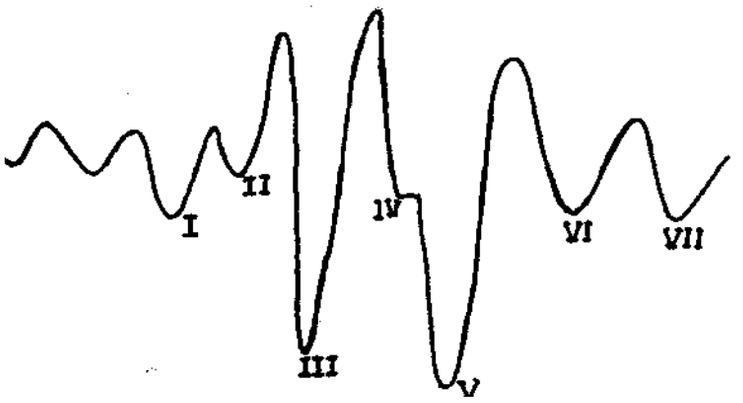
NEUROLOGICAL APPLICATIONS OF BRAIN STEM EVOKED RESPONSE AUDIOMETRY IN ADULTS: A REVIEW



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AN INBEPENDENT PROJECT WORK SUBMITTED IN PART FULFILMENT FOR FIRST YEAR M.Sc.(SPEECH AND HEARING) TO THE UNIVERSITY OF MYSORE.

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

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I DEDICATE THIS TO

MY 'PAPA' WHO ALWAYS LED ME TO BELIEVE WHAT I SHOULD BE . . . . . .

TO MY 'MAMMA' WHO MADE MB REALISE WHAT I AM . . . .

TO MY 'TEACHERS' WHO TAUGHT ME

AND

TO THE 'ONE' WHO GUIDED ME

TO BE WHERE I AM . . . . . .

CERTIFICATE

This is to certify that the Independent Project entitled "Neurological Applications of Brain-Stem evoked response Audiometry in Adults: A Review" is the bonafide work on part fulfilment for the degree of Master of Science (Speech and Hearing) of the student with Register No.8809.

17/5/89

Director
All India Institute of Speech and Hearing, Mysore-6

CERTIFICATE

This is to certify that this Independent Project entitled "Neurological Applications of Brain-Stem Evoked Response Audiometry in Adults: A Review" has been prepared under my supervision and Guidance.

Dr. M.N.Vyasamurthy
GUIDE

ACKNOWLEDGEMENTS

"GURUBHYAM PRANATOSMYAHAM". . . . . .

My "Dandhawath" to the aureole, pinnacle and Zenith of knowledge* my revered "Guru" Dr.M.N.VYASAMURTHY, who with this aura sowed within me the seeds for the quest to know.

Gratitudes to Dr.N.RATHNA, Director, A.I.I.S.H., for permitting me to undertake this project.

I am indebted to Dr.S.NIKAM, Professor and HOD Audiology, AIISH for allowing me to work on this project.

The project required many a help from books, journals, and other periodicals. I hence thank the Library staff for the "treasure hunt"..

"SAATHI HAATH BADHANA". . . . . .

- A friendly pat on the back for my chum Jyothi, who made munching yums and thinking pump when writing was glum.

- When thoughts were helter-skelter and things topsy-turvy, she put it right with a cup of tea... Thanks a million Radhe . . .

Melodies of 'Paean' to Mohan for sounding away the blues with patience and sounding in vigour and zeal.

Mumming was fine when the three musketers suchitra, Alka and Uma rode in, in time.

Beauty lies in the hands that glided smoothly on the alphabet keys. My "VANDANESALU" to Ms. Rajalakshmi R.Gopal

" THANKS HEAVEN "

"GRACIAS", pals, thou gals - Indu, Kiran, Nagpu, Maya, Vidya Laxmi and Yamini for the potpourri of gusto.

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INTRODUCTION

Now we are in the area of evoked potentials. We owe all of this to the pioneering observations of DanGeisler, who was first to demonstrate an auditory evoked potential based on the principle of signal averaging by the computer. He described an average waveform with a positive peak at about 30 msec, the response which we now call the MLR. Bat little farther research on auditory evoked potentials was carried out until Davis and his group at "central Institute for the Deaf" began serious work on what we know call the date or V potentials as a vehicle for "objective audiometry". Then interest in clinical exploitation of auditory evoked potentials began to flower.

"Sohmer and Feinmesser (1967) were the first to report the measurement of eighth nerve action potentials with the use of external electrodes. In 1971 Jewett and Williaton published their paper on what we now tall the auditory brain-stem response (ABR) and the configurations what we use now are the ones that were again first used by Jewett et al and later used by Hecox and Galambos (the configuration mentioned are the Reman numerals as used to identify the various components of the auditory system as seen on Brain-stem evoked response audiometry (BSERA).

According to Stockard at al (1978) "If one could directly record from several different levels of the subcortical auditory

pathways in man, one would seen in first 10msec following an appropriate acouatie stimulus aeries of potentiala corresponding to the successive activation of peripheral, pontomedullary, pontine and mid-brain portions of the pathway. When these acoustic nerve and brain-stem potentials are volume conducted to recording electrodes at the vertex and earlobe, they form a composite series of potentials which are known as the brain-stem auditory evoked responses. Study of the spontaneous activity of the brain has a well established place in clinical medicine and so does brain electrical activity which is brought about by an experimenter or clinician and hence "evoked".

Auditory brain-stem response technique has emerged as vital adjunct to the clinical armamentarium of the Radiologists, Otologists and Neurologists, who jointly determine hearing sensitivity, lesion site and central nervous system integrity, pathology and maturation. ABR can provide information of value from both an audiologic and neurologic standpoint. Although certain laboratories use the technique solely for audiologic purposes and others interested primarily in the neurologic information the response can provide as the 2 cannot be separated. Hearing impairment and neurologic dysfunction may not be mutually exclusive events. As the neurologic status of the patient can influence ABR estimates of hearing impairment and vice-versa.

In order to put the past into proper perspective, several lines of historical evidence must be examined. Andiologie "site of lesion tests were first developed in the late 1950's

in an attempt to localize 'retrocochlear foci". These efforts were spearheaded by people like James Jerger aad the North-western group with the development of their special audiometric test battery. This type of diagnostic audiometry served to focus otologic attention en those diseases beyond the cochlea affecting sensorineural function. Hence the evolution of diagnostic and therapeutic measures use to manage acoustic tumors is a most interesting saga of medical history. Selters was the first to report the used of BSERA to detect acoustic neuromas. Then roughly around the 1970s otologic interest in surgical treatment of acoustic tumors was aroused by the work of William House. He revised, developed and perfected the micro-oto-neurological techniques currently used to successfully remove acoustic tumors.

In early 1970s Arnold Starr along with associates Achor and Hamilton was gathering data on diagnostic applications of the brain stem evoked response audiometry by showing how acoustic tumors* brain stem tumors and higher level disorder* uniquely modified these brain stem potentials.

Evoked potentials measurement have come to play an extremely important role in diagnosis of patients who present with symptoms suggesting possible multiple sclerosis. Robinson and Rudge did the first extensive study of brain stem evoked response audiometry in multiple sclerosis, which was a widely quoted paper and one of the semial studies of the era.

Therefore the recent application of brain stem evoked response audiometry haa been its use in neurologic diseases. Brain stem lesions cause a selective absence or alternation of one or more of the response components; patients with brain stem damage (due to various types of tumors, demyelinating diseases, diminiahed brain-stem circulation and even brain death) show either an absence of certain components or prolonged latency and reduced amplitude of reaponse components This is what is described in the following chapters under separate categories.

To add to the potpourri of the bowl of tests BSERA leads us to the modern era of neuroaudiology.

NEURAL GENERATORS OF THE AUDITORY BRAIN STEM RESPONSE

Introduction:

The usefulness of auditory brainstem responses (ABRs) in asking otoneurological diagnoses depends upon knowing the anatomical origin of the various components of the ABR that can be identified and upon knowing how various pathologies change these potentials. It is generally accepted that the ABR recorded from electrodes placed on the scalp represent the far field of the potentials generated by the fiber tracts and nuclei of the ascending auditory pathway.

Throughout the first decade that ABRs were used to make otoneurological diagnoses the origins of the potentials were determined on the basis of results of animal experiments (Achor and Starr, 1980s, b; Britt and Rossi, 1980; Buchwald and Huang, 1975; Huang and Buchwald, 1977; Rossi and Britt, 1980).

Recent studies in which a comparison has been made between the ABR and the potentials recorded directly from different structures of the ascending auditory pathway in man have provided new insights into the neural generators of the human ABR (Moller and Jannetts, 1981, 1982a, b, 1983b, e, 1984; Moller, Jannetta, Bennett, and Moller, 1981; Moller, Jannetta and Moller, 1981). In other studies abnormalities in the ABR patterns of patients with confirmed lesions in the ascending auditory pathway were examined to gain insight into the origins of the ABR. By correlating the location of the lesion with

ehanges in the ABR, information about the origin of the different components of the ABR was obtained (Sohmer, Feinmesser, and Szabo, 1974; Starr and Achor, 1975; Starr and Hamilton, 1976y stockard and Rossiter, 1977).

Even more difficult to determine than the origins of components of the ABR is the relationship between the type of anatomical changes observed during intracranial surgical procedures and the changes in the ABR. At present this problem is being studied primarily by creating specific lesions in animals and then analyzing the changes which occur in the recorded far-field potentials (Achor and Starr, 1980b). However, in these studies the differences between the auditory nervous systems of animals and man must also be considered.

The interpretation of ABRs is complicated by the complexity of the ascending auditory pathway; the auditory system is more complex than other sensory systems and there are several connections between the left and right sides. The auditory nerve terminates in the cochlear nucleus eomplex, which mainly contains second-order neurons, but also contains neurons of higher order. These fiber tracts connect the hemispheres: nuclei of the most dorsal, the stria of Monakow, mainly terminate in the nucleus of the contralateral-lateral lemniscus sad the inferior colliculus; the other two tracts are the medial stria (stria of Held) and the ventral stria (trapezoidal body). All three striae make connections with the numerous subnuclei of the superior olivary complex. Seme fibers leaving the cochlear nucleus reach the nucleus of the ipsilateral lateral lemniscus. The superior olivary complex contains mainly third-order neurons and serves as the first relay nucleus that receives input from both ears.

From the superior olivary complex connections are made to the inferior colliculus via the lateral lemniseus, mostly by neurons that receive their input from the opposite ear. Fibers leaving the inferior colliculus reach the thalamic auditory relay nucleus (medial geniculate body) via the brachium of the inferior colliculus. The primary auditory cortex receives its input from this nucleus. It is generally assumed that ABRs represent electrical events generated is subcortical structures.

Potentials recorded from the auditory nervous system at a distant to the generators (far-field potentials) are thought to be of two kinds, namely, summations of the neural discharges of many fibers or nerve cells and potentials generated by dendrites. Potentials of the first type are dependent upon the locking of discharges to the time pattern of the stimulus sound, and are characterized by sharp peaks. The latter type of potentials are alow potentials that are much less dependent on synchrony of firing and are thus less dependent on the transient nature of the stimulus.

Neural generators:

Electrical potentials of the ear and the auditory nerve:

Several different sound- evoked potentials can be recorded from the cochlea: the cochlear microphonic (CM), the summating potential (SP), and the compound action potential CAP) see, e.g., Dallos, 1973). These potentials can he recorded from an electrode placed on the round window or from various

types of electrodes placed inside the cochlea. Different types of sounds may evoke all three potentials bat each potential is most clearly elicited in response to a particular type of sound. Thus, the CM is best seen in response to pure tones of relatively low frequency, the SP is best elieited by bursts of high-frequency tones, and the CAP is seen beat in response to transient sounds. In small animals such as cats, guinea pigs, and rats and CAP that can be recorded from the cochlea shows two negative peaks (N_1 and N_2), the earliest one (N_1) representing the synchronization in many nerve fibers of the auditory nerve and the latter one (N_2) representing the discharges of nerve cells in the cochlear nucleus (Fisch and Ruben, 1962; Miller, 1983ay Ruben, Hudson and Chiong, 1982).

The potential recorded intracranially from the auditory nerve in man has a triphasic shape: the earliest potential is a small positive deflection, which is followed by a large negative peak, which in turn is followed by a smaller deflection (Miller and Jannetta, 1981). This type of response is to be expected when recording from a long nerve with a field potential which is the second derivative of the action potential (Lorente, de No.1947).

More distal responses have shorter latencies than do those recorded more prominally. The latency of the negative peak varies with the sound intensity. It is lightly more than 3 ms in response to short bursts of a 2000 Hz tone at 100 dB equivalent

above normal hearing threshold (Moller, Jannetta, Bennett, and Moller, 1981;Moller and Jannetta, 1961),a time which la much longer than the latencies recorded from snail animals and about 1 ma longer than the N_1 that can be recorded from the round window of the human cochlea (Eggermont, 1974; Eiberling, 1976). This additional delay in N_1 is one to the greater length of the auditory nerve in man, which leads to a rather slow conduction time (20 m/s) (Engstrom and Rexed, 1940; Lazorthes, Lacomme, Ganbert, and Planel, 1961). This may also explain why there is no clear evidence of an N_2 potential whan recording fro* the promontorium in man (Eggermont, 1974; Elberling, 1976; Spoor, Eggermont, and Odenthal, 1976) In small animals the N_2 has been shown to originate in the cochlear nucleus and is conducted well to the recording site (round window) because the distance is short. The much longer distance between the cochles and the cochlear nucleus in man compared to that in small animals leads to poor conduction of the evoked potentials of the cochlear nueleas to the recording side (promontorium).

A comparison of the potential recorded directly from the eighth nerve and the ABR recorded differentially from electrodes placed on the vertex and just above the pinna shows that the potential recorded from the proximal end of the auditory nerve appears with the same latency as does peak II of the ABR. Moller, Jannetta, Bennett, and Moller, 1961; Moller, Jannetta, Moller, 1981, 1982; Moller and Jannetta, 1983c; spire Dohrmann, and Prieto, 1982). The recordings were Obtained in patients

undergoing neurosurgical operations to treat cranial nerve dysfanctions; in most cases microvascular decompression was performed to relieve hemifacial spasm or trigeminal neuralgia (Jannetta, 1977; Jannetta, 1981a, b). The results of analyzing these recordsing lad to revise earlier interpretations of the origins of the ABRa in man that assumed that the second peak was generated by secondary neurons located in the cochlear nucleus.

Potentials Generated by the cochlear nucleus and superior olivary complex;

When a recording electrode on the eighth nerve is moved from a location near the porus acusticus to a location that is close to the brainstem, the amplitude of the potential decreases and the shape of the potential changes. The potentials recorded from the eighth nerve near the porus acusticus have shorter latencies than do those recorded from the nerve at a location near the brainstem. In addition, when responses are recorded near the brainstem a slow negative potential is seen to follow the sharp negative peak and a second negative potential is seen about lms after the first negative peak. This second negative peak is most likely generated by sound-order auditory neurons located in the cochlear nucleus, while the slow potential is probably generated by dendrites in the coehlear nucleus (Moller and Jannetta, 1982a).

