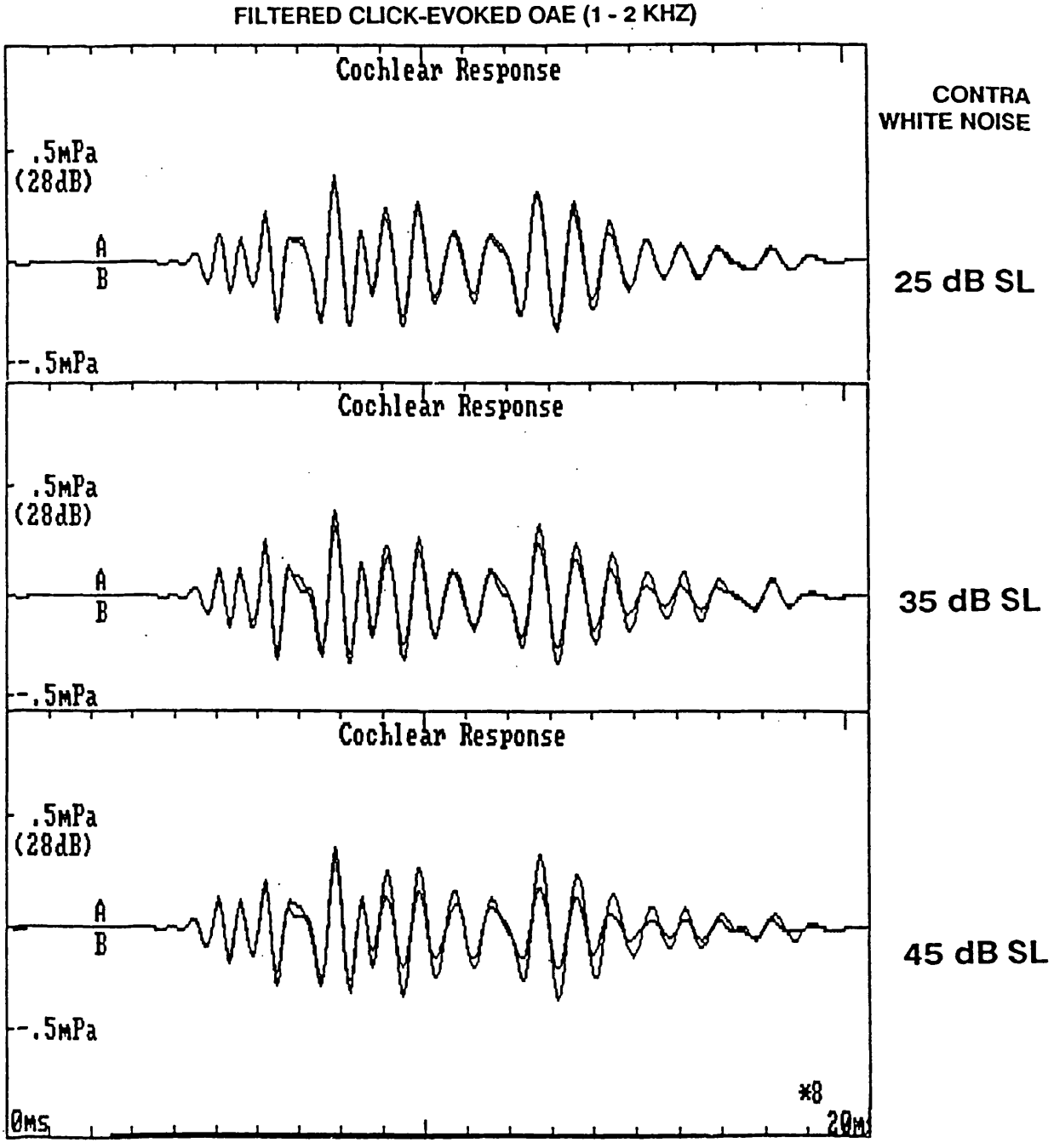
Efferent Auditory Effects in Normal Subjects: As a Function of Stimuli and Recording Parameters

Inhibition of Efferent Auditory Effects as a Function of Contralateral Stimulus Level

The normal group's inhibition as a function of contralateral noise levels were calculated for temporally adjacent quiet noise pairs giving a measure of "fast" efferent auditory effects (Formula 1). This provided a measure of the fractional change in OAE amplitude per individual. That is, the % change in amplitude, expressed as a fraction of *that individual's* emission amplitude in quiet (See Guinan and Stankovitch 1996). The figures below demonstrate this yields a similar pattern of inhibition to measurement using dB ratio change (Formula 2). Fractional % inhibition calculations first converted measures to a linear scale (re. 20 μPa) before statistics were calculated.

Figure IV.1
Efferent Auditory Effects in a Normal Subject

Illustrates the reduction in peak-peak amplitude of CEOAE waveforms collected in noise relative to those recorded in quiet conditions. The peak – peak difference increases with increasing sensation levels (dBSL) of contralateral white noise. Filtered click evoked emission waveforms (1000-2000 Hz): recorded in quiet conditions (A) superimposed over emission waveform in noise conditions (B), plotted as amplitude (mPa) as a function of time (msec).



Normative Efferent Auditory Effects

Means and standard deviations of inhibition were calculated for adjacent quiet/noise pairs during 0, 35, and 45dBSL (n=20 ears per level) with OAE linear click stimuli at 67+/7dBpeSPL. Means and standard deviations are also calculated for 15dBSL, 25dBSL, and 55dBSL. (See Figures below.) Mean inhibition from normal subjects showed little change in response amplitude during repeated measurements in the quiet condition [0dBSL =1.4%, 3.9SD, n=20]. Contralateral noise at 15dBSL was associated with increased inhibition relative to quiet recordings, although without statistical significance. Statistically significant differences ($p<0.001$) were demonstrated with contralateral noise $\geq$25dBSL. On the basis of these statistics, the criterion of normal efferent function was considered relative the normal group's mean, SD and confidence interval for inhibition during 35dBSL and 45dBSL contralateral white noise. (See Table IV. 1, Figure IV. 2.)

Table IV.1: Mean Inhibition of CEOAE in Normal Subjects During Contralateral White Noise

% Change relative to Response Amplitude in Quiet Conditions

Subject group	Obs n	CAS dBSL	Mean %inhib	Std Dev %inhib	Min %inhib	Max %inhib	Mean +2SD	Mean -2SD	Conf Interval Upper	Lower
Normals	20	0	1.4	3.8	-7.2	7.7	8.9	-6.2	3.1	-0.3
	5	15	2.8	4.7	-4.7	6.7	12.2	-6.6	6.9	-1.3
	10	25	10.5	2.2	6.7	13.9	14.9	6.1	11.9	9.1
	20	35	20.5	4.7	13.9	31.6	29.9	11.1	22.6	18.4
	20	45	26.0	6.2	15.9	37.4	38.4	13.6	28.7	23.3
	4	55	29.0	5.2	25.0	35.4	39.4	18.6	34.1	23.9

Efferent Auditory Effects Expressed as DeciBel Ratio

The change in CEOAE amplitude was also measured using the total response dB values provided by the ILO OAE recording system. (See Formula 1; Figure IV.3). This demonstrated a similar pattern to the fractional % inhibition formula, with a significant decrease in CEOAE amplitude for all white noise level => 25dBSL ($p<0.001$). The method of analysis chosen for this study utilized a measure of the decrease in OAE amplitude relative to the amplitude of each individual's response in quiet (i.e. % inhibition, or fractional inhibition).

Table IV.2 : Mean Inhibition of CEOAE in Normal Subjects During Contralateral White Noise

dB Ratio of Amplitude of Quiet - Noise Response Level

CAS dB SL	Mean	Std dev	Mean -2 st dev	Mean +2st dev	count
0	0.1	0.3	-0.6	0.8	20
15	0.3	0.4	-0.6	1.1	5
25	1.0	0.2	0.5	1.4	10
35	2.0	0.5	1.0	3.1	20
45	2.6	0.8	1.0	4.2	20
55	3.1	0.6	1.8	4.4	4

Figure IV.2
Mean Inhibition of CEOAE Amplitude in Fractional % Change as a Function of Contralateral Acoustic Stimulation Level

Inhibition of CEOAE amplitude was calculated as the fractional change in amplitude of CEOAE collected in noise, compared to the CEOAE collected in quiet, and expressed as % change from amplitude of adjacent recording in quiet. (Filled square) Mean inhibition; (X) +/- 2SD from mean for the normal subject group.

dBSL	0	15	25	35	45	55
n	20	5	10	20	20	4

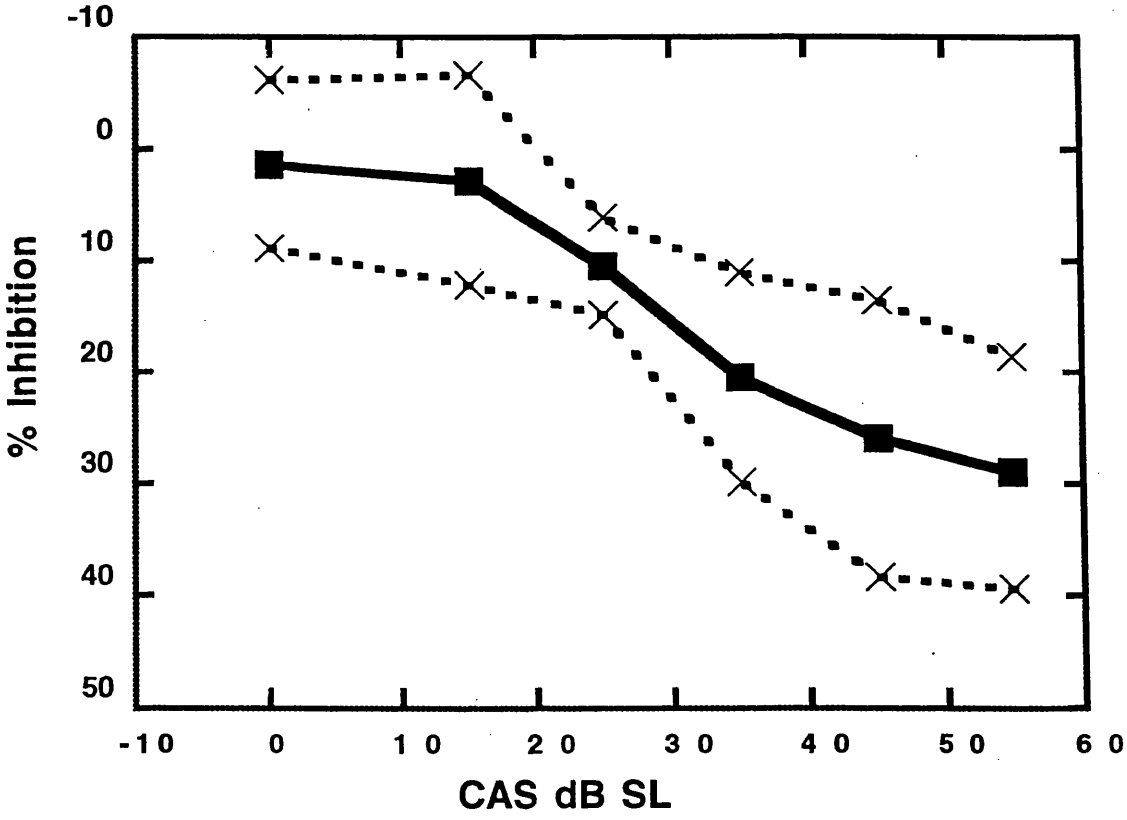
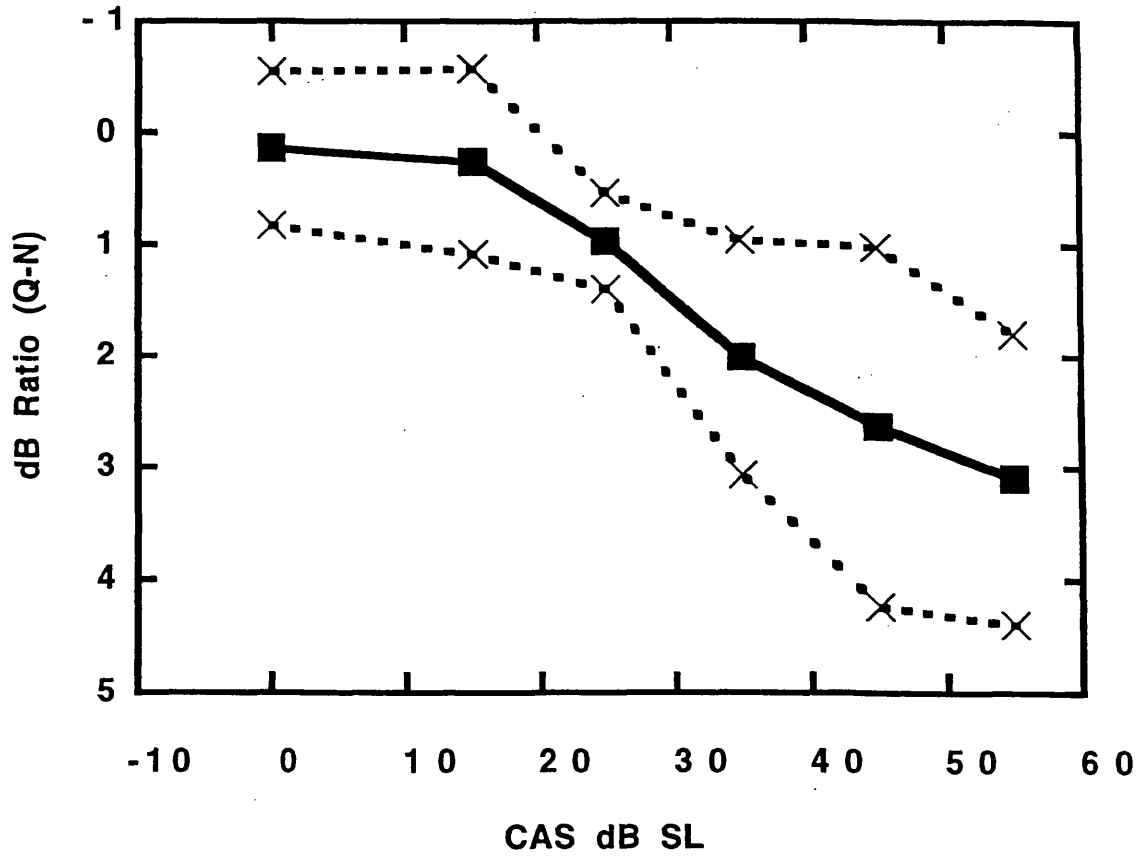


Figure IV.3
Mean Inhibition of CEOAE Amplitude in dB Ratio as a Function of Contralateral Acoustic Stimulation (CAS) Level

Inhibition of CEOAE amplitude collected in noise (N) relative to the amplitude recorded in quiet (Q) was calculated for each individual at each contralateral intensity, and expressed as a dB Ratio (Q-N) relative to that individual's amplitude in quiet. (Solid squares) means for the normal; (X) +/- 2SD of mean. Contralateral acoustic stimulation (CAS) is expressed in dB relative to sensation level above threshold (dB SL).

dBSL	0	15	25	35	45	55
n	20	5	10	20	20	4



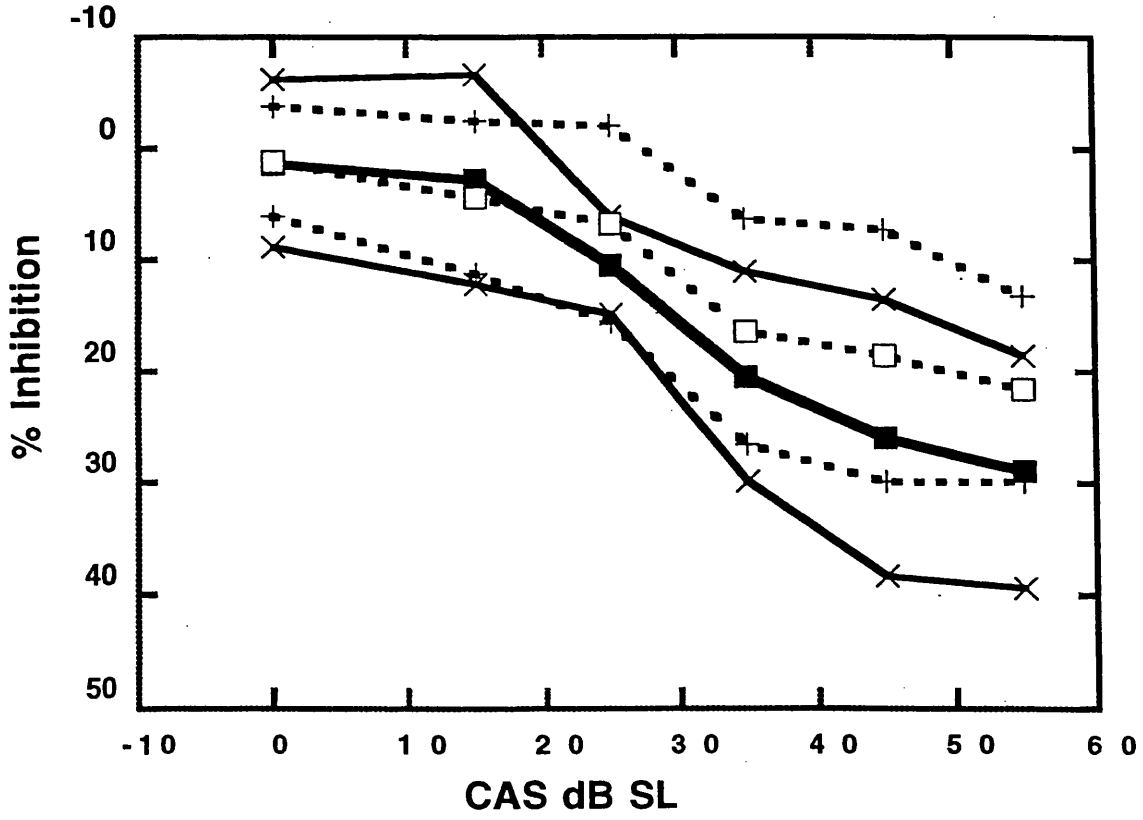
Efferent Auditory Effects as a Function of Window Onset Time

The data described above was calculated from the amplitude of otoacoustic emission pressure across the measurable frequency bandwidth of the ILO system that fell within a 4.5 (+/-0.5) to 20.5 msec time window (with a 2.5 msec cosine onset ramp). A similar pattern of inhibition was observed when the time window began at 2.5 msec (with a 2.5 msec cosine onset ramp). Student's t-tests demonstrated that, above 30dBSL, responses in noise were significantly different to responses recorded in quiet ($p<0.001$ two tailed t-test). Comparison of the % inhibition measured using 2.5 and 5.0 msec onset windows revealed that the magnitude of inhibition was enhanced by removing the initial 2.5 msec period. It is likely that this reflects the result of removing linear middle ear oscillations. These are most likely to affect the first 5 msec of the recording window when using the "linear" click amplitude technique (which does not reject linear changes in amplitude). Such middle ear artifacts should, hypothetically, be unresponsive to the effects of the intra-cochlear efferent fibers acting upon outer hair cells, and hence show no amplitude change in the presence of olivocochlear activity. Thus it is likely that inhibition calculations using the 2.5 - 20.5 msec window would be artificially lower due to the confounding effects of linear middle ear response which are not inhibited by contralateral noise. The 4.5 (+/- 0.5) - 20.5 msec window was therefore chosen as the time filter for the test protocol described below. (See Figure IV.4)

Figure IV.4
Efferent Inhibition as a Function of Window Onset Time and Contralateral Acoustic Stimulation Level

Inhibition of CEOAE amplitude collected in noise relative to the amplitude recorded in quiet was calculated for each individual at each contralateral intensity, and expressed as a fractional % of the amplitude recorded in quiet. (Solid squares) mean % inhibition with an analysis time window beginning at 5.0 msec; (X) & solid lines represent +/- 2 SD from mean. (Open squares) mean inhibition with a time window onset of 2.5 msec; (+) & dashed lines represent +/-2 SD from mean. Contralateral acoustic stimulation (CAS) is expressed in dB relative to sensation level above threshold (dB SL).

dBSL	0	15	25	35	45	55
n	20	5	10	20	20	4



Efferent Auditory Effects in Normal Subjects: As a Function of Biological Effects

Effective Efferent Inhibition as a Function of Ipsilateral Click Intensity

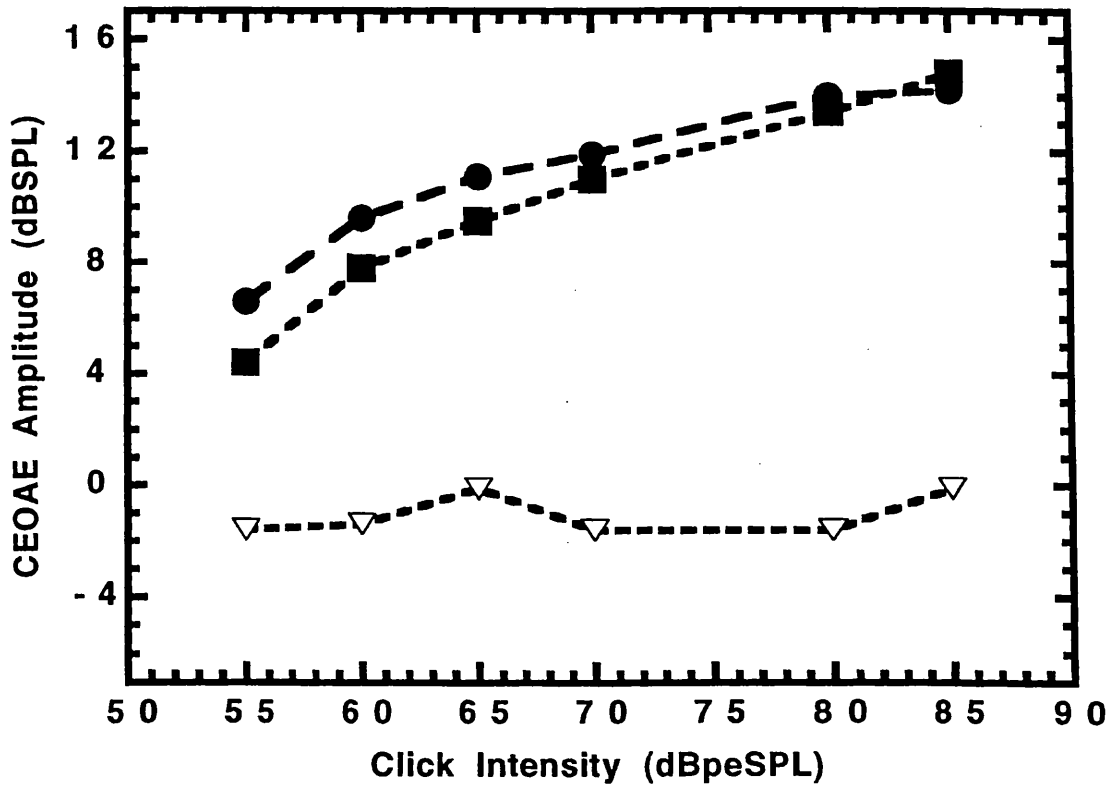
In animal studies, a measure of "effective" inhibition has been used to quantify a decrease in response amplitude in terms of an equivalent loss of amplitude that would result from a decrease in the intensity of the ipsilateral stimulus (Puria et al. 1996). The protocol requires measurements across a range of ipsilateral stimulus intensities and thereby offers information about the dynamic range of the efferent effects, and the rate of increase of inhibition. This measure tends to yield inhibitory values of greater magnitude than comparisons of temporally related quiet / noise pairs. (See Figure IV.5.)

Normal subjects were tested with click stimuli at levels from 55 to 88 dBpeSPL with contralateral white noise at 35 and 45 dB SL. At the lowest click levels, the signal to noise level of the recordings determined the detection level of otoacoustic emissions, and conclusions were not drawn from data collected when the signal to noise ratio was less than one, or the reproducibility was less than 50%. As click intensity increased, the signal to noise ratio improved. Those recordings during the highest click levels, which showed marked increases in the noise floor, were excluded from analysis. Observations revealed that inhibitory effects were greatest with clicks ranging from 60 - 75 dBpeSPL. Inhibition tended to decrease at higher click intensities, and was not observable in several cases with click levels equal to or above 80-85 dBpeSPL. Pilot data recording inhibition of distortion product emissions also verified the importance of using lower intensity stimuli (55-65 dBSPL).

Figure IV.5
Input / Output Function of CEOAE

Emission Amplitude in Quiet and in Noise as a Function of Ipsilateral Click Intensity

The convergence of the two lines show that difference between the OAE amplitude in quiet and in noise decreases as click intensity increases. At the highest levels, virtually no inhibition is observed. (Circles) CEOAE amplitude (dBSPL) in quiet conditions; (Squares) CEOAE amplitude (dBSPL) during 35dBSL contralateral white noise. (Triangle) noise level of recording.



Repeatability of Efferent Auditory Effects

Inter-test variability of % inhibition was minimal during repeated recordings with alternating quiet / noise conditions for each series of 10 recordings using a fixed level of contralateral noise (e.g. 5 in quiet, 5 in noise). Individually and across the normal group, there was little overlap between the response amplitude measured in quiet, and amplitudes during CAS levels above 30dBSL when comparing immediately adjacent "quiet / noise" pairs. Similar to observations reported in animals, relative to the initial level in quiet, inhibition slowly increases and decreases over time (Sridhar et al. 1995). (See Figure IV.8.) Whilst the mean inhibition at 25 dBSL was significantly greater than at 0 dBSL ($p<0.01$), the distributions overlap sufficiently to make it more difficult to immediately observe suppression. Therefore, 35dBSL was chosen as the stimulus intensity to establish normal response criteria. (See Table IV.1, Figure IV.6.)

Bilateral Efferent Auditory Effects

For those subjects (n=8 subjects) completing efferent auditory effect tests in both ears (n=16 ears), bilateral inhibitory effects were observed in all cases. Inter-aural differences between the magnitude of inhibition in right and left ears were minimal with a mean difference of 2.9% across contralateral levels from 0-45dBSL. (See Figure IV.7.)

Figure IV.6
Inhibition over a Repeated Series as a Function of Intensity

The % inhibition over repeated recordings during contralateral acoustic stimulation at different levels relative to sensation level (dBSL). (Circles) %CEOAE amplitude change in repeated recordings made in quiet, relative to the initial amplitude in quiet. (Squares) the % changes in CEOAE amplitude relative to the initial amplitude in quiet, during repeated recordings with 25 to 45 dBSL noise.

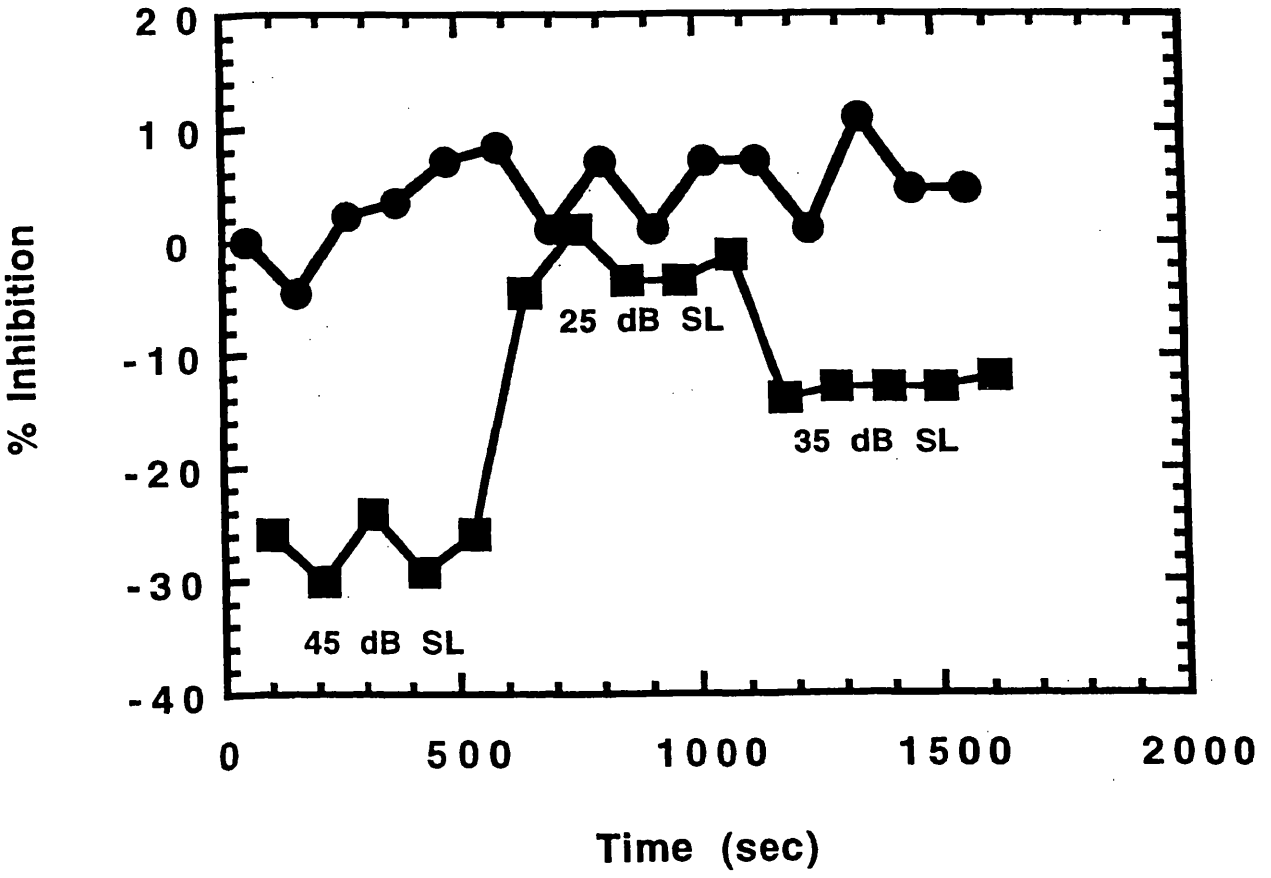
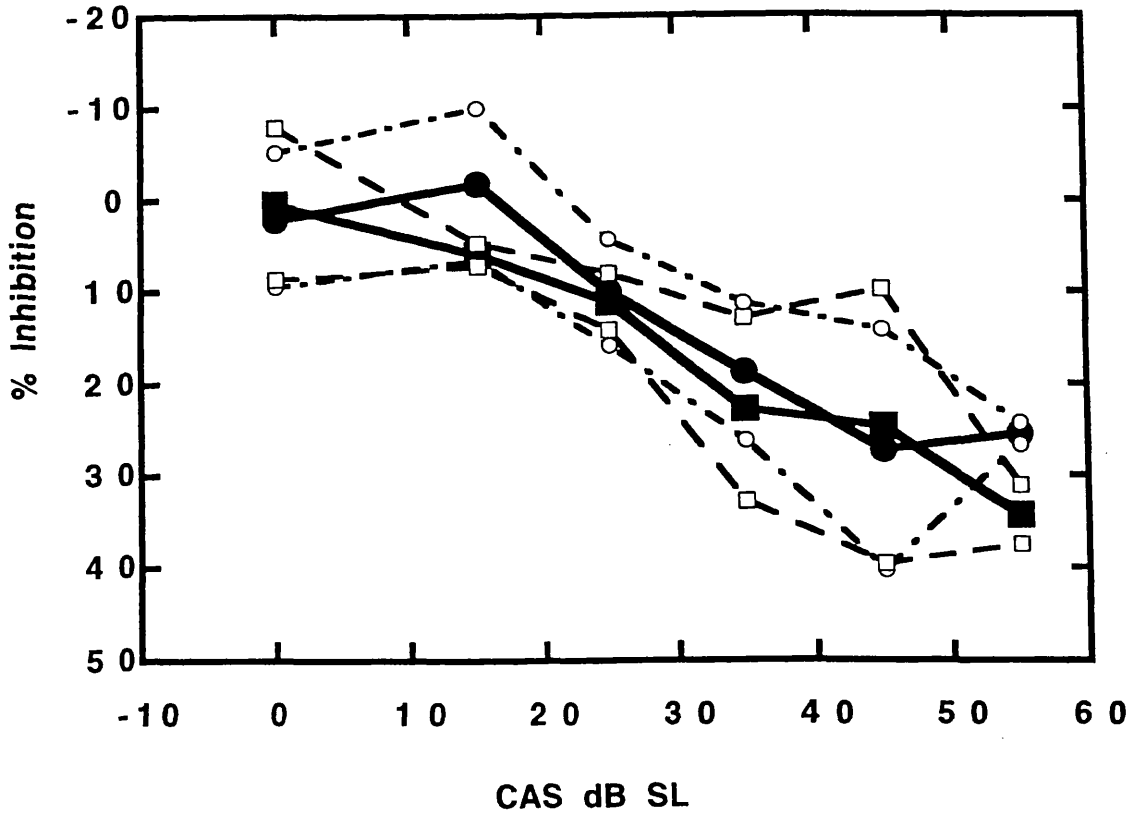


Figure IV.7
Bilateral Inhibition in Normal Subjects

The mean % inhibition of CEOAE amplitude in right and left ears of normal subjects, plotted as a function of contralateral acoustic stimuli levels relative to dB sensation level (CAS dBSL).

Inhibition magnitude represents the change in CEOAE amplitude in noise conditions as a fraction of the individual's CEOAE amplitude in quiet. (Solid Circles) right ear mean inhibition. (Open circles) right ear +/- 2 SD of right mean inhibition. (Solid Squares) left ear mean inhibition. (Open Squares) left ear +/- 2 SD of left mean inhibition.

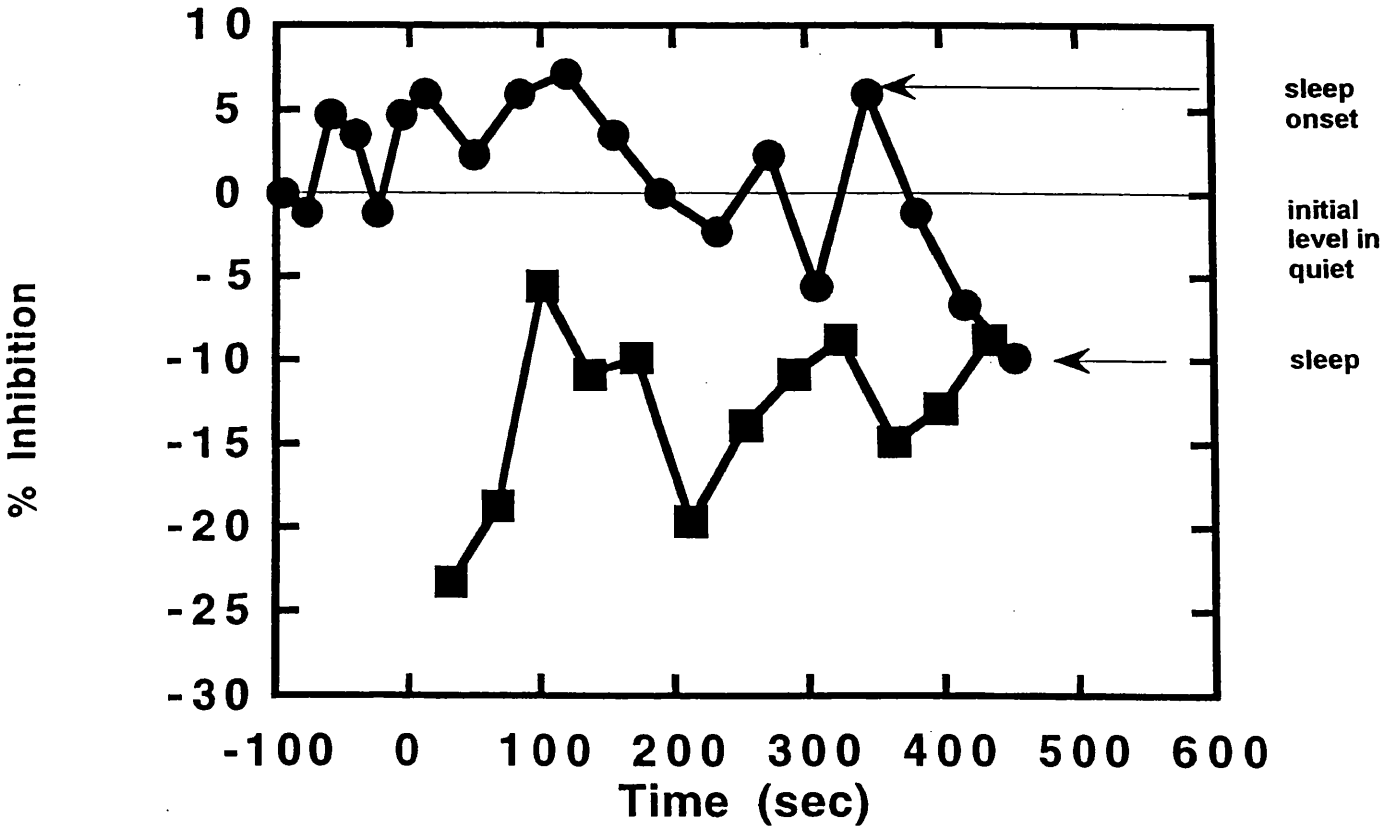


Impact of Attention and Slow Efferent Auditory Effects

Loss of inhibition was observed in normal subject during changes in attention, fatigue or distraction and in particular during the onset of sleep. This study did not seek to replicate the correlation of sleep EEG with efferent effects reported by others; however, the loss of inhibition was readily observed during clinical testing. The amplitude of the emissions recorded in quiet conditions tended to fall towards the amplitude of emissions recorded during noise, resulting in a loss of "fast efferent effects", whilst inhibition relative with the initial baseline were maintained. It was noted that whilst the amplitude of emissions recorded in noise fluctuated, the onset of sleep appeared to have less effect on the recordings in noise. The amplitude rarely increased to the level of the initial amplitude in quiet. (See Figure IV.8.) Evidence of attention and sleep state was gathered by observation and by confirmation from the subject. Further validation of these observations using psycho-acoustic or electrophysiologic measures would be more informative.

Figure IV.8
Inhibition over a Repeated Series
Attention and Slow Efferent Effects

The % inhibition during repeated recordings with alternating contralateral white noise stimulation at 35dB sensation level (dBSL). Slow efferent effects are noted as variation in the % inhibition of the responses collected during noise. The onset of sleep and full sleep are marked by arrows. The horizontal line at 0% represents no change from the initial amplitude in quiet. (Circles) % CEOAE amplitude in quiet, relative to the initial CEOAE amplitude in quiet. (Squares) % CEOAE amplitude change in recordings during noise, relative to the initial amplitude in quiet conditions.



CHAPTER V

EXPERIMENTAL RESULTS

VESTIBULAR NERVE SECTION PATIENTS

SECTION A.

Pre and Post-Operative Comparisons

of Efferent Auditory Effects

with Interruption of the Olivocochlear Efferents

PRE AND POST-OPERATIVE VESTIBULAR NERVE SECTION RESULTS

Efferent Auditory Effects In Vestibular Nerve Section Patients (VNS)

Vestibular nerve section patients provided an experimental paradigm for studying the effect of loss of olivocochlear innervation to the cochlea. The olivocochlear bundle, traveling within the inferior vestibular nerve was severed (by Gerald Brookes) proximal to the vestibulo-cochlear anastomosis by means of retro-labyrinthine vestibular nerve section for the treatment of intractable peripheral labyrinthine disorders.

Audiometric Results:

The Appendix includes raw data on all cases, including pure tone thresholds, tympanometry, acoustic reflex thresholds, auditory brainstem and caloric responses. The mean pure tone averages (PTA) of 500, 1000 and 2000Hz from eight vestibular nerve section patients were within the normal range before and following surgery. The mean PTA from the surgical side was 10dBHL before surgery and 14dBHL following nerve section. (See Appendix: Table A1.) The mean for the intact side was 11dBHL before, and 5dB after surgery, showing an improvement of only 6dB. (Thresholds tested in 5dB steps.)

Post-operatively, seven of eight VNS patients had pure tone thresholds in the operated ears between 0-35dBHL for 500, through 2000Hz, and normal ABR results. Bilateral thresholds were $\leq$25dBHL in four patients. Three had thresholds between 0-10dBHL at those frequencies. Post-operative thresholds improved in both ears in two cases, and one stayed the same. Four cases had hearing loss $\geq$4kHz (35-55dBHL); 2 cases had moderate to severe loss $\geq$4kHz (65-100dBHL). There was a mean decrease of 14dB at 4kHz and 11dB at 8kHz. For both operated and intact ears, the average air bone gap was 10dB or less at all bone conduction frequencies for three patients.

The Appendix records the values recorded in electro-physiological tests for all patients. (Appendix: Tables A.1-8.)

Pre/Post-Operative Comparisons: Vestibular Nerve Section Case Studies

Case v : History and Audiology

This 37 year old female presented with a 6 year history of episodic dizzy spells precipitated by movement. Attacks became increasingly severe, lasting 2-3 weeks at time at frequent intervals. There was no evidence of cervical spine disorders. The patient reported that left divergent ocular strabismus had been present since birth or early childhood. The patient did not complain of hearing loss or tinnitus. The patient did report that hearing was subjectively better in the left ear. Pitch perception was symmetrical.

Pre-operative investigations (3 months and also 1 day before surgery) revealed pure tone thresholds between 0-10dBHL bilaterally. Tympanometry was normal in compliance and pressure. Acoustic reflex thresholds were normal for ipsilateral conditions, and were at the upper limit of normal for contralateral stimuli presented at 1000 and 2000 Hz. Contralateral ART were slightly elevated at 500 and 4000 Hz recording from the right, and at 500 Hz recording from the left. Reflex decay measures were normal in both ears. ABR were tested on three different occasions, and wave morphology was clearly formed. On two tests showed very early wave I and wave III, and slightly prolonged inter-wave intervals. These observations were not repeated on other recordings. Inter-aural differences were normal.

Vestibular tests revealed a right canal paresis with bithermal caloric tests. Gait was normal, spontaneous nystagmus was not observed. Pursuit, saccades, VOR and OKN eye movements were normal. Gadolinium enhanced MRI and air tomography were normal.

Post-operative measurements were conducted 28 months following surgery, at which time the patient reported full recovery from vestibular dysfunction, with full facial function. The patient reported diminution of hearing in the right ear, with occasional difficulty understanding some words. She was able to hear, but unable to comprehend speech.

Audiometric thresholds remained normal, and within 10dB of pre-operative levels bilaterally. Tympanometry and ART were normal. The ABR showed a slight delay in wave III in right ipsilateral recordings, though inter-wave intervals were normal. The absolute latency of wave III in the right ear was slightly above normal limits (0.07 msec), however this was considered insignificant give normal wave morphology, inter-wave intervals and inter-aural differences. (See Appendix: Table A1, A3).

Case v: Pre and Post Nerve Section Comparison of Efferent Auditory Effects

Pre-operatively, otoacoustic emissions were measurable across the 0.5-4kHz range using standard clinical protocol. Linear responses using lower stimulus levels were associated with weaker emissions. Dominant responses were within the 1-2 kHz range for both ears. The intact ear displayed 16.8% inhibition during 45dBSL stimulation, and 12.9% in the operated ear.

Post-operative measurements revealed unilateral loss of inhibitory effects in the sectioned ear, whilst the intact ear maintained inhibition (28 months following surgery). Following nerve section, the right "de-efferented" ear demonstrated virtually no change in CEOAE amplitude with increasing contralateral noise levels (2.3% at 45dBSL). The minimal fluctuations in amplitude observed were more consistent with fluctuations in amplitude in quite. (Table V.1) The intact ear, however, maintained inhibition following surgery, within 5% of the ear's pre-operative measures. At 35 dB SL, inhibition of 9.8% was slightly less than 2 SD from normal means, but was greater than variability observed in quiet (0dBSL). Inhibition at 40-45dBSL was within normal limits (16.8%). (See Figures V.1, V.2.)

Figure V.1
Case v: Inhibition of CEOAE Pre and Post Vestibular Nerve Section in the Operated Ear

Filtered CEOAE waveforms (1000 – 2000 Hz) are superimposed to show the waveform recorded in quiet (A) and the waveform during 35dBSL contralateral white noise (B), plotted as amplitude (μPa) versus time (msec). The upper trace illustrates pre-surgical peak to peak inhibition in the operative ear. The lower trace shows reduced emissions and reduced inhibition in the operated ear, following vestibular nerve section.

