UNIVERSITY OF SOUTHAMPTON

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# Auditory Brainstem Response in Metabolic Disorders

by

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To my Family

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ABSTRACT

The validity of the auditory brainstem evoked response (ABER) technique as a diagnostic tool was investigated in metabolic disorders, hypo-thyroid, hyper-thyroid and diabetic patients. The aim was to show the effect of these diseases on the ABER components and to explore the mechanism by which the thyroid dysfunction and diabetes mellitus act on the auditory system. The research programme was formulated into four experimental studies:

1. ABER was recorded in 31 normal subjects using click intensities of 80, 70 and 60 dBSL (above individual threshold), with a repetition rate of 21 per s. From each record the latency, amplitude and interwave intervals of waves I, III and V were measured. The mean, standard deviation and 95% confidence limit for each component were obtained. There was no effect of age and sex on these parameters. The result of this study is in agreement with results in the literature.

2. In this study ABER was recorded in 21 hypo-thyroid patients. There was a prolongation of latency and a reduction in amplitude of waves III and V and a delay in brainstem conduction time (I-V) interval in relation to the normal controls ($p = 0.02$). These changes were reversed towards normal after replacement therapy with thyroxine when the temperature of the patients was raised to the normal level. Hearing impairment associated with hypo-thyroidism in this study was about 36%.

3. Twelve hyperthyroid patients were investigated using the ABER technique. There was no significant difference between hyperthyroid patients and those of normal ones. However the significant difference was clear between hyper- and hypothyroid patients ($p = 0.01$).

Recording of ABERs seems to be useful in distinguishing between euthyroid and hypothyroid subjects on the one hand and between hypo- and hyperthyroid patients on the other. However it is not helpful in distinguishing between hyperthyroid and euthyroid subjects.

The effect of hypothyroidism on hearing was most probably due to a reduction in the body temperature without any neurological deficit. The mean and standard deviation of the body temperature of the sample of hypothyroid patients who were tested was; $35.99 \pm 0.5°C$ and in normal controls; $36.9 \pm 0.19°C$.

4. The ABER was recorded in 13 insulin dependent diabetes mellitus (IDDM) patients with and without diabetic complications and with different durations of illness and blood glucose level. The findings of this study revealed that hearing impairment in the case of diabetes mellitus does not depend on the duration of the illness nor glycosylated haemoglobin (HbAlC). However, there is a relationship between the existence of diabetic complications and ABER abnormality. The ABER was found to be abnormal only in patients with the following complications: retinopathy; nephropathy and neuropathy. The effect of diabetes mellitus on ABER appeared to be retro-cochlear in the form of prolongation of the absolute latency and reduction of amplitude of waves III and V as well as the prolongation of the I-V interval. There is also prolongation of wave I latency in some patients. The findings of this study are in agreement with the theory which attributes the effect of diabetes mellitus on the auditory system to the microangiopathy in the brainstem tissue.

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# CHAPTER ONE

## INTRODUCTION

In the following chapters an attempt has been made to investigate the changes of parameters of ABER of the human auditory system in the thyroid dysfunction - hypo and hyper function - and in diabetic patients. In view of the published experimental data on humans and animals and results developed from closely related responses, it seemed that such investigation would provide a new interesting and useful addition to the field of clinical auditory research, and to the audiological diagnostic tests which is the aim of this study. The aim was to gain full advantage of a comprehensive review of the previous studies and relevant published reports of this subject. An idea on the ABER technique; what is it? what is the origin of its components, its clinical applications, its clinical diagnostic criteria and, finally, the advantages and disadvantages of this technique? This is made in Chapter 2. The aim of this study and the reason I chose to carry out the research programme are outlined in Chapter 3. The instrumentation and procedure of the ABER technique are well established in the literature. The main problem facing this technique was how to pick up the auditory potentials which are very weak in relation to the surrounding spontaneous electrical activity of the brain and muscular potential; that is to say how to improve signal-to-noise ratio. The ideal stimulus parameters and the best place electrodes attachment and the best conductor media were taken from the published reports of relevant research. The instrumentation and procedure of the ABER technique are described in detail in Chapter 4.

From the literature review it was clear that there are several factors which might affect the ABER recordings. These factors are not related to

the subject. They are related to the equipment, to the environment and to the stimulus parameters. To overcome these problems it was decided to investigate some normally hearing subjects of both sexes and at different ages in order to make the baseline with which the pathological recordings could be compared. The basis of the choice of normal subjects, the method, the results and the statistical properties of this investigation and the discussion of these results are described in Chapter 5.

As the aim of this study is to investigate the hearing impairment which might be associated with some metabolic disorders; thyroid dysfunction and diabetic patients were chosen for this study. The hypothyroid function which is now established to be associated with hearing impairment was comprehensively reviewed. This review, with the method by which the hypothyroid patients were investigated, the results of this investigation and the discussion of the results are described in Chapter 6.

