AUDITORY MIDDLE LATENCY AND LONG LATENCY REPONSE IN SUBJECTS WITH AUDITORY NEUROPATHY

Reg. No. M.2K21

An Independent project submitted in part fulfillment for the first year M.Sc (Speech & Hearing) to University of Mysore

ALL INDIA INSTITUTE OF SPEECH & HEARING
MYSORE - 570 006.

MAY-2001.

Dedicated To

.... *Bawasahab, Mummy & Papa*

for all your love and support throughout the years.

.... *Vanaja ma'am*

for inspiring me to soar great heights , and for keeping me

on firm ground with constructive criticisms.

Certificate

This is to certify that this independent project entitled **"AUDITORY MIDDLE LATENCY AND LONG LATENCY REPONSE IN SUBJECTS WITH AUDITORY NEUROPATHY"** is a bonafide work in part fulfillment for the degree of Master of Science (Speech and Hearing) of the student (Register No. M2K21).

Mysore,
May, 2001

DIRECTOR
All India Institute of
Speech and Hearing.
Mysore - 570 006.

Certificate

This is to certify that this independent project entitled **"AUDITORY MIDDLE LATENCY AND LONG LATENCY REPONSE IN SUBJECTS WITH AUDITORY NEUROPATHY"** has been prepared under my supervision and guidance. It is also certified that this has not been submitted earlier in any other University for the award of any diploma or degree.

Guide

Mysore,
May, 2001

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Declaration

This independent project entitled **"AUDITORY MIDDLE LATENCY AND LONG LATENCY REPONSE IN SUBJECTS WITH AUDITORY NEUROPATHY"** is the result of my own study under the guidance of **Mrs. Vanaja,** C. S., Lecturer in Audiology, Department of Audiology, All India Institute of Speech and Hearing, Mysore and not been submitted earlier in any other University for the award of any diploma or degree.

Mysore,
May, 2001

Reg. No. M2K21

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I thank God

For giving me all the dedication to work,

And making me all that i am today.

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INTRODUCTION

The history of Audiological Science is marked by a slow but steady progress from unknown to what it is today; It has been built brick by brick and laboriously fashioned over years even centuries. Each new finding provides an immediate solution to an existing problem but poses another question in its term. Though the tower of elecrophysiological measures available to examine the audiovestibular systems is well based; it cannot be considered complete.

The evidence for this comes from the study in 1979 by Davis and Hirsh that reported of the incidence of absent/abnormal auditory brainstem response (ABR) in patients with relatively good hearing responding to moderate or low intensity sounds. But is this truly an error or paradox? Literature findings show that there can occur a condition with normal outer hair cell function and abnormal function at the level of VIIIth (vestibule cochlear) nerve. These characteristics are manifested on clinical audiological tests as normal otoacoustic emissions (OAEs) when ABR is absent or severely abnormal. This condition has been labeled as auditory neuropathy (Starr, Picton, Sinniger, Hood and Berlin, 1996; Hood, 1998).

Auditory neuropathy can thus be stated as congenital or acquired demyelinating disorder of the VIIIth nerve in which there is absent ABR not corresponding to the subject's audiometric thresholds (which may indicate only a mild to moderate hearing loss) or to relatively normal OAEs and/or cochlear microphonics (CM). (Starr et al., 1996, Hood 1998, Berlin, 1999). These patients have poor speech identification scores relative to their audiometric status. One of the first reports of this disorder comes from Davis and Hirsh (1979) and since then many patients with auditory neuropathy has been described (Worthington and Peters, 1980; Berlin,

Hood, Cecola, Jackson & Szabo, 1993; Starr et al., 1996, Deltnere, Mansbach, Bozet Clercx & Hecox, 1996; Ranee et al., 1999).

The characteristics of auditory neuropathy reflect more than a single etiology and the disorders) may more accurately be described as "auditors' neuropathies" (Hood, 1998). The pattern of normal OHC function combined with abnormal ABR places the site of auditory neuropathy in the area that contains the inner hair cells (IHCs), the connection between IHCs and cochlear branch of VIIIth cranial nerve . and perhaps auditory pathways of the brainstem (Starr et al., 1996; Hood, 1998). Hood (1998) states that the neural problems may be axonal or demyelinating, and afferent as well as efferent pathways may be involved. The specific sites and mechanism of auditory neuropath}' is yet to be determined.

Thus auditon^{r} tests for auditor}' neuropathy patients are those sensitive to cochlear and auditory nerve function. Outer hair cell function can be evaluated by measuring otoacoustic emissions and cochlear microphonics. Clinical tests that are specifically sensitive to auditory nerve dysfunction are middle ear reflexes (ipsilateral and contralateral), auditory brainstem response, masking level difference, efferent suppression of OAEs, and to a limited extent word recognition with an ipsilateral competing message or noise (Starr et al., 1996; Berlin et al., 1998; Hood, 1998).

The status of inner hair cells cannot be assessed, as there are no procedures currently available for this purpose. Nevertheless whatever causes inner hair cell damage, it will not be confined to the hair cells. It is well established that after inner hair cell degeneration, there is associated spiral ganglion cell loss (Spoendlin, 1975) and that more central neurons (at least to the mid-brain) also will show some degeneration (Morest and Bohne, 1983; Salvi, Wang, Ding, Stecker and Arnold, 1999). Thus, although the entity of auditory neuropathy might originate with cochlear lesion , consequent central deficits can develop (Harrison, 1998). Middle-

latency and long latency auditory evoked potentials may provide some information on central auditory functions in auditory neuropathy. The significance of middle-latency and long latency responses in subjects with auditory neuropathy is not well documented and appears to be inconclusive. Starr et al.. (1996) found absent or abnormal middle latency responses (MLRs) and long latency responses (LLRs) in six patients and normal in one patient. Kraus, Ozdamar. Stein and Reed (1984) found absent MLRs in nine ears out of ten ears they evaluated. It was found to be normal in one ear. A recent study by Kraus et al., (2000) revealed presence of LLR and MMN for a speech stimuli in a subject of auditors' neuropathy whose hearing threshold were within normal limits.