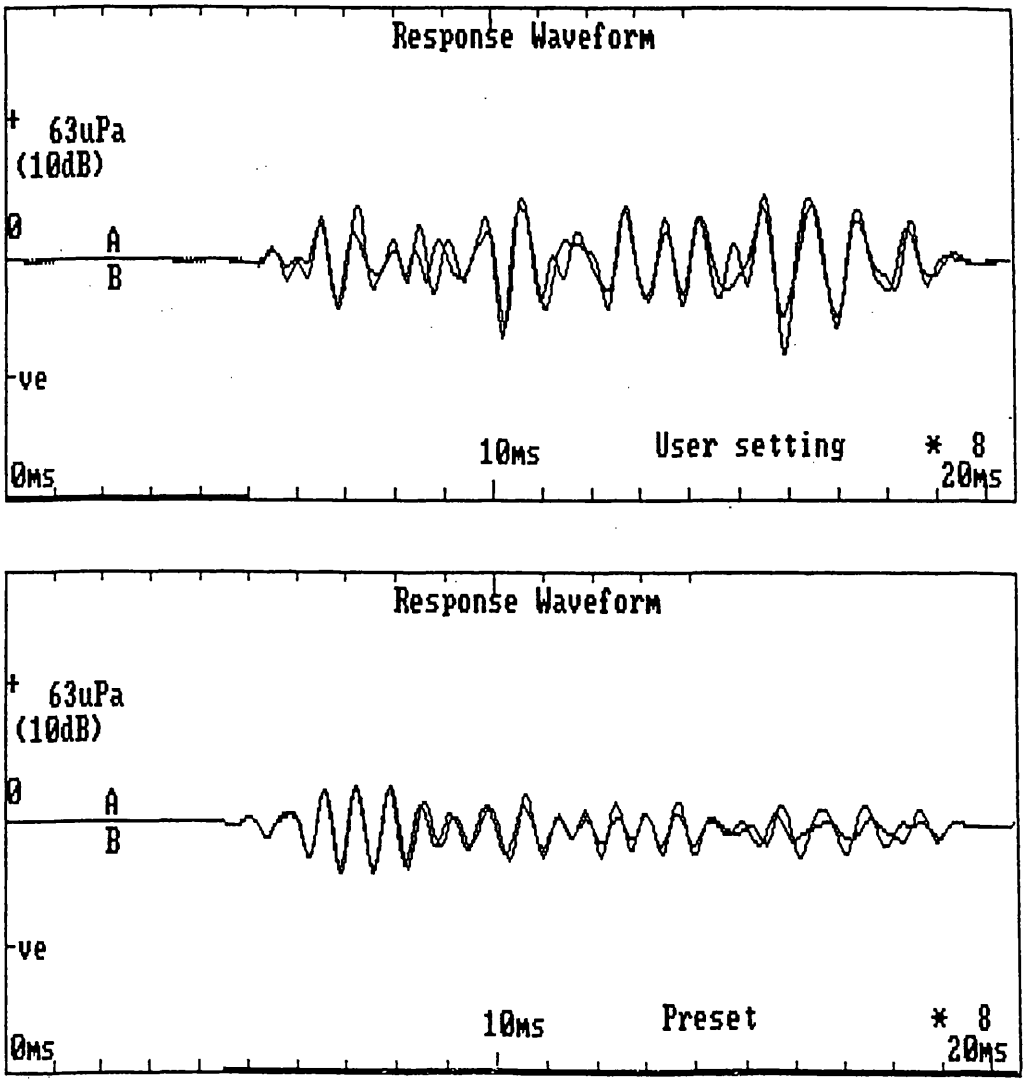
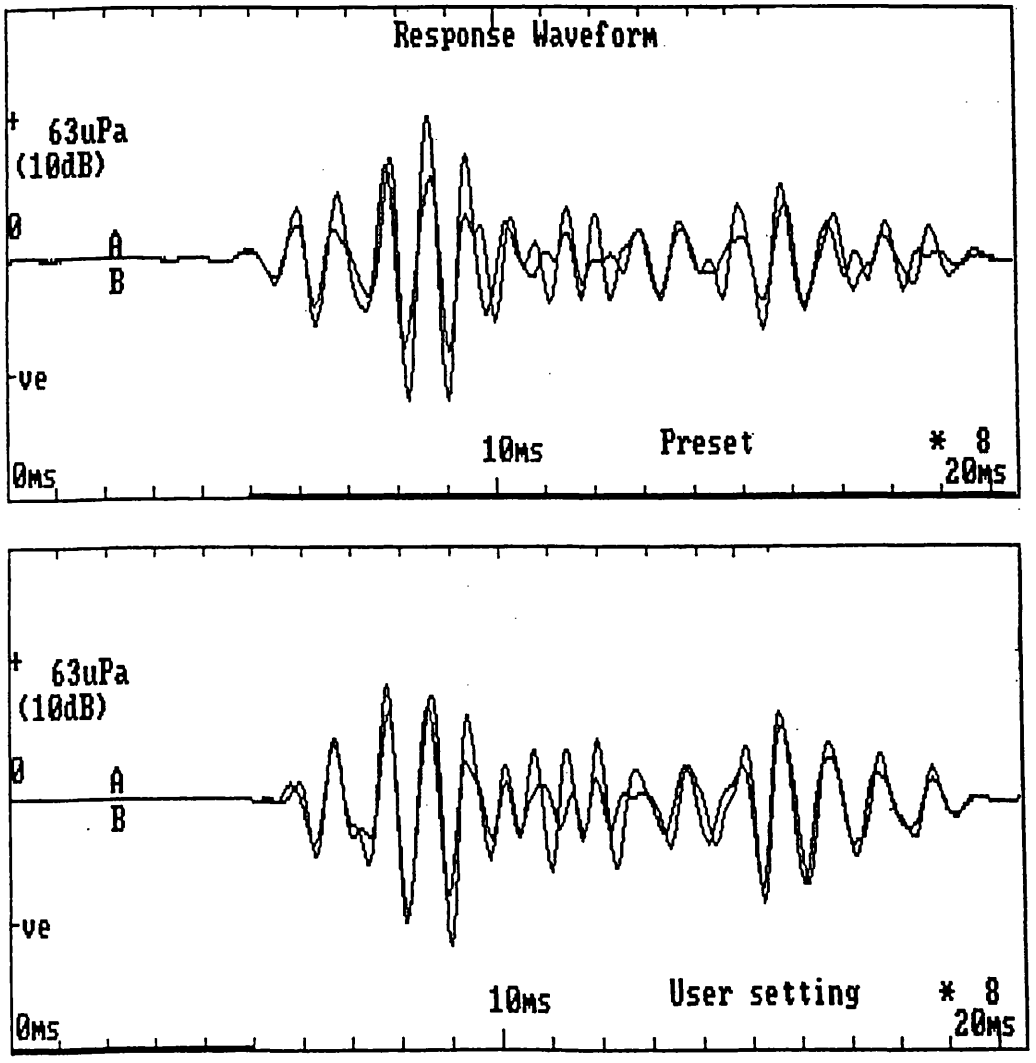


Figure V.2

Case v: Inhibition of CEOAE Pre and Post Vestibular Nerve Section in the Intact Ear

Filtered CEOAE waveforms (1000 – 2000 Hz) are superimposed to show the waveform recorded in quiet (A) and the waveform during 35dBSL contralateral white noise (B), plotted as amplitude (μPa) versus time (msec). Upper trace shows pre-surgical peak to peak inhibition of waveforms during noise in the intact ear. Lower trace shows inhibition is maintained in the intact ear following surgery.



Case vi: History and Audiology

This 47 year female presented with a 6 year history of recurrent bouts of vertigo which increased in frequency to monthly intervals with symptoms lasting 1-2 weeks. The patient reported no difficulties with hearing function or tinnitus.

Pre-operative audiometric and efferent evaluations were conducted 10 days before left vestibular nerve section. Pure tone audiometry was normal bilaterally up to 3 kHz. At age 51 there was a bilaterally high frequency loss (maximum 40 dBHL). Tympanometry revealed normal middle ear pressure and slightly low compliance in both ears (0.3 ml), with normal ART with ipsilateral and contralateral stimuli, and reflex decay. ABR responses were normal in morphology, absolute and inter-wave latencies, and inter-aural difference.

A left canal paresis with right directional preponderance was evident upon caloric testing. Gait, pursuit, saccades and electro-oculography were normal. Spontaneous nystagmus was not observed. CT scans were normal.

Post-operative investigations and efferent auditory effects were conducted 18 months after surgery. Post-surgical recovery was uncomplicated; the patient's balance was stable, and facial function normal. The patient was unable to undergo full audiological evaluation prior to hospital discharge but did report an extreme sensitivity to the traffic noise one week after surgery, which she found "overwhelming". The patient reported difficulty in occasionally misinterpreting a word within a sentence, but had no further complaints of noise sensitivity.

Pure tone thresholds up to 3kHz were normal and within 5dB of pre-operative measures, with persistence of the bilateral high frequency loss. Tympanometry, ART and ABR were normal and similar to pre-operative latencies. (Table A.1 and A.3)

Case vi: Pre and Post Nerve Section Comparison of Efferent Auditory Effects

Pre-operative measurements from both ears demonstrated normal levels (+/-1SD) of inhibition. The left and right ear both demonstrated 19.6% inhibition with 35 - 45 dBSL.

However, after vestibular nerve section, inhibition in the left "de-efferented" cochlea was not observed. The amplitude of emissions during 35dBSL noise was 2.3% greater than OAE in quiet. In contrast, the intact right ear maintained the same level of inhibition to pre-operative measures during 35 dBSL contralateral noise (19.6%). (See Figures V.3 and V.4.)

Figure V.3
Case vi: Inhibition of CEOAE Pre and Post Vestibular Nerve Section in the Operated Ear

Filtered CEOAE waveforms (1000 – 2000 Hz) are superimposed to show the waveform recorded in quiet (A) and the waveform during 35dBSL contralateral white noise (B), plotted as amplitude (μPa) versus time (msec). The upper trace illustrates pre-surgical peak to peak inhibition in the operated ear. The lower trace shows lack of inhibition of CEOAE recorded in noise following nerve section, the waveform recorded in noise was *larger* than the waveform recorded in quiet (see arrows).

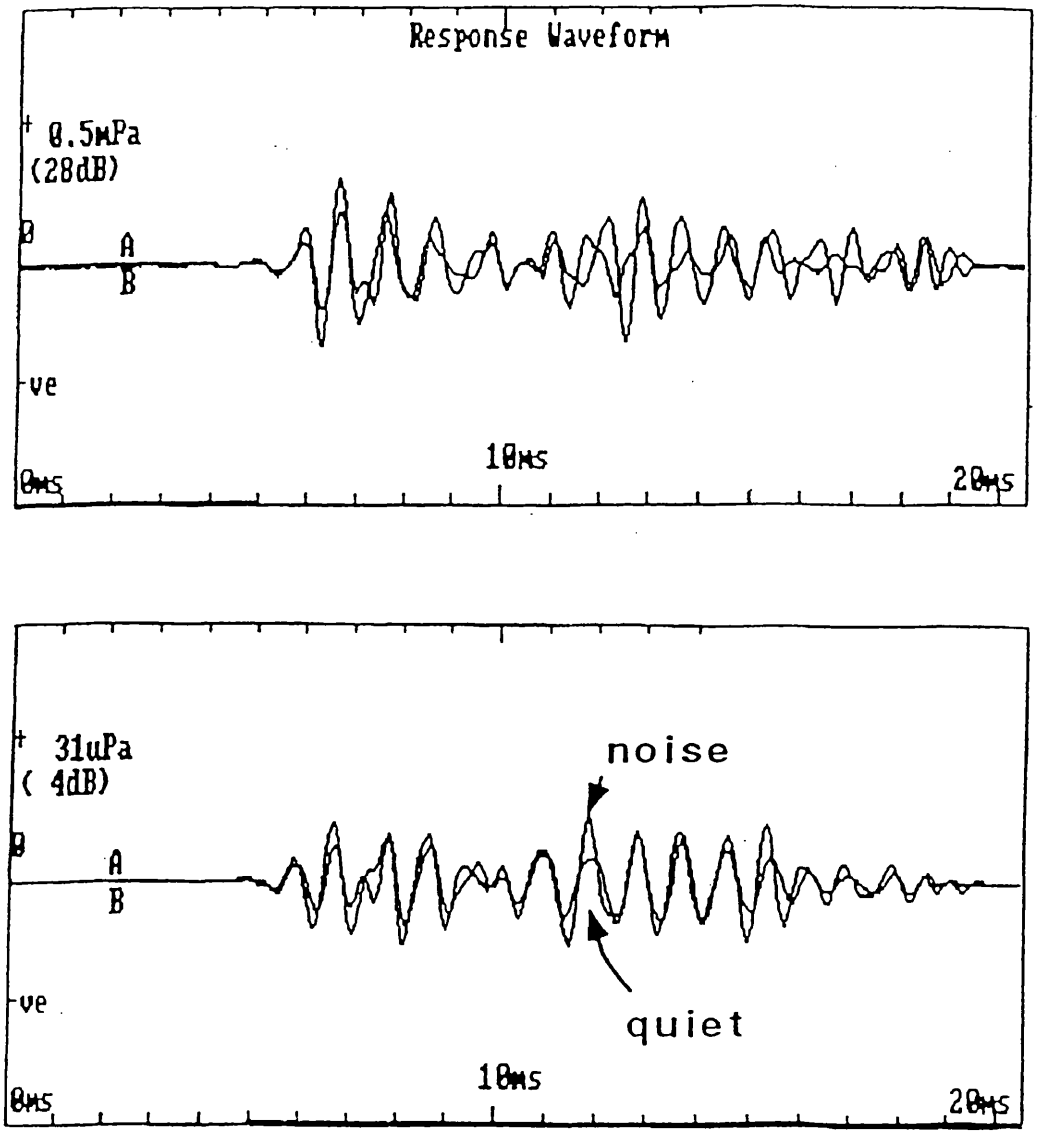
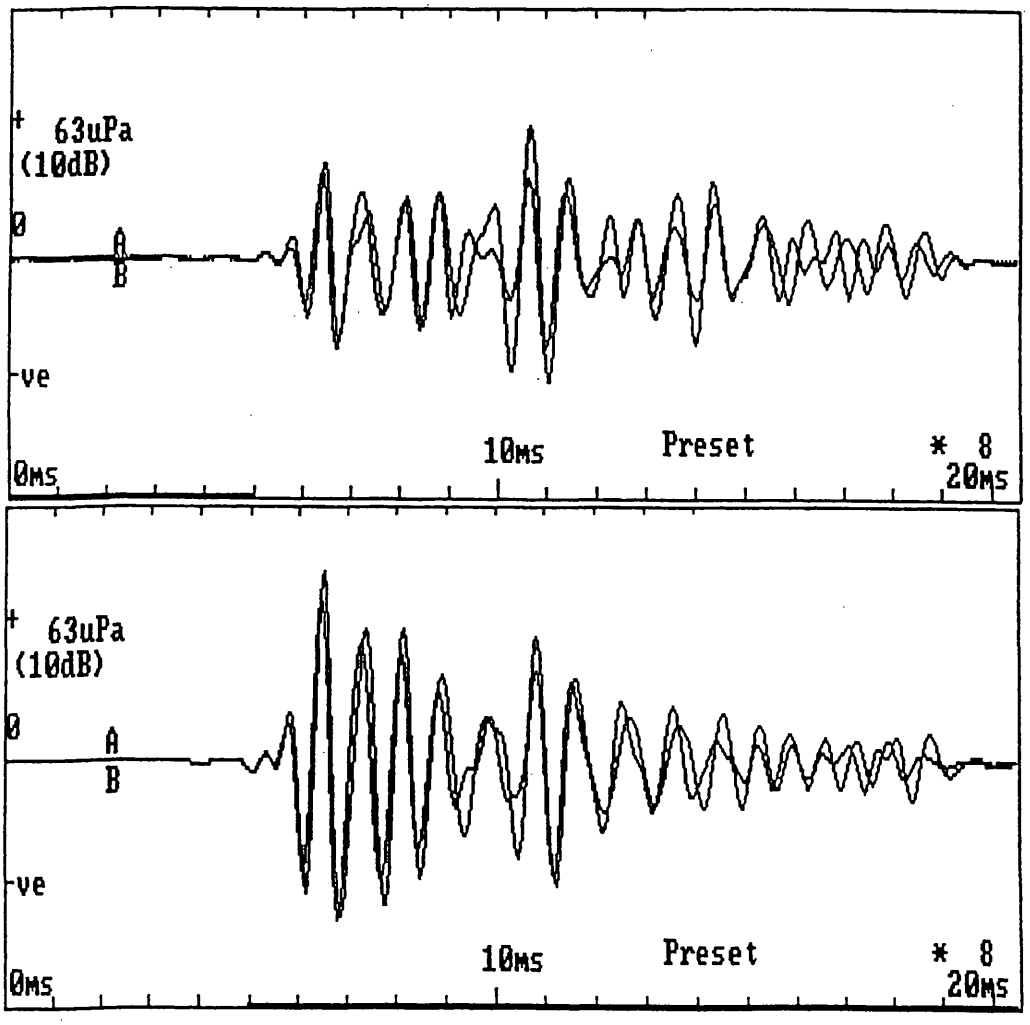


Figure V.4
Case vi: Inhibition of CEOAE Pre and Post Vestibular Nerve Section in the Intact Ear

Filtered CEOAE waveforms (1000 – 2000 Hz) are superimposed to show the waveform recorded in quiet (A) and the waveform during 35dBSL contralateral white noise (B), plotted as amplitude (μPa) versus time (msec). The upper trace illustrates pre-surgical peak to peak inhibition and a phase lead of CEOAE recorded in noise from the intact ear. The lower trace shows post-surgical results from the intact ear, which maintained peak to peak inhibition and a phase lead of waveforms recorded during contralateral noise.



Case vii: History and Audiology

This 43 year old male presented with 6 years of balance disorders. Medical therapy was unsuccessful in controlling the vertigo and nausea. The patient had no complaint of hearing loss. Tinnitus in the left ear was reported.

Pre-operative investigations were completed 3 weeks before surgery. Pure tone audiometry was in the normal range in the right ear, and was normal in the left for frequencies up to 8kHz which showed 35 dBHL thresholds. Tympanometry and acoustic reflex thresholds were normal and symmetrical for ipsilateral and contralateral stimuli. Reflex decay was normal bilaterally.

Vestibular tests confirmed a left canal paresis with no other ENG abnormalities. Gait, spontaneous nystagmus, saccades, pursuit and oculo-vestibular responses were normal. CT Tomograms of the internal auditory meati were normal.

Post-operative evaluations were conducted 41 months following surgery. Recovery was uncomplicated, with no nystagmus one week following surgery, and Romberg test was negative. Balance was well compensated by 15 months following surgery, with no further episodes of vertigo.

Pure tone audiometry revealed a high frequency hearing loss in the operated ear, whilst the right ear remained within the normal range. Tinnitus remained. Tympanometry remained normal bilaterally. ART were normal for right ear stimulation for ipsilateral and contralateral recordings, although left ear stimulation yielded no responses for ipsilateral or contralateral recordings. Auditory brainstem responses were normal for right ipsilateral conditions, but abnormal for left ipsilateral and both contralateral conditions. The results are consistent with the high frequency hearing loss in the left ear. (See Table A.1 and A.3.)

Case vii: Pre and Post Nerve Section Comparison of Efferent Auditory Effects

Efferent tests were conducted three weeks before and 41 months after surgery.

Pre-operative CEOAEs were robust in both ears. Bilateral inhibition was in the normal range preceding surgery with 40dBSL (left: 13.9%; right: 16.8%).

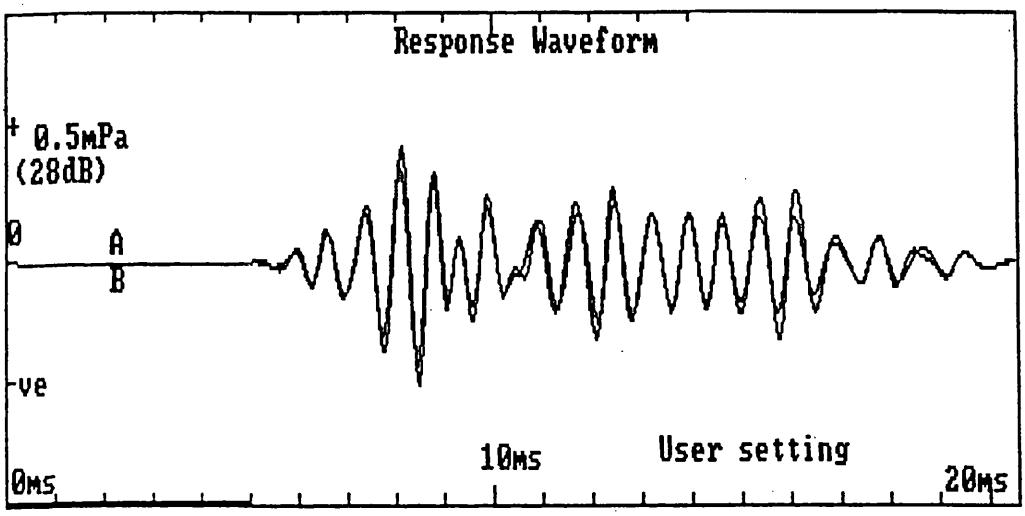
Following surgery, emissions from the operated ear were much reduced relative to pre-operative levels with a frequency range primarily between 0.5 - 1.5 kHz (5.0ms window onset), consistent with the remaining thresholds better than 35dBHL. Inhibition was abnormal in the operated ear. Responses during 35dBSL were -7.2% greater than in quiet, but only 6.7% smaller during 40dBSL.

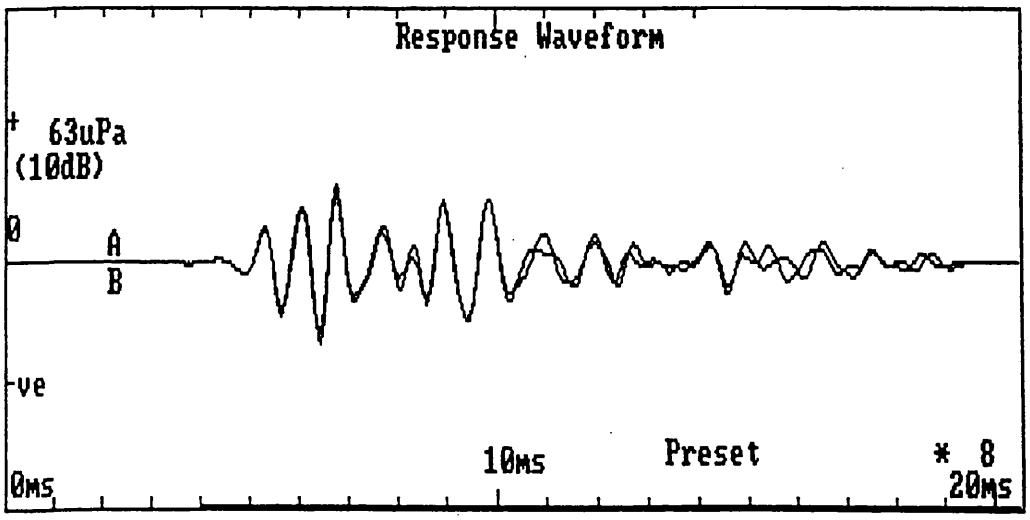
In contrast, responses in the intact ear were robust across the frequency range, and similar to pre-operative levels. Inhibition reached 16.8% during 35dBSL. (See Figure V.5.)

The unilateral loss of inhibition in the operated ear is consistent with findings in other vestibular nerve section patients, and with loss of olivocochlear innervation. However, it is possible that reduced auditory function played a role in the loss of inhibition. The persistence of inhibition in the intact ear suggests normal efferent function. However the perception of the full frequency spectrum of the white noise presented to the operated ear is likely to have been distorted, and may have resulted in less effective stimulation of the efferent fibers at the mid to high frequency range where the hearing loss was greatest. It is thus possible that the magnitude of inhibition in the intact ear was reduced as a result of this distortion.

Figure V.5
Case vii: Unilateral loss of Inhibition of CEOAE Post Vestibular Nerve Section in Intact and Operated Ears

Filtered CEOAE waveforms (1000 – 2000 Hz) are superimposed to show the waveform recorded in quiet (A) and the waveform during 35dBSL contralateral white noise (B), plotted as amplitude (uPa) versus time (msec). The upper trace illustrates that following surgery, the intact ear maintains peak to peak inhibition of CEOAE during contralateral noise. The lower trace shows lack of inhibition in the operated ear following surgery.





Summary of Pre/Post-Operative Efferent Auditory Effects Following Vestibular Nerve Section:

Pre-operative testing demonstrated bilateral inhibition of otoacoustic emissions. Responses from the operative and intact sides were similar to normal responses. In contrast, post-operative responses demonstrated a unilateral loss of inhibition in the operated ears, relative to pre-operative levels in the intact and operated ears, relative to normal mean responses, and relative to post-operative responses from the intact ears. The intact ears, maintained inhibition at magnitudes consistent with normal mean responses, or pre-operative intact response means. The magnitude of inhibition increased as a function of contralateral noise intensity, as observed in normal subjects. (See Figures V.6, V.7.)

Conclusion

These intra and inter-subject pre and post-operative studies of vestibular nerve section patients offered evidence that section of the olivocochlear fibres within the vestibular nerve was associated with significant loss of contralateral inhibitory effects. The unilateral absence of inhibition in these cases contrasts the bilateral presence of inhibition observed in the normal group.

Figure V.6
Pre-Vestibular Nerve Section
Bilateral Efferent Inhibition

Bilateral inhibition of CEOAE amplitude is within +\- 2SD of normal means for both ears before Vestibular Nerve Section. (Open circles) pre-operative intact ears. (Open diamonds) pre-operative ears before undergoing nerve section. (X) +/- 2SD of normal mean inhibition magnitude expressed as a percentage of CEOAE amplitude in quiet.)

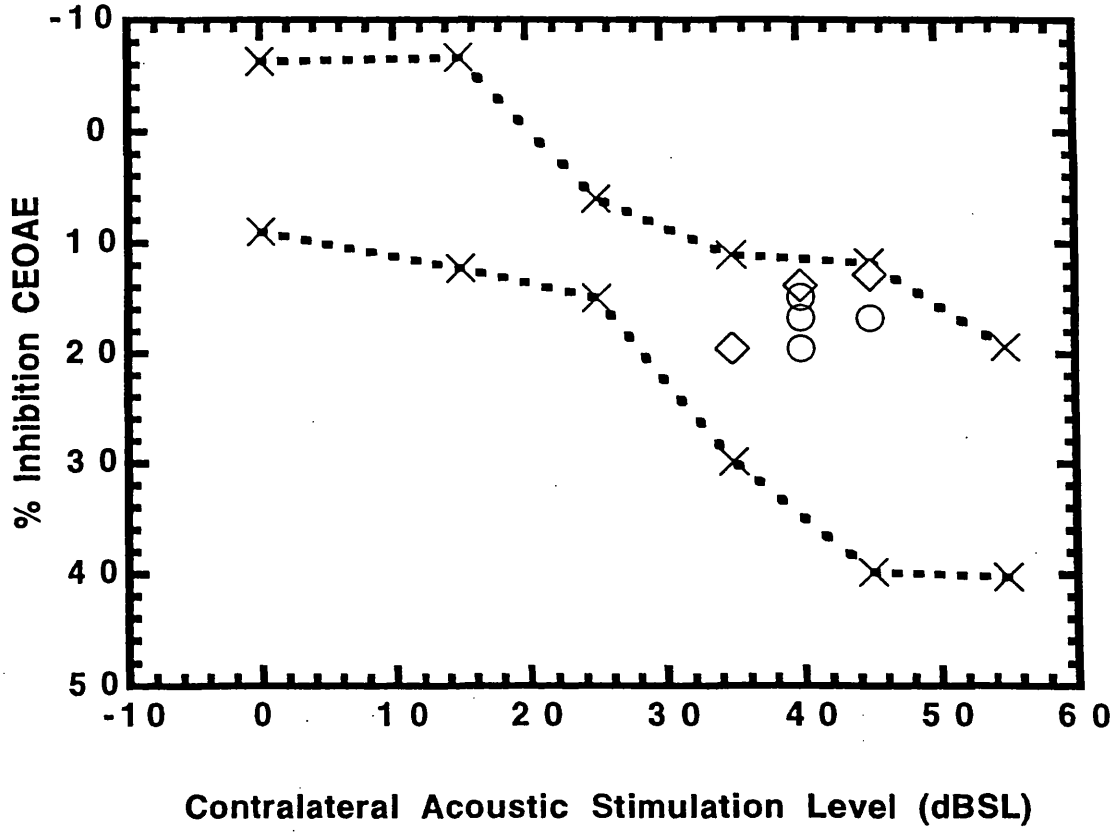
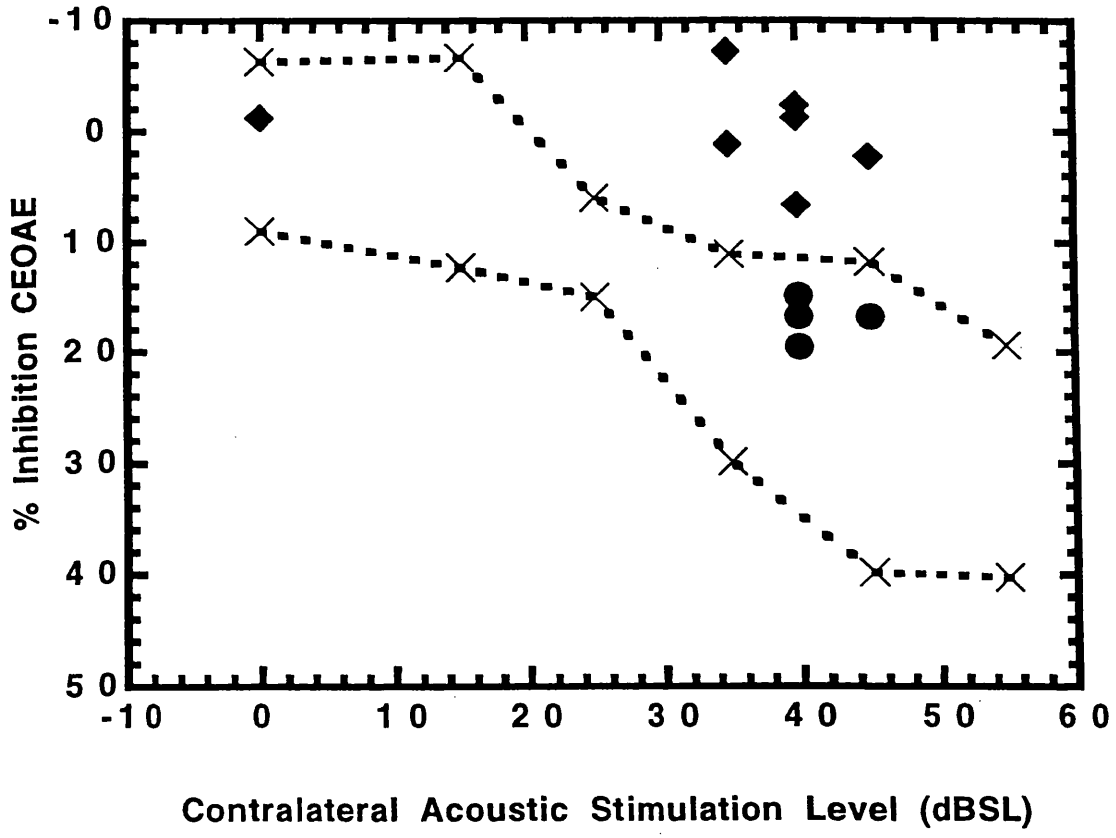


Figure V.7
Post-Vestibular Nerve Section
Unilateral Loss of Inhibition in Operated Ears

The post-surgical results are plotted for intact and operated ears in terms of % magnitude of inhibition of CEOAE amplitude recorded in noise versus quiet, as a function of contralateral acoustic stimulation (re. DB sensation level (SL). Results are plotted in comparison to mean normal responses, and show that de-efferented ears demonstrate minimal inhibition (less than +\- 2SD of normal means) after vestibular nerve section. In contrast, intact ears maintain normal levels of inhibition. (Diamonds) post-nerve section ears. (Circles) intact ears. (X) +/- 2SD of normal mean inhibition magnitude (expressed as a percentage of CEOAE amplitude in quiet).



CHAPTER V

EXPERIMENTAL RESULTS

VESTIBULAR NERVE SECTION PATIENTS

SECTION B.

Post-Operative Efferent Auditory Effects

Following Interruption of the Olivocochlear Efferents

Post-Operative Vestibular Nerve Section Case Studies

The findings from intra-subject pre / post operative comparisons were replicated in an additional study of a group of post-operative patients. The post-operative findings from de-efferented ears are contrasted with results from their intact ears, and with the mean results from the normal group.

Case i: History and Audiology

This 43 year old woman presented with a 7 year history of persistent dizziness of increasing severity. Tinnitus and hearing dysfunction were absent. This case is of particular interest, as her post-operative pure tone hearing thresholds remained very sensitive across the entire frequency range in both ears. Indeed, pure tone audiometry improved after vestibular nerve section.

Pre-operative pure tone audiometric thresholds were $\leq$10dBHL for both ears. Normal responses were observed bilaterally for tympanometry, ART, and auditory brainstem response morphology, absolute, inter-wave and inter-aural differences. Caloric tests revealed a left canal paresis. Second degree right spontaneous nystagmus was present without optic fixation. Gait, pursuit, saccades, OKN, and vestibulo-ocular responses were normal. A CT scan was normal, though a large cysterna magnum was noted.

Post-operative investigations were completed 2 months, 6 months and 41 months following right vestibular nerve section, during which time vestibular symptoms were resolved. Following surgery, pure tone thresholds showed bilateral improvement by 5-15dB. Tympanometry and acoustic reflexes remained within normal limits. ABR responses recorded also remained normal. (See Appendix: Table A.1.)

Case i: Efferent Auditory Effects Following Vestibular Nerve Section

Post-operative efferent emission tests were recorded two months and 6 months following surgery. Additional post-operative recordings were made 41 months following surgery.

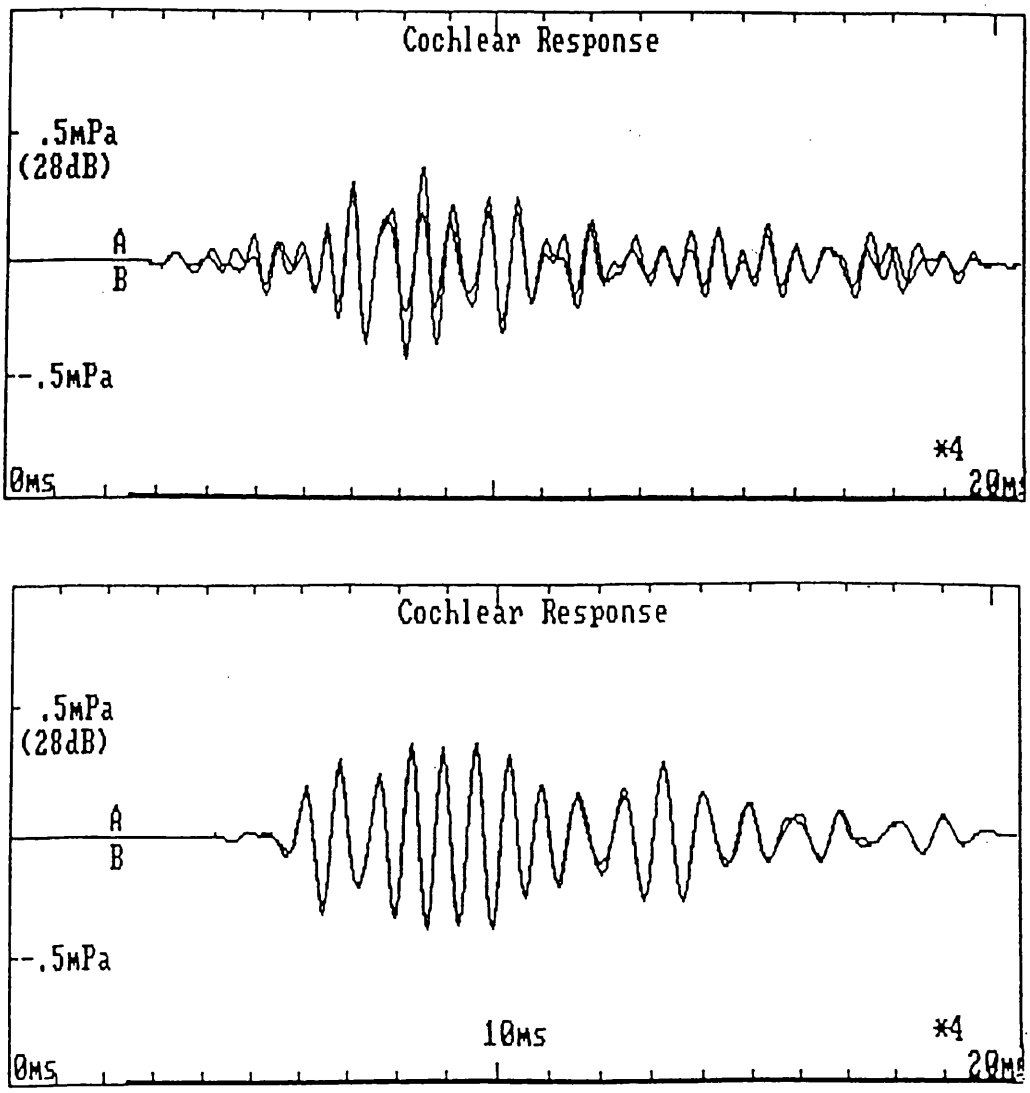
Normal click evoked otoacoustic emissions were recorded from both sides, with frequency spectra consistent with the patient's pure tone hearing thresholds ≤15dBHL. Inhibition from the ear with severed efferent fibres showed minimal changes with contralateral acoustic stimulation that was un-related to increasing contralateral intensity. The minimal variation in amplitude observed was more consistent with inter-test amplitude fluctuations in normal subjects in quiet conditions. The waveform of the dominant emissions (1000-2000Hz band) from the operated ear, showed virtually no observable change in amplitude or phase of emissions produced by the cochlea with severed efferent fibres. (Max. range –4.5 -7.0 dB inhibition with up to 45dBSL contralateral stimulation).

In contrast, otoacoustic emission amplitude from the normal ear decreased under contralateral noise stimulation, with an evident phase shift. The magnitude of inhibition increased with contralateral intensity (13.9% with 25dBSL, 19.6% during 45dBSL). (See Table V.11, and Figure V.8).

Figure V.8
Case i: Inhibition of CEOAE Post Vestibular Nerve Section in the Intact and Operated Ears

Filtered CEOAE waveforms (1000 – 2000 Hz) are superimposed to show the waveform recorded in quiet (A) and the waveform during 35dBSL contralateral white noise (B), plotted as amplitude (uPa) versus time (msec).

The upper trace shows post-surgical CEOAE from the intact ear, with preservation of peak to peak inhibition of CEOAE collected in noise relative to CEOAE recorded in quiet. The lower trace shows post-surgical results from the operated ear, with virtually no observable inhibition of peak to peak amplitude recorded in noise relative to CEOAE recorded in quiet.



Case viii: History and Audiology

This 46 year old male presented with episodic vertigo and tinnitus occurring occasionally over a period of 20 years. Recurrent vertiginous episodes increased over the last 4 years preceding surgery.

Pre-operative audiometry was normal across the frequencies apart from a very slight bilateral sensorineural loss at high frequencies (max. of 35 dB HL at 8 kHz in the left ear). Tympanometry, ART, and ABR were normal.

A slight left canal paresis was measured with caloric testing. First degree spontaneous nystagmus in absence of optic fixation was present. Pursuit, saccades and vestibulo-ocular responses were normal. The CT scan was normal.

Post-operative evaluations were conducted 9 months following left vestibular nerve section. The patient reported a change in hearing such that the operated ear was "more sensitive". Audiometry revealed pure tone averages that were normal bilaterally, except for a slight notch at 6 and 8kHz (30-35dBHL. Tympanometry and ABR remained normal in terms of morphology, absolute latency, and inter-wave and inter-aural intervals.

Vestibular symptoms were well compensated until 8 months post-operatively. Thereafter a recurrence of muzziness and unsteadiness was reported that was much less severe than pre-operative symptoms. First degree spontaneous nystagmus was noted. MRI revealed normal internal auditory meati and CPA. Inflammatory changes in left mastoid air cells and middle ear cleft were noted, with tiny high signal focus in the left medial lemniscus noted, which was possibly ischaemic.

Case viii: Efferent Auditory Effects Following Vestibular Nerve Section

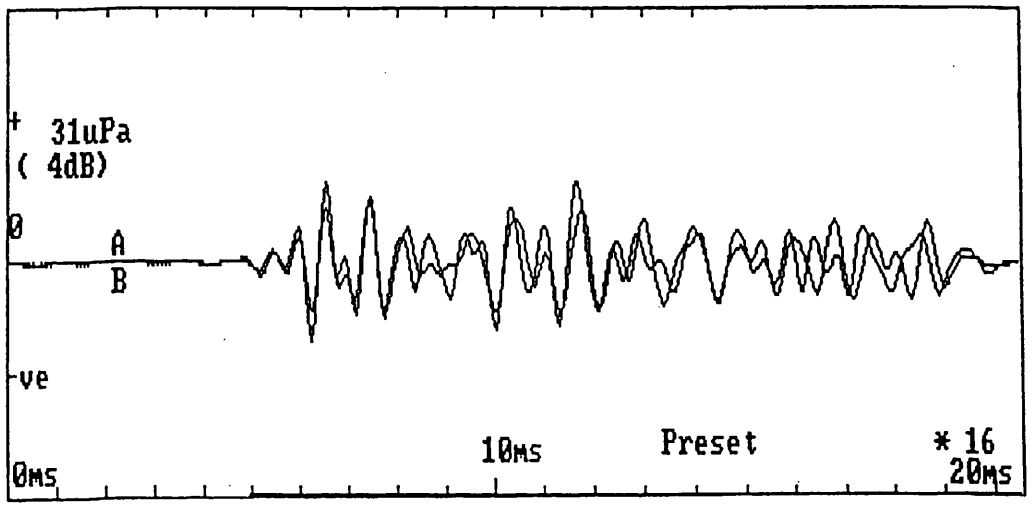
Efferent tests were conducted 9 months following surgery. Otoacoustic emissions were present, and of low amplitude, consistent with slight hearing loss and difficulty in positioning the probe in his meati, which were sharply turned.

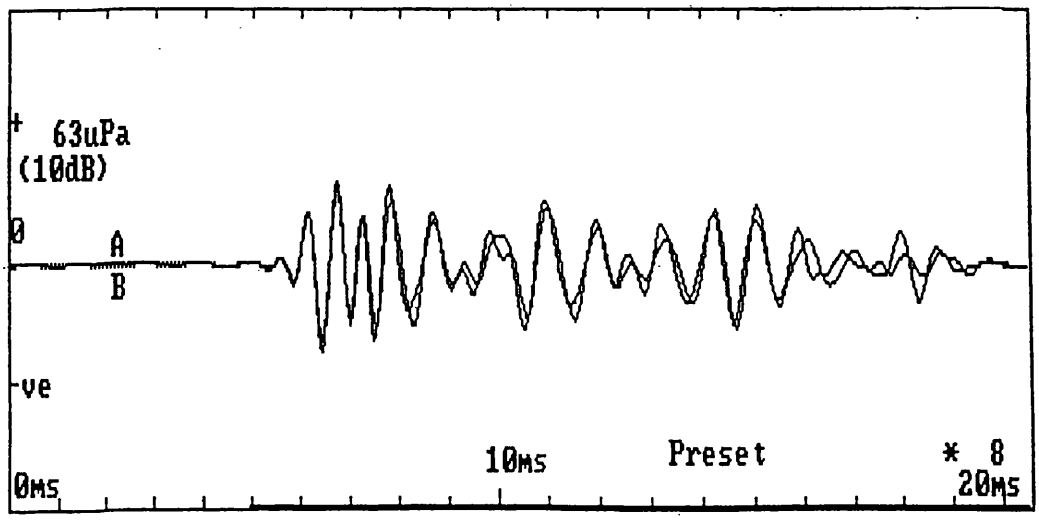
Responses were sufficient to record OAE above the noise floor (and $\geq$50% reproducibility) in both ears. Inhibition was clearly abnormal in the operated ear, with amplitude changes during 40dBSL only reaching 3.4% of the response in quiet. At 35dBSL, responses in noise were 5.9% larger than those in quiet. The intact ear however, demonstrated normal levels of inhibition, with CEOAE amplitude inversely related to contralateral noise intensity (from 14.9% at 25dBSL to 21.5% with 40dBSL). (See Figure V.9.)

Figure V.9
Case viii: Inhibition of CEOAE Post Vestibular Nerve Section in the Intact and Operated Ears

Filtered CEOAE waveforms (1000 – 2000 Hz) are superimposed to show the waveform recorded in quiet (A) and the waveform during 35dBSL contralateral white noise (B), plotted as amplitude (uPa) versus time (msec).

The upper trace shows post-surgical results from the intact ear, with preservation of peak to peak inhibition and a phase lead of CEOAE collected in noise relative to CEOAE recorded in quiet.
The lower trace shows post-surgical results from the operated ear, with minimal inhibition of peak to peak amplitude of CEOAE recorded in noise relative to CEOAE recorded in quiet.





Case iv: History and Audiology

The 41 year old female patient presented with a 10 year history of episodic vertigo with increased severity over the preceding 3 years. Occasional tinnitus was noted, but no other hearing dysfunction was reported.

Pre-operative audiometry was normal bilaterally with pure tone averages ≤15dBHL. Middle ear and brainstem responses were normal.

Caloric tests showed a right canal paresis. Observation of pursuit, saccades, and vestibulo-ocular responses confirmed a right peripheral labyrinthine disorder. Gait was unsteady, with a suggestion of a functional component. Bilateral first degree right and left spontaneous nystagmus was present. A CT scan was normal.

Post-operative efferent tests and audiometric studies were conducted 4 1/2 years following surgery, at which time vestibular symptoms were resolved.

Audiometry showed a mild loss in the right with a conductive component, plus a high frequency loss up to 55dBHL at 8kHz. The intact ear maintained normal thresholds. Tympanometry was slightly negative (-65 daPa) with low compliance (0.2ml) in the left, and normal in the right. Acoustic reflex thresholds were normal in both ears. (See Table: A.1.) Auditory brainstem responses were normal for absolute latency, inter-wave and inter-aural differences.

Seven years following surgery, the patient suffered episodic bouts of mild unsteadiness and imbalance, tinnitus and bi-temporal headaches. Her pure tone audiometry revealed in the left ear a sloping mild to moderate sensorineural hearing loss, with normal ABR. ENG revealed left lateral gaze fine rotatory nystagmus, with no evidence of central vestibular pathology, but rotational VOR were attenuated to left and right. Pursuit and saccadic eye movements were normal, there was no gaze evoked nystagmus and OKN was symmetrical. Bithermal caloric responses were normal in the left, and showed complete canal paresis on the right. MRI showed no intracerebral abnormality. Cawthorne-Cooksey exercises were prescribed. The symptoms resolved after 2 months.

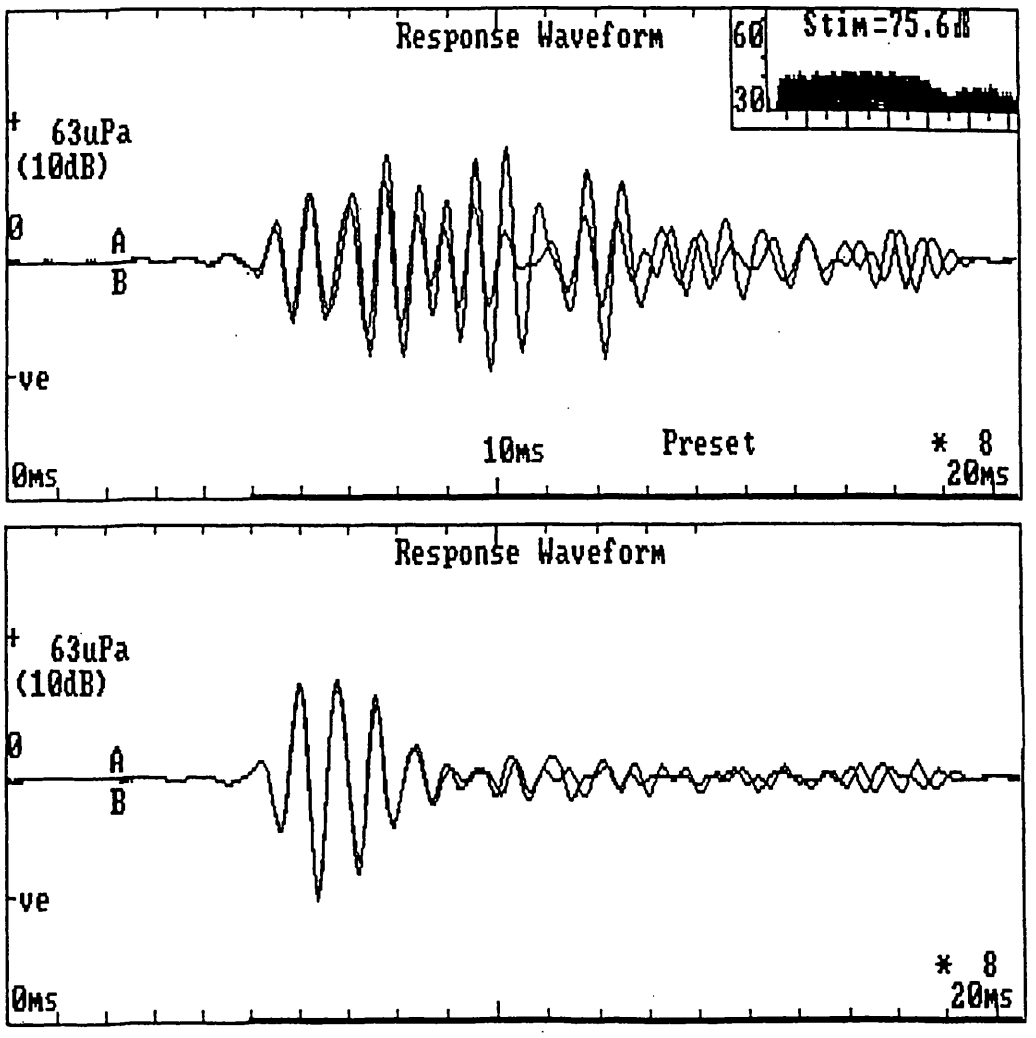
Case iv: Efferent Auditory Effects

Click evoked otoacoustic emissions were concentrated within the 1 - 2 kHz frequency range in the right ear and from 0.5 - 4.0 kHz in the left ear. Inhibition of emission amplitude was absent in the operated ear during contralateral noise at 40 dB SL (-4.7%), whilst present at normal magnitude (25.9%) in the intact ear. (See Figure V.10.)