What is related to the study of hyperthyroid patients, the literature review, the method and patients, the results of investigation and the discussion of these results are described in Chapter 7.

The last chapter in this study, Chapter 8, deals with diabetic patients, and includes a review of relevant reports, the results of the experiment on chosen patients, the method and a discussion of these results.

# CHAPTER TWO

# AUDITORY EVOKED POTENTIALS

## 2.1 Introduction

The electric responses arising from the auditory system as a result of sound stimulation of the ear are very weak in relation to the background noise that arises spontaneously from the surrounding brain. The recent development of small averaging computers has given a great deal of help in extracting these minute potentials and it has become possible to use these electric responses as a practical diagnostic tool.

During the past 15 years electric response audiometry has become an important and reliable clinical diagnostic tool in audiology, otology and neurology and is used in many clinics and research centres all over the world.

There are three types of electric response audiometry used in practice now: electrocochleography, brainstem electric response audiometry and cortical electric response audiometry. The electrocochleography is the measurement of potentials arising from the cochlea-cochlear microphonic, and summating potentials and auditory nerve action potentials. The auditory brainstem evoked response audiometry is the measurement of electric rsponses arising from auditory nerve and brainstem structures. The cortical electric response audiometry is the measurement of electric response potentials arising from the auditory system further to the brainstem structure.

The aim of this study is the use of brainstem response techniques as a diagnostic tool with patients of thyroid disorders and diabetic patients. The review will be given only in respect of brainstem electric response audiometry.

## 2.2 Auditory Brainstem Evoked Response

The auditory brainstem evoked response (ABER) is those electrical events which appear following auditory stimulation of the ear and are recorded from the scalp through electrodes; positive, negative and earth. They appear as a waveform of seven peaks with an amplitude less than one microvolt ($\mu$V) and latencies less than 10 ms (Jewett and Willston, 1971). Although these seven components are recorded by many workers, there are five main components which are found to be most constant (Thornton, 1975a).

Sohmer and Feinmesser (1967) for the first time could record the VIIIth nerve action potential; they reported the presence of two additional peaks. They could not give the precise interpretation for these additional waves and considered them either as repetitive auditory nerve action potentials or as arising from brainstem structures. Jewett (1970) could demonstrate, after experimental study on a cat, that the additional waves arose from brainstem structures. Then Jewett and Willston studied these responses in humans and could record a series of seven waves with latencies of less than 10 ms and amplitudes of less than one $\mu$V. They labelled them in Latin numerals as wave I to wave VII and gave name to the ABER technique as "far field" to distinguish it from the transtympanic electrocochleography which is considered as a "near field", as in the latter the electrode is attached near to the site of the origin of the waves.

As a result of both animal and human studies (Jewett, 1970; Lev and Sohmer, 1972; Buchwald and Huang, 1975; Thornton, 1975a,c; Starr and Hamilton, 1976; Stockard and Rossiter, 1977) the site of origin of the seven components has been suggested to reflect electrical activity for the following sites:

Wave I - from auditory nerve

Wave II - from cochlear nucleus

Wave III - from superior olivary complex

Wave IV - from nucleus of lateral lemniscus

Wave V - from inferior colliculus

Wave VI - from lateral geniculate body

Wave VII - from cortical radiation

A differing viewpoint was expressed following intra-cranial recordings in neuro-surgical patients (Moller, 1981). His findings indicate that wave II came from the proximal part of the VIIIth nerve; wave III from the cochlear nucleus and waves IV and V from the more peripheral nuclei of the ascending pathway than was previously assumed.

## 2.3 Clinical Application

Jewett and Willston were the first who suggeted the possibility of using the ABER technique in clinical application in 1971. Since then many studies on patients with normal and abnormal hearing were performed by many investigators at different clinics and research centres all over the world. These studies showed that abnormalities of ABER waveforms were indicative of auditory pathway pathologies (Thornton, 1975b; Starr and Hamilton, 1976 and Terkildsen et al., 1977) and reliability and usefulness of ABER technique as a tool of investigation and diagnosis in the fields of audiology, otology and neurology were established.

These are some examples of applications of the ABER technique in the fields of audiology, otology and neurology.

2.3.1 Audiology: The main application of ABER is;

a) In obtaining objective threshold and auditory acuity, ABER was found to be very useful in this purpose particularly with patients who cannot perform the subjective tests such as neonates, infants and young children (Hecox and Galambos, 1974), in mentally retarded and handicapped people (Buchwald and Squires, 1979) and with uncooperative subjects such as malingerers (Stein et al., 1979).

b) In a differential diagnosis between end-organ peripheral and central nervous system disorders.