The fact that MLRs and LLRs were absent or abnormal in some patients suggests deficits in auditory processing or communicative problems, which cannot be explained by peripheral hearing loss alone. On the other hand, the fact that MLRs and LLRs were observed in some patients indicates that neural signals are indeed reaching auditory pathways central to brainstem which in turn suggest that some form of auditory function exists. (Kraus et al., 1984; Kraus et aL 2000). Thus, it is of paramount essence to carry out investigations relating to MLRs and LLRs in subjects with auditory neuropathy.

Need for the study:

As already discussed, the review of literature on MLRs and LLRs in-patients with auditory neuropathy are inconclusive and have been given least attention. This study aims at determining the middle-latency and long latency auditory evoked potentials in auditory neuropathy subjects in order to provide information on auditory pathways central to brainstem and to observe if there is any central auditory processing deficiencies.

Aims of the study:

This investigation aimed at studying the following potentials in subjects with auditors' neuropathy:

- Auditory middle latency responses (AMLRs).
- Auditory late latency responses (ALLRs).
- Mismatch negativity (MMN) for intensity deviance.

REVIEW OF LITERATURE

The review of literature on auditor}' neuropathy is discussed in this chapter under the following headings -

- The definition of auditory neuropathy.
- Etiological factors.
- Signs and symptoms.
- Peripheral Vs central affects.
- Behavioral Vs evoked potential used to evaluate central auditory processing.
- Auditory evoked potential studies in patients with auditory neuropathy.

A) **Definition of auditory neuropathy**

Auditory neuropathy is a term currently used to describe a condition in patients ranging in age from infants to adults, in which the patient displays characteristics consistent with normal outer hair cell function and abnormal function at the level of the VIIIth (Vestibulo-Cochlear) nerve. These characteristics are observed on clinical audiologic tests as normal otoacousitic emissions (OAEs) and absent or severely abnormal auditory brainstem responses (ABRs). (Hood, 1998).

Retrospectively, in literature, the earliest study was by Davis and Hirsh in 1979, where they reported the incidence of absent/abnormal auditory brainstem response in patients with relatively good hearing-

responding to moderate or low intensity sounds. Worthington and Peter (1980) published four case reports of patients with absent ABR and no worse than severe hearing loss. Galambos and Galambos (1979) warned that such findings might be due to technical error. However Kraus et al., (1984) refuting this justification, said that these reports indicate the need for reexamining and further delimiting cases where the audiological findings appear "paradoxical". Literature, till date, shows that there can occur a condition where ABR is absent or severely abnormal, not corresponding to subject audiometric threshold (which may indicate only mild to moderate hearing loss). This condition has been labeled as auditory neuropathy (Starr et al., 1996; Deltenere et al., 1997a; Hood; 1998, Rance et al., 1999; Berlin, 1999).

B) Etiological factors

Proposed etiologies of auditory neuropathy have been diverse and include neonatal hyperbilirubinemia (Stein, Tremblay, Pasternak, Banerjee, Lindeman and Kraus, 1996), severe illness during the neonatal period (Deltenere et al., 1997b), a part of a generalized metabolic toxic or inflammatory neuropathy (Berlin et al., 1993; Starr et al., 1996). Some patients also may have an accompanying generalized neuropathy affecting other cranial and/or peripheral nerves (Starr et al., 1996). The other etiologies which can lead to occurrence of auditory neuropathies include genetic factors as in hereditary sensory motor neuropathy (Musiek, Weider and Muller, 1982; Raglan, Prasher, Trinder and Rudge, 1987), hereditary sensory and autonomic neuropathy (Hallpike, Harriman and Wells, 1980; Wright and Dyck, 1995), and the neuropathy accompanying Friedrich's ataxia (Cassandro, Mosca, Sequino, De falco and Campanella, 1986). The demyelinating neuropathy of the Guillian-Barre syndromes may at times involve the auditory neuropathy (Rooper and Chiappa, 1986).

C) Signs and Symptoms

The symptoms that these patients manifest are primarily with varying deficits of hearing. Patients with auditory neuropathy display auditory thresholds to pure tone stimuli by air and bone conduction varying from mild to severe degree and the nature of problem is usually reported to be progressive (Starr et al., 1996; Deltenere et al., 1996; Sinmger et al., 1995; Rance et al., 1999).

A majority of these patients have bilateral, low frequency, sensorineural hearing loss (Starr et al.. 1996). Speech identification scores are generally poorer both in quiet as well as in noise than those obtained by patients with comparable pure tone loss due to cochlear damage (Starr et al., 1996; Hood. 1998). These patients do not complain of absence of tinnitus and vertigo/dysequilibirum (Starr et al., 1996; Hood. 1998). However Sheykholeshami, Kaiga, Morofishi and Hughes (2000) reported that in patients with isolated auditors' neuropathy, the vestibular branch of VIIIth nerve and its innervated structures may also be affected leading to dysequilibirum.

The general clinical findings in these patients are that response requiring intact auditory nerve/or brainstem pathways, such as the acoustic reflex, the auditory brainstem response and efferent suppression of otoacoustic emission are abnormal (Starr et al., 1996; Hood, 1998; Berlin, 1999; Rance et al., 1999), whereas cochlear responses that involve outer hair cell function, which include OAEs and cochlear microphonics are normal (Starr et al., 1996; Berlin. 1999; Rance et al.. 1999).

D) Peripheral Vs Central affects

Auditory neuropathy manifests a hearing loss which has been classified as neural (Hood 1998), but the available data on OAEs permits the identification of the site of lesion as being post outer hair cells. The presence of OAEs indicates that the OHCs are functional; the abnormality could be at the inner hair cells and their dendrites, the spiral ganglion, eighth nerve fibres or a combination of any of the above (Hood. 1998).

The histological findings from animal studies (Salvi,Wang.Ding. Stecker and Arnold, 1999; Harrison, 1998) showed that auditory neuropathy could arise from scattered IHCs loss. Whatever causes inner hair cell damage; it will not be confined to hair cells (Harrison, 1998). It is well established that after inner hair cell degeneration there is associated spiral ganglion cell loss (Spoendlin, 1975) and that more central neurons (at least to the mid-brian) also will show some degeneration (Morest and Bohne, 1983).Thus although the entity of auditory neuropathy may originate from cochlear lesions, consequent central deficits will develop.