Figure V.10
Case iv: Inhibition of CEOAE Post Vestibular Nerve Section in the Intact and Operated Ears

Filtered CEOAE waveforms (1000 – 2000 Hz) are superimposed to show the waveform recorded in quiet (A) and the waveform during 35dBSL contralateral white noise (B), plotted as amplitude (uPa) versus time (msec).

The upper trace shows post-surgical CEOAE from the intact ear, with preservation of peak to peak inhibition and phase lead of CEOAE collected in noise relative to CEOAE recorded in quiet.
The lower trace shows post-surgical results from the operated ear, with minimal inhibition of peak to peak amplitude of CEOAE recorded in noise relative to CEOAE recorded in quiet.



Case ii: History and Audiology

This 24 year old female presented with positional vertigo and left ear pain. Tinnitus and hearing dysfunction were not reported.

Pre-operative investigations revealed normal audiometric thresholds in the right, with a slight sensorineural loss at 6000 – 8000 Hz in the left. Tympanometry revealed negative pressure bilaterally. Ipsilateral ART were normal, and contralateral thresholds were elevated bilaterally relative to ipsilateral thresholds. Reflex decay was normal.

ABR were repeated on three occasions. Responses had well formed morphology. On one occasion, there was a slight elevation in I-V left ipsilateral waveform, and one occasion there was a slight elevation in III-V right contralateral waveform. However, these observations were not repeated in other recordings.

Gait, stance and extra-ocular movements including saccades, pursuit and VOR were normal. No nystagmus was observed on Hallpike manoeuvre. Calorics revealed a marked left canal paresis.

CT and a gadolinium enhanced MRI were normal, and air-meatography showed no evidence of a vascular loop.

The left vestibular nerve was sectioned, and vestibular symptoms resolved over the course of the following 18 months. Post-operative investigations were conducted 27 months following surgery, during which time vestibular symptoms were resolved. Audiometry revealed in the left, a mild gently sloping hearing loss from 25 – 40dBHL. There was a 10-15dB air bone gap, with bilateral negative pressure on tympanometry (-95 to -170 daPa). ART were elevated as would be expected given a conductive loss.

Case ii: Efferent Auditory Effects Following Vestibular Nerve Section

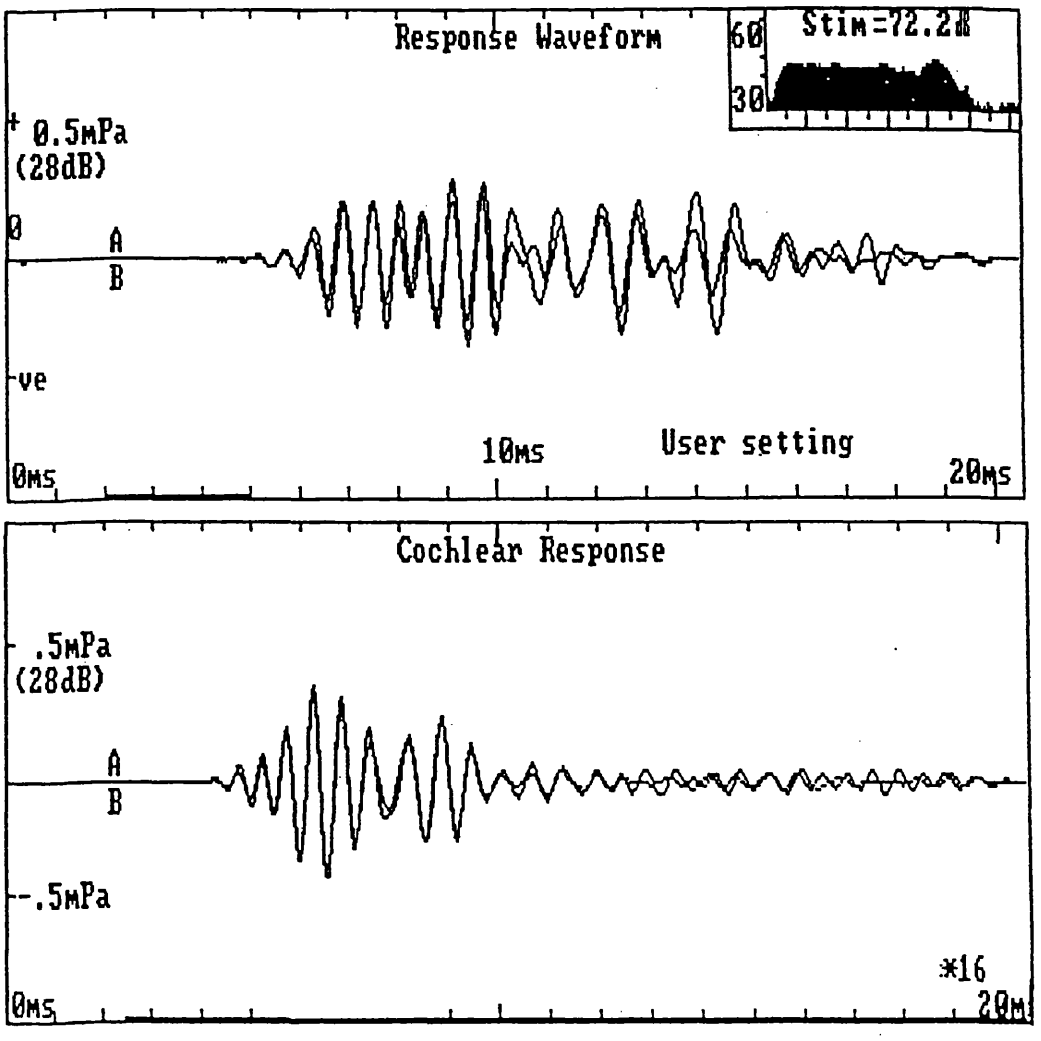
Efferent tests were conducted 27 months following surgery at which time vestibular symptoms had resolved. Middle ear pressure was elevated, and whilst OAE amplitude was low, emissions were recordable.

Bilateral otoacoustic emissions were present with a frequency spectrum from 0.5 - 5.0 kHz. (Left CEOAE = 4.4 dB SPL, 59%, A-B 1.7; Right CEOAE = 2.5 dB SPL, 69%, A-B -1.8.) This is consistent with reports which show the presence of CEOAE with hearing levels less than 35 dB HL, and negative pressure below 200 daPa (Robinson and Houghton 1991). Suppression of otoacoustic emissions was only 5.6% in the left operated side during contralateral stimulation (45 dB SL). In contrast, CEOAE amplitude from the intact side decreased by 31.6% from amplitudes recorded in quiet. (See Figure V.11.)

Figure V.11
Case ii: Inhibition of CEOAE Post Vestibular Nerve Section in the Intact and Operated Ears

Filtered CEOAE waveforms (1000 – 2000 Hz) are superimposed to show the waveform recorded in quiet (A) and the waveform during 35dBSL contralateral white noise (B), plotted as amplitude (uPa) versus time (msec).

The upper trace shows post-surgical CEOAE from the intact ear, with preservation of peak to peak inhibition and phase lead of CEOAE collected in noise relative to CEOAE recorded in quiet.
The lower trace shows post-surgical results from the operated ear, with minimal inhibition of peak to peak amplitude recorded in noise relative to CEOAE recorded in quiet.



Case iii: History and Audiology

This female presented with a two year history of vertigo, tinnitus and fluctuant hearing loss.

Pure tone audiometry showed normal hearing in the left ear, and a 30-40dBHL sensorineural loss in the right. ABR were normal in morphology, absolute latency, inter-wave and inter-aural differences. Electrocochleography was consistent with Meniere's disorder.

Caloric tests revealed a right canal paresis, with reduced function in the left. Pursuit and saccades were normal. Stance and gait were also normal. There was a slight unsteadiness on Romberg, but heel /toe gait was fine. A CT scan revealed no abnormalities.

Post-operative tests 7 months following right vestibular nerve section, revealed pure tone thresholds were normal in the left (5-15dBHL) un-operated ear, and displayed a domed loss in the operated right ear with the most sensitive hearing at 2kHz (35dBHL). Auditory brainstem responses were normal.

Electronystamography revealed second degree left spontaneous nystagmus in the absence of optic fixation. There was a left directional preponderance on VOR testing, while central VOR suppression was normal. There was no directional preponderance of OKN, and smooth pursuit was normal. Caloric tests with 20oC revealed a total right canal paresis, and a canal paresis in the left ear.

Vertiginous attacks resolved. The patient noted oscillopsia when walking, though managed well if she could utilize visual and proprioceptive stimuli.

Case iii: Efferent Auditory Effects

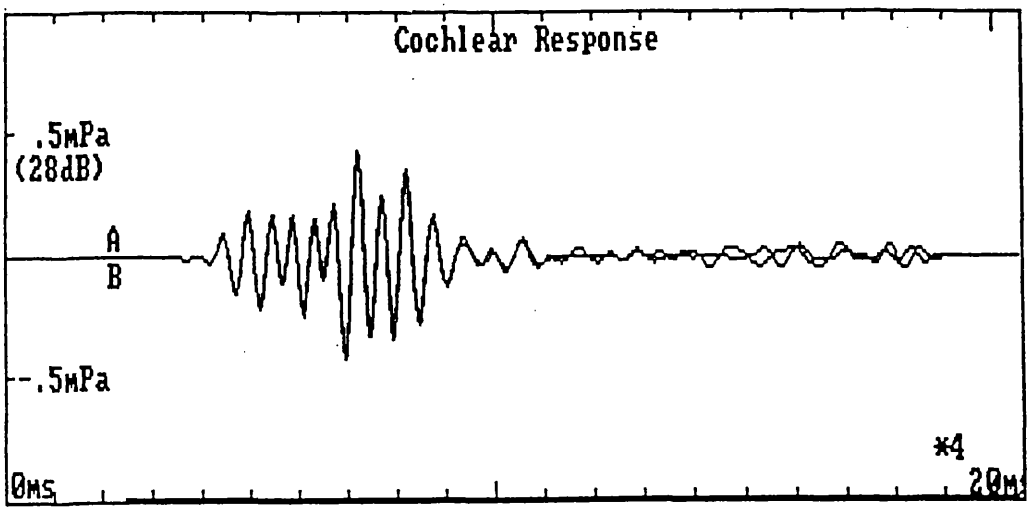
Post-surgical evaluations were conducted 7 months following surgery.

Otoacoustic emissions were present bilaterally [right=8.0dBSPL, 80%, A-B1.4; left=17.6dBSPL, 96%, A-B 3.4]. Whilst the total response pressure was reduced in the ear with hearing loss, emissions were dominant at 2kHz which corresponds to pure tone thresholds at 35dBHL at that frequency. The amplitude of CEOAE responses in operated ear varied by only 3.4% during contralateral stimulation at 35dBSL. (See Figure V.12, and Table V.11.)

Figure V.12
Case iii: Inhibition of CEOAE Post Vestibular Nerve Section in the Operated Ear

Filtered CEOAE waveforms (1000 – 2000 Hz) are superimposed to show the waveform recorded in quiet (A) and the waveform during 35dBSL contralateral white noise (B), plotted as amplitude (uPa) versus time (msec).

The trace shows post-surgical results from the operated ear, with minimal inhibition of peak to peak amplitude recorded in noise relative to CEOAE recorded in quiet.



Summary : Vestibular Nerve Section Results

Unilateral Absence of Efferent Auditory Effects in Operated Ears Following Vestibular Nerve Section

The findings from the post-operative vestibular nerve section group showed a significant absence of suppression in the operated ear as did the pre/post cases reported above ($p<0.01$). The mean inhibition in all sectioned ears was negligible compared to normal responses, and to the intact post-operative ears.

The student's t-test (two tailed) was used to analyze all vestibular nerve section results. (See Table V.11 below.) KS testing verified normal sample distributions. A complete statistical analysis is also reported at the end of this chapter, comparing all subject groups, levels, sides and gender.

Pre-surgical results:

Before surgery, inhibition with 40-45dBSL stimulation was not significantly different between ears ($p=0.07$).

Post-surgical results:

The intact side showed no significant change in inhibition following surgery during 40-45dBSL ($p=0.27$). Intact ears were not significantly different to normal ears ($p=0.5$) during 45dBSL.

In contrast, significant differences existed between pre and post-operative inhibition in the operated ears during 40-45dBSL contralateral noise ($p<0.001$). A significant difference also existed between post-operative ears and normal responses during 35 and 45dBSL noise ($p<0.001$).

Post-nerve section results during noise, were not significantly different to normal ears in quiet (35dBSL: $p=0.12$; 40-45dBSL: $p=0.09$; 45dBSL: $p=0.05$). Indeed, in 6 out of 7 recordings during 35dBSL, OAE amplitude was greater in noise than in quiet. However, these fluctuations were not significantly different to normal mean responses to 0 dB SL contralateral stimulation ($p=0.12$). No significant difference existed between post-operative inhibition during 40-45dBSL and intact post-operative ear responses at 0dBSL ($p=0.93$). (Table VI.13.)

Conclusion: Efferent Auditory Effects in Vestibular Nerve Section Cases

The pre and post-operative results from vestibular nerve section patients evidence documenting the impact of removing olivocochlear innervation on cochlear function.

The findings demonstrate that vestibular nerve section is associated with significant loss of inhibition of otoacoustic emission amplitude in the operated ears ($p<0.01$). Pre-operative data provided an important baseline to show that normal levels of inhibition had been present before surgery. Whilst pre-operative baselines were not available in all cases, post-operative intra-subject comparisons also showed that unilateral inhibitory effects were maintained only in the intact ears. This was in contrast to normal subjects who demonstrated bilateral inhibitory effects. This unilateral absence of inhibition following vestibular nerve section appears to result from the loss of olivocochlear fibre innervation. (See Figure V.13.)

Table V.1: Inhibition of CEOAE Amplitude in Vestibular Nerve Section Cases

(preint) pre-operative % inhibition from non-operative side.
(preop) pre-operative % inhibition from side to receive surgery.
(postint) post-operative % inhbition from non-operated side.
(postop) post-operative % inhibition from operated side.

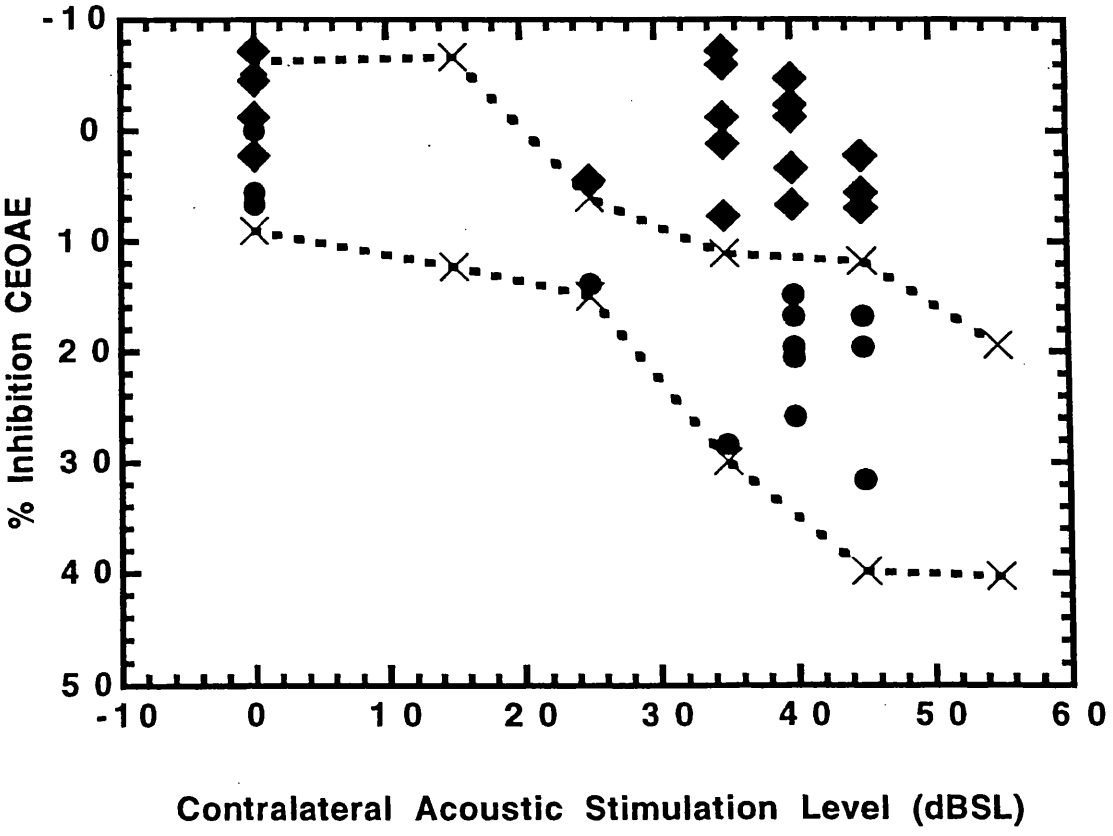
	% Inhibition in Vestibular Nerve Section Cases									
	preint	preop	postint	postop	postint	postop	postint	postop	postint	postop
dBSL	40-45	40-45	0	0	35	35	40-45	40-45	45	45
	14.9	13.9	0.0	-4.5	25.9	7.7	14.9	-1.2	19.6	7.0
	16.8	12.9	5.6	-7.2	19.6	-1.2	21.5	6.7	31.6	5.6
	16.8		6.7	-1.2	16.8	-4.7	19.6	3.4	16.8	3.4
	19.6			2.3		-1.2	31.6	7.0		2.3
						-2.3	16.8	5.6		
						-7.2		3.4		
						-5.9		2.3		
Mean	17.0	13.4	4.1	-2.6	20.8	-2.1	20.9	3.9	22.7	4.6
SD	1.9	0.7	3.6	4.1	4.7	4.9	6.5	2.9	7.9	2.1
n	4	2	3	4	3	7	5	7	3	4

Figure V.13

Unilateral Loss of Inhibition in Vestibular Nerve Sectioned Ears Compared to Intact Ears and to Normal Responses

Operated ears demonstrated minimal inhibition that was less than 2 SD from mean responses in normals, for all intensities of contralateral noise assessed (35 – 45dBSL). The intact ears maintained inhibition within 2 SD of normal means at all intensities.

The magnitude of inhibition (% change in amplitude of CEOAE in noise relative to CEOAE in quiet) is illustrated for operated ears (diamonds) and intact ears (circles). (X) +/- 2 SD from mean inhibition in normal subjects as a function of contralateral white noise intensity re. dB sensation level (dBSL).



CHAPTER VI

CONTROL RESULTS

SURGICAL PATIENTS

Efferent Auditory Effects

with Intact Olivocochlear Efferents

Following Neuro-otological Surgery

CONTROL RESULTS

Efferent Auditory Effects in Surgical Control Patients:

A group of patients was studied following neuro-otological surgery without section of the olivocochlear system. These patients provided control information, relating to the specificity of efferent auditory test procedures to olivocochlear dysfunction. The findings also indicated the influence of the middle ear reflex system, general anesthesia, intra-operative noise and drilling, opening of the cerebello-pontine angle, neural movement and compression, and physical alteration of the structure of the mastoid.

Efferent Auditory Effects Following Retro-Labyrinthine Surgery for Vascular Decompression of the Vestibulo-Cochlear Nerves

The impact of retro-labyrinthine surgery on otoacoustic emission inhibition was investigated in patients undergoing surgical micro-vascular de-compression of the VIII and VII nerves. The surgical approach was similar to that utilized in vestibular nerve section, except that vascular loops found on the vestibulo-cochlear nerves were moved, and the nerves were left intact. (See Methods: Inclusion Criteria.) Precise definition of vascular compression can be difficult, especially via imaging alone (Lempert 1998). In the cases reported here, efferent responses were assessed to indicate the effect of retrolabyrinthine surgery, and not to determine if compression was the sole aetiology related to the patients' disorders.

Case a: Vascular Decompression Case History and Audiology

This 39 year old female presented with intractable very severe right sided tinnitus, but no vestibular or auditory complaints. The patient reported great difficulty coping with the tinnitus, and had developed secondary depression and attempted suicide twice.

Evaluations 2 ½ months before surgery revealed normal pure tone thresholds bilaterally. Tympanometry, acoustic reflex thresholds and reflex decay were normal. Auditory brainstem responses displayed normal morphology, absolute latencies and inter-wave and inter-aural differences.

Gait, pursuit, saccades, OKN and vestibulo-ocular reflexes were normal. Spontaneous nystagmus was not observed. A right canal paresis was noted on caloric testing. A CT scan was normal.

Efferent tests were carried out 2 ½ months before, and 1 month after surgery. Following surgery, the tinnitus initially resolved completely, but then recurred coincident with a post-surgical viral infection. Efferent testing was conducted following recovery.

Post-surgically, audiometric thresholds in the intact ear decreased by 5-10 dB across all frequencies except 8kHz which remained the same. The operative ear decreased 5-10dB from 0.5-2kHz with no change at the other frequencies. Acoustic reflex thresholds and auditory brainstem responses remained normal.

Eighteen months later, the patient reported a swimming, muzzy sensation in her head. MRI confirmed that a vascular loop was again in close association with the VIII nerve. Examination revealed difficulties in gait (could not undertake heel toe manoeuvre), and 3rd degree left spontaneous nystagmus. Pursuit and saccades were normal. Calorics revealed no response at 20oC in the left with fixation, and 1'5" without fixation. Revision surgery was conducted, and her tinnitus resolved, though psychotropic drugs for depression were likely to have interfered with vestibular compensation.

Case a: Efferent Auditory Effects

Efferent tests conducted 2 ½ months before, and 1 month following surgery, during which time symptoms had resolved.

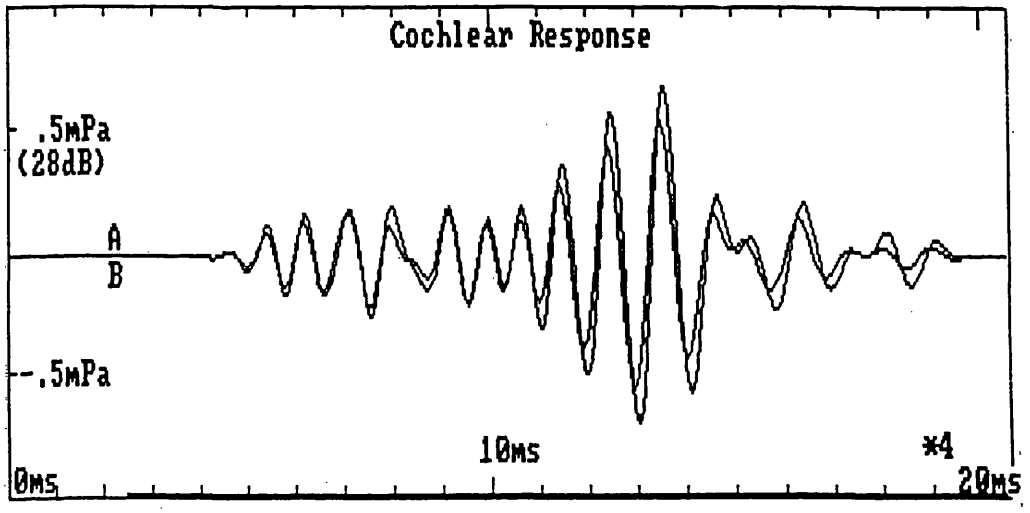
Pre-operative inhibition was normal bilaterally. Inhibition was consistent with normal levels (11.9 at 25dBSL and 22.4% at 45dB in the intact ear, and 18.7% with 40dBSL in the pre-operative ear).

Following surgery, contralateral inhibition was maintained in both the operated and intact ears. The magnitude of inhibition was consistent with normal responses. A phase lead was demonstrable in emissions recorded during noise relative to emissions recorded in quiet. The operated ear demonstrated 18.7% with 35dBSL, and 25% with 55 dBSL. The intact ear displayed 18.7% with 35dBSL, and 24.1% with 55dBSL (See Figure VI.1, Figure VI.2.)

Figure VI.1
Case a: Pre and Post-Surgical Inhibition of CEOAE Following Vascular Decompression Operated Ear

Filtered CEOAE waveforms (1000 – 2000 Hz) are superimposed to show the waveform recorded in quiet (A) and the waveform during 35dBSL contralateral white noise (B), plotted as amplitude (uPa) versus time (msec).

The upper trace shows pre-surgical CEOAE from the ear before surgery, with inhibition of peak to peak amplitude recorded in noise relative to CEOAE recorded in quiet.
The lower trace shows post-surgical results from the operated ear, with maintained peak to peak inhibition of CEOAE collected in noise relative to CEOAE recorded in quiet.



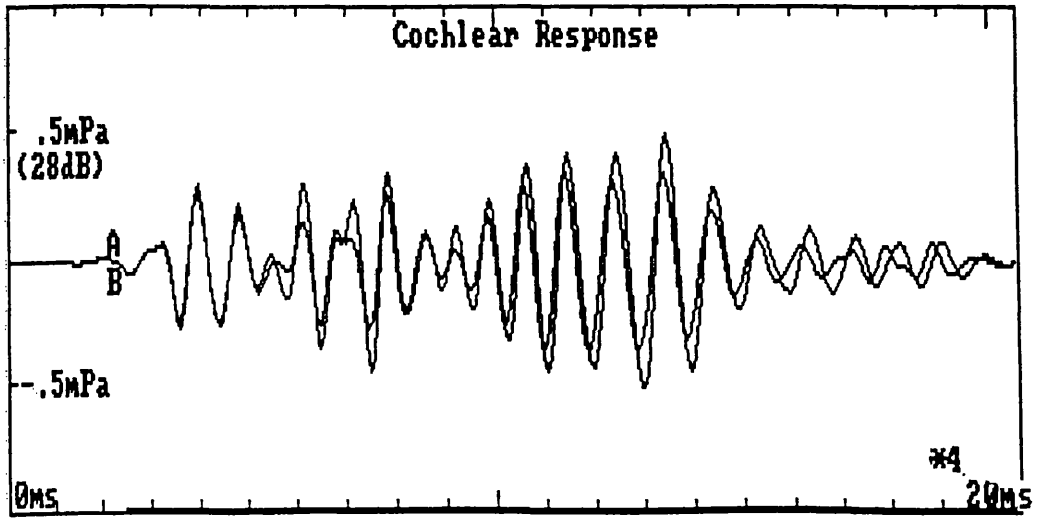
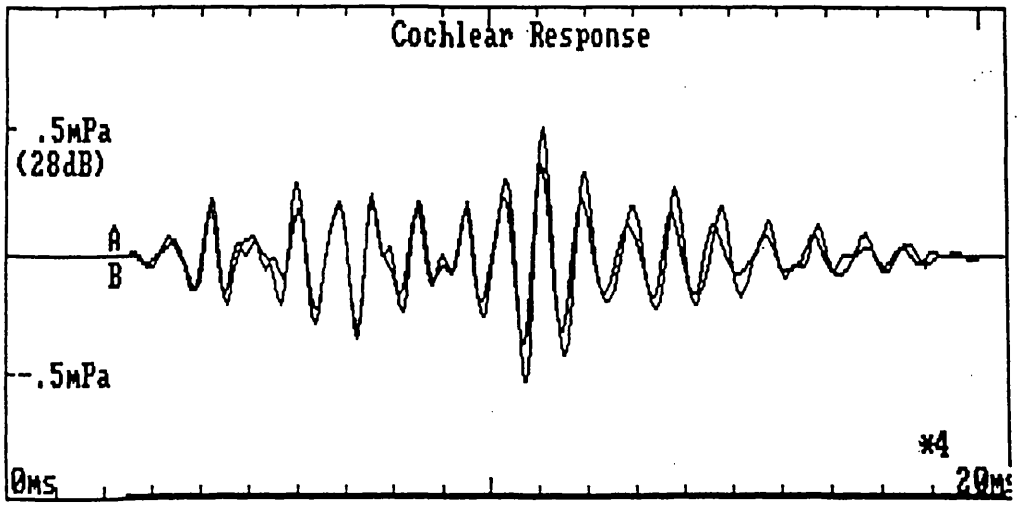
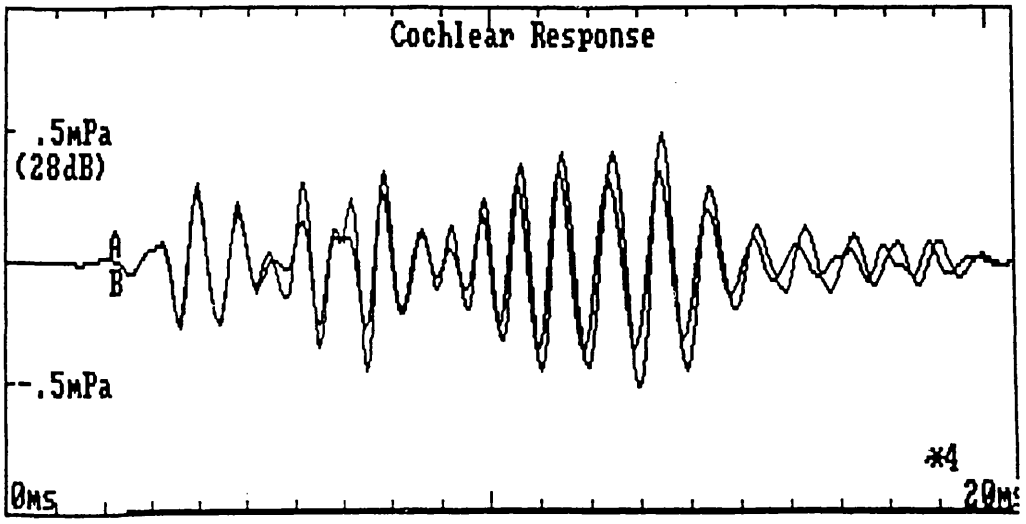


Figure VI.2
Case a: Inhibition of CEOAE Following Vascular Decompression
Intact and Operated Ears

Filtered CEOAE waveforms (1000 – 2000 Hz) are superimposed to show the waveform recorded in quiet (A) and the waveform during 35dBSL contralateral white noise (B), plotted as amplitude (uPa) versus time (msec).

The upper trace shows post-surgical CEOAE from the intact ear, with inhibition of peak to peak amplitude recorded in noise relative to CEOAE recorded in quiet.
The lower trace shows post-surgical results from the operated ear, with preserved peak to peak inhibition of CEOAE collected in noise relative to CEOAE recorded in quiet.





Case c: Vascular Decompression Case History and Audiology

This 41 year old male presented with a four year history of disorientation, imbalance and vertiginous sensations without auditory dysfunction. He also reported aural blockage and bilateral low level tinnitus (matched to 0dBHL at 125 Hz or lower). The patient had a history of migraines and panic attacks. Subjective hearing dysfunction was not reported.

Pre-operative audiometry revealed normal thresholds in the right, and a slight sensorineural loss in the left from 4000 – 8000 Hz. Tympanometry, acoustic reflexes, and reflex decay were normal. Auditory brainstem responses had normal morphology, absolute latencies, inter-wave and inter-aural intervals.

Gait was normal, and spontaneous nystagmus was not present. Pursuit, saccades, OKN and VOR were normal. Calorics revealed a slight left directional preponderance. CT scans revealed no abnormalities. Air-meatography confirmed a vascular loop on the left vestibulo-cochlear nerve.

Decompression of the left vestibular nerve was conducted. There was no loss in audiometric threshold function following surgery. Tympanometry, acoustic reflex thresholds and auditory brainstem responses were normal before and after surgery. Efferent tests were conducted three months before, and three months after surgery, during which time symptoms had resolved.

Vestibular symptoms resolved for 12 months, before recurring with a slight degree of muzziness and aural blockage, with left Eustachian tube dysfunction. Seven months following efferent testing, he was re-assessed and found to have a mild high frequency hearing loss in the left, no neuro-otological symptoms, but recurrent panic attacks. One year later, he developed a mild high frequency loss in the right ear, and had elevated acoustic reflexes on ipsilateral recordings, with slightly low middle ear pressure, and left sided tinnitus. Panic attacks recurred. Examination including a full battery of ENG tests revealed normal responses and normal calorics. A MRI was normal. There was a suggestion of basilar migraine to his symptoms. Revision surgery was conducted. Muzzy headed symptoms recurred two years thereafter, and thorough neuro-otological assessment showed no objective measure of dysfunction and the patient subsequently improved.

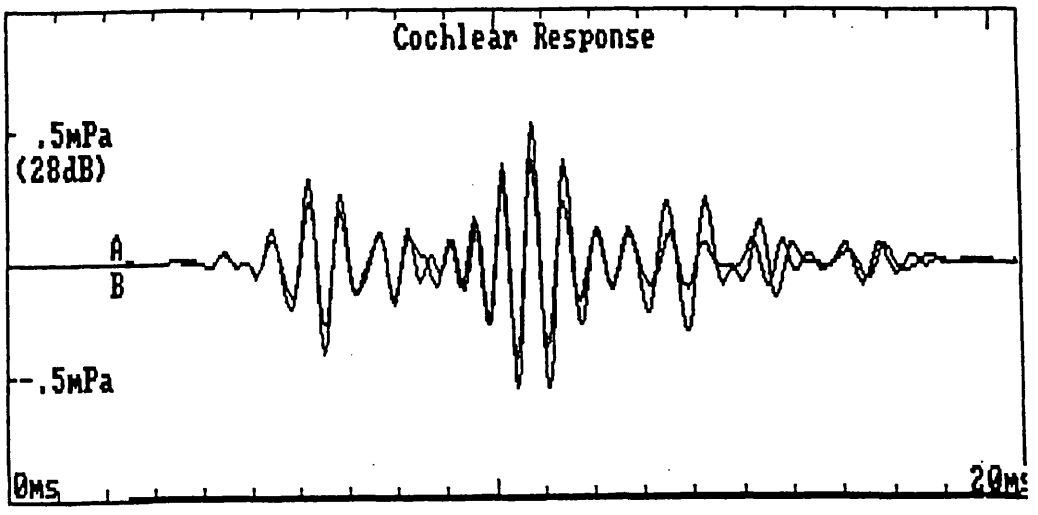
Case c: Efferent Auditory Effects

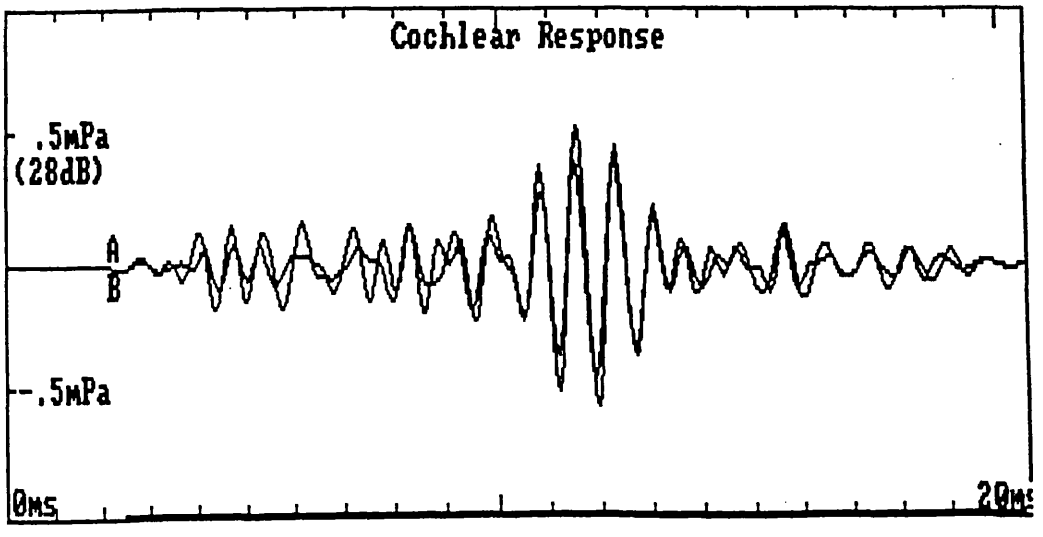
Efferent tests were conducted 3 months following surgery, during which time symptoms had resolved. Inhibition in operated side remained within +/-2SD of normal responses (23.3% during 35dBSL and 25.9% during 45dBSL). Unfortunately, clinical constraints necessitated the patient leave before the intact side could be measured. (See Figure VI.3.)

Figure VI.3
Case c: Inhibition of CEOAE Following Vascular Decompression
Intact and Operated Ears

Filtered CEOAE waveforms (1000 – 2000 Hz) are superimposed to show the waveform recorded in quiet (A) and the waveform during 35dBSL contralateral white noise (B), plotted as amplitude (μPa) versus time (msec).

The upper trace shows post-surgical CEOAE from the intact ear, with inhibition of peak to peak amplitude recorded in noise relative to CEOAE recorded in quiet.
The lower trace shows post-surgical results from the operated ear, with preserved peak to peak inhibition of CEOAE collected in noise relative to CEOAE recorded in quiet.





Case b: Vascular Decompression Case History and Audiology

This 28 year old man presented with a three year history of recurrent attacks of vertigo and right sided tinnitus. Fluctuant hearing loss was recordable with head lateral position.

Pre-operative pure tone thresholds were normal bilaterally, as were tympanometric, acoustic reflex and reflex decay results. Auditory brainstem responses were normal in morphology, absolute latency, inter-wave and inter-aural latencies.

Gait was normal. An ill-sustained first degree spontaneous nystagmus was observed in the dark. Pursuit was normal, though the task enhanced subjective dizziness. Saccades, OK and VOR were normal. Caloric tests revealed a right canal paresis. Magnetic resonance images excluded an acoustic neuroma and showed a blood vessel in close association with the VIIIth cranial nerve. A vascular loop, compressing the VIII nerve, was confirmed at surgery and decompression performed.

Vestibular symptoms were much improved for two years following surgery, with only occasional unsteadiness reported. Three years following efferent testing, the patient experienced slight recurrence of vertigo and increased right aural pressure and tinnitus. Calorics revealed significant right canal paresis, with normal function on the left side. Pure tone audiometry was unchanged. No active treatment was required.

Case b: Efferent Auditory Effects

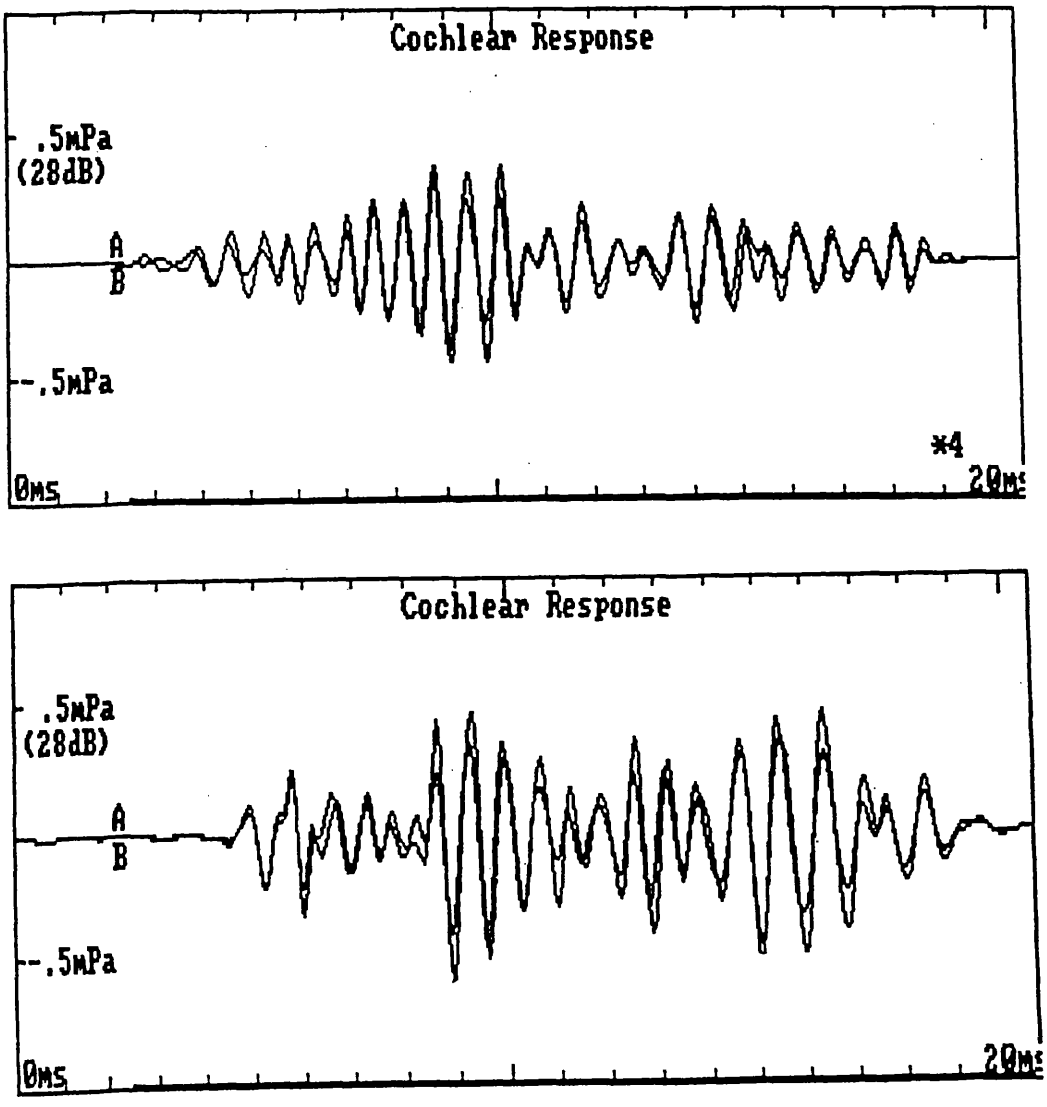
Efferent tests were carried out one year following surgery during complete resolution of symptoms.

Click evoked emissions were normal bilaterally following surgery for vascular decompression. Post-operatively, inhibition remained within normal levels for both the intact and operated ear, with the magnitude of inhibition increasing with contralateral stimuli levels. In the intact ear, with stimuli from 25 – 45dB, inhibition was from 10.9 – 19.7% respectively. The operated ear displayed inhibition 12.9% to 31.2% with contralateral stimuli from 25 to 45dBSL respectively. (See Figure VI.4.)

Figure VI.4
Case b: Inhibition of CEOAE Following Vascular Decompression
Intact and Operated Ears

Filtered CEOAE waveforms (1000 – 2000 Hz) are superimposed to show the waveform recorded in quiet (A) and the waveform during 35dBSL contralateral white noise (B), plotted as amplitude (uPa) versus time (msec).

The upper trace shows post-surgical results from the intact ear, with peak to peak inhibition of CEOAE collected in noise relative to CEOAE recorded in quiet.
The lower trace shows post-surgical CEOAE from the operated ear, with preserved inhibition of peak to peak amplitude recorded in noise relative to CEOAE recorded in quiet.



Summary:
Efferent Auditory Effects Following Retrolabyrinthine Surgery for Vascular Decompression

Bilateral inhibition of otoacoustic emissions was observed before and following vascular decompression surgery. During contralateral stimulation, CEOAE amplitude decreased with increasing stimulus intensity for both the operated and intact sides.

Following surgery, the mean inhibition for all intact and operated ears during 35dBSL was 18.7% (SD=3.3, n=5), consistent with normal vaules. With 45dBSL mean inhibition was 28.6% (SD =3.7, n=2). There was no significant difference (two tail t-test, $p>0.01$) between vascular decompression means and normal means at 35 and 45dBSL. Statistical comparisons with the entire study sample are discussed in the following chapters. (See Figure VI.5.)

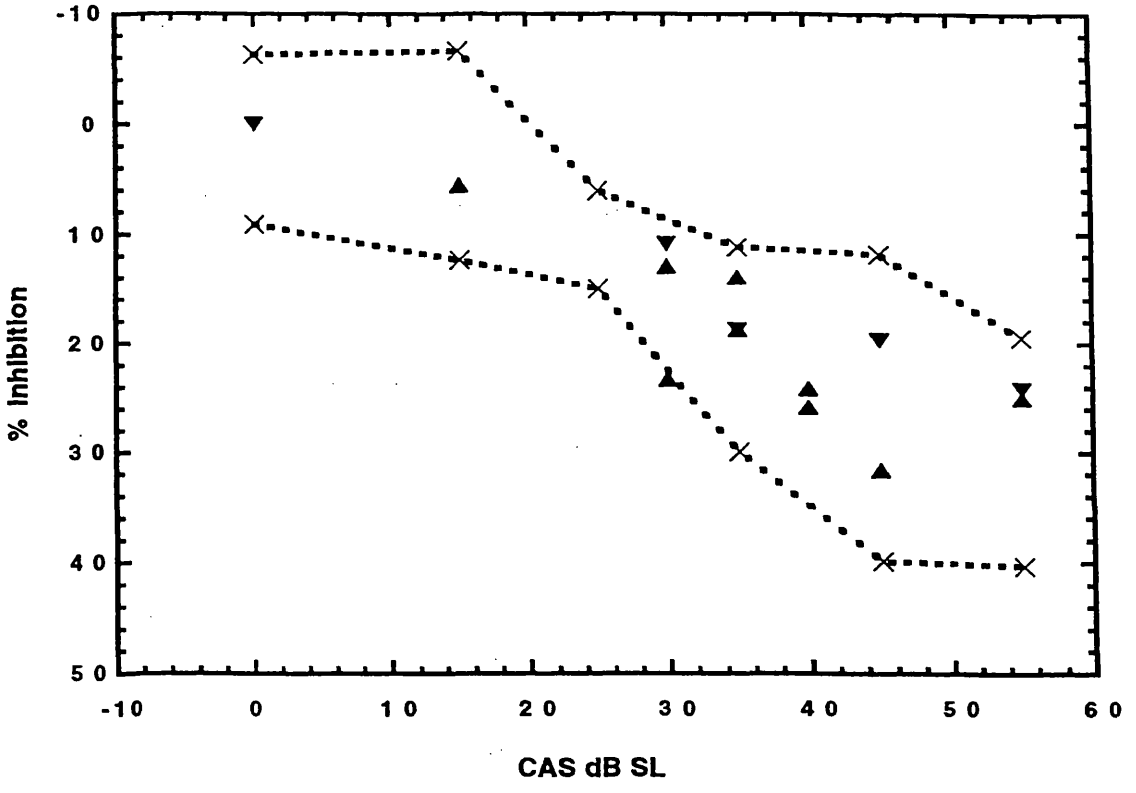
Observation of normal bilateral inhibition before and after surgery suggests that the retrolabyrinthine surgical procedure itself need not interfere with the inhibitory effects on otoacoustic emissions. As the olivocochlear fibres remained intact, the findings also suggest that the efferent auditory tests were specific to olivocochlear function. The findings support the conclusion that the lack of efferent auditory effects in vestibular nerve section cases does not result primarily from the surgical procedure itself.

It can be difficult to assess vascular compression via MRI or CT alone (Lempert 1998). Thus, it remains possible that compression was not the sole disorder associated with the patients' symptoms. Regardless of aetiology, these findings suggest that retrolabyrinthine surgery itself does not affect the inhbition of CEOAE in these cases.

Figure VI.5
Inhibition in Operated and Intact Ears Following Vascular Decompression

Both operated and intact ears demonstrated inhibition within 2 SD of normal means at all intensities.

