PRIMARY AUDITORY NEUROPATHY : A REVIEW

Reg.No.M9819

Independent Project as a part fulfilment of first year M. Sc, (Speech and Hearing), submitted to the University of Mysore, Mysore

ALL INDIA INSTITUTE OF SPEECH AND HEARING
MYSORE 570 006
MAY 1999

Dedicated to
JoJo
my Pest and my Love

CERTIFICATE

This is to certify that this Independent Project entitled: **PRIMARY AUDITORY NEUROPATHY : A REVIEW** is the bonafide work in part fulfilment for the degree of Master of science (Speech and Hearing) of the student with Register No.M**9819.**

Mysore
May, 1999

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CERTIFICATE

This is to certify that this Independent Project entitled **PRIMARY AUDITORY NEUROPATHY : A REVIEW** has been prepared under my supervision and guidance.

Mysore
May, 1999

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DECLARATION

This Independent Project entitled : **PRIMARY AUDITORY NEUROPATHY : A REVIEW** is the result of my own study under the guidance of Dr.K.Rajalakshmi, Lecturer in Audiology, All India Institute of Speech and Hearing, Mysore and has not been submitted earlier at any University for any other diploma or degree.

Mysore
May, 1999

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INTRODUCTION

The incidence of absent/abnormal auditory brainstem response (ABR) in patients with relatively good hearing has been reported (Davis and Hirsh, 1979). The patients respond to moderate or low intensity sounds. Here ABR and audiological findings appear paradoxical. But is this truly an error or paradox ? Literature reports findings showing that, there can occur a condition with normal outer haircell function and abnormal neural function at the level of VTIIth (vestibulo-cochlear) nerve. These characteristics are observed on clinical audiological tests as normal Otoacoustic Emissions (OAEs) when ABR is absent or severely abnormal. This condition is currently termed as 'auditory neuropathy' and is found in patients ranging in age from infants to adults.

Auditory neuropathy is not a new hearing disorder. But our ability to identify this is new. This is due to the use of OAE. OAE allows us to identify persons who have normal outer haircell function despite abnormal ABR.

The patients may have other neural disorders associated with it. The common ones are Hereditary Motor Sensory neuropathy (HMSN Charcot-Marie Tooth syndrome), Friedrick's ataxia, loss of deep tendon reflex and motor system disturbances.

The etiology of auditory neuropathy is thought to be more than single. But all patients have shown a cohesive set of auditory

symptoms. The pattern of normal outer haircell function combined with abnormal ABR places the site of auditory neuropathy in the area that contains the inner hair cell (IHC) connections between IHC and cochlear branch of VIIIth cranial nerve, the VIIIth nerve itself and perhaps auditory pathways.

Possible sites include IHC. tectorial membrane synaptic juncture between EHC auditory neurons in spiral ganglion, VIIIth nerve fibers or any combination. Problems may be axonal or demyelinating. Afferent as well as efferent path may be involved. Biochemical abnormality involving neurotransmitter release can be a problem (The specific sites and mechanisms of auditory neuropathy are yet to be determined).

The clinical auditory tests most sensitive to auditory neuropathy would be those sensitive to cochlear and auditory nerve function. Measuring OAEs and cochlear microphonics would evaluate OHC function.

Tests most sensitive to auditory nerve dysfunction are middle ear reflexes (ipsilateral and contralateral) ABR, masking level difference (MLD) efferent suppression of OAE and to a limited extent word recognition with ipsilateral competing noise or message.

Of these measures, OAE and auditory ABR when used together, offer insight into preneural as well as neural function in auditory system and thus may form the most sensitive combination.

Expected Results in Auditory Neuropathy Patients :

Test	Outcome
Puretone thresholds	Normal to severe/profound hearing loss (any configuration can be asymmetric)
Speech recognition in quiet	Variable, slightly reduced to greatly reduced
Otoacoustic emission	Normal
Middle ear muscle reflex	
• Ipsilateral	Absent
• Contralateral	Absent
• Non-acoustic	Present
Cochlear Microphonic	Present (inverts with stimulus polarity reversal)
Auditory brainstem response	Absent (severely abnormal)
Masking level difference	No MLD (i.e. 0 dB)
Efferent suppression of Transient evoked otoacoustic emission	No suppression
Speech recognition in noise	Generally poor

Auditory neuropathy is least sensitive to puretone thresholds and speech recognition scores.

ABR or OAE are not direct tests for hearing. OAE evaluates OHC functions, representing preneural phenomena related to

mechanical process in the cochlea. The ABR tests neural synchrony and the timing precision to external stimuli. Under appropriate conditions both OAE and ABR can give us information about function of peripheral auditory function.

Specific risk factorsfor auditory neuropathy are not clearly understood. However, a number of infants with auditory neuropathy have a history of major neonatal illness including hyperbilirubinemia and other risk factors. Auditory neuropathy is also associated with other non-auditory peripheral neuropathies siblings have been identified with auditory neuropathy suggesting underline genetic factors as well.

Efferent suppression of OAE involves the reduction in amplitude are change in phase of emission resulting from addition of another stimulus. Auditory neuropathy patients demonstrate a lack of suppression of otoaocustic emission under any circumstances, wihich may reflect efferent pathway dysfunction and/or a compromise of access to the efferent system resulting in a lackof efferent suppression of OAEs. Middle latency responses (MLR) are generally normal, while late potentials example (N1-P2, P300) where longer duration stimuli can be used may be present.

Normal OAEs with hearing difficulty is manifested because the mechanical function of cochlea alone remain insufficient for normal hearing. IHC function is also needed to activate the sensory process that transmit incoming information to the auditory nerve and central auditory system.

Most cases identified to-date are bilateral (often asymmetrical). However, a few have unilateral auditory neuropathy. Functionally these unilateral cases are similar to patients with unilateral hearing loss.

At present, the management approach in these patients is similar to that used in other more common types of unilateral hearing loss, such as directing speech to normal ear and maximizing the signal to noise ratio.

Hearing loss have been to be progressive in some patients, though is not characteristic in all patients. The occurrence would depend on underlying etiology.

Auditory neuropathy gets misdiagnosed in infants and children where evidence of otitis media is higher than in older children and adults, where OAEs may be absent.

While any disorder of the auditory neural pathways from the VIIIth nerve to the cortex might be defined as an auditory neurpathy, the current use of the term relates specifically to more peripheral portions of the auditory pathway in the area between OHC and brainstem. The patients may display characteristics of central auditory processing (CAP) problems (eg. inattention, missing some information, inconsistencies in responses etc). Peripheral measures as middle ear muscle reflexes and the ABR are abnormal in auditory neuropathy the function at the brainstem level is more often normal in patients with CAP disorders.

Patients with auditory neuropathy have trouble communicating in everyday situations. They have discrimination deficits due to neural tuning deficits limiting the ability to follow rapid transitions of normal speech.

Patients may heavily rely on lip reading to supplement the auditory information available.

However, patients generally have normal sounding speech and vocal qualities, suggesting an intact monitoring system.

In infants and children, they do not have the advantage of accurate auditory information to help them discriminate and learn appropriate speech language patterns.

Management

The most important consideration is facilitating the development of langauge in children.

Use of visual communication system (Sign language, cued speech) would be helpful. The goal is to expose children to conversation as it normally occurs at home. If ability to use auditory information improves, spoken language can be assimilated to a system that follows the required language structure.

In patients who have already developed spoken language, goal is to maximise the available auditory information and provide

supplementary speechreading cues. Training to improve speechreading skills may be beneficial.

Adult patients generally find hearing aids to be of little benefit. Some find frequency modulated (FM) systems helpful (situation where enhanced SN ratio allow residual speech understanding).

If hearing aids are recommended high quality, low gain, wide-dynamic range compression aids should be the choice (If hearing aids are tried, frequent monitoring of OAEs for either temporary or permanent effects on OAEs should be a part of the management program).

Cochlear implants would be least useful in any condition with etiology involving neural function. If in a particular patient auditory neuropathy is cochlear in origin with intact nerve, it can however be tried.

The condition is progressive in adults with Hereditory Motor Sensory Neuropathy (HMSN) and the case may remain stable or fluctuate:; in cases of temperature sensitivity or auto-immune disorders.

In infants fluctuations are very common (depending on neural maturely).

Until the etiologies underlying auditory neuropathy can be identified and distinguished clinically it will be impossible to make accurate predictions about changes in auditory ability. For now, changes either improvement or decline can be ascertained only through long term follow up.