E) **Behavioral Vs Auditory evoked potential used to evaluate Central Auditory Processing**

A number of central auditory tests, both behavioral and electrophysiological, have been successfully used in defining central auditory processing disorder (CAPD). It is very difficult to understand the relationship between results of behavioral and electrophysiological tests. While selecting the type of central test to be administered to patients with auditory neuropathy certain factors have to be taken into consideration. The most important factor seems to be their ability to understand speech. It is observed during routine audiological evaluation that these patients respond very inconsistently, which could be due to poor understanding of instructions. This is also evident from the poor speech identification score.

Thus, it is possible that these patients may not respond adequately for behavioral tests where the understanding of instructions is very important. However with electrophysiological test, except for P_{300} where patients with auditory neuropathy may find difficult to understand instructions, this limitation is not there.

Also, it is possible that there is post outer hair cell pathology in these patients, that is, inner hair cells and/or other cochlear structures, may be affected accounting for some degree of peripheral hearing loss. In such cases, the results of tests such as dichotic CV would be affected more than potentials such as LLR (Chermak and Musiek. 1997). This may be due to the greater complexity of intensity and frequency interactions, especially over a restricted range thus leading to greater peripheral influence(Chermak and Musiek, 1997).. Hence subjects with associated cochlear hearing loss generally perform better on electrophysiologic tests for central auditory processing evaluation. Thus, electrophysiological tests are better than behavioral tests, in assessing auditory processing in patients with auditory neuropathy.

F) Auditory evoked potential studies in patients with auditory neuropathy

The first auditory evoked potential study in patients with auditory neuropathy was done by Kraus et aL (1984). He described four patients with audiometric findings ranging from normal hearing to moderate hearing loss all of that had absent ABRs. They showed ABR abnormalities, which was out of proportion to the pure tone hearing loss. The localization of eighth nerve lesion could not be done, as methods for defining outer hair cell function using OAEs were not widely used at that time. It was found that MLR was normal in one out of five patients. In the remaining four, the

MLR was reported to be absent. Hence a neuropathology of brainstem was suspected in those patients.

Starr et al., (1996) studied ten patients with hearing impairment and administered behavioral and physiological test that were compatible with a disorder of the auditory portion of the VIIIth cranial nerve. Evidence of normal cochlear outer hair cell function was provided by the confirmed presence of OAEs and cochlear microphonics in all of the patients. Auditory brainstem potentials showed the evidence of abnormal auditory pathway beginning with the VIIIth nerve. The study showed that it was possible to detect other types auditory evoked potentials in five patients even though their brainstem potentials were absent. Middle latency responses were detected in one out of five patients with absent brainstem potentials and long latency components (N100,P200) were detected in three out of four patients with absent ABR. Cognitive potential (P300) evoked in an auditory discrimination target detection task, were also present in the two patients tested.Kraus et al., (2000) studied perception skills ranging from pure tone to sentence level in a subject with auditory neuropathy having hearing within normal limits. Findings were viewed in the context of the sound structure of the signals and the physiological activity along the auditory pathway. It was observed that speech elicited cortical potentials (LLR and MMN) were present.

Thus, MLRs and LLRs were absent or abnormal in a few patients suggests deficits in auditory processing or communicative problems that cannot be explained by peripheral hearing loss alone. On the other hand, the fact that MLR and LLRs were observed in some patients indicated that neural signals are indeed reaching auditory pathways central to brainstem. that is some form of auditory function exists.

The present study aimed at determining middle latency and long latency auditory evoked potentials in subjects with auditory neuropathy in order to provide information regarding auditory pathways central to brainstem, and to detect the presence of any central auditory processing deficiency.

METHODOLOGY

Subjects:

Seven subjects (two males and five females) who reported to All India Institute of Speech and Hearing (AIISH) with a complaint of difficulty in understanding speech and who satisfied the following criteria were chosen for the study.

a) Poor speech identification scores (disproportionate to pure tone average) given by Owens (1971) criteria.

b) 'A' type tympanogram with absent ipsilateral and contralateral reflex.

c) Absent or severely abnormal ABR at 90dBnHL.

d) Presence of TEOAEs.

The demographic data of these patients is shown in Table 1.

Instrumentation:

The following instruments were used for the study.

1. A calibrated two channel diagnostic audiometer GSI-61 with TDH-50P earphone in MX-41/AR ear cushions and Radio ear B-71 bone vibrator was used for pure tone and speech audiometry.

2. A calibrated middle ear analyzer, GSI-33 was used in examining middle ear status.

3. The Nicolet Bravo (version 3.0) evoked potential system was used to record ABR, MLR and MMN. The stimuli were calibrated in dBnHL(0 dBnHL = 40dBSPL for clicks and 25dBSPL for l000Hz tone burst).

4. Click evoked otoacoustic emissions were measured using biologic Scoutplus OAE (version 3.07).

Features	*Category*	**Number**
Age Range	10-20 years	3
	21-30 years	2
	31-40 years	2
Gender	Male	2
	Female	5

Table 1: Summarizes the demographic profile of patients with auditor}' neuropathy.

Test Procedure:

- Pure tone thresholds were obtained at octave intervals for a frequency range of 250 Hz to 8000Hz for air conduction stimuli and from 250 Hz to 4000 Hz for bone conduction stimuli using Carhart-Jerger modified Hughson-Westlake method (Carhart and Jerger. 1959).

- Speech recognition threshold (SRT) were obtained using Kannada paired word list (Rajshekhar. 1976) and speech identification scores were obtained using monosyllables given by Mayadevi (1978). Speech identification scores were obtained at most comfortable level (MCL).

- Immittance evaluation included the measurement of tympanometry and acoustic reflexes (ipsilateral and contralateral) for 500 Hz, lOOOHz, 2000Hz and 4000 Hz to rule out middle ear pathology.

- For recording AEPs, subjects were seated comfortably in an armchair and were asked to relax the jaw and neck muscles. Stimuli were presented through TDH-39 earphones placed in MX-41/AR ear cushions. Electrode site were cleaned, before placing electrode at vertex (Cz), parietal (Pz), forehead (FPz) and the two mastoids (M,and M_2).For ABR and MLR recording, four-electrode montage was used with Cz as non-inverting, FPz as common, left ear (M1) and right ear (M2) as inverting. For MMN recording, five-electrode montage was used with Pz, Cz as non-inverting .FPzas common, left ear (M1) and right ear (M_2) as inverting. The two inverting electrode were linked with jumper. It was ensured that impedance at each electrode was less than 5kΩ and the interelectrode impedance difference was less than 3kΩ. The protocol used for ABR and MLR is shown in Table 2 and protocol for MMN is shown in Table 3.