The magnitude of inhibition (% change in amplitude of CEOAE in noise relative to CEOAE in quiet) is illustrated for left ears (upward triangles) and right ears (downward triangles). Dashed lines illustrate +/- 2 SD from mean inhibition in normal subjects as a function of contralateral white noise intensity re. dB sensation level (dBSL).



Efferent Auditory Effects Following Section of the Middle Ear Tendons for Myoclonus

The middle ear muscles provide an efferent reflex system to alter the admittance and resistance of the middle ear ossicles, thereby controlling the stimulus level to the cochlea. In order to differentiate between the role of the olivocochlear reflex system and the middle ear reflex system, patients were examined who underwent unilateral section of the middle ear stapedial and tensor-tympani tendons for myoclonus. Whereas palatal myoclonus is commonly associated with bilateral symptoms, the patients in this study, presented with unilateral audible myoclonus, suggesting the more unusual condition of myoclonus of the middle ear muscles. Surgical section via tympanotomy was very successful in relieving these symptoms (Badia et al. 1994).

Case x: History and Audiometry

This 32 year old woman presented with a 10 year history of unilateral middle ear myoclonus which resulted in audible clicking in the right ear with earache and aural blockage. Subjective hearing dysfunction was not reported. The patient was unaware of palatal movement. Vestibular and facial function was normal.

Palatal movement was not observed during audible clicking. Pre-operative audiometry revealed normal pure tone thresholds ranging from -5-10dBHL across all frequencies tested. Tympanometry and acoustic reflex thresholds were normal bilaterally. Middle ear impedance, acoustic reflexes and acoustic decay were normal, with no observable compliance changes in association with symptoms.

Surgical section of the stapedius and tensor tympani tendons was successful in relieving the clicking sensations, ear ache and aural blockage. Post-operative audiometry showed that the pure tone thresholds were little changed for both ears (+/-5dB). Tympanometry was normal and similar to pre-operative values. Acoustic reflex thresholds showed complete loss of reflexes recorded from the operated side in response to ipsilateral or contralateral stimulation, with no observable deflection of the baseline at any frequency or level (up to 120dBHL). Reflex thresholds from the un-operated ear in response to ipsilateral and contralateral stimuli were normal, and within 5 dB of pre-operative measures.

Efferent tests were conducted 9 months following surgery, while clicking symptoms were resolved.

Case x: Efferent Auditory Effects Following Middle Ear Tendon Section

Contralateral inhibition of otoacoustic emissions was maintained post- in both ears following unilateral section of the tensor-tympani and stapedial tendons. Indeed, the magnitude of inhibition with noise from 15-25dBSL was greater than observed in normals, and more consistent with inhibition during stimuli 10dB louder. The operated ear showed inhibition from 15.9% at 15dBSL to 28.4% with 55dBHL. The intact ear revealed 20.6% inhibition at 35dBSL, increasing to 25.9% at 55dBSL. (See Figure VI.6, Figure VI.7.)

Effective efferent inhibition in the operated ear, revealed substantial changes in amplitude with contralateral noise at 35 dB SL (over a range of click intensities from 65 - 85 +/- 2 dB). The magnitude of inhibition did not decrease at higher intensities as was often observed in normals (16.8 - 28.4% in the operated ear at $\geq$35dBSL, across the range of click intensities noted above.)

Figure VI. 6
Case x: Inhibition of CEOAE Post Section of Middle Ear Tendons in the Intact and Operated Ears

Filtered CEOAE waveforms (1000 – 2000 Hz) are superimposed to show the waveform recorded in quiet (A) and the waveform during 35dBSL contralateral white noise (B), plotted as amplitude (uPa) versus time (msec).

The upper trace shows post-surgical CEOAE from the intact ear, with peak to peak inhibition and phase lead of CEOAE collected in noise relative to CEOAE recorded in quiet.
The lower trace shows post-surgical results from the operated ear, with preservation of inhibition of peak to peak amplitude and phase lead of CEOAE recorded in noise relative to CEOAE recorded in quiet.

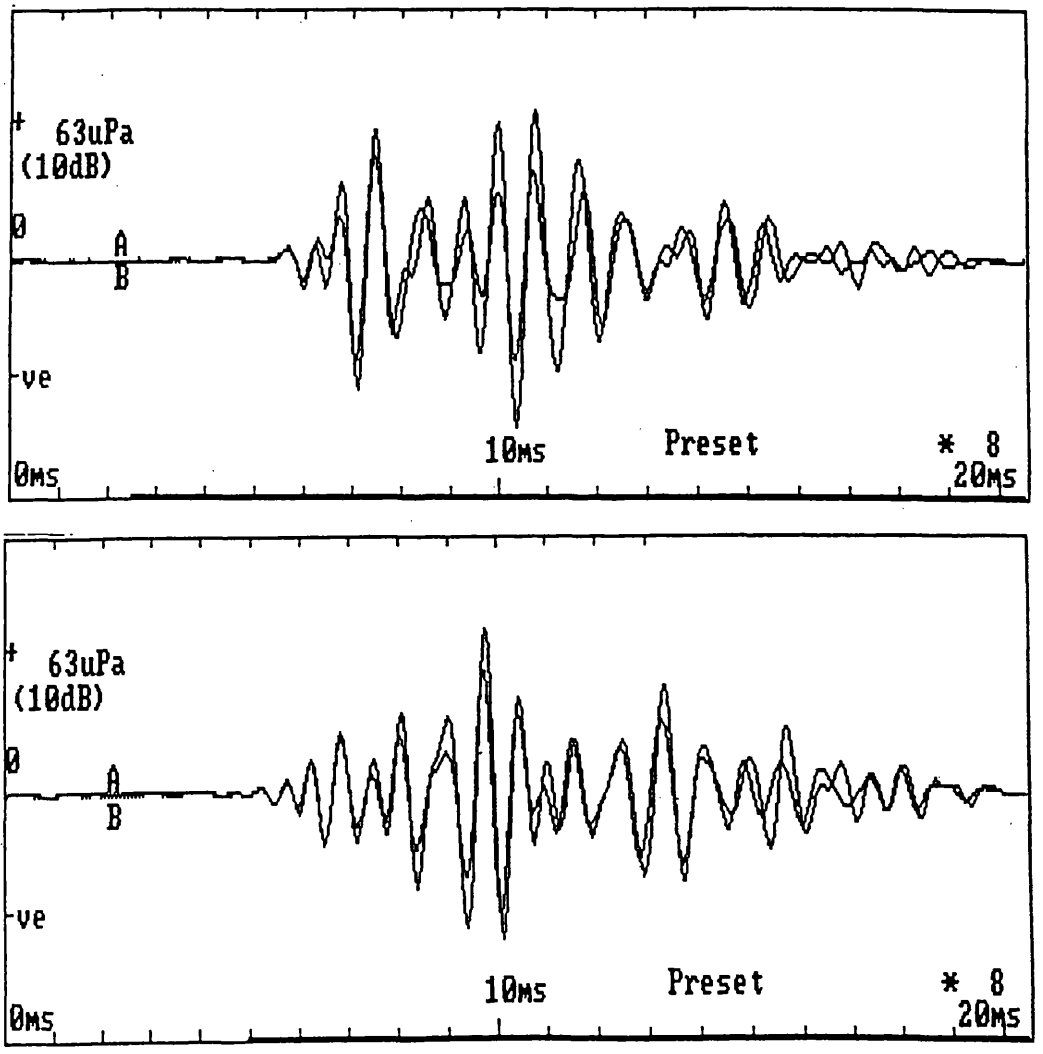
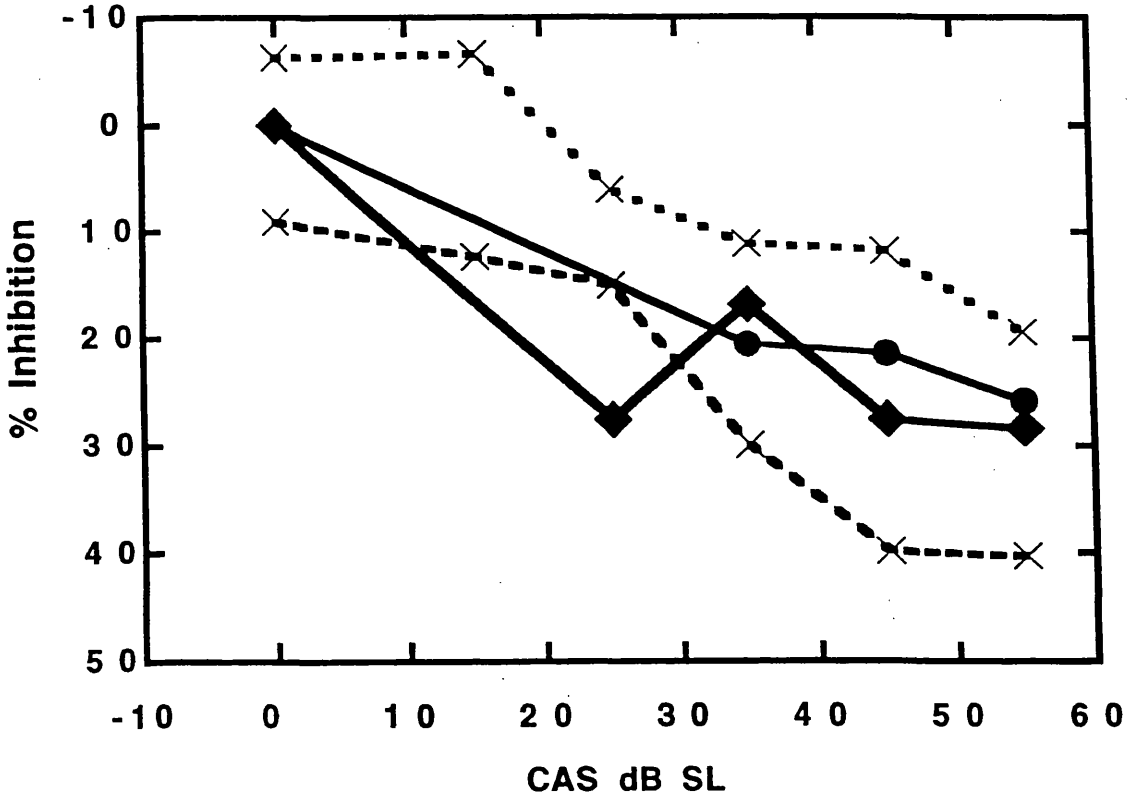


Figure VL 7
Case x: Bilateral Inhibition of CEOAE Following Middle Ear Muscle Section

Both intact and operated ears demonstrated inhibition greater than normal mean responses minus 2 SD. Inhibition from the operated ear showed greater than 2 SD plus normal mean inhibition with stimuli at 25dBSL. (X) normal inhibition +/- 2 SD.

The magnitude of inhibition of CEOAE amplitude (% reduction of response in noise compared to response in quiet) for the intact side (circles) are compared to the operated side (diamonds), as a function of contralateral acoustic stimulation levels (CAS) relative to dB sensation level (dBSL).



Case y: Middle Ear Section History and Audiology

A 35 year old male presented with a history of clicking sensations in his left ear, consistent with middle ear myoclonus. Pre-operative hearing thresholds revealed normal levels in the left ear, and a mild mixed loss in the right ear with air conduction thresholds at 35-40 dB HL with a 10-15dB air-bone gap between 500-2000Hz. Tympanometry was normal, and acoustic reflex measures did not reveal alterations coincident with clicking. Internal auditory meati were normal on X-ray scans. A high dehiscent jugular bulb was observed on the right side. There was no report of vestibular dysfunction. Gait, saccades and pursuit were normal.

Tympanotomy and surgical division of the stapedial tendon and tensor tympani of the left ear were performed, and the clicking sensations resolved.

Pure tone audiometry in the operated ear showed a mild sloping hearing loss (up to 35dBHL at 8000Hz), with an air-bone gap at 1000 Hz, but no gap at 2000Hz. The left ear retained normal pure tone thresholds within 10dB of pre-operative levels. Right ear thresholds ranged from 10-25 dB with improvement of the air-bone gap. Hearing in the right was essentially flat at 20-25dBHL rising to10dB at 6000 Hz.

Middle ear pressure was normal. Tympanic compliance was normal in the right ear (1.3 ml), but hyper-mobile in the left ear (1.8ml). Acoustic reflex thresholds were absent bilaterally, consistent with the conductive elements, and taking into consideration the unstable baselines resultant from the hyper-mobile tympanum. The patient reported greater discomfort from loud stimuli (above 100dB) in the left (operated) ear equivalent to an increase sensitivity of 15dB compared to the right ear. This likely reflected the loss of acoustic reflex protection from loud sounds.

Case y: Efferent Auditory Effects in the Absence of Middle Ear Reflexes

Efferent auditory effects were measured 2 ½ years following surgery. Clicking sensations were resolved. Inhibition was clearly observed in the waveform from the operated ear following surgery, though inhibition values were not very robust. (Operated/left: 35dBSL=9.8%; 45dBSL=10.9%.)

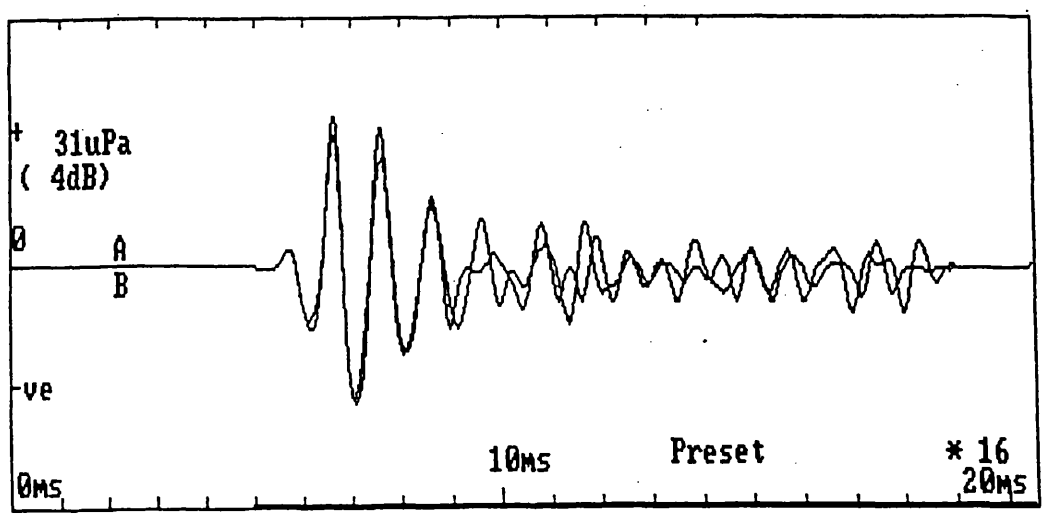
Emission amplitude in the intact ear was low, probably due to the slight conductive loss in that ear at frequencies below 4 kHz. Emission amplitude during contralateral noise fell below the recording noise floor, and thus precise quantification of the magnitude of inhibition could not be measured, but a decrease in amplitude was noted. (See Figure VI.8.)

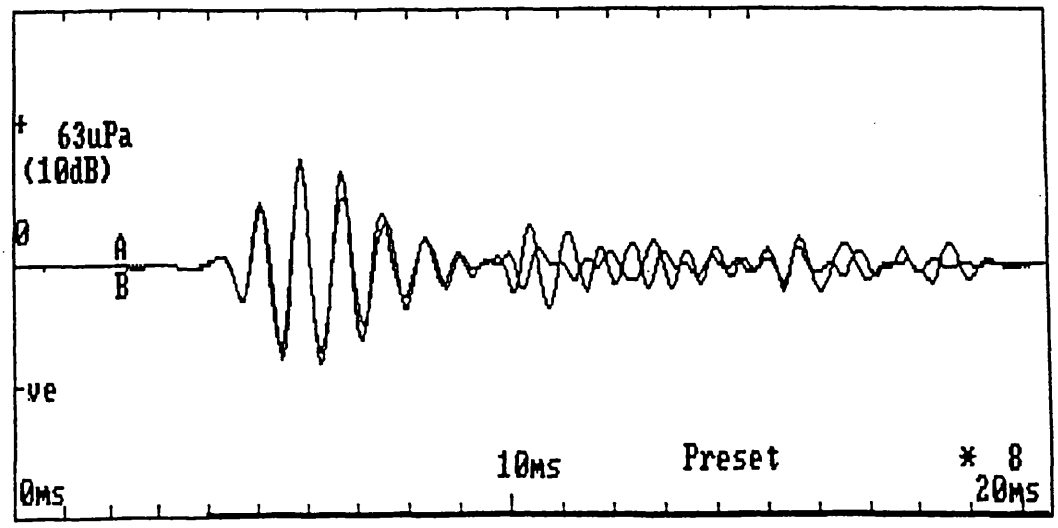
Figure VI.8

Case y: Inhibition of CEOAE Post Section of Middle Ear Tendons Intact and Operated Ears

Filtered CEOAE waveforms (1000 – 2000 Hz) are superimposed to show the waveform recorded in quiet (A) and the waveform during 35dBSL contralateral white noise (B), plotted as amplitude (uPa) versus time (msec).

The upper trace shows post-surgical CEOAE from the intact ear, with preservation of peak to peak inhibition and phase lead of CEOAE collected in noise relative to CEOAE recorded in quiet.
The lower trace shows post-surgical results from the operated ear, with inhibition of peak to peak amplitude and phase lead of CEOAE recorded in noise relative to CEOAE recorded in quiet.





Summary: Middle Ear Muscle Section

Bilateral inhibition of otoacoustic emissions was maintained despite unilateral loss of the middle ear muscle reflexes, following surgical section of the middle-ear muscle tendons. Acoustic reflexes from the operated ear were completely unresponsive to all stimuli. In these cases, it can be confidently stated that the contralateral stimuli did not elicit middle-ear reflexes. Thus, efferent auditory effects were not solely reliant on middle ear reflexes.

CHAPTER VII

NEURO-OTOLOGICAL PATHOLOGIES

Efferent Auditory Effects

in the Presence of Neuro-otological Pathologies

PATHOLOGICAL CASES

Cases with lesions along the olivocochlear pathways were tested to determine if interruption of the olivocochlear system would result in loss of CEOAE inhibition. The study included lesions affecting the olivary nuclei and brainstem at the level of olivocochlear decussations, the cerebello-pontine angle, vestibular nerve root, and inferior vestibular nerve. Presumed disruption of outer hair cells, via ototoxic and noise exposures were also studied.

The precision with which one can define a site of lesion is limited. CT or MRI images might not reveal all cerebral derangement or very small lesions. Space occupying lesions are likely to affect both the afferent and efferent auditory system traveling in close proximity. Further, compressive, oedemic or ischaemic effects may also affect fibres distant to the site of lesion. Whilst the study of lesions may not provide an uncomplicated experimental paradigm, it provides information about the specificity of the test.

Central Pathologies:

Case g: Lesions of the Olivary Nuclei

A 43 year old male presented with headaches, dizziness, imbalance, slight ataxia, and visual disturbance over the preceding two years. The patient had viral meningitis 16 years previously. Neuro-otological assessment, comprising a complete vestibulo-ocular evaluation (see Methods), confirmed central abnormalities including fast horizontal oscillopsia and a directional preponderance on caloric testing. The patient's MRI images were studied and reported by two Consultant neuro-radiologists to have areas of enhancement which indicated bilateral changes in the olivary nuclei and slight cerebellar atrophy with fairly focal symmetrical degeneration of the cerebello-olivary connections. (See two slices of magnetic resonance image in Figures VII.1a, VII.1b.) The cause was undetermined, but typical of olivo-ponto-cerebellar degeneration. There was no evidence of inflammatory disease such as multiple sclerosis, ischaemia, congenital malformation or tumor. Despite the observed foci of lesions to the olives and cerebellum, it is possible that additional CNS derangement's were present in more cortical centers, resulting from the olivo-ponto-cerebellar disorder, or compressive or ischaemic effects.

Neuro-otological assessment revealed grossly unsteady ataxic gait, with a tendency to fall with eyes open and closed. Extra-ocular movements were abnormal. Constant fast (10-15 Hz) microsaccadic vibration of the fundus with some horizontal and vertical flutter and square wave jerks. Left beating nystagmus and flutter episodes in vertical and horizontal channels were observed. Volitional movements were slow and hypometric. Optic chiasmatic nystagmus was present in horizontal plane with upward directional preponderance.

Pursuit was mildly abnormal, being broken, but probably full, with a tendency to converge, inducing rapid eye movements that looked like convergent nystagmus. Electro-nystamography did not document convergence nystagmus. Electro-nystagmography was extremely difficult to interpret, though occasional absence of nystagmus on rotation intermittent with normal responses suggests convergence. Sinusoidal rotation suggested a left directional preponderance. Parts of the OKN were normal in the horizontal plane, but there was a directional preponderance upwards. Caloric responses were normal, but opsoclonus developed on caloric testing with warm water.

The patient did not report any hearing difficulty, tinnitus or hyperacusis. Pure tone thresholds on the right showed a slight sensorineural loss bilaterally from 250-2000 Hz, falling to a moderate loss at 6000-8000 Hz. The left ear shoed a mild sensorineural loss notched to 30dBHL at 4000Hz. Tympanometry was normal bilaterally in terms of middle ear pressure and compliance. Acoustic reflex thresholds with ipsilateral stimulation were normal in the right, and slightly lower than normal in the left. ART with contralateral stimulation were slightly elevated in the right, and normal in the left. Reflex delay in the right was abnormal at 500 and 1000 Hz (4 and 3 seconds respectively), and normal in the left ear.

Auditory brainstem responses were abnormal. Wave amplitude was low bilaterally. Right ipsilateral responses were delayed for Wave III and V, with a prolonged I-III and I-V inter-wave interval. Contralateral right recording with left stimuli revealed a delayed Wave V, and an inter-wave III-V interval at upper limit of normal. Left ipsilateral recordings revealed a delay in Wave V, and prolonged I-III and I-V inter-wave intervals. Contralateral recordings from the left with right stimuli, revealed delayed Waves III and V. Inter-aural differences were in the normal range, due to bilaterally prolonged responses.

Speech discrimination thresholds using the AB word list showed normal discrimination at 40dB bilaterally, with no roll over at higher intensities. Masking level differences were abnormal at 5dB (normal values >9dB). Dichotic speech tests revealed no abnormality (performed by M. Cohen).

Case g: Efferent Auditory Effects

Tests were conducted at the initial visit to the hospital, coincident with the complete neuro-diagnostic and neuro-otological battery. Efferent auditory effects were measured ten months later, when the patient returned for follow-up assessment. At this time, auditory function had declined (further loss in pure tone thresholds) and OAE tests revealed lower amplitude emissions. Efferent results are reported from the initial visit, during which time thresholds ranged showed a bilateral mild loss, except in the right at higher frequencies (6000-8000 Hz) where a moderate loss was present.

Efferent Effects in the presence of Bilateral Olivary Lesions:

Analysis of right ear responses revealed no inhibition of otoacoustic emission amplitude during 45dBSL of noise (0% = 0dB difference ratio). The left side showed a decrease of only 10.9% during 45dBSL, which is less than +/-2SD from normal responses at 45dBSL. Frequency analysis of the left ear emissions within 500 Hz bands revealed abnormal levels of inhibition in all frequency bands from 2.2-9.8% (See Williams et al. 1994 for frequency analysis). However, inhibition in the 1.0-1.5kHz band was 27.5%. (See Figure VII.2.)

Summary:

Efferent tests and audiometric responses showed bilateral deficits. Efferent suppression was virtually absent in the right ear and less than 2 SD from normal means in the left ear (with inhibition limited to a narrow frequency band). At this time, audiometric tests demonstrated a moderately severe sensorineural loss at high frequencies in the right, and only a mild sensorineural loss in the left.

Figure VII. 1a

Case g: Bilateral Lesions of the Olivocochlear Nuclei

T1 weighted (3mm) magnetic resonance image of Case g showing enhancement of both olivary nuclei

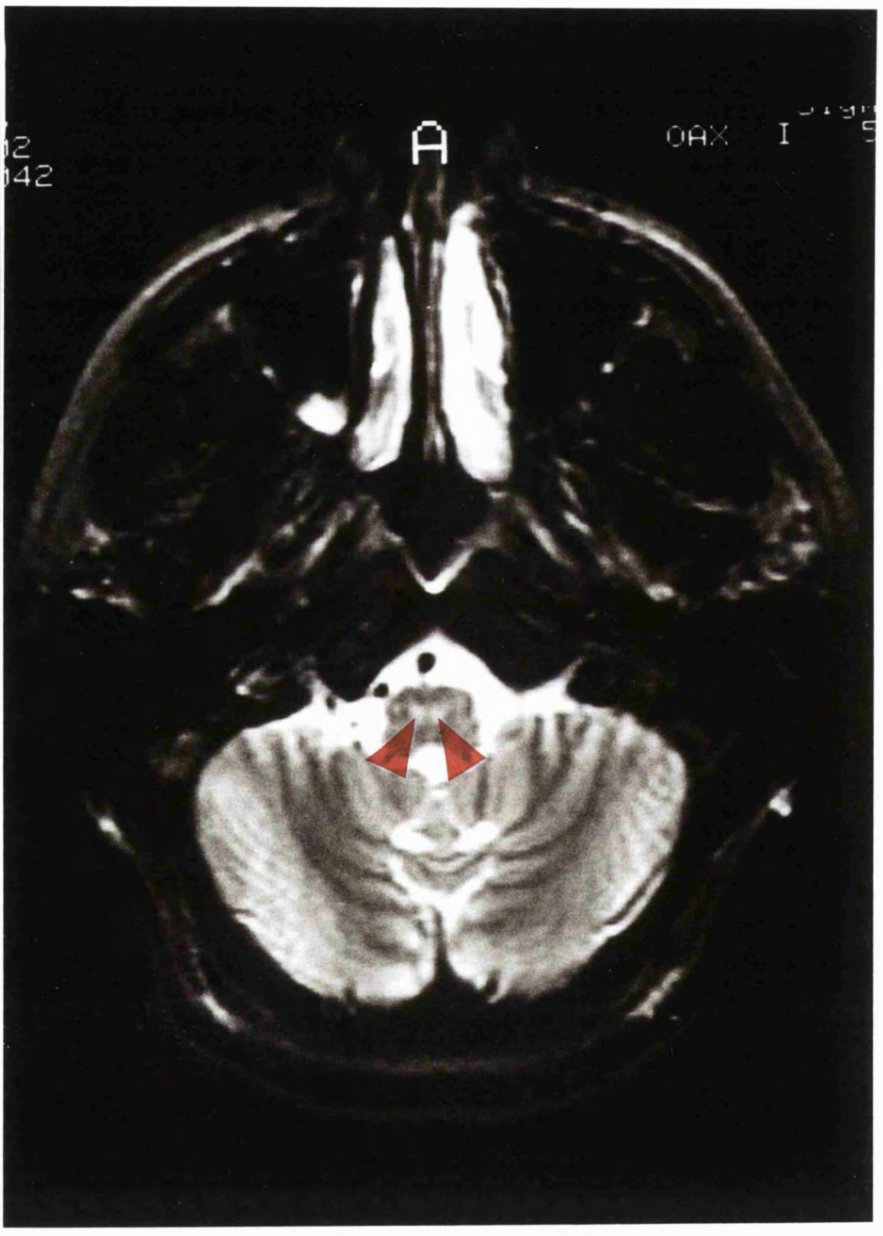


Figure VII. 1b

Case g: Bilateral Lesions of the Olivocochlear Nuclei

T1 weighted (3mm) magnetic resonance image of Case g showing enhancement of both olivary nuclei

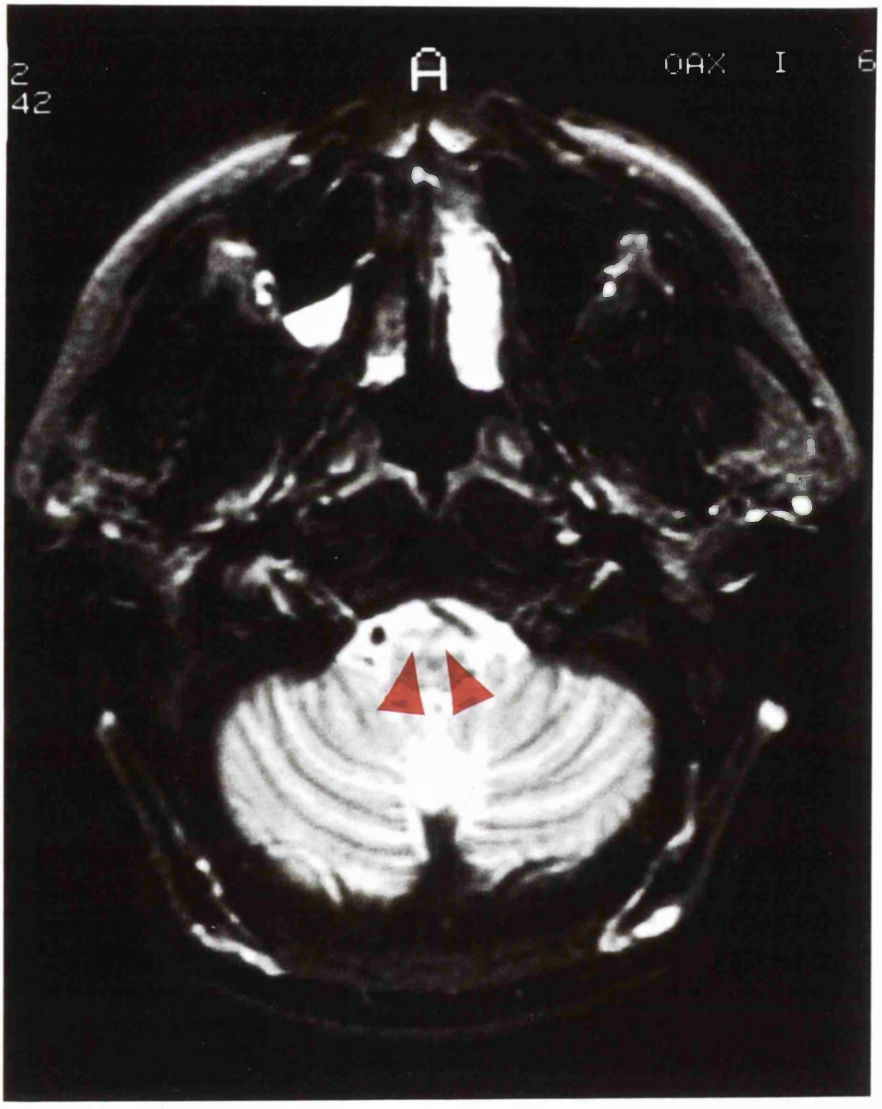
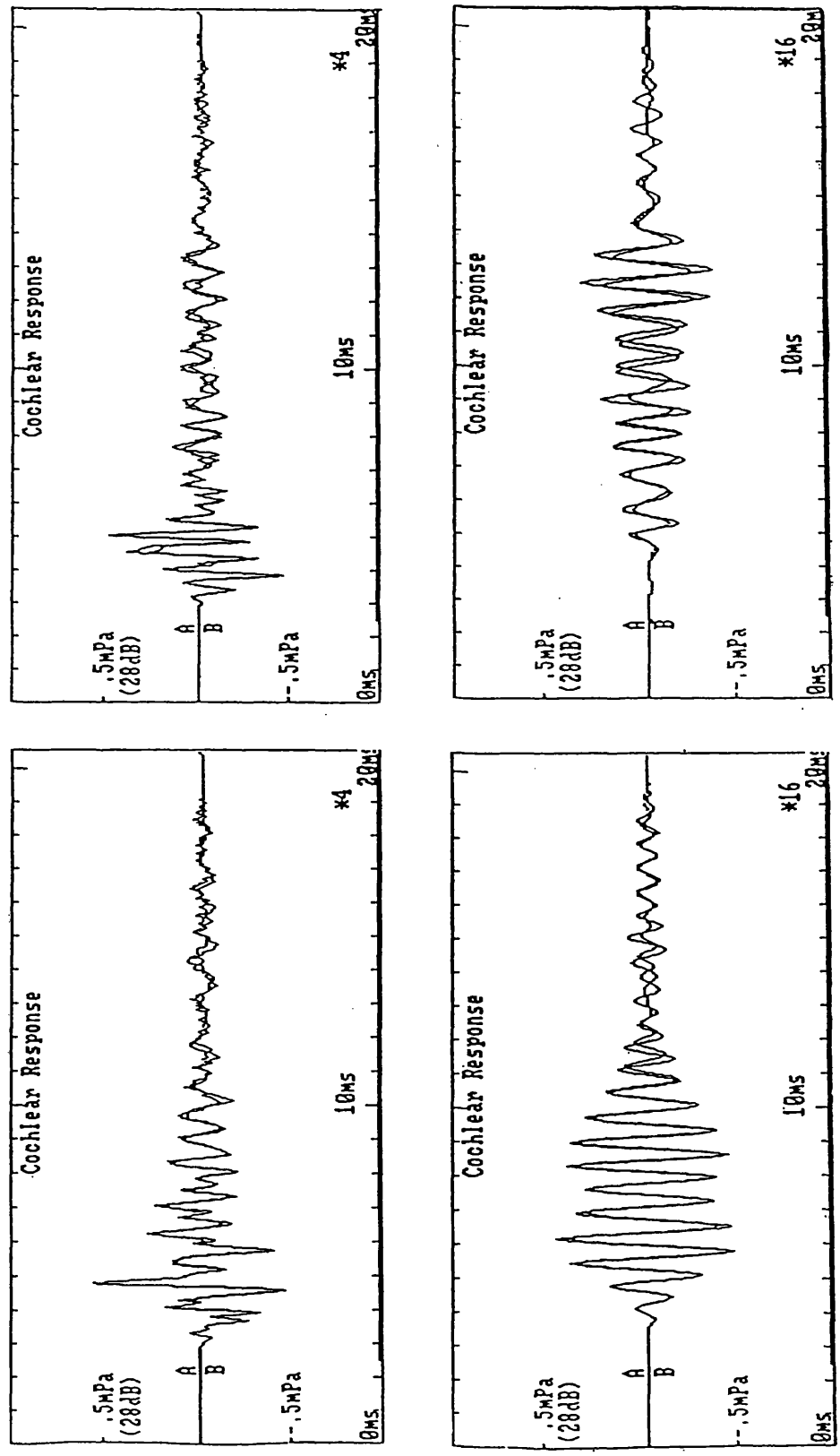


Figure VII.2

Case g: Absence of Efferent Inhibition in a Case with Olivo-Ponto-Cerebellar Degeneration



The top row illustrates CEOAE in the right and left ears. The lower row illustrates efferent auditory effects in the right and left ears. Efferent auditory effects are illustrated in the lower row for right and left ears. The filtered CEOAE (1000 – 2000 Hz) are superimposed to illustrate the lack of peak to peak inhibition in the right ear, and the existence of inhibition in a narrow frequency band in the left ear.

Epidermoid Cyst in the Cerebello-Pontine Angle:

Case f: History and Audiometry

This 43 year old male presented with complete hearing loss in the right ear, reduced right corneal reflex, and persistent balance difficulties. At 26, he had been treated medically for trigeminal neuralgia which had resolved, but shortly after he suffered from repeated blackouts and vertigo. At 40 he first noticed progressive hearing loss and tinnitus in the right ear.

Pre-operative audiometry confirmed complete loss of hearing in the right, with normal hearing in the left ear. Tympanometry was normal bilaterally. Ipsilateral acoustic reflexes were absent in the right, and normal from the left ear. Contralateral reflexes were normal recording from the right, and absent recording from the left.

An MRI revealed a mass expanding the right cerebello-pontine angle cistern, and displacing the pons and cerebellum away from the petrous. The lesion was of high signal on T2 weighted sequences, and of similar signal to CSF on T1 weighted sequence. There was no enhancement after gadolinium. A left vertebral angiogram catheter study showed no pathological circulation to the right cerebellar pontine angle mass. There was reflux into the right vertebral and predominant filling of the left posterior cerebral artery.

Observations during surgery revealed that the upper border of the mass extended up to the tentorial hiatus and the inferior border down to the level of the jugular foramen. There was no hydrocephalus or additional abnormalities. The mass was seen to stretch the VII and VIII nerves, splitting them into many separate bundles. Histology confirmed an epidermoid cyst. There was no pathological circulation to the right cerebello-pontine angle mass. Following surgery, the patient reported persistence of deafness and ringing tinnitus in the right ear.

Continuous tinnitus in right ear remained following surgery, exacerbated by movement of the eyes to the right. Two years following excision, tinnitus began in left side. A MRI showed the brainstem to be a little deformed but no evidence of recurrence of tumor on right and no evidence of abnormality on left. Right sided neurological deficits improved, with near normal facial function and sensation, with corneal reflex remaining a little depressed.

Otoacoustic emissions, and efferent auditory effects were recorded pre-surgically revealing robust emissions bilaterally (1 and also 4 days before surgery). Post-surgical efferent effects were recorded 1 and 1 ½ weeks following excision of the cyst.

Case f: Otoacoustic Emissions in the Presence of an Epidermoid Cyst in the CPA

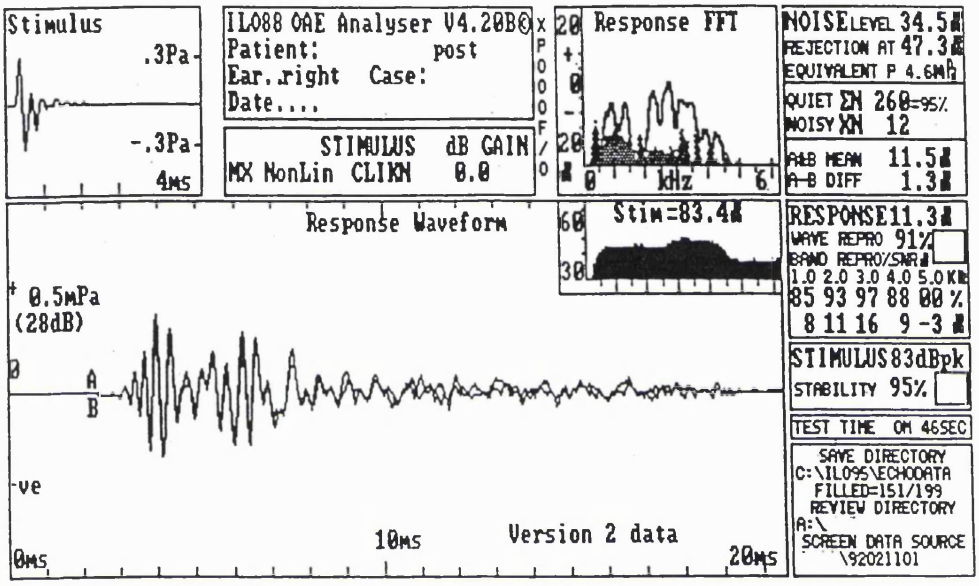
Otoacoustic emissions were observed in both ears during pre-operative testing one and four days before surgery. This suggests that the central cyst had not disrupted cochlear function.

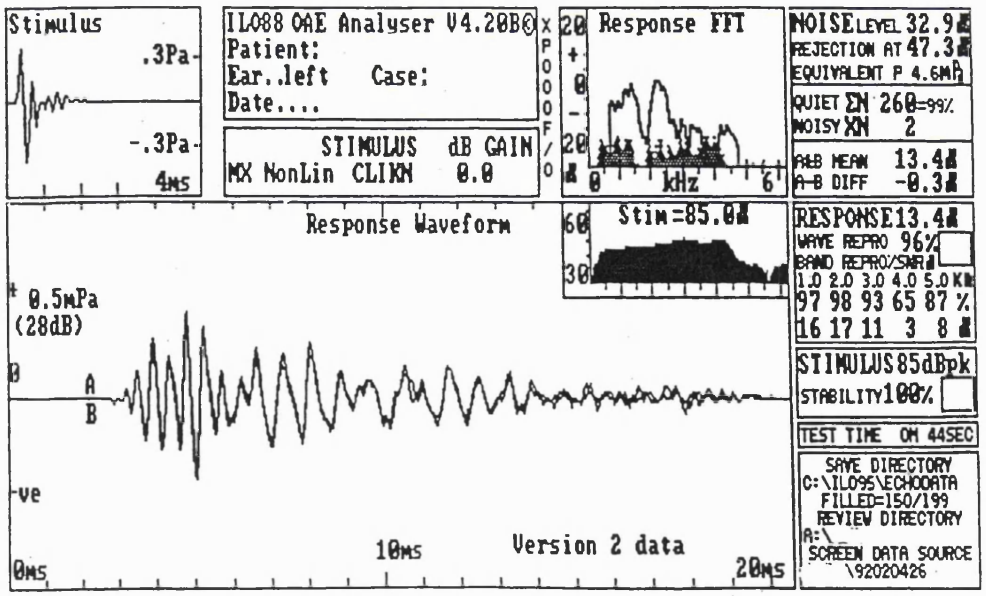
The right ear (ipsilateral to the cyst) demonstrated normal amplitude CEOAE (14.8dBSPL, 0.4dB difference, 96% reproducibility) with 83.7dBpeSPL non-linear click stimuli. Spectral analysis of 1kHz bands showed normal amplitudes (8-19dB) for frequencies from 1-4kHz. The waveform showed maximal oscillations in the initial 10 msec, with relatively low amplitude oscillations from 10-20msec. In order to ensure that middle ear oscillations were not the primary source of the first portion of the waveform, the non-linear emissions were windowed to begin at 5msec. Normal amplitude emissions remained across the entire spectrum (9.6dBSPL, -0.3dB diff., 90% repro.), and within 1-3kHz range on band analysis (11-13dB from 1-3kHz bands). (See Figure VII.3, VII.4, VII.5.)

Figure VII.3

Presence of CEOAE in Case with Epidermoid Cyst of the Cerebello Pontine Angle

Non-linear click evoked emissions from the ear ipsilateral to the cyst (top trace) and the ear contralateral to the cyst (lower trace). CEOAE waveform in central panel of each trace. Frequency spectrum of response in panel titled "Response FFT".





Right ear responses to tone-pip stimuli confirmed the presence of frequency specific evoked emission in the ipsilateral ear from 500-4000 kHz. (See Figures VII. 4, VII.5.) The dispersion of low frequencies up to 1000Hz occurred in the first 10msec of the waveform, revealing a similar pattern to click evoked emissions. However, it should be noted that normal subjects show great variability in the dispersion of frequencies relative to time. Responses to the 4000Hz tone pip were visible in the emission waveform and spectrum, but the signal to noise ratio was insufficient to be certain that a valid response was present.

Table VII.1

Pre-Operative Tone Evoked Emission Responses from the Ear Ipsilateral to CPA Cyst (Right)

Tone Frequency	CEOAE (dBSPL)	Diff. (dB)	Repro %
500 Hz, 2 cycle:	1.7	0.0	69
1000 Hz, 2 cycle:	5.0	2.6	63
2000 Hz, 4 cycle:	3.8	0.2	70
4000 Hz, 4 cycle:	-1.7	1.2	28

The left ear (contralateral to the cyst) revealed normal CEOAE responses of 14.4dBSPL (0.7dB diff., 96% repro.) with 84.7dBpeSPL non-linear click stimuli. An onset time window of 5msec demonstrated normal total response (11.6dBSPL, -0.2dB diff., 94% repro.), with normal responses at 1 and 2kHz (17dBSPL, and 10dBSPL, 98% repro. respectively), and 0dBSPL (47% repro.) at 3kHz. (See Figures below.) Tone evoked emissions from the left ear were also normal for tone pips ranging from 500-2000Hz.

Table VII.2

Pre-Operative Tone Evoked Emission Responses from the Ear Contralateral to CPA Cyst (Left)

Tone Frequency	CEOAE (dBSPL)	Diff. (dB)	Repro %
500 Hz:	11.3	-2.8	96
1000 Hz:	14.0	-0.3	96
2000 Hz:	13.3	-0.9	96
4000 Hz:	3.8	-2.3	82

Otoacoustic Emissions Following Surgical Removal of the Cyst

The right ear (ipsilateral to the cyst) maintained otoacoustic emissions following surgery. Fourteen days after surgery, response amplitude remained within the normal range (CEOAE = 11.3dBSPL, 1.3dB diff, 91% repro) with 83.4 dBpeSPL non-linear clicks) (Ryan et al. 1990). Responses were also measurable with a 5.0msec window onset (CEOAE = 4.9dBSPL, 0.3dB diff, 74% repro.). Band analysis showed responses remained in the 1-3kHz range (5-8dBSPL range, 74-87% repro), although reduced compared with pre-operative recordings.

Responses to tone stimuli confirmed the presence of OAE in the right ear at 500 and 1000Hz, consistent with pre-operative recordings (within 2.7 dB). Tone evoked emissions at 2000 and 4000Hz were robust and were >4dB above pre-operative levels. The presence of emissions is considered to be the significant finding in this case, as changes in amplitude are as likely to arise from inter-test variability or spectral scatter of the tone pip, as they are from surgical effects. Unfortunately, the patient was not available to complete repeated testing to establish a baseline for amplitude comparisons.

Table VII. 3

Post-Operative Tone Evoked Emission Responses from the Ipsilateral (Right) Ear:

Tone Frequency	CEOAE (dBSPL)	Diff. (dB)	Repro %
500 Hz:	1.0	-0.5	63
1000 Hz:	7.7	1.9	80
2000 Hz:	8.6	1.4	84
4000 Hz:	4.5	-0.6	77

Following surgery, left ear (contralateral to the cyst) emissions were little changed from pre-operative recordings (CEOAE = 13.4dBSPL, -0.3dB diff, 96% repro, 85.0 dBpeSPL non-linear clicks). An onset time of 5.0msec resulted in a normal response of 9.6dBSPL (-1.0dB diff, 92% repro) from 0.5-3kHz (1kHz = 17dB, 97%; 2kHz = 8dB, 86%; 3kHz =3 dB, 66%). Tone evoked emissions in the left ear were within 2dB of pre-operative levels.

Table VII: 4

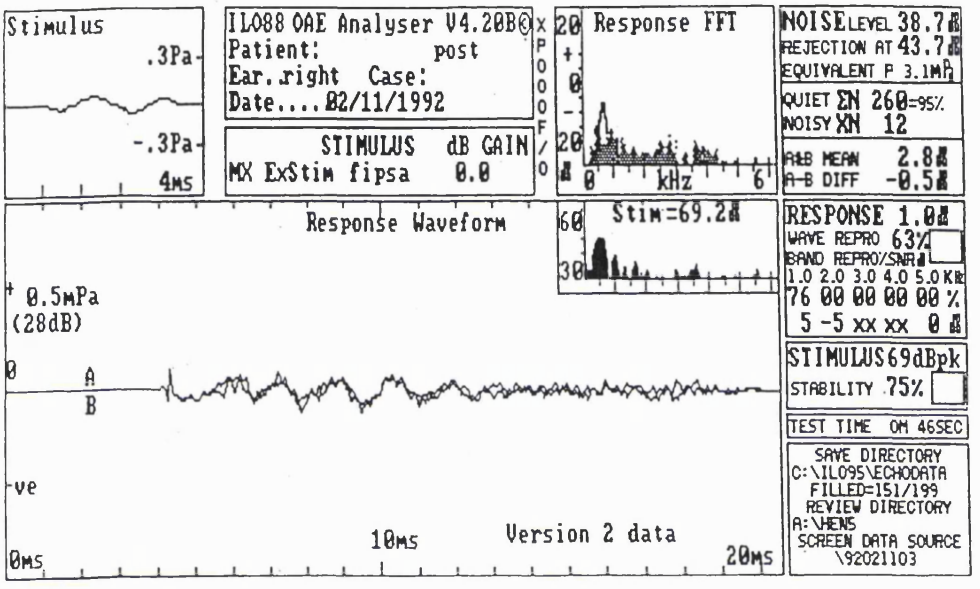
Post-Operative Tone Evoked Emission Responses from the Contralateral Ear (Left)

Tone Frequency	CEOAE (dBSPL)	Diff. (dB)	Repro %
500 Hz:	10.0	0.0	91
1000Hz:	13.6	0.1	95
2000Hz:	13.3	0.0	95
4000Hz:	3.5	0.0	70

Figure VII.4

Case f: Tone Evoked Otoacoustic Emissions in the Ear Ipsilateral to Epidermoid Cyst of the CPA

Top trace illustrates emissions evoked by 500 Hz tone. The lower trace illustrates emissions evoked by 1000 Hz tone. The emission waveforms in the main panels show oscillations replicating the frequency of the tone stimuli seen in the upper left panels. The FFT of the response is illustrated in the upper right panels of each trace.