An auditory neuropathy patient, in addition to speech language and audiology considerations should be evaluated by a neurologist, paediatrician, otolaryngologist and a general physician for comprehensive care.

WHAT IS AUDITORY NEUROPATHY?

Auditory Neuropathy is congenital or acquired a. demyelinating disorder of the VIIIth nerve in which there is an absent or severely abnormal auditory brainstem evoked potential (ABR) (starting from Wave I, the component reflects activity of the VIIIth nerve within the cochlea) that does not correspond to the subject's audiometric thresholds (which may indicate only a mild to moderate hearing loss) or to relatively normal OAEs (OAEs and/or cochlear microphonics (CM) reflecting the integrity of OHC of cochlea). These patients have poor speech discrimination scores relative to their audiometric status particularly in the presence of noise. One of the first reports of this disorder come from Worthington and Peters (1980) since then many patients with auditory neuropathy have been described (Berlin, et al. 1993; Deltenre, et al. 1997, Starr etal. 1991, Stein, etal. 1996).

Before the use of otoacoustic emissions (or cochlear microphonic (CM) recordings), the locus of the disorder was unclear, however the finding of relatively normal OAEs excluded the possibility that damage to the outer hair cells was the primary cause because these are the major generators of the OAEs.

Another significant diagnostic feature of auditory neuropathy is that the ABR waveform is severely abnormal beginning at wave one, suggesting that the hearing disorder arises from a cochlear or VIIIth nerve pathology rather than from some more central lesion (Starr, et al. 1996).

Otoacoustic emissions (OAEs), originally described by Kemp (1978) are faint sounds emitted by the cochlea either spontaneously or in response to an acoustic signal. These emissions are thought to be generated by active movements of the outer hair cells and are left intact after severance of the auditory nerve (Seigel and Kim, 1982). OAEs can be detected by a sensitive microphone placed within the external ear canal. Stimulation with clicks, evokes emissions in the form of a brief acoustic echo lasting approximately 20 ms. Specific testing of a restricted region of hair cells can be carried out by stimulation with two continuous tone of different frequencies (Fl and F2) to evoke distortion product otoacoustic emission which are the largest at the 2F1-F2 frequency.

Auditory neuropathy is infrequently seen relative to sensory hearing loss. It manifests with a hearing loss which is more accurately classified as neural, but the available data on OAEs permit the identification of the site of lesion as being post outer hair cells. The presence of OAEs indicate that the outer hair cells are functional, but the abnormality in auditory neuropathy could be at the inner hair cells and their dendrites, the spiral ganglia, the eighth nerve fibres or a combination of any of the above. The disorder probably arises from a pathological condition in which some inner hair cells and/or associated spiral ganglion cells are inactive or have degenerated.

The absence of wave I in auditory brainstem resonse (ABR) in case of patients with auditory neuropathy, suggests the possibility as lesion that is not merely restricted to cochlear nucleus. It may also seem possible to have auditory pathway abnormalities, in addition to

more peripheral lesions. However, there are no diagnostic tests available at this time to differentiate these conditions.

Absent ABRs or the selective loss of the later waveforms may result from the disruption of neural synchrony necessary for ABR generation. Insults to the nervous system may have resulted from myelinization deficits or destruction of cell bodies. However, it may be possible that pathways responsible for ABR may be damaged while hearing is presumed through other pathways.

One of the intriguing feature of this disorder is that thresholds measured using puretone audiometry can be markedly better than ABR thresholds. In some cases there may be only a mild to moderate sensorineural hearing loss. This means that if there is cochlear damage, it is not extensive enough to prevent some relatively low threshold cochlear afferent activity across a range of frequency locations. On the other hand, to reduce the number of synchronized neurons that contribute to the ABR, the deterioration has to be quite significant. These conditions could arise from scattered IHC loss. Given the findings of relatively normal OAE, the OHC are minimally involved.

In a study done by Starr, et al. (1996), they presented ten children with hearing-impairments that, by behavioural and physiological testing 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 preservation of OAE and cochlear microphonics in all of the patients. Auditory brainstem

potentials showed evidence of abnormal auditory pathway function beginning with the VIII nerve : the potentials were absent in some patients and severely distorted in one. Auditory brainstem reflexes (middle ear muscles, crossed suppression of OAE) were absent in all of the tested patients. Behavioural audiometric testing showed a mild to moderate elevation of puretone thresholds in nine patients. The extent of the hearing loss, if due to cochlear receptor damage, should not have resulted in the loss of auditory brainstem potentials.

The shape of the puretone loss varied, being predominantly low frequency in five patients, flat across all frequencies in three patients and predominantly high frequency in two patients. Speech intelligibility was tested in eight patients, and in six was affected out of proportion to what would have been expected if the puretone loss were of cochlear origin. The patients were otherwise neurologically normal, when the hearing-impairment first manifested. Subsequently eight of these patients developed evidence for a peripheral neuropathy. The neuropathy was hereditary in three and sporadic in five. They suggest this type of hearing-impairment is due to a disorder of auditory nerve function and may have as one of its causes, a neuropathy of the auditory nerve, occurring either in isolation or as part of a generalized neuropathic process.

Another study by Doyle, et al. (1998) also described a group of eight children with hearing loss for puretones impaired word discrimination out of proportion to pure tone loss, absent or abnormal ABR and normal OHC function as measured by OAE and CM. And they suggest that hearing deficits are due to neuropathy of the eight

nerve. Recent advances in OAE testing permit differentiation of the neural deafness from sensory deafness.

The middle latency response (MLR) in one subject showed that neural signals indeed reach auditory pathway central to the brainstem. Hence some form of auditory function exists as evidenced by audiometric thresholds for understanding speech.

Spoendlin (1974) described the temporal bones of two individuals with Friedrich 's ataxia. He noted that the organ of corti was normal, but that there was damage to the spiral ganglion cells in these patients.

Hallpike et al. (1980) also found normal hair cells, but degeneration of spiral ganglion cells and auditory nerve fibres in a patient with hereditary hearing loss, poor speech comprehension and peripheral neuropathy.

Kraus et al. (1984) described four patients with audiometric findings ranging from normal hearing to moderate hearing loss, all of whom had absent ABRs. They showed ABR abnormalities far out of proportion to the puretone loss. The localization of eighth nerve could not be made as methods for defining outer hair cell function (OAE) or (cochlear microphones) were not widely used. And hence Kraus suspected a neuropathology of the brainstem.

ETIOLOGY, CLINICAL SYMPTOMS, AUDIOLOGICAL EVALUATIONS AND DIFFERENTIAL DIAGNOSIS

Etiologies of auditory nerve disorders have been diverse and include neonatal hyperbilirubenia (Stein, et al. 1996), severe illness during the neonatal period (Deltenre, et al. 1997a) a part of a generalized hereditary metabolic toxic, or inflammatory neuropathy (Alexander, et al. 1995; Berlin et al. 1993; Hardin, 1995; Jabbari, et al. 1993; Kalaydjieva et al. 1996; Starr et al. 1996) and an isolated neuropathy of the VIIIth nerve. Some patients also may have an accompanying generalized neuropathy affecting other cranial and/or peripheral nerves (Starr et al. 1996).

A number of etilogies related to the occurrence of auditory neuropathies have been found. These include (1) genetic factors as in hereditary sensory motor neuropathy (Hardin, 1995; Kalaydjieva et al. 1996) and Friedrich's ataxia (Cassandro et al. 1986). (2) Immune disorders as in Gullian - Barre syndrome (Nelson, et al. 1988), (3) Infections processes such as mumps (Sawada, et al. 1979) and (4) Toxic-metabolic disorders during neonatal period as in hyperbilirubemia (Stein, et al. 1996) a lesion to the cochlear nucleus and anomia (Deltenre et al. 1997 a).

In patients with an auditory nerve disorder, the development of deafness with slight elevation of body temperature is noticed. This is most consistent with a demyelinating neuropathy of the auditory nerve. In myelinated mammalion nerves, the ionic processes accounting for the generation of action potential are restricted to the

nodes of Ranvier, the junction points between adjacent myelin glial cells (oligodendroglia for central pathways and schwann cells for peripheral nerve). The nodal membrane is rich in Na+ channels essential for the generation of the nerve action potential, whereas paranodal and internodal membrane sites have few Na+ channels but are rich in K+ channels. Thus the generation of Na+ current contributing to the development of action potential in myelinated nerve is not continuous along the nerve but is restricted to the nodes of Ranvier. The restriction of the action potential to the nodes of Ranvier results in a discontinuity of conduction from node to node known as saltatory conduction and accounts in part for the rapid conduction velocity of myelinated fibers.