- The MLR waveforms obtained by the subjects were stored and later analysed for the peak latencies for Po, Na, Pa, Nb and Pb and amplitude Na-Pa.LLR was studied by analyzing the peak latencies for P_1, N_1 ,P_2 and amplitude of N_1 .P_2 from the response for frequent stimuli in MMN recording. The MMN response for intensity deviance was obtained by subtracting the response for the frequent stimulus from that of infrequent stimulus. The peak latency and total duration of MMN were analysed.

- TEOAEs evoked by clicks, ranging from 60-70 dBSPL were recorded.the probe with a foam tip was positioned in the external ear canal and adjusted to give flat stimulus spectrum across the frequency range. The response of 256 stimuli were averaged to obtain the standard nonlinear click emissions .The presence of TEOAEs was determined by response amplitude (noise subtracted) of at least 3dB and waveform replicability of at least >80%.

Parameters	ABR	MLR
Stimulus type	Click	Tone burst
Stimulus intensity	90dBnHL	60-80dBnHL (depending on the hearing Loss
Stimulus Frequency	Not applicable	lOOOHz
Plateau	lOOusec	20cys
Rise time/fall time	Not applicable	10/10
Stimulus polarity	Rarefaction	Alternating
Filter Bandwidth	100-3000 Hz	30-100 Hz
Stimulus Rate	11.1/sec	7.7/sec
Sweep	1500	500
Time window	10ms	100ms
Number of channels	Two	Two
Electrode montage	Cz-M,/Cz-M_2	Cz-M_l/Cz-M_2

Table 2:Summarizes the recording protocol for ABR and MLR.

Parameters	MMN
1. Stimulus Type	Tone burst
2. Stimulus intensity (frequent/infrequent)	60-80/65-85 dBnHL
3. Stimulus Frequency (frequent/infrequent)	1/1 KHz
4. Plateau (frequent/infrequent)	30/30 cys
5. Percent (frequent/infrequent)	80/20
6. Stimulus polarity	Alternate
7. Filter Bandwidth	0.1-30Hz
8. Stimulus Rate	0.9/sec
9. Sweep	500
10. Time window	500 msec
11. Number of channels	Two
12. Electrode montage	Cz-Mi/Pz-M_2

Table 3:Summarizes the recording protocol for MMN.

RESULTS

The information collected from case history, results of pure tone audiometry, speech audiometry. immittance evaluation, auditory brainstem response and otoacoustic emissions of seven subjects with manifestations of auditory neuropathy are presented in this chapter.

Clinical history"

It can be observed from Table 4 that all the seven subjects reported with the complaint of difficulty in understanding speech both in quiet and in noise. The duration of problem ranged from 8 months to 9 years. The nature of the problem was reported to be progressive in six subjects. Only one subject had a positive medical history with a complaint of weakness in the anterior two third of tongue and blurring of vision. The subject reported that the problem increases when exposed to sunlight. The nature of the Problem was thus reported to be fluctuating. Positive family history was reported in one subject whose cousin was also having similar problem.

Audiological profile

Pure tone audiometry revealed normal hearing in only one subject. Four subjects had mild to moderate hearing loss whereas, the degree of hearing loss ranged from moderate to severe in two subjects. As shown in table 4 the configuration of audiogram was either rising or flat type in a majority of the subjects. Only one subject showed an irregular pattern .All the subjects had poor speech identification scores, absent acoustic reflex and abnormal ABR However, TEOAEs were normal, meeting the criteria of auditory neuropathy as given by Starr et al., (1996).

Features/subjects	1	2	3	4	5	6	7
Duration of problem	7yrs	3yrs	3yrs	2yrs	**8 mths**	2yrs	9yrs
Nature of problem	Progressive	Progressive	Progressive	Progressive	Flucluniit	Progressive	Progressive
Medical history	Negative	Ncgalivc	Negative	Negative	Positive	Ncgalivc	Negative
Family History	Negative	Negative	Negative	Negative	Negative	Negative	Positive
Self report of speech understan-ding	Poor	Poor	Poor	Poor	Poor	Poor	Poor
Tinnitus	Absent	Absent	Absent	Absent	Present	Absent	Absent
Giddiness	Absent	Absent	Absent	Absent	Present	Absent	Absent
Symmetry of hearing loss	Asymmetrical	Symmetrical	Asymmetrical	Asymmetrical	symmetrical	Symmetrical	Asymmetrical
Degree of hearing loss (R/L)	Modcraje/Modc-rately severe	Moderate/Mode-rate	Mild/Moderate	Moderate/Mild	Moderate/Mode-rate	Normal hearing	Modcratc/Modc-rately severe
Slope of hearing loss (R/L)	lrregular/Irregula-rf	Rising/Rising	Irregular/Falli-ng	Rising/Falling	Falling/Falling	Falling/Falling	Rising/Rising
Speech identification score	Disproptionatc to PTA	Disproptionale to PTA	Disproplionate to PTA	Disproptionatc to PTA	Disproptionalc to PTA	Disproplionate to PTA	Disproptionatc to PTA
Acoustic reflex	Absent	Absent	Absent	Absent	Absent	Absent	Absent
ABR(90dBnHL)	Absent	Absent	Absent	Absent	Absent	Absent	Absent
OAE (60-70dBpeakSPL)	Present	Present	Present	Present	Present	Present	Present

Table 4. Summarizes the Clinical and Audiological profile of seven subjects with auditory neuropathy.

Test	! 1	2	3	4	5	6	7
MLR	Noisy	Present	Noisy	Present	Absent	Absent	Absent
LLR	Present	Present	Present	Present	Present	Absent	Present
MMN	Present	Absent	Present	Present	Present	Absent	Present

Table 5:Summarizes test results of MLR, LLR and MMN in seven subjects with auditory neuropathy.

