EFFERENT INDUCED CHANGES ON ACOUSTIC REFLEX

Register No. M9901

An Independent Project submitted as part fulfillment foi the I year M.Sc. (Speech and Hearing) to University of Mysore

ALL INDIA INSTITUTE OF SPEECH AND HEARING, MYSORE-570 006

MAY, 2000

Certificate

This is to certify that the Independent Project entitled "Efferent Induced Changes on Acoustic Reflex* is a bonafide work done in part fulfillment for the degree of Master of Science (Speech and Hearing) of the student with Register No.M 9901.

Mysore,
May, 2000

Director
All India Institute of
Speech & Hearing
Mysore - 570 006

Certificate

This is to certify that the Independent Project entitled "Efferent Induced Changes on Acoustic Reflex" has been prepared under my supervision and guidance.

Mysore,
May, 2000

Animesh Barman
Lecturer,
Dept. of Audiology,
A.I.I.S.H., Mysore - 570 006

Declaration

I hereby declare that this Independent Project entitled "Efferent Induced Changes on Acoustic Reflex" is the result of my own study under the guidance of Mr. Animesh Barman, Lecturer, Department of Audiology, All India Institute of Speech and Hearing, Mysore, and has not been submitted earlier in any other University for any other Diploma or Degree.

Mysore,
May, 2000

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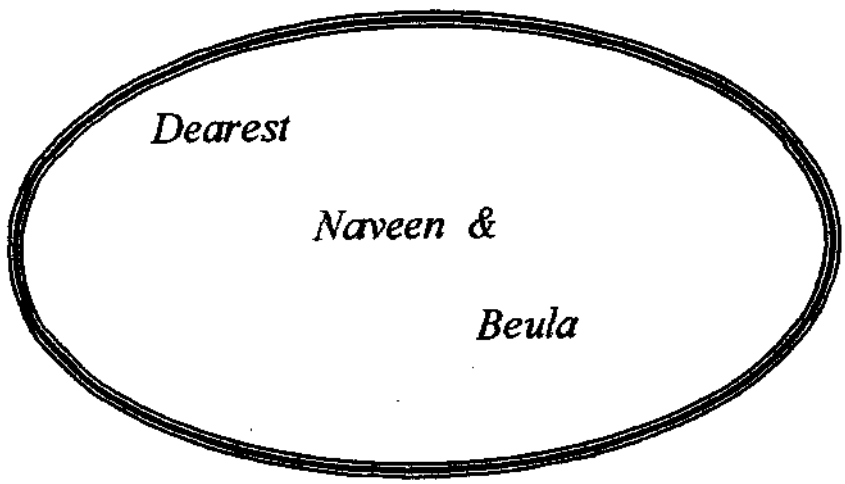
Dedicated to



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INTRODUCTION

In humans, the role of ear is extremely important. It is one of the most important links in speech chain, which enables proper communication. All the information from peripheral receptor organ of the ear is carried to the central organ, the brain for analysis, by means of the auditory or eight cranial nerve. The higher organs can have control over the peripheral receptor the cochlea by means of two major efferent feed back pathways viz., middle ear muscle, reflex, and olivocochlear reflex [Liberman & Guinan, 1999].

The acoustic reflex (AR) is the contraction of the stapedius muscle of the middle-ear in response to an acoustic activating signal. This contraction can be monitored by recording the resultant change in the acoustic immittance of the middle ear.

The acoustic reflex center is situated in superior olivary eomplex(SOC) of the brainstem. There are four acoustic-reflex arcs, two epsilateral and two contralateral (Borg,1978). The ipsilateral acoustic reflex arc consists of

1. The primary auditory neuron of the eighth cranial nerve from the hair cells of the cochlea to ventral cochlear nuclei (CN),

2. The second order neuron from the ventral cochlear nuclei through the trepezoid body to the ipsilateral superior olivary complex,
3. The third-order neuron from the ipsilateral superior olivary complex to the ipsilateral facial-nerve nuclei (FMN). But some neurons from VCN bypass the superior olivary complex and synapses directly with the FMN constituting second ipsilateral path way.
4. Fourth-order neuron from the ipsilateral facial-nerve nuclei to the ipsilateral stapedius muscle.

Contralateral acoustic reflex arc has,

1. The first-order neuron to the ipsilateral ventral cochlear nuclei.
2. The second-order neuron from the ipsilateral ventral cochlear nuclei to the ipsilateral superior olivary complex. Some fibers from ipsilateral ventral cochlear nuclei may cross over and synapses with the contralateral superior olivary complex and sends fibers to the contralateral FMN
3. The third-order neuron from ipsilateral superior olivary complex to the contralateral facial-nerve nuclei.
4. Fourth-order neuron from contralateral facial-nerve nuclei to contralateral stapedius muscle.

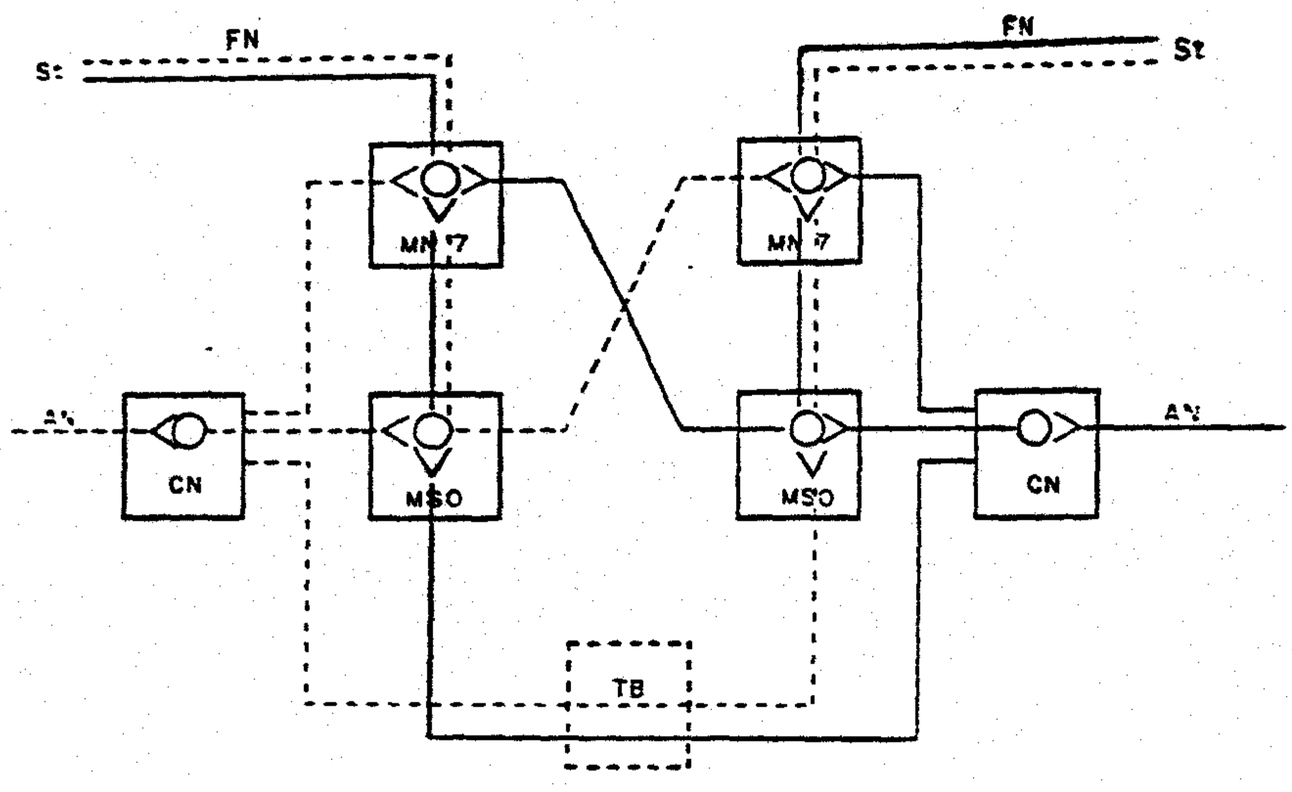

Fig.1. Schematic diagram of the acoustic reflex arc. Solid lines indicate right ear pathways, clashed lines indicate left ear pathways. AN: auditory nerve (cranial nerve VIII). CN: cochlear nucleus. TB: trapezoid body. MSO: medial superior olivary complex. MN7: motor nucleus of cranial nerve VII. FN: facial nerve (cranial nerve VII). St: stapedius muscle.

The reflex contraction after a loud acoustic stimulus causes the stapes foot plate to swing outward and backward from oval window. This action attenuates the vibrations of stapes foot plate, thereby reducing the fluid motion of inner ear.

The efferent innervation that terminates in the cochlea consists of two sub-systems: the lateral and medial efferent pathways (Warr & Guinan, 1979). The lateral olivocochlear efferents orignate from small neurons in and near the lateral superior olivary nucleus. They have unmyelinated axons, and terminate on the dendrites of auditory nerve radial afferent fibres in the region beneath IHCs. Medial olivocochlear efferents originate from larger neurons located medial, ventral and anterior to the medial superior olivary nucleus. These have myelinated axons, and terminate directly on OHCs (Warr and

Guinan, 1979; Guinan, Warr, and Norris, 1983). The auditory afferents fibres terminate in the cochlear nuclei which sends connections to both ipsilateral and contralateral superior olivary complex from where the efferent are originated. Thus the olivo cochlear bundle forms an inter-cochlear loop, where by stimulation of one cochlea modifies the functioning of the opposite cochlea.