Internodal conduction velocity in a segmentally demyelinated axon is slowed and varies with the extent of demyelination (Razminsky, 1973), when the nerve impulses passes a demyelinated region and encounters a normally myelinated segment, conduction velocity resumes, normal speeds. If the length of the demyelinated zones in these axons differs, conduction spreads of demyelinated axons of comparable size will vary and affect the degree of synchrony of discharge between adjacent axons. This dysynchrony in conduction may account for the failure to average auditory brainstem potentials in patients with auditory neuropathy (Starr, et al. 1991,1996). Dysynchrony of auditory nerve fiber discharges also could account for the difficulties these patients have in perceptual judgements dependent on temporal information contained in auditory signals such as in gap detection, masking level differences and lateralization of binaural signals (Starr et al. 1991, 1996).

As more is learned about the disorder, different forms of auditory neuropathy will be demonstrated, and classified according to the anatomic areas.

Clinical Symptoms

The symptoms that these patients manifest are primarily with varying deficits of hearing. Speech recognition in noise very poor compared to when quiet. Absent or severely abnormal ABRs are almost always seen. But, preservation of OAE and cochlear microphonic indicating normal OHC status remain a striking feature of the disorder.

Responses that require intact auditory nerve and/or brainstem pathways as in middle ear muscle reflex, the ABR, MLD and efferent suppression of OAEs are abnormal. One of the intriguing features is that threshold measured using puretone audiometry can be markedly better than ABR thresholds. In some cases there may be only a mild to moderate sensorineural hearing loss. This means that if there is cochlear damage its not extensive enough to prevent some relatively low threshold cochlear afferent activity across a range of frequency locations. On the other hand to reduce the number of synchronized neurons that contribute to the ABR, the deterioration has to be quite significant These conditions could arise from scattered inner hair cell loss. Given the findings of relatively normal OAEs, the outer hair cells are minimally involved. MLR are generally abnormal while late latency responses (LLR) may be present.

Starr et al. (1991, 1996) studied the hearing function of children and young adults with auditory nerve carefully and found the loss to be typically of insidious onset, initially affects a moderate elevation of puretone threshold, particularly of low and middle frequencies. Impaired speech comprehension was noticed out of proportion to the puretone threshold loss, impairs auditory perception could be dependent on temporal cues of the auditory signals and can be slowly progressive.

Audiological Evaluation and Differential Diagnosis

The following studies explain the audiological evaluation done in case of auditory neuropathy patients.

Doyle et al. (1998) studied a group of Paediatric patients out of which 8 children identified to have hearing loss and absent or severely abnormal auditory brainstem response, with normal cochlear functions as measured by OAEs.

Method

Subjects : Five boys and three girls of (4-15 years) age range from different parts of California, served as subjects. All children were initially diagnosed to have sensori-neural hearing loss though later confirmed with absent or abnormal ABRs and normal OAEs. One of the patient had Friedricks ataxia and another had Stevens-Johnson syndrome. Both had absent deep tendon reflexes on neurological evaluations. No other known neurological or medical abnormalities noted.

Audio logical Testing

Puretone audiometry was done for the frequencies 250, 500, IK, 2K, 4K and 8K for all children. Masked bone-conduction could not be accomplished for three youngest children and speech audiometry was not possible in the four youngest subjects.

Click-evoked OAEs were measured with a range from 80 to 87 dB SPL. The presence of normal click evoked OAE was determined by response signal-to-noise ratio of atleast 4 dB and wave reproducibly in atleast 3 octave bands of more than 75%.

ABR recorded (in to two electrode configurations in a vertical channel, vertex to seventh cervical vertebra to optimise detection of wave V). Rarefaction click stimuli were presented monaurally at rates from 5 to 25 and at 65, 75, 85 and in most cases at 95 dB nHL. The average were made at each test level and reproduciable components of the ABR was evaluated.

Results

Puretone audiometry revealed seven ears to have an up sloping hearing loss, four had high frequency loss, three had flat configuration and two had profound loss. Severity ranged from mild to profound. Three had poor to fair word discrimination. One had high speech discrimination (SD) scores and the rest were too young to be tested.

All children had normal OAEs and abnormal or absent ABRs except for one child who showed profound SN loss with absent OAEs in one ear.

Kaga et al. (1996) found two patients who showed absence of auditory brainstem response but broad compound action potentials on electrocochleaograms and almost OAE, together with absence of caloric response and preservation of per rotatory nystagmus for both ears.

The patient 1 was a 53 year old woman who had noted auditory and vestibular problems since the age of 15 years. Patient was a 68 year old woman who had noted problems of the same type since the age of 30 years. They could hear and understand sentences if spoken slowly, but could not disseminate monosyllables very well. The auditory examination disclosed mild threshold elevation in puretone audiometry and markedly poor scores in speech audiometry and good scores in auditory comprehension test. They were diagnosed to have auditory nerve discourse of unknown cause.

Auditory Function Tests

Patient 1

Puretone audiogram revealed bilateral symmetric threshold curves with moderate threshold elevation at low frequency and mild threshold elevation at middle and high frequencies. The maximum discrimination score in speech audiometry was 45% for the left ear and 35%. for the right ear.

Click evoked ABRs of each ear at 100 dB HL were absent.

Click evoked EcochG showed large negative summating potentials and small compound action potentials.

In this patient TEOAE and DPOAE were normal around 1 KHz but DPOAEs were slightly reduced around 2 and 4 KHz in the left ear and OAEs were almost normal around 1 and 2 KHz but slightly reduced around 4 KHz in the right ear.

Patient 2

Puretone audiometry revealed bilateral symmetric threshold curves with moderate threshold elevation at low frequency and moderate threshold elevation at middle and high frequencies Maximum discrimination score in speech audiometry was only 25% for the left ear and 20% for the right ear.

ABRs of each ear at 100 dB HL were absent. EcochG revealed a broad summating potential at 100 dB HL, 90 dB HL, 85 dB HL and 80 dB HL. The threshold of EcochG was 80 dB for both the right and left ears.

TEOAEs and DPOAEs were almost normal below 2 KHz but reduced around 4 KHz in both ears.

Differences of puretone audiometry and speech audiometry in patients 1 and 2 suggested retrocochlear problems, since the

maximum discrimination scores were remarkably low despite the mild elevation of the puretone audiogram. The stapedial reflex in the two cases were off the scale.

Vestibular Function Tests

In both patients response to 20 cc ice water irrigated caloric test was absent for both ears. The electric nystagmalographic (ENG) recording in patients 1 and 2 obtained during the damped rotation test to the right and left direction on the horizontal place were performed to examine vestibular function (Kaga et al. 1981). Right and left rotation tests elicited prominent per rotatory nystagmus but no post rotatory nystagmus. The computerized balance board test demonstrated severe ataxia in the Romberg position with eyes closed in patient 1 and with eyes open and closed in patient 2.

MRI and CT Scan

In patients 1 and 2, neither brain magnetic resonance imaging (MRI) nor computerized Tomography (CT) could reveal any abnormalities of the inner ear, the eighth cranial nerve as the cerebellopontine angle or brainstem on the image.

Results of the series of tests suggest that in both the patients lesions could exist at the auditory nerve but with slight involvement of cochlear or vestibular organs and brainstem. With the uses of OAEs the functioning of outer hair cells in the mid and high frequency regions can be confirmed. The authors conclude that the given two

patients have shown the above audiological symptoms due to a proposed "auditory nerve disease".

A study done by Berlin et al. (1998) revealed that the identification of auditory neuropathy in infants was possible by reversing click polarity. The objective of the study was to identify patients with primary auditory neuropathy whose cochlear potentials to a 100 microseconds click persist after the click cessation, stimulating synchronous auditory brainstem responses.

The design of the study was to obtain ABRs to condensation and rarefaction clicks as well as maximum length sequence ABRs and a transtympanic electrocochleogram (EcochG). This was collected from five infants with absent middle ear reflexes and normal or near normal otoacoustic emissions. These infants failed ALGO screens, which used alternating polarity clicks, and/or failed full ABRs done elsewhere with alternating polarity clicks.