Electrophvsiological study:

The results of Middle latency response (MLR), Late latency response (LLR) and Mismatch negativity (MMN) are summarized in Table 5.

1. **MLR** Response:

Middle latency response was present in only two subjects and in both the subjects only Po, Na and Pa could be visually recognized and peak latencies were comparable with that reported for normal subjects by Paul (1997).The peak latency of Po was 19.6 and 18 msec.for Na it was 27 and 28 msec and for Pa it was 35 and 33 msec for both the subjects respectively. The Na-Pa amplitude was less than 1.26uV in both the subjects. Figure 1 shows the MLR waveform obtained from one of the subjects. In two subjects no clear peaks could be identified other than Pa as the waveforms were very noisy, even when replicated and the latency of Pa was 43.40msec in these two subjects. In the remaining three subjects MLR was absent.

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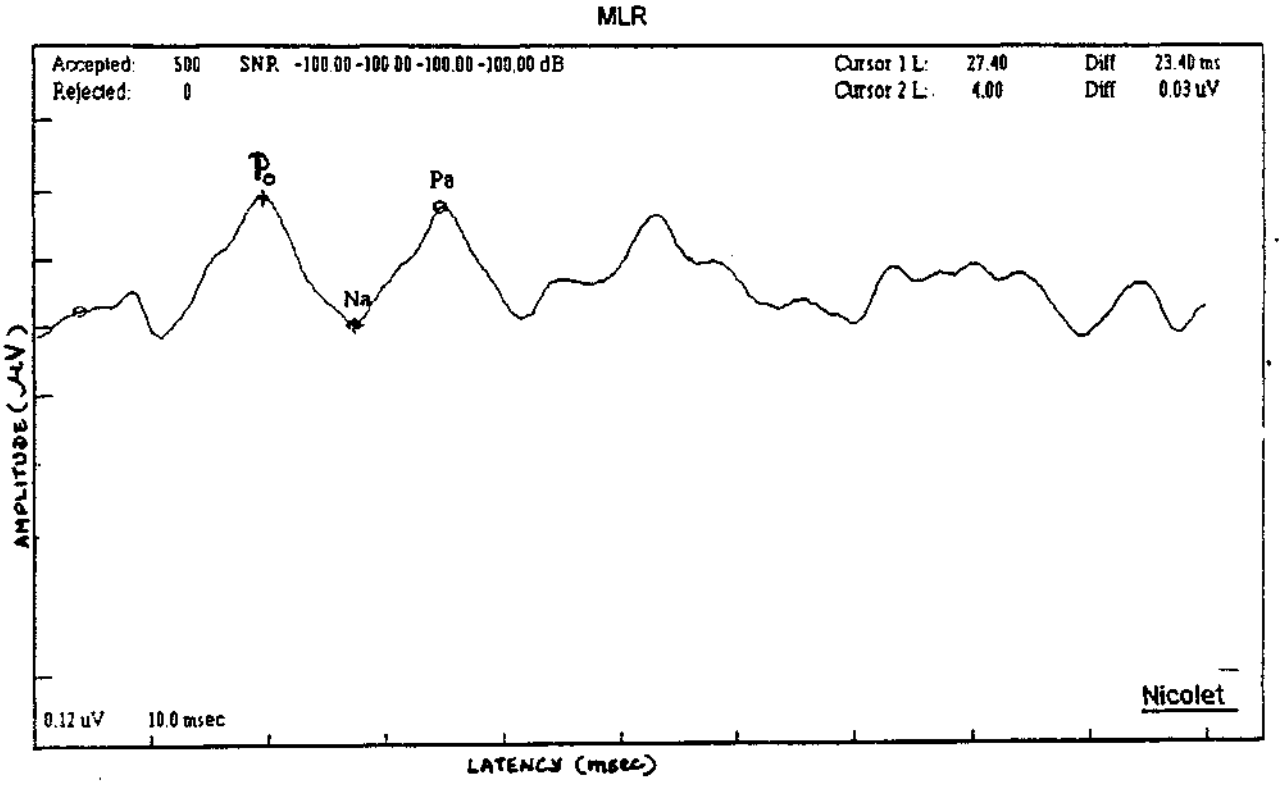

Figure 1: Shows Middle latency reponse obtained at the vertex (Cz) in subject with auditory neuropathy. The peak latency of P_0 is 19.6msec, N_a is 27.8msec and P_a is 35msec. The amplitude of- N_a- P_a is 1.20uV.

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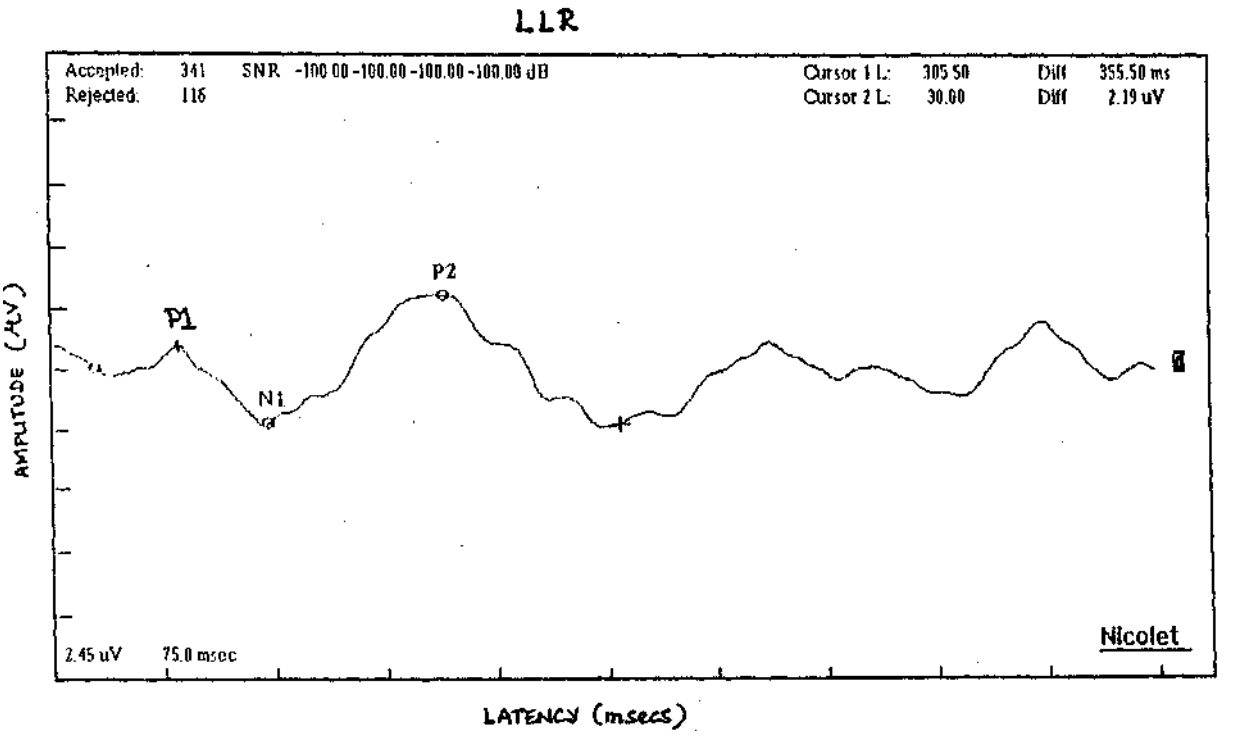