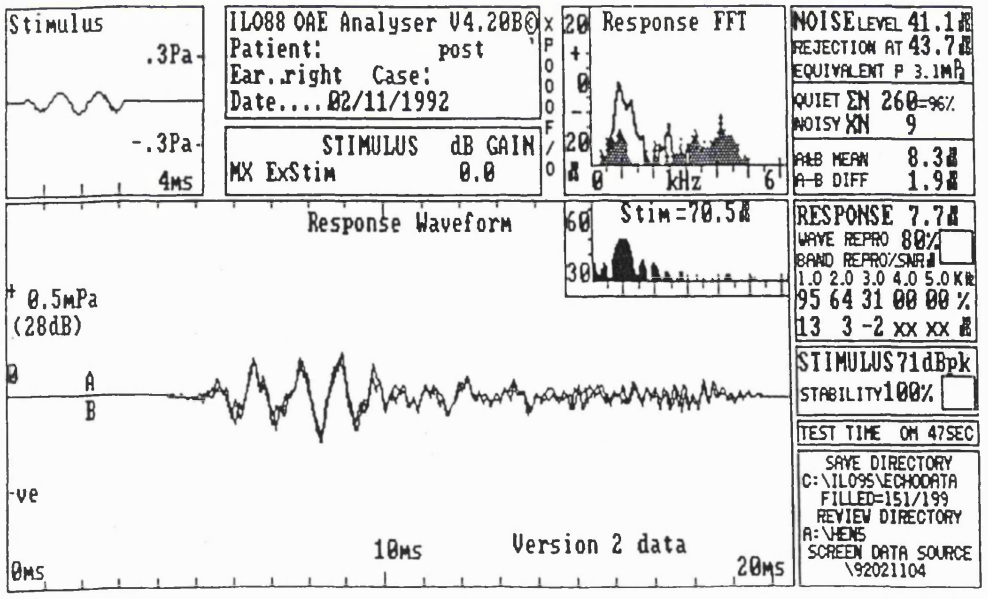
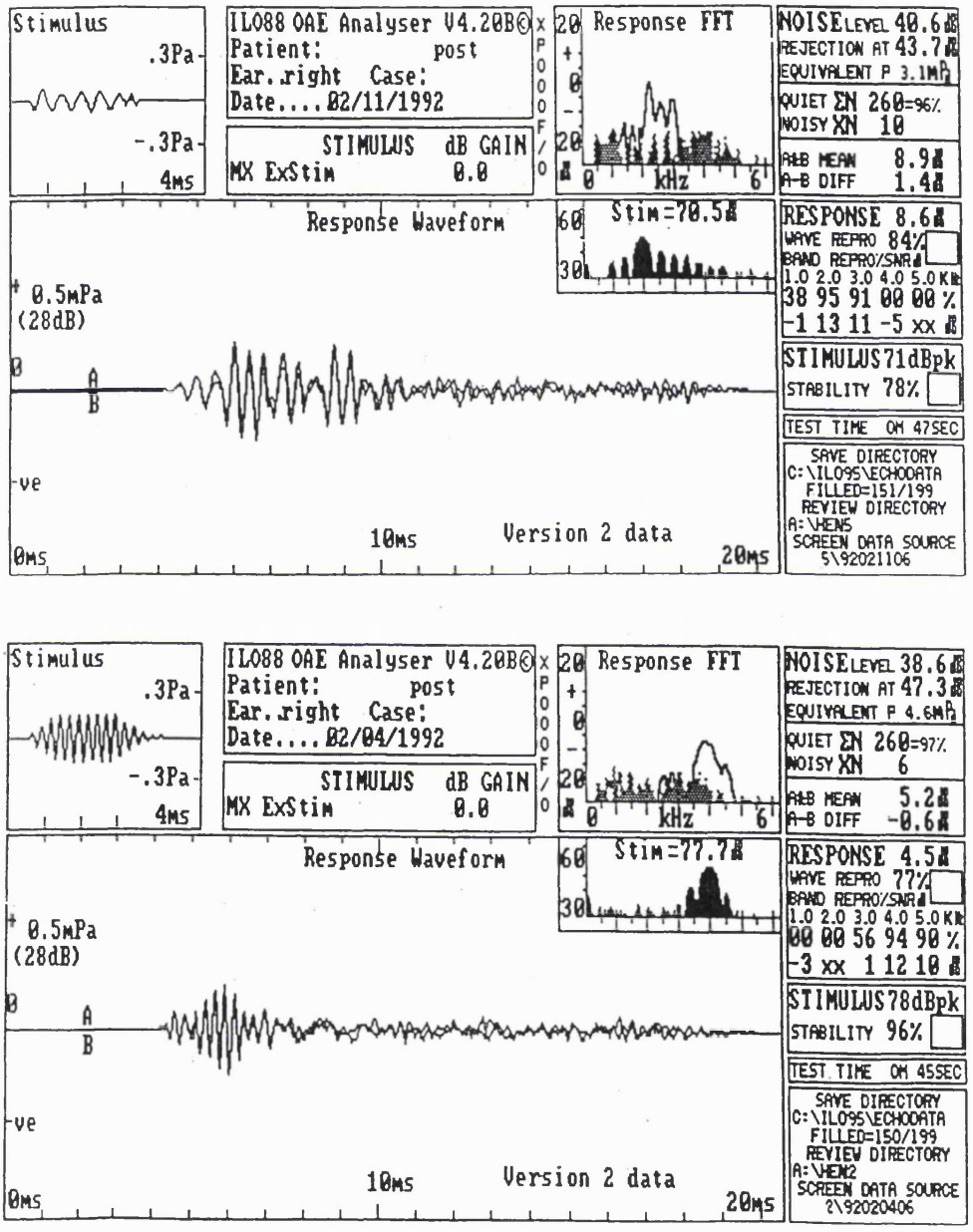


Figure VII.5
Case f: Tone Evoked Otoacoustic Emissions in the Ear Ipsilateral to Epidermoid Cyst of the CPA

Top trace illustrates emissions evoked by 2000 Hz tone. The lower trace illustrates emissions evoked by 4000 Hz tone. The emission waveforms in the main panels show oscillations replicating the frequency of the tone stimuli seen in the upper left panels. The FFT of the response is illustrated in the upper right panels of each trace.



Case f: Efferent Auditory Effects in the Presence of Epidermoid Cyst of the CPA

Suppression of otoacoustic emissions was negligible in both the ear ipsilateral to (right) and the ear contralateral to (left) the epidermoid cyst. Efferent tests conducted one day and four days before surgery demonstrated that minimal levels of inhibition in the right ear ranging from -4.7 to 9.8% with contralateral white noise intensities from 0 to 50dBSL (=20 to 70dBHL). The magnitude of inhibition was less than in normals at equivalent noise levels. Similarly, minimal levels of inhibition (2.3 %) were observed in the left ear during right contralateral white noise stimulation at 70dBHL. However, the sensation level of the white noise could not be calculated, as the subject had no sensation of perception in the right receiving the contralateral noise stimulus. (See Figure VII.6.)

Summary

The absence of efferent auditory effects in this patient with a cerebello-pontine angle mass and displacement of the pons was associated with bilateral loss of inhibition. The lack of inhibition in both ears is likely to reflect compression of the pons, leading to bilateral dysfunction of the olivary nuclei or olivocochlear bundles within the brainstem. Alternatively, the absence of inhibition in the left ear could have arisen from disruption of the right ipsilateral afferent pathway resulting in lack of normal perception of the contralateral stimuli. Based on normal studies (Gorga et al. 1999), it could be assumed that the presence of CEOAE in the right ear suggested normal cochlear function better than 30dBHL. Thus, 70dBSL white noise presented to the right ear (ipsilateral to the cyst) could have been perceived at 40dBSL or more at the cochlea. However, the cyst was observed to be stretching and splitting the right afferent cochlear nerve. It is therefore unlikely that contralateral noise presented to the right ear was accurately transmitted to the cochlear nucleus and thus was ineffective in inhibiting OAEs from the left ear.

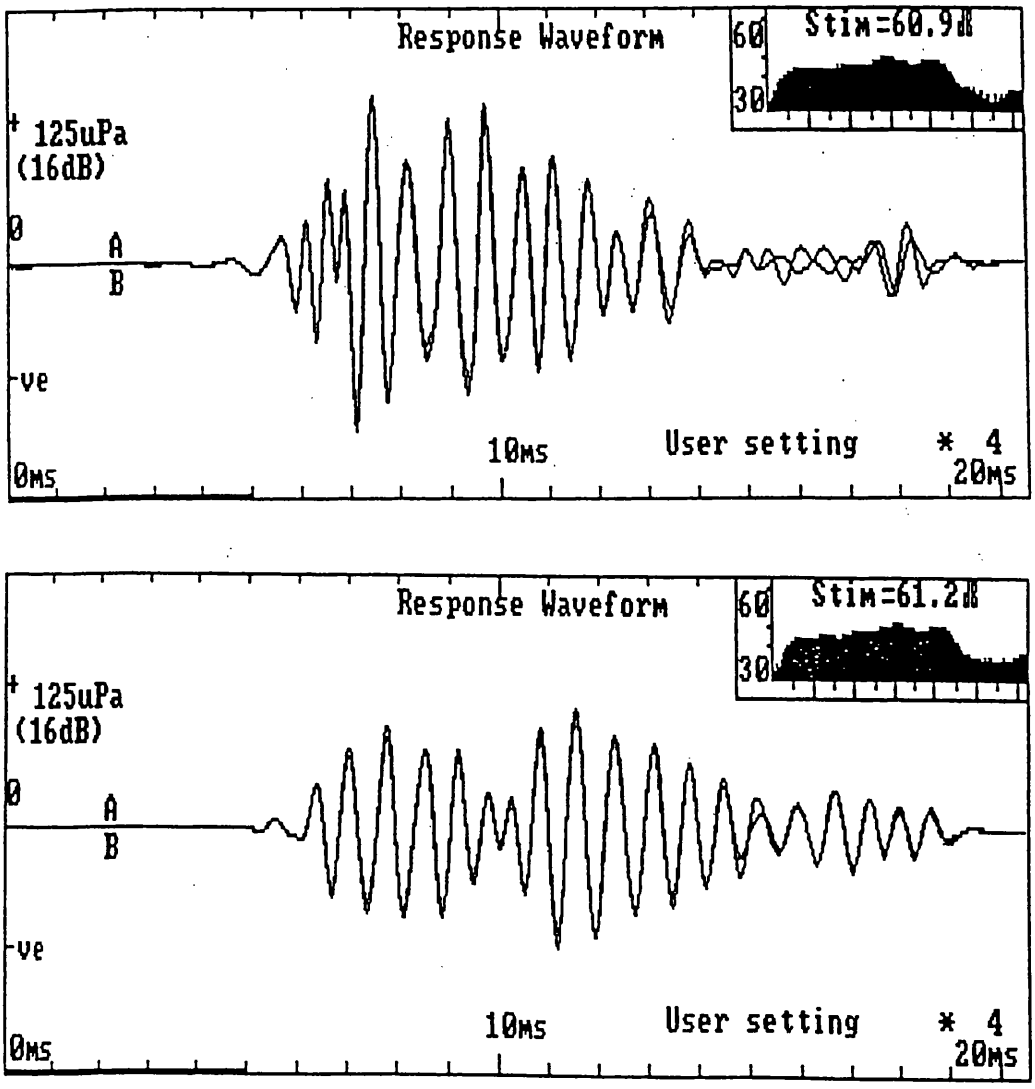
The presence of click and tone evoked emissions in the ear ipsilateral to the cyst suggests that the mass had not completely destroyed peripheral cochlear function (although there was some indication of disruption of the frequency dispersion of the emissions). Nonetheless, brainstem dysfunction was revealed by the application of the efferent test procedures. This suggests the efferent emission test offers a differential diagnostic function in distinguishing cochlear function versus olivocochlear feedback dysfunction.

Figure VII.6

Case f: Absence of Efferent Inhibition in Case with Epidermoid Cyst of the Right Cerebello-Pontine Angle

Filtered CEOAE waveforms (1000 – 2000 Hz) are superimposed to show the waveform recorded in quiet (A) and the waveform during 35dBSL contralateral white noise (B), plotted as amplitude (uPa) versus time (msec).

The upper trace shows lack of peak to peak inhibition in the left ear (contralateral to the cyst). The lower trace shows lack of peak to peak inhibition in the right ear (ipsilateral to the cyst).



Ototoxic Drug Therapy

Case z: - History and Audiology

The crossed medial olivocochlear fibres directly innervate the base of the outer hair cells, which are an essential component for the generation of otoacoustic emissions. Outer hair cells are sensitive to ototoxic agents, including quinine based medications. Efferent tests were performed on a 23 year female who reported hearing and balance disturbances following preventative treatment with Chloroquine. The patient described over-sensitivity to sounds in both ears, and subsequently a loss of sensitivity.

Initial pure tone thresholds showed a slight low frequency loss (20-25dBHL at 250-500 Hz), but threshold levels at the time of efferent testing were normal. Audiograms repeated one month later were normal in both ears, with a range of ¯10-5dBHL across all frequencies. Tympanometry, acoustic reflexes and decay were normal. ABR were normal in wave morphology, absolute latency, inter-wave interval and inter aural differences. Tinnitus was not reported.

Vestibular tests failed to reveal any significant vestibular disturbance. There was no sustained nystagmus on ENG testing, and smooth pursuit, optokinetic and vestibulo-ocular suppression tests of central vestibular function were normal. There was a slightly reduced labyrinthine function on the left side on caloric testing, with a left directional preponderance.

The findings suggested inner ear damage as a result of quinine hypersensitivity, with a possibility that bilateral effects lead to continuation of vestibular symptoms (due to lack of compensation). (See Table A.2.)

Efferent tests were conducted one month after the initial presentation, when auditory symptoms had resolved.

The frequency spectrum of non-linear otoacoustic emissions differed between the two ears despite symmetrical and sensitive thresholds. The total pressure of emissions in the right ear was 13.2dBSPL (diff -0,1, repro 95%) with non-linear clicks at 79 dB pe SPL. The spectrum revealed robust responses from 18-5 dB SPL (77 - 98% repro) for frequencies between 0.5 - 5.0 Hz. CEOAE from the left ear were approximately half the size of the right (Resp = 7.5 dB SPL, diff -0.8, 87% repro) with frequency responses ranging from 12 - 5 dB SPL (76 - 93% repro range) between 0.5 - 5.0 kHz. The primary difference between the two ears were found around 1kHz (8 dB) and 3 kHz (9 dB) (1 kHz bands).

At the level of stimuli used, the left ear displayed no responses at frequencies above 2kHz and the right ear displayed responses up to 3kHz. Whilst the spectra of adult subjects often decreases above 3kHz, the amplitude of responses was not as robust as often observed given the patient's sensitivity to pure tones and age. Further testing with more intense stimuli might prove useful to determine input - output function of CEOAE amplitude across the frequency spectra. Suppression of otoacoustic emissions was consistent with normal subjects (35dBSL: right=15.9%; left=11.9%). (See Figure VII.7.)

Summary

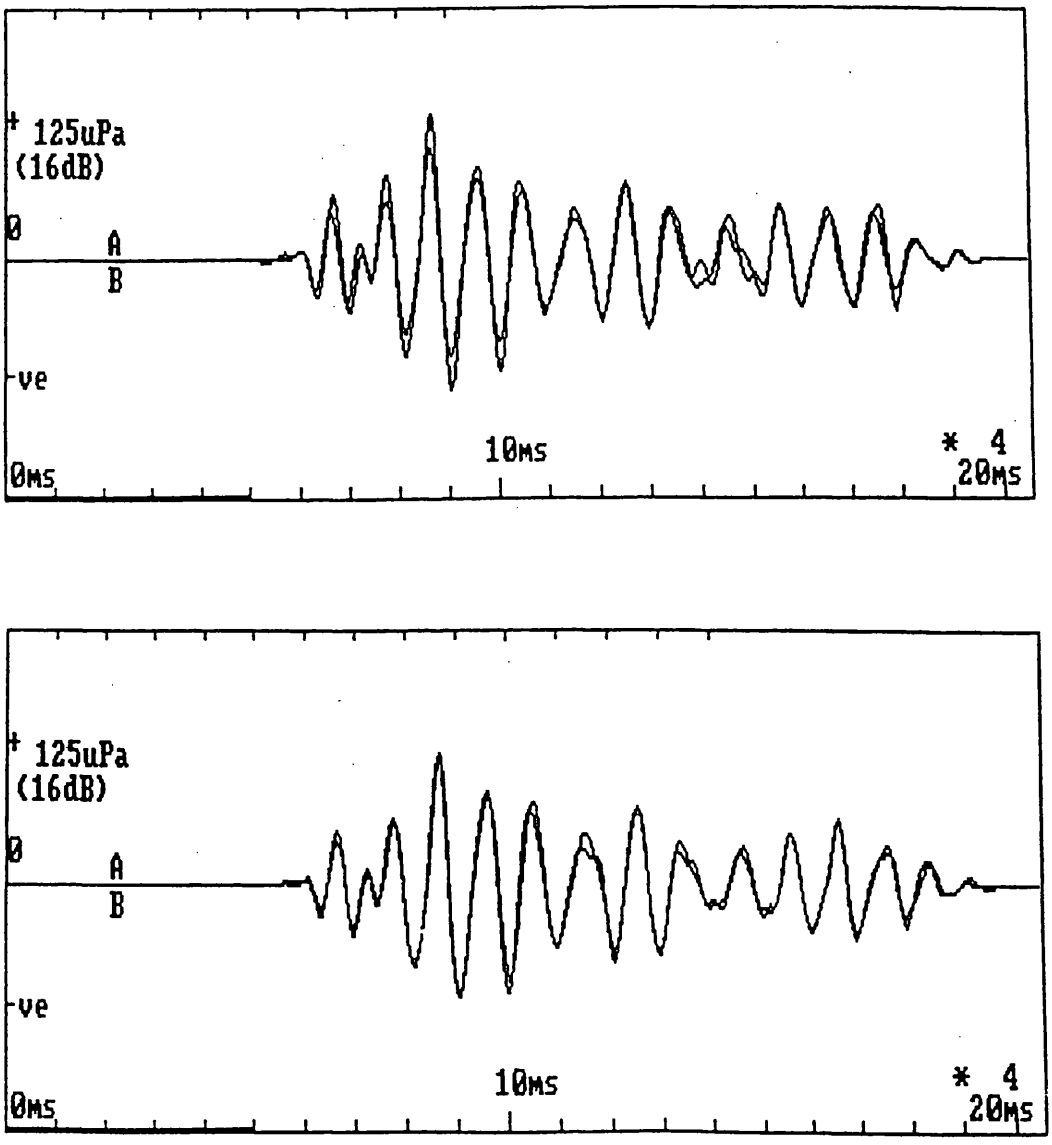
This patient demonstrated only mild signs of vestibular damage, and a slight loss in low frequency pure tone thresholds, which recovered within one month. Whilst it is not possible to determine the exact site of dysfunction in this patient, it is likely that the symptoms represent early stages of ototoxia which might not have affected efferent structures or function. Alternately, it is possible that recovery of efferent function had occurred before efferent testing was conducted. (The efferent tests were conducted after pure tone thresholds had recovered). Of interest, is the possibility that efferent function was preserved whilst there was some damage to the structures that affect the production of CEOAE. The amplitude of emissions in the left ear were notably less than in the right. However, it is not yet possible to quantify the expected amplitude of CEOAE relative to pure tone thresholds, and conclusions should be drawn with caution from these observations.

Figure VII.7

Case z: Efferent Inhibition Following Recovery from Exposure to Ototoxia

Filtered CEOAE waveforms (1000 – 2000 Hz) are superimposed to show the waveform recorded in quiet (A) and the waveform during 35dBSL contralateral white noise (B), plotted as amplitude (uPa) versus time (msec).

The top trace illustrates peak to peak inhibition in the right ear. The lower trace shows lesser peak to peak inhibition in the left ear.



Difficulty Discriminating Speech in Noise

Case e: History and Audiology

This 30 year old male volunteered as a normal subject, with normal pure tone audiometry, tympanometry, and ABR. However, an in-depth history revealed that his wife often complained that he mis-heard speech, especially in background noise (television). Ten years ago he participated in a rock band for about a year. Currently, he avoids loud environments as it induces bilateral ringing tinnitus. Family history includes his mother who developed a bilateral mild-moderate mid-frequency hearing loss from the age of 50. (See Appendix: Table A.2, A.3.)

The subject wished to complete a full evaluation. Pure tone thresholds were normal at all frequencies. Tympanometry was normal bilaterally, as were acoustic reflexes. Auditory brainstem responses were normal in wave morphology, absolute latency, inter-wave and inter-aural differences. Middle latency and late latency auditory evoked responses were normal.

Additional tests showed normal responses including speech reception threshold, loudness discomfort levels, and word intelligibility. The SCAN-A test for central auditory processing revealed very poor function in filtered words (rank 1%) and competing words (rank 1%) (Keith 1986). There were no complaints of vestibular symptoms.

Case e: Efferent Auditory Effects

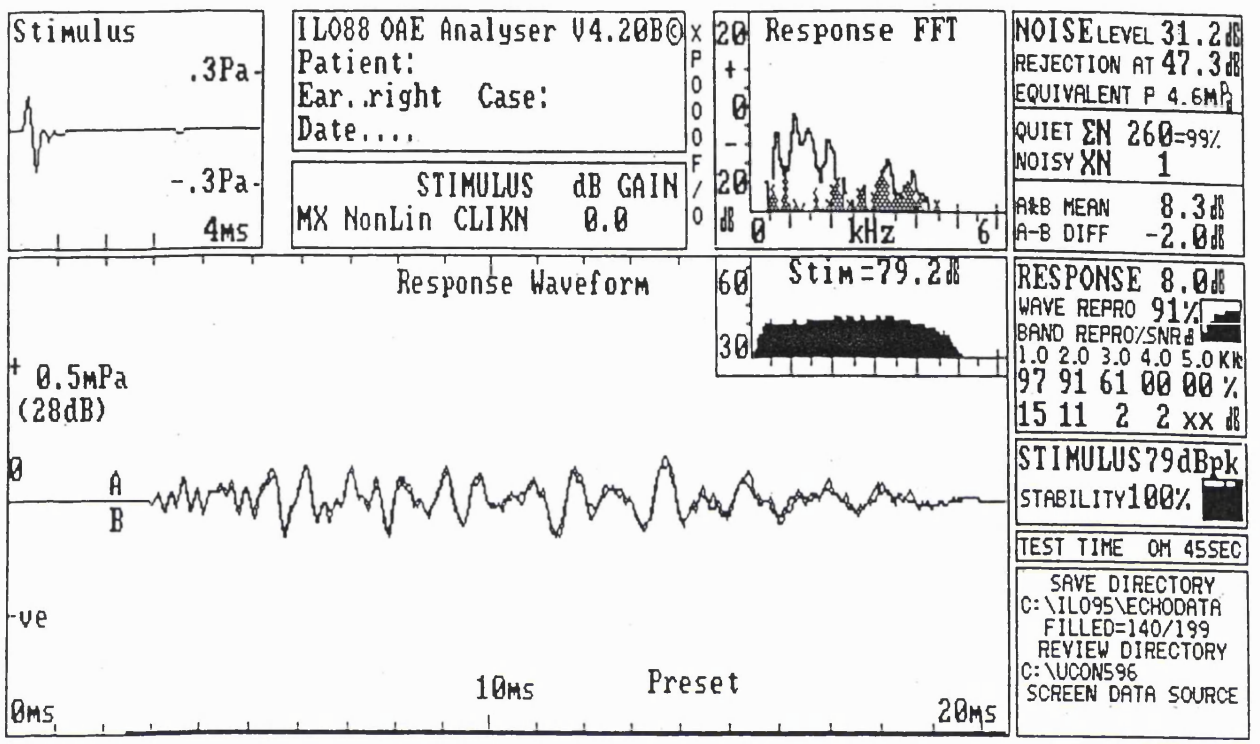
Efferent tests were conducted as part of the audiometric battery.

Cochlear OAE and efferent tests suggested diminished cochlear function. CEOAE spectra were unusual, showing a 1500Hz wide notch in responses in both ears. (See Figure VII.8.) Efferent inhibition was abnormal in both ears, with the right ear being more affected than the right (Right: 2.3 to -7.2%; Left: 2.3 to 9.8%.). It is possible that earlier noise exposure affected damaged the mid frequency responses of both cochleae, which were inadequate to elicit inhibition in the other ear. (See Figure VII.9.)

Figure VII. 8

Case e: Abnormal CEOAE in Case with Difficulty Hearing Speech in Noise

The upper trace shows right sided CEOAE. Lower trace shows left CEOAE responses. Both ears displayed a 1500Hz notch in emission amplitude at mid-frequencies, illustrated in the upper right panels "Response FFT".



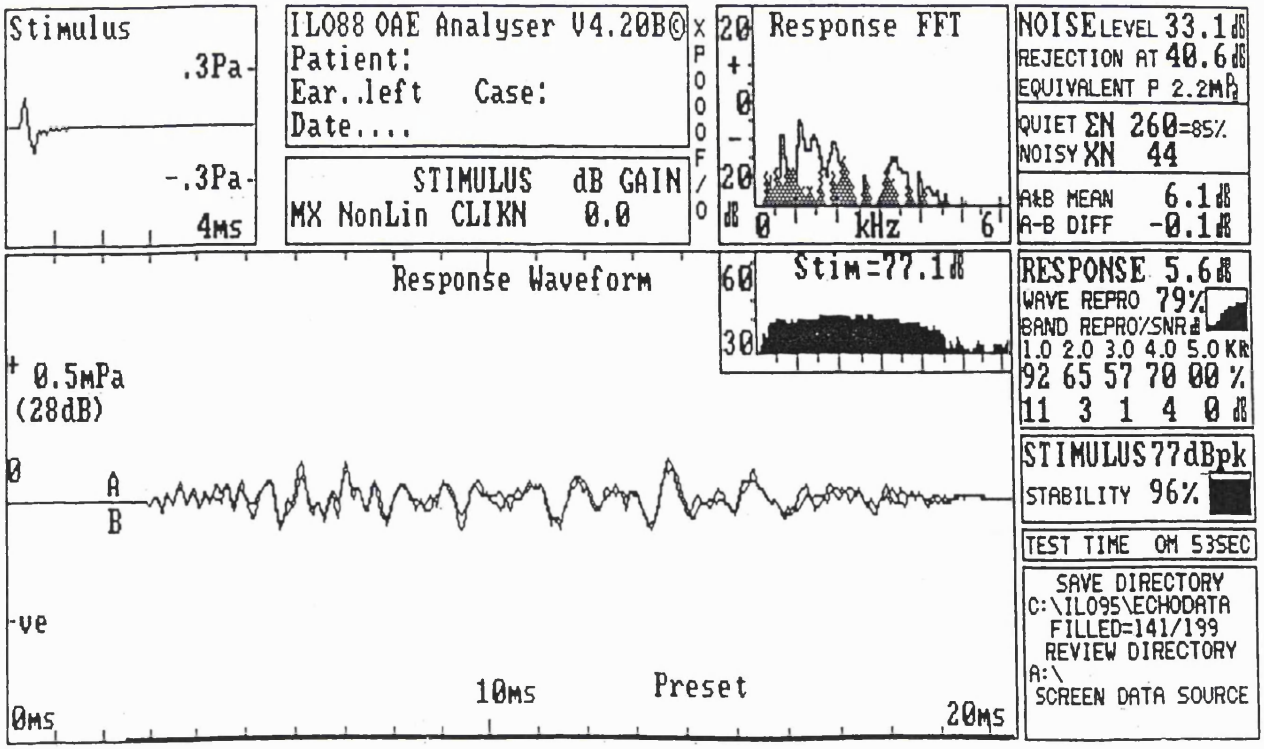
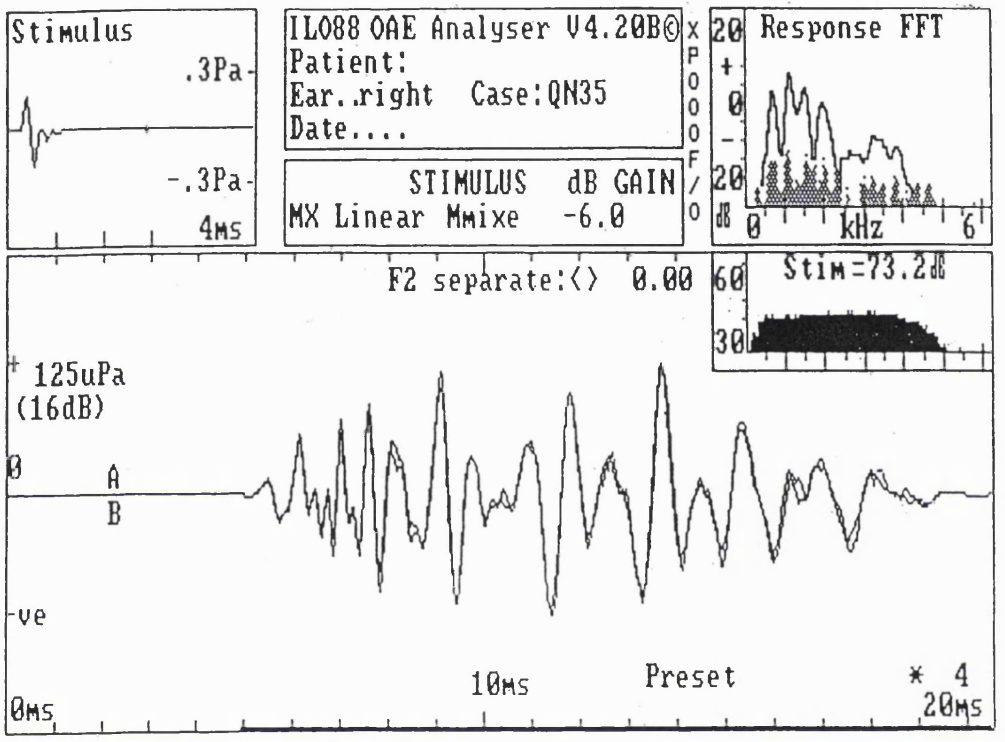
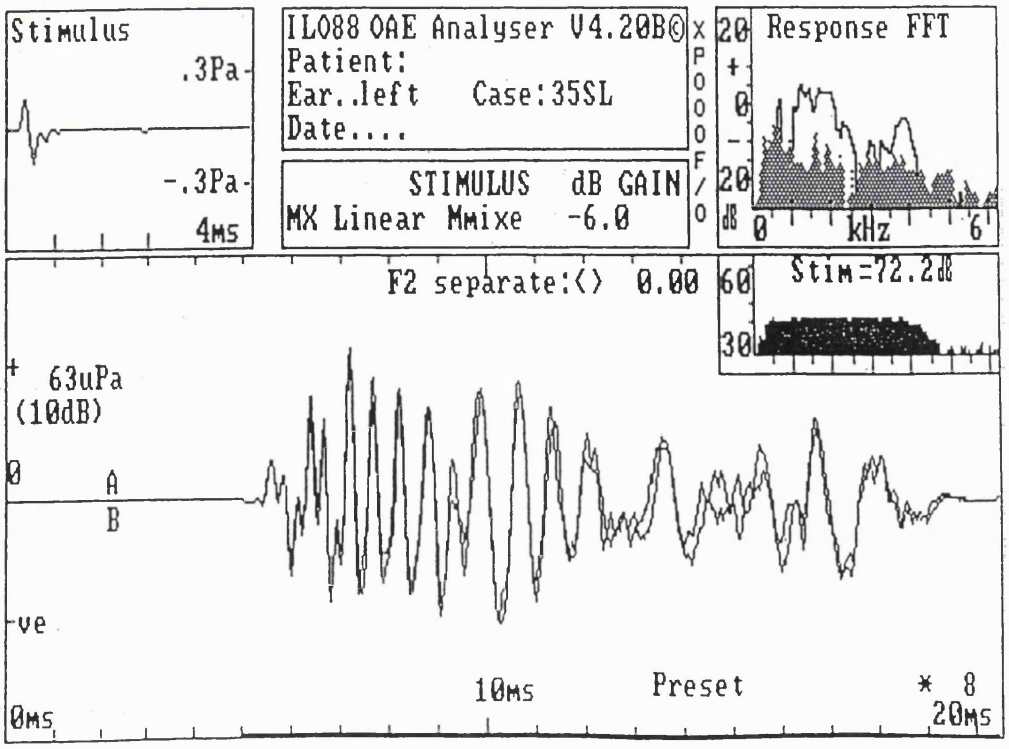


Figure VII.9
Case e: Lack of Efferent Inhibition with Difficulty Hearing Speech in Noise

CEOAE waveforms (500-6000 Hz) are superimposed to show the waveform recorded in quiet (A) and the waveform during 35dBSL contralateral white noise (B), plotted as amplitude (uPa) versus time (msec).

The upper trace shows lack of peak to peak inhibition in waveform recorded from the right side.
The lower trace shows minimal peak to peak inhibition in waveform from the left side with 45dBSL noise.





Difficulty Discriminating Speech in Noise

Case d: History and Audiology

This 27 year old male was referred following otological assessment for a progressive difficulty understanding speech in background noise, over the previous year. He heard segments of words, but found the sounds and words mixed. He had no trouble following speech in one to one conversations, or on the telephone. Occasional tinnitus was reported.

The patient reported no difficulties with balance or gait. The patient reported that he had bacterial meningitis at the age of four, and recurrent middle ear infections, familial hearing loss and occupational noise exposure.

Pure tone audiometry, tympanometry, and acoustic reflexes were normal. Word recognition tests were normal. Unfortunately, auditory brainstem results were not reported.

The SCAN-A test of central auditory processing function revealed a composite score equal to 90, which is in the normal range (Keith 1986). The competing words sub-set was the most difficult, with a score one standard deviation below normal means. Normal scores were obtained for filtered words, auditory figure-ground, and competing sentences were obtained.

Case d: Otoacoustic Emissions and Efferent Auditory Effects

Efferent tests were conducted 4 months following speech and central auditory assessment. CEOAE had unusual morphology and spectra. Right OAE had virtually no response from 2 to 3kHz (with a minimal noise floor), whilst the left displayed frequency responses from 0.5-4.0kHz, but without the dominant 1-2kHz peak usually observed. (See Figure VII.10.) DP OAE dipped from 1-4kHz, though remained above 5dB in the right, which could be considered normal. However, the left ear DP's fell to the recording floor of the instrument (-10dBSPL) from 1.5-3kHz. (Se Figure VII.12.)

Inhibition in the left ear was virtually absent, whereas the right ear demonstrated normal inhibition at 35dBSL and above. (Right: 16.8 - 25%; Left: 2.3 - 3.7%.) (See Figure VII.11.)

Summary

Efferent effects using clicks and white noise tend to be maximal at the dominant frequencies of the CEOAE spectrum (1-2kHz). It is possible that the right ear did not "hear sufficiently" in the mid frequencies, in order to inhibit the left ear. On the contrary, the left ear had low, but "adequate" responses to the white noise spectrum, and thus could sufficiently elicit activity from the contralateral OC system in order to inhibit OAE from the right ear. Of interest is the reduced DPOAE amplitude in the left ear, which could result from the normal lack of interaction of DP with CEOAE, hence the "flat"

spectral response in this ear. History revealed noise exposure, and it is possible that resultant cochlear damage was represented by reduced emissions and loss of efferent activation in the mid-frequency range in advance of pure tone threshold loss.

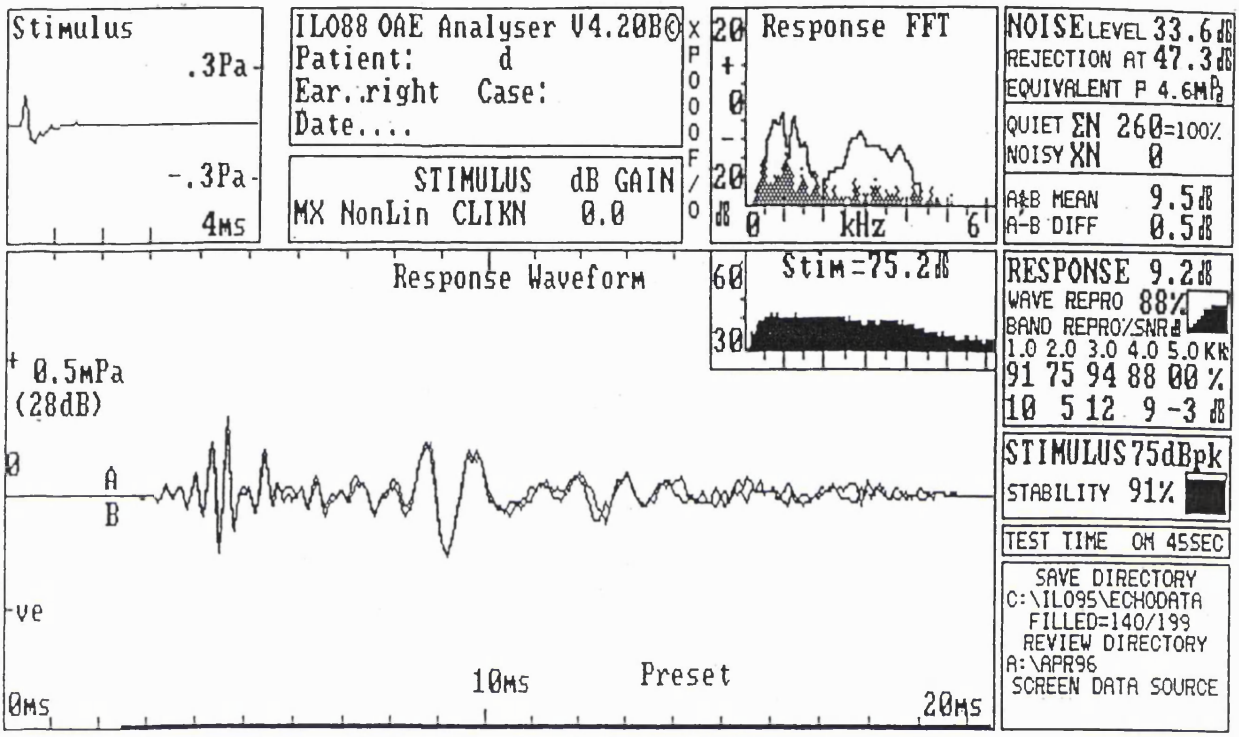
Summary: Pathological Cases

Pathological lesions along the olivocochlear pathway, from brainstem to cochlea were associated with a loss of efferent auditory effects. A patient with bilateral olivary lesions and cerebral degeneration demonstrated a lack of inhibition of otoacoustic emissions. Similar findings from a patient with a lesion within the cerebello-pontine angle showed bilateral presence of otoacoustic emissions, but lack of efferent effects. However, additional CNS derangement, pathology or effects from secondary compression or ischaemia may be related to these findings, thus precise location of the site of lesion relative to dysfunction is limited when considering pathological cases. Loss of efferent auditory effects were also observed in subjects suspected of peripheral damage as a result of noise exposure.

Figure VII. 10
Case d: Abnormal CEOAE in Case with Difficulty Hearing Speech in Noise

The upper trace shows right sided CEOAE, with a large notch in emission amplitude at mid-frequencies, illustrated in the upper right panels "Response FFT". The waveform of the emission (main panel) shows an unusual pattern, with uneven distribution of oscillations across the time window.

The left ear (lower trace) has frequencies across the 500 – 4500 Hz range, however of low amplitude across the range, as seen in the waveform in the main panel.



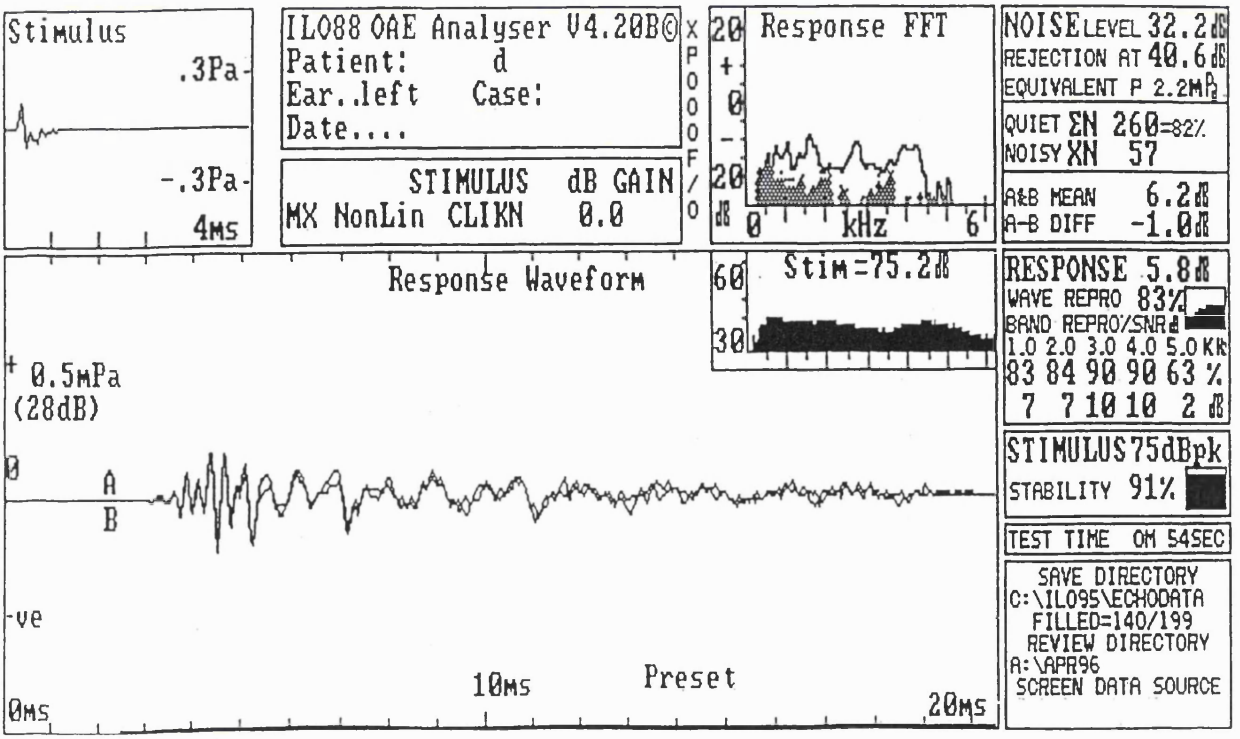
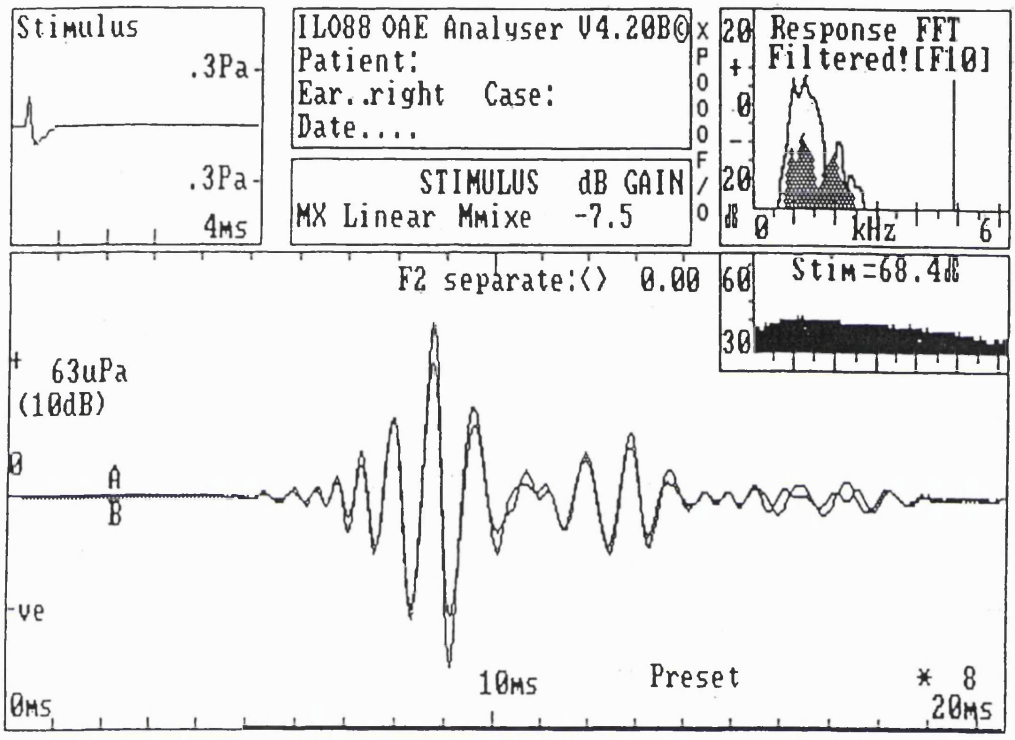


Figure VII.11

Case d: Lack of Efferent Inhibition with Difficulty Hearing Speech in Noise

CEOAE waveforms (filtered 1000 - 2000 Hz) are superimposed to show the waveform recorded in quiet (A) and the waveform during 35dBSL contralateral white noise (B), plotted as amplitude (uPa) versus time (msec).

The upper trace shows presence of peak to peak inhibition in waveform recorded from the right side. The lower trace shows minimal peak to peak inhibition in waveform from the left side.