The results showed that when ABRs were collected to respond to a single polarity pulse, they revealed robust reproducible waveforms over 4 to 6 msec, that initially were mistaken for a normal ABR by the referring agents. However when condensation and rarefaction click data were compared, the waveforms changed polarity when the stimulus got inverted. Furthemore, the waves failed to shift in latency as the intensity of the elimination was reduced. Transtympanic electrocochleography (EcochG) on one of the children revealed the same polarity reversal and fixed latency functions, confirming that they were cochlear rather than the neural responses.

Berlin et al. (1998) They concluded by saying, comparison of responses with positive versus negative polarity clicks may help separate ABRs from cochlear potentials and alert clinicians to the possibility of an auditory neuropathy. Therefore, absent or abnormal ABRs in the presence of the normal otoacoustic emissions need not always implicate a purely central "disorder", but might be consistent with dysfunction between outer hair cells and primary afferent fibers.

Starr et al. (1996) conducted a study on ten patients who presented as children or young adults with hearing impairments that by behavioral and physiological testing were compatible with a disorder of the auditory portion of the VIII cranial nerve. Evidence of normal cochlear outer hair cell were provided by the preservation of OAE and cochlear microphonics in all the patients. ABR showed evidence of abnormal auditory pathway function beginning with the VIIIth nerve.

Methods

Audiometric Tests

Patients were tested with standard clinical procedures. Puretone audiometry (250 - 8 KHz) was performed by air and bone conducted signals. Speech intelligibility assessment was made in 8 patients (The remaining two had to be exempted from the test as one was with retardation of speech and language and the other spoke Vietnamese for which word list was not available).

Tyrnpanometry along with acoustic reflex thresholds for puretone stimuli from 500 to 4000 Hz were made. Reflexes ipsilateral/

contralateral to the stimulated ear were considered absent when there was no response to test intensities upto and including 110 dB hearing level.

Psychoacoustic Evaluations

Extensive testing was performed in two patients. Discrimination limens for frequency, intensity, duration and gap detection were obtained by having the patient choose which of the three stimuli was different from the other two.

The standard stimulus was (the one presented twice) a 60 dB HL, 1000 Hz tone lasting 750 ms. The changes in frequency, intensity and duration were all positive. The gap occurred in the centre of the tone with full rise times of 5 ms. The difference between the target and the stimulus was automatically adjusted on the basis of patient's response until a discrimination threshold was consistently bracketed. Masking level difference was also found in these patients.

Auditory Physiological Tests

Otoacoustic Emissions : Click evoked OAEs were measured with a click range of 80 to 86 dB peak sound pressure. Responses to as many as 260 stimuli were averaged over a 20 ms. window and stored in two separate buffers. The presence of normal transient evoked otoacoustic emissions in the 2.5 -20ms. post stimulus period was determined by response amplitude at least 4 dB and waveform reproducibility in at least three octave bands of >75%.

The presence of contralateral noise induced reflex suppression of the transient evoked emissions was tested by presenting a white noise at 5 dB above the level of click as monitored by a probe microphone. Three trials each with and without contralateral noise were interleaved and amplitude changes and time delays analysed for transient evoked otoacoustic emission suppression as **a** function of post stimulus time. The presence of normal contralateral suppression was defined by a reduction of the transient evoked otoacoustic emission of > 1 dB.

Evoked Potentials

Auditory brainstem evoked potentials were recorded in two electrode configurations in a vertical channel (vertex to 7th cervical vertebra to optimize detection of wave V and vertex to the ipsilateral ears) using band pass between 30 and 100-3 kHz. Click stimuli were rarefaction clicks presented monoaurally at rates from 5-25 S and at intensities of 65, 75 and when necessary at 85 dB normal hearing level (nHL). Two averages were made at each signal and the presence of reproducible components defined. MLR, LLR, pattern reversal visual and median and posterior tibial nerve somatosensory evoked potentials were recorded in some patients using standard clinical protocols.

Peripheral Nerve Tests

Nerve conduction studies were performed on sural and peroneal nerve in eight out of 11 patients. Abnormality was defined

according to established criteria (Kimura, 1989). Usage of clinical measures of peripheral nerve function (absence of deep tendon reflexes at the ankles, diminished vibratory sensibility in the feet to a 128 Hz tuning fork) served as indices of peripheral neuropathy.

RESULTS

Out of 10 patients pure tone audiometry revealed five patients to have a low frequency loss, three patients to have a flat frequency loss and two to have high frequency loss. Word recognition scores were found to be impaired bilaterally out of proportion to what was expected, if the loss were of cochlear origin in four (Yellin et al. 1989). Among five patients who did not have this finding too had an impairment greater than would have been expected in only one of the ears. One had word intelligibility scores beyond the conservative *2%* cut off point used by Yellin et al. (1989); one had as severe hearing loss (puretone average threshold loss of 90 dB) with a predicted and actual intelligibility score of 0%.

All of these patients (except the young child) reported that speech comprehension was a major problem.

Masking levels differences were absent in the six patients tested. In two patients the absence of the masking level difference was of uncertain significance because of the severely or the asymmetry of the puretone hearing loss (Schoreny and Tabott, 1994). In the other four, there was failure to demonstrate any improvement of monaural masked thresholds for low frequency tones by the addition

of correlated contralateral noise that distinguished them from patients with cochlear or conductive loss.

All patients had absence of absolute reflexes, middle ear muscle contractions and an absence of noise induced contralateral suppressions of OAEs.

Auditory brainstem potentials were bilaterally absent in 9 out of 10 patients. There were a number of patients with cochlear microphonic components reversed polarity with reversal of the which phases from condensation to rarefaction.

MANAGEMENT OF AUDITORY NEUROPATHY

Auditory neuropathy being a recently described clinical entity, is characterized by sensorineural hearing loss in which the auditory evoked potential is absent but otoacoustic emissions are present. Typically word recognition is reduced out of proportion to the puretone thresholds. The audiometric patterns documented on puretone testing includes low frequency, flat, high frequency and fluctuating configuration.

The precise pathological correlate to electrophysiological pattern is yet to be defined. This confounds the therapeutic challenges in the management of these patients.

The impairment in speech understanding causes failure in the development of spoken language in case of patients with pre-lingual onset. In spite of the hearing loss being mild, the patients fail to develop spoken language. In such situations an alternative input method can be of most help.

Hood (1998) has recommended the cues of a visual communication systems such as cued speech or signed English. The choice of the method can be made using local resources. The goal is to expose children to conversation as it normally occurs in the home and daily activities by allowing them to 'eavesdrop' on all conversations among family members.

In patients who have already developed spoken language the goal is to maximize the available auditory information and provide

supplementary cues to speech reading. Since some can understand some speech in quiet surroundings but experience difficulty in background noise, enhancing signal-to-noise ratio may be helpful. Training to improve speech reading skills may also be helpful.

Until the underlying etiologies of auditory neuropathy are better understood the appropriateness of using hearing aids and cochlear implant is difficult to determine. Adults report that hearing aids are of little or no benefit. Some patients find FM systems helpful in situations where enhanced signal-to-noise ratio allow use of residual speech and understanding.

It is pointed out that hearing aids are contra indicated in the face of intact outer hair cell function, because of the risk of noise induced damage to the outer hair cells. However ancedotally, hearing aids are tried to a limited extent in some children with auditory neuropathy. This is done mainly to enhance the awareness of sound. A high quality, low gain wide dynamic range compression hearing aids are usually recommended. This approach is intended to minimize any deleterious effect of amplification on otoacoustic emission until the importance of maintaining OAE - in these patients is better understood. Use of more powerful hearing aids for limited periods in one ear only is being tried by some, where trial with stronger amplification is desired. If hearing aids are tried, frequent monitoring of otoacoustic emissions for either temporary or permanent effects on OAEs should be a part of the management program.

Speech reading classes are strongly recommended for adults with auditory neuropathy, initially sign language and intensive speech

and language therapy provide the base line of habilitation for children with the disorder.

The potential benefit for cochlear implants are considered for auditory neuropathy patients, but it is unknown whether electrical stimulation will 'resynchronize' neural activity.

If the underlying etiology of the auditory neuropathy in a particular patient is cochlear in origin (i.e. the like inner hair cells and/or the hair cell nerve juncture) and neural function is intact, then a cochlear implant may be potentially beneficial. In cases where the underlying etiology invovles neural function, then the anticipated results with a cochlear implant may be less predictable, based on current experience.

A study done by Miyamoto et al. (1998) provide detailed accounting of the clinical course of a child with Friedrick's ataxia who received a Nucleus 22 channel cochlear implant.