Figure 2: Shows the Late latency reponse obtained at the vertex (C_z) in subject with auditory neuropathy. The peak latency of P_1 is 73msec, N_1 is I47sec, and P_2 is 255msec. The amplitude of N_rP_2 is 2.19uV.

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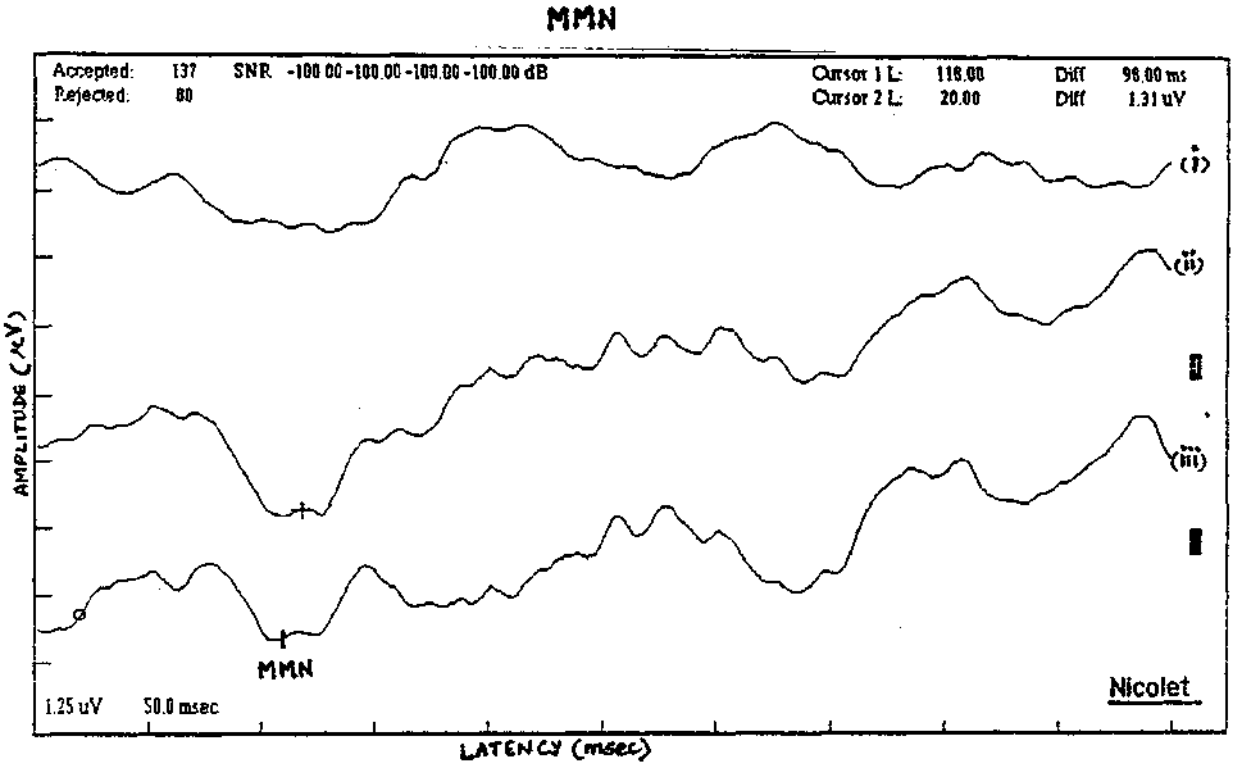

***Figure 3**: Shows the Mismatch negativity response obtained at the vertex (Cz) in subject with auditory neuropathy . The MMN peaks at 118msec and is seen in the difference waveform (Hi) produced by subtracting the reponse for the frequent stimuli (i) from that of the infrequent stimuli (ii)*

2. LLR Response:

LLR was present in six subjects and absent in only one subject. The peak latency of P_1 varied from 51 to 84 msec, N_1 from 96 to 145 msec, P_2 from 167 to 255 msec and N_1-P_2 amplitude varied from 0.65 to 4.93uV .These values are comparable with that reported for normal subjects by Shankar (1997).Figure 2 shows LLR waveform obtained from one of the subject.

3. MMN Response:

MMN for intensity deviance could be identified in five subjects and was absent in two subjects.The peak latency of MMN varied from 153 to 214 msec at Cz and at Pz, the peak latency varied from 121 to 166 msec. The total duration of negativity for the waveform obtained from Cz and Pz ranged from 40-109 msec and 37-11 msec respectively. The peak latency and total duration of MMN for Pz and Cz were comparable with that reported in normal subjects by Jose (1999).Figure 3 shows the MMN waveform obtained from one of the subjects.

Only in one subject all the potentials i.e., MLR, LLR and MMN were absent even though hearing was within normal limits.

DISCUSSION

In the present study, long latency responses and mismatch negativity were present in a majority of the subjects but middle latency responses were either noisy or absent. These result are in congruence with previous investigations using MLR (Kraus et al., 1984;Starr et al, 1996), LLR (Starr et al., 1996;Kraus et al., 2000) and MMN (Kraus et al., 2000). The presence or absence of these potentials in some of the subjects and the discrepancy between the test results are discussed in this chapter.