The coehlear nucleus in small animals dominates the brainstem and is located near the entrance of the eighth nerve, but

FIGURE
Schematic illustration of the neural generators of the ABR in man.

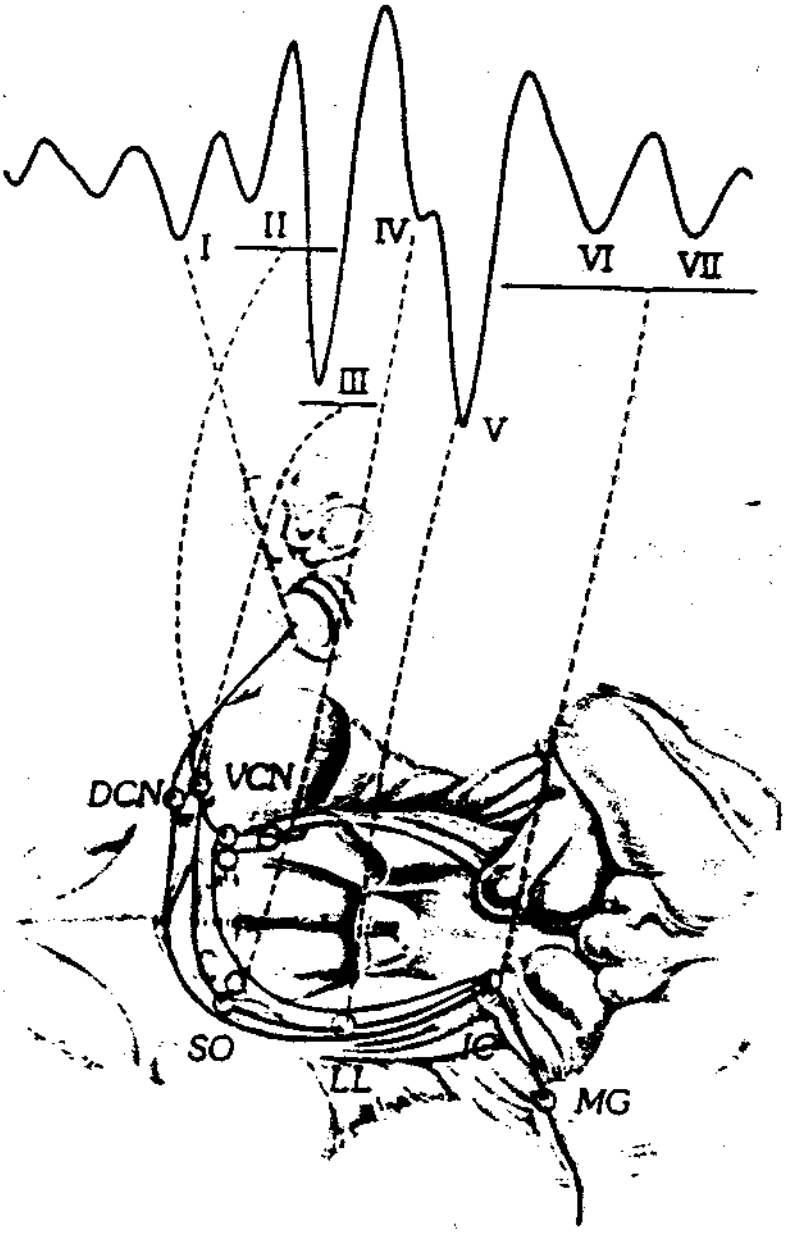
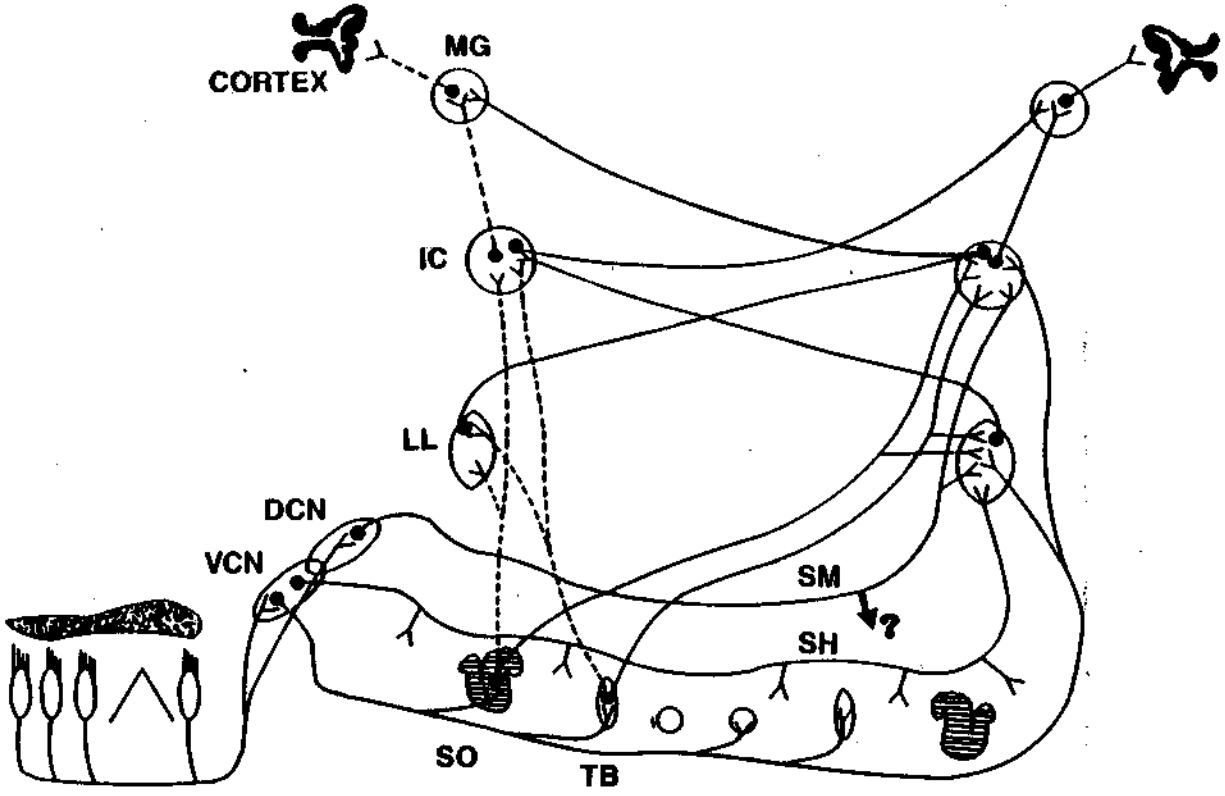


FIGURE [redacted].
Schematic drawing of the ascending auditory pathway. VCN: ventral cochlear nucleus; DCN: dorsal cochlear nucleus; SO: superior olivary complex; TB: trapezodial body; SM: stria of Monakow (dorsal stria); SH: stria of Held (intermediate stria); LL: lateral lemniscus; IC: inferior colliculus; MG: medial geniculate body (from Møller, 1983b).



in man it is a comparatively small part of the brainstem and is pushed backwards by the larger inferior cerebellar peduncle. It is, therefore, difficult to gain direct access to the cochlear nucleus of man in a lateral approach. Conclusion that second peak is located inthe brainatem and not in the nerve trunk along which the electrode ia moved (Moller and Jannetta, 1982a, 1983a). When these intracranial recordinga are compared to the ABRs recorded simultaneously from scalp electrodes, this peak is seen to appear with the same latency as does peak III of the ABR.

In a patient who was operated upon for a tumor of the fourth ventricle it was possible to obtain direct access to the medial side of the cerebellar peduncle and thus the cochlear nucleus or ita vicinity (Moller and Jannetta, 1983b). Recordings from this location showed a potential with a large negative peak, the latency of which was similar to this second negative peak in the recording from a root entry zone of the eighth nerve. The initial positive deflection ia assumed to have originated in the proximal portion of the auditory nerve, where it enters the cochlear nucleua. It may therefore be assumed that this aecond peak ia generated by secondary auditoty neurona located in the cochlear nucleua. This leds strong support to the hypothesis that peak III ia generated mainly in the cochlear nucleus. Originally, it was thought that peak III originated in the superior olivary complex, but the facts that as additional delay occurs in the auditory nerve and that peak III has a much larger amplitude than peak II support the hypothesis that peak III ia generated by a relatively large nucleus, such aa the cochlear nucleus.

While it is relatively easy to record the evoked potentials from the superior olivary complex in animals, it is difficult to record from this nucleus in man due to the relatively small size of these nuclei, which necessitate a very precise placement of the recording electrode, and the fact that the nuclei are located below the lateral of the brainatem. When the recording electrode is moved from the REZ to a location on the brainstem that is presumed to be ever the superior olivary complex, this third peak rose in amplitude, indicating that this latter location is closer to the source of this third peak than was the entrance to the brainstem. The latency of this third peak is about 1 ms longer than that of the second negative peak, indicating that its source is third-order auditory neurons. Third-order auditory neurons are known to be located mainly in the superior olivary complex, although presumably there are a number of third-order neurons also in the cochlear nucleus of man, as has been shown to be the case in animals. Although this third peak has a latency that is close to that to peak IV in the ABR recorded simultaneously determination of the generators of peak IV is complicated by the fact that the major parts of the ascending auditory pathway cross the midline at this level while some parts continue uncrossed toward higher auditory centers.

The conclusions that can be drawn from the results of this work are that peak I originates exclusively from the

distil part of the eighth nerve; that peak II originates mainly from the proximal part of the eighth nerve, although there may be some small contribution from other more distal parts of the auditory nerve; that peak III is mainly generated by the neurons in the cochlear nucleus but may receive some small contribution from nerve fibers entering the cochlear nucleus; and that the neural generator of peak IV is third-order neurons, mostly those located in the superior olivary complex but also those in the cochlear nucleus and probably also in the nucleus of the lateral lemniscus. Although other studies of the neural generators of ABRs in man based en intracranial recordings have obtained essentially similar results (Hashimoto, Ishiyama, Yoshimotos and Nemoto, 1981; Spire et al, 1982), this interpretation, particularly regarding peaks III and IV, should be taken as a simplification. There is no doubt that other sources in addition to these two nuclei also contribute to peaks III and IV of the ABR.

In comparing potentials recorded intracranially to the ABRs recorded in the traditional way (the difference between responses from electrodes places on the vertex and the ipsilateral mastoid) we found that the intracranial potentials did not always occur precisely with the same latencies as did peaks in the ABBs (Miller, 1983 a). There was thus not always an exact match in time between potentials recorded intracranially and those recorded extracranially. A similar observation was made by Hashimoto et al (1981). He ascribe that

occasional lack of an exact match between the peaks of potentials recorded intracranially and those recorded extracranially to the way ABRa are traditionally recorded: namely, differentially between electrodes placed at the vertex and the ipsilateral mastoid. Since both of the recording electrodes are located at sites that are electrically active (vertex and mastoid), the resulting potential will be the difference between the potentials recorded at these two locations. If the peaks of the potentials recorded at these two sites do not occur at precisely the sane time, the resulting difference potential will have peaks that occur with latencies that are different from those of the peaks in the potentials occuring at either of the two electrode locations.

More often, earlier components of recordings from the vertex have smaller amplitudes and peaks V, VI and VII are more evident. In recordings from the mastoid the first three or four peaks usually have the largest amplitudes while peaks V, VI and VII have relatively low amplitudes.

Potentials Recorded from the Inferior Colliculus:

It has generally bean assumed that peak V in the ABR is generated by the inferior colliculus. While this is most likely true in the snail experimental animals usually used in auditory research, recordings from the inferior colliculus in man show that this is unlikely to be the case in man.

Typical potentials recorded from the inferior colliculus in man in response to contralateral sound simulation.

When the potentials recorded from the inferior colliculus are compared to the ABR, both being recorded in such a way that low frequencies are preserved, it is seen that the negative peak in the response from the inferior colliculus has about the same latency as does the vertex negative potential (Miller, and Jannetta, 1982b, 1983c), usually known as the SN_{10} (Davis and Hirsh, 1976). This indicates that the main neural generator of this potential is most likely the inferior colliculus.

When the slow potential is removed by filtering, a aeries of two to three peaks is seen to follow the initial positive peak. These sharp peaks probably represent synchronized firing of neurons in the inferior colliculus. When the potentials recorded intracranially from the inferior colliculus are compared to those recorded from the vertex using a noncephalic reference, the latencies of peaks V,VI, and VII of the potentials recorded from the scalp and the first, second, and third peaks of the potentials recorded intracranially look nearly identical (Miller and Jannetta, 1983c). When the intracranially recorded potentials are compared to the AHRs recorded in the traditional way, differentially between a mastoid and a vertex electrode, the match between the peaks in the intracranial and scalp recordings is less perfect. This discrepancy is due to the fact that the

two locations (mastoid and vertex) from which the ABRs are recorded differentially from the scalp are both active and the latencies of the peaks are slightly different for the two locations. A differential recording from these two locations consequently differs from the recordings made from either of the two locations alone.

It is important to emphasize that the neural generaters of peaks IV, v, VI, and VII are complex in that more than one anatomical structure contributes to each peak and that each anatomical structure contributes to more than one peak.

Effects of Pathologies on Near-field and Far-field Potentials:

To understand the changes in the far-field potentials (ABRs) that result from pathological changes in the nerves it is necessary to understand the changes that such pathologies cause in the near-field potentials. However, the effects of various pathologies on the potentials that can be recorded from nerve tracts and nuclei have not been studied to the same extent as has the normal response. Thus, the changes that can be expected as a result of certain insults are largely unknown. Clinical experience, however, has shown that various types of pathologies result in a prolongation of the latencies of the various peaks in the ABR.

The effects of pathologies such as tumors on the far-field potentials (ABR) have been studied extensively in patients whose site of lesion is known.

Studies of patients with acoustic neuromas has been the moat useful in correlating specific changes in the latencies of the peaks in the ABR to the particular lesion involved. ABRs are generally assumed to be among the more important data obtained in otonearological testing of patients with intracranial lesions.

The uncertainty as to just what the neural generators of elements of the ABR are has, however, made it difficult to determine exactly which of the changes seen in ABRs are most specifically correlated with certain diseases. For instance, an increase in the latency of wave V of the ABR had generally been regarded as being indicative of an acoustic neuroma. However, when more information about the neural generators of the ABR was obtained, it became evident that in most patients who had acoustic nerve tumors a shift in latency of peak III occured, a finding which agreed with previous findings that peaks I and II are generated by the auditory nerve and that peak III is generated by the cochlear nucleus (Moller and Moller, in press). The amplitudes of the potentials and their wave form morphology also Change as a result of injury, bat the two latter parameters are not as well utilized in clinical diagnosis as is the change in latency.