These efferent fibers can be activated by the electrical stimulation at the floor of forth ventricle (Galambos, 1956) or by contralateral acoustic stimulation (Buno, 1978). The stimualation of efferent system by these method reduces the compound action potentials of the auditory nerver (N 1 , or reduces the amplitude of both spontaneous (Mott et al., 1989) and evoked otoacoustic emission (Collet et al., 1990; Veuillet et al., 1991). This is due to reduction of gain of cochlear amplifier.

Although early literature emphasizes efferent effects at low sound levels (Galambos, 1956; Mountain, 1980), recent work suggests that the most significant effect of medial efferents may be at moderate and high sound levels. (Guinan and Stonkovic, 1995). Other recent data suggest a role of efferents in preventing damage to cochlea due to intense sounds (Rajan & Johnstone, 1983a: Rajan, 1988: Reitor and Liberman, 1995).

Similarly, stapedial acoustic reflex is also produced at high sound levels, can be used as a noninvasive technique to study the effect of efferent stimulation at high sound levels.

Since, there is a dearth of literature on effects of efferents for high sound levels, this study was aimed.

1. to examine the effect of contralateral wide and narrow band noise presentation on acoustic reflex.
2. To see whether OCB has a protective effect or not.
3. To develop a test for efferent pathway using acoustic reflex.

REVIEW OF LITRATURE

The mammalian cochlea receives efferent innovation from both ipsilateral and contralatexal superior olivary complex (SOC). These descending fiber tracts, known as olivocochlear bundle (OCB), represents the final link of chain of neurons from the cortex to the cochlea (Desmedt 1975). The OCB is composed of two separate systems. The medial olivocochlear (MOC) projections primarily to outer hair cells (OHCs) and lateral olivocochlear (LOC) projections primarily to inner hair cells (IHCs) (Warr and Guinan, 1979).

Approximately 72 to 74% of MOC fibers travel to the contralateral cochlea. The remaining 26 to 28% course ipsilaterally (Guinan, et aL 1983, 1984; Warr, 1975). Approximately 89 to 91% of LOC fibers destined to terminate in the ipsilateral cochlear IHC region and remaining 9% to 11% project to contralateral IHCs (Guinan, et aL, 1983,1984; Warr, 1992).

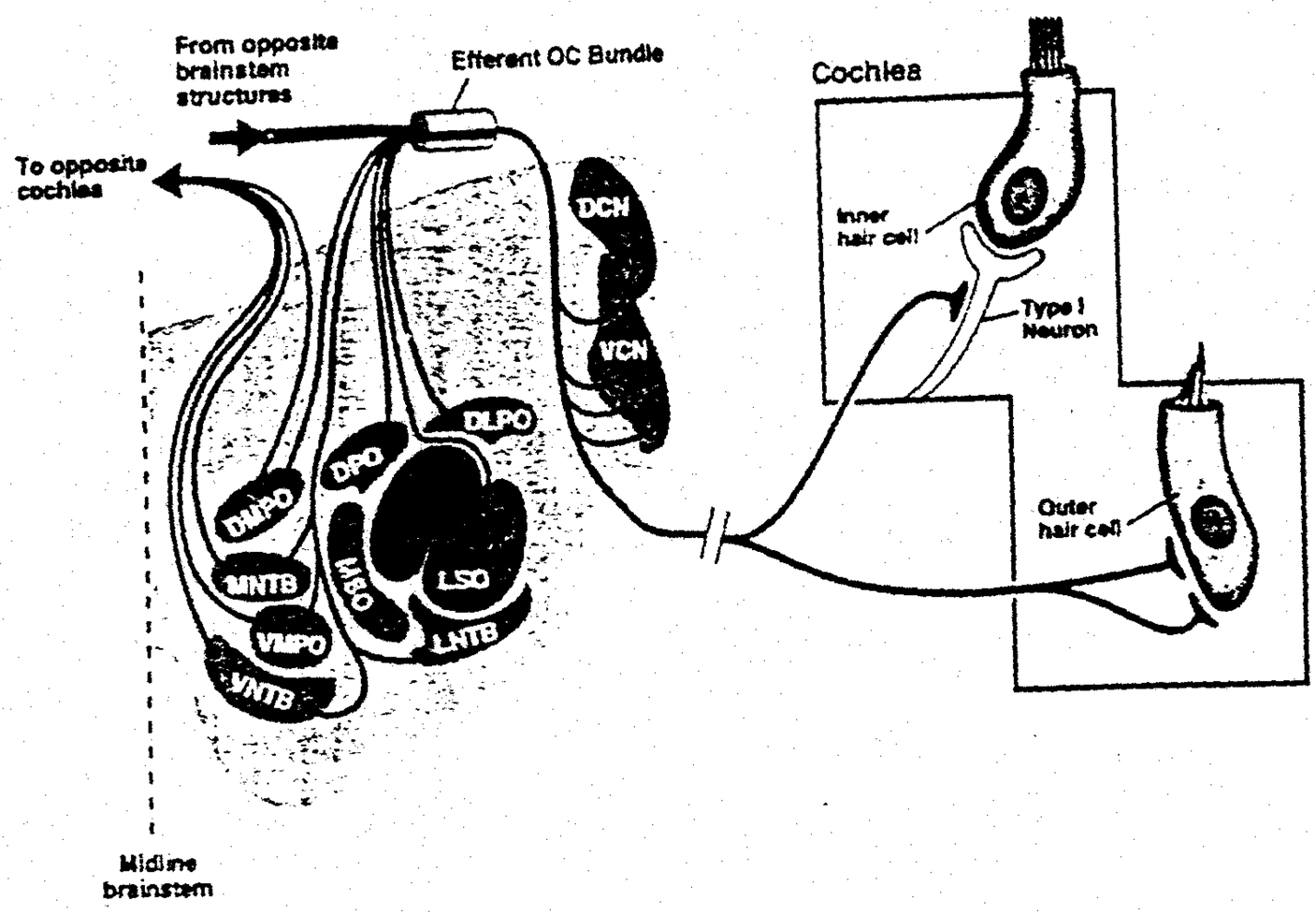

Fig. 2: Schematic of the efferent olivocochlear system showing the distribution of fiber projections from efferent nuclei to targets withn the cochlea.

Medial efferent innervation is largest near the centre of the cochlea, with the crossed innervation biased towards the base compared to the uncrossed innervation. In contrast, lateral efferent innervation is relatively constant in the center and base of the cochlea. (Guinan, Warr and Norris, 1984; Liberman, Dodds and Pierce, 1990).

Although the existence of an efferent innervation of the mamalian cochlea was described more than 50 years ago (Rasmussen, 1946), the functional role of these fibers remain unclear. In general, the OCB has an inhibitory effect on the auditory periphery. Because of its predominently inhibitory nature, it has been hypothesized that the efferent system serves a

protective role in the auditory system (Rajan, 1988). It also hypothesized that the activation of OCB enhances the detection of sound in noise (Michely & Collet, 1996) and maintains the cochlea at an optimum mechanical state for efficient function of active processes (Johnstone et al, 1986).

Although biological significance of medial efferent fibers remains ambiguous, it is clear that activation of MOCB alters the cochlear output. For example, electrical stimulation of MOC bundle at the floor of forth ventricle inhibits cochlear and neural potentials (Galambos, 1956 , Gifford and Guinan 1983,1987; Fex, 1959, Mountain, 1980) MOC fibers can also be activated by acoustic stimulation (Buno, 1978). BBN presented to the ear opposite to the test ear reduces the amplitudes of several auditory responses such as compound action potential (Galambos, 1956, Gifford and Guinan, 1987) spontaneous rate (SR) of auditory nerve fibers (Wiederhold & Kiang, 1970; Buno, 1978) and oto-acoustic emissions.

The review of literature about the physiology of efferent system can be classified under the following headings.

1 Effect of medial efferent system

a) On cochlear potentials;

b) On cochlear amplifier, and

c) Beyond cochlear amplifier.

II Effects of lateral efferents on cochlear mechanics.

III Effects of efferent over stapedial acoustic reflex.

I Effect of medial efferent system

(a) On cochlear potentials

Perhaps the best known effect of efferent activity is to depress the compound action potential of auditory nerve, N1 (Galambos. 1956; Desmedt 1962; Wiederhold and Peake, 1966). This inhibition can be seen with N1 S evoked by clicks or by tone pips. Efferent activity evoked by electrical stimulation and contralateral sound produces qualitatively similar effects (Buno, 1978; Murata et al, 1980; Folsom & Owsley, 1987; Liberman, 1989). These inhibition was greatest at low sound levels (Galambos, 1956).

In addition to inhibiting N1 medial efferents also affect non neural cochlear potentials. Efferent stimulation increases the amplitude of cochlear microphonics (CM). This increase is typically larger at high sound levels than at low sound levels and can be as large as 4 dB (Fex, 1959; Kittrell and Dalland, 1969; Mountain et aL, 1980; Gilford & Guinan, 1987).

The endochochlear potential bathing the haircell cillia is around +80 to +90mv. Stimulation of OCB decreases this endocochlear potential by few milivolts. This decrease in large positive endocochlear potential is termed as

"Medial olivocochlear potential" (MOC) (Fex, 1959, 1962; Konishi and Slepian 1971; Brown and Nuttall, 1984; Gifford and Guinan, 1987).