The absence of MLR in a majority of the subjects can be attributed to either generation of myogenic response while recording MLR or disrupted neural discharge of the afferent pathway to auditory cortex. The absence of MLR in some of the subjects can be attributed to the generation of myogenic response as in these subjects the hearing threshold at 1kHz was more than 45dB HL and high stimulus intensity (80dBnHL) was used to elicit the response. At such high intensity, several reflexes may have originated from scalp musculature. (Picton, Hillayrd, Krausz and Galambos, 1974), which would have masked the MLR waveforms. The interpretation can also be supported by the observation of normal MLR in two subject whose hearing threshold level at 1kHz was less than 30dBHL and MLR was present at lower intensity .MLR was absent in one subject even though the hearing was normal. Absence of MLR in this patient may be attributed to disrupted neural discharge of the afferent pathway to auditory cortex because of auditory neuropathy.

Presence of LLR in subjects with absent MLR can be attributed to the difference in stimulus - duration used for the two potentials and/or to the difference in the neural synchrony required for these potentials. Auditory neuropathy subjects have impaired processing for short duration stimuli

compared to long duration stimuli (Starr et al., 1991), and this may have lead to absence of MLR where shorter duration of stimuli were used compared to LLR. Also cortical potential like LLR require different neural synchrony compared to the synchrony required for relatively shorter latency responses (Kraus et al., 2000). It is possible that in subjects.ABR and MLR which require high synchronization may be disrupted whereas slow neural synchrony (in order of several milliseconds) required for LLR may be intact. This may result in presence of LLR in subjects with absent MLR and ABR.

In the present study MMN for intensity deviance was recorded from five subjects reflecting intact neuronal response to intensity change. MMN is an objective neurophysiological test of auditory discrimination. (Sams, Paavilainnen, Alho and Naatanen, 1985). Absences of MMN in two subjects suggest possibility of impaired intensity discrimination. Starr et al., (1991) found impaired discrimination of pure tones with the subject requiring twice the normal intensity change to discriminate a difference . Thus, absence of MMN in the present study can also be, because the intensity deviance was small for the subject to discriminate.

Absence of all the three cortical potential in one of the subjects with normal hearing can be attributed to disrupted neural discharge of the auditory pathways as mentioned before, resulting in absent MLR; impaired stimuli-related-timing neural synchrony at cortical level resulting in the absence of LLR and MMN. These results suggest that this subject in future may constitute a clinical subgroup of auditory processing disorder consequent to brainstem and cortical dysfunction.

SUMMARY AND CONCLUSIONS

Auditory neuropathy could be one etiology for some cases with central auditory processing dysfunction (Starr et al., 1996). Thus, assessment of central auditory processing in subjects with auditory neuropathy is of paramount importance from clinical point of view. Application of electro-physiological test such as auditory evoked potential provides objective information on the central auditory processing abilities, critical for effective assessment and management of neurologically impaired patients,however very few studies have investigated middle latency response and long latency response and endogenous potentials in subjects with auditory neuropathy.(Kraus et al., 1984; Starr et al., 1996;Kraus et al., 2000).

Thus, this study was undertaken to see if the electrophysioiogical tests such as MLR, LLR and MMN reveal any auditory processing problem in subjects with auditory neuropathy.

Auditory evoked potentials (ABR, MLR, LLR & MMN for intensity deviance) were recorded in seven subjects with auditory neuropathy using Nicolet Bravo (Version 3.0) evoked potential system. Obtained MLR waveforms were analysed for peak latencies of Po, Na, Pa, Nband Pb and amplitude of Na-Pa. LLR was studied by analysing peak latencies of P_l, N_l, P2 and amplitude of N_1-P2 from repense of frequent stimuli in MMN recording. Peak latency and duration of MMN was analysed after subtracting the response to frequent stimuli that of infrequent stimuli. All the subjects met the criteria of auditory neuropathy given by Starr et al., (1996).

Analysis of results showed that in a majority of the subject MLR was absent but LLR and MMN were present. In one subject, all the potentials

were absent even though the hearing was within normal limits. However there were some subjects in whom MLR was present but MMN was absent.

To conclude, the results of present study suggest variability in subjects with auditory neuropathy. This suggest that central auditory processing ability can either be intact or disrupted, and is reflected by presence, absence or abnormal auditory evoked potentials in subjects with auditory neuropathy. Thus, these potentials (MLR, LLR & MMN) can be used in order to supplement clinical information in identifying central auditory processing dysfunction in auditory neuropathy subjects.

BIBLIOGRAPHY

1. Berlin, C.I., Hood, L.J., Cecola, R.P., Jackson, D.F., & Szabo, P.P. (1993). Does type II afferent neuron dysfunction reveal itself through lack of efferent suppression? Heaing Research, 65, 40-50.

2. Berlin, C.I., Hood, L.J., Murley, A., & Wen, M. (1994). Contralateral suppression of otoacoutstic emissions: An index of the function of the medical olivocochlear system. Otolaryngol Head Neck Surgery, 100,3-21.

3. Berlin, C.I., Bordelon, J., St.. John, P., Wilensky, D., Murley, A., Kluka, E., & Hood, L.J. (1998). Reversing Click Polarity may uncover auditory neuropathy in infants. Ear and Hearing, 19, 37-47.

4. Berlin, C.I. (1999). Auditory neuropathy using OAEs and ABRs from screening to management. Seminars in hearing, 19 (5), 355-361.

5. Carhart, R., & Jerger, J.F. (1959). Preferred method for clinical determination of pure tone thresholds. J. Speech Hearing Disorder, 24, 330-345.

6. Cassandro, E., Mosca, F., Sequino, L., De Falco, F.A., & Campanella, G. (1986). Otoneurological findings in Friedrich's ataxia and other inherited neuropathies. Audiology, 25, 84-91.

7. Chermak, G.D., & Musiek, F.E. (1997). Central Auditory Processing Disorders: New Perspectives. San Diego-Singular Publishing Group.