There are several factors that may change the amplitude of the evoked potentials, one of which is insult to the nerve, When recordings are made from the auditory nerve, cochlear

nucleus, and probably also from more centrally located structures, the degree of synchrony (phase locking) of discharges is a large factor in determining the amplitude and the shape of the potential. If synchrony is impaired, the amplitude will change will change but the latency may be relatively unchanged.

It is more difficult to obtain accurate and reproducible measures of the amplitudes of evoked potentials than of their latencies. This is true of near-field as well as far-field potentials. Thus, the amplitudes of near-field potentials may be greatly affected by such factors as the exact placement of the recording electrode or shunting of fluid, while these same factors do not affect latency to any noticeable extent. This is one important reason why examining changes in latency has been preferred over studying changes in amplitude to detect various abnormalities. Nevertheless, there is no doubt that the amplitude and the waveform of the evoked potentials carry much information that can be of value in the diagnosis is disorders of the auditory nervous system. This is shown, for instance, in the discovery that putting traction on the auditory nerve in patients undergoing operations for cranial nerve dysfunction produces a number of changes in the shape of the CAP that can be recorded directly from the nerve, as well as causing an increase in the latency of the ABR (Moller and Jannetta, 1983a)

another reason for studying characteristics of ABRs other than their latencies is that non-neural factors can affect

latency. Notable among these is hearing loss resulting from defects in the conduction of sound to the inner ear (middle ear disorders) or from damage to hair cells in the inner ear. These factors prolong the latency of impulse conduction, and if not taken into account may lead to a mistaken interpretaion of the ABR. When click sounds with broad spectra are used as stimuli, it is mainly the high-frequency part of the spectrum that is the effective stimulus in people with normal hearing. Since high-frequency sounds only travel a short distance on the basilar membrane, this travel time contributes only slightly to the latency of the ABR in people with normal hearing. However, in people who have lost their high-frequency hair cells (commonly the elderly or people who have noise-induced hearing losses) the lower-frequency components constitute the effective stimulus? since these components travel a longer distance on the basilar membrane there is an additional delay which adds to the latency time of all the peaks. If not taken into account, this latency increase may be confused with an increased neural conduction time. There are several ways of compensating for this possibility in testing for neural conduction deficits. One way is not to use absolute latency values but instead to use the interwave latencies between waves I and III or waves I sad V; another way is to test the responses to tone bursts rather than click sounds. The latter method works because of location of maximal deflection of the basilar membrane in response to tones is independent of the sensorineural hearing loss, which

in turn means that the time it takes for the traveling wave to reach the location of maximal response of a pare tone is independent of the population of sensory hair cells. Consequently, the latency of the response to tone bursts is relatively independent of the size of the hair cell population, as long as there are some hair cells present. For this reason the latency of the response to low-frequency tone bursts (of e.g., 2,000 Hz) is lessdependent on degree of cochlear hearing loss than are the latencies of the responses to click sounds.

AUDITORY BRAIN STEM RESPONSE IN EIGHTH NERVE AND BRAINSTEM LESIONS

Auditory brain stem (ABR) in 8th nerve and low brain stem lesions:

Introduction:

From the first reports of abnormal auditory behavior in the 1890s until the present the patient with acoustic nerve tumor has been the subject of considerable discussion.

The advent of auditory brain stem response (ABR) in the site of lesion testing has markedly enhanced sensitivity in the detection of eight nerve and low brain stem lesions. In these patients changes may occur in latency morphology or both in the affected ear. In large tumors responses from the contralateral side may be affected as well. The changes affect waves I and II on the affected side so that I to III are prolonged.

ABR is so sensitive to 8th nerve tumors that it may act as a monitor for patients who have lesions small enough to escape routine radiologic evaluation. Thus ABR is helpful in screening relatives of Von Recklinghausen's syndrome so much ao that after baseline screening with computerized axial tomography or magnetic resonance imaging (MRI) and hearing tests with ABR, annual re evaluation is only audiologic utilizing hearing tests and ABR. ABR has also been effective in detecting vascular lesions of the low brain stem, it yielded no response or latency delays of ABR (Coats. 1978; Stockard. 1980).

Pathophysiology:

While considering the various pathologies of the 8th nerve and low brain stem tumors, specifically the acoustic neuroma or schwannoma head the list. The tamors of the brain stem can also be called as posterior fossa tumors and can be classified into two types.: Intraaxial and extra-axial tamors. Intra axial tamor is a neoplasm which originates within the brain stem. The extra-axial tamor originates outside but close to the brainstem. The extra axial tumor influences the auditory nerve resulting as neuromas or meningiomas. Vascular lesions of the brain stem are also of great clinical significance.

The most common tumor found in the cerebellopantine angle and low pontine area is the acoustic schwannoma or acoustic neuroma. When small, the neuroma is usually located within the internal auditory canal but with growth it insinuates into the cerebellopontine angle. In moat cases the neuroma erodes the walls of the internal auditory canal which can be seen in radiological studies. Symptoms of auditory and labyrinthine involvement occur early in the disease and include deafness, tinnitus and disequilibrium. A meningioma originates in the tentorium of the dura covering the cere-bellopontine angle. Initially the meningioma compresses only cerebellopontine angle structures and not the auditory nerve, but continued growth will usually affect the auditory

nerve, symptoms of auditory and labyrinthine involvement occur in cases of neuroma later.

When the tumor stretches or compresses nerve fibers it may slow the conduction velocity of the nerve impulse. The desynchronization of the firing rate of neuroma as a result of a variety of pathologies may be more plausible explanation (Eggermont, Den and Brackman, 1980).

Changes in vascular supply to the internal auditory meatus and low brain stem may also occur with resultant symptoms and clinical findings to space-occupying lesions (Mailer and Moller in press, Starr and Achor, 1975). Because vertrobasilar system is the origin for the anterior inferior cerebellar artery (which arises from the basilar artery and travels superiorly to the IAM)and its collaterals, including the internal anditory artery, deficiencies inthis network may subsequently be noted in the eight nerve and other cranial nerve functions. The arteries may become restricted in diameter secondary to arteriosclerotic changes and compromise osygenation in this area. These results may also compress the adjoining nerves, causing damage to the central myelin. The pulsatile pressure of the artery on the nerve may create hyperfunction or total loss of function. These nerves then may be disrupted from their normal activity, resulting in tinnitus hearing loss and vestibular disorders (Moller and Moller in press).

The eighth nerve is not only nerve sensitive to vascular compression. The facial (VIII and trigeminal (V) nerves may also be damaged doe to compression of a similar nature.

The pulsatile pressure may create artificial stimulation or compression of the nerve, resulting in hemifaeial spasm and trigeminal neuralgia. In cases of hemifacial spasm, the close proximity of the dysfunctioning nerve to the eight nerve may result in disruption of auditory nerve function with subsequent changes in the ABR (Moller, Moller and Jannetta, 1982). Hence the greatest otoneurological value of ABR is its high detection rate for eighth nerve and low brain stem lesions. This sensitivity is better than any other audiological test for the detection of eighth nerve and cerebello—pontine angle tumors (Musiek, Mueller, Kobbe and Rackllffe, 1983b).

ABR findings:

Selters was the first to report the use of ABR to detect acoustic neuroma and the most consistent finding was the absence or increased latency of wave V. Later Eggermont et al in 1980 found that selective action of a tumor on high and low frequency fibers of the auditory nerve may be responsible for ABR wave V delays.

Further aberrations of the ABR caused by an acoustic tumor include missing components, increased absolute latencies.

increased interpeak intervals and reduced amplitudes.

There are 3 ABR latency measures in defining eighth nerve and low brain stem lesions. Absolute interwave and interaural latency differs (ILD) are helpful in detecting retrocochlear involvement.

1. Inter wave measure or inter peak intervals:

The most powerful latency measure in the detection of otoneurological deficits is the interwave measure on inter peak interval determination specifically I-V interval. The primary purpose for determining these is to localize the lesion.

A variety of studies have indicated that the 'normal' I-V interval is approximately 4.0 ms with a standard deviation of 0.2 ms (Chiappa ,Gladstone and Young, 1979? Eggermont et al. 1980; Musiek and Geurkink, 1982). The I-V latency interval can be broken down into I-III and III-V intervals.

The normal I-III latency is slightly greater than 2.0 ms while the normal mean III-V latency is slightly less than 2.0 ms Standard deviations for I-III and III-V intervals range between 0.1 and 0.2 ms (Chiappa et al 1979; Eggermont et al, 1980; Stockard, 1982).

In the majority of cases with acoustic tumors the early waves may be undefinable. Hence I-III or III-V intervals cannot be measured. In the cases where the waves I, III and V

could be identified, the I-III interval was more affected than the III-V (Eggermont et al). Harris and Almquist in 1981 found that tumors of the acoustic nerve and cerebello-pontine angle can result in an increased 111-V and a normal I-III latency. In a patient with a suspected newroma of the auditory nerve only wave I demonstrated normal absolute latency. The interpeak intervals werE prolonged for waves I-III and I-V but were normal for 111-V. These results were interpreted as indicating that the lesion was between the generators of waves I and III. Surgical results confirmed to location of the neuroma as being on the auditory nerve.

In subjects with vertebral basilar disease, as reported by Ragazzoni, Amantine, Rossi et al (1982) increased inter-peak intervals were observed. Rosehall et al (1981) noted abnormal I-V intervals in patients with vascular disease of the low brain stem region. Increased interwave intervals were observed in subjects with compression of the arterial loop in the cerebello pontine angle. Increased I-III and III-V wave Intervals have been reported for patients with hemifacial spasm secondary to vascular compression (Moller and Moller). Also in patients with vascular compression in the brain stem resulting in trigeminal neuralgia have yielded an increased III-V interwave latency.

2. <u>Absolute latency:</u>

In Cases where wave I is absent some alternate measure to the interwave or interpeak interval must be employed and

absolute Latency being an example of the neurological function. One of the most consistent finding in the detection of acoustic neuromas has been the absence or increased latency of wave V. In the normal ears the latency of wave V is 5.0 to 5.8 ms. The absolute latency of wave V greater than two standard deviations beyond the mean for normal hearers i.e. any latency greater than 6 ms was suggestive of a retrocochlear lesion (selters).

In a study conducted by -John W.House and Brackmann in 1979 on 136 patients with acoustic neuromas they found either a delay or the absence of wave V in 143 patients. Inthe vascular disorders of the brain stem the absolute latency of wave V was found to be prolonged.

Further in patients with acoustic neuromas or meningiomas the latency of the waves distal to the tumor are typically within normal limits while those that originate proximally will be prolonged. Absolute latencies have been shown to be of value in detecting eighth nerve cerebellopentine angle tumors and vertebrobasilar lesions in a number of studies like (Bauch et al 1982; Clemis and McGee, 1979; Glaascock, 1979; Rosehall et al, 1981).

3. <u>Interaural latency difference (ILD):</u>

It is one of the most commonly used latency measures. Here the comparison of wave V absolute latencies for each ear is carried out. According to Clemia and McGee (1979) and Terkildsen et al (1981) the ILD of greater than 0.3 ms are significant

tad may indicate a retroeochlear lesion. Hearing loss must also be kept into account. Clemis and McGee in 1979 said that when hearing loss is greater than 65 dB HL a 0.4 ms ILD criteria must be employed.

Wave form morphology: This is most subjective index and ean be classified as -

1. Totally absent or unreadable waves.
2. Absence of certain waves.
3. Noisy waveforms.

1. **Total absence:**- An acoustic neuroma will typically reduce the number of components of the ABR and result in absence of all waves or unreadable wave forme. Selters and Brackmann (1977, 1979) reported that approximately one-half of their acoustic neuroma subjects had no response for ABR. Harker (1960) reported 28% of his patients with acoustic tumors showed no ABR. It must be kept in mind that if the hearing loss is severe enough, there may be an absent of ABR without any retrocochlear involvement.

Total absence of ABR waves is more likely to occur in an eighth nerve or low brain stem lesion if there is hearing loss. In patients with meningiomas the absence of specific waves is generally determined by the location and effects of the tumor.

If the menigiomas originates high in cerebellopontine angle tumor, compression of the brain stem may affect only the later waves. If the meningioma is located closer to the pens, only

the early ABR components can be modified. If the hearing is good only wave I is noted (House and Brackmann, 1979). Wave I is generated at the more lateral aspect of the auditory nerve and most acoustic tumors arise more medially, close to the cerebellopontine angle. In the lesions of the cerebello-pontine angle or low brain stem the acoustic nerve segment is responsible for generating wave I has a probability of being intact.

2. **Partial absence:** Eighth nerve or low brain stem lesions yield a variety of other wave form abnormalities. The waves I and II may be present and wave V absent. This finding is more common in high brain stem lesions and has been reported in the lesions of the cerebellopontine angle (Harris, and Almquist, 1981, Rosehall, 1981). An absence of wave III with a normal I and V wave also has been reported (Miller et al, 1982, Howe, 1981).

3. **Noisy wave forms:** This is the most subjective analysis. If the patient is quiet during testing and has good hearing and no technical problems (eg. electrode contact), yet the wave form is noisy and poorly formed, retrocochlear involvement should be considered (Musiek, 1982). This must be viewed as a 'soft sign'.

To reiterate interpretation of noisy waveform and totally absent wave must be based on audiometric information as these can occur with cochlear involvement and hence be ruled out.

Amplitude ratio : Another index of value in detecting retrocochlear lesions with ABR is the amplitude ratio (Musiek, Kibbe, Rackliffe and Weider, 1984) and can be applied specifically to eighth nerve and low brain stem lesions (Hecox, 1960, Musiek et al 1984, Stockard, 1977).

Amplitude ratio is the amplitude of wave V compared to wave I. A ratio of less than 1.0 is considered abnormal in the adult population. Musiek found that of 25 ears with retrocochlear lesions where both waves I and V were present. 11 patients had abnormal amplitude ratio further it was noted that in 4 of the 25 ratrocochlear ears the only ABR abnormality was amplitude ratio.

Repetition rate: There have been several reports of eighth nerve or brain stem lesions that have shown significant wave V latency shifts or degradation of wave V morphology at high repetition rates (Paludetti, Mausizi and Ottavini, 1983; Weber and Fuizibawa, 1977; Yaga and Yaga, 1979). It is believed that the use of high repetition rate stresses the auditory system and in some cases can uncover an abnormality. The physiological basis for repetition rate studies is the neural refractory period The absolute refractory period is the time interval in which the nerve cell cannot respond. If the nerve cell or cells are not functioning properly a longer refractory period may be detected by employing a high repetition rate.

To examine the repetition rate effect, comparison of the latency of wave V at high and low repetition rates is reqaired. In normal subjects there is an increase in wave V latency for the high repetition condition (Don, Allen and Starr, 1977? Paludetti, 1983). Hecox in 1980 gave a formula for finding the upper limit of acceptable latency shift, which is determined by 0.006 ms multiplied by the difference between high and low repetition rates plus 0.4 ms.