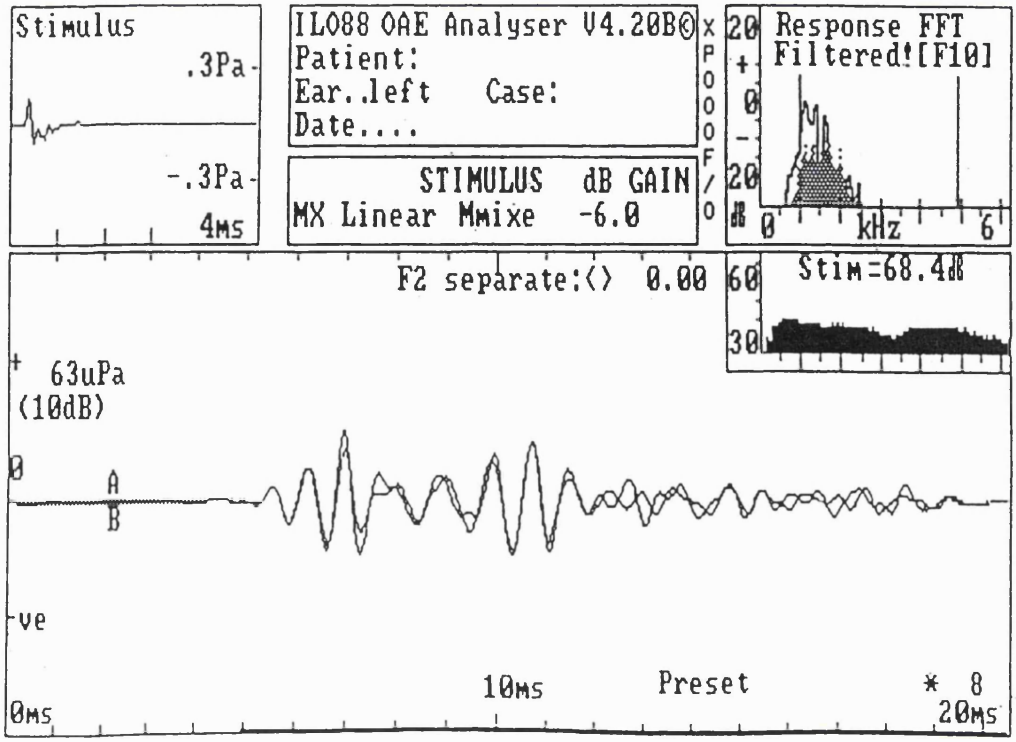
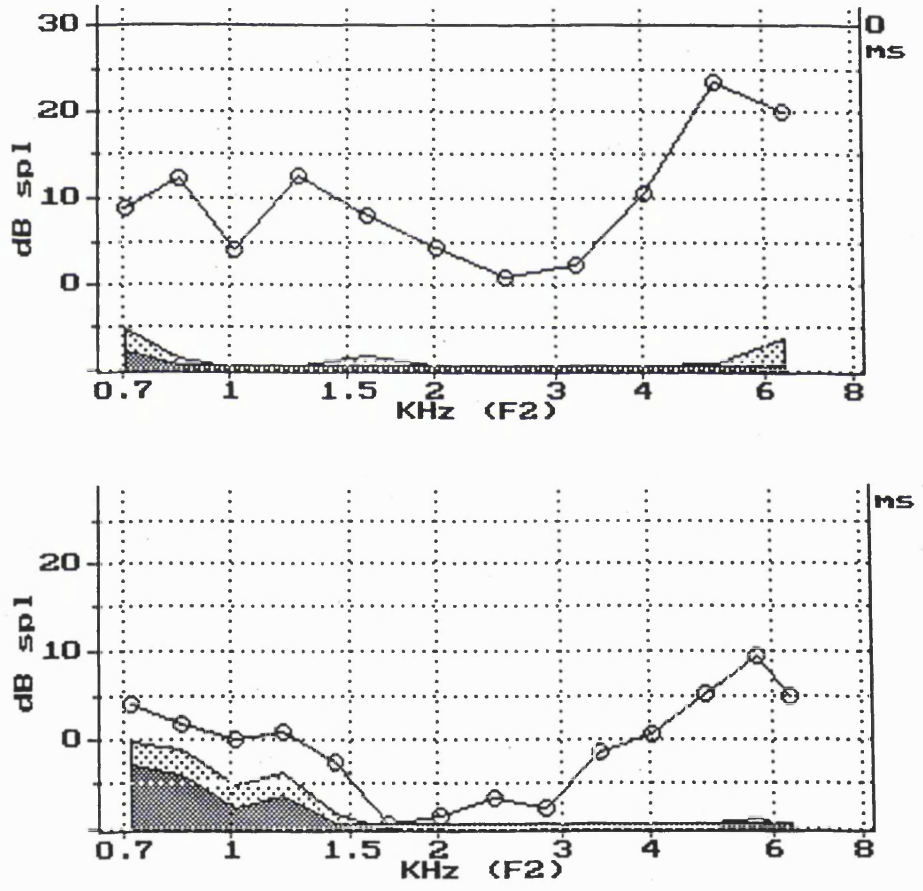


Figure VII.12

Case d: Distortion Products Otoacoustic Emissions

Distortion Product Emissions demonstrated reduced amplitude in the left ear (lower trace) in a frequency range similar to low amplitude click evoked emissions. The right ear (upper trace) showed normal amplitude distortion product emissions. DP Amplitude is plotted in dBSPL as a function of frequency of the f2 stimulus (kHz).



CHAPTER VIII

SUMMARY OF RESULTS

SUMMARY OF RESULTS

Statistical Comparisons between Normal Ears, Intact Ears, and Ears with OC Disruption

Multi-way analysis of variance with multiple comparisons was used to examine the interaction between three groups: 1) "Normal" ears, 2)"Control" ears with intact OC systems that were contralateral to surgery, or subject to surgery that did not section the OC system, 3)"OC Disrupted " ears with surgery or pathologies likely to sever or disrupt the OC system (from experimental and pathological groups). These groups were compared to contralateral stimulus level (0, 35, 45dBSL CAS), side (CEOAE from right or left ear) and gender (male or female). Data from each subject's audiometry, history, OAE and efferent tests are recorded in the Appendix (Tables A1 through A8.)

ANOVA analysis of first order effects between groups, level, side and gender showed that the groups were significantly different ($p<0.001$) and that there were significant differences with the level of contralateral stimulation ($p<0.001$). Thus, normals, controls and OC disrupted ears did not have similar levels of inhibition during contralateral stimuli from 0-45dBSL. Second order effects showed a significant difference between group and level ($p<0.001$), and between groups and gender ($p=0.033$). There were no significant third order effects between group, level, side, and gender. (See Statistical Analysis Table VIII.1 below.)

Multiple comparison analyses (Scheffe) analysed first, second and third order differences between group, level, side and gender. First order comparisons of group differences shows significant differences between the group of normal ears and the OCB disrupted ears ($p<0.001$). The group of control ears was also significantly different to the OC disrupted group ($p<0.001$). There was no significant difference between the normal and control group ($p=-15.98$). (See Statistical Analysis Table VIII.1.)

First order effects of differences in inhibition relative to contralateral stimulus level showed a significant decrease in mean inhibition levels between 0dBSL and 35dBSL ($p<0.001$), and a significant difference between 0dBSL and 45dBSL ($p<0.001$). At a level of 0.05 significance, there was a significant difference between 35 and 45dBSL ($p=0.012$).

Significant second order effects were noted between group and contralateral stimulus level, and between group and gender. There were no significant third order effects.

In normal ears, and in control ears, there was a significant increase in inhibition with contralateral stimuli of 35 and 45dBSL, compared with emissions in quiet (0dBSL) ($p<0.001$). Normal and control

ears did not show significantly more inhibition in 45dBSL than with 35dBSL respectively for each group.

This was not the case in OC disrupted ears, where no significant difference was observed between inhibition with 0dBSL, 35dBSL or 45dBSL. Normal and control ears were significantly different to OC disrupted ears with contralateral noise levels at 35dBSL and 45dBSL ($p<0.001$). However, OC disrupted ears at all levels (0, 35 and 45dBSL) were not significantly different from normal or control responses at 0dBSL. Thus, disrupted ears behaved similarly to normal / control ears in quiet.

Second order comparisons also revealed significant effects on inhibition with comparisons of group and gender. Analysis showed that the OC disrupted group was significantly different to the normal group ($p\leq0.001$). Control males and females were also significantly different to OC disrupted ears in males and females ($p=0.001$ and $p=0.004$). However, within each group, males were not significantly different to females. There were no significant third order effects.
(See Table VIII.1.)

Table VIII.1
Statistical Analysis

ANOVA: Normal, Intact, OC Disrupted Ears

Source	df	F	Prob>F
group	2	101.52	<0.001
level	2	94.66	<0.001
side	1	3.87	0.052
gender	1	1.77	0.187
group x level	4	13.45	<0.001
group x side	2	0.81	0.446
group x gender	2	3.56	0.033
level x side	2	0.63	0.537
level x gender	2	0.58	0.563
side x gender	1	0.01	0.924
group x level x side	4	0.17	0.953
group x level x gender	4	0.92	0.458
group x side x gender	2	1.02	0.363
level x side x gender	2	0.60	0.550

First Order Effects: Comparison of Inhibition by Group (Scheffe)

p value	Normal	Intact
Intact	1.000	
OC Disrupted	<0.001	<0.001

First Order Effects: Comparison of Inhibition by Level (Scheffe)

p value	0dBSL	35dBSL
35dBSL	<0.001	
45dBSL	<0.001	0.012

Comparison of Inhibition by Group and by Contralateral Stimulation Level (Scheffe)

		Normal			Intact			OC Disrupted		
	p value	0 dBSL	35 dBSL	45 dBSL	0 dBSL	35 dBSL	45 dBSL	0 dBSL	35 dBSL	45 dBSL
Normal	0 dBSL									
	35dBSL	<0.001								
	45dBSL	<0.001	0.066							
Intact	0 dBSL	1.000	<0.001	<0.001						
	35dBSL	<0.001	0.977	0.003	<0.001					
	45dBSL	<0.001	1.000	0.370	<0.001	0.898				
OC Disrupte	0 dBSL	0.941	<0.001	<0.001	0.966	<0.001	<0.001			
	35dBSL	0.900	<0.001	<0.001	0.961	<0.001	<0.001	1.000		
	45dBSL	0.963	<0.001	<0.001	0.997	<0.001	<0.001	0.516	0.358	

Comparison of Inhibition by Group and Gender (Scheffe)

		Normal		Intact		OC Disrupted	
	p value	male	female	male	female	male	female
Normal	male						
	female	0.912					
Intact	male	0.998	0.997				
	female	0.975	1.000	1.000			
OC Disrupte	male	<0.001	<0.001	0.001	0.001		
	female	0.001	0.001	0.004	0.004	1.000	

CHAPTER IX

DISCUSSION

DISCUSSION

This study investigated the utility of otoacoustic emissions as a means of observing efferent modulation of cochlear activity in humans. Further, it explored whether loss of olivocochlear innervation was associated with loss of otoacoustic emission modulation. A protocol was developed using contralateral acoustic stimulation to evoke olivocochlear activity. Responses from normal subjects demonstrated robust and repeatable inhibitory effects on otoacoustic emission amplitude. A site of lesion study was conducted, applying the protocol to patients with a variety of surgical or pathological lesions affecting the olivocochlear system, from the brainstem to the outer hair cells. The results from these cases were compared to control surgical and control pathological cases in whom the olivocochlear fibres remained intact. Methods to optimize the clinical measurement of efferent auditory dysfunction, and concepts about the functional significance of the efferent olivocochlear system are discussed.

Efferent Auditory Effects of the Olivocochlear System in Normal Subjects

In normal subjects, presentation of contralateral white noise was associated with inhibition of otoacoustic emission amplitude, and a phase lead of responses recorded during contralateral noise. Relative to emissions recorded in quiet conditions, emission amplitude was significantly reduced ($p<0.01$) with contralateral white noise stimulation >=25 dBSL. The data revealed that the magnitude of inhibition increased with increasing white noise intensity. These findings were reported (Williams 1992, Williams et al. 1993, 1994), and found to be consistent with human studies describing inhibition on transient, tone, spontaneous and distortion product emissions (Collet et al. 1990, 1992 Berlin et al. 1994, Berlin et al. 1993). This study found bilateral inhibitory effects in normal subjects, with minimal inter-aural difference.

The protocol chosen to measure inhibition was referenced in terms of the total change in otoacoustic emission response pressure across a 20 msec time period, including all frequencies falling within the effective recording bandwidth of the ILO system. Normal subjects demonstrated obvious inhibition of CEOAE amplitude from the middle portion of the recording time window. The magnitude of the measured effect was enhanced by time windowing between 4.5 (+/- 0.5) - 20 msec. This excluded middle ear artifacts that may occur within the initial portion of the waveform as a result of continued oscillations in the ear canal. The ear canal stimulus artifact should not change during olivocochlear activity, whereas the cochlear response should be inhibited by efferent. The averaging of such artifacts within the emission response would reduce the apparent magnitude of inhibitory effects. This study showed greater inhibition if the first 5 msec of the response waveform was excluded. Although delayed time window analysis yields lower otoacoustic emission amplitude, inhibition magnitude was slightly increased. These results, and the findings of others (Collet 1994, review, Prasher 1994),

suggest that simple windowing of the OAE response forms an effective yet simple means of measuring CEOAE inhibition. This method offers a clinically viable protocol, enabling rapid and immediate analysis of the results. Other protocols for measuring inhibitory effects have been demonstrated by Hood et al. (1993). They report maximal inhibition in the middle to later portion of the post- stimulus period (10 - 20 msec), using a system that analyzes the changes in otoacoustic emissions within rolling short time segments.

The intensity of the ipsilateral click stimuli was found to be an important parameter affecting the magnitude of the inhibitory effects. During protocol development, it was observed that in humans, efferent effects were greatest with click stimuli between 55 and 75 dBpeSPL, with lesser effects, and in some cases a total absence of inhibition at higher intensities (above 80 dBpeSPL). These findings have been confirmed in other human studies by Veuillet et al. (1996) and Lina-Grandade et al (1997) who found the largest suppression at lower stimulus levels, which were unrelated to the baseline amplitude of the CEOAE or their input / output function. Rajan (1983, 1990), Reiter & Liberman (1995), and Kujawa & Liberman (1999) note that the efferent system may also provide protection from intense noise stimulation. Input / output functions may reveal the interaction between efferent function at low to medium sound levels, intense sound levels, and for middle ear protection (Guinan 1996: review).

When considering clinical protocols, the balance between otoacoustic emission detection level, efferent effect detection level, and the optimal range for stimulating the efferent olivocochlear system in humans must be considered. The efferent auditory test is likely to be applied to patients who may have less robust otoacoustic emissions for a variety of reasons. Therefore, it would be prudent to develop procedures and clinical norms with click levels most likely to yield emissions with acceptable signal to noise ratios. This study found that click stimuli set below 65 dB were often insufficient to yield robust emissions, making emission detection and therefore efferent function detection difficult. Thus, despite the increased magnitude of efferent effects at lower stimuli settings, the findings suggested that click stimuli around 70dB pe SPL would be preferable to obtain robust otoacoustic emissions and robust inhibitory effects. This may provide the best starting point for the development of routine clinical protocols for efferent testing.

Higher click levels are associated with greater signal to noise ratios and improved reproducibility. However, this must be balanced against the saturation of efferent auditory effects at mid to high levels, the interaction of "passive" or high intensity functions, and the middle ear the auditory feedback systems. It may be that at low levels, the medial OCB efferents act to enhance signal detection in noise by reducing the response to background noise - or anti-masking (Kawase et al. 1993a, b). At mid to higher intensities, the medial OCB efferents may inhibit responses by adaptation (Guinan 1996: review). At higher intensity the OC system may re-set the operating point of the cochlear partition input / output function, conditioning the ear to resist noise damage. The middle ear provides an

additional protective auditory feedback system which decreases masking by reducing acoustic input before it reaches the cochlea (Guinan 1996). Clinical protocols, which utilize more than one level of ipsilateral click stimuli to obtain input / output efferent functions, may provide information regarding the rate of increase of inhibition. This could provide differential information about auditory dysfunction of these different synergistic systems, including ability to detect signal in noise, recruitment, and noise exposure damage or conditioning.

Careful choice of click and noise stimuli intensities is warranted to exclude the possibility of cross-masking of otoacoustic emission response, and to avoid elevation of the recording noise floor during the recording period. (Collet et al., 1990; Veuillet et al., 1991). Emissions with elevated noise floors should be excluded from analysis. Further, insert earphones are highly recommended to avoid erroneous measurements resulting from collapsed meati due to headphones (Mahoney and Luxon 1996).

Middle ear reflexes must be taken into account when setting efferent protocol. The stimuli (both efferent elicitor, and OAE elicitor) must be sufficiently low, or confounding effects from middle ear muscle inhibition will be combined with OCB inhibition.

Improvement in the signal to noise ratio of otoacoustic emissions can be achieved by use of a "non-linear" method which utilizes click stimuli of different intensities and polarity within each emission average to cancel artifacts and remove linear (non-cochlear) responses (Kemp et al. 1990). Inhibition of emission amplitude was observed in "non-linear" recordings from a pilot sample of normal subjects, and it may be a useful technique for low level stimuli (50 - 75 dB pe SPL) (Hood et al. 1996). However, the "non-linear" technique was not used in this study, as it would necessitate the averaging of inhibitory changes from two different levels of click stimuli, and two different polarities. Since inhibition was shown to vary as a function of click intensity level, this could result in the averaging of inhibition effects in the linear portion of the efferent dynamic range, with inhibition effects from the saturated portion of the dynamic range. This may result in an apparent reduction in the magnitude of inhibition. However, there would be value in defining the optimal click intensity range for use with the non-linear technique, as benefits would be gained from enhanced artifact rejection. Normal values would have to be established for non-linear and linear techniques and applied appropriately.

Cumulative increases in inhibitory effects over repeated otoacoustic emission recordings during alternating contralateral stimulation have been observed in guinea pigs (Sridhar et al. 1995, 1997). They noted a slow increase in the magnitude of inhibition of compound action potential responses occurring with a 25-50 second time constant, relative to the initial baseline recorded in quiet conditions. Such "slow efferent effects" may reflect the time course of intra-cellular second messenger metabolic system of the efferent neuro-transmitters which exceeds the rapid time frame of

the stimuli. Slow increases in the magnitude of efferent inhibition were observed in this study, during repeated recordings.

The role of attention and fatigue should not be neglected during clinical application of the test procedures. In several cases, loss of normal levels of inhibition was coincident with the onset of sleep, or visual distraction, and this observation was repeatable on several occasions. Following the loss of inhibition due to sleep onset, testing was stopped and then resumed after subjects were asked to direct their attention to the acoustic stimulus. It was found that inhibition returned to normal values. Other reports of the effect of sleep confirm the effect of attention on contralateral inhibition of otoacoustic emissions (Meric and Collet 1994 Review).

Clinical procedures should thus account for an attention component to the efferent auditory effects. Sleep, hyperactivity, visual, auditory or physical interruptions should be controlled, and data collected during such changes in attention should be excluded. The effects of general anesthesia or other medications should also be considered. Brookes et al. (1994) noted a change in emission amplitude during anesthesia, and animal studies suggest that efferent activity is not elicited with certain anesthetic agents. These findings add support to the role of attention in directing efferent olivocochlear effects.

Animal studies have shown that bilateral noise enhances the efferent effects (May et al. 1995), suggesting a synergistic relationship between the ipsilateral and contralateral efferents that improves signal perception in competing noise. These findings are consistent with anatomical data which show olivocochlear nerves response to bilateral acoustic stimuli (Guinan et al. 1996: review). Development of bilateral stimuli protocols may well be the most effective means of clinically measuring efferent auditory effects that are more closely related to natural physiological stimuli (Berlin et al. 1995). However, the presence of coincident noise interferes with recording OAE responses. A suitable alternative is to use of forward masking paradigms that take into account the timing of efferent activity in terms of fast and slow efferent effects. Of course, asymmetrical hearing dysfunction would have to be accounted for when incorporating bilateral stimulation into clinical tests.

Loss of Otoacoustic Emission Inhibition in the Absence of Olivocochlear Innervation

The study of patients before and after unilateral section of the vestibular nerve, which carries the efferent olivocochlear bundle, offers the most direct means for examining cochlear function in the absence of efferent control in humans.

During vestibular nerve section surgery the isolation of the vestibular nerves is assisted by observation of a fine septum between the cochlear and vestibular nerves in 75%-80% of patients. However there can be an intermingling of cochlear and vestibular fibers along the apparent line of division, with an overlapping zone occupying approximately 16 - 33% of the area of the cochlear subdivision (Schefter & Harner 1986, Natout et al. 1987). Warren and Liberman (1989) provided evidence of the efficacy of vestibular nerve section in interrupting the entire OCB in cats, as demonstrated by the lack of retrograde labeled neurons in the superior olivary complex following perfusion with horseradish peroxidase. It is not always possible to be certain that all of the inferior vestibular fibers or the entire efferent auditory bundle traveling within it, will be completely severed. However, a clear anatomical demarcation between the cochlear and vestibular nerves was apparent in the vestibular neurectomy patients at operation, and their vestibular symptoms improved.

Intra-subject comparison of responses before and after vestibular nerve section demonstrated that interruption of the efferent olivocochlear bundle resulted in a loss of inhibition of otoacoustic emission amplitude during contralateral noise stimulation. Pre-operative inhibitory effects were normal bilaterally. Post-operatively, however, the "de-efferented" ears showed a dramatic loss of inhibition, with minimal fluctuations of amplitude during noise. The responses from operated ears were more consistent with the responses observed in quiet conditions. In contrast, the intact ears maintained normal levels of inhibition after surgery, with post-operative measures being similar to pre-operative levels, and not significantly different to normal responses at equivalent levels ($p<0.01$).

Direct observation of the loss of CEOAE inhibition following neurectomy is consistent with observations from the post-surgical group of vestibular neurectomy patients reported in this study. The "de-efferented" ears in all post-neurectomy patients demonstrated abnormal inhibitory effects. The minimal fluctuations in emission amplitude observed during $\geq$35dBSL contralateral stimulation were significantly different to inhibitory responses found in normals ($p<0.01$). However, these fluctuations were not significantly different to the inter-test fluctuations of emissions observed in normal subjects in quiet conditions. In contrast, the patients' intact ears, taken as controls, were not significantly different to normal inhibition. Thus, all nerve section cases tested demonstrated abnormally low levels of inhibition of otoacoustic emissions in the operated ears, whilst maintaining normal efferent function in the intact ear. (Williams 1992, Williams et al. 1993, Williams et al. 1994). Philibert et al. (1998) demonstrated asymmetrical and inversely related uncrossed and crossed efferent effects related to handedness of the subject. Handedness was not examined in this study, and thus correlations regarding

asymmetries and OAE or efferent inhibition magnitude cannot be drawn. The magnitude of asymmetry of efferent inhibition between ears in subjects with disruption to the olivocochlear system was far greater than the inter-aural difference reported in normals (Khalfa et al. 1998). This data supports the conclusion that unilaterally abnormal inhibition of OAE reflects efferent dysfunction.

Neurectomy cases with normal pre and post-operative hearing levels are not common, but normal pure tone thresholds can be preserved after vestibular nerve section despite severance of the entire efferent olivocochlear bundle to the operated ear. This suggests that olivocochlear innervation is not essential for pure tone threshold function. This is consistent findings from physiological experiments which show that OCB fibres spontaneously fire above the threshold of the least sensitive nerve (Guinan 1996; review).

In the 3 cases with entirely normal post-surgical audiometric thresholds, the results revealed virtually no inhibition of otoacoustic emissions in the operated ears while the control (intact) ears maintained normal levels of inhibition. Thus, loss of inhibitory effects in the operated ear after neurectomy can occur even when pure tone thresholds are maintained. Findings were similar in the cases who maintained normal thresholds from 500 - 3000 Hz. Cases who displayed mild or moderate high frequency hearing loss also lacked inhibition in the operated ears, but maintained inhibition in the intact ears despite the loss. Collet et al. (1992) confirmed the presence of inhibitory effects in subjects with high frequency sensory neural hearing loss. It can be assumed that the impact of hearing loss below 500 Hz and above 3000 Hz is minimized when assessing inhibition via CEOAE amplitude measure (the bandwidth and roll-off of the emission recording system). Nonetheless, the possibility that an underlying pathology affected the responses cannot be excluded.

The possibility that section of the vestibular nerve resulted in cochlear ischaemia and hence efferent dysfunction should be considered. The vasculature supplying the cochlear and vestibular nerves is unlikely to be damaged during retrolabyrinthine surgery, although one could hypothesize that a local post-operative inflammatory effect following CPA surgery might occur (pers. comm. GBB). The presence of normal otoacoustic emissions are probably the most sensitive test of hair cell function that can be applied to human studies, and suggests that vascular damage is unlikely. Similar surgical procedures were carried out for vascular decompression cases with no loss of inhibitory function, suggesting that the loss of inhibitory effects in vestibular nerve cases were unlikely to result from ischaemia or inflammation.

Veuillet et al. (1992) considered the effect of conductive hearing loss on olivocochlear effects by altering middle ear pressure in the external ear canal. They show that changes in middle ear pressure exert greater influence on a different frequency range than the most effective range of olivocochlear stimulation. Their findings suggest that conductive changes are unlikely to interfere with the

contralateral inhibition of emissions providing that middle ear pressure is within the +/-200daPa range (Veuillet et al. 1992).

In this study, conductive hearing losses were minimal following vestibular nerve section (except for in one case where pressure was -95 to -170daPa). The studies of Robinson and Haughton (1991) suggest that middle ear pressure changes observed in this study would have insignificant effects on the measurement of efferent cochlear responses.

Olivocochlear fibres arise from the superior olivary complex, thought to be one of the primary neural generators of Wave III (Hill, et al. 1997, Prasher et al. 1982, Moffat et al. 1989). Brainstem function, as demonstrated by evoked auditory brainstem responses, were normal for most cases who maintained normal to mild pure tone threshold function. One case showed a slight delay in pre and post-operative Wave III latency. Large changes were not observed in the latencies or intervals of the evoked responses before or after vestibular nerve section surgery, except in one case with a moderate - severe post-surgical high frequency hearing loss. Yokata et al. (1994) found post-operative changes following vascular decompression surgery for trigeminal neuralgia, with a decrease in latency of Wave V of the contralateral ABR from the unaffected side, and a parallel prolonged latency in Wave V of the operated side. They suggested that damage to the efferent system resulted in loss of suppression of the contralateral responses.

It should be noted however, that whilst the entire olivocochlear bundle to the operated ear is severed as a result of the vestibular nerve section procedure, inter-aural innervation from olivocochlear fibres remains at the level of the brainstem. A small number of fibres form a collateral path from the olivocochlear bundle within the vestibular nerve root to innervate the cochlear nucleus (Guinan 1996: review). Thus, it is possible that tests at the level of the cochlea will show a complete loss of efferent effects, whilst tests of auditory function at the level of the brainstem or higher centres might still reflect the involvement of olivocochlear collaterals. The possibility that these remaining collateral efferents adapt to compensate for the loss of peripheral efferent control should be considered. The collateral fibres may provide an inhibitory function after the uninhibited responses from the cochlea arrive at the cochlear nucleus. This anatomical arrangement may explain, in part, the variability in responses to psycho-acoustic tests reported in the literature. It may also explain the resolution of noise sensitivity noted by the patients in this study, who reported hyperacusis immediately following vestibular nerve surgery. Behavioural and psycho-acoustic tests beyond the scope of this study would offer fascinating information regarding the difference between efferent function at the peripheral and brainstem levels.

Experimental Control Patients

Retrolabyrinthine Surgical Procedures

Control data was provided by the study of subjects who had undergone surgical procedures for vascular decompression of the vestibulo-cochlear nerves. The surgical approach was similar to the vestibular nerve section procedure, but without severing the OCB. Efferent tests conducted before and following surgery, assessed the affect of general anesthesia, intra-operative noise and drilling, opening of the CPA, neural movement and compression, alterations of the mastoid, and possibly ischaemia or oedemia on efferent auditory effects. The absence of central abnormalities were confirmed with evoked auditory brainstem responses, vestibular assessment and radiography. These patients demonstrated bilateral inhibition of CEOAE pre and post-surgically. The magnitude of inhibition was not significantly different from normal mean responses at all contralateral noise levels (Williams et al. 1994). Giraud et al. (1995) found similar results in subjects who had undergone facial nerve decompression for hemifacial spasm using a retrolabyrinthine approach to move the vascular loop.

Whilst it is possibile that aetiologies other than vascular compression were involved, normal efferent effects were observed in the cases studied, both before and after surgery. The findings suggest that the lack of contralateral inhibition observed in vestibular nerve section patients need not result from surgical effects, and suggest that loss of cochlear inhibition following nerve section was related to the loss of olivocochlear innervation.

Presence of Efferent Effects in the Absence of Middle Ear Muscle Reflexes

Middle ear reflexes alter the admittance of the tympanum in response to ipsilateral or contralateral pure tones at intensities ranging from 75 - 100 dB HL in normal hearing subjects (Katz 1994). If the contralateral noise during the efferent test procedures was sufficient to stimulate the middle ear reflex, it is possible that the muscular reflex could alter the amplitude or frequency of sound transmission through the middle ear. This could cause decreased intensity of the click stimuli received at the stapies, or affect the reverse transmission of the otoacoustic emissions through the middle ear structures.

The possibility that contralateral efferent auditory effects resulted from activation of the middle ear reflexes was considered. Patients with unilaterally absent middle ear reflexes following surgical section of the middle ear muscle tendons for treatment of myoclonus were tested. In these patients, bilateral inhibition of otoacoustic emissions were maintained following surgery. These findings suggest that inhibitory effects are unlikely to be mediated by middle ear muscle activity.

These findings confirm other investigations which demonstrated the persistence of inhibitory effects on otoacoustic emissions in subjects with pathological loss of the acoustic reflex due to Bells palsy (Collet

et al. 1990, Veuillet et al, 1991). Their comparison between normal subjects and patients without acoustic reflexes, showed no difference between the two groups except for a slightly stronger suppressive effect (Giraud et al. 1995). A stronger efferent effect was also noted in this study at lower contralateral levels (15-25 dBSL). In Giraud et al.'s study (1995), the muscles to the tensor tympani remained intact, and might have contributed to the responses. In contrast, in this study, patients had both stapedial and tensor tympani muscles sectioned. The increased magnitude of inhibition observed may reflect the relationship between the olivocochlear and middle ear reflex systems. Perhaps the loss of middle ear reflexes resulted in increased acoustic input to the cochlea, providing more intense stimuli to the efferent system, resulting in greater efferent auditory effects.

To avoid middle ear muscle activation in all subjects, the protocol utilized noise and OAE stimuli at intensities below measured reflex thresholds for ipsilateral clicks and contralateral noise. The criterion for detection of threshold was set to the minimum sensitivity of the immitance device, a more stringent criterion than used in diagnostic testing. However, one cannot entirely exclude the possibility that the muscles were active at levels below the thresholds measured using standard tympanometric devices.

Data from the vestibular nerve section patients also argue against the theory that contralateral inhibition of otoacoustic emissions is mediated by acoustic reflexes. Results from vestibular nerve section patients with *intact acoustic reflexes* which showed *negligible suppression* after olivocochlear section, diminishes the possibility that the efferent effect was mediated solely via the middle ear muscles. In one case, acoustic reflex thresholds improved slightly following vestibular nerve section (becoming more sensitive at some frequencies). If middle ear muscle activity was the source of inhibition, then one might expect to observe greater inhibition in this case where the middle ear reflex system had become more sensitive. Instead, minimal inhibition was observed in the de-efferented ear.

In summary, it was found that interruption of the olivocochlear pathway via vestibular nerve section was associated with lack of inhibition of otoacoustic emission responses in the operated side. Further, section or surgical manipulation of the internal auditory canal, VII or VIII nerves, or middle ear musculature which left the inferior vestibular nerve and olivocochlear bundle intact, were not associated with loss of inhibitory effects. The findings support the contention that otoacoustic emission inhibition associated with contralateral acoustic stimulation is related to efferent olivocochlear activation (Williams 1992, Williams et al. 1992, Williams et al. 1993, Williams et al. 1994).

Pathologies of the Olivocochlear Pathway

Efferent tests were applied to patients with lesions of neuro-otological sites that fell along the olivocochlear pathway, from brainstem to cochlea. The sensitivity of the efferent tests for detecting olivocochlear dysfunction was supported by the study of a case with bilateral lesions of the olivary nuclei. Bilateral loss of efferent effects was observed. The right ear, which displayed the greatest audiometric and evoked brainstem abnormalities, revealed a complete loss of inhibitory effects. The left ear, which was abnormal to a lesser degree, also displayed lack of inhibition of overall OAE response, although some inhibition in otoacoustic emission amplitude was noted in the 1-1.5 kHz frequency band alone. In this subject, unlike the unilateral vestibular nerve section cases, all olivocochlear innervation to both ears may have been lost, including the MOC, LOC and fibres traveling to the cochlear nucleus. Interestingly, this patient also had a mild to moderate bilateral hearing loss across the frequencies (30-55 dBHL). One could speculate this resulted from complete loss of efferent information to the outer-hair cells, which may be essential for hearing up to 40dBHL. Of course, the precise site of lesion and the full extent of functional disruption are extremely difficult to ascertain. Even in the case of discrete lesions of the olivary nuclei, it must be recognize that both the afferent as well as efferent auditory pathways could be disrupted.

The case presented in this study who had a CPA meningioma provided evidence of the sensitivity of the efferent test to central disruption. This fascinating case showed a functional cochlea with normal levels of click evoked and tone evoked emissions, in the presence of a large epidermoid cyst and abnormal central auditory evoked potentials. Following successful surgical removal of the cyst, hearing did not improve in the ear ipsilateral to the cyst, despite maintenance of normal click and tone evoked OAE. Return of hearing is an extra-ordinarily rare occurrence following surgery of the cerebello-pontine angle, though it has been reported (Farrell et al. 1991).

Berlin et al. (1993, 1994) note the absence of efferent auditory effects in patients with central neural disorders. They note the test's utility in distinguishing hair cell deafness from nerve deafness, and identify patients with absent efferent function in association with auditory neuropathy or desynchrony of the primary afferent nerve system, who also have difficulty discriminating speech in competing noise (Hood 1999, Berlin 1993, Starr et al. 1996). Absent or abnormal ART, ABR and efferent auditory effects in the presence of normal OAE are essential diagnostic indicators of "auditory neuropathy" (Starr et al. 1996). Cochlear microphonic (CM) oscillations during the initial two milliseconds of the ABR are observed in neuropathy cases by comparing ABR recorded with opposing polarities.

In contrast to auditory neuropathy cases, all but two of the vestibular nerve section and vascular decompression cases described here displayed acoustic reflexes in the normal range. Of those with elevated ART, one had a mild mixed hearing loss with an air-bone gap of 10 to 15 dB. The other

patient had a sensorineural hearing loss post-operatively, consistent with elevated ART. This patient also had delayed ABR in the affected ear. The other vestibular nerve section cases had normal auditory brainstem responses except for two cases, who had early Wave I's, with concomitant slightly prolonged I-III or I-V interval above clinical norms. Three patients had early contralateral III, with concomitant prolonged III-V intervals. The ABR recorded in this study used averaged alternating polarity responses, and no obvious CM oscillations were observed.

Neuropathy indicators were not obvious in the pathology cases studied. The case with olivo-ponto-cerebellar degeneration had normal acoustic reflexes thresholds. The case with a large cerebello-pontine angle lesion had present OAE, absent efferent effects, and unilaterally absent acoustic reflexes. However, his clearly present central lesion, and complete unilateral deafness makes his profile unlike the "neuropathy" cases (Starr et al. 1996). Both noise-exposed cases and the case exposed to ototoxic medication had normal ART, and thus could not be considered a neuropathies.

Efferent tests may prove useful in detecting central auditory dysfunction. Patients with unilateral acoustic neuromas could offer insight as to the extent of the swelling on the schwannoma of the vestibular nerve, as indicated by secondary disruption of the olivocochlear system (Baguley et al. 1997, Prasher et al. 1995). The efferent test may not be able to differentiate between the possible causes of dysfunction, though Prasher et al. (1994) found absence of efferent effects to be related to the size of lesion, with extrinsic and intrinsic sites related to whether absence of efferent effects were unilateral or bilateral

Efferent auditory effects may also provide useful information as part of a differential diagnostic battery of tests. In this study, patients were examined who had difficulty hearing in background noise despite normal pure tone thresholds. These cases had been exposed to noise that was likely to have damaged the "effectors" of the olivocochlear reflex arc, the outer hair cells. These subjects had unusual spectral representations of their CEOAE, and abnormal efferent inhibition.

Efferent tests have been shown to be sensitive to ototoxic damage at lower concentrations than those found to include permanent alterations in hearing threshold (Perry & Smith 1996). Efferent tests may thus provide an effective test for cochlear / hair cell damage, or for monitoring medical therapy with ototoxic medications. In this study, one patient with hyperacusis had taken large doses of quinine. This may have been related to her asymmetrical CEOAE responses, despite symmetrical pure tone thresholds. At the time of efferent testing, the patient's threshold had returned, and inhibition was normal.

Whilst extensive studies of the mammalian olivocochlear system have been conducted, our knowledge of the role of the olivocochlear feedback system in humans has been limited. Earlier human studies relied almost solely on behavioural psycho-acoustic tests following vestibular nerve section (pure tone and Bekesy audiometry, SISI, speech reception and discrimination tests), and failed to reveal a loss of function imputed to the efferent system. (Fisch 1970) A review of the literature revealed that most neurectomy patients maintain pure tone and speech threshold relative to preoperative levels (53 - 86 %), whilst up to 27% have worse pure tone scores, and up to 32% have worse speech scores. (McElveen et al. 1988, Wazen et al. 1990). Interestingly, most of the authors reviewed report a small proportion of patients whose pure tone (9 - 16%) and speech test (13 - 28%) improve post-operatively. Fisch (1970) observed that discrimination improved with a concomitant disappearance of the recruitment phenomenon, although this might have been attributed to the loss of tinnitus, but he was not able to detect any consistent postoperative change in cochlear function.

In this study, 3 vestibular nerve section patients reported post-surgical changes in hearing, in the absence of significant pure tone threshold change. Following vestibular nerve section, the auditory symptoms most often reported included difficulty in hearing conversation in a noisy environment, and a crackling tinnitus. One case reported shortly after surgery, that previously acceptable levels of traffic noise were "over-whelming". This suggests that the "de-efferented" auditory system may have had difficulty in suppressing the cochlear response to background noise. It is interesting to speculate whether central compensation via the remaining efferent fibres to the cochlear nucleus were responsible for her subsequent post-surgical compensation.

The contralateral presentation of noise allows a viable means of using clinically available emission equipment to activate the efferent system. Micheyl & Collet (1996) note that contralateral suppression of emissions correlated with behavioural detection thresholds in response to 1 and 2kHz tone pips in noise. Micheyl et al. (1995) found a significant correlation with detection threshold of a multi-tone complex stimulus in contralateral noise, suggesting the role of the OCB in detecting signals in noise.

However, unilateral contralateral noise with click or tone stimuli in the ipsilateral ear, is not a natural sound condition. It is reasonable to assume that physiological activation of the efferent auditory system would comprise bilateral transient signals occurring in the presence of bilateral noise. As previously noted, the medial olivocochlear complex provides both ipsilateral and contralateral innervation to the outer hair cells of each ear, and could thus produce bilateral responses to such stimuli. Indeed, noise stimulation to both ipsilateral and contralateral ears enhance efferent auditory effects on neural responses in animals (Liberman 1988, Kawase et al. 1993, May 1995). Kawase et al. 1993 conclude in their study on cats, that in continuous background noise, the olivocochlear reflex

enhances responses to transient stimuli as it suppresses the responses to steady background noise (anti-masking).

In human studies, Kawase and Takasaka (1995) found anti-masking of compound action potentials in normal subjects. The responses from patients with absent acoustic reflexes (as a result of facial palsy) were not significantly different to the normal group, suggesting that the phenomena was not solely a result of middle ear activity. Berlin et al. (1993, 1994) noted absent efferent function in association with afferent nerve desynchrony and difficulty in discriminating speech in competing noise. Zeng et al. (1994) demonstrated that after vestibular neurectomy, the operated ears' ability to detect a tone at the onset of noise presented bilaterally was significantly reduced (overshoot effect). They also demonstrated that intensity discrimination in noise was significantly worse in the operated ear, and that speech recognition in noise required higher than normal signal to noise ratio in some subjects, but not others (although hearing loss may have affected these results). Scharf et al. (1994, 1997) also report a reduction in overshoot in their post-neurectomy subject, although they did not investigate enhancement during bilateral broad band noise.

If the natural physiological stimuli for efferent activation are supra-threshold transients in the presence of bilateral background noise, it may explain the lack of change in threshold function following OCB section that has been reported here and in Scharf et al.'s study (1994, 1997). Micheyl et al. (1997) note an efferent role in intensity discrimination in dichotic noise. Elevation of threshold with loss of tuning was observed in neonatal cats after 1 year of de-efferentation, but with minimal hair cell loss. It is possible that the efferent system is critical in the early development of the active cochlear response yielding thresholds up to about 40dBHL.

Several studies have reported the loss of ability to detect signals in noise following OCB disruption. (Scharf et al. 1994, 1997, Zeng et al. 1994, Kawase et al. 1995). Scharf et al. (1994) noted a marked improvement in detection of unexpected signals in noise, reflecting impaired selective attention (i.e. the patient responded to an abnormally wide frequency range of unexpected stimuli, compared to his pre-surgical responses and to normals).

If a role of the olivocochlear system is related to the ability to focus selectively on a particular frequency region when attempting to detect signals in noise (Scharf et al. 1997, Micheyl & Collet 1996), then the role of attention becomes more relevant when considering the performance of the efferent system under clinical test conditions (Meric & Collet 1994 a, b). Froehlich et al. (1993) demonstrated the influence of visual and auditory attention on evoked emission responses, with visual effects predominant at 960-1920 Hz, and auditory effects of attention at 1920-2880 Hz. However, Micheyl et al. (1996) found that simple attention switches between fixed auditory objects do not support active cochlear involvement in selective attention. Thus, the role of attention should not be

overlooked in protocol design or test execution. In addition, the importance of attention effects should be taken into account when comparing human findings with the results of anaesthetized animal studies of de-efferentation.

It is possible that the olivocochlear system has been preserved in mammalian species in order to provide a pathway for central control of both cochleae. Given recent psycho-acoustic and electrophysiologic data, it is interesting to speculate that the central system uses the efferent feedback system, enhanced by an attention component and slow cumulative effects over time, to facilitate detection of signals in the presence of bilateral noise, by regulating cochlear micro-mechanics to modify response amplitudes. Clearly, the role of the olivocochlear bundle in humans is deserving of further study, and its relation to central masking phenomena should be explored. It is also interesting to speculate about the role of the remaining OCB collateral fibres that run from the olivary nuclei to the cochlear nucleus. It is possible that the collateral efferents play a role in central masking.

Efferent / Cochlear Mechanism

The mechanism by which contralateral acoustic stimulation inhibits OAE amplitude is thought to involve activation of the medial efferent system innervating the outer hair cells. As the OHC are coupled to the tectorial and basilar membranes, efferent induced changes in the frequency, phase or amplitude of their movement, could affect the movement of the cochlear partition, thereby modifying the local mechanical input to the sensory hair cells in a frequency specific manner. In addition, a change in the electrical environment, induced within or external to the hair cells as a result of release of the efferent transmitter, could alter the potential differences across other hair cell membranes, and hence modify the potential driving forces controlling outer hair cell motile responses and afferent response (Ashmore, 1994, Guinan 1996). Nadol and Burgess (1994) found supra nuclear innervation of the outer hair cells and Dieter cells apparently derived from the olivocochlear system. Recent observations which show the cuticular plate to be composed in part of actin / protein compound (Slepecky 1996, p.91) may suggest that the efferent system alters the set position of the cuticular plate, and thereby alters the shear input to the stereocilia. Murugasu and Russell (1996), using laser diode interferometery, found that OCB activity changes the gain of outer hair cell motility without changing the stiffness or position of the basilar membrane, but it does not broaden the tuning curve function, or cause a phase change. However, perfusion with acetylcholine was observed to change the phase of responses (Russell pers. com.). Thus it has been suggested that efferent fibres and the associated OHC and structures alter receptor cell responses via mechano-electrical feedback induced by release of efferent neuro-transmitters (Ashmore 1994).

The question has arisen whether the efferent system has a tonic function on cochlear responses. Liberman and Brown (1986) note that in animal studies olivocochlear neurones rarely exhibit

spontaneous activity. However, the natural environment is rarely as quiet as the threshold of hearing, and would continually provide stimuli that could activate the efferent system. Therefore, continual efferent control may exist, whether it be "tonic" or evoked. If the primary function of the medial efferents is inhibitory, one might expect loss of tonic efferent function to result in a concomitant increase in the amplitude of otoacoustic emissions. In humans, Brookes et al. (1994) noted an increase in OAE baseline during surgical procedures. Kakigi et al. (1997) observed an increase in amplitude of emissions above 2kHz in chinchilla following section of the crossed OCB. It is possible that this increase in amplitude was a consequence of increased spontaneous emissions due to the loss of inhibitory efferent feedback, as observed in disinhibition reported by Ceranic, et al. (1998). Moulin et al. (1993) demonstrated that spontaneous emissions influence the amplitude of click evoked responses. However, spontaneous emissions per se were not measured by Brookes et al. (1994), or in this study.

Behavioural results offer some information in this regard. Interestingly, one patient in this study showed that the transection of the olivocochlear bundle following vestibular nerve section was associated with an improvement in pure tone audiometry, but without hyperacusis. Two vestibular nerve section patients reported hyperacusis or increased sensitivity following surgery. Increased threshold sensitivity has been occasionally reported in the literature in a small (<20%) proportion of post neurectomy cases (McElveen et al. 1988; Silverstein et al. 1990; Wazen et al. 1990). However, increased sensitivity was not coincident with obviously large emissions. OAE recorded following vestibular nerve section were of normal to low amplitude, and not suggestive of the undamped oscillations which may be presumed to result from a loss of tonic negative feedback, or from increased spontaneous emissions. Low amplitude emissions were observed in additional studies of vestibular nerve section cases (Hine et al 1997, Giraud 1995). Tewary et al. (1998) found a slow deterioration of hearing levels in 25 vestibular nerve section cases, with an average of 7dB after 2 post-surgical years, and a total decline of 29dB over the course of 20 years. It is possible that the underlying disorder or loss of efferent innervation was involved, in addition to expected changes from presbyacusis. However, the role of the lateral efferents, which may provide a positive feedback control, should be considered. If this were the case, vestibular nerve section would result in the loss of both excitatory and inhibitory feedback control, which could lead to a diminution of OAE amplitude. Such complexity should be taken into account when considering the role of the efferent auditory system.

CHAPTER X

CONCLUSION

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This study examined whether acoustic activation of the contralateral olivocochlear system results in measurable efferent auditory effects on otoacoustic emission responses. The effect of surgical disruption of the olivocochlear system on efferent auditory effects was also investigated.

The results from the sample of normal hearing subjects suggested that the intact olivocochlear efferent system acts to significantly inhibit the amplitude of cochlear micro-mechanical responses during alternating contralateral noise conditions above 20 dB SL ($p<0.001$). These robust and repeatable inhibitory effects were present bilaterally. Detailed investigation of a variety of stimuli and response parameters were conducted in order to gain information about the dynamic range of human efferent olivocochlear function.

Pre and post operative comparisons of efferent effects were conducted on patients with unilateral section of the olivocochlear bundle as a result of vestibular nerve section. Results revealed that complete section of the medial and lateral olivocochlear fibres to one cochlea was associated with unilateral loss of OAE inhibition in the operated ear. The loss was statistically significant from pre-operative measures and from normal subjects ($p<0.001$). Post-nerve section inter-aural comparisons demonstrated a significant loss of inhibitory effects in de-efferented inner ears relative to the intact (un-operated) inner ears ($p<0.001$). The findings confirm initial studies that demonstrated minimal inhibition in the post nerve section ears (Williams et al. 1993, 1994). The experimental findings support the conclusion that disruption of the olivocochlear fibres is associated with a loss of inhibitory effects on otoacoustic emissions.

Control information was provided by the study of surgical patients who underwent neuro-otological surgery but without section of the olivocochlear bundle. Patients who had undergone similar retrolabyrinthine surgical procedures for vascular decompression of the cochlear or vestibular nerves, but leaving the efferent fibres intact, demonstrated no significant changes in inhibition of otoacoustic emissions. Bilateral inhibitory effects were observed in these patients preceding and following surgery, and the magnitude of the efferent auditory effect was not significantly different to normal subject responses. Observations in patients who maintained normal levels of inhibition following unilateral section of the tendons of the middle ear muscles for the treatment of unilateral middle ear myoclonus. The results indicate that the middle ear reflex system is not essential for the production of inhibitory effects. The presence of bilateral inhibitory effects in these surgical control cases suggest that the unilateral loss of inhibitory effects in the vestibular nerve section cases need not be imputed to either the effects of surgery or loss of middle ear reflex function.