This change in the CM and EP potential can be understood from the electrical properties of the cochlea. Efferent stimulation increases OHC basolateral conductance and hyperpolarizes OHCs. This results in increase in current flow and thereby increase in CM (Davis, 1965; Dallos and Cheatham. 1975). The increased conductance and hyperpolarization of the OHCs causes an increased DC current flow through OHC stereocilia thereby decreasing the large positive endocochlear potential. This decrease in large positive endocochlear potential is termed as 'MOC' potential.

b) On cochlear amplifier:

OHCs are known to be cochlear amplifier, OAEs are believed to be generated by active mechanisms in the cochlea which involves OHCs. Since OHCs receive direct efferent innervation they may be affected by contralateral acoustic stimulation of olivocochlear bundle (Kim, 1986).

Distortion product otoacoustic emmissions (OPOAEs) are tones produced by distortion in the cochlea in response to two externally supplied tones, the primary tones ($f_1 < f_2$) the $2f_1 - f_2$ distortion product has the highest amplitude and has been moststudied. Efferent stimulation usually decrease the amplitude of DPOAEs, (Mountain 1980; Siegel & Kim, 1982). On

average, efferent inhibition of DPOAEs is greatest for low level primaries and decreases as primary tone level is increased (Mountain, 1980; Moulin, Collet and Duclaux, 1993).

Similarly, activity of medial efferent inhibits transient evoked OAEs and stimules frequency evoked OAEs (Guinan, 1986, 1991; Ryan, et al., 1991).

Medial efferents produce small changes in SOAEs. SOAE frequency shifts to higher frequencies and amplitude can change in either direction (Mott et al., 1989; Harrison and Bums, 1993).

There are wide variety of machanisms by which medial efferents might affect OAEs.

* At low to moderate sound levels, medial efferent induces depression of basilar membrane. (Dolan and Nuttall, 1994).
* It affect the operation of OHCs, i.e., it may reduce the OHC receptor potential, which would reduce OHC motion (Santos-sachi and Dilger, 1988).
* It hyperpolaries the cell, which moves the membrane potential away from the optimum voltage for voltage to length transduction (Roddy et al., 1994).

* Efferent induced-contractions of OHCs distort the organ of corti, thereby lowering the gain of the cochlear amplifier (Rajan, 1990).
* Finally, medial efferents reduces the endocochlear potential which reduces the gain of cochlear amplifier (Seweli, 1984).

c) Beyond Cochlear Amplifier;

These are efferent effects that are not completely explained by medial efferent control of cochlear amplifier. This include

1. Medial efferent induced changes in auditory nerve spontaneous rate
2. Medial efferent inhibition of auditory nerve responses to high level sounds
3. Potection of cochlea from high level sounds.

1. Efferent induced changes in auditory nerve spontaneous rate.

The discharge of neural impulses by auditory nerve in the absence of acoustic stimulation is called "spontaneous firings". The stimulation of medial efferent reduces the spontaneous activity of auditory nerve fibers, even in very insensitive fibers (Wiederhold and Kiang, 1970; Guinan and Gifford, 1988; Kawase et al., 1993). This observation is not due to an efferent induced reduction of cochlear amplifer gain. Guinan and Gifford (1988) hypothesized that this is due to the MOC potential.

1 **On High Sound Levels:**

In addition to the well known changes for low sounds, medial efferents also decrease auditory nerve fiber responses to high level sounds. In most studies of efferent effects as a function of sound level (Wiederhold, 1970; Gifford and Guinan, 1983; Guinan and Gifford, 1988), rate versus sound level functions were obtained by presenting low level to high level sounds in sequence with efferent stimulation (by electrode placed at IV ventricle) and no efferent stimulation conditions alternating at each sound level. Such a level functions show a region in which the rate increases Tapidly with the sound level and at high sound levels there is a "saturated" or "plateau" region. In these level functions efferent stimulation produced small depression in plateau region (Guinan & Stankovic, 1995).

For mid frequency auditory nerve fibers, efferent stimulation reduced plateau rates in high-SR fibers by 5% and in low-SR fibers by more, often 15% to 20% (Guinan & Gifford, 1988). Although these data demonstrate that efferents have substantial effects at high sound levels, the interpretation of these experiment is difficult because with the sequential paradigm, the firing rates are strongly influenced by adaptation.

Recent experiments show that medial efferent produces large effects on responses to high-level sounds (Guinan and Stankovic, 1995) even when the influence of adaptation is minimised by randomising the sound level

function . These experiments have shown that, high spontaneous rate fibers show little effect of efferent stimulation, however, for medium SR and low SR fibers, efferent stimulation has a strong effect, even at 100 dB SPL. At 100 dB SPL, efferent inhibition can reduce the rate by an amount equivalent to more than 20 dB reduction in sound level. At these high sound levels, 20 dB of efferent inhibition is unlikely to be produced by reduction in basilar membrane motion.

3 . <u>Protective Effect:</u>

Efferents appear to provide some protection from temporary threshold shift (TTS) due to intense sounds. In the last few years, many reports have been published on this phenomenon, with conflicting results; some found a protective effect (Cody and Johnstone, 1982; Rajan and Johnstone 1983a; Rajan, 1988; Putuzzi and Thompson, 1991). Some did not (Trahiotis and Elliott, 1970; Liberman, 1991), and some found that it depended on experimental conditions (Reiter and Liberman, 1995).

Cody and Johnstone (1982) found that monoaural losses in hearing sensitivity induced by an intense pure tone could be reduced if an acoustic stimulus of the same frequency was simultaneously delivered to the other ear. The reduction was eliminated after the administration of strychnine a known blocker of auditory efferent activity. They concluded that acoustic activation of auditory efferents is responsible for reduced TTS.

In his review of "Protective functions of the efferent pathways to the mammalian cochlea", Rajan (1992), concluded that brain stem electric stimulation, contralateral acoustic stimulation (CAS) and contralateral cochlear distraction (CCD) resulted in decrease in the TTS produced by intense sound. He attributed these protective effects were due to the crossed olivocochlear bundle because these effect was eliminated by administration of strychnine and lesioning at the floor of forth ventricle which destroys MOCB.

Takeyama et al, (1992) concluded that there was significant protective effect for intermediate intensity and no protective effect for greater or milder intensities, by exposing guinea pigs to sounds of varying intensity (110-130 dB SPL) with and without electrical stimulation of COCB, using threshold shift for compound action potentials as an indicator.

Pujol, (1994) in his reviewed efferent neurochemistry and pharmacology, with an emphasis on the protective roles. He concluded that lateral efferent neurotransmitters, particularly enkephalons and dopamine may play role in protecting the auditory nerve dendrites against excessive noise and/or oto-toxicity. The cholinergic medial efferents synapsing with OHCs play a role in altering and/or modulating cochlear micromechanics.

II Effects of lateral efferents:

Although there is no direct evidence of effects of lateral efferents, it has been reported that lateral efferents that contain Ach may excite auditory-nerve fibers (Felix and Ehrenbergen 1992; Liberman, 1990) and lateral efferents that contain GABA may inhibit AP of auditory nerve fibers (Flexi and Ehrenberger, 1992).

Sahley and Colleagues (1991; 1994) have suggested that enkephalins found in lateral efferents may increase auditory sensitivity near threshold.

III Efferent effect over acoustic reflex:

Higson, Stephenson and Haggard (1996) reported the binaural summation of acoustic reflex. They found out ipsilateral acoustic reflex threshold (ART) with and without contra lateral stimulation. Contralateral stimuli was of the same frequency as that of reflex activating stimulus and intensity was ipsilateral ART+ (contralateral ART- ipsilateral ART). They noted an improvement in the acoustic reflex threshold by about 4.4 dB. But 3 subjects out of 34 showed negative summation i.e., elevation in threshold and some showed no difference.

Downs and Cram (1980) reported four case studies with low acoustic reflex threshold. All of them had some retrocochlear and/or CNS impairment as suggested by neurologic, audiologic, speech pathological and psychological evaluation. In these patients acoustic reflex thresholds were found with values as low as 55 dB. It is suggested that these low thresholds represents reduced central inhibitory influence on peripheral auditory function.

Borg (1971) measured the acoustic reflex threshold in the awake rabbit, before and after the COCB sectioning. He found that ART were decreased by 12 dB after the sectioning. These results indicate that the efferent system has some influence over the acoustic reflex.

METHODOLOGY

This study was taken up to examine the effect of contralateral broad and narrow band noise presentation on acoustic reflex and its physiological basis.

SUBJECTS

Comprised of 60 volunteers (30 males and 30 females) age ranged from 17 to 23 years (mean age = 20 years). All the subjects had pure tone hearing thresholds less than 15 dB HL in the frequency range from 250 Hz to 8 kHz. The immittance measures revealed 'A type' tympanograms and normal reflexes on screening. None of the volunteers reported of any history of ototoxic drug usage, noise exposure, previous history of otologic disease, tinnitus or giddiness etc.

Equipment used:

The following equipment were used in the study.

a) The GRASON-STADLER (GS1-16) clinical audiometer with standard accessories as specified by manufacturer was used to obtain pure tone thresholds which was calibrated as per ANSI S3.6-1969.

b) The GRASON-STADLER (GSI-33) middle ear analyzer, version-2 (calibrated as per ANSI, 1969) was used to assess the middle-ear function of volunteers and to measure the acoustic reflex thresholds (ART) and amplitude of AR at 10 dBSL.

Test Environment:

The tests were carried out in a sound treated room. Noise levels were within the limits as specifies by ANSI S3.1-1977. The test room had adequate lighting and comfortable temperature.