The effects of increased repetition rate on the ABR have been documented in normal (Don, Allen and Starr, 1977; Hydestephens and Thornton, 1976? Weber and Fujikawa, 1977) and neurologically impaired human subjects (Hecox, Cone and Blaw, 1981). Generally an increase in repetition rate will differentially prolong wave latency while decreasing wave amplitude. The more rostral the response the greater the; latency shift.

Opposite ear effects in cerebellopontine angle tumors:

A large CPA tumor in an individual may displace or compress the brainstem enough to effect the ABR from the ear opposite the lesion (Lynn and Gilroy, 1980; Musiek, 1982). This finding has several important clinical implications. One of these is a rationale for performing an ABR or patient with absent or very poor hearing in an ear which is suspected of having an acoustic tumor. Since the hearing may be too poor for the ear in question to be tested by ABR, the opposite

ear can be assessed for any ABR abnormality. If ABR results are abnormal in the ear opposite the suspected lesion, there may be brainstem involvement resulting from a large CPA tumor and can be an importent information to relay to the surgeon. The most common finding has bean that only the ABR waves TV and V are affected for the ear opposite the tumor (Musiek, Kibbe and Strojny, 1983 a).

Laterality:

Excluding large CPA tumors, acoustic tumors typically affect the ipsilateral ABR. When there is a lesion of the low brain stem the effects may not be clear when the lesion is in the brain stem, ipsilateral and bilateral findings are more common (Musiek and Geurkink, 1982). However to a lesser extent, contralateral abnormalities may also exist (Stockard, Stockard and Sharbrough, 1979). Laterality findings depend on many factors such as ABR recording sites, the level (rostral or caudal to the level of auditory decussation), size and type of lesion.

Finally not all the discussed indices should be viewed as having equal clinical value. The latency measures remain the most valid and reliable tool for ABR assessment.

Auditory brain stem response in upper brain stem lesions:

The principal auditory centers and pathways of the upper brain stem that give rise to components of the ABR -

1. Rostral extension of the lateral leminiscus in the upper part of the Dons.

2. Inferior colliculus located in the caudal region of the midbrein, and
3. Medial geniculate body of the caudal thalamua (Most rostral part).

The lateral leminiscus (LL) is the principal ascending tract in the brain stem. Initially this bundle lies lateral and rostral to the superior olivary nuclei and the lower pons and courses nostrally along the lateral edge of the pontine tegmentum to assume a more dorsal position as it approaches the inferior colliculus in the midbrain clumps of cell located among the fibers of this bundle constitute the ventral and dorsal nuclei of the LL. The IC receives its major input from the contralateral cochlear nucleus, the ipsilateral and contra-lateral nuclei of the superior olivary complex and the IC of the opposite side via the commissure of the IC. Afferent neurons of the lemniscal tract terminate almost entirely in the ventra lateral region of the central nucleus of the IC and from here projected to the MSB via the brackium of the IC. Extra axial structures namely the cerebellum, blood vessels tentorium and pineal gland are relevant to this system because extrinsic pressure from mass lesions arising from these extra axial sites may affect upper brain stem auditory functions.

Pathophysiology:

Intrinsic or intra axial lesions originate within the substance of the brain stem examples being - mass such as tumor

infiltrating the brain tissue, a plaque resulting from a demyelinating process like multiple sclerosis, an infarction resulting from insufficient blood supply to a particular region resulting from stenosis or occlusion of blood vessel or a hemorrhage resulting from rupture of a blood vessel. Extra axial lesions affect the brain stem secondarily by pressure, distortion, local extension into the substance of the brain stem or by compromising the brain stems blood supply. These factors then alter the ABEs if generators or pathways in the auditory system are involved. Four mechanisms account for the ABR alterations.

1. The lesion may involve the generators directly
2. Fibers which course through the area of the 1 sion to terminate in the remote generators may be damaged.
3. The secondary effects of lesions remote from the primary site may effect the ABRs.
4. The function of uninvolved generators may be affected by lesions located elsewhere.

ABR data can contribute to an anatomical localization of a lesion.

ABR findings:

Since the first description of scalp-recorded auditory evoked brain stem potentials (Jewett, Romano, Williston, 1970), the consensus has been that the human ABR waves IV, V and possibly VI reflect electrical activity occuring primarily from auditory centers and pathways in the upper brainstem.

The effects of upper brain stem lesions on the ABR are varied, changes in latency, amplitude and waveform alone or in combination and on one or both sides have been described in clinical human stadias. Because of the predominance of the contralateral pathway of the auditory system in the brain stem, ABRs in unilateral upper brain stem lesions should be expected to reflect abnormalities when the ear opposite the involved side is stimulated. Some authors believe that the abnormal ABR features occur on stimulating the tar ipsilateral to the lesion (Chiappa, 1983; Oh Kuba Soyer, Bonikowski, 1981). Whereas (Epstein and Stappenbeck and Karp 1980) found ABR abnormalities may occur in rostral brain stem lesions when the stimulus is presented to the contralateral ear.

Starr and Hamilton (1976) reported one case of a hemorrhagic tumor (germinoma of the pineal gland), oblite-rated most of the midbrain and a portion of the rostral pontine tegmentum. ABR waves IV through VII were absent bilaterally to monoaural stimulation and waves II and III were slightly prolonged in latency, due to secondary effects of pressure from the tumor.

Starr and Hamilton concluded that intact midbrain auditory structures are essential for detection of components after wave III. Amplitudes of Wave IV and V were reduced.

Epstein et al (1980) in a study of a patient with palatal myoclonus found the same results. In this case there was vertical diplopia, left sided hemisensory loss and right sided

in coordination. Clinically the lesion was localized to the right side of the brain stem with definite involvement of the midbrain on that side. The ABR showed a delayed wave V latency with significant amplitude reduction only when stimulating the left or contralateral ear. Waves TV and V were normal in latency aad amplitude when stimulating the ipsilateral ear.

Differentiation of low brain stem and high brain stem lesions

Low Brain Stem	High Brain Stem
1. Earlier waves or entire wave form may be absent	1. Earlier waves present, later waves absent.
2. Most common interpeak interval prolongation between I-III	2. Prolongation between III-V
3. Ipsilateral abnormalities are commonly observed.	3. Bilateral, ipsilateral and contralateral, abnormalities present.

Hence ABR helps to confirm the clinical suspicion of brain stem involvement.

Vascular disorders of the brain stem:

The cardinal feature of brainstem vascular disorders is the stroke, which is the sudden development of a focal neurological deficit due to an infacet or hemorrhage (Fisher, Mohr Adams, 1975). An infarct occurs from an obstruction of an artery and results in necrosis of brain tissue. In a hemorrhage, blood leaks from the artery and disrupts the function of surrounding tissue through infiltration.

ABR elicited from 19 patients evaluated due to brain stem strokes have been described inthe literature (Green and McLord, 1979? Hashimoto, Ishiyama and Tozka, 1979).

In patients with generalized brain stem infarcts, the majority lack ABR components, or display increases in absolute latencies and IPIS. These characteristics were found in patients evaluated at KUMC and reported in the literature (Ragazzoni, Amantini, Rosi, et al, 1982, stem Krumholz Weiss, et al 1982). The majority of these patients were diagnosed as having an infarct in the vertegro-basilar artery system.

When the infarct involves the corticospinal and cortico-bulbar traits a conditions known as locked in syndrome occurs. Typically, these patients have no effective verbal or motor responses, but are awake and in contact with the environment. In some cases vertical eye movements and eye blinking occur. While inlocked in syndrome is very uncommon, ABRs have been reported in seven cases. In two of these cases, the ABR showed normal waves I, II, III, but prolonged IV, V waves - bilaterally (Gilory and Lynn, 1978; Series, et al 1981). The I-III IPIS were normal but the III-V and 1-V were abnormal bilaterally. The ABRs in the remaining 5 cases were normal (Hammond and Wilder, 1982; Fischer Mohr and Adams et al 1981). The discrepancy between these studies is attributed to different locations of the infarCt.

Tumor detection: Patients are considered to have positive test result for tumor detection when their latencies showed one of the three characteristics.

I. Wave V latencies are significantly different from the normal mean.

II. The interaural latency difference greater than 0.3 msec (0.4 msec when hearing loss greater than 65 dB HL).

III. No response recognized at suprathreshold levels.

Results of the study conducted by Clemis and McGee for the differential diagnosis of the acoustic tumors.

They took 26 patients with surgically proven vestibular Schwannomas, out of these, 25 had unilateral tumors and one with Von Recklinghausen's disease (bilateral tumors).

Wave V latencies were obtained from 23 tumors ears (2 of which were from the patient with bilateral tumors). Nineteen had abnormally delayed latencies while 4 had latencies within the normal range. ILDs were determined for 21 patients with vestibular Schwannomas of thse 20 had abnormal ILDs and one had an ILD within the normal range. Four tumor patients demonstrated no response at suprathreshold levels.

Two patients with unilateral vestibular schwannomas had normal absolute latencies but abnormal ILDs. This suggests that the ILD is a more sensitive measure than absolute latency. On the contrary a disadvantage of ILD measure is the inability to detect bilateral tumors, or to detect a tumor in an only hearing ear. One of the patients who had Von Recklinghausen's

disease had a 2.5 cm tumor on the right side and a 0.4 cm intracanicular tumor on the left. The ILD was abnormal 0.8 msec, with the right ear more delayed. Using the ILD value in this case the larger tumor was identified and the smaller tumor was not. Seleters and Brackman also report such a case and suggest comparing the latencies to normative data.

No response at suprathreshold levels: In half of the patients with acoustic neuromas no wave V values could be obtained. In the Selters and Brackmann series, tumor size ranged from 1.0 to 5.0 cm. In the study by Clemis and McGee 16% of the patients demonstrated no response. This may be due to a difference in patient populations. Reviewing the tumors of comparable size in the two studies, Selters and Brackman have a higher proportion of cases of no response (30% of tumors under 2.5 am) Another factor involved in this discrepancy may be the difference in the type of stimulus used i.e. tone pip vs click. It is unlikely that a tumor would press equally on all fibers of the nerve. Rather, some nerve fibers would be involved more than others. Therefore assuming that the pressure of the tumor causes the latency shift in the response it very likely would not be a constant shift for all the fibers.

A nonfrequency - specific stimulus such as click stimulates a broad range of fibers and the variability in the latencies may tead to 'smear' the responses. Perhaps a frequency

specific stimulus such as a tone pip would be less likely to have such an effect because a narrower range of fibers would be stimulated. Although the latencies would still be delayed, thezeduced variability would make the response more detectable by BSERA methods.

Tuamer size vs ILD: Clemis and McGee found correlation between the tumor size and ILD. However in one case, a patient with a relatively small tumor (0.8 cm) demonstrated a rather large ILD (over 3.0 m.sec) and for the patients in which no response could be recorded, the tamor size varied widely. This suggests that it is not only the size of the tumor per se, bat possibly the locus of the pressure of the tumor, which determines the magnitude of the effect on the physiological response.

A small, strategically- placed acoustic neuroma may cause as much latency shift in the response as a larger tamor in a different locus. Although, in general a large tumor should exert greater pressure on the nerve than a small tumor.

Effect of stimulus parameters on brain stem responses:

I. Frequency:- Clemis and McGee tested 17 patients with abnormal ILD measures at more than one frequency only one tumor patient demonstrated an abnormal ILD at one frequency but a normal ILD at another. For 7 of 17 patients, the abnormal ILDs varied more than 0.3 m.sec.across frequencies. Another patient showed a response at 500, 1000 and 2000 Hz. but not

at 4000 Hz although all signals were presented at supra-threshold levels. Thus ILD measurements varied across frequencies. These variances across frequency and the difference in "no response" patients between this study and Selters and Brackman suggest that tone pips may have an advantage over clicks in tumor detection, contrary to previous reports. Hence it is better to establish latency values in a suspect ear at more than one test frequency.

II. Intensity: The wave response can be recorded to within 10 dB of behavioural threshold. However at lower intensities the amplitude of wave V is greatly reduced. Because of this, for the purpose of tumor diagnosis, wave V latencies were obtained only at relatively high stimulus levels (60 to 90 dB HL).

Individual variance in latency values is apparently related to the degree and distribution of the pressure exerted by the tumor and can thus be related to tumor size. Stimulus variables i.e. a click vs a tone pip also may produce differences in the brain stem responses.

Despite the words of caution BSERA is the most efficient audiomgtric test available in the search for tumors affecting the auditory nerve.

FIGURE [redacted]

Case [redacted] is a 36-year-old female who complained of left-sided numbness and tingling of the face, arm, and leg for about 6 months to 1 year. During this period she had occasional bilateral tinnitus and mild imbalance. Her main complaint, surprisingly, was a clicking noise in her left ear. She reported her hearing as being very good. Radiological and surgical findings revealed a large (4.0 cm) CPA tumor which was displacing the brainstem (Figure 2b). The left ear ABR shows wave V, by our interpretation, at about 7.3 ms (see arrow). Therefore, absolute and interwave latencies (I–V—5.7 ms) are abnormal for the left ear. In addition, the relatively "flat" response at 60 dB HL is inappropriate for a patient with a normal audiogram.

The right ear ABR is missing wave V, though waves I through IV (4.8 ms) seem robust. This absence of wave V is probably due to brainstem compression. [redacted].

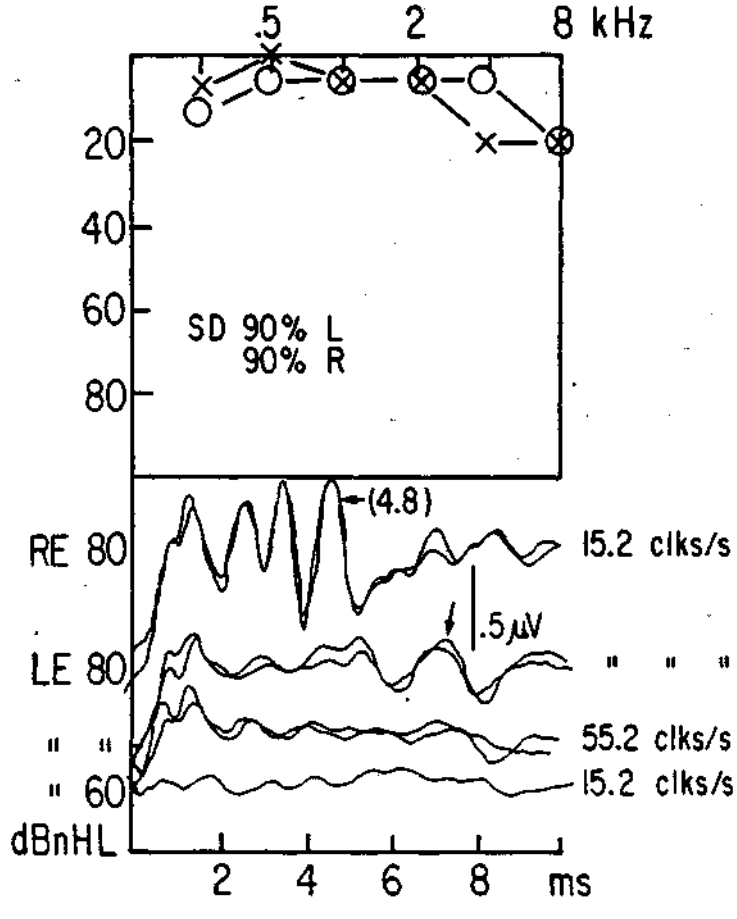


Figure 10–2a.