The results observed in this child with auditory neuropathy who received a cochlear implant are presented and compared with those of a matched group of children who were recipients of implants.

A single subject, repeated-measures design, evaluating closed-set and open set word recognition abilities was used to assess the subject and a control group of matched children with implants who had also experienced a progressive sensorineural hearing loss.

The subject demonstrated improvements in vowel recognition (82% correct) by one year after implantation, which were only slightly lower than the control group. Consonant recognition and open set word recognition scores were significantly lower.

Caution should be exercised when considering cochlear implantation in children with auditory neuropathy.

SYNDROMES

The majority of patients are identified to have either overt or enable neuropathies outside the auditory system. Some report symptoms of other non-auditory peripheral neuropathies, while neurologic dysfunction in other patients is revealed only upon clinical neurologic examination. Some appears to have only an auditory abnormality. Among the neurologic abnormalities identified in patients with auditory neuropathy are hereditary motor sensory neuropathy. Sensory neuropathy (HMSN, Charcot Marie Tooth Syndrome) Friedreich's ataxia, gait ataxia, loss of deep tendon reflexes and motor system disturbances. Most patients who are old enough to provide subjective reports complain first of hearing difficulty.

Hereditary sensory neuropathies are a group of disorders characterized by progressive loss of one or several modalities of sensation, depending upon the type of neurons or sensory receptors primarily involved in the gradual process of degeneration.

The most frequently encountered are HMSNI and HMSN II. Most patients with HMSN in whom hearing loss has been reported have features indicating more widespread involvement of the nervous system, particularly optic atrophy. It is found from brainstem evoked potential studies that the auditory pathways are sometimes involved though the proportion of such patients uncertain. It is suggested that the hearing loss in HMSNI and HMSNN II is due to an affection of VIII nerve fiber comprising demyelination or loss of ganglion cells analogous to abnormalities found in spinal nerves.

Autosomal dominant HMSN (Charcot-Marrie Tooth (CMT) disease or cases of personal muscular atrophy) shows typical neuropathological findings of demyelination of onion bulb formation. CMT is heterogeneous with loci described on chromosome 17 (CMT 1 A), chromosome 1 (CMT IB) and an unknown possible third locus (CMT 1C). Classically exhibits degenerations of peripheral nerves and roots, resulting in detail muscle atrophy that begins in the feet and legs and spreads on to the hands later. Atrophy of anterior tibial calf muscles (Stork legs) and wasting of lower thigh muscles are usually observed. Deep tendon reflexes are usually diminished or absent. The disease may become progressive and severe or may spontaneously arrest at any time.

Features of hereditary cerebellar ataxias, optic atrophy and other cranial nerves involvement may occur in combination with the previously mentioned classic description. Specific sensory dysfunction in reference to Charcot Marrie Tooth disease has been reported for both visual and auditory modes. Tackman and Rad (1980) have shown abnormal visual evoked responses in patients with CMT disease. Rosenberg and Chutorian (1967) have reported both visual and auditory disturbances in family members with CMT disease. Cruse et al. (1977) reported deafness as one of the main features of the patients who were examined in their study of CMT disease.

HMSN type I is well characterized by dominant autosomal inheritance a slowing of nerve conduction and histological findings of nerve hypertrophy with segmental demyelination. Dyck et al. (1973) says that segmental demyelination is caused by a primary

axonal derangement. Lewis and Sumner (1982) howeyer observed a uniform slowing of conduction along different segments of the peripheral nerves of patients with HMSN I suggesting a primary myelinic pathogenesis.

CMT neuropathy is the commonest group of genetic disorders of the peripheral nerve. There are two subgroups of CMT according to nerve conduction velocity HMSN type I has slow motor nerve conduction velocities and are more common compared to HMSN II, an axonal disorder with relatively normal conduction velocities.

Molecular genetic techniques have chosen that CMT type I is heterogenous and include disorders due to abnormalities in schwann cell myelin proteins. The most common variety of CMI type 1 is CMTIA. The next most common form of CMIA. The next most common form of CMT type I after CMTIA, has a locus on the X-chromosome (X-linked CMT, CMTX) and has recently been shown to be caused by mutations in the gap junction gene connexin 32.

Friedrich's ataxia classified as one of the cerebellar degenerations manifests hearing dysfunction if the spiral ganglion may gets affected.

In general, neuropathies show a distoproximal gradient in conduction velocities due to a primary axonal defect. Hence its to be expected that primary axonal neuropathies would affect conduction velocity much more in long than in short nerves. Whereas any

conduction impairments due to primary myelin involvement should affect short and long nerves similarly.

Scaioli et al. (1992) evaluated conduction along the proximal and distal segments of motor and sensory long limb nerves, as well as along the very short acoustic nerve. F response and somatosensory and brainstem auditory evoked potential were studied in a series of patients with hereditary motor and sensory neuropathy (HMSN) types I and II. A diffuse and comparable slowing of conduction in proximal and distal nerve segments, as well as along the acoustic nerve, favours a primary myelin defect in HMSN I. F response and motor conduction velocity showed a similar derangement in both proximal and distal motor segments. Latencies of somatosensory evoked potentials were symmetrically prolonged and correlated with motor nerve impairment. Central conduction times were normal. Studies of brainstem auditory evoked potentials showed a high incidence of acoustic nerve involvement. The most evident abnormality was a statistically significant increase in the latency of the wave I. The data hence support the presence of a primary myelinopathic damage.

The prolongation of conduction in the auditory pathway studied and abnormal evoked potentials were obtained in a study done by Satyamurthy et al. (1979). A kinship with a dominantly transmitted motor sensory neuropathy was studied. Two brothers on whom brainstem auditory evoked potentials and behavioral audiometric tests were run. They had abnormal prolongations of I-III interpeak intervals. Wave V was poorly developed. Conventional

audiometric tests did not reveal a peripheral hearing loss. These changes could be due to the probable pathophysiological process or in the auditory nerves and spiral ganglia analogous to the changes in their peripheral nerves. Evidence suggests that wave I reflects activity at the eighth nerve. Waves II and III result from activities predominantly at the cochlear nucleus and superior olivary complex respectively. While activities in lateral leminiscus and inferior colliculus contribute largely to the generation of waves I and II, anatomical and physiological integrity of the more caudal structures in essential for full development of these later waves. Thus the I-III interwave interval represents conduction times in the eighth nerve and the pontomedullary portions of the auditory pathways. In the mentioned boys waves IV and V were not well developed. Temporal dispersion of incoming impulses from caudal areas could account for such an alternation of waves IV and V

A study done on parallel lines with Scaioli et al., (1992), Nicholseon et al. (1993) observed slowing of central conduction in X-linked CMT neuropathy shown by brainstem auditory evoked responses.

CMT 1A manifests slow nerve conduction velocities. It is caused by a submicroscopic duplication of a region of DNA on chromosome 17 including the PMP 22 gene. This gene is expressed in peripheral nerve but not in the CNS. X-linked CMTX is caused by mutations in the connexin 32 genes in the X chromosome. Connexin 32 is expressed both in brain and peripheral nerve. However, these molecular variants are difficult to be clinically distinguished.

Brainstem auditory evoked responses (BAERs) were measured in patients with CMTX and CMT1A.

ABRs showed central conduction slowing in patients with CMTX which did not overlap the normal range. Patients with CMT1A had a delay in wave I latency but otherwise normal responses. These results are consistent with the pattern of expression of PMP 22 in the peripheral portion of the eighth nerve (myelinated by Schwann cells) and of connexin 32 in the central portion in the brainstem auditory pathways (myelinated by oligodendrocytes).

Conclusion

It can be concluded that ABRs are useful to distinguish CMTX from CMT1A in terms of conduction.

Another study in 1996 done by Qattrane et al. through clinical, electrophysiolgic and genetic aspects of a large family found autosomal recessive hereditary motor and sensory neuropathy associated with focally folded myelin sheaths.

Ten patients from a large family with early onset of motor and sensory neuropathy served as subjects. Six of them were still living at the time of the study. In all cases, early motor milestones had been achieved. Mean age at onset of symptoms was 34 months; these included progressive distal and proximal muscle weakness of lower limbs. Slight facial weakness was present in four patients; and one had bilateral facial synkinesia. Intellectual function was

normal in all cases. There was no evidence of thickned peripheral nerves. All three adult patients (mean age 27 years) were seriously handicapped and wheel chair bound. Death occurred in the fourth to fifth decade of life and duration of illness varied from 27 to 30 years. Motor nerve conduction velocities ranged from 15 to 17 msec, in the upper limbs of youngest patients and were undetectable in adult patients. Sensitive action potentials were almost always absent. In all patients, auditory evoked potentials show abnormality consisting of irregular redundant loops and folding of the myelin sheath.