Test Procedure

Subjects who met the above mentioned criteria are chosen for the study. For the acoustic reflex testing the subjects were made to sit on a chair comfortably and were instructed not to move their head, jaw, swallow or to talk.

Measurements were performed in two experimental settings (Expt. A &B)

EXPT A: This was further divided in to two steps

Step 1: Acoustic reflex threshold was measured at 500 Hz, 1 kHz and 2 kHz using pure tones bracketed in ldB steps. Probe tone frequency was 226 Hz. ART was defined as the minimum intensity of Teflex activating stimulus which produced a reduction in admittance by 0.03cc.

ARTs were measured again in the presence of broad band noise (BBN) in the contralateral ear, fed through the insert receiver using GSI-16 clinical audiometer.

Step 2: This step included measurement of ART, with and without the presentation of narrow band noise (NBN) in contralateral ear. NBN were centered around the frequency of reflex activating signal.

5 minutes of resting period was given to each subjects between Stepl and Step 2, to overcome the adaptation effect if any. To counter balance the order effect, 30 subjects underwent step 1 first and other 30, step 2 first.

In both the conditions intensity of noise was kept at 30 dBSL (re: threshold of noise).

Intensity of the noise was chosen based on two factors.

1. Intensity should be high enough to produce the activation of olivocochlear bundle (OCB). Berlin et al, 1993 reported that 30 dBSL is sufficient to activate OCB.

2. Intensity should be below the level at which significant interaural transmission of sound or activation of the acoustic reflex could be expected. Hence, the insert receiver was used to present contralateral

acoustic stimuli because minimum inter aural attenuation of insert is knowntobe70dBSPL.

EXPT. B In this, reflex activating stimulus was presented al 10 dBSL with Tespect to acoustic reflex threshold and amplitude of reflex was measured in terms of equivalent volumes.

After the baseline experiment, amplitude was measured in the presence of BBN & NBN at 30 dBSLs (re: threshold of noise) in the contralateral ear and readings were noted separately.

Analysis: A paired T-test was used to find the significant difference between means of two conditions.

RESULTS

The results of this study were examined under the following sections:

1) Effects of contralateral BBN & NBN presentation on ART.

2) Effects of contralateral BBN & NBN presentation on AR amplitude at 10 dB SL with respect to ART. Statistical analysis was carried out to see the significant differences in ART as well as change in amplitude in different conditions and results obtained are as discussed below.

1) Effect of contralateral BBN stimulation on ART:

The ART in the two experimental conditions (with and without BBN) were obtained at 3 frequencies, Mean, Standard deviation and t values are as shown in table .1.

Table 1.shows the meanlSD values of ART with and without contralateral BBN along with t-values.

	500 Hz		1kHz		2kHz	
	Without BBN	With BBN	Without BBN	With BBN	Without BBN	With BBN
Mean	79.93	81.08	82.9	86.9	86.76	90.38
S.D.	7.36	8.10	6.7	7.0	6.8	7.09
t values	0.793		3.2**		3.016**	

**P<0.01

The analysis of the data reveals a significant difference (at .01 level) between ART with and without contralateral BBN presentation at 1 kHz and 2 kHz. However, at 500 Hz theTe was no significant difference between two conditions either at 0.01 or at 0.05 level.

Out of 60 subjects tested, 60% showed increase in ART in the presence of contralateral BBN. which ranged between 1-3 dB (Mean =1.15 dB) at 500 Hz. 95.56% of the subjects showed increase in ART at 1 kHz which ranged between 1 to 8 dB (Mean = 4 dB) and 93.3% showed increase in ART at 2 kHz which ranged between 1 to 10 dB (Mean = 3.62 dB). Rest of the subjects showed either improvement in the ART or no change in ART.

Mean of ARTs with and without contralateral BBN across 3 frequencies are graphically presented in Fig.l

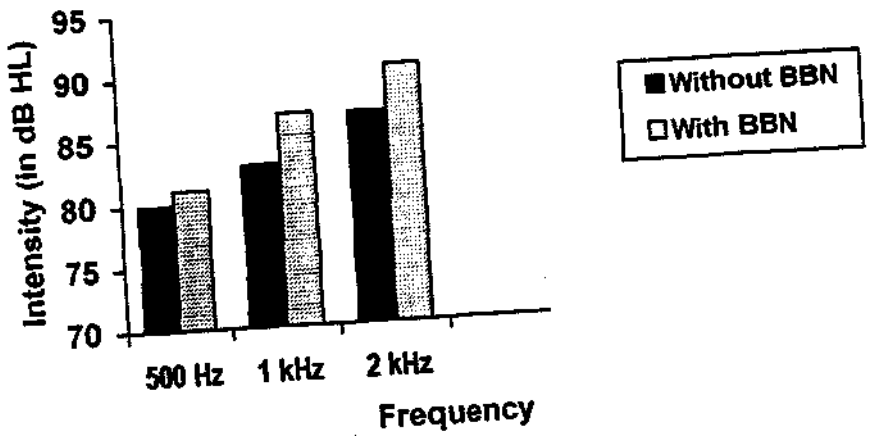

Fig.l: Mean of ARTs with and without contralateral BBN across 3 frequencies -

2) Effect of contralateral NBN on ART:

Effect of contralateral NBN on ART are as shown in table2.

Table. 2.shows the Mean and SD values of ART with and without contralateral NBN along with, t-values.

	500 Hz		1 kHz		2 kHz	
	Without NBN	With NBN	Without NBN	With NBN	Without NBN	With NBN
Mean	80.23	80.31	84.11	84.35	87.56	88.46
S.D.	8.16	7.88	7.12	6.9	8.75	8.91
t values	0.05		0.2		0.6	

Results indicate that there was no significant difference between ART obtained with and without contralateral NBN stimulation across all the 3 frequencies.

Mean of ARTs with and without NBN across 3 frequencies are graphically presented in Fig.2.

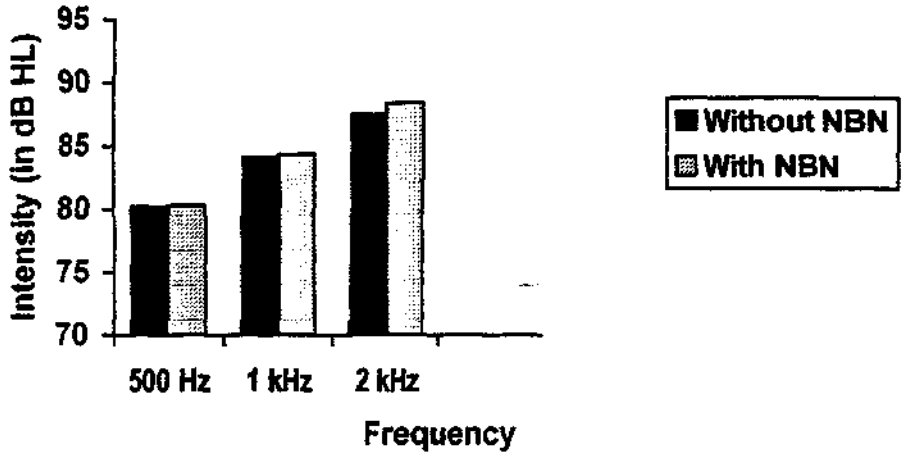

Fig.2 : Mean of ARTs with and without NBN across 3 frequencies.

3) Effect of contralateral BBN on AR amplitude at 10 dB SL (with reference to ART)

AR amplitudes in terms of equivalent volumes were measured with and without contralateral BBN at 3 frequencies and results are as shown in Table 3.

Table3.shows the mean SD values of AR with and without contralateral BBN along with t-values.

	500 Hz		1kHz		2kHz	
	Without BBN	With BBN	Without BBN	With BBN	Without BBN	With BBN
Mean	.093	.09	.1	.07	.09	.06
S.D.	.04	.04	.037	.034	.044	.039
t values	.428		4.8**		4.22**	

**p<0.01

Inspection of the table.3.reveals that there is a significant reduction in the amplitude of AR at 1 kHz and 2 kHz (at .01 level). However, no significant reduction was seen at 500 Hz.

Out of 60 subjects, 91% showed reduction in the amplitude, at 1 kHz which ranged between .01 to .07cc (Mean = 03cc). 90% showed reduction in amplitude at 2 Hz with the range of .01 to .12cc (Mean = .03cc) and 66.5% showed reduction at 500 Hz with range of .01 to .03cc (Mean = .003 cc). None of the subjects showed increase in the amplitude in the presence of contralateral BBN.

Mean and SD of AR amplitudes with and without contralateral BBN is graphically shown in Fig. 3.