Illustration continued on following page.

FIGURE [redacted]

Case [redacted] is a women in her early thirties who 5 months prior to diagnosis reported a vague facial numbness along the right eye, nose, and lateral upper lip. A few months later she noted bilateral tinnitus and intolerance to loud sounds. Neurological examination revealed hyposensitivity of the second and third divisions of the fifth cranial nerve. Radiological and surgical findings documented a 4-cm, right-sided fifth nerve neuroma intimately attached to the low to midpons. The tumor was removed and the hearing preserved. (Figures 3a, 3b are pre- and post-operative audiograms; Figure 3c is the pre- and post-operative ABR.)

The right ear ABR shows an abnormal amplitude ratio and an abnormally "flat" waveform at 60 dB HL. However, latency measures are normal. Note that postoperatively the amplitude ratio is appropriate, and there is a much better waveform at 60 dB HL (taken in part from Musiek, Weider, & Mueller, 1983c).

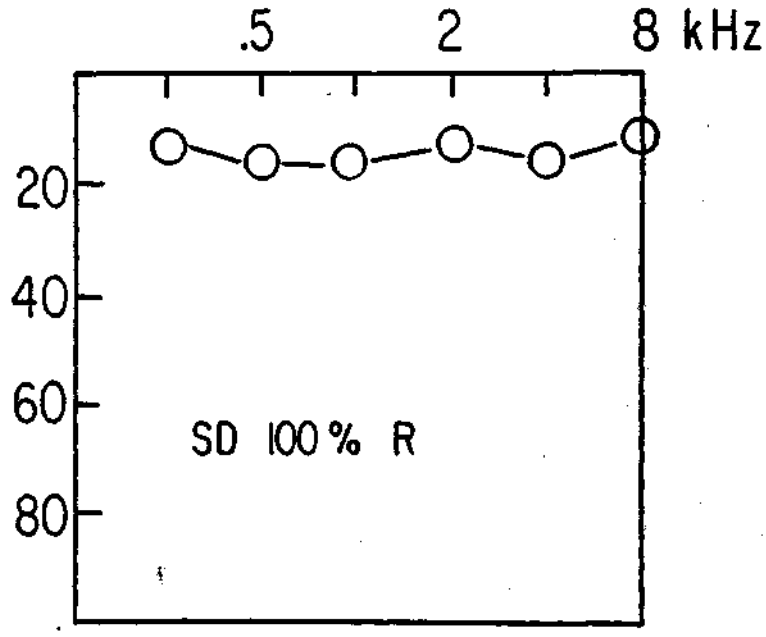
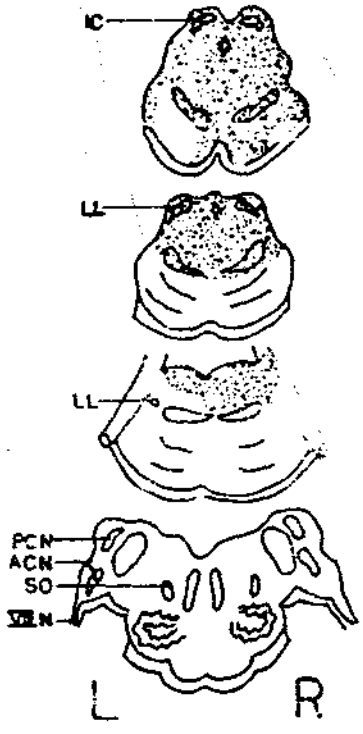


FIGURE [redacted].
Distribution of neuropathology in the upper brainstem (stippled areas) of a patient with a germinoma and ABRs compared to a normal response. R and L refer to stimulated ear: right (R) or left (L). IC, inferior colliculus; LL, lateral lemniscus; PCN, posterior cochlear nucleus; ACN, anterior cochlear nucleus; SO, superior olive; VIII N, eighth cranial nerve. Reproduced with permission from Starr and Hamilton (1976).



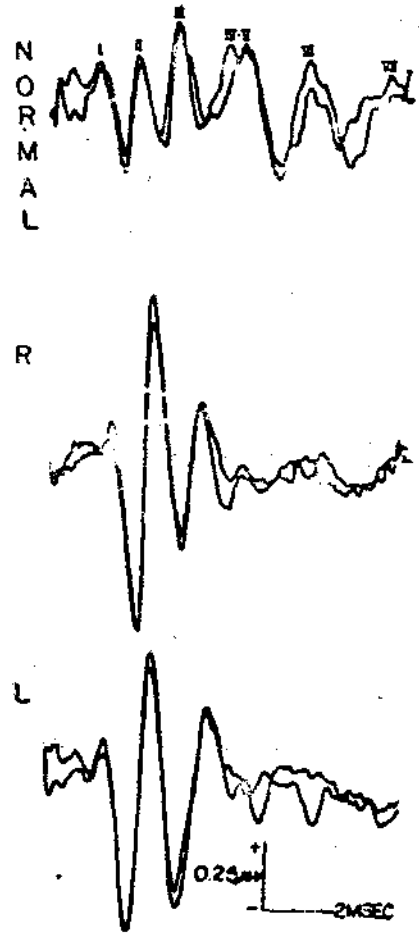


FIGURE [redacted].
Distribution of neuropathology on the l[illegible] side of the brainstem (stippled areas) of a patient with tuberous sclerosis with [illegible]emistocytic astrocytoma and ABRs compared to a normal response. Abbreviations are the same as in Figure 11-1. Reproduced with permission from Starr and Hamilton (1976).

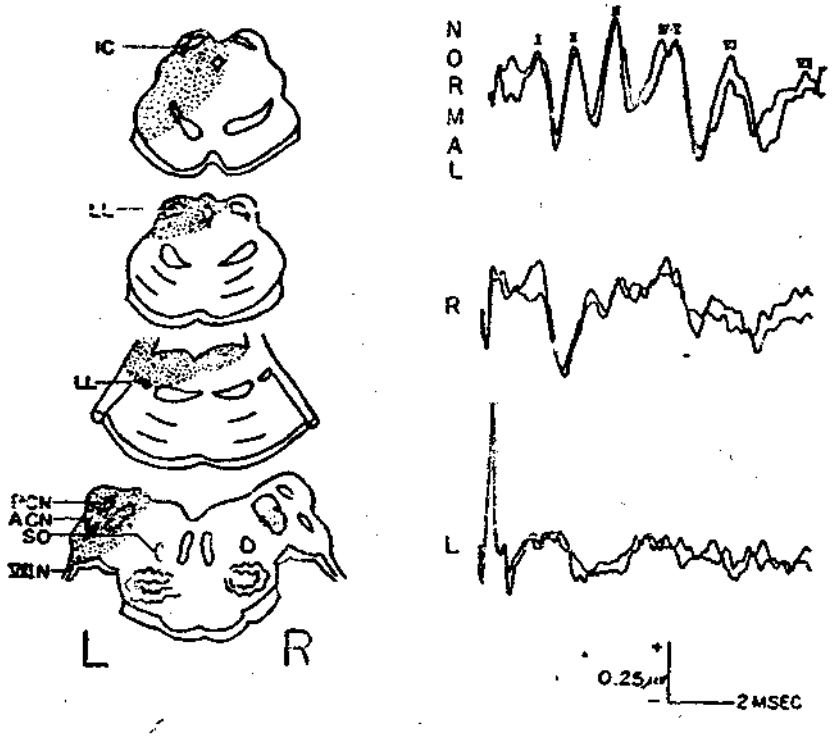
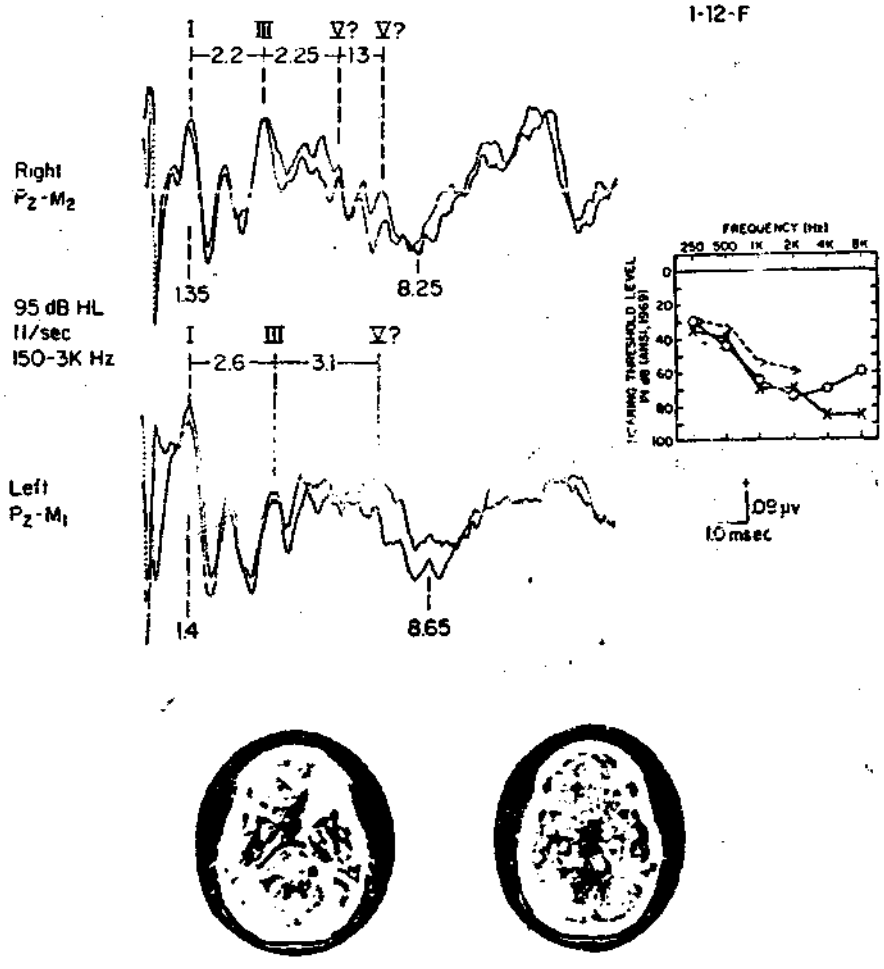


FIGURE [redacted]

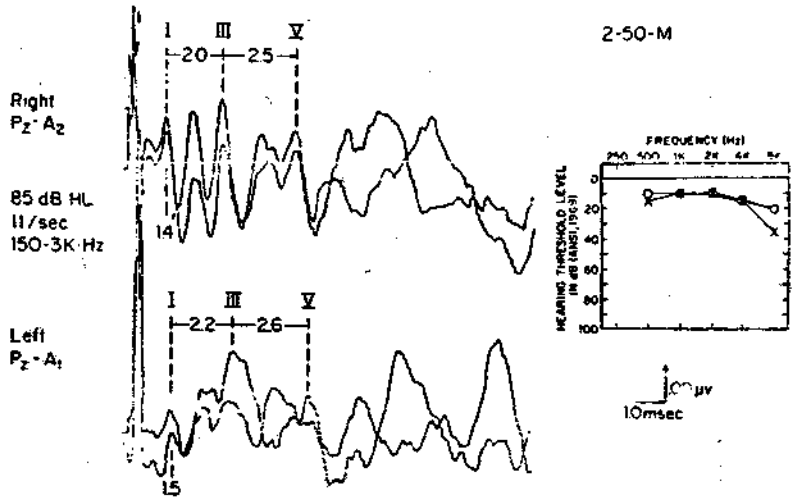
Case [redacted]: 12-year-old female with an upper brainstem tumor. CT scan shows enlargement of the midbrain with involvement of the pons (arrows). The audiogram reveals a severe, bilateral sensorineural hearing loss, congenital in origin. ABRs show abnormal waves IV through VII bilaterally with abnormal I-III interpeak latency on the left side.



[redacted] ABRs were repeated with no significant changes relative to the first tests. The patient continued to deteriorate after initial transitory improvement following the insertion of a shunt for the hydrocephalus. A year later the patient died. An autopsy revealed a pinealoblastoma which had replaced the pineal gland and had metastisized to the cerebellum, splenium of the corpus callosum, spinal cord, and leptomeninges with pressure on the quadrigeminal plate of the midbrain.

FIGURE [redacted]

Case [redacted]: 50-year-old male with an upper brainstem infarction. CT scan shows a lucency in the midbrain and pontine areas (arrows). The audiogram reveals normal hearing bilaterally. ABRs show bilaterally prolonged III-V and I-V interpeak latencies with reduced amplitudes on the left side compared to the right.



AUDITORY BRAIN STEM RESPONSE IN MULTIPLE - SCLEROSIS

Introduction:

ABR has been used as a nominative electrophysiological procedure in the detection and diagnosis of neurological disorders. ABR wave components show minimal subject variability and are easily replicated, and appear insensitive to attention, sleep, sedation or general anesthesia. The value of brain stem response measurement lies in its ability to monitor neural conduction within the auditory mechanism and to objectively demonstrate subclinical lesions.

Multiple sclerosis produces widespread and well documented changes in brain stem structures. For this reason patients with multiple sclerosis provide an unique population in which to study the effects of brain-stem pathology on certain auditory tasks.

The diagnosis of multiple sclerosis is dependent on the clinical demonstration of at least two separate lesions in the central nervous system (McAlpine et al 1972; McDonald and Halliday, 1977). However in the early stages of the disease it is common to find only a single lesion by clinical examination. In order to improve the early diagnosis, both visual and auditory evoked potentials have been explored and proved to be useful in the detection of clinically silent lesions (Halliday et al 1973; Asselman et al 1975; Robinson and Ridge, 1977; Stockard, et al, 1977).

Prevalance of abnormalities:

The advent and development of electrophysiological measures resulted in a systematic approach to differential diagnosis in patients with various VIIIth nerve and brain stem lesions including multiple sclerosis (MS).

Studies by Robinson and Rudge (1975, 1977) Shanon, Gold Himmelfarb and Carzsso (1979), Starr and Achor (1975) and Lynn, Taylor and Gilroy (1980) indicated that a substantial number of patients with MS showed ABR abnormalities. The estimates of abnormalities range from 34% (Chiappa and Norwood, 1977) to 73% (Robinson and Rudge, 1975). These were classified as - definite, probable 6r possible MS.