In a study done by Raglan et al. (1987) fourteen patients with HMSN, 12 of type I and 2 of type II were assessed for auditory dysfunction.

Routine audiometry

Puretone audiometry, loudness discomfort level, tone decay, speech audiometry and masked speech audiometry were performed (puretone audiograms were considered abnormal if the hearing loss exceeded 20 dB). Acoustic reflex and the reflex decay were measured. Reflex decay test was classified as abnormal, when the amplitude of its trace declined to less than half of the initial amplitude in less than 6 sec.

Speech audiometry

A. Unmasked speech - Speech was presented using Peters AP5 audiometer from a cassette player. The speech material consisted

of 10 monosyllabic words which were scored by phonemes. These were shown as the percentage of the maximum possible score.

B. Masked speech audiometry

The masking noise was the internal speech masking of the instrument. The lowest level at which optimum score was obtained in test-A was the speech level for test B. The masking level was relative to this. There were 8 normal control subjects with optimum speech discrimination scores of 90 to 100%. The masked speech discrimination scores at the presentation level of 40 dB S/N ratio were 70 to 100%.

Brainstem auditory evoked potentials and electgrocochleography

BAEP recordings were monaurally and binaurally done with a 100 ms. click of various intensities upto 103 dB at a rate of 10/sec. Signal emerging in the band 3.2 Hz to 3.2 kHz was carried out using a minicomputer with an analysis window of 10 ms duration compressing 1024 sampling points. The test was repeated to check on response reliability.

For EcochG the active electrode was a fine needle placed through the tympanic membrane onto the promontory. The ipsilateral mastoid acted as reference. The same recording procedure as BAEP was done with only 128 sweeps averaged.

The results of the study showed puretone audiogram to be a abnormal in six out of fourteen patients.

Thirteen patients underwent speech audiometry, where one showed scores which were worse than the expected (from the puretone audiogram). In 4 others with abnormal puretone audiogram, speech discrimination was as expected. All others with normal puretone audiogram had a normal speech audiogram.

Masked audiometry was done on twelve patients. It was abnormal in four patients with abnormal puretone audiograms. In addition one patient with normal puretone audiometry had abnormal masked speech bilaterally and two other related patients with normal, puretone audiograms had abnormal masked speech bilaterally and two other patients with normal puretone audiograms and loudness function had abnormal masked speech audiometry from one ear.

Loudness function

Tone decay and DDL were normal in all patients with normal audiograms. Of the patients who complained of hearing loss 2 had marked tone decay at two frequencies, and the remainder had type I or type II tone decay. Only one had equivocal LDL and this patient had the most severe tone decay. The remainder had full recruitment, including one patient with type IV tone decay at 2 and **4** kHz.

Stapedial Reflex

Thirteen patients underwent this test. All with normal puretone audiogram had a normal stapedial reflex thresholds without decay and normal middle ear pressures. The stapedial reflex was studied only in 5 of the 7 patients with definitely abnormal audiograms.

Threshold was elevated in 4 of these including the two with the most masked tone decay. There was an abnormal decay of the stapedial reflex in these two patients but this were confined to one ear in both cases and 500 Hz in one.

Brainstem auditory evoked potentials (BAEP)

BAEP were recorded in 4 of the 5 symptomatic patients and in 3 the response was about or inconsistent as to render identification of possible component. In the other patient with symptomatic hearing loss components could be identified. The interval between components I and III was at the upper limit of the normal range, bilaterally. The responses were also absent in one patient with an abnormal puretone audiogram who did not complain of hearing loss. All patients with normal hearing had normal latencies of the various component of the BAEP.

Electrocochleography was performed in one patient who had a hearing loss and it was abnormal. The threshold of the action potential was at least 60 dB greater than the puretone threshold at 4 KHz. The action potential increased in amplitude with no alteration of latency as the stimulus increased from threshold to 120 dB. The BAEP were absent in this patient.

A case study was done on a 54 year old CMT syndrome patient by Musiek et al. in 1982. They noted the following audiological findings.

Puretone air conduction thresholds showed mild hearing loss bilaterally. Bone conduction test results indicated sensorineural loss bilaterally. Spondee thresholds were borderline normal and agreed with Fletcher average bilaterally. Speech discrimination ability accomplished by using the Northwestern University Auditory Test No.6 at 30 dB SL in reference to spondee threshold was excellent in the right ear and good in the left ear.

At 5 dB SL speech discrimination scores decreased severely yielding a roll over index on performance intensity PI-PB function. Tone decay test showed adaptation.

ABR waves showed extremely poor wave morphology and abnormal absolute latency.

Central auditory assessments were done using various tests.

Masking Level Difference (MLD)

Based on a large sample of normal hearing persons, the range for MLD test is 8 to 14 dB. The MLD for this patient was 5 dB.

Rapidly Alternating Speech Perception (RASP)

The normal performance show 90% or better scores. The patient's performance showed 50% which is below the normal level.

Binaural Fusion

The nonnal performance is 90% or better. Patient had notable difficulty with the task since the score of 65% was well below normal levels.

Staggered Spondaic Word Test (SSW)

The normal performance is 90% or better. The results in competing condition showed a severe deficit in the left ear (33%) while that of the right ear was (80%) that is slightly below normal.

Dichotic Digit

Normal performance is 90% or better and the results indicated a bilateral deficit.

Competing Sentences

Normal performance, 90% or better. The subject had moderate left ear deficit (60%) while score for right ear was within the normal range (90%).

Frequency Patterns

Normal performance, 80% or better scores obtained were severely reduced bilaterally.

Low-pass filtered speech (LPFS)

Normal performance, 70% or better. The patient was unable to understand any of the words presented. Of all the tests this was the most difficult Qne for the patient.

In interpreting results from various tests available, a particular auditory area cannot be isolated exclusively but rather trends that seem to emerge from the entire auditory picture must be considered.

The roll over noticed in the patient is consistent with auditory nerve lesions, brainstem lesion or both. Similarly lack of appropriate response on ABR and the excessive acoustic reflex decay could denote auditory nerve dysfunction, brain dysfunction or both. Acoustic reflex thresholds were absent at 4K and 2K. But at middle and lower frequencies they were present at a normal or reduced SL. The former finding is consistent with retrocochlear lesion and the better is considered with cochlear involvement.

MLD, RASP and binaural fusion are often considered tests of brainstem function and deficits were noted on all of these in this patient. It has been shown that peripheral and with the exception of MLDs, cortical lesions can also affect performance on these tests.

The LPFS test competing sentences the SS W test, dichotic digits and frequency patterns essentially test cortical function. This patient performed below normal or these especially for the left ear.

Some of these tests are known to be affected by peripheral and brainstem lesions and hence a clear out analysis is difficult.

Interpretation of these findings would suggest a conclusion of cochlear, eighth nerve, brainstem and cortical manifestations. However, the overall results suggest the major auditory deficit to be central.

Garg et al. (1982) did a study on three patients with hereditory motor sensory neuropathy (HMSN) Type I. They studied brainstem auditory evoked responses and observed prolongation of latency of all maj or components. Interpeak latency I-III was prolonged but the III-V interval was normal and the separation of waves I and II accounted for the prolonged I-III interval.

Wright et al. (1995) noticed sensorineural deafness and early onset dementia in a kindred with autosomal dominantly inherited sensory neuropathy. This kindred provided evidence of clinical variability among kindreds with hereditary sensory neuropathy, suggesting genetic heterogeneity. Hereditary SN. SNHL and a dementing process are linked in an autosomal dominantly inherited disorder.

The findings of study done in 1980 by Satyamurthy et al. in four Friedrich's ataxics showed auditory dysfunction. The puretone audiograms showed some degree of sensitivity loss. Air conduction approximated bone conduction thresholds, including normal hearing or sensorineural hearing loss. No air bone gap was noticed in any patients.

Three out of four patients tested, showed good agreement with puretone averages.

In three of the four patients roll over was observed.

Synthetic Sentence Identification with - Ipsilateral Competing Message (SSI-ICM) modality revealed a performance deficit in all patients. In one, however, peripheral hearing loss may have contributed to this finding. In all the three tested, SSI-CCM Synthetic Sentence Identification with - Contralateral Competing Message (SSM-CCM) was normal.