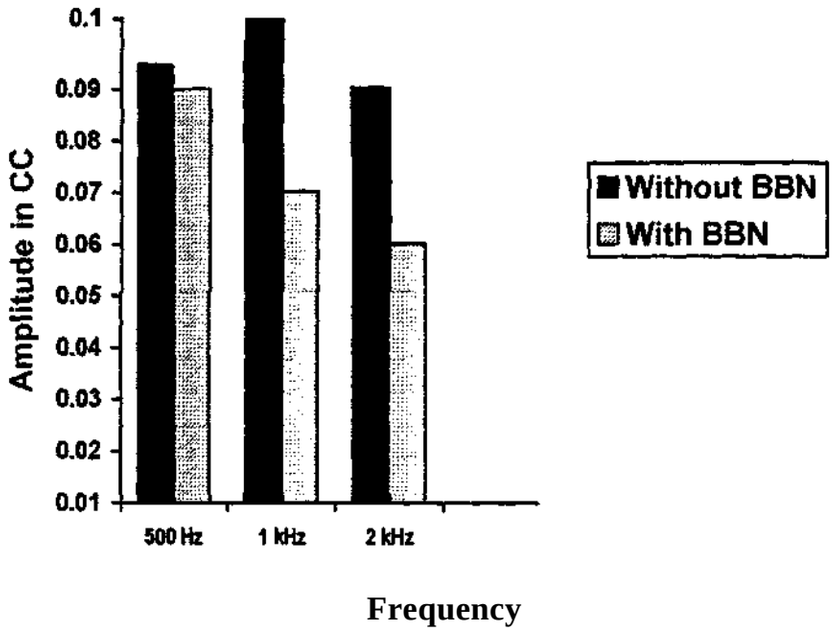

Fig. **3:** Mean of AR amplitudes with and without contralateral BBN.

4) Effect of contralateral NBN on AR amplitudes at 10 dB SL (re: ART)

Effect of contralateral NBN presentation on AR amplitudes are as shown in the table.

Table.4,shows the Mean, SD values of AR with and without contra-lateral NBN presentation along with t-values.

	500 Hz		1kHz		2kHz	
	Without NBN	With NBN	Without NBN	With NBN	Without NBN	With NBN
Mean	.10	.09	.09	.089	.09	.08
S.D.	.0428	.0425	.042	.038	.042	.041
t values	1.27		.166		0.57	

A glance at the table 4 shows that there was no significant changes in amplitude between two experimental conditions (with and without contralateral NBN presentation). Fig. 4 shows the graphical representation of means and S.D. of acoustic reflex amplitudes with and without NBN presentation.

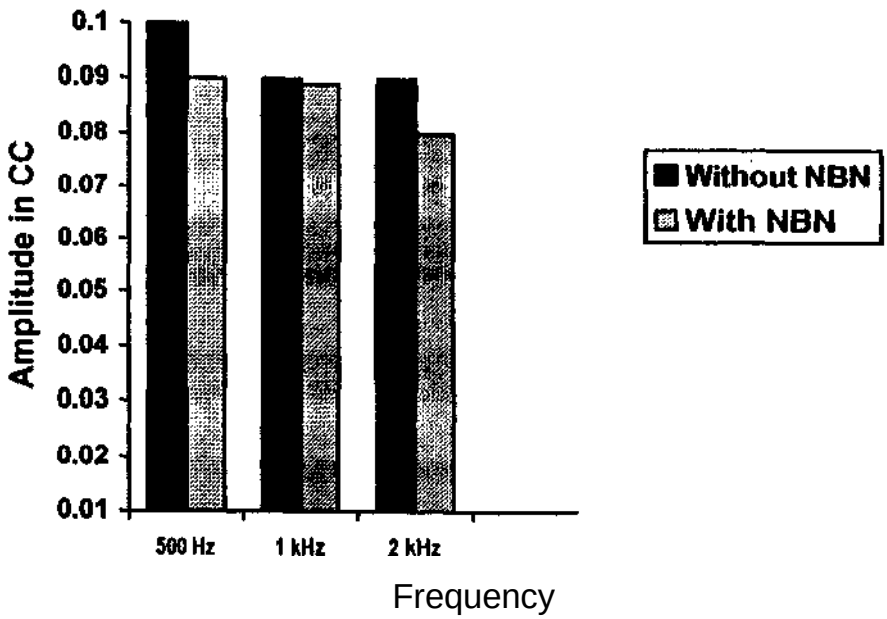

Fig.4 : Mean and Acoustic Reflex amplitudes with and without contralateral NBN

DISCUSSION

The results indicate that contralateral stimulation by BBN can increase the ART and reduce the acoustic reflex amplitude. This suppressive effect of contralateral BBN stimulation on acoustic reflex could be a result of several factors:

1. The middle ear acoustic reflex elicited by contralateral noise itself.
2. Masking effect due to the inter aural cross over.
3. Central masking effect.
4. An action of olivo-cochlear bundle.
5. Some systemic or unknown mechanics.

* The possibility of middle ear acoustic reflex elicited by contralateral noise or masking due to inter aural cross over can be ruled out since the intensity of noise was 30 dB SL which is insufficient to elicit the acoustic reflex in normals and as the noise was presented through an insert receiver interaural cross over is unlikely. Moreover, stapedial reflex attenuates the sound reaching to the cochlea maximally at low frequencies (Zemlin, 1988) and maximum cross over also takes place at low frequency. So, maximum suppression would have been present for 500 Hz when compared to 1 kHz and 2 kHz. However, suppression was seen only at 1 kHz and 2 kHz, not at 500 Hz. So, these two possibilities can be ruled out.

Central Masking:

Masker presented to one ear can cause a threshold shift for a signal at other ear even when the masker level is too low for it to cross over to the signal ear. This effect is called central masking and is attributed to the interaction of masker and test signal within the central auditory pathway, particularly at the level of SOC (Gelfand, 1998).

However, efferent induced reduction in the sensitivity can be another explanation for central masking, because there are few similarities between central masking and action of efferents, such as,

1) The amount of threshold shift produced by both the phenomenon are small.
2) Efferent suppression and central masking occurs more for high frequency stimuli than for low frequencies (Gelfand, 1998). So although not fully efferents may play a role in the central masking phenomenon.

* Therefore, the observed effect may be attributed to the change in the electrical/mechanical properties of the cochlea brought by the efferent system. The mechanism by which efferent stimulation alters the electrical properties of the cochlea and thereby acoustic reflex can be understood by the following physiological model:

Physiological model: Fex (1962) was the first to suggest that medial efferent system produces a drop in the endocochlear potential by shunting the transduction current through the hair cells, and this theory has been gaining in popularity (Erostegui et al., 1994). The release of ACh by medial efferent terminals produces OHC hyperpolarisation via ca^{++} dependent outward K^+ conductance (Doi and Ohmori, 1993; Erostegui et al., 1994; Housley and Ashmore, 1991). The increased OHC negativity brought about by the hyperpolarising efflux of intracochlear K^+, also increase the electro-chemical gradient on intracellular cations (ca^{++} and/or K^+). The increased driving force on cations could conceivably augment the apical inward cation conductance during the depolarizing phase of OHC-stereociliar displacement. An augmented inward K^+ conductance could produce an even greater concentration gradient for intracellular K^+, leading to an additional outward driving force on K^+. This combined increase in the inward and outward transduction current brought about by a medial efferent-induced by hyperpolarizing K^+ efflux, is responsible for increase in CM, since CM is postulated to be proportional to the endolymphatic transduction current passing through individual hair cells (Corey and Hudspeth, 1979a, 1979b; Dallos, 1984; Hudspeth, 1986: Pickles, 1988). The same shunting of K^+ transduction current through many rows of OHCs, leads to decline in scala-media

generated EP and may serve to shunt a proportion of the K^+ transduction current away from the IHC transducer. This might reduce the IHC depolarizing DC current and reduces IHC tuning (Brown et al., 1983; Nultall, 1984, 1985). This will lead to less transmitter being released by IHCs (Guinana and Stankovic, 1995). Hence, it may produce the reduction in discharge rates of auditory nerve fibers which may increase the acoustic reflex threshold and reduce its amplitude at supra threshold (re: ART) level.

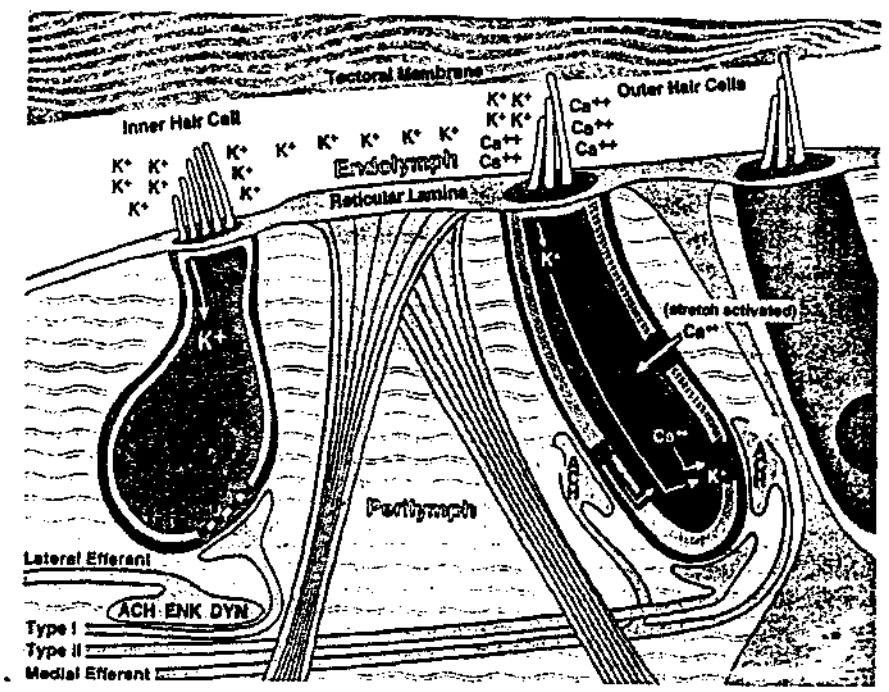

Fig.3: A model of Mammalian Efferent Physiology.