Lynn et al (1979) showed that 75% definite, 33% probable, 29% - possible Mere MS patients with ABR abnormalities.

There is a higher rate of ABR abnormalities in patients with evidence of brainstem involvement as compared to no evidence of brain stem disorder.

Manifestation of brainstem abnormalities include internuclear opthalmoplegla, sixth or seveth nerve palsy, horizontal or vertical gaze nystagmus (Robinson and Rudge, 1977), dizziness, gait disturbance, cerebellar signs and sensory or motor abnormalities (Chiappa, Brooks, Harrison and Young, 1980). A study by (Stockard and Rossiter, 1977) has shown estimates as high as 93% with definite clinical brain stem involvement.

Types of ABR abnormalities:

1. Abnormality of symmetry
2. Delay in latency
3. Fragmented response
4. Decrease in amplitude or absence of peaks
5. Poor response reliability
6. Abnormal responses to changes in rate and abnormal latency - intensity function.

Latency and amplitude:

Chiappa, Young and Goldie (1979) report that 13% of 202 patients had abnormal 1-V separation, 55% had only wave V amplitude abnormalities and 33% had both abnormalities. Stockard and Rossitec (1977) - 69% abnormalities were related to latency and 31% - amplitude.

Interwave interval (IWI) latency abnormalities appears to occur in the III-V separation supported by Chiappa (1980), Lynn et al (1980), Shanon, Gold and Himmerfarb, (1981). But Shanon et al (1981) found that I-III interval to be prolonged more thaa 111-V interval.

Starr and Achor (1975) report that with the exception of wave I all of their MS patients showed reduced amplitude.

Peripheral nerve involvement:

New evidence has shown segmental demyelination (Pollack, Calder and Allpress, 1977) and abnormal refractory periods

(Hopf and Eysholdt, 1978) in the peripheral nerves of MS patients. Using ABR and EcochG to confirm wave I presence, Hopf and Maurer (1983) tested 71 Ms patients. Eight (11%) exhibited prolonged wave I latencies (73 SD). They attributed peripheral involvement to segmental demyelination of the distal part of the acoustic nerve.

Anatomical support -

The neuroglial - neurolemmal junction of the acoustic nerve is located 7 to 13 mm distal to the brain stem near the fundus of the internal meatus. (Nager, 1969). This junction may prove to be the functional site of peripheral demyelination.

Repeatability: Test-retest repeatability in normal is excellent with highly reproducible wave form morphology and latency. But a common finding in MS patients is poor repeatability of ABR results with investigators reporting poor agreement on retest in - 80% of MS patients (Graza et al 1982, Nodar, 1978, Prasher and Gibson, 1980, Robinson and Badge, 1980).

Latency-intensity eaffects: Parving, Elberling and Smith (1981) studied 15 patients with definite Ms using EcochG, ABR and an objective technique of analyzing electrophysiological data.

They found difficulty in the ability to assign values to ABR components and latency intensity function was abnormal for both latency and amplitude at low stimulus intensities despite normal hearing.

ABR and Psychophysical data:

Clinically the authors have observed patients for whom no repeatable ABR could be recorded who had normal hearing sensitivity with 100% word discrimination scores in quiet. Patients with abnormal just -noticeable difference had abnormal ABRs on atleast one side. Hence this suggests that the same auditory structure of the brain stem subserves intraaaral time discrimination and short-latency click evoked potentials.

ABR Finding:

There are a wide variety of ABR results possible in multiple sclerosis with disseminated lesions possible at all levels of the brain stem. Normal wave I pattern proves that peripheral portion of the auditory nerve where the myelin sheath is formed by Schwann cells rather than glial cells is not affected. (Hausler and Levine, 1980). The III-V internal is likely to be prolonged since the area between the superior olivary complex and the inferior colliculus is the "longest tract of white matter inthe CNS and therefore the most susceptible to the effects of demyelinacting disease (Shanon et al 1979) Also demyelinization results in increased refraction period of transmission of the axons with reduced conduction velocity along the central auditory pathways; yielding delays in latency of progressive waves of the auditory evoked potential.

Recording of ABR has been found to be reliable method in the assessment of brain stem lesions (Starr and Achor, 1975, Starr and Hamilton 1976? Thornton and Hawkes, 1976, Stockard and Rossiter, 1977? Stockard et al 1977). Thus a 65% of patients suffering from a definite or suspected MS, BSER were abnormal as judged by latency and amplitude parameters (Robinson, Rudge, 1977? stockard, et al.1977).

In a report on the early components of ABR in patients with MS, Robinson and Rudge (1975) found that 22 patients of 30 had abnormal responses judged by latency and amplitude although none was clinically deaf. According to further investigations (Robinson and Rudge, 1977), 65% of the patients with definite Ms had abnormal BSER and it was stated that latency was a more reliable discriminator of abnormality than amplitude. They found component V to be the most important one being abnormal in every patient in whom any abnormality was found. In some patients other components were also altered, but in none was component I, thought to arise from the eight nerve - abnormality (Rudge, 197).

Relating the BSER to the clinical examination the method was found to be highly sensitive as 82% with definite brain stem affection had abnormal responses. (Robinson and Rudge, 1977).

Thornton (1976) found systematically increase latency and a much flatter shape of the components in 1 patients with MS. Based upon further investigations, 90% of with definite MS had increase latency of responses (Thorntal et al 1978) Starr

and Achor (1978) refused to an investigation performed at university of California. In this investigation, a measure of central conduction time was used to help define brain stem alteration in MS and was found abnormal in approximately 90% of the tests.

Maureen Hannley, James F.Jerger, Victor M.Rivera (1983) took 20 subjects and divided into 3 groups.

Group-A - had 5 subjects with essentially normal ABR on both ears.

In 3 subjects, waves I1-V were observed with absolute and inter-peak latencies falling within 2 standard deviations of the norm established 2 subjects showed wave V at a slightly prolonged 0.1 m.sec latency on one ear.

Group-B - consisted of 7 subjects with wave III present bilaterally, but prolonged by an average of 0.4 - 0.6 ms beyond the range encompassing 95% of normal results ($\pm$ 2SD). 2 subjects in this group 1 and 3 showed no repeatable wave V an one or both ears.

Group-C consisted of 8 subjects in whom wave III as well as subsequent waves, was absent from one or both ears.

In all subjects the latency of wave I fell within the normal range. Abnormalities in latency were confined to the later waves and to the interpeak intervals. In group B the I-III interpeak latencies were prolonged by 0.1 - 0.8 in 8 of

FIGURE [redacted].
ABR responses obtained on a normal and several MS subjects. Responses were obtained and are displayed under identical conditions. [redacted]

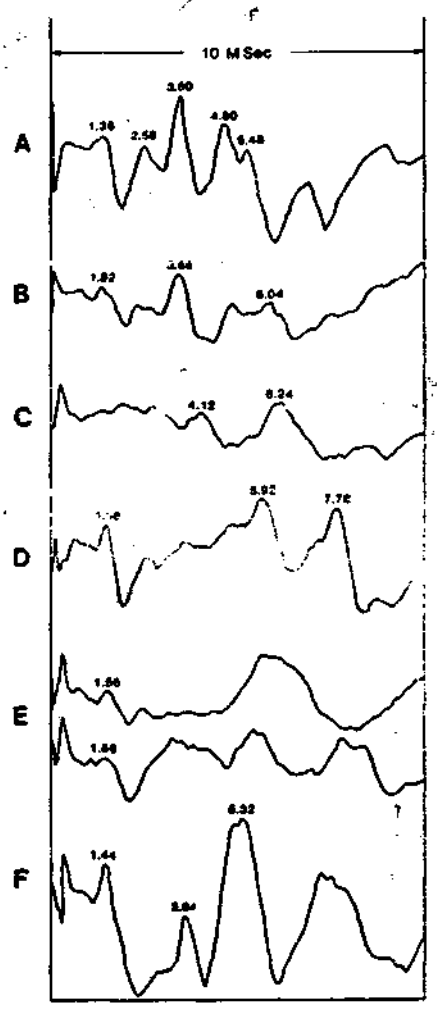


FIGURE [redacted].

ABR responses obtained from a patient with MS using click rates from 10 to 80/s. Note the abnormal change in response morphology that results from an increase in click rate.

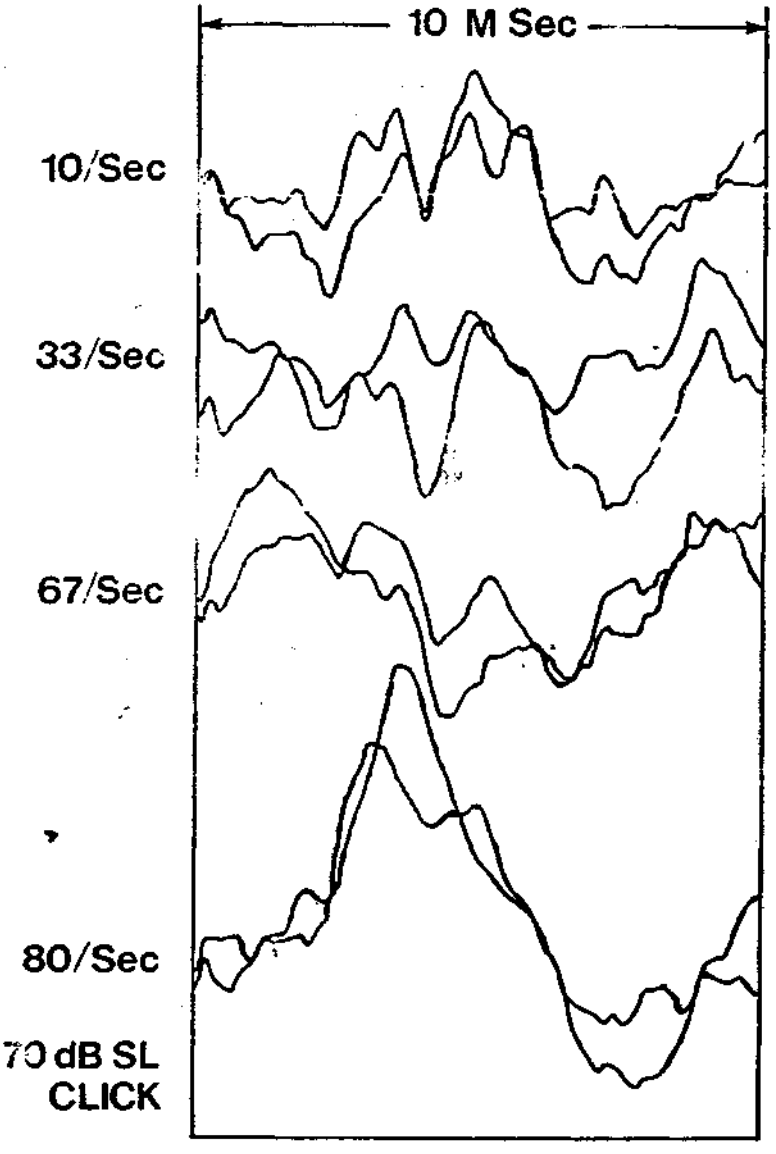
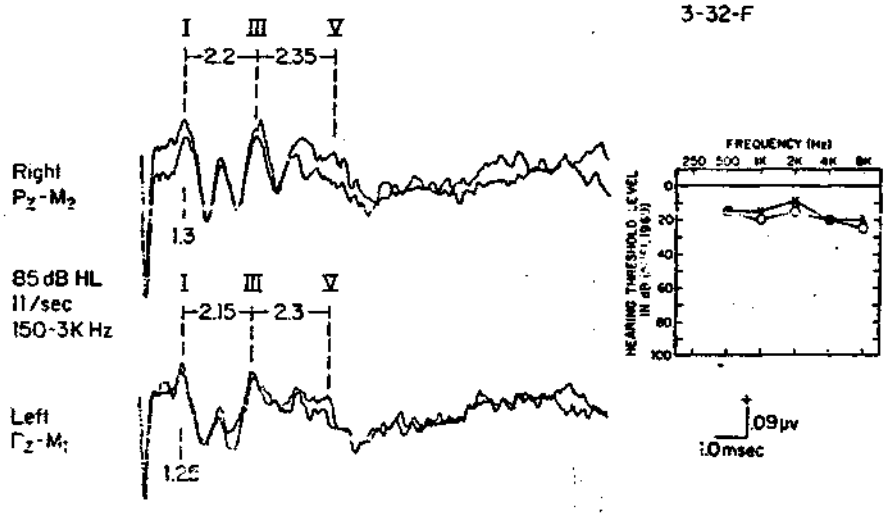


FIGURE [redacted].

Case [redacted]: 34-year-old female with multiple sclerosis. The audiogram shows normal hearing sensitivity, bilaterally. ABRs demonstrate bilaterally prolonged III-V and I-V interpeak latencies with reduced amplitudes for the IV-V wave complex and waveform distortion.



AUDITORY BRAIN STEM RESPONSE IN NEUROLOGIC STATUS OF COMATOSE PATIENTS

Introduction:

There is an important need for a clinical method of objectively monitoring neurologica status in patients, comatose as a result of severe brain injury. There are 10 criterias for meeting the clinical utility and feasibility. These are as follows:

1. Noninvasivenss
2. Safety
3. Mobility (Assessment can be carried out at bedside)
4. Brief test time
5. Objectivity (test results can be quantified and subjected to mathematical/statistical analysis.
6. Reliability
7. Sensitive and comprehensive index of neurologic status. (This method yields information on multiple levels of the central nervous system and is sensitive to changes, even subtle ones in neurologic function.
8. Independence of level of consciousness (Results are not-influenced by degree of coma).
9. Resistance to drugs (Results are not influenced by commonly used medical therapies in severe brain-injured patients, including paralyzing agents, sedatives and barbiturates.
10. Cost effectiveness.

The ABR meets these criteria and has multiple applications in monitoring neurologic function of comatose patients.

Pulmonary, cardiovascular and nutritional system functions and intracranial pressure are routinely monitored in comatose, brain-injured patients in the intensive-care unit. An adequate cardiac output and excellent cerebral oxygenation are reassuring but do not directly reflect brainfunction. Although ICP below 20 mm Hg is considered beneficial a substantial portion of comatose patients with severe brain injury do not have elevated intracranial pressure. Thus there exists an extremely important need for clinical feasible monitor of msuronal integrity, particularly a method that is sensitive to subtle changes in neural function.

Among the electrophysiologic procedures the somatosensory (SSEPs) and auditory evoked potentials (AEPs) have been applied with greatest regularity in comatose patients. The SSEPs and AEPs have peripheral, brainstem and cortical neuroanatomic components which are relatively easy to interpret and can be reliably recorded in an ICU setting from patients that are deeply comatose (with eyes closed) and often sedated or under the influenceof intoxicants or therapeutic CNS suppressants.