8. Davis, H., & Hirsh, S.K. (1979). A slow brainstem response for low frequency audiometry. Audiology, 18,445-461.

9. Deltenere, P., Mansbach, A.L.. Bozet C, Clercx, A.. & Hecox, K.E. (1997a). Temporal distortion product (kernel slices) evoked by maximum length sequences in auditory neuropathy: Evidence for a cochlear pre synaptic origin. Electroencephal Clin Neurophysiol, 104, 10-16.

lO. Deltenere, P., Mansbach, A.L., Bozet, C.I., Clercx, A., & Hecox, K.E. (1997b). Auditory neuropathy: A report on three cases with early onsets and major neoratal illness. Electroencephal clin Neurophysiol. 104, 17-22.

ll. Hallpike C.S., Harriman, D.G.F.. & Wells, C.E.C. (1980). A case of afferent neuropathy and deafness. J.Layngol Otol, 94, 945-64.

12. Harrison, R.V. (1998). Animal model of auditory neuropathy. Ear and Hearing, 19 (5), 355-361.

13. Hood, L.J. (1998). Auditory neuropathy: What is it and what can we do about it? The hearing journal, 5(8) 10-18.

14. Jose, B; (1999). Effects of intensity deviance on mismatch negativity. Unpublished Master's Independent Project, University of Mysore, Mysore.

ls. Kaga, K., Nakamora, M., Shinogami,M., Tsuzuku, T., Yamada, K., & Shindo, M. (1996). Auditory nerve disease of both ears revealed by auditory brainstem response, electorcochleography and otoacoustic emissions. Scandinavian Audiology, 25, 233-238.

16. Kraus, N., Ozdamar, O.. Stein, L,, & Reed, N. (1984). Absent auditory brainstem response. Peripheral hearing loss or brain stem dysfunction. Laryngoscope, 94, 400-406.

17. Kraus, N., Bradlow, R., Cheatham, M.A., Cunningham, J., King, CD., Koch, D.B., Nicol, T.G., McGee, T.J., Stein, L.K., & Wright, B.A. (31st May, 2000). Consequences of neural asynchrony: A case of auditory neuropathy. Journal of the Association for the research in Otolayngology (online). Available: World Wide Web: http//www.cns.nyu.edu/earclub/ artfiles/Kraus2000.html. (Retried on 14th April 2001).

18. Morest D.K., & Bohne, B.A. (1983). Noise induced degeneration in brain and representation of inner and outer hair cells. Hearing Research, 9, 145-151.

19. Musiek, F.E., Weider, D.J., & Mullen R.J. (1982). Audiological findings in Charcot-Marie tooth disease. Arch Otolaryngol, 108, 595-599.

20. Owens, E. (1971). Audiological evaluation in cochlear Vs. retero-cochlear lesions. Acta otolaryngol (Stockh), 79, 310-314.

21. Paul, P. (1997). Age related changes in MLR. Unpublished Master's Independent Project. University of Mysore. Mysore.

22. Picton, T.W., Hillyard, S.A., Krausz, H.I., & Galambos. R. (1974). Human auditory evoked potentials. I. Evaluation of components. Electroencephal clin neurophysiol. 36, 179-190.

23. Picton, T. (1995). The neurophysiological evaluation of auditory discrimination. Ear and Hearing. 16, 1-5.

24. Raglan, E., Prasher, D.K.. Trinder, E., & Rudge, P. (1987). Auditory function in hereditary motor and sensor}' neuropathy (Charcot-Morei-Tooth disease). Acta otlaryngol (stock; 103, 50-55.

25. Rance, G., Beer, D.E., Cone-Wesson, B., Shephard, R.K., Dowell, R.C., King, A.M., Rickards, F.W., & Clark, G.M. (1999). Clinical findings for a group of infants and young children with auditory neuropathy. Ear and Hearing, 20, 238-252.

26.Rooper, A.H., &Chiappa, K.H. (1986). Evoked potential in Guillain-Barfe Syndrome. Neurology, 36, 587-590.

27. Salvi, R.J., Wang, J., Ding, D., Stecker, M., & Arnold, S. (1999). Auditory deprivation of the central auditory system resulting from selective inner hair cell loss: Animal model of auditory neuropathy. Scandinavian Audiology, 28 (supp 151). 1-12.

28. Sams, M., Paavilainen, P., Alho, K., & Naatanen, R.C. (1985). Auditory frequency discrimination and event related potential. Electroenceph clin Neurophysiol, 62, 437-448.

29. Schulman, Galambos, C, & Galambos, R. (1979). BSER Audiometry in newborn hearing screening. Arch otolaryngol, 105, 86-90.

30. Shankar, D. (1997). Age related changes in auditory late latency responses. Unpublished Master's Independent Project. University of Mysore. Mysore.

31.Sheykholeslami, K., Kaga, K., Murofushi, T., & Hughes, D.W. (2000). Vestibular function in auditory neuropathy. Acta Otolaryngal (stockh), 120, 849-854.

32.Sinniger, Y.S., Hood, L.J., Starr, A., Berlin, C.I., & Picton, T.W. (1995). Hearing loss due to auditory neuropathy. Audiology Today, 7, 10-13.

33. Spoendlin, H. (1975). Retrograde degeneration of the cochlear nerve. Acta oto-larynga] (stockh), 79. 266-275.

34. Starr, A., McPherson, D.. Patterson, J., Luxford, W., Shannon, R., Sinniger, Y., Tonokawa. L., & Waring, M. (1991). Absence of both auditory evoked potentials and auditory percepts dependent on time cues. Brain, 114, 1157-1180.

35. Starr, A., Picton, T.W., Sinniger, Y.S., Hood L.J., & Berlin C.I. (1996). Auditory neuropathy. Brain, 119,741-753.

36. Stein, L., Tremblay, K., Pasternak, J., Banerjee, S., Lindemann, K., & Kraus, N. (1996). Brainstem abnormalities in neonates with normal otoacoustic emissions. Seminars in hearing, 17. 197-213.

37. Worthington, D.W., & Peters, J.F. (1980). Quantifiable hearing and no ABR: Paradox or Error? Ear and Hearing, 5, 281-285.

38. Wright, A., & Dyck, P.J. (1995). Hereditary Sensory neuropathy with sensorineural deafness and early onset dementia. Neurology, 45, 560-562.