Alternatively, the MOC potential (drop in large positive EP, caused by efferent) in the region of the dendrites of radial auditory nerve fibers may cause there to be fewer action potentials in response to a given transmitter release, and this may account for medial efferent effects on high intensity sounds (Guinan, 1996) hence, on acoustic reflex.

Other possibilities by which efferent can modify the discharges of auditory nerve fiber at high intensity are:

1. Efferents can produce a mechanical change (e.g., a distortion of organ of corti) that reduces the mechanical coupling of basilar membrane motion to sound-frequency bending of IHC Stereocilia (de Boer, 1990)
2. Mechanical rectification in OHCs leads to a slow bending of IHC stereocilia (this could be the primary mechanism of exciting of auditory nerve fibers for high-frequency acoustic signal) and efferent activity may inhibit auditory nerve discharges by reducing the OHC rectification or the coupling of the resulting motion of IHCs (Guinan, 1996).

Reduction in the amplitude at 10 dB SL (re: ART) indicates that efferent system is capable of inhibiting auditory nerve discharges even at intensities such as 100-105 dBHL.

Why only for BBN?

Significant suppressive effect was seen only for the presentation of contralateral WBN not for NBN. This may be because the acoustic reflexes are elicited at high intensities where many auditory nerve fibers are activated simultaneously. So a large percentage of efferents should be activated to inhibit the responses from afferent auditory nerves. It has been shown that OCB activation increases with stimulus bandwidth even when the overall energy is maintained constant. This can be explained by the spatial integration properties of certain neurons in the cochlear neucleus (Evans & Zhoo, 1991; Young et al., 1992). Onset units have large tuning curves with occasionally inhibitory lateral bands in their response maps. These units are able to carry out spatial integration of several auditory-nerve fiber responses of different best frequencies, due to which OCB activation increases with stimulus bandwidth, whether or not the overall energy is kept constant. Similar results were also reported by Norman & Thornton (1993) that contralateral EOAE suppression effect increased with the contralateral stimulus bandwidth. So by the BBN large number of efferents can be activated than NBN. This might explain the observation that suppressive effect was seen only for BBN not for NBN.

Why only for 1 and 2 kHz?

Sound in the one ear influences the responses in other ear mainly through the uncrossed medial olivo-cochlear bundle. This is because majority of medial fibers, which belongs to the crossed medial olivo-cochlear (MOC) system, project on to the cochlea from which they receive afferent innervation. Furthermore, ipsilateral suppression is really a double-crossed reflex, that is signal crosses the midline twice, once in the input to the medial efferents and a second time in the crossed efferent fibers (Liberman & Brown, 1986).

However, some fibers constituting the uncrossed MOC system project on to the contralateral cochlea. These uncrossed fibers are involved in the inter-cochlear pathway that enables sound in one ear to influence responses in the other ear. However, the possibility of crossed MOCB causing the suppression is also cannot be excluded, because few afferent fibers does not crossover at midline, and projects to ipsilateral SOC. These fibers might activate the crossed MOCB which projects to contralateral ear (Cody & Johnstone, 1982). So the observed reduction may be a combined effect of both crossed and uncrossed efferent fibers from either sides. These uncrossed medial efferent innervation is largest near the center of the cochlea (Guinan, Warr and Norris, 1984; Liberman, Dodds and Pierce, 1990). This might explain the observation that there was no suppression effect in low frequency

(500 Hz) where apical part is active and is supplied by less MOCB fibers. In contrast, for mid frequencies (1 kHz & 2 kHz) suppressive effect was seen, because the center part of basilar membrane is active and is supplied by large number of uncrossed MOC efferent fibers. This observation is also consistent with the interpretation that suppression of stapedial acoustic reflex was due to medial efferents, not due to lateral efferents, because lateral efferent inervation is relatively constant throughout the length of the cochlea (Guinan, Warr & Norris, 1984; Liberman, Dodds & Pierce, 1990).

Does OCB feed back protect the cochlea from acoustic injury?

Reduction in the amplitudes of AR at 10 dB SL (re: ART) suggests that the efferent system can reduce the auditory nerve fibers discharge rates even at intensities above 100 dBHL. Rajan (1988), Rajan and Johnstone (1983a, 1983b) reported that the compound action potential threshold shift induced by acoustic over stimulation was significantly reduced by simultaneous electrical stimulation of OCB. Cody and Johnstone (1982) obtained similar results, when contralateral sound was used to activate efferent system. The results of present study is also consistent with the above findings that OCB can protect the cochlea from damage caused by loud sounds.

Test for MOCB:

Collet et al., (1990) suggested a possibility of investigating into the function of olivo-cochlear bundle, using contralateral EOAE suppression. Thus, EOAE recording during contralateral stimulation provides a non-invasive means of investigating auditory efferent system functioning in humans. This test has been found useful in identifying various retero-cochlear pathologies. This suppression is reduced or absent in patients with RCP and size and site of the lesion determines whether the suppression is affected unilaterally or bilaterally.

However, use of OAE to investigate the efferent functioning has the following pitfalls:

1) The cochlea should be normal.
2) This test fails to evaluate the efferent system when cochlear pathology as well as retrocochlear pathology exist in the same ear.
3) OAEs evaluate the efferent system only at low intensities.
4) Majority of the clinics in India do not have sophisticated instrumentation like OAE.

On the other hand, AR can be used to evaluate the efferent pathway at higher intensities and the instrument required is also readily available in most of the audiology clinics.

A suggested protocol to investigate the auditory efferents in humans using acoustic reflex would be to,

1) record the acoustic reflex threshold at 1 kHz or 2 kHz in one ear in the absence of a contralateral acoustic stimuli.
2) Present a BBN stimulus at 30 dB SL (ref: threshold of BBN) using on insert receiver to contralateral ear and record the ART again, in the presence of BBN.
3) Find the difference between ART in both the conditions. From the preliminary- data obtained in the present study, it can be said that in normals with contralateral BBN there is an elevation of ART by an average of 4 dB at 1 kHz and 3 dB at 2 kHz.
4) Repeat the same procedure by monitoring the reflex in the other ear.
5) Present the reflex activating stimulus at ART +10 dB at 1 kHz and 2 kHz and record the amplitude of AR in the presence and absence of contra-lateral BBN.
6) In normals, this amplitude is decreased by .03cc in the presence of noise. In cases of RCP this phenomenon may not be seen. However, further investigations in pathological population is needed before any conclusion is drawn.

SUMMARY AND CONCLUSIONS

Although the biological significant of efferent fibers remains ambiguous, it is clear that activation of medial olivo-cochlear fibers has an inhibitory effect on the auditory periphery (Abdal, Ma. & Sininger, 1999). The OAE which reflect the OHC integrity, provide an appropriate index of changes in cochlear function as MOC fibers are activated However, OAEs evaluate MOCB only at low intensities. In contrary, acoustic reflex can be used to monitor the MOCB effects on high intensity levels. Since there was a dearth in the literature in this area, this study was taken with the aim

1) to examine the effect of contralateral WBN and NBN on AR
2) To see whether OCB has any protective effect or not.
3) To develop a test to evaluate efferent pathway using AR.

Sixty subjects (30 males and 30 females) were included in the study. ART and AR amplitudes were measured across three frequencies (500 Hz, 1 kHz and 2 kHz) with and without the contralateral wide and narrow band noise presentation at the intensity level of 30 dB SL through the insert receiver to avoid cross over or stapedial reflex caused by noise itself. The results indicated that with contralateral BBN presentation, there was significant increase in the ARTs at 1 kHz and 2 kHz (4 dB & 3 dB respectively). But there was no significant change in the ART at 500 Hz.

None of the frequencies showed significant change with the contralateral NBN presentation.

AR amplitude also reduced by an average .03cc at 1 and 2 kHz with contralateral BBN presentation. But 500 Hz did not showed any significant change. Contralateral NBN presentation did not showed any significant difference in the amplitude at all the frequencies tested.

This suppression effect seen can be attributed to the change in the electrical and mechanical properties of the cochlea brought by the efferent system. Since MOCB innervation is largest near the center of the cochlea (Guinan, Warr & Norris, 1984; Liberman, Dodds & Pierce, 1990), suppression was seen only in mid frequencies (1 kHz & 2 kHz) but not at low frequency (500 Hz). BBN showed more suppressive effect because OCB activation increases with stimulus bandwidth, even when overall energy is maintained constant (Norman &. Thornton, 1993).

Thus, the study on the effect of contralateral acoustic stimulation on AR opens the door to further research on the efferent effects at high intensities. From the results it can be inferred that efferents may play a role in protecting the cochlea from loud acoustic stimulation and it can be used as a objective noninvasive technique to evaluate the descending auditory pathway.

REFERENCES

Abdal , C, Ma, E. Sininger, Y.S. (1999). Maturation of medial efferent system function in humans. Journal of Acoustical Society of America, 105,2392-2402.

American National Standards Institute (1970). ANSI S3.6-1969. Cited in Silman, S.,& Silverman, C.A. (1991). Auditory diagnosis principles and applications. New York: Academic Press, INC.

American National Standards Institute (1977). ANSI S3.6-1977. Cited in Silman, S.,& Silverman, C.A. (1991). Auditory diagnosis principles and applications. New York: Academic Press, INC.

Berlin, C.I., Hood, L.T., Wen, R, Szabo, P., Cecola, R.P.,JRigby, P. (1993). Conrralateral suppression of non-linear click evoked otoacoustic emissions. Hearing Research, 71,1-11.