Factors influencing ABR measurements in the ICU:

The ABR is influenced by myriad factors, including subject characteristics (age, sex, auditory status, body temperature), stimulus parameters (eg. intensity, frequency, duration rate) recording parameters (electrodearray, neural filtering) and drugs.

FIGURE [redacted].
Glasgow Coma Scale, GCS (Jennett &-Teasdale, 1981). A GCS of 8 or less defines sev e re brain injury and comatose state. [redacted].

Glasgow Coma Scale

Eye Opening	Spontaneous	4	**Total Glasgow Coma Scale Points**
	To Voice	3	
	To Pain	2	14-15=**5**
	None	1	11-13=**4**
Verbal Response	Oriented	5	8-10=**3**
	Confused	4	5- 7=**2**
	Inappropriate Words	3	3- 4=**1**
	Incomprehensible Words	2	
	None	1	
Motor Response	Obeys Command	6	
	Localizes Pain	5	
	Withdraw (pain)	4	
	Flexion (pain)	3	
	Extension (pain)	2	
	None	1	
Total Trauma Score			**1-16**

TABLE [redacted].
Relationship between Glasgow Coma Score (see Figure 14–1) and initial auditory brainstem response (ABR) outcome in 83 comatose, brain-injured patients.

Glasgow Coma Score	Auditory brainstem response[a]			
	No response[b]	Abnormal		Normal
		Missing wave component	Latency prolongation	
9–10				3
7–8				15
5–6		1	2	27
3–4	14	1	3	15

NOTE. ABR data were obtained within 48 hours post-injury.

[a] ABR symmetry was observed in 62 (75%) of the patients. With asymmetrical findings, data from the better side were tabulated.

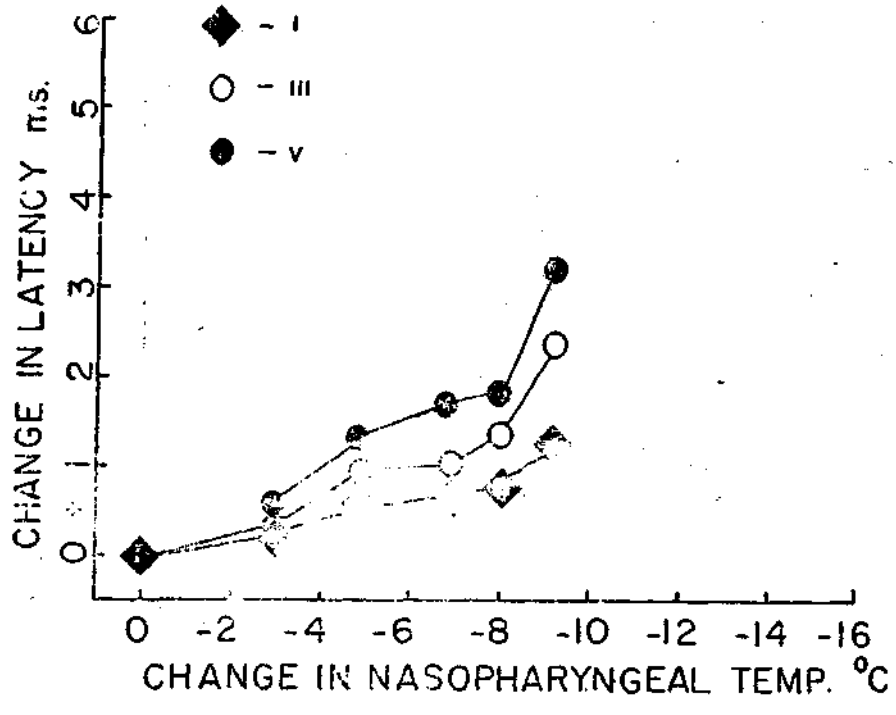
[b] Wave I only (62% of category) or no response (38% of the category).

The five mainfactors of concern with the comatose patient in the ICU environment are the degree of coma, patient characteristics, environmental contaminents, otologic pathology qnd therapeutic drugs.

I. Coma: A commonly used clinical grading system for severity of brain injury is the glassgow coma scale (gCS). This was developed by Jenett and colleagues in 1974. The GCS is based on the evaluation of eye opening, verbal and motor responses to sensory stimulation. Patients with highest possible score (15) are grossly intact neurologically, where as patients with dowest score (3) are totally unresponsive to even painful stimulation. The accepted criterion for severe brain-injury is a GCS of 8 or less. Patients with severe brain injury are, therefore comatose and typically do not open their eyes do not vocalize (as are intubated for mechanical ventilation) and have only abnormal (posturing) motor responses to painful stimulation.

The ABR is not influenced by degree of coma in patients without primary or secondary brain stem injuries. Completely normal ABR may be recorded in these patients with GCS as low as 3. In 200 severely head injured patients, over 70% initially showed normal ABR. Abnormal ABRs were recorded in these patients with GCS of 3 to 4 because this group is more likely to have structural brain damage or brain stem dysfunction secondary to massive cerebral swelling. Among the patients with GCS of 3 are those meeting criteria for brain death. ABR patterns of brain death are discussed in the chapter.

FIGURE [redacted].
The relationship between body temperature and auditory brainstem response components.



It is important to keep in mind that a GCS of 3 does not imply irreversible and eminent death or a poor neurologic outcome.

Patient characteristics:

1) Body temperature - The body temperature must be routinely taken into account in the interpretation of ABR findings in comatose patients. Comatose patients especially those in barbiturate - included coma, tend to have lower than normal body temperatures and may for this reason show increased ABR latencies. Body temperature is usually monitored continuously in ICU patients and the digitally displayed value should be recorded at the start of the evaluation and periodically checked throughout testing. Body temperature documentation is extremely important in interpretation of subtle changes in serially recorded ABR data.

2) Alcohol - Blood alcohol levels are often excessive upon hospital admission in traumatically head injured patients. Alcohol abuse is frequently an important factor in motor vehicle accidents and accidental falls. In normothermic patients alcohol probably does not seriously affect the ABR (squires, Chu and Starr in 1978) although chronic alcohol abase may have an effect. This is again discussed in the chapter

3) Neuromuscular state - The neuromuscular status varies in the comatose patient. Patients is deep coma with Glasgow coma scores of 8 or less rarely move spontaneously to light touch

or acoustic stimulation, some are flaccid. Following severe brain injury the patient is intubated and placed on mechanical ventilation. Chemical muscle paralyzing agents (eg. metacurine or pavulon) are frequently administered during this period. For these reasons, muscle artifact is an infrequent problem in ABR measurement in the acute - phase after severe brain injury.

In less severely injured patients or those recovering neirologically, ABR recordings can be seriously contaminated by excessive muscle movement. Decorticate or decrebrate posturing, torsion of neck musculature or a generally agitated highly active state can all introduce an unacceptable amount of artifact. The best solution to this artifact problem is induced patient relaxation during testing by means of a sedative. Further more, the post auricular muscle (PAM) artifact appears to be more common in muscularly active or tense patients. Muscle paralyzing agents, when medically appropriate reduce the influence of muscle contamination including the PAP reflex, if sedatives or chemical paralyzing agents cannot be used or are not effective, the deleterious influence of muscle artifact on the response can sometimes be reduced by more restricted high-pass neural filtering - for example changing the filter setting from 30 to 150 or even 300 to 3000Hz neural filtering well also alter amplitude and latency characteristics of the ABR (Bastan and Ainslie, 1980; Laukli and Mair, 1981). The use of artifact

rejection features and increasing the number of averages will contribute to signal enhancement and noise reduction.

ENVIRONMENTAL CONTAMINANTS:

The key factors for successful ABR measurement in an ICU are quality instrumentation and a flexible test protocol. Airborne electromagnetic interference and 60Hz line noise are not uncommon in an ICU. There are numerous sources of electrical artifact close to the patient, including fluorescent light, mechanical ventilators, monitoring devices and thermal blankets. Also, other sources of electrical interference may be located adjacent to, or above or below the ICU, or share power lines with the ICU. Precautions have to be taken to reduce the deleterious influence of electrical artifact.

Inspite of the precautions in electrode type and placement 60 Hz 'hum' and high frequency 'snow' may be present in ABR measurement still. Therefore a power outlet is used at a nearby empty bed. Combination with digitally smoothing and adding acquired, replicated averaged waveforms, generally yields a valid interpretable ABR.

OTOLOGIC PATHOLOGY:

Peripheral auditory abnormalities are not uncommon following traumatic brain injury (Grove, 1947? Hall, et al 1982) clinical findings and records confirm the high incidence of otologic pathology and immittance abnormalities in severe head injury (Aguilar, Hall and Mackey-Hargadine, 1983; Hall et al 1982).

In most cases ABR assessment of patients in ICU is carried out for evaluation of CNS status, rather than peripheral auditory function. Circumaural earphone cushions were used to reduce the likelihood of collapsing ear canal walls. In patients with excessive head dressings, or neck collars which partially cover the ear, use a miniature insert transducer. Patients with evidence of middle ear pathology by otologic examination or air conduction. ABR stimuli are assessed by bone conduction ABR, mainly in an attempt to observe wave components, I,III and V and therefore define brain stem function.

THERAPEUTIC DRUGS:

The commonly used drugs in comatose ICU patients that act on the nervous system are chemical paralyzers, sedatives, anticonvulsants and barbituarates chemical paralyzing agents do not adversely effect ABR measurement and eliminate bothersome muscle artifact. Likewise latency of ABR does not appear to be influenced by sedatives (eg. Haldol, Morphine) or therapeutic doses of anticonvulsants (eg. Dilantia).

The possible influence of high dose barbiturates on the ABR has been studied experimentally (Bobbin, May and Lemoine, 1979, Cohen and Britt, 1981? Suttan, Frewen, Marsh Jaggi and Bruce, 1982) but has not been systematically investigated in comatose, brain-injured patients.

ABR is extremely resistant to the effects of high dose barbiturates, clinically significant changes in ABR during barbiturate

coma, then may be attributed to neurologic improvement or deterioration.

MONITORING NEUROLOGIC STATUS WITH ABR:

Applications of the ABR in comatose patients are varied. ABRs are often requested for patients with CT evidence of impending serious neurologic deterioration (eg. apparent compression of perimesencephalic cisterns and rostral brain stem, particularly when their medical therapy includes paralysis or barbiturates. ABRs can be used in the determination brain death and hence contribute to the medical management of patients. Findings of gross ABR abnormalities, coupled with supplemental clinical evidence of extensive neurologic dysfunction lead to the decision to provide supportive care management Or to initiate the assessment of candidacy for organ donation.

MEDICAL MANAGEMENT AND NEUROLOGIC DETERIORATION:

ABR findings are useful in management of acute brain injury. In approximately 20% of the patients, medical or surgical therapy has been initiated upon the development of ABR abnormalities. In other patients surgical or medical intervention dictated by CT has been postposed or deferred entirely on the basis of consistently normal ABRs, particularly in patients with unstable ICP or some contraindication to surgery such as sepsis.

Initial ABR abnormalities (slight wave III-V prolongation) precede neurologic (pupillary) changes.

ABR abnormalities can reflect transtentorial hermiation associated with increased intracrnial pressure (ICP). There is experimental evidence of a relationship between the ABR and increased ICP(Klug, 1982; McPherson, Blanks and Foltz, 1984). But Keith, Jabie and Heerse (1983) reported that ICP upto 50 cm of H_2O did not affect clinical ABR recordings. Cerebral perfuslon pressure (i.e. mean arterial pressure minus ICP) is the critical factor, rather than ICP alone. Increases in ICP with associated increases in arterial pressure may not produce ABR abnormalities. Sohmer et al 1983 found that persistently reduced cerebral perfusion pressure below 60 mm Hg approximately leads to ABR abnormalities and below 10 mm Hg the ABR is usually no longer recorded. Progressive brain stem ischemia is the pathophysiologic basis for this finding (Hassler, 1967).

The ABR wave I and II components may be observed in patients meeting clinical neurologic criteria for brain death and with no measurable cerSbral blood flow . This observation supports evidence Erom depth -electrode studies in humans (Holler, Jannetta, Bennett, and Holler, 1981) and recent pathologic ABR findings (eg. Garg Harkland and Bustion, 1982) suggesting the wave II component arises from the intracrnial portion of the eighth cranial nerve rather than the cochlear nucleus. Later, with further increases in ICP and decreases in vertebrobasilar cirulation and blood supply to the sensorineural apparatus (Larsen, 1982) only wave I is usually observed or there is mo measurable peripheral component.

Inexplicably, with severe brainstem dysfunction as in deep barbiturate coma - there may be an abnormal augmentation of ABR wave I amplitude. The phenomenon has been observed in patients during neurologic decompensation and sepucalates on the possibility that it reflects suppression or elimination of the inhibiting influences of brainstem efferent components of the auditory mechanism (Musiek Weider, and Mueller, 1983). Finally, the investigation of these complex - interactions between pathophysiology and ABR have apparent clinical application and long-term implications for basic neuroscience.

AUDITORY BRAIN STEM RESPONSE IN SOME MISCELLANEOUS CONDITIONS

1. ABR in Hereditary motor - sensory neuropathy:

It involves degeneration and atrophy of peripheral motor and sensory neurons. In addition there is usually evidence of primary destruction of anterior horn cells or posterior root ganglia. One of the best known of these neuropathies is Charcot-Marie tooth disease.

ABR elicited from five patients with charco^ Marie tooth disease demonstrated increased absolute latency of waves I to V, increased IPIS from I-II and III or reduced amplitude of waves 3V and V (Garg, Markland and Bustion 1982? Satya-Murthy, Cacae and Hanson, 1979). In three of these cases morphology was normal for all the waves and in all five cases III-V IPI was normal. Abnormalities were attributed to pathophysiological processes involving the auditory nerves and spiral ganglia.

2. Charcot-Marie tooth disease:

Charcot Marie tooth disease is a hereditary disease belonging to a broad spectrum of degenerative diseases that include olivoponto-cerebellar, cerebelloparenchymal and spinocerebellar disorders and neuropathies. There is chronic degeneration of peripheral nerves and roots resulting in distal muscle atrophy that begins in the feet and legs and later develops in the hands. There is extreme atrophy of the anterior tibial and calf muscles and wasting of the lower thigh muscles.d Deep tendon reflexes are

usually diminished to absent. The disease may become progressive and severs or may spontaneously arrest at any time.

ABR findings: Questionable wave v responses were present, for example waveform morphology was poor and absolute latency was abnormal and around 6.5 ms. This denotes auditory nerve dysfunction brain stem dysfunction or both but the greatest deficit being in the central auditory system.

3. ABR in spinocerebellar degeneration

Several studies have reported the influence of spinocerebellar degeneration of ABR. These studies have been limited primarily to Friedrech's Ataxia and Olivopanto-cerebellar atrophy.