Application of the efferent auditory tests to a neuro-otological patient population revealed that the responses from patients with lesions affecting the olivocochlear nuclei or the path of innervation of the olivocochlear system, were sensitive to the efferent test procedures. An absence of inhibitory function was observed with lesions of the olivary nuclei (olivo-ponto-cerebellar degeneration) and meningioma of the cerebello-pontine angle. Although precise definitions of the aetiology, exact sites of disruption or extent of metabolic dysfunction were not possible in the pathological cases reported, continued efferent studies may provide data on the correlation between the extent of damage and the loss of feedback function.

The study provided support for further consideration of efferent auditory tests as a component of a neuro-otological test battery of brainstem or cochlear function. The test may offer useful information to track the progression of pathologies affecting the vestibular nerve (such as acoustic neuromas), in which the olivocochlear bundle travels before reaching the cochlea. It may also provide sensitive and early indication of disruption to the outer hair cell and cochlear mechanisms that are vulnerable to ototoxia, ischaemia and noise exposure. Further test development is necessary to differentiate between sites of lesion along the olivocochlear pathway, and may rely on the correlation of results from a battery of audiological tests. It will be important that the test protocols are standardized and evaluated with regard to the role of attention. Validation of the otoacoustic emission tests as an indicator of efferent auditory dysfunction will enable the correlation between loss of olivocochlear function and the its function. Future studies will provide the basis for understanding the role of the olivocochlear system in humans.

XI. REFERENCES

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XII. APPENDIX

Appendix Table A.1. Audiometry

Condition	Case	Age	Site of Lesion	Pre or Post Op	Ear	Pure Tone Audiometry 250	500	1000	2000	3000	4000	6000	8000	PTA AVE	IMPANOMETRY Press	Compl	ART Rec	Ipsi Stim	1000	2000	click	Contra Rec	Stim	1000	2000	Contra BBN
VNS	I	43	L	pre	L	20	20	10	10		15		10	13	0	0.3	L	L	80	80		L	R	100	85	
				pre	R	15	20	15	10		20		10	15	10	0.5	R	R	75	85		R	L	95	90	
			L	post	L	15	15	0	-5		10		15	3	-45	0.5	L	L	80	75		L	R	95	90	
				post	R	15	10	10	0		5		5	7	-10	0.6	R	R	75	85		R	L	85	80	
	V	37	R	pre	R	10	5	0	5		5		10	3	0	0.6	r	r	90	95		r	l	100	100	
				pre	L	5	0	0	0		0		0	0	5	0.5	l	l	85	85		l	r	90	85	
				post	R	15	5	5	5		15		10	5	15	0.4	r	r	90	90	90	r	l	95	100	90
				post	L	10	5	0	0		0		5	2	10	0.4	l	l	85	85	80	l	r	80	85	80
	VI	47	L	pre	L	15	5	5	5		30		40	5	0.5	0.3	L	L	80	95		L	R	85	85	
				pre	R	15	5	5	10		20		35	7	0.5	0.3	R	R	85	90		R	L	85	90	
				post	L	35	25	10	10		45		50	15	1	0.4	L	L	95	90	105	L	R	100	100	85
				post	R	10	0	0	5		30		40	2	5	0.3	R	R	75	80	90	R	L	85	80	75
	VII	43	L	pre	L	5	5	20	10		5	20	35	12	5	0.3	L	L	85	80		L	R	85	85	
				pre	R	15	15	15	15		15		20	15	5	0.3	R	R	80	80		R	L	80	80	
				post	L	25	25	30	35		100		85	30	-15	0.3	L	L	>110	>105	>110	L	R	90	95	85
				post	R	20	20	15	20		15		20	18	-20	0.5	R	R	85	80	90	R	L	>115	>100	>115
	VIII	46	L	pre	L	25	15	15	20		25		35	17			L	L								
				pre	R	20	15	15	20		30		30	17			R	R								
				post	L	10	10	5	10	10	10	35	35	8	15	0.7	L	L	95	90	100	L	R	90	90	80
				post	R	5	0	5	5	5	5	30	20	3	10	1.4	R	R	95	85	100	R	L	95	85	80
	II		L	pre	L									0			L	L								
				pre	R									0			R	R								
				post	BC		20	15	20		30															
				post	L	35	30	30	25		40		35	28	-95	0.6	L	L	90	95		L	R	105	110	95
				post	R	25	15	15	10		15		10	13	-170	0.9	R	R	95	100		R	L	110	105	85
	IV	41	R	pre	R	15	15	10	10		5	15		12			r	r								
				pre	L	15	10	5	5		0		15	7			l	l								
				post	BC		-5	0	10		15															
				post	R	30	25	30	30		45	50	55	28	-65	0.2	r	r	100	95	105	r	l	100	100	85
				post	L	15	5	10	5		10		15	7	-10	0.5	l	l	90	90	100	l	r	95	90	85
	III	32	R	pre	R																					
				pre	L																					
					BC																					
				post	R	70	60	45	35		40		65	47												
				post	L	15	10	5	15		10		10	10												

Appendix Table A.2. Audiometry

Condition	Case	Age	Site of Lesion	Pre or Post Op	Ear	Pure Tone Audiometry 250	500	1000	2000	3000	4000	6000	8000	PTA AVE	IPANOMETRY Press	Compl	ART Ipsi Rec	Stim	1000	2000	click	Contra Rec	Stim	1000	2000	BBN
VOC	a	39	R	pre	R	0	0	0	10		0		5	3	5	0.4	r	r	85	85		r	r	90	90	
				pre	L	5	-5	-5	0		0		10	-3	10	0.5	l	l	85	85		l	l	95	95	
				post	R	10	5	5	15		5		5	8												
				post	L	5	5	0	10		0		15	5												
				pre	R	10	10	10	5		15		10	8	-15	0.6	r	r	80	75		r	r	90	85	
VOC	b	28	R	pre	L	15	10	5	5		5		0	7	-40	0.7	l	l	75	80		l	l	90	90	
				post	R	20	10	10	0		5		10	7	-35	0.4	r	r	85	80		r	r	90	90	
				post	L	15	0	-5	-10		0		-5	-5	-25	0.4	l	l	80	85		l	l	90	85	
				pre	L	5	5	5	15		25		25	8												
VOC	c	41	L	pre	R	5	5	5	0		15		15	3												
				post	L	15	10	5	10		40		45	8												
				post	R	5	0	5	5		15		20	3												
MEM	x	32	R	pre	R	5	5	0	-5		5		10	0	10	0.8	r	r	95	90		r	l	85	85	
				pre	L	0	0	5	0		0		5	2	5	0.4	l	l	85	85		l	r	90	95	
				post	R	5	0	5	0	0	5	15	15	2	-15	5	r	r	NR	NR		r	l	NR	NR	
				post	L	5	5	0	0	0	0	10	5	2	0.5	0.5	l	l	85	85		l	r	85	85	
MEM	y	35	L	pre	L	5	5	15	20	15	20	25	35	13												
				pre	R	20	20	25	25	20	25	10	15	23												
					BC		20	25	30																	
				post	L	10	5	15	25		10		15	15	0	1.8										
				post	R	35	35	35	40		20		20	37	0	1.3										
OAD/NIHL	e	30		pre	R																					
				pre	L																					
				post	R	10	5	5	5	5	5	10	10	5	25	1.4	r	r	90	95		r	l	100	90	
				post	L	15	10	15	5	5	10	15	10	10	55	1	l	l	100	100		l	r	100	100	
OAD/NIHL	d	27		pre	R																					
				pre	L																					
				post	R	5	5	10	5		10		15	7	10	1	r	r	90	95	75	r	l	90	90	85
				post	L	10	5	5	5		10		10	5	5	1.8	l	l	95	95	70	l	r	95	90	70
OTOTOX	z	23	R>L	pre	R																					
				pre	L																					
				post	R	5	0	5	0	-5	-5	5	-5	2	5	0.6	r	r	80	90		r	l	85	85	
				post	L	5	5	0	-10	-10	0	-5	-5	-2	-5	0.7	l	l	80	85		l	r	90	90	
CCB	g	43	R>L	post	R	30	30	30	20		30	55	85	27	-45	1.3										
				post	L	20	25	15	10		30		25	17	-15	0.5										
				Oct-92	R	30	25	35	30		35		70	30			r	r	80	85		r	l	95	90	
				Oct-92	L	30	25	25	25		45		30	25			l	l	75	75		l	r	85	85	
CPA	f	43	R	Dec-91	R	>80	>90	>120	>120		>120		>120	>110	5	0.6	r	r	nr	nr		r	l	90	90	
				Dec-91	L	0	5	-5	0		15		20	0	-10	0.6	l	l	85	85		l	r	nr	nr	

Appendix: Table A.3 Auditory Brainstem Responses

CLINICAL NORMS

	Biologic	1.23-1.69	3.41-3.69	5.20-5.74	1.60-2.40	1.40-2.20	3.6-4.4	<0.4							
	Medelec	1.30-1.90	3.30-4.10	5.20-6.00	1.60-2.40	1.40-2.20	3.6-4.4					3.30-4.10	5.20-6.00	1.40-2.20	

Case	ABR Rec	Ipsi Stim	I	III	V	I-III	III-V	I-V	ILD - V (R-L)	Contra Rec	Stim	III	V	III-V	Case
i	Pre														
	R	R	1.36	3.56	5.68	2.20	2.12	4.32		R	L	3.48	5.80	2.32	i
	L	L	1.44	3.68	5.80	2.24	2.12	4.36	-0.12	L	R	3.52	5.72	2.20	
	Post														
	R	R	1.48	3.50	5.62	2.02	2.12	4.14							
	L	L	1.42	3.68	5.74	2.26	2.06	4.32	-0.12						
v	Pre														
	R	R	1.32	3.84	5.76	2.52	1.92	4.44		R	L	3.12	5.64	2.52	v
	L	L	1.40	3.84	5.60	2.44	1.76	4.20	0.16	L	R	3.92	5.80	1.88	
	Post														
	R	R	1.46	3.76	5.74	2.30	1.98	4.28							
	L	L	1.40	3.64	5.70	2.24	2.06	4.30	0.04						
vi	Pre														
	R	R	1.40	3.36	5.48	1.96	2.12	4.08		R	L	3.30	5.56	2.26	vi
	L	L	1.44	3.44	5.60	2.00	2.16	4.16	-0.12	L	R	3.36	5.56	2.20	
	Post														
	R	R	1.40	3.44	5.44	2.04	2.00	4.04		R	L	3.40	5.56	2.16	
	L	L	1.52	3.38	5.52	1.86	2.14	4.00	-0.08	L	R	3.36	5.56	2.20	
vii	Post														
	L	L	1.52		6.52			5.00		L	R	3.04	6.08	3.04	vii
	R	R	1.88	3.88	5.92	2.00	2.04	4.04	0.60	R	L	4.16	6.36	2.20	
viii	Post														
	L	L	1.52	3.88	5.68	2.36	1.80	4.16		L	R	3.68	5.80	2.12	viii
	R	R	1.56	3.88	5.52	2.32	1.64	3.96	-0.16	R	L	3.72	5.80	2.08	
iv	Pre														
	R	R	1.40	3.40	5.20	2.00	1.80	3.80							iv
	L	L	1.40	3.50	5.30	2.10	1.80	3.90	-0.10						
	Post														
	R	R	1.28	3.48	5.48	2.20	2.00	4.20							
	L	L	1.62	3.44	5.42	1.82	1.98	3.80	0.06						
iii	Pre														
	R	R	1.72	3.68	5.32	1.96	1.64	3.60		R	L	3.48	5.48	2.00	iii
	L	L	1.52	3.52	5.24	2.00	1.72	3.72	0.08	L	R	3.60	5.48	1.88	
ii	Pre														
	R	R	1.40	3.88	5.56	2.48	1.68	4.16		R	L	3.16	5.84	2.68	iii
	L	L	1.48	3.72	5.76	2.24	2.04	4.28	-0.20	L	R	3.76	5.80	2.04	
a	Post														
	R	R	1.36	3.56	5.28	2.20	1.72	3.92		R	L	3.56	5.36	1.80	a
	L	L	1.36	3.48	5.28	2.12	1.80	3.92	0.00	L	R	3.48	5.40	1.92	
b	Pre														
	R	R	1.48	3.76	5.40	2.28	1.64	3.92		R	L	3.68	5.52	1.84	
	L	L	1.44	3.64	5.40	2.20	1.76	3.96	0.00	L	R	3.60	5.44	1.84	b
e	Post														
	R	R	1.58	3.74	5.64	2.16	1.90	4.06		R	L		5.66		
	L	L	1.66	3.92	5.58	2.26	1.66	3.92	0.06	L	R		5.70		e
g	Initial														
	R	R	1.52	3.96	5.92	2.44	1.96	4.40		R	L	3.88	6.16	2.28	
	L	L	1.80	3.96	6.08	2.16	2.12	4.28	-0.16	L	R	4.16	6.08	1.92	
	Post-efferent tests														
	R	R	1.68	4.12	6.24	2.44	2.12	4.56		R	L	3.84	6.24	2.40	
	L	L	1.48	4.04	6.16	2.56	2.12	4.68	0.08	L	R	4.12	6.24	2.12	g

Table A. 4 Subject Data: Vestibular Nerve Section

Case	Group 1=norm, 2=ctl 3=exp, 4=oad	Condition	VNS =1; VDC=2 CPA=3; OCB =4 MEM=5; NIHL=6; NORM=7; OTO=8	Test pre/post Pre-op = 1 Post-op= 2 Normal=3	Side of Pathol. Intact side = 1 Pathol side= 2 Normal = 3	Gender male = 1 female=2	Side left = 1 right=2	Level (dBSL) 0; 15; 25; 35; 40; 45; 55	% Inhibition
			vns	pre	intact				
v	3	VNS	1	1	1	2	1	40	14.9
vii	3	VNS	1	1	1	1	2	40	16.8
v	3	VNS	1	1	1	2	1	45	16.8
vi	3	VNS	1	1	1	2	2	45	19.6
			vns	pre	oper				
vi	3	VNS	1	1	2	1	1	35	19.6
vii	3	VNS	1	1	2	1	1	40	13.9
v	3	VNS	1	1	2	2	2	45	12.9
			vns	post	intact				
i	3	VNS	1	2	1	2	2	0	0
ii	3	VNS	1	2	1	2	1	0	5.6
viii	3	VNS	1	2	1	1	2	0	6.7
i	3	VNS	1	2	1	2	2	25	13.9
viii	3	VNS	1	2	1	1	2	25	14.9
iv	3	VNS	1	2	1	2	1	35	25.9
vi	3	VNS	1	2	1	2	2	35	19.6
vii	3	VNS	1	2	1	1	2	35	16.8
v	3	VNS	1	2	1	2	1	40	14.9
viii	3	VNS	1	2	1	1	2	40	21.5
i	3	VNS	1	2	1	2	2	45	19.6
ii	3	VNS	1	2	1	2	1	45	31.6
v	3	VNS	1	2	1	2	1	45	16.8
			vns	post	oper				
i	3	VNS	1	2	2	2	1	0	-4.5
iii	3	VNS	1	2	2	2	2	0	-7.2
v	3	VNS	1	2	2	2	2	0	-1.2
viii	3	VNS	1	2	2	1	1	0	2.3
i	3	VNS	1	2	2	2	1	35	7.7
iii	3	VNS	1	2	2	2	2	35	-1.2
iv	3	VNS	1	2	2	2	2	35	-4.7
v	3	VNS	1	2	2	2	2	35	-1.2
vi	3	VNS	1	2	2	2	1	35	-2.3
vii	3	VNS	1	2	2	1	1	35	-7.2
viii	3	VNS	1	2	2	1	1	35	-5.9
v	3	VNS	1	2	2	2	2	40	-1.2
vii	3	VNS	1	2	2	1	2	40	6.7
viii	3	VNS	1	2	2	1	1	40	3.4
i	3	VNS	1	2	2	2	1	45	7
ii	3	VNS	1	2	2	2	2	45	5.6
iii	3	VNS	1	2	2	2	2	45	3.4
v	3	VNS	1	2	2	2	2	45	2.3

Table A. 5 Subject Data: Pathologies

Case	Group 1=norm, 2=ctl 3=exp, 4=oad	Condition	VNS =1; VDC=2 CPA=3; OCB =4 MEM=5; NIHL=6; NORM=7; OTO=8	Test pre/post Pre-op = 1 Post-op= 2 Normal=3	Side of Pathol. Intact side = 1 Pathol side= 2 Normal = 3	Gender male = 1 female=2	Side left = 1 right=2	Level (dBSL) 0; 15; 25; 35; 40; 45; 55	% Inhibition
a	2	VDC	2	1	1	2	2	25	11.9
a	2	VDC	2	1	1	2	2	45	22.4
a	2	VDC	2	1	2	2	1	40	18.7
			vdc	post	intact				
a	2	VDC	2	2	1	2	2	0	0
a	2	VDC	2	2	1	2	2	35	18.7
a	2	VDC	2	2	1	2	2	55	24.1
b	2	VDC	2	2	1	1	2	25	10.9
b	2	VDC	2	2	1	1	2	35	18.7
b	2	VDC	2	2	1	1	2	45	19.7
			vdc	post	oper				
a	2	VDC	2	2	2	2	1	35	18.7
a	2	VDC	2	2	2	2	1	55	25
b	2	VDC	2	2	2	1	1	25	12.9
b	2	VDC	2	2	2	1	1	35	13.9
b	2	VDC	2	2	2	1	1	40	24.1
b	2	VDC	2	2	2	1	1	45	31.2
c	2	VDC	2	2	2	1	1	35	23.3
c	2	VDC	2	2	2	1	1	45	25.9
			paths	post	pathol				
f	3	CPA	3	2	2	1	1	0	1.1
f	3	CPA	3	2	2	1	1	45	2.3
f	3	CPA	3	2	2	1	2	0	-4.7
f	3	CPA	3	2	2	1	2	35	-4.7
f	3	CPA	3	2	2	1	2	45	1.1
f	3	CPA	3	2	2	1	2	55	9.8
g	3	OCB	4	2	2	1	2	35	0
g	3	OCB	4	2	2	1	1	45	10.9
			mem	post	intact				
x	2	MEM	5	2	1	2	1	0	0
x	2	MEM	5	2	1	2	1	35	20.6
x	2	MEM	5	2	1	2	1	45	21.5
x	2	MEM	5	2	1	2	1	55	25.9
			mem	post	operated				
x	2	MEM	5	2	2	2	2	0	0
x	2	MEM	5	2	2	2	2	15	15.9
x	2	MEM	5	2	2	2	2	25	27.6
x	2	MEM	5	2	2	2	2	35	16.8
x	2	MEM	5	2	2	2	2	45	27.6
x	2	MEM	5	2	2	2	2	55	28.4
y	2	MEM	5	2	2	1	1	0	0
y	2	MEM	5	2	2	1	1	35	9.8
y	2	MEM	5	2	2	1	1	45	10.9
			oad	post	operated				
e	4	NIHL	6	2	2	1	1	35	2.3
e	4	NIHL	6	2	2	1	1	45	9.8
e	4	NIHL	6	2	2	1	2	25	2.3
e	4	NIHL	6	2	2	1	2	35	-7.2
e	4	NIHL	6	2	2	1	2	45	-3
d	4	NIHL	6	2	1	1	2	35	16.8
d	4	NIHL	6	2	1	1	2	45	25
d	4	NIHL	6	2	2	1	1	35	2.3
d	4	NIHL	6	2	2	1	1	45	3.7
			oto-resolved	post	operated				
z	4	OTO	8	2	1	2	2	35	15.9
z	4	OTO	8	2	1	2	1	35	11.9

Table A. 6 Subject Data: Normals

Case	Group 1=norm, 2=ctl 3=exp, 4=oad	Condition	VNS =1; VDC=2 CPA=3; OCB =4 MEM=5; NIHL=6; NORM=7; OTO=8	Test pre/post Pre-op = 1 Post-op= 2 Normal=3	Side of Pathol. Intact side = 1 Pathol side= 2 Normal = 3	Gender male = 1 female=2	Side left = 1 right=2	Level (dBSL) 0; 15; 25; 35; 40; 45; 55	% Inhibition
	1	NORM	7	3	3	1	1	1	6.7
	1	NORM	7	3	3	1	1	1	0
	1	NORM	7	3	3	1	1	2	29.2
	1	NORM	7	3	3	1	1	2	21.5
	1	NORM	7	3	3	1	1	2	31.6
	1	NORM	7	3	3	1	1	3	33.9
	1	NORM	7	3	3	1	2	1	2.3
	1	NORM	7	3	3	1	2	1	7.7
	1	NORM	7	3	3	1	2	1	5.6
	1	NORM	7	3	3	1	2	1	0
	1	NORM	7	3	3	1	2	2	24.1
	1	NORM	7	3	3	1	2	3	27.6
	1	NORM	7	3	3	1	2	3	19.6
	1	NORM	7	3	3	1	2	3	32.4
	1	NORM	7	3	3	1	2	3	34.7
	1	NORM	7	3	3	1	2	3	23.3
	1	NORM	7	3	3	2	1	1	-7.2
	1	NORM	7	3	3	2	1	1	1.1
	1	NORM	7	3	3	2	1	1	-1.2
	1	NORM	7	3	3	2	1	1	0
	1	NORM	7	3	3	2	1	1	4.5
	1	NORM	7	3	3	2	1	1	-1.2
	1	NORM	7	3	3	2	1	2	21.5
	1	NORM	7	3	3	2	1	2	22.4
	1	NORM	7	3	3	2	1	2	25
	1	NORM	7	3	3	2	1	2	17.8
	1	NORM	7	3	3	2	1	2	19.6
	1	NORM	7	3	3	2	1	2	16.8
	1	NORM	7	3	3	2	1	3	15.9
	1	NORM	7	3	3	2	1	3	25.9
	1	NORM	7	3	3	2	1	3	37.4
	1	NORM	7	3	3	2	1	3	30
	1	NORM	7	3	3	2	1	3	24.1
	1	NORM	7	3	3	2	1		21.5
	1	NORM	7	3	3	2	1	3	25
	1	NORM	7	3	3	2	1	3	25.9
	1	NORM	7	3	3	2	1	3	25.9
	1	NORM	7	3	3	2	2	1	3.4
	1	NORM	7	3	3	2	2	1	-2.3
	1	NORM	7	3	3	2	2	1	1.1
	1	NORM	7	3	3	2	2	1	-2.3
	1	NORM	7	3	3	2	2	1	6.7
	1	NORM	7	3	3	2	2	1	3.4
	1	NORM	7	3	3	2	2	1	-3.5
	1	NORM	7	3	3	2	2	1	3.4
	1	NORM	7	3	3	2	2	2	17.8
	1	NORM	7	3	3	2	2	2	17.8
	1	NORM	7	3	3	2	2	2	15.9
	1	NORM	7	3	3	2	2	2	17.8
	1	NORM	7	3	3	2	2	2	20.6
	1	NORM	7	3	3	2	2	2	17.8
	1	NORM	7	3	3	2	2	2	16.8
	1	NORM	7	3	3	2	2	2	26.7
	1	NORM	7	3	3	2	2	2	13.9
	1	NORM	7	3	3	2	2	2	16.8
	1	NORM	7	3	3	2	2	3	18.7
	1	NORM	7	3	3	2	2	3	30
	1	NORM	7	3	3	2	2	3	34.7
	1	NORM	7	3	3	2	2	3	26.7
	1	NORM	7	3	3	2	2	3	16.8

Table A. 7 Efferent Auditory Effects: Vestibular Nerve Section

Case i	Condition	Side	Gender	CAS dBSL	% Inhibition
i post-operative	intact	R	2	0	0
i			2	25	13.9
i			2	45	19.6
i VNS	operated	L	2	0	-4.5
i			2	35	7.7
i			2	45	7

Case ii	Condition	Side	Gender	CAS dBSL	% Inhibition
ii post-operative	intact	L	2	0	5.6
ii			2	45	31.6
ii VNS	operated	R	2	45	5.6

Case iii	Condition	Side	Gender	CAS dBSL	% Inhibition
iii post-operative	operated	R	2	0	-7.2
iii VNS			2	35	-1.2
iii			2	45	3.4

Case iv	Condition	Side	Gender	CAS dBSL	% Inhibition
iv post-operative	intact	L	2	35	25.9
iv VNS	operated	R	2	35	-4.7

Case v	Condition	Side	Gender	CAS dBSL	% Inhibition
v pre-operative	intact	L	2	40	14.9
v			2	45	16.8
v VNS	operative	R	2	45	12.9
v post-operative	intact	L	2	40	14.9
v			2	45	16.8
v VNS	operated	R	2	0	-1.2
v			2	35	-1.2
v			2	40	-1.2
v			2	45	2.3

Case vi	Condition	Side	Gender	CAS dBSL	% Inhibition
vi pre-operative	intact	R	2	45	19.6
vi VNS	operative	L	1	35	19.6
vi post-operative	intact	R	2	35	19.6
vi VNS	operated	L	2	35	-2.3

Case vii	Condition	Side	Gender	CAS dBSL	% Inhibition
vii pre-operative	intact	R	1	40	16.8
VNS	operative	L		40	13.9
vii			1		
vii post-operative	intact	R	1	35	16.8
vii VNS	operated	L	1	35	-7.2
vii			1	40	6.7

Case viii	Condition	Side	Gender	CAS dBSL	% Inhibition
viii post-operative	intact	R	1	0	6.7
viii			1	25	14.9
viii			1	40	21.5
viii VNS	operated	L	1	0	2.3
viii			1	35	-5.9
viii			1	40	3.4

Table A.8 Efferent Auditory Effects: Pathologies

	Case a	Test	Side	Gender	CAS dBS	% Inhibition
a	pre-operative	intact	R	2	25	11.9
a				2	45	22.4
a	VDC	operative	L	2	40	18.7

a	post-operative	intact	R	2	0	0
a				2	35	18.7
a				2	55	24.1
a	VDC	operated	L	2	35	18.7
a				2	55	25

	Case b	Test	Side		CAS dBS	% Inhibition
b	post-operative	intact	R	1	25	10.9
b				1	35	18.7
b				1	45	19.7
b	VDC	operated	L	1	25	12.9
b				1	35	13.9
b				1	40	24.1
b				1	45	31.2

	Case c	Test	Side		CAS dBS	% Inhibition
c	post-operative	operated	L	1	35	23.3
c	VDC			1	45	25.9

	Case f	Test	Side		CAS dBS	% Inhibition
f	post-pathology	contralat	L	1	0	1.1
f		to CPA cyst		1	45	2.3
f		ipsilatera	R	1	0	-4.7
f		to CPA cyst		1	35	-4.7
f				1	45	1.1
f				1	55	9.8

	Case g	Test	Side		CAS dBS	% Inhibition
g	post-pathology	bilateral	R	1	35	0
	OCB	olivary				
	lesions	lesions	L		45	10.9

	Case x	Test	Side		CAS dBS	% Inhibition
x	post-operative	intact	L	2	0	0
x				2	35	20.6
x				2	45	21.5
x				2	55	25.9
x	MEM	operated	R	2	0	0
x				2	15	15.9
x				2	25	27.6
x				2	35	16.8
x				2	45	27.6
x				2	55	28.4

	Case y	Test	Side		CAS dBS	% Inhibition
y	post-operative	operated	L	1	0	0
y	MEM			1	35	9.8
y				1	45	10.9

	Case e	Test	Side		CAS dBS	% Inhibition
e	post-pathology	affected	L	1	35	2.3
e				1	45	9.8
e	NIHL	affected	R	1	25	2.3
e				1	35	-7.2
e				1	45	-3

	Case d	Test	Side		CAS dBS	% Inhibition
d	post-pathology	un-affect	R	1	35	16.8
d				1	45	25
d	NIHL	affected	L	1	35	2.3
d				1	45	3.7

	Case z	Test	Side		CAS dBS	% Inhibition
z	post-pathology		R	2	35	15.9
z	OTOTOX		L	2	35	11.9

XIII. ABBREVIATIONS

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ABR	Auditory Brainstem Response
ART	Acoustic Reflex Threshold
CAS	Contralateral Acoustic Stimulation
CEOAE	Click Evoked Otoacoustic Emission
CPA	cerebello-pontine-angle
daPa	deca Pascal
dB	decibel
dBHL	decibel Hearing Level
dBpeSPL	decibel peak equivalent Sound Pressure Level
dBSL	decibel Sensation Level
dBSPL	decibel Sound Pressure Level
DP	Distortion Product
DPOAE	Distortion Product Otoacoustic Emission
EAE	Efferent Auditory Effect
IHC	Inner Hair Cell
kHz	kilo Hertz
LOC	Lateral Olivocochlear
MEM	Middle Ear Muscle
MOC	Medial Olivocochlear
MRI	Magnetic Resonance Image
ms	milli seconds
msec	milli seconds
N1	first Negative wave
OAE	Otoacoustic Emission
OC	Olivocochlear
OCB	Olivocochlear Bundle
OHC	Outer Hair Cell
PLF	Perilymph Fistula
PTA	Pure Tone Average
SD	Standard Deviation
SL	Sensation Level
SOC	Superior Olivocochlear
TEOAE	Transient Evoked Otoacoustic Emission
WN	White Noise

XIV. PUBLICATIONS

XIV. PUBLICATIONS

Submitted as attachments to Thesis

Williams E. A., Brookes G. B. and Prasher D. K. (1994) Effects of Olivocochlear Bundle Section on Otoacoustic Emissions in Humans: Efferent Effects in Comparison with Control Subjects. Acta Otolaryngol 114: 121-129.

Williams, E. A., Brookes G. B. and Prasher D. K. (1993) Effects of Contralateral Acoustic Stimulation on Otoacoustic Emissions Following Vestibular Neurectomy. Scand Audiol 22:197-203.

Scand Audiol 1993; 22: 197–203

EFFECTS OF CONTRALATERAL ACOUSTIC STIMULATION ON OTOACOUSTIC EMISSIONS FOLLOWING VESTIBULAR NEURECTOMY*

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ABSTRACT

Effects of contralateral acoustic stimulation on otoacoustic emissions following vestibular neurectomy. Williams, E.A., Brookes, G.B. and Prasher, D.K. (Department of Neuro-otology and MRC Human Movement and Balance Unit, National Hospital for Neurology and Neurosurgery, London, UK).

Scand Audiol 1993; 22: 197–203.

This study demonstrates that, following unilateral vestibular neurectomy, the inhibitory effect of contralateral acoustic stimulation on evoked otoacoustic emissions is absent. The patient acts as her own control in that the unoperated side shows normal suppression of otoacoustic emission amplitude with contralateral acoustic stimulation. The lack of interaural suppression of otoacoustic emissions on the sectioned side, in the presence of normal acoustic reflex threshold levels, provides evidence that observed phenomena are not merely a function of middle ear reflex activity. It is concluded that the lack of inhibition in the operated ear is due to the sectioning of the olivocochlear bundle within the inferior vestibular nerve, removing the efferent control of the receptor cells. Otoacoustic emissions recorded during contralateral acoustic stimulation may thus provide a rapid, non-invasive means of investigating the functional of the efferent auditory system.

Key words: acoustic reflex, auditory, cochlea, efferent, hair cells, human, neural pathways, olivocochlear bundle, otoacoustic emissions, vestibular neurectomy.

INTRODUCTION

Anatomical and physiological evidence suggest that the efferent olivocochlear system directly controls the sensitivity and frequency specificity of the cochlea by modulating its mechanical response to acoustic stimuli. The olivocochlear bundle (OCB) projects from the superior olivary complex to the cochlea along two pathways. The lateral efferent fibres are unmyelinated neurons arising from the superior olivary nucleus which predominantly travel to the ipsilateral cochlea where they innervate the dendrites of the inner hair cells. The medial efferent fibres comprise large myelinated neurons, originating from the contralateral medial nuclei of the superior olivary complex, that cross the floor of the fourth ventricle before entering the vestibular nerve root where they are joined by the lateral fibres. The entire OCB exits the brainstem travelling within the inferior vestibular nerve until just distal to the saccular ganglion whereupon the OCB crosses to the organ of Corti via the vestibulocochlear anastomosis (Rasmussen, 1946; Schuknecht, 1974). The contralateral medial efferent fibres primarily form axosomatic synapses along the base and sides of the outer hair cells (Warr & Guinan, 1979).

The outer hair cells have been shown to be motile (Ashmore, 1987; Brownell 1990, Review) and could provide a mechanism for creating the nonlinear, highly tuned movement of the basilar membrane. Otoacoustic emissions (OAEs), first described by Kemp (1978), are thought to be generated by a portion of this movement being reflected back along the cochlear partition to the middle ear, and provide the most direct evidence of active mechanical processing within the cochlea. Thus it is postulated that the efferent system directly controls the micromechanical system of the cochlea via the outer hair cells, and that otoacoustic emissions provide a means of measuring efferent-induced changes in cochlear mechanics.

Contralateral acoustic stimulation apppears to provide a method for investigating the crossed efferent system in humans. Using electrocochleographic recordings in humans Prasher & Gibson (1984) found a reduction of compound action potential amplitude with contralateral acoustic stimulation, which has been confirmed in further studies (Folsom & Owsley, 1987), and is consistent with numerous animal studies of the effect of contralateral acoustic stimulation on afferent nerve activity (Buno, 1978; Liberman, 1989).

* Read at the Politzer Society International Conference: Otology in the 90s, Cortina, Italy, March 17, 1992.

Inhibition of evoked emission amplitude during contralateral acoustic stimulation has recently been documented in normal human subjects (Collet et al., 1990; Veuillet et al., 1991). Several studies show that this effect appears to be independent of transcranial transmission of middle-ear effects, and can also be observed in pathological cases with sensorineural hearing loss provided that there was sufficient hearing to produce emissions (Collet et al., 1992).

In guinea-pigs the inhibitory effect of contralateral acoustic stimulation on DP otoacoustic emissions has been shown to disappear after sectioning the efferent auditory fibres at the floor of the fourth ventricle (Puel & Rebillard, 1990). Warren and Liberman (1988) reported the loss of suppression of auditory nerve fibre responses after sectioning of the entire OCB in the VIIIth nerve in cats. There have been no studies to date that examine the effect of sectioning the efferent auditory fibres on human OAE. Patients with intractable vertigo who have normal auditory function and undergo vestibular neurectomy (which entails the sectioning of both the medial and lateral olivocochlear fibres travelling within the inferior vestibular nerve) provide a physiological model for examining the effect of removing the efferent supply on cochlear mechanical responses. This study examined such a patient with a view to documenting the effect of contralateral stimulation on otoacoustic emissions.

MATERIAL AND METHODS

Case description

A 43-year-old woman with an uncompensated left peripheral labyrinthine disorder first noted symptoms 7 years prior to admission when she had an acute episode of vertigo and vomiting which took several weeks to resolve. Thereafter she suffered from periodic bouts of recurrent vertigo and imbalance lasting about 6 weeks. A number of auditory and vestibular tests were conducted to establish the diagnosis. Pure tone audiometric thresholds were within the normal range for both ears. Tympanometry showed normal middle ear pressure and compliance, and normal ipsilateral and contralateral acoustic reflex thresholds (ART). Auditory evoked brainstem potentials were within normal limits for both absolute and inter-wave latency. Electronystagmographic (ENG) recordings of horizontal eye movements showed second degree spontaneous nystagmus in the absence of optic fixation, and the Fitzgerald–Hallpike bithermal caloric test showed a left canal paresis. Vestibulo-ocular reflexes and pursuit movements in response to 0.2–0.4 Hz target velocities were normal. The preoperative CT scan was normal although a large cisterna magna was noted. Medical therapy using a variety of vestibular sedative drugs were found to be ineffective in alleviating the patient's symptoms. A left vestibular neurectomy was performed using the retrolabyrinthine approach which allows for the preservation of hearing. The patient made a good recovery with normal facial movements. Postoperative audiometry, evoked otoacoustic emissions and the efferent emission tests were recorded 2 months postoperatively, and repeated at the same time interval over the next 6 months. The results of these tests are described below.

Audiometry

Standard pure tone audiometry was performed before and after the operation in a soundproof booth using a Madsen OB 802 audiometer. Threshold measurements are reported relative to dB HL (ISO). Tympanometry and acoustic reflex thresholds were measured using a GSI 33 Middle Ear Analyzer.

Otoacoustic emission procedures

Click-evoked OAEs were recorded using an Otodynamic Ltd ILO88 acoustic emission analyser as described by Kemp et al. (1990). The stimulus was a non-filtered 80 us click, presented at a rate of 50/s. Spectral analysis and amplitude measurement of the responses were performed by the system. The OAE responses to 260 clicks were averaged, using the artefact rejection facility, at stimulus levels of 81 dB SPL ($\pm$2 dB) and 61 dB SPL ($\pm$2 dB), followed by the 'efferent test' procedures.

Efferent test procedures

White noise, generated by a Madsen OB 802 audiometer via a TDH 39 earphone was presented to the ear contralateral to the OAE probe. The patient's threshold to white noise was measured for each ear, and intensities corresponding to 5, 15, 25, 35 and 45 dB above sensation level (SL) (30–70 dB HL) were used. The ILO88 was set to present OAE click stimuli at 61 dB SPL ($\pm$2 dB) peak reception level. Ten sets of 60 click-evoked OAE responses were averaged, and contralateral continuous white noise was presented during alternate sets of stimuli (see Ryan et al., 1991). OAE amplitude was measured within the 5–20 ms post-stimulus epoch and within the 1000–2000 Hz frequency band for those emissions with a reproducibility $\geqslant$50%. The responses in quiet (no contralateral stimulus) and in noise (with contralateral white noise) were averaged by the ILO88 software into separate buffers, and the two results compared in terms of total emission amplitude as measured on the ILO88, and by superimposing the emission waveforms.

RESULTS

The pure tone audiograms (Fig. 1) recorded before and after surgery show bilateral improvement by 5–15 dB at frequencies from 500 to 4000 Hz. Changes of 5 dB which are within the range of inter-test variability were noted at 8000 Hz in both ears. Tympanometry showed normal compliance measurements (right 0.5 ml, left 0.3 ml) that were stable bilaterally following surgery (within 0.1 ml of preoperative recordings). Middle ear pressures remained within normal limits (shifting to -45 daPa in the left, and by -10 daPa in the right). Ipsilateral acoustic reflex thresholds (250–4000 Hz) remained essentially unchanged for both ears, improving by at most 5 dB which is within

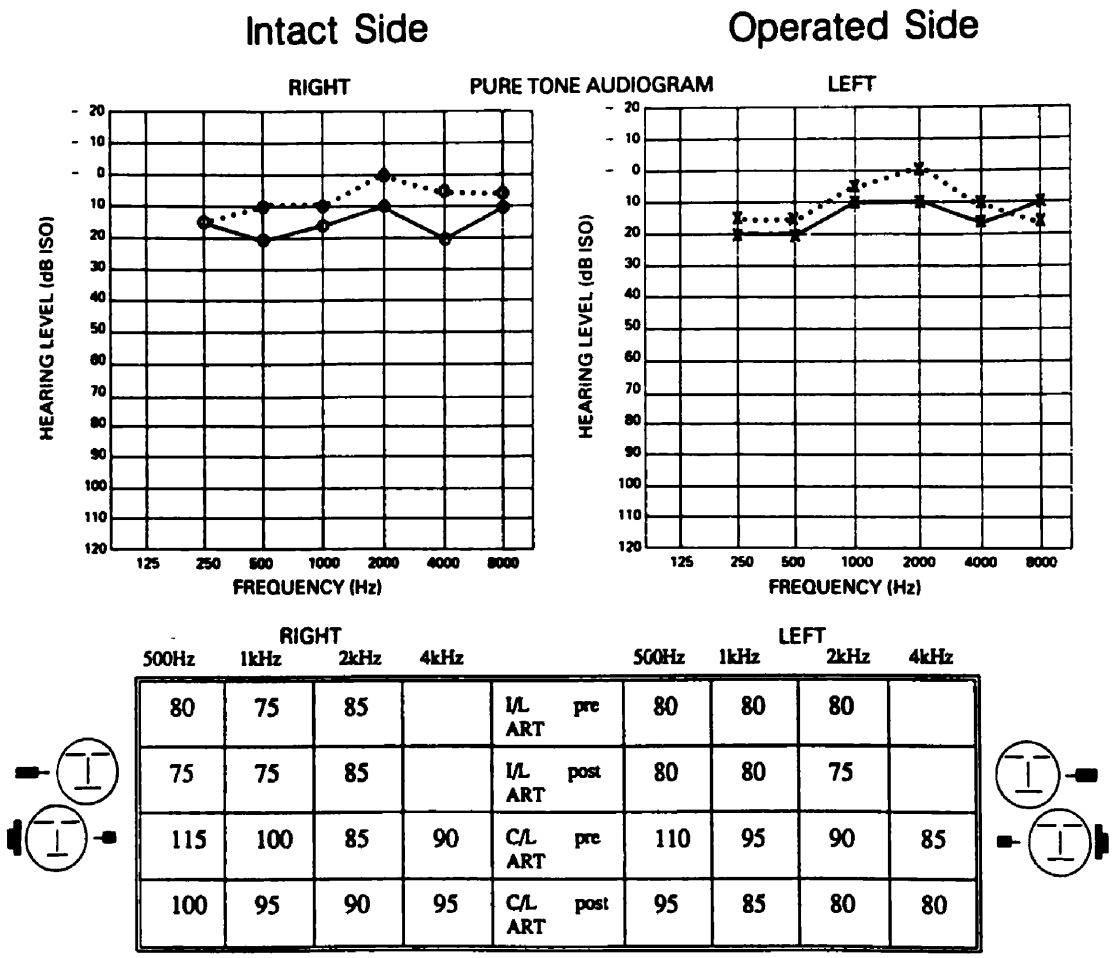

Fig. 1. Pure tone thresholds (dB HL ISO) from the operated side (left X) and intact side (right O) before (solid lines) and after (dotted lines) left vestibular neurectomy. Ipsilateral and contralateral acoustic reflex thresholds expressed in dB HL (ISO) are shown pre- and postoperatively.

expected inter-test variability. Contralateral acoustic reflexes recorded from the intact ear whilst stimulating the operated side improved by 5–15 dB across the frequency range. Contralateral acoustic reflex thresholds recorded from the severed side while stimulating the intact ear decreased by up to 15 dB at 1000 Hz and 500 Hz, but were increased by only 5 dB at 2000 and 4000 Hz.

Otoacoustic emissions

Normal click-evoked otoacoustic emissions were recorded from the sectioned side (13.0 dB, 94% reproducible, A–B 0.9 dB at 83 dB spl), and from the intact side (10.2 dB, 85% reproducible, A–B 2.3 dB at 80 spl) (Fig. 2). The frequency spectrum of these responses are consistent with the patient's pure tone hearing thresholds which were better than 20 dB HL (ISO). The amplitude and spectral content of the OAE from the cochlea with the severed efferent fibres (left) was similar in nature to that from the cochlea with intact efferent innervation (right).

Efferent auditory effect (EAE) from the intact side

The subjective perception threshold to white noise was found to be 25 dB HL for both ears. OAE amplitude from the normal ear decreased under contralateral noise stimulation and was inversely related to the intensity of the stimulus. The decrement in amplitude as a function of contralateral stimulus intensity is shown in Fig. 3. The greatest magnitude of suppression was observed with contralateral noise levels of 45 dB SL (70 dB HL), such that the total averaged OAE responses decreased by 1.8 dB relative to the total averaged amplitude of the emissions recorded in quiet, which is equivalent to a drop of 28.2% relative to the amplitude in quiet conditions. Contralateral stimulation at 25 dB SL (50 dB HL) was associated with a 1.3 dB decrease in OAE amplitude, equivalent to a

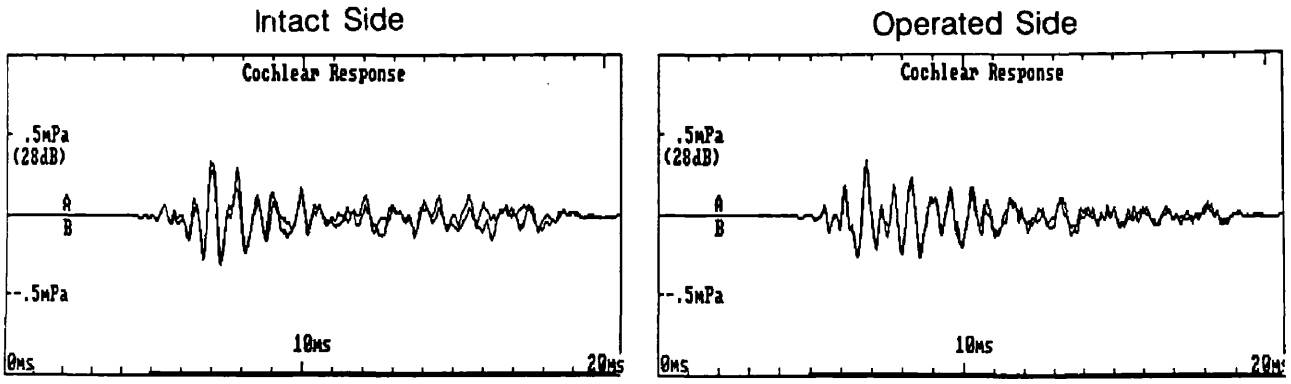

Fig. 2. Click-evoked otoacoustic emissions recorded postoperatively from the sectioned and intact sides. The cochlear responses were recorded in quiet conditions using the non-linear artefact rejection method. The averaged waveforms from buffers A and B for each ear are displayed in the 2.5–20 ms post-stimulus epoch. The amplitude of the OAE from the intact side was 10.2 dB, 85% reproducible, A–B 2.3 dB, in response to 80 dB spl click stimuli. The amplitude of the OAE from the sectioned side was 13.0 dB, 94% reproducible, A–B 0.9 dB in response to 83 dB spl.

decrease of 22.4% relative to the total OAE amplitude without noise. However, negligible suppression (−0.2 dB) was induced with contralateral stimulation at 30 dB HL which was only 5 dB above the patient's perceptual threshold to white noise. Observation of the spectral analysis of the emissions shows that the frequencies of the dominant emissions were within the 1000–2000 Hz band. Inhibition was most noticeable within this band, and was inversely related to contralateral stimulus levels. Within this frequency band, the phase of the emissions recorded with contralateral noise lead the filtered responses recorded in quiet conditions. Fig. 4 shows the effect of 25 dB SL (50 dB HL) contralateral white noise on the 1000–2000 Hz band of the OAE frequency spectrum for both ears.