Borg, E. (1971). Cited in Wiederhold, M.L. (1986). Physiology of the ohvo-cochlear system. In R.A. Altschuler, R.P. Bobbin,^D.W. Hytman (Eds.), Neurobiology of hearing: The cochlea (pp.349-370). New York: Raven Press.

Borg, E. (1973). Cited in Silman, S.,& Silverman, C.A. (1991). Auditory diagnosis principles and applications. New York: Academic Press, INC.

Brown, M.C., Nuttall, A.L. Masta, R.L. (1983). Intracellular recordings from cochlear inner hair cells: Effects of stimulation of the crossed olivocochlear efferents. Science, 222,69-72.

Brown, M.C., and Nuttall, A.L., (1984). Cited in Guinan, J.J. Jr., (1996). The physiology of olivocochlear efferents. In P. Dallos, A. Popper, R. Fay (Eds.), The Cochlea, (pp.435-502). New York: NY: Springer-Verlag.

Buno, W. (1978). Cited in Guinan, J.J. Jr., (1996). The physiology of olivocochlear efferents. In P. Dallos, A. Popper, R. Fay (Eds.), The Cochlea, (pp.435-502). New York: NY: Springer-Verlag.

Cody, A.R & Johnstone. B.M. (1982). Temporary threshold shift modified by binaural acoustic stimulation. Hearing Research, 6,199-205.

Collet L., Kemp, D.T., Vevillet, E., Duclaux, R., Moulin, A.& Morgon, A., (1990). Effects of contralateral auditory stimuli on active cochlear micro-mechanical properties in human subjects. Hearing Research, 43,251-262.

Corey, D.P. Hudspeth, A.J. (1979a). Ionic basis of the receptor potential in vertebrate hair cell. Nature, 281,675-677.

Corey, D.P., Hudspeth A.J. (1979b). Cited in Sahley, T.L., Nodar, R.H., Musiek, F.E. (1997). Efferent auditory system. Structure and function. SanDiego: Singular Publishing Group Ltd.

Dallos, P. (1984), Cited in Sahley, T.L., Nodar, R.H .Musiek, F.E. (1997). Efferent auditory system. Structure and function. SanDiego: Singular Publishing Group Ltd.

Dallos, P. Cheatham, M.A. (1975). Production of cochlear potentials by inner and outer hair cells. Journal of Acoustical Society of America, 60, 510-512.

Davis, H (1965). Cited in Guinan, J.J. Jr., (1996). The physiology of olivocochlear efferents. In P. Dallos, A. Popper, R Fay (Eds.), The Cochlea, (pp.435-502). New York: NY: Springer-Verlag.

de Boer, E. (1990). Cited in Guinan, J.J. Jr., (1996). The physiology of olivocochlear efferents. In P. Dallos, A. Popper R. Fay (Eds.), The Cochlea, (pp.435-502). New York: NY: Springer-Verlag.

Desmedt J.E., (1962). Cited in Guinan, J.J. Jr., (1996). The physiology of olivocochlear efferents. In P. Dallos, A. Popper R. Fay (Eds.), The Cochlea, (pp.435-502). New York: NY: Springer-Verlag.

Desmedt, J.E., (1975). Auditory evoked potentials from cochlea to cortex as influenced by activation of the efferent olivocochlear bundle. Journal of Acoustical Society of America, 34,1470-1496.

Doi, T., Ohmori, H. (1993). Cited in Sahley, T.L., Nodar, R.H. Musiek, F.E. (1997). Efferent auditory system. Structure and function. SanDiego: Singular Publishing Group Ltd.

Dolan, D.F. NuttalL A.L. (1994). Cited in Guinan, J.J. Jr., (1996). The physiology of olivocochlear efferents. In P. Dallos, A. Popper R. Fay (Eds.), The Cochlea, (pp.435-502). New York: NY: Springer-Verlag.

Downs, D,W. Crurn M.A. (1980). The hyperactive Acoustic reflex. Four case studies. Acta Otolaryngology, 116,401 -404.

Evans, E.F. Zhao, W. (1991). Cited in Maison, S., Micheyl, L. Collet, L. (1999). The medial olivocochlear efferent system in humans: Structure and function. Scandinavian Audiology, 28 Supp, 51, 77-84.

Erostegui L., Noirrs, C.H., Bobbin.P. (1994). Cited in Sahley, T.L., Nodar, R.H. Musiek, F.E. (1997). Efferent auditory system: Structure and function. SanDiego: Singular Publishing Group Ltd.

Felix, D. Ehrenberger, K. (1992). Cited in Guinan, J.J. Jr., (1996). The physiology of olivocochlear efferents. In P. Dallos, A. PopperiR. Fay (Eds.), The Cochlea, (pp.435-502). New York: NY: Springer-Verlag.

Fex, T. (1959). Cited in Guinan, J.J. Jr., (1996). The physiology of olivocochlear efferents. In P. Dallos, A. Popper R. Fay (Eds.), The Cochlea, (pp.435-502). New York: NY: Springer-Verlag.

Fex, T. (1962). Cited in Guinan, J.J. Jr., (1996). The physiology of olivocochlear efferents. In P. Dallos, A. Popper R. Fay (Eds.), The Cochlea, (pp.435-502). New York: NY: Springer-Verlag.

Folsom, R.C. Owsley, R.M. (1987). N1 action potentials in humans. Influence of simultaneous contralateral stimulation. Acta Otolaryngologica (Stockh), 103, 262-265.

Galambos, R. (1956). Cited in Guinan, J.J. Jr., (1996). The physiology of olivocochlear efferents. In P. Dallos, A. Popper R. Fay (Eds.), The Cochlea, (pp.435-502). New York: NY: Springer-Verlag.

Gelfand, S.A. (1998). Hearing: An introduction to psychological and physiological acoustics, (3rd edn.), New York: Marcel Dekker.

Gifford, M.L. Guinan, J.J., Jr. (1983). Effects of corss-olivocochlear bundle stimulation on cat auditory nerve fiber responses to tones. Journal of Acoustical Society of America, 74,115-123.

Gifford, M.L. Guinan, J.J., Jr. (1987). Effects of electrical stimulation of medial olivocochlear neurons on ipsilateral and contralateral cochlear responses. Hearing Research, 29,179-194.

Guinan, J.J. Jr. (1986). Effect of efferent neural activity on cochlear mechanics. Scandinavian Audiology, 54, Suppl.25,53-62.

Guinan, J.J. Jr. (1991). Inhibition of stimulus frequency emissions by medial olivocochlear efferent neurons in cats. Assoc. Res. Otolaryngol, 14.129.

Guinan, J.J. Jr. (19%). The physiology of olivocochlear efferents. In P. Dallos, A. Popper R Fay (Eds.), The Cochlea, (pp.435-502). New York: NY: Springer-Verlag.

Guinan, J.J. Jr Gifford, ML. (1988). Cited in Guinan, J.J. Jr., (1996). The physiology of olivocochlear efferents. In P. Dallos, A. Popper, R Fay (Eds.), The Cochlea, (pp.435-502). New York: NY: Springer-Verlag.

Guinan, J.J. Jr., Stonkovic, K.M. (1995). Medial olivocochlear efferent inhibition of auditory-nerve firing mediated by changes in endocochlear potential. Associate Research Otolaryngology abstracts, 18,172.

Guinan, J.J. Jr., Warr, W.B. Norris, B.E. (1983). Cited in Guinan, J.J. Jr., (1996). The physiology of olivocochlear efferents. In P. Dallos, A. Popper, SL R-Fay (Eds.), The Cochlea, (pp.435-502). New York: NY: Springer-Verlag.

Guinan, J.J. Jr., Warr, W.B. Norris, B.E. (19841 Cited in Guinan, J.J. Jr., (1996). The physiology of olivocochlear efferents. In P. Dallos, A. Popper,R. Fay (Eds.), The Cochlea, (pp.435-502). New York: NT: Springer-Verlag.

Handrock, M. Zeisberg, T. (1982). The influence of the efferent system on adaptation, temporary and permanent threshold shift. Archives of Otorhinolaryngology, 234,191-195.

Harrison, W.A. Bums, E.M. (1993). Effects of contralateral acoustic stimulation on spontaneous otoacoustic emissions. Journal of Acoustical Society of America, 94,2649-2658.

Higson, J.M., Stephenson, H.,Hiaggard, M.P. (19961 Binaural summation of the Acoustic reflex. Ear and Hering, 17, 334-340.

Hildesheimer, M., Makai, E., Muchnik, C. Rubinstein, M. (1990). Cited in Guinan, J.J. Jr., (1996). The physiology of olivocochlear efferents. In P. Dallos, A. Popper R. Fay (Eds.), The Cochlea, (pp.435-502 \ New York: NY: Springer-Verlag.

Housley, G.D Ashmore, J.F. (1991). Cited in Sahley, T.L., Nodar, R.H., Musiek, F.E. (1997). Efferent auditory system. Structure and function. SanDiego: Singular Publishing Group Ltd.

Hudspeth, A.J. (1986). The ionic channels of a vertebrate hair cell. Hearing Research, 22,21-27.

Johnstone, B., Patuzzi, R. Yates, G. (1986). Basilar membrane measurements and the travelling wave. Hearing Research, 22,147-153.

Kawase, T. Liberman, M.N. (1993). Cited in Guinan, J.J. Jr., (1996). The physiology of olivocochlear efferents. In P. Dallos, A. Popper R. Fay (Eds.), The Cochlea, (pp.435-502). New York: NY: Springer-Verlag.