The major cites of degeneration in Frieddaich's Ataxia are the cortico-spinal tracts, dorsal root ganglia and the spinocerebellar tracts, Symptoms include ataxia, impaired position and vibration sense hypotonia and pes cavua. ABRs elicited from patients with Friedereich's Ataxia have beea categorized as being normal with an absence or prolongation of the early or late components.

Category - 2 ABRs have been interpreted as indicating degeneration primarily within the spinal ganglion (Satya-Murti, Cacace and Hanson, 1980) or within the cochlear nucleus and SOC (Shannon, Himelfarb sad Shlomit, 1981). Category-3 data were consistent with a primary site of degeneration within the brainstem.

The relation between duration of disease and presence of hearing loss who determined. The patients were those evaluated at KUMC and those adequately described in the literature (Pederaen and Trojaborg, 1981; Satya-murti et al 1980, Shannon et al 1981y Taylor McMenamin, Andarmann et al 1982; Jabarri Schwartz, McNeil et al 1983; Nuwver, Perlman, Packwood et al 1983). The only significant correlation was between the presence of a hearing loss and ABR category. If hearing was normal, 20% of the patients yielded a category 2 response and 80% a category. If a hearing loss was present 69% fell within category 2 and 31% in category 3.

The major sites of degeneration in olivopontocerebellar atrophy are the brain stem and cerebellum symptoms include ataxia of gait and fine movement with LMH and brain stem signs. The literature describes the ABR elicited from 10 patients diagnosed with OPCA (Gilory and Bynn, 1978, Nuwer et al 1983; Satya-Murti et al 1980). In 2 patients reported by Satya-Murti et al (1980) the ABRa were normal. The remaining 3 patients had absent components or prolonged absolute latency and IPIS. When ABRa abnormality occurred, they were occasionally asymmetrical

4. <u>ABR in patients with dementia of the Alzheimer type:(DAT)</u>

Alzheimer's disease or dementia of the Alzheimer's type is characterized by diffuse brain lesions including among other areas, the CANS. The primary site of CANS involvement in DAT is the temporal cortex (Gray matter) with little evidence of

white matter involvement. Lesion of the CANS theoretically result in impairment of auditory functions, either behavioral or eleetrophysiological subserved by the lesion area. It disrupts the function of CANS as a result of temporal lobe pathology. ABR and MLR were studied in a group of patients with DAT to determine whether a correlate of dementia existed in these electrophysiological potentials.

Comparison of absolute and interwave latencies on ABR and absolute latency and amplitude of the MLR in patients with DAT and normal aged controls showed no significant differences between groups for any measure. It was concluded that the temporal lobe atrophy and hypemetabolism seen in DAT is not generally sufficient be disrupt the generating of ABR and MLR potentials, however slow comtical and cognitive evoked potentials may be more sensitive to CANS impairment in DAT.

The failure to discern significant group differences in ABR values between normal aged subjects and patients with DAT relates directly to the predominant cortical pathology of this disease. But there is evidence that some brain stem or mid brain nuclei are abnormal in Alzheimer's disease. In particular the corus coeruleus and dorsal raphe nuclei have been shown to be pathological in patients with DAT.

These nuclei both of which are at approximate anatomical level of the nucleus of the LL are involved in cortical lesion. These nuclei are different in several ways from the nuclei of

the central auditory pathway in that they have direct projections to the cortex while auditory nuclei believed to be responsible far the ABR (i.e. cochlear superior olivary and lateral lemnesic nuclei) project to the thalamus rather than directly to the cortex.

The finding of normal auditory brain stem potentials is more consistent with the current understanding of the loci and nature of the pathology associated with Alzheimer's disease. But there were a few patients in whom the absolute or interpeak latencies on ABR fell outside of the normal distribution. It ia most reasonable to assume that these patients have subtle brain stem dysfunction affecting the CANS which was not apparent on CT scan. Such brain stem impairment might exist either as an unrecognized and rate component of DAT, or equally possibly as a phenomenon unrelated to the dementia.

5. ABR in Ramsay Hunt Syndrome:

Bright in 1831 first recognized herpes Zoster as a cutaneous manifestation of a disease of the nerve.

The first autopsy in 1861, by Von Baren sprung indicated a definite inflammatory lesion at the posterior root ganglion but it was Koerner in 1904 who first linked the triad of signs of vesicular eruption in the auricle, facial paralysis, and inner ear disturbance. However it was Ramsay Hunt in 1907 who investigated it in some detail and outlined a theory according

to herpetic infection of the geniculate ganglion was the cause of herpes zoster appearing at a certain area of the external ear which he tensed the "geniculate zone*. By farther investigations he proved that increasing pressure of the swollen, ganglion produced facial palsy and infection of the associated 8th nerve caused auditory symptoms.

ABR findings: Audiologic investigations of the patients have revealed hearing loss to the eoehlear origin and in some neural. Absence of recruitment by ABLB test was reported my Welsh and Welsh. In a ease without vesicular eruption. No TDT and ABLB and SISI indicated recruitment. Study carried out by Solmon Abromovich and Deepak Brasher in 1986. They took 13 patients from 21 to 73 years. And found vesicular eruption facial palsy and eochleovestibular symptoms. 7/13 had abnormal ABRs and 6/13 had interwave intervals prolonged from the normal. In 1 patient the brain stem response morphology was abnormal. In another patient no response because of severe hearing loss was obtained.

In all the patients tested ABRs were presented only on the affected side. Striking features being the prolongation of the latencies of waves III aad V with the preservation of wave I which clearly suggest retrocochlear involvement greater abnormal in patients with complete facial paralysis.

Hence the recording of ABRs has clearly demonstrated retrocochlear involvement in patients with aural herpes zoster, the

latencies of wave III and in particular, wave V were prolonged or morphology was abnormal. The latency of wave I was within normal limits.

Brain stem or 9th nerve involvement can result in similar abnormality of ABRs therefore making the differentiation difficult. Small acoustic tumors that are clearly extrinsic and with out brain-stem compression can produce abnormally prolonged waves III and V. This would imply that in patients with aural herpes zoster with abnormal ABR the lesion may be at the level of spiral ganglion or the 8th nerve which may result in the deaynchronization and impairment of neural transmission. The abnormality of particular brain stem components may also be due to a lesion at the site of its generator or at a level preceding it. ABR detected in patients with aural herpes zoster may also reflect brain stem involvement, however it is not clear how distorted input from the nerve to the brain stem may affect the subsequent component generator.

These have been only six hostologic studies to date of herpes zoster limited to the temporal bone sections. The findings of Friedmann and Blackley et al indicated that the organ of corti, the ganglion in the modiolus and the 7th and the 8th serves can be affected in the case of aural herpes zoster. Head and Campbell later reported degeneration of the gasserion ganglion the sensory root of the trigeminal nerve and through the pons.

Inflammation of neural and perineural structures in herpes zoster could be a factor responsible for the underlying process of desynchronization and poor conduction which may result in prolonged interwave intervals of the brain stem components and abnormality of wave morphology. The abnormalities were seen only on the side of vesicular eruptions, these describes the effects of the varicella zoster virus on the auditory pathway.

6. Alcoholism:

There are 2 mechanisms by which alcohol influences the ABR structural changes include pseudobulbar palsy and quadriplegia due to central pontine myelinolyais and progressive ataxia due to cerebellar/degeneration. Of the 66 eases reported in the literature approximately 42% demonstrated increased I-V IPIS (Chu, Squires and Starr, 1982? stockard, Rossiter and Weiderholt, 1976). The incidence of ABR abnormalities was related to the type and number of neurological complications, subject's age and cerebellar atrophy revealed by CT scans.

Alcohol induced hypothermia influences the ABR by increasing IPIS, consequently, when recording the ABR of alcoholics it is necessary to monitor body temperature during the procedure sad preferably at more than one location. If hypothermia cannot be controlled, it has been suggested that 0.15 msec should be subtracted from the I-V IPI for every degree centigrade the body temperature falls below 36 degree (Rutschg et al, 1983).

7. Brain death:

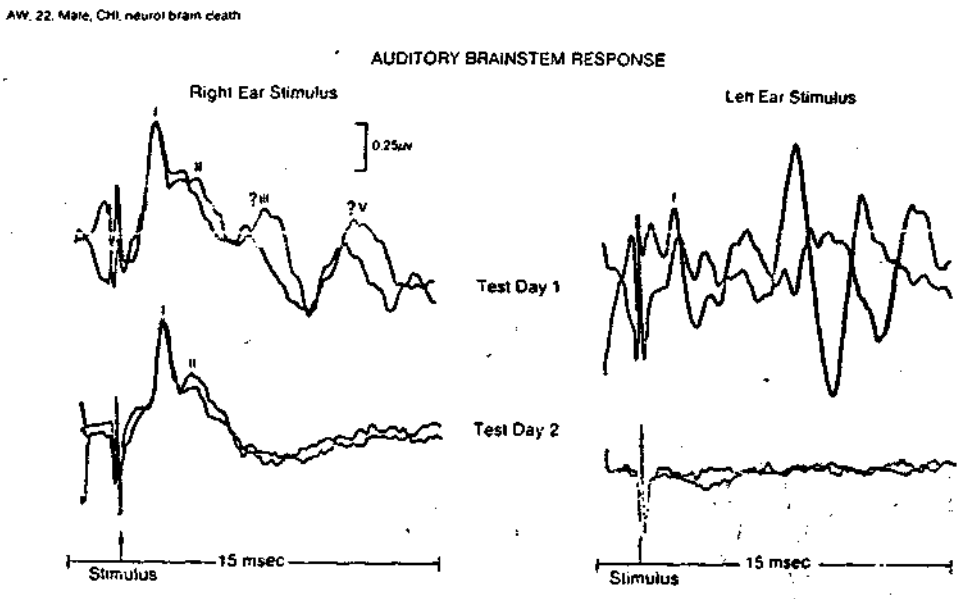
ABR is clinically useful ancillary test in the determination of brain death. Unlike neurologic examination and EBB. ABR measurement is not invalidated by aeuite medical therapies such as chemical paralyzing agents and high-dose barbiturates It is possible to record a well-formed reliable ABR with barbiturate blood Bevels in excess of 200 mg/L with suppression of all neurologic signs of CHS integrity. Furthermore ABR outcome is highly correlated with the results of nuclear CEP studies in the determination of brain death. Patients with normal ABR have normal cerebral blood flow (CBF) and conversely patients with no ABR or only a wave I component have no cerebral circulation.

The finding of a wave I component without wave III or V is the most clear cut ABR outcome. The majority of the cases were managed with high dose barbiturates. In 1/3 series the ABR was used in determination of brain death, always In conjunction with nuclear cerebral blood flow studies.

Patient 1 43 year old woman who was involved in motor vehicle accident (suffered multiple trauma including severe facial crush, chest, injury and closed head injury).

The ABR was well with in normal limits. Follow-up after 3rd and 5th days again showed normal ABR. The patient's condition was subsequently aggressively managed and improved neurologically. Evaluation of brain death was initiated on the basis

FIGURE [redacted].
Auditory brainstem response (ABR) recordings on two successive test days for a 22-year-old male meeting clinical neurologic criteria for brain death.



of severe neurologic decompensation/evidence of apparently fatal injury by computed tomography on physiologic factors (Grossly elevated ICP hypotension, hypoxia etc)with brain death patients. The patients demonstrating this pattern have fulfilled clinical neurologic criteria for brain death a non have survived with discontinued ventilation support. This finding is interpreted as evidence of irreversible brain stem destruction (dysfunction).

The ABR wave II may also be observed in patients with no brain stem reflexes and no CHP. This may be an evidence that wave II component arises from the proximal portion of the 8th cranial nerve rather than cochlear nucleus. The persistence of these ABR components despite elevated ICP and depressed blood pressure in consistent with experimental evidence of a differed tial sensitivity of peripheral vs central auditory structures to severe CNS pathephysiology.

The augmentation of ABR wave I in severe brain stem dysfunction is a characteristic features in some cases of severe head injury. Perhaps the usually large amplitude of wave I reflect loss of efferent auditory CHS inhibition of cochlear activity. Leas likely is the possibility that elimination of acoustic reflex are activity by widespread brain stem pathology results in increased cochlear activity.

8. ABR in leukodvatrrophy:

It is a white-matter disease characterized by progressive ataxia and paralysis. Abnormal ABRs have been elicited ia two forms of disease - Adrenoleukodystrophy (ALD) and metachromatic leukodystrophy (MLD).

ALD occurs only in males and is the result of atrophy of the adrenal cortex and ballooning of cortical cells. ABRS eliatited from 6 patients with ALD were abnormal in five. Abnormalities included prolonged I-III,III-V, or I-V IPIS.(Fariello and Chun 1979, Garg at al 1982, Ochs, Markan and BeMeyer, 1979) and missing components (Ochs et al 1979).

9. ABR in Wilson's disease:

It is a rare inherited metabolic disorder characterized by an accumulation of copper in the liver, central nervous system, cornea and kidneys. Neurological symptoms include rigidity, ataxia and choreoathetoid movements. One study has reported the effect of Wilsons disease on the ABR (Fugita, Hosoki and Miyazoki, 1981). ABRs were elicited from six normal hearing patients with this disease, three that were symptoaa - free and three that were not. ABRs were normal in symptom - free pttiaata While responses elicited from the remaining three patiaata showed varied abnormalities. In two out of three patients with symptom absolute latencies of waves II through VI and I M S e% 1-111, 111-V were prolonged* In the remaining one patient the absolute latencies of waves III through V were prolonged. The

increased latencies were attributed to brainatem lesions, the locations of which were not identified.

All of the patients showed disturbances of consciousness and a score of sevea or less on the Glasgow coma scale. The ABRs were classified as 1) Normal (N=27), 2) prolonged or Missing wave V (N-13) (3) Missing waves II-V or I-V (B-23). Of the 27 patients that did not show brain stem dysfunction, 22 (813) yielded a type 1 ABR and the remaining 5 (19%) a type 2 ABR. The 36 remaining patients yielded either type 2 or type 3 ABR.

Results hence indicate that when clinical signs suggest involvement of lower portions of the brainstem, the ABR becomes progressively more abnormal. This relation between site of lesion and ABR type emphasizes the relatively poor sensitivity of the ABR to high brain stem abnormadties.

SUMMARY

The tentacles of ABR hence have gripped the area of audiology maximally.

Starting from the studies on generation of nerve potentials to the clinical application. Farther boring deep into the neuro-otologic implications. The detailed overview of which has just been provided in the previous chapters.

In brief ABR helps in differential diagnosis of acoustic tumors depending on the tumor size and site of invasion (i.e. low brain stem or high brain stem!. Multiple sclerosis and other demyelinating diseases can also be studied extensively depending on the ABR findings. But most recently ABR is being used in ICU for monitoring the neurologic status of comatose patients.

The last chapter deals with ABR findings in some miscellaneous conditions affecting the various parts of the body and its effect on ABR.

Last but not the least ABR saga in neuro-otologic diagnosis has been, one of the most mystical studies of the era.

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