EAE results from the sectioned side

In contrast, the amplitude of OAE recorded from the ear with severed efferent fibres showed minimal changes with contralateral acoustic stimulation from

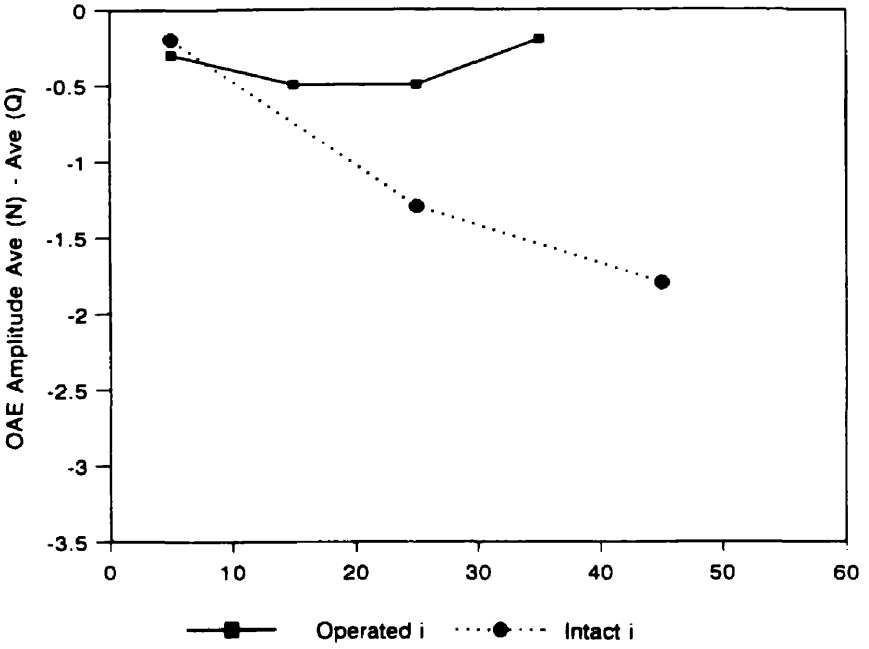

Fig. 3. Decrement in averaged OAE amplitude as a function of contralateral stimulus intensity. For each ear, the difference of the averaged OAE amplitude recorded in noise (N) minus the averaged OAE amplitude recorded in quiet (Q) is plotted against the intensity of contralateral acoustic stimulation (dB SL ISO).

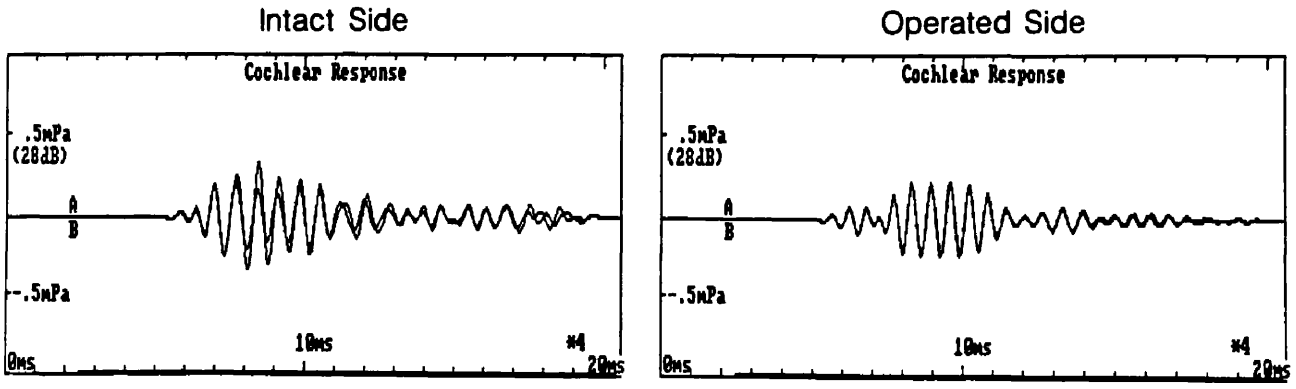

Fig. 4. Comparison of click-evoked OAE within the filtered band of 1000–2000 Hz for both intact and operated sides. The averaged OAE recorded during 25 dB SL (50 dB HL) contralateral stimulation (A) is superimposed over the averaged OAE recorded in quiet (B) for each ear.

25 to 35 SL (30–60 dB HL). The extent of suppression observed was negligible (3.0–7.16% reduction in the average OAE amplitude recorded without contralateral noise) in comparison with that recorded in the normal ear, and was not directly related to the intensity level of the contralateral noise (see Fig. 3). The total averaged OAE amplitude recorded in noise was within 0.5 dB of the averaged OAE amplitude in quiet, for all intensity levels. No suppression was observed with 70 dB HL of noise, but these data have been excluded because of the low reproducibility of the emissions caused by patient movement. The minimal inhibitory values observed from the operated side are within the range of inter-test variability (+0.4 to −0.5 dB) observed in this patient for emissions recorded without contralateral stimulation, and it is therefore assumed that the results reflect a random fluctuation in amplitude that is not related to responses of the auditory system to the contralateral stimuli. Observations of the dominant emissions (1000–2000 Hz band) from the operated ear showed virtually no observable change in amplitude or phase of emissions produced by the cochlea with severed efferent fibres (see Fig. 4).

DISCUSSION

Patients with normal hearing who undergo vestibular neurectomy provide a human model for examining the effect of removing efferent auditory innervation on otoacoustic emissions. The inhibitory effect of contralateral acoustic stimulation on otoacoustic emission amplitude and phase was absent in the operated side following surgical division of the efferent auditory fibres to the cochlea by vestibular neurectomy. OAE measurements from the patient's unoperated side provide control information, and show a clear reduction in amplitude and a phase lead during contralateral stimulation.

The retrolabyrinthine neurectomy involves sectioning of the inferior vestibular fibres which carry both the medial and lateral efferent bundles, whilst preserving the cochlea and afferent auditory fibres. Because of the intermingling of fibres along the apparent line of division between the cochlear and vestibular nerves (Schefter and Harner 1986; Natout et al., 1987), one cannot always be certain that all of the inferior vestibular fibres, or all of the efferent auditory bundle within it, will be completely severed. However, in the case reported, a clear anatomical demarcation between the cochlea and vestibular nerves was apparent, and in clinical terms the patient experienced a complete resolution of vestibular symptoms. The standard audiometric test battery showed normal responses. Postoperative pure tone thresholds improved slightly, and it is therefore unlikely that undetected surgical disruption of the afferent auditory system occurred, although one cannot entirely exclude the possibility that the underlying pathology affected our findings. Middle ear pressure shifted up to −45 daPa, but this is considered by Robinson and Haughton (1991) to be insufficient to cause a significant reduction in the OAE amplitude or change in the spectral content, or to account for the difference in OAE amplitude when recorded in the quiet vs contralateral white noise.

The mechanism by which contralateral acoustic stimulation inhibits OAE amplitude is thought to involve activation of the medial efferent system which primarily innervates the outer hair cells, causing them to alter their biomechanical response to sound. As the

outer hair cells are coupled to the tectorial and basilar membranes, changes in their movement could affect the damping and thus the frequency and amplitude of the movement of the cochlear partition, thereby modifying the local mechanical input to the sensory hair cells. Thus it has been suggested that an efferent fibre and its associated outer hair cells could act as a motor unit, inhibiting the receptor cells by means of inter-cochlear feedback via the crossed medial fibres.

One might construe that sectioning of the efferent fibres should result in disinhibition of the cochlear response, and in this case the patient's pure tone thresholds improved following surgery. Similar effects have also been reported in the literature in a small (< 20%) proportion of post-neurectomy cases (McElveen et al., 1988; Monsell et al., 1988; Silverstein et al., 1990; Wazen et al., 1990). The bilateral improvement reported here may suggest that the loss of inhibition to the sectioned ear changes its afferent output in such a way as to modify inter-aural interaction and thus the response of the other ear. Hyperacousis was not reported in this case, and it is interesting to note that the amplitude of the emissions evoked in quiet surroundings from the sectioned cochlea were similar to the OAE evoked from the intact side, and not suggestive of the undamped oscillations one might speculate would arise from loss of a gross inhibitory feedback function on an inherently unstable mechanism such as the non-linear amplification of basilar membrane movement. Unfortunately, preoperative comparisons are not possible as the patient was not available for testing. Further investigations are currently underway to throw light on these findings and their relevance to theories of cochlear mechanics.

It has been suggested that the contralateral 'efferent auditory effect' on OAE amplitude could be a function of the bilateral activation of the acoustic reflexes by the contralateral noise, resulting in reduced transmission of the OAE to the ear canal. To avoid middle ear muscle activation, the protocol utilized noise and OAE stimuli at intensity levels below postoperative reflex thresholds for both sides. Although one cannot entirely exclude the possibility that the muscles were active at levels below the thresholds measured using standard tympanometric devices, the fact that in this study the patient with intact normal acoustic reflexes thresholds showed no significant suppression after vestibular nerve section argues against the possibility that the effect is mediated via the acoustic reflex. Human studies have demonstrated that the inhibitory effect of contralateral acoustic stimulation persisted in subjects with unilateral loss of the acoustic reflex after surgical removal of the stapedius muscle or with Bell's palsy (Veuillet et al., 1991). A comparison of the effect between normal subjects and patients without acoustic reflex showed no difference between the two groups except for a slightly stronger suppressive effect, especially in the case with Bell's palsy. Inter-aural suppression of distortion products after section of the middle ear muscles in animals (Puel & Rebillard, 1990), along with findings by Williams and Russell (unpublished observations) which demonstrate the inhibitory effect of electrical excitation of the OCB on intracellular hair cell responses in paralysed animals, further supports the supposition that the inter-aural suppression using low level stimuli is not a result of acoustic reflex activity.

Suppression of OAE amplitude by contralateral noise is unlikely to be explained by ipsilateral masking of the OAE stimulus via transcranial transmission as the contralateral stimulus intensities were below levels reported to cause cross-masking in normal subjects (Collet et al., 1990; Veuillet et al., 1991). Furthermore, contralateral acoustic stimulation has been demonstrated to have a frequency-specific effect on tone evoked (Veuillet et al., 1991), spontaneous emissions (Mott et al., 1989), distortion products (Brown et al., 1983) and click-evoked emissions (Collet et al., 1990). Liberman (1989) argues that the frequency selectivity of the inhibitory effect on emission amplitude cannot be accounted for on the basis of middle ear activity. This frequency-specificity is consistent with the inhibitory effect of electrical excitation of efferent fibres on hair cell tuning curves as observed by Brown et al. (1983) and by Williams and Russell (unpublished research), as well as the well documented suppressive effect on auditory nerve responses (Galambos, 1956; Guinan and Gifford, 1983).

CONCLUSION

This study supports the hypothesis that inter-aural suppression of otoacoustic emissions provides a mirror of efferent events occurring at the cellular level of the organ of Corti. The results demonstrate that the inhibitory effect of contralateral acoustic stimulation on emission amplitude and phase is absent following section of the efferent auditory bundle as a consequence of vestibular neurectomy. Otoacoustic emis-

sions techniques used in conjunction with contralateral acoustic stimulation may thus provide a non-invasive means of investigating the efferent auditory system, and may prove to be of diagnostic value.

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Effects of Olivocochlear Bundle Section on Otoacoustic Emissions in Humans: Efferent Effects in Comparison with Control Subjects*

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The effects of contralateral acoustic stimulation on evoked otoacoustic emissions (OAE) were examined in three subject groups in order that the impact of efferent olivocochlear bundle section (as a consequence of vestibular neurectomy) could be compared with normal findings, and with a control surgical population. Results demonstrated that the inhibitory effect of contralateral noise on OAE amplitude was absent from the cochlea with severed efferent fibers. These findings appear to be independent of acoustic reflex activity, as suppression was absent despite normal reflexes. Inter-aural suppression of emissions recorded from the patients' intact cochleae act as a control and show a clear reduction in amplitude during contralateral stimulation in a frequency specific pattern consistent with normal findings. Patients who had undergone a similar surgical approach for vascular decompression of the VIIIth nerve without vestibular nerve section, were studied in order to assess the impact of retrolabyrinthine surgery on inter-aural suppression. Inhibition of OAE amplitude was maintained in all control cases in both the operated and intact sides, and was consistent with suppression observed in normal subjects, suggesting that the surgical procedures had not disturbed inter-aural suppression of otoacoustic emissions. It is concluded that the olivocochlear efferent system, when activated by low level contralateral acoustic stimulation, has an inhibitory role in controlling the cellular mechanisms responsible for the generation of otoacoustic emissions in humans. OAE techniques in conjunction with contralateral acoustic stimulation may thus prove to be of value in providing a rapid and non-invasive clinical test of efferent function and offer a means of investigating the functional significance of the efferent auditory system in humans. *Key words: acoustic reflex, auditory, cochlea, contralateral acoustic stimulation, medial efferent system, outer hair cell, olivary nuclei, vestibular neurectomy.*

INTRODUCTION

Physiological research has demonstrated that the receptor cells (1) and the basilar membrane (2) of the organ of Corti respond to sound in a non-linear and sharply tuned manner. Otoacoustic emissions (OAE), first described by Kemp, (3) are thought to be generated by the motion of the cochlear duct, and provide a noninvasive means of observing these responses. It has been demonstrated that the biomechanical activity of the outer hair cells (OHC) are essential to cochlear tuning and to the production of emissions (4). The OHC receive direct axosomatic innervation from the medial efferent auditory fibers, and it therefore follows that excitation of the efferent system or interruption of efferent innervation should alter the nature of otoacoustic emissions. Otoacoustic emissions may thus provide a method for studying not only the nonlinear responses of the organ of Corti, but also the role of the efferent auditory system in modulating cochlear output.

The efferent auditory fibers project from the superior olivary complex to the cochlea along two pathways. The lateral efferent pathway comprises unmyelinated neurones which predominantly innervate the dendrites of the inner hair cells. Large myelinated neurones form the medial efferent pathway, which originates from the medial region of the superior olivary complex and primarily form direct axosomatic synapses with the outer hair cells (5). Both medial and lateral pathways enter the vestibular nerve root within the brainstem, where they form the olivocochlear bundle (OCB). The OCB travels within the inferior vestibular nerve until just distal to the saccular ganglion, whereupon it crosses to the organ of Corti via the vestibulo-cochlear anastomosis (6, 7).

Animal studies have demonstrated that activation of the medial efferent system by electrical stimulation at the floor of the fourth ventricle alters the phase and amplitude of tone evoked emissions (8), as well as the amplitude of click evoked (9) and distortion product (DP) emissions (10, 11). Removal of the observed suppressive effect by perfusion of the cochlea with d-turbocurarine, an efferent blocker, provides further evidence that the efferent system influences cochlear mechanics (11). These findings are consistent with the inhibitory effect of electrical stimulation on intracellular receptor potentials (12), and the observed decrease in auditory nerve responses (13). It has been suggested that electrical excitation at the fourth ventricle overstimulates the efferent and surrounding fibers (9), whereas presentation of sound to the contralateral cochlea has been shown to physiologically

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activate the medial efferent system (14). In keeping with this theory, acoustic stimulation of one cochlea has been found to suppress contralateral otoacoustic emission amplitude (15) and afferent output (16). Warren & Liberman (1989) demonstrated that sectioning of the entire OCB within the inferior vestibular nerve completely removed the inhibitory effects.

In humans, a number of normal studies have documented the inhibitory effect of contralateral acoustic stimulation on click evoked otoacoustic emissions (17, 18) and it has been suggested that inter-aural suppression of OAE may be used for the clinical assessment of efferent auditory dysfunction. Williams et al. (19) utilized inter-aural techniques to investigate OAE following unilateral surgical section of the olivocochlear efferent bundle as a consequence of vestibular neurectomy, and found that inter-aural inhibition of OAE amplitude was absent on the operated side. Measurements of the suppressive effect from the patient's intact side, taken as a control, were found to be normal.

The current study aimed to examine the effect of de-efferentation on otoacoustic emissions and inter-aural suppression in neurectomy patients, and compare the results with normal subjects and a control surgical group undergoing a similar approach to the cerebello-pontine angle for vascular decompression of the vestibulo-cochlear nerve but without nerve section. The control group provided a means of investigating the impact of retrolabyrinthine surgical procedures on inter-aural inhibition of otoacoustic emissions. The results suggest that in humans the olivocochlear efferent system has an inhibitory role in controlling cochlear responses when presented with low to moderate levels of contralateral noise. This function is presumably mediated via the outer hair cells which are believed to be essential for the production of otoacoustic emissions.

MATERIAL AND METHODS

The effects of contralateral acoustic stimulation on click evoked otoacoustic emissions (CEOAE) were studied in three subject groups selected from the following populations: *i)* normal healthy volunteers, *ii)* vestibular neurectomy patients who had undergone retrolabyrinthine surgery with efferent olivocochlear bundle section as a consequence of division of the vestibular nerve, and *iii)* vascular decompression patients who formed surgical controls having undergone a similar retrolabyrinthine approach for vascular decompression of the VIIIth nerve, but without nerve section. Individuals were selected for study from the above populations on the basis of the following profiles:

Normals. Normal subjects were admitted to the study from healthy volunteers if they had no history of hearing disorder, normal otoscopy, pure tone thresholds ≤ 20 dB HL (0.25–8 kHz), and normal tympanometry (± 50 mm H_2O middle ear pressure, 0.3–1.5 ml compliance). Eight subjects (20–43 years, 2 male, 6 female) with pure tone thresholds less than or equal to 20 dB HL, normal ipsilateral and contralateral acoustic reflex thresholds between 80–105 dB (0.5–4 kHz), and with no history of hearing disorder were admitted to the study. CEOAE were present bilaterally with amplitudes for the whole non-linear response (2.5–20 ms) from 8 to 22 dB spl in response to 80–86 dB spl peak level stimuli.

Vestibular neurectomy patients. The selection criteria for vestibular neurectomy patients required normal otoscopy and tympanometry as defined above. Post-operative pure tone audiometric thresholds (0.25–8 kHz) were required to be within 15 dB or better than preoperative levels. In order to reliably record OAE, thresholds better than 35 dB HL at a minimum of two adjacent frequencies were required. Patients were also selected on the basis of normal auditory evoked brainstem potentials for both absolute and inter-wave latencies (Wave I: 1.3–1.9 ms, III: 3.3–4.1 ms, V: 5.2–6.0 ms; Inter-Waves I–III: 1.6–2.4 ms, III–V: 1.4–2.2 ms, I–V: 3.6–4.4 ms). Vestibular function examinations including electronystagmographic (ENG) recordings of horizontal eye movements, and the Fitzgerald-Hallpike bithermal caloric test confirmed peripheral vestibular disorder. CT scans, CT air meatography, and MRI scans were performed in order to exclude central lesions, and/or to confirm the diagnosis. Only those patients with no evidence of central pathologies were considered for this study.

Over half of the 72 cases undergoing vestibular neurectomy during the past 6 years suffer from Meniere's disease with thresholds of 35 dB HL or better pre-operatively, and two of these patients (32–43 years, females) with recurrent peripheral vestibular dysfunction but with good hearing function, normal auditory evoked brainstem potentials, and no evidence of central dysfunction were available for post-operative investigations.

Case i, had normal pre- and post-operative hearing levels (10–20 dB HL) in both ears at all frequencies tested (0.25–8 kHz). In this case, bilateral improvement in pure tone audiometry was observed following surgery, with an increase of 5–15 dB, except for at 8 kHz which decreased by 5 dB in the operated ear. Acoustic reflexes remained within the normal range, with ipsilateral thresholds falling within 5 dB of pre-operative values, and contralateral thresholds at least 5 dB of pre-operative levels or improved by up to

15 dB. Otoacoustic emissions were present bilaterally with amplitudes and frequency spectra consistent with pure tone hearing levels. Click stimuli levels of 83 dB spl produced non-linear CEOAE whole echo amplitudes of 13.0 dB, 94% reproducible, A-B 0.9 dB from the operated ear; levels of 80 dB spl produced CEOAE with amplitudes of 10.2 dB, 85% reproducible, A-B 2.3 dB from the intact ear. Neurectomy cases with good hearing levels at all frequencies are most uncommon, and this case provided a rare opportunity to conduct a more thorough examination of the effect of de-efferentation on hearing, and the effect of contralateral acoustic stimulation on otoacoustic emissions as a function of intensity and frequency.

Case ii maintained post-operative pure tone hearing levels between 25–35 dB HL on the operated side, and 10–25 dB HL on the intact side for frequencies between 0.25–8 kHz. Otoacoustic emissions were present bilaterally, with non-linear CEOAE amplitudes of 5.7 dB, 59% reproducible, A-B 3.1 dB with 87 dB spl click stimuli to the operated side, and 5.3 dB, 65% reproducible, A-B 1.7 dB with 82 dB spl stimulus levels on the intact side. At the time of submission, it had not been possible to obtain pre- and post-operative data from the same patient, but our ongoing research is addressing this comparison.

Vascular decompression patients. Patients who underwent retrolabyrinthine surgery for vascular decompression of the VIIIth cranial nerve, formed a control group. They were admitted to the study from the surgical population according to the same criteria as the neurectomy group, having normal otoscopy, tympanometry and pure tone thresholds better than 35 dB HL at a minimum of two adjacent frequencies, which remained within 15 dB of pre-operative levels. The selected cases also demonstrated auditory evoked brainstem potentials within the normal limits noted above for both absolute and interwave latency. CT scans, CT air meatography and MRI scans were conducted to exclude central abnormalities and/or confirm the diagnosis. The diagnosis of vascular compression is suggested by atypical Meniere's-like symptoms including imbalance and tinnitus, but excluding fluctuation in hearing levels. Symptoms may be exacerbated by positional changes and are invariably refractory to medical treatment. Three patients (28–42 years, 2 male, 1 female) who underwent vascular decompression have been studied. The vascular loops, evident via CT air meatography, were confirmed during surgery. Pre- and post-operative measurements have been conducted in one case to date.

Case P had pure tone pre-operative thresholds between 0–10 dB in the intact side which decreased by 5–10 dB for all frequencies except 8 kHz which remained the same. Thresholds in the operated side were ⁻5–15 dB before surgery and decreased post-operatively by 5–10 dB from 0.5–2 kHz with no change at the other frequencies. Pre-operative CEOAE amplitudes from the operated side produced 13.4 dB, 90% reproducible, A-B 3.6 dB with 88 dB spl click stimuli, and the intact side were 14.5 dB, 95% reproducible, A-B 1.4 dB with 86 dB spl stimulation. Post-operative CEOAE amplitudes on the operated side measured 12.0 dB, 89% reproducible with A-B 2.8 dB with 87 dB spl stimulation. Case D also had normal pure tone audiometry, with thresholds better than 20 dB HL for all frequencies tested (0.25–8 kHz) and no loss in function following surgery, thresholds varying 5–10 dB around the pre-operative values. CEOAE from the operated side were 17.7 dB spl, 97% reproducible, A-B −5.1 dB with 85 dB spl stimulation, and 14.4 dB, 95% reproducible, A-B 0.7 dB with 85 dB spl stimulation of the intact side. Case B had pre-operative hearing levels from 0–15 dB on the intact side which varied by at most 5 dB following surgery. The operated side had thresholds from 5–25 dB, with 4 and 8 kHz being less sensitive. Post-operative values varied from 0–10 dB of the pre-operative thresholds except for 4 and 8 kHz values which decreased by 15 and 20 dB. CEOAE were present in both ears with amplitudes of 7.7 dB, 59% reproducible, A-B 4.9 dB from the operated side with 83 dB spl click stimuli, and emissions of 9.5 dB, 75% reproducible, A-B 4.2 dB in the intact side with stimuli at 80 dB.

Surgical procedure. The retrolabyrinthine surgical approach to the cerebello-pontine angle was performed for both patient groups, as described by Silverstein & Norell (20). Vestibular neurectomy performed at this site removes both medial and lateral components of the olivocochlear bundle traveling within the inferior vestibular nerve. The patients made an uncomplicated recovery, with no evidence of facial nerve compromise. Audiometric profiles, evoked otoacoustic emissions and the efferent auditory tests were recorded between one week and twelve months post-operatively.

Audiometry. Standard pure tone audiometry was performed before and after the operation in a soundproof booth using a Madsen OB 802 audiometer. Threshold measurements at 0.25, 0.5, 1, 2, 4, and 8 kHz are reported relative to dB HL (ISO). Tympanometry and acoustic reflex thresholds at 0.5, 1, 2, 4 kHz and to broad band noise were measured using a GSI33 Middle Ear Analyzer. Auditory evoked brainstem potentials to click stimuli at 90 dB HL were recorded bilaterally using a Medelec ST10.

Otoacoustic emission procedures. Click evoked OAE were recorded using an Otodynamic Ltd.

ILO88 acoustic emission analyzer as described by Kemp et al. (21). Spectral analysis and amplitude measurement of the responses was performed by the system. The ILO88 probe was positioned in the external meatus and adjusted to ensure that the power of the frequency spectrum of the click stimulus was as equal as possible across the frequency range of 0.5–3.0 kHz. The OAE responses to 260 clicks were averaged, with and without use of the artifact rejection facility, at peak stimulus levels of 88 dB spl to 61 dB spl, followed by the "efferent test" procedures. The probe position remained stable, and was not adjusted or removed until the recording process was completed for the test ear.

Efferent test procedures. The contralateral stimulus was white noise generated by a Madsen OB802 audiometer via a TDH 39 earphone. The patients perceptual threshold to white noise was measured for each ear. The ILO88 was set to present OAE click stimuli at 61 dB spl ($\pm$ 2 dB) peak reception level in order to minimize interference from middle ear reflexes. Ten sets of 60 click responses were averaged and each set recorded separately. With each alternate set of ten recordings, a fixed level of continuous noise was presented to the ear contralateral to the probe. Three to four series were presented for each ear using different intensities of white noise at levels between 15–70 dB HL (equivalent to 5–55 dB sensation level (SL) above threshold). Contralateral stimuli were chosen to be at least 15 dB less than the individual's acoustic reflex threshold to white noise. The responses in quiet (no contralateral stimulus) and in noise (with contralateral white noise) were averaged into separate buffers. Averaged responses with less than 50% reproducibility (due to patient movement or environmental noise) were excluded from analysis. To give a measure of suppression, the averaged OAE amplitude of the whole response (5–20 ms) and of 1000 Hz and of 500 Hz frequency bands from 500–3000 Hz were converted from the dB SPL values calculated by the ILO88 spectral analysis system into microPascals, and the relative difference was expressed as a percentage change of the averaged response amplitude recorded in noise compared with the averaged OAE amplitude recorded in quiet.

RESULTS

Normals. All normal subjects ($n = 8$) demonstrated suppression of emission amplitude during contralateral acoustic stimulation. The amplitude of emissions were inversely related to the intensity of the contralateral stimuli. Comparing the difference in microPascal output in noise and in quiet for all subjects, the relative change in CEOAE amplitude of the whole response (5–20 ms) was associated with a mean decrease of 26.9% (sd 3.0) with 45–55 dB SL; 14.5% (sd 1.2) with 30–40 dB SL; and 8.14% (sd 1.9) with 15–25 dB SL contralateral stimulation. Direct observation of the filtered emission waveform shows a clear difference in peak to peak amplitude and a phase lead of responses recorded with noise versus quiet. A frequency specific inhibitory effect was observed by filtering the click evoked response within 500 Hz bands and comparing the responses recorded in quiet with responses during moderate levels of contralateral white noise (35–45 dB SL). The greatest suppression occurred within the 1.0–2.5 kHz range, with lesser effects at 0.5–1.0 kHz, and 2.5–3.0 kHz. The mean values of suppression observed in normals ($n = 8$) was 30.0% (sd 3.35) in the 1.0–1.5 kHz range; 25.7% (sd 2.5) in the 1.5–2.0 kHz range; 23.7% (sd 4.0) in the 2.0–2.5 kHz range; 18.7% (sd 2.8) in the 0.5–1.0 kHz range; and 18.4% (sd 4.5) suppression in the 2.5–3.0 kHz range.

Vestibular neurectomy patients. In all neurectomy patients examined, inhibition of CEOAE amplitude during contralateral stimulation recorded from the ear with severed efferent fibers was negligible in comparison with that recorded from the intact side or with normal values.

The findings are readily observed in Case i in whom contralateral stimulation produced virtually no observable change in amplitude or phase of emissions from the cochlea with severed efferent fibers during 25 dB SL noise (showing a decrease of only 4.5% in CEOAE amplitude). In contrast, a clear peak to peak decrease in amplitude equivalent to a 13.9% reduction, and a phase lead can be observed in the waveforms recorded from the intact side with 25 dB SL noise versus those recorded in quiet (Fig. 1). Case ii demonstrated similar results. Suppression of otoacoustic emissions was absent (0.0% change) from the operated side with moderate levels of contralateral stimulation (45 dB SL), whilst CEOAE amplitude from the intact side decreased by 11.9% from amplitudes recorded in quiet (Fig. 2).

Efferent auditory effect as a function of contralateral stimulation intensity. The decrement in amplitude as a function of contralateral stimulus intensity for both ears in Case i is shown in Fig. 3. The amplitude of emissions from the sectioned side was clearly not related to the intensity of the contralateral stimuli for levels from 5–45 dB SL (30–70 dB HL). The averaged amplitude of the whole response from the sectioned side decreased by at most 7.74% with 35 dB SL (60 dB HL) contralateral noise, relative to recordings in quiet, which is less than 2 standard deviations from the decrease observed in normals. CEOAE amplitude from the intact side decreased with contralat-

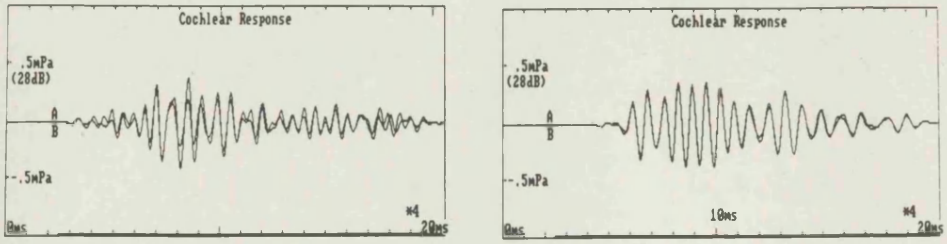

Fig. 1. Vestibular neurectomy Case i. The effect of contralateral white noise on click evoked OAE waveforms. The intact side (*left trace*) shows a decrease in peak to peak amplitude and a phase lead of the filtered (1000 Hz band) waveform recorded in 25 dB SL noise (trace A) relative to quiet conditions (B). The operated side (*right trace*) shows virtually no observable difference in amplitude or phase of filtered waveforms recorded without or with 25 dB SL of contralateral noise.

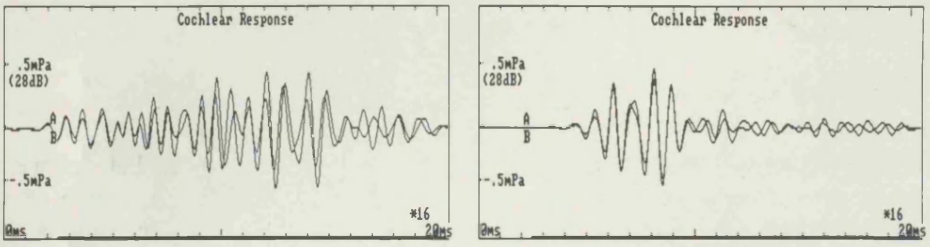

Fig. 2. Vestibular neurectomy Case ii. Superimposed filtered OAE from the operated side (*right trace*) demonstrates the lack of inter-aural suppression following neurectomy with 45 dB SL contralateral noise. Inhibition of OAE amplitude with contralateral noise at 45 dB SL was maintained on the intact side (*left trace*).

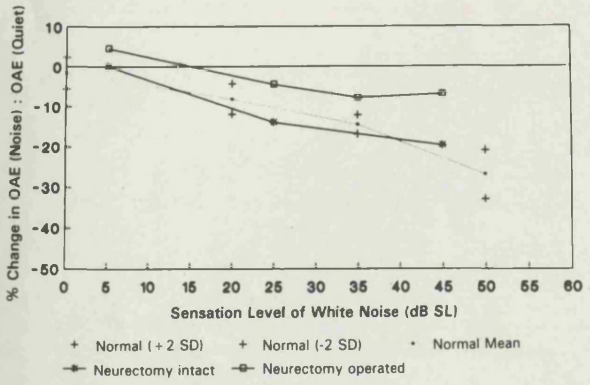

Fig. 3. Suppression of OAE amplitude as a function of contralateral stimulation level following vestibular neurectomy. In comparison with normal measures (mean and ± 2 standard deviations), Case i demonstrates negligible suppression of OAE amplitude on the operated side (*square symbols*), whilst inter-aural suppression is maintained at normal levels on the intact side (*star symbols*), and is inversely proportional to the level of contralateral stimulation.

eral noise stimulation, and was inversely related to the intensity of the stimulus. Contralateral stimulation at 25 dB SL (50 dB HL) was associated with reduction of CEOAE amplitude by 13.9%. Increasing the level of contralateral noise to 45 dB SL (70 dB HL) suppressed the amplitude by 19.64%.

Efferent auditory effect as a function of OAE frequency. Bilateral CEOAE from Case i had spectral response patterns well above the noise floor within the frequency range of 0.5–3 kHz for which the ILO88 microphone response function is relatively constant. Spectral analysis of the emissions within 500 Hz bands from the intact side demonstrated a frequency specific pattern of inhibition with 25–35 dB spl noise which was consistent with our normal results, for all frequencies from 0.5–3.0 kHz, except within the 1.0–1.5 kHz band. In contrast, CEOAE suppression in the operated side was less than 2 standard deviations from the mean observed in normal subjects for all frequency bands measured (Fig. 4).

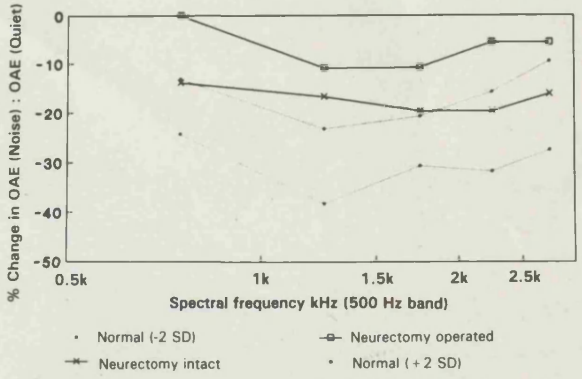

Fig. 4. Frequency specificity of OAE inhibition following vestibular neurectomy. The effect of contralateral white noise (35 dB SL) on 500 Hz bands of the click evoked OAE waveforms from the operated and intact sides of Case i in comparison with the response in normal subjects (± 2 standard deviations).

Vascular decompression patients. In all cases examined a decrease in amplitude and phase lead was observed in emissions recorded during contralateral stimulation from both operated and intact sides following vascular decompression. Fig. 5 shows the filtered emissions (1000 Hz band) from the operated sides of three cases with the waveforms recorded in noise superimposed over those recorded in quiet. Fig. 6 illustrates the relative decrease in CEOAE amplitude as a function of stimulus intensity for both the operated and intact sides of these cases. CEOAE amplitude recorded in noise was inversely related to the intensity of the contralateral stimuli. Suppression was induced with contralateral stimulation greater than 15 dB SL (30 dB HL), and was comparable for both sides, showing a drop in CEOAE amplitude from 10.87% with 30 dB SL to a maximum decrease of 31.61% with 45 dB SL (35–65 dB HL). These values of inhibition were within at least 2 standard deviations of the range recorded in normals.

The emissions from Case P showed that 35 dB SL contralateral noise was associated with inter-aural suppression of equivalent magnitude (18.72%) in both the operated and intact sides. This patient was

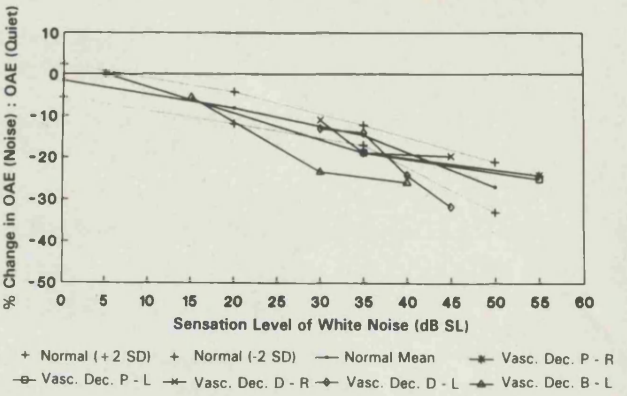

Fig. 6. Suppression of OAE amplitude as a function of contralateral stimulation level following vascular decompression. The relative suppression of OAE amplitude (% change of amplitude in noise versus quiet) as a function of contralateral stimulation is illustrated for the operated and intact sides (R = right, L = left) of Cases D, P, B. The control data is comparable to suppression observed in normals (mean ± 2 standard deviations).

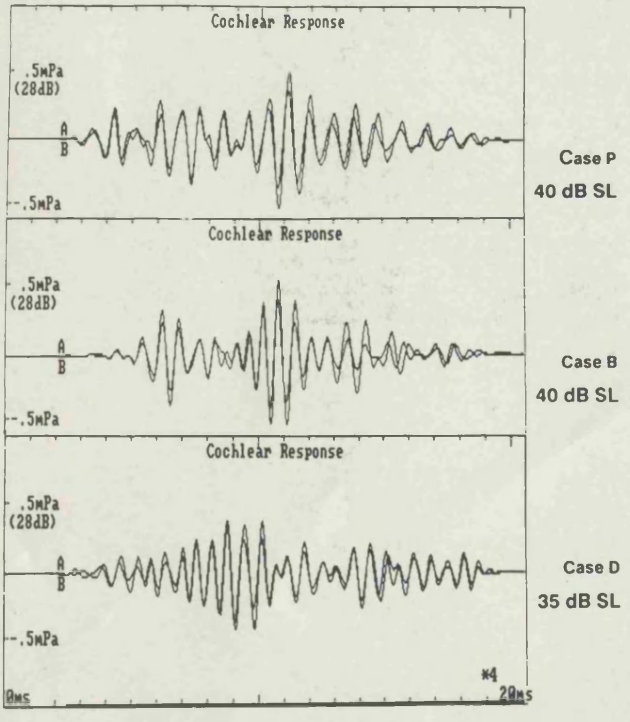

Fig. 5. OAE suppression in surgical controls. Inter-aural inhibition of OAE amplitude was maintained following vascular decompression of the VIIIth nerve. The effect of contralateral white noise on filtered (1000 Hz band) CEOAE from the operated side of 3 cases show a peak to peak decrease in amplitude of OAE recorded in noise (B) relative to responses recorded in quiet (A). Contralateral intensities are expressed in dB sensation level (SL).

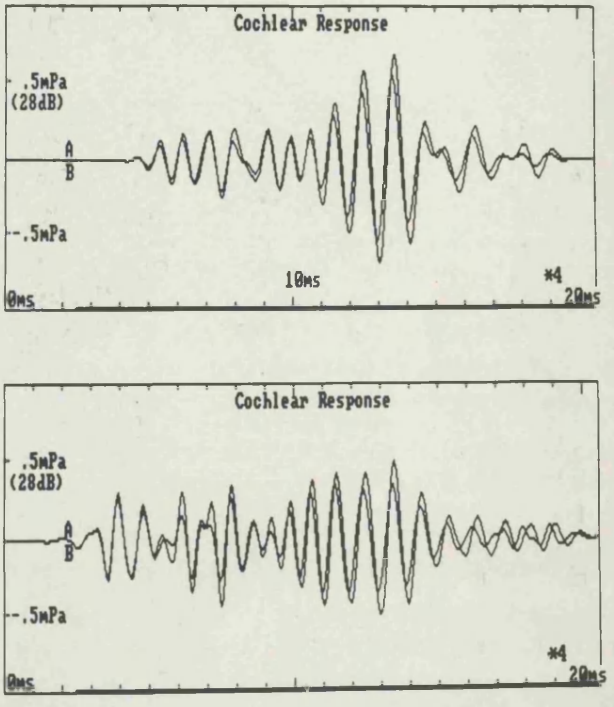

Fig. 7. The suppressive effects of contralateral acoustic stimulation are maintained following vascular decompression surgery (Case P). Filtered waveforms (1000 Hz band) from the operated side were recorded pre-(*upper trace*) and post-(*lower trace*) operatively. OAE responses with 30 dB sensation level of contralateral white noise (B) are superimposed over emissions recorded in quiet (A) revealing a decrease in peak to peak amplitude of waveforms recorded in quiet.

studied before and following surgery, and demonstrated that contralateral suppression was maintained relative to pre-operative levels (Fig. 7).

DISCUSSION

The study of patients undergoing vestibular neurectomy resulting in section of the efferent olivocochlear bundle traveling within the inferior division of the vestibular nerve, provides a human physiological model for examining the role of the efferent auditory system in controlling cochlear responses (see Williams et al. (19)). Otoacoustic emission measurements demonstrated that in the absence of efferent innervation, contralateral acoustic stimulation had no observable effect on the amplitude or phase of emissions recorded from ears with severed nerve fibers. In contrast, control information from the patients' intact side showed that inhibition of OAE was maintained, exhibiting a clear phase lead and reduction in amplitude that was inversely related to the level of contralateral noise intensity and with a frequency specific pattern which was consistent with our normative results and with recently reported normal studies (17, 18). These findings suggest that the inhibitory effect of contralateral noise on cochlear emissions was absent as a result of sectioning the efferent olivocochlear bundle.

During surgery the isolation of the vestibular nerves is assisted by observation of a fine septum between the cochlear and vestibular nerves in 75%–80% of patients, however there can be an intermingling of cochlear and vestibular fibers along the apparent line of division, with an overlapping zone occupying approximately 16–33% of the area of the cochlear subdivision (21). Warren & Liberman (16) provided evidence of the efficacy of vestibular nerve section in routinely interrupting the entire OCB in cats, as demonstrated by the lack of retrograde labeled neurons in the superior olivary complex following perfusion with horseradish peroxidase. Although it is not always possible to be certain that all of the inferior vestibular fibers or the entire efferent auditory bundle traveling within it, will be completely severed, a clear anatomical demarcation between the cochlear and vestibular nerves was apparent in the vestibular neurectomy patients at operation, and in clinical terms they experienced a complete resolution of vestibular symptoms. As there was no significant loss in the pure tone audiometry after the operation, it is unlikely that the absence of OAE suppression observed following neurectomy was a result of undetected surgical disruption of the afferent auditory system.

In order to assess the impact of retrolabyrinthine surgery on inter-aural suppression of emissions, patients who had undergone a similar surgical approach for vascular decompression of the VIIIth nerve, but without nerve section were studied. In all cases examined, inter-aural suppression of OAE was observed in both the operated and intact sides, with OAE amplitude decreasing with increasing contralateral noise levels. Post-operative measures of OAE amplitude and inhibition were comparable with pre-operative values in the case examined. This further indicates that the retrolabyrinthine surgery itself need not interfere with inter-aural suppression of otoacoustic emissions.

Our normal group displayed similar results to the control surgical population. Normal hearing adults showed that low to moderate levels of contralateral noise (15–45 dB SL) were consistently associated with inhibition of OAE amplitude. The magnitude of suppression was inversely related to the level of the contralateral stimuli, and was most effective at frequencies above 1 kHz in a broadly tuned pattern. Given that the test measured the effect of a broad band contralateral noise on a broad band eliciting ipsilateral stimulus, a sharper tuning curve need not be expected.

It has been suggested that the contralateral effect could be a function of the bilateral activation of the acoustic reflexes resulting in reduced transmission of the OAE to the ear canal. To avoid reflex activation, the protocol utilized noise and OAE stimuli at intensity levels below reflex thresholds, although the possibility that the muscles were active below the levels measurable with standard clinical tympanometric devices cannot be entirely excluded. Our results, which show that vestibular neurectomy patients *with intact acoustic reflexes* showed *negligible suppression* after OCB section, diminishes the possibility that the effect is mediated solely via the middle ear muscles. Other studies have demonstrated that the effect of contralateral stimulation persisted in subjects with unilateral loss of the acoustic reflex after surgical removal of the stapedius muscle or as a result of Bells Palsy, and comparisons between normals and patients without acoustic reflex showed no difference between the two groups in OAE suppression except for a slightly stronger suppressive effect, especially in the case with Bells Palsy (18). These observations, and the findings in this study, might be imputed to the age or underlying pathologies of the subjects, however animal experiments also report that inter-aural suppression of DP emissions (15) and auditory nerve responses (16) were maintained after section of the middle ear muscles suggesting that inhibition cannot be accounted for solely on the basis of middle

ear activity. In addition, Warren & Liberman (16) argue that the frequency dependence of the effect is more consistent with the frequency distribution of efferent innervation in the middle range of frequencies, and is incompatible with the acoustic reflex activity which is most effective at a lower frequency range. In this study the maximum effect of contralateral white noise was seen above the frequencies of the response spectrum thought to be within the most effective range of the acoustic reflex.

Cochlear responses can, of course, be inhibited by transcranial masking of the OAE stimulus if the contralateral noise intensities are sufficiently loud. The protocol was therefore designed to avoid masking of the OAE stimuli via transcranial transmission by using low to moderate contralateral stimuli intensities, well below that found to cause cross-masking in normal subjects (17, 18).

Previous studies of post-operative hearing function in vestibular neurectomy patients utilizing the available psycho-acoustic techniques (pure tone and Békésy audiometry, SISI, speech reception and discrimination tests) have thus far failed to reveal a loss of function that could be imputed to the efferent system (23). Most neurectomy patients reviewed in the literature appear to maintain pure tone and speech threshold relative to pre-operative levels (53–86%), whilst up to 27% have worse pure tone scores, and up to 32% have worse speech scores (24, 25). Interestingly, most of the authors reviewed report a small proportion of patients whose pure tone (9–16%) and speech test (13–28%) improve post-operatively. Fisch (23) observed that discrimination improved with a concomitant disappearance of the recruitment phenomenon, although this might have been attributed to the loss of tinnitus, but he was not able to detect any consistent postoperative change in cochlear function.

Our methods, which measure the change in otoacoustic emissions associated with the presentation of contralateral acoustic stimulation, were able to detect postoperative loss of an inhibitory efferent function, suggesting that the human efferent olivocochlear fibers have a similar role in modulating cochlear responses to that observed in animal studies. Warren & Liberman (16) reported that in cats contralateral acoustic stimulation produced a relative decrease in afferent nerve activity from 10–55% of the response rate recorded in quiet. No significant suppression was seen in any units following section of the entire OCB at the vestibulo-cochlear anastomosis, whereas cutting the crossed medial fibers alone at the floor of the fourth ventricle had little effect on inter-aural suppression. The relative contributions of the lateral and medial efferent systems to inter-aural suppression remains unclear, although the observation that the medial olivary neurons innervate the outer hair cells (essential for the production otoacoustic emissions) and respond to contralateral stimulation (14) further suggests that the loss of inter-aural suppression of otoacoustic emissions observed in this study was a consequence of the absence of efferent innervation.

Interestingly, our results showed that the transection of the olivocochlear bundle in one vestibular neurectomy case was associated with an improvement in pure tone audiometry, but without hyperacusis. OAE recorded 2–12 months following sectioning were of normal amplitude, and not suggestive of the undamped oscillations which might be presumed to result from a loss of tonic negative feedback. This is consistent with the observation by Liberman & Brown (14) that olivocochlear neurons rarely exhibit spontaneous activity. One could argue that homeostatic changes altered the cochlear responses post-operatively in order to compensate for de-efferentation. Alternatively, the observations could be explained by the loss of positive as well as negative feedback function, and perhaps reflect the loss of lateral as well as medial efferent systems. It should also be noted that otoacoustic emissions are a reflection of a portion of the summated response of many elements, and the manifestation of loss of efferent control will be related in a complex manner to the gross emission waveform.

Currently, further pre- and post-operative tests are being conducted to provide a more rigorous investigation of the impact of sectioning the efferent bundle, with a view to exploring the role of the efferent auditory system in human cochlear micro-mechanics and the potential of otoacoustic emission techniques as a rapid non-invasive test for investigating olivocochlear bundle dysfunction. Our investigations were able to detect a loss of inhibition as a result of de-efferentation after vestibular neurectomy, which was not observed in the control surgical population, suggesting that the techniques described may provide a useful clinical procedure for the assessment of efferent auditory function in humans.

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