All four had normal tympanogram acoustic reflex abnormalities indicative of retrocochlear dysfunction were present. Two patients had reflex decay at 0.5 and 1 kHz bilaterally.

ABR waveforms could not be clearly obtained in any of the patients.

The results of the study is in congruence with the literature. Friedrich's ataxias have been noticed with deficits in hearing sensitivity. Roll over is usually an indication of retrocochlear pathology though may be associated with cochlear pathology rarely.

The greater performance of ICM task than CCM is characteristics of brainstem dysfunction.

Abnormaliteis in ABR could be associated with egeneration of dorsal root ganglion cells and axonal processes which accounts for

the total absence or diminshed amplitude of sensory nerve action potentials in Friedrich's atoxia. Similar process is thought to occur in the spiral ganglia, homologue of dorsal root ganglion, affecting the auditory nerve and its central connections. This could account for the abnormalities in ABR.

Clinically manifested and symptomatic deafness may occur in spino cerebellar degenerations, especially in Friedrich's ataxia as one component among the spectrum of difficulties. Neuronal degeneration in spiral ganglia and loss of haircells in cochlea are reported in the literature. Studies have shown that Friedrich's ataxia show degenerative changes in the auditory pathways of the brainstem. Spoendlin (1974) found selective and extensive damage to neurons and the spiral ganglia, whereas the organ of corti was essentially intact and the outer spiral fibers destined for the outer hair cells of the organ of corti, being presumed.

Deltenre et al. (1996) reported of three children without auditory evoked potential (BAEP) neural component, although they exhibited a prominent early fast oscillation identified as an isolated microphonic potential. All these three children went through major neonatal health problems and the results of physiological testing indicated a pattern of auditory neuropathy in the few months of their lives. All the patients retained isolated cochlear microphonic potentials as well as click evoked otoacoustic emissions. Two of them demonstrated only moderately impaired audiometric thresholds.

MISCELLANEOUS

Animal Model of Auditory Neuropathy

Harrison (1998) reported an animal model of auditory neuropathy where Chinchillas with extensive but not total (i.e. Scattered) IHC degeneration showed normal OAEs (and CMs) while ABR thresholds were severely elevated. Single unit recording from auditory mid-brain (inferior colliculus CIC) show near normal response thresholds. Other aspects of this model fit with the human condition.

The scattered IHC loss was caused by carboplatin ototoxicity. This does not however reflect a naturally arising condition, but there is evidence that scattered IHC loss also can arise from a mild sustained cochlear hypoxia. This could constitute an etiology of the disorder in many humans.

Adult Chinchillas (500 to 700g) free from ear disease were used in this study. Animals were treated with 500mg/m of carboplatin injected into the internal jugular vein.

It was observed that treatment of Chinchillas with carboplatin produces cochleas with good survival of outer hair cells but with severe inner hair cell degeneration. In general, IHC degeneration tends to be scattered throughout the length of the cochlea but is most severe toward the cochlear base.

Electrophysiological and OAE Recordings

The survival of outer hair cells in carboplatin treated subjects accounts for the preservation of good OAEs. ABR thresholds are elevated across all frequencies tested by 40 to 70 dB. Although behavior audiograms were not checked in the animal model, it is assumed that central auditory neurons can have thresholds that differ significantly from those of the ABR.

Carboplatin caused scattered inner hair cell generation with little or no OHC loss. This explains ABRs having considerably elevated thresholds while functional indication of outer hair cell activity, including OAE and CM recordings appeared normal. These features specifically define auditory neuropathy.

It cannot of course be suggested that in human subjects auditory neuropathy results exclusively from carboplatin drug treatment. But one natural mechanism for producing inner hair cell damage is long term cochlear hypoxia. It has been observed that after about a three hours mild hypoxia, inner hair cells form swelling and other damage in cochlear regions where outer hair cells appear normal. It is well established that after inner hair cell degeneration, there is associated spiral ganglion cell loss. More central neurons will also show some degeneration. Thus although the entity of auditory neuropathy might originate with a cochlear lesion, consequent central effects certainly will develop. The above can be deemed as underlying pathology in cases of auditory neuropathy patients.

Cochlear Implantation in Auditory Neuropathy

Miyamoto et al. (1999) worked on J.G. 4 year old boy who experienced progressive hearing loss and imbalance. He was also experiencing progressive visual loss. Initial audiogram of the patient demonstrated a mild hearing loss in the right ear and a moderate loss in the left ear. Word recognition scores (PBK word list) showed 92% on the right and only 12% on the left. ABR demonstrated no response at 95 dB HL for click stimuli.

Eleven months later word recognition dropped to 56% on the right and 0% on the left. A loaner hearing aid when fitted showed 50 dB functional gain. The patient initially seemed to respond better with the hearing aid in the right ear, but by one month of hearing aid use it was apparent that minimal, if any enhancement had occurred.

During the ensuring two years, the patient experienced periodic fluctuations in hearing and by twenty two months a moderate bilateral flat sensorineural hearing loss was present with word recognition scores of 12% on the right and 4% on the left. A course of Prednisolone therapy results in a 15 dB improvement in the right ear for 500 and 1000 Hz. The left ear remained uncharged. Word recognitions scores were 20% on both right and left. An FM system was recommended and fit. A further neurologic evaluation at this time led to the diagnosis of Friedriech's ataxia and in 6 3/4 years had reached profound levels (90 dB on the right and 95 dB on the left) word recognition scores were 8% on the right and 0% on the left.It was necessary to use finger spelling with speech to communicate with the patient.

Interestingly, transient evoked otoacoustic emissions were present bilaterally. By then progressive visual loss had progressed leaving only one quadrant of his visual field. Ataxia had progressed and needed a wheel chair.

Control Group

Seven children with a progressive, postlingually profound hearing loss who received the Nucleus 22 channel cochlear implant served as the control group. On an average children in the control group became profoundly deaf at 6.2 years (ranges 3.7 -10.3 years) and received their cochlear implant at 7.8 years of age (age range 6.2 -11.9 years). The range of hearing loss was 90 to 112 dB HL with a mean of 103 dB HL. Four children in the control group used oral communication and three used total communication.

Procedure

JGs performance was assessed at the preimplantation interval and then again at six months and 1 year post implantation intervals. Two assessment procedures were used to evaluate JGs performance. The minimal pair test was administered to assess JGs closed set recognition, word recognition abilities. The test fields a score for individual speech features as well as composite scores for vowels and consonant recognition. Openset word recognition was assessed using the PBKs.

At each testing interval, his performance was compared with that of average performance of the control group. Before

implantation JG was tested using his personal FM system and the control subjects were tested while using personal amplification. At both post implantation intervals all subjects were tested using only their nucleus 22 channel cochlear implant.

Results

JGs average warble tone thresholds were similar to those obtained from the control group and within the range normally seen for children with cochlear implants.

Closed set word recognition

Since JG tired easily, closed set word recognition was not administered at pre-implant interval. Preimplantation score for the control group were 74% and 61% respectively. After 6 months of cochlear implant JG correctly identified 72% of the words on the basis of vowel and consonant speech features. The average vowel and consonant recognition scores for the control group at 6 months after implant were 89% and 82% respectively.

At the 1 year post implantation interval the patient showed continued improvement in closed set vowel recognition of the minimal pair test with a score of 82%. This was slightly lower than the vowel score of 92% obtained by the control group. In contrast, his consonant recognition on minimal pair test did not improve from 6 months to 1 year in interval remaining nearly 70% correct. At this interval children in the control group obtained an average consonant recognition score of 93%.

Open set word recognition

Before implantation both JG and the children in the control group demonstrated minimal open set speech perception abilities JG correctly identified 4% of the words and 12% of the phonemes at this interval compared with mean scores of 3% word correct and 13% phonemes correct for the control group.

After 6 months of devices use, children in the control group showed substantial improvement in their openset word recognition abilities. They correctly identified an average of 25% of the words and 54% of the phonemes on the PBK at the testing interval. In contrast JG failed to identify correctly any word or phoneme after 6 month post implantation interval. When JG was retested after one year of cochlear implant use, his open set speech perception performance was similar to that of prior implantation. Children in the control group continued to show improvement in open-set word recognition abilities with increased experience using the cochlear implant. After 1 year of device use they identified 39% of word and 61% of the phonemes on PBK.