Kim, DO. (1986). Active nonlinear cochlear biomechanics and the role of outer hair cell subsystem in mammalian auditory system. Hearing Research, 22, l(b-114.

Kittrell, B.J.,& Dalland, J.I. (1969). Frequency dependence of cochlear microphonic augmentation produced by olivocochlear bundle stimulation Laryngoscope, 79,228-238.

Konishi, T., Slepian, J.Z. (1971). Effects of the electrical stimulation of the crossed olivocochlear bundle on cochlear potentials recorded with intracochlear electrodes in guinea pigs. Journal of Acoustical Society of America, 49, 1762-1769.

Liberman, M.C. (1989). Rapid assessment of sound evoked olivocochlear feedback: suppression of compound action potentials by contralateral sound. Hearing Research, 38,47-56.

Liberman, M.C. (1990). Cited in Guinan, J.J. Jr., (1996). The physiology of olivocochlear efferents. In P. Dallos, A. Popper R. Fay (Eds.), The Cochlea, (pp.435-502). New York: NY: Springer-Verlag.

Liberman, M.C. (1991). Cited in Guinan, J.J. Jr., (1996). The physiology of olivocochlear efferents. In P. Dallos, A. Popper R. Fay (Eds.), The Cochlea, (pp.435-502). New York: NY: Springer-Verlag.

Liberman, M.C Brown, M.C. (1986). Physiology and anatomy of single olivocochlear neurons in the cat. Hearing Research, 24, 17-36.

Liberman, M.C, Dodds, L.W., Pierce, S. (1990). Cited in Guinan, J.J. Jr., (1996). The physiology of olivocochlear efferents. hi P. Dallos. A. Popper R. Fay (Eds.), The Cochlea, (pp.435-502). New York: NY: Springer-Verlag.

Liberman, M.C., Guinan, J.J. Jr. (1999). Feedback control of the auditory periphery: Anti-masking effects of middle ear muscles Vs. olivocochlear efferents. Journal of Communication Disorders, 31,471-483.

Micheyl, C, and Collet, L. (1996). Involvement of the oliovocochlear bundle in detection of tones in noise. Journal of Acoustical Society of America, 99, 1604-1610.

Mott, J.B., Norton, S.J., Neely, S.T. Warr, W.B. (1989). Changes in spontaneous otoacoustic emissions produced by acoustic stimulation of the contralateral ear. Hearing Research, 38, 229-242.

Moulin, A., Collet, L. Duclaux, R (1993). Contralateral auditory stimulation alters acoustic distortion products in humans. Hearing Research, 65,193-210.

Mountain, D.C. (1980). Changes in endolymphatic potential and crossed olivocochlear bundle stimulation alter cochlear mechanics. Science. 210,71-72.

Murata, K., Tanahashi, T., Horidawa, J Funai, H.M. (1980). Cited in Guinan J J. Jr., (1996). The physiology of olivocochlear efferents. In P. Dallos, A. Popper, R. Fay (Eds.), The Cochlea, (pp.435-502). New York: NY: Springer-Verlag.

Norman, M. Thomton, A.R.D. (1993). Frequency analysis of the contralateral suppression of evoked otoacoustic emissions by narrow-band noise. British Journal of Audiology, 27,281-289.

Nuttall, A.L. (1985). Influence of direct current on DC receptor potentials from cochlear inner hair cells in the guinea pig. Journal of Acoustical Society of America, 77 165-175.

Nuttall, A.L. (1984). Dynamic aspects of guinea pig inner hair cell receptor potentials with transient asphyxia. Hearing Research, 16,1-16.

Patuzzi, R.B., Thompson, M.L. (1991). Cited in Guinan, J.J. Jr., (1996). The physiology of olivocochlear efferents. In P. Dallos, A. Popper, R. Fay (Eds.). The Cochlea, (pp.435-502). New York: NY: Springer-Verlag.

Pickles, J.O. (1988). An introduction to physiology of hearing (2^{nd} ed). New York: Academic Press.

Pujol, R. (1994). Lateral and medial efferents: a double neurochemical mechanism to protect and regulate inner and outer hair cell function in the cochlea. British Journal of Audiology, 28,185-191.

Rajan, R. (1990). Cited in Guinan, J.J. Jr., (1996). The physiology of olivocochlear efferents. In P. Dallos, A. Popper R. Fay (Eds.), The Cochlea, (pp.435-502). New York: NY: Springer-Verlag.

Rajan, R. (1988). Cited in Rajan, R. (1992). Protective functions of the efferent pathways to the mammalian cochlea: A Review. In A.L. Darner, D. Handerson, R.J. Salvi (Eds.), Noise induced hearing loss, (pp.429-444). St. Louis. Mosby Yearbook.

Rajan, R |Johnstone, B.M. (1983a). Crossed cochlear influences on monaural temporary threshold shifts. Hearing Research, 9, 279-294.

Rajan, R. Johnstone, B.M. (1983b). Residual effects in monaural temporary threshold shifts to pure tones. Hearing Research, 12,185-197.

Rasmussen, G.L. (1946). Cited in Cited in Guinan, J.J. Jr., (1996). The physiology of olivocochlear efferents. In P. Dallos, A. Popper,R. Fay (Eds.), The Cochlea, (pp.435-502). New York: NY: Springer-Verlag.

Reiter E.R.Liberman, M.C. (1995). Cited in Guinan, J.J. Jr., (1996). The physiology of olivocochlear efferents. In P. Dallos, A. Popper,R. Fay (Eds.), The Cochlea, (pp.435-502). New York: NY: Springer-Verlag.

Roddy, T., Hubbard, A.E., Mountain, D.C.|Xue, S. (1994). Cited in Guinan, J.J. Jr.. (1996). The physiology of olivocochlear efferents. In P. Dallos, A. Popper, R. Fay (Eds.), The Cochlea, (pp.435-502). New York: NY: Springer-Verlag.

Ryan, S., Kemp, D.T Hinchcliffe, R. (1991). The influence of contralateral acoustic stimulation on click evoked emissions in humans. British Journal of Audiology, 25,391-397.

Sahley, T.L., Kalish, R.B., Musiek, F.E. Hoffman, D.W. (1991). Cited in Guinan, J.J. Jr., (1996). The physiology of olivocochlear efferents. In P. Dallos, A. Popper R. Fay (Eds.), The Cochlea, (pp.435-502). New York: NY: Springer-Verlag.

Sahley, T.L.,Nodar, R.R (1994). Improvement in auditory function following pentozocine suggests a role for dynorphins in auditory sensitivity. Ear and Hearing, 15,422-431.

Santos-Sacchi, J Dilger, J.P. (1988). Cited in Guinan, J.J. Jr., (1996). The physiology of olivocochlear efferents. In P. Dallos, A. Popper R. Fay (Eds.). The Cochlea, (pp.435-502). New York: NY: Springer-Verlag.

Sewell, W.F. (1984). The effects of furo semide on the endocochlear potential and auditory nerve fiber tuning curves in cats. Hearing Research, 14,305-314.

Siegal, T.H., & Kim, D.O. (1982). Efferent neural control of cochlear mechanics? Olivocochlear bundle stimulation effects cochlear biomechanical nonlinearity. Hearing Research, 6, 171 -182.

Takeyama, M., Kusokori, J., Nishikawa, N. Wawla, T. (1992). The effect of crossed oliocochlear bundle stimulation on acoustic trauma. Acta Otolaryngologica (Stockh), 112,205-209.

Trahiotis, C. EUiott, D.N. (1970). Behavioural investigation of some possible effects of sectioning the crossed oliovocochlear bundle. Journal of Acoustical Society of America, 47,592-596.

Veuillet, E., Bazin, F Collet, L. (1991). Cited in Veuillet, E., Khalfa, S., Collet, L. (1999). Clinical relevance of medial efferent auditory pathways. Scandinavian Audiology, 28 Suppl. 51, 53-62.

Warr, W.B., (1975). Cited in Guinan, J.J. Jr., (1996). The physiology of olivocochlear efferents. In P. Dallos, A. Popper,iR. Fay (Eds.), The Cochlea, (pp.435-502). New York: NY: Springer-Verlag.

Warr, W.B. (1992). Organisation of olivocochlear efferent systems in mammals. In D.B. Webster, AN. Popper, R. Fay (eds.), Mammalian Auditory Pathway.

Warr, W.B., and Guinan, J.J., Jr. (1979). Cited in Guinan, J.J., Jr. (1996). The physiology of olivocochlear efferents. In P. Dollos, A. Popper & R Fay (Eds), the cochlea (pp.435-502). New York, NY: Springer-Verlag.

Wiederhold, M.L Kiang, N.Y.S. (1970). Effects of electric stimulation of crossed olivocochlear bundle on single auditory-nerve fibers in the cat. Journal of Acoustical Society of America, 48, 950-965.

Wiederhold, M.L., and Peake, W.T. (1966). Cited in Guinan, J.J. Jr., (1996). The physiology of olivocochlear efferents. In P. Dallos, A. PopperJR. Fay (Eds.), The Cochlea, (pp.435-502). New York: NY: Springer-Verlag.

Young, E.D., Spirou, G., Rice, J. Voigt, H. (1992). Cited in Maison, S., Micheyl, L. Collet, L. (1999). The medial olivocochlear efferent system in humans: Structure and function. Scandinavian Audiology, 28 Supp, 51,77-84.

Zemlin, W.R., (1988). Speech and hearing science anatomy and physiology (3rd ed.). New Jersy: Prentice Hall.