Conclusion

The case JG was diagnosed to have Friedrich's ataxia which is one of the spino cerebellar degeneration. Many of the clinical deficits in this case are explained on the basis of neuronal loss with dorsal root ganglion as a major site of neuronal degeneration. Auditory dysfunction could be explained on the basis of involvement of a sensory ganglion (The spiral ganglion).

Notwithstanding, cochlear implantation was recommended in the case as an attempt to ameliorate the devastating effects of progressive deafness.

The benefits of cochlear implantation observed in JG were modest as noted by the comparison with the control group. It is difficult to know whether the progressive nature of the patient's disease contributes to the limited speech perception benefits he has obtained with cochlear implant.

Transient Deafness Due to Temperature - Sensitive Auditory Neuropathy

Starr et al. (1998) identified three children with a temperature - dependent disorder of auditory nerve function who became transiently deaf when their core body temperature is raised by as little as one degree Celsius. Their hearing sensitivity returned when body temperature becomes normal again. They have no evidence of a generalized neuropathic disorder nor of any systemic illness. An analysis of their clinical course and the results of auditory function tests performed when afebrile and when febrile provide insights into the neurophysiological mechanisms accounting for auditory nerve dysfunction.

Case Reports and Results

Three children, two siblings a girl aged 6, a boy aged 2 and an unrelated girl aged 15 become transiently deaf when afebrile within

an hour which is have after treatment with antipyretic agents the children regained their ability to responds to sounds and to speak. The children's speech and auditory behaviour otherwise have been entirely normal except that the two of the children have difficulty in understanding speech in noisy environments. The two related children have two older siblings who do not have hearing or communication problems when either febrile or afebrile. Subject 3 has siblings with normal hearing who are unaffected by fever.

Subject 1

The affected girl was born normally after a normal gestation. The developmental highlights were normal for motor and social functions. Speech and language functions were slightly delayed though speech language errors were not evident at the time of the study. She had talked late (2 years) and had made articulation errors. She attended regular school and class performances was normal. When she was 3 years 1 month of age, had the first episode of transient deafness in association with an upper respiratory infection and a low grade fever. She was unresponsive to sounds and would not speak. She resumed talking and responding to sounds within a few hours after treatment with acetaminophen. The following day when afebrile, puretone audiometry showed a mild low frequency loss with normal tympanograms and an absence of acoustic middle ear muscle reflexes bilaterally.

Subject 1 underwent series of tests in both febrile and afebrile conditions. There were differences noted in the test results in both conditions in case of pure tone threshold, speech and ABR.

Subject 2

The subject was born of normal pregnancy and delivery. He had developed normally, walked at 1 year of age and has appropriate speech langauge development. He had atleast two episodes of deafness accompanying mild elevation of body temperature before becoming 2 year of age.

This child is a brother of subject 1. The child, underwent a series of tests in afebrile conditions.

1. Audiogram showed a mild 30 dB, low frequency hearing loss.
2. Speech awareness thresholds were normal.
3. Tympanogram wasnormal.
4. Acoustic middle ear muscle reflexes were absent bilaterally to ipsilateral and contralateral stimulation.
5. ABR showed a delayed III-V complex to 80 dB nHL clicks. There were early deflections that were cochlear microphonics, and waves I-III could not be identified.
6. Cochlear microphonic of large amplitude was present.
7. TEOAEs were of normal amplitude bilaterally. There was no suppression of OAE with contralateral noise stimulation.
8. Long and middle latency responses showed no reproducible components.

Subject 3

This 15 year old girl's first episode of deafness accompanied a high fever after a DPT inoculation when she was four years of age.

She continued to experience an impairment of hearing whenever she was febrile and used to take antipyretic agents immediately when she experienced hearing loss. She had also noted difficulty in understanding speech in moving environments. Her development otherwise had been normal. She was excellent in school and was an athlete She had no symptoms suggestive of other cranial or peripheral neuropathies.

Afebrile Test Results

1. Audiogram showed normal puretone thresholds.
2. Speech perception was normal. Sentence comprehension was below the 10th percentile for her ages in both quiet and noise.
3. Tympanogram was normal.
4. Acoustic middle ear muscle reflexes were absent bilaterally.
5. ABRs to 85 dB nHL clicks showed cochlear microphonics and a delayed IV-V complex.
6. Without waves I-III cochlear microphonic of large amplitude was present.
7. TEOAEs were of normal amplitude bilaterally. There was no suppression of OAEs with contralateral noise stimulations.
8. Long and middle latency auditory evoked potentials were present.

In patients with an auditory nerve disorder the development of deafness with slight elevation of body temperature is most consistent witha demyelinating neuropathy of the auditory nerve. In myelinated mammalian nerves, the ionic processes accounting for generation of action potential are restricted to the nodes of Ranvier, the junction

point between adjacent myelin glial cells (Oligodendroglia for central pathways and schwann cells for peripheral nerves). The nodal membrane is rich in Na+ channels essential for generation of the nerve action potential, whereas paranodal and inter modal membrane site have few Na+ channels but rich K+ channels. Thus the generation of Na+ current contributing to the development of action potential in myelinated nerve is not continuous along the nerve but is restricted to the nodes of Ranvier. The restriction of the action potential to the nodes of Ranvier results in a discontinuity of conduction from node to node known as saltatory conduction and accounts in part for the rapid conduction velocity of myelinated fibres.

Internodal conduction velocity in a segmentally demyelinated axon is slowed and varies with the extent of demyelination. When the nerve impulse passes a demyelinated region and encounters a normally myelinated segment, conduction velocity resumes normal speeds. If the length of the demyelinated zones in these axons differs, conduction speeds of demyelinated axons of comparable size will vary and affect the degrees of synchrony of discharge between the adjacent axons. The dysynchrony of conduction is the deficit in patients with multiple sclerosis when they experience fevers. Its particularly relevant that the oldest child (subject 3) uses the changes in hearing as the first indication of development of a fever and treats herself with antipyretic agents.

It is likely that the children of this report have a demyelinating disorder of the auditory nerve and experience both a conduction block of auditory nerve and deafness when their body

temperature gets elevated. The site of demyelination is not known but could be in the peripheral or schwann cell myelinated portion of auditory nerve distal to the dura matter and/or in its "central portion "proximal to the duramatter where the axons are myelinated by oligodendroglial cells. All other patients with auditory neuropathy need not have aggravation of hearing-impairment with febrile episodes. It may be that the pathology in these patients with auditory neuropathy differed from that present in the ones of this study. Other possible sites of damage in the auditory periphery that could lead to impaired auditory nerve function include the generation of receptor potentials by the IHC, inner hair transmitter release, nerve impulse generation in VIIIth nerve dendrites and VIII nerve ganglion cell function.

The demonstration in these children of an episodic hearing deficit compatible with a demyelinating disorder of auditory nerve in the presence of normal cochlear outer hair cell function emphasizes the importance of establishing criteria to distinguish among varieties of hearing losses, including auditory nerve dysfunction (neural deafness), sensory receptor disorders (sensory deafness) and mixed impairment.

The results from ABRs and OAEs appears to be important for distinguish among the various hearing disorders V1H nerve fibers is one of the mechanisms that may account for the failure to average auditory brainstem potentials in patients with auditory neuropathy (Starr et al. 1991, 1996). Dysynchrony of auditory nerve fiber discharges could also account for the difficulties these patients have

in making perceptual judgements dependent on temporal information contained in auditory signals such as in gap detection masking level differences and lateralization of binaural signal (Starr et al. 1991, 1996).

The maintenance of nerve transmission in the paranodal region of demyelinated axons is temperature dependent. With slight elevations of temperature, the voltage dependent Na+ channels become inactivated more rapidly than at normal temperatures, resulting in a failure of impulse generation and a conduction block can develop (Razminsky, 1973). The appearance of the block in certain demyelinated axons in experimental conditions can occur with temperature elevations of as little as 0.5oC. Its relevant that one of the patients noted as that hearing was affected 'suddenly' as temperature increased. An increase of core body temperature of approximately loC was accompanied by a profound hearing loss. Conduction block accompanying slight exercises of body temperature also has been suggested as accounting by transient reappearance of neurological deficits in patients with multiple sclerosis when they expereince fever.

The authors conclude that auditory neuropathy can be temperature sensitive and audiological findings would vary from febrile to afebrile condition.

Auditory neuropathy, being a newly identified disorder poses challenges in terms of early diagnosis and better management. Otoacoustic emission test has proved to be an important tool in identifying auditory neuropathy.

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