Conductive hearing loss: it was found that conductive hearing impairment affects the absolute latencies of all ABER waves but does not change in the inter-wave latency (Coats and Martin, 1977; Coats, 1978; Chiappa et al., 1979). It was reported that there is prolongation of wave I in the case of conductive hearing impariment (Sohmer and Cohen, 1976). The increase in latency of the wave I and IV/V complex is because the signal intensity is reduced in the cochlea (Stockard et al., 1979; Glasscock et al., 1979). By plotting the input/output function curve of wave V in the case of conductive hearing impairment, it is shown to be parallel to but displaced from the normal input/output function curve. The amount of this displacement is the amount of conductive hearing loss (Brackmann, 1977).

Sensorineural hearing loss: In the case of cochlear lesion, the recruitment phenomenon is frequently observed and is often manifested in ABER as an abnormal rapid decrease in wave V latency with increasing stimulus intensity (Galambos and Hecox, 1977; Yamada et al., 1975). By plotting the latency intensity function curve it shows a dramatic deviation from the normal curve and gives a typical "L" shaped curve (Picton and Smith, 1978;

Galambos and Hecox, 1978). It was also found that the cochlear lesions affect the inter-wave interval; it was reported that the I-V interval is slightly shortened at lower click intensity (Coats, 1978; Coats and Martin, 1978; Chiappa et al., 1980).

Retro-cochlear disorders; In the case of retrocochlear disorders the abnormality of ABER is manifested as follows: loss of all or one waves after wave I (Jerger et al., 1980); loss of all waves (Jerger and Mouldin, 1978; Starr and Hamilton, 1976); abnormality of absolute latency and amplitude of one or more late waves, particularly wave V, so retrocochlear lesions tend to increase the I-V interval (Jerger et al., 1978; Sander et al., 1978 and Brackmann, 1977).

2.3.2 In otology: the main applications of ABER in otology are:

a) Detection of acoustic neuroma. ABER has been found to be the best audiometric test for the acoustic tumour detection. The success and reliabilty of this technique in the diagnostic process has reached about 98%. The mechanism of ABER diagnosis of an acoustic tumour depends on the fact that acoustic tumours stretch or compress the auditory nerve and this results in producing a delay in the response latency which can be easily detected by ABER (Selters and Brackmann, 1977).

b) Differential diagnosis between cochlear and retrocochlear pathologies as mentioned above.

2.3.3 In neurology: in this field the main application of ABER is:

a) Detection of brainstem tumours. It was found that brainstem lesions had an effect in inter-wave latencies I-III, I-V and III-V rather than the absolute latencies (Rowe III, 1978).

b) Multiple sclerosis. ABER found to be characterised in multiple sclerosis patients by erratic waveform and lack of reproducibility. Nodar (1978) reported that 20 out of 25 multiple sclerosis patients showed ill defined waveforms. He also reported prolongation of latency and/or reduction of amplitude of waves; and both prolongation of latency and reduction of amplitude (Maurer et al., 1980).

## 2.4 Clinical Criteria of ABER

As the results of various clinical studies performed at research centres worldwide, criteria of ABER were established as follows:

1. Absolute peak latency. Seven Jewett peaks to be measured in patients and to be compared with the normal ones, particularly wave V, for given sensation levels. Latencies 0.4 ms longer than normal suggest an abnormality along the auditory pathway of the tested ear (Starr and Achor, 1975).

2. Inter-peak latency. Starr and Achor (1975) were the first to suggest that central conduction time could be obtained by measurement of I-V, I-III and III-V inter-peak intervals. The inter-peak conduction time is found to vary with structural and physiological disorders of the brainstem (Starr and Hamilton, 1976; Stockard et al., 1976a). A delay in I-III interval would seem to indicate an abnormality in the pontine-meduallary region.

Prolongation of III-V may suggest an abnormality in the mid brain-pontine region, while a delay in I-V interval may indicate dysfunction in the brainstem without specific localising value (Rowe III, 1978).

3. Interaural peaks: this criterion depends on comparison between IV latency differences of two ears in the same subject. This criterion is useful in unilateral disorders. The comparison should be at the same intensity level. A latency difference greater than 0.4 ms is considered to be abnormal and suggests a dysfunction along the auditory pathway of the delayed ear (Selters and Brackmann, 1977).

4. Amplitude: the absolute peak to peak amplitude is very variable between subjects and even in the same subject, so using a ratio amplitude as a criterion to judge abnormalities of waves is more reliable than using an absolute amplitude (Starr and Achor, 1975; Chiappa et al., 1979).

5. Peak presence: any absence of ABER peaks will be considered abnormal and might determine the site of lesion, e.g. the absence of wave V suggests that the lesion is in the mid brain region. However, the absence of wave II and wave IV cannot be taken as a sign of abnormal response, it occurs even in normal subjects (Sohmer, 1984).

## 2.5 Advantages and Disadvantages of ABER

ABER is an easy performance technique; it does not need a medical person but it can be performed even by trained technicians. ABER is non-invasive, that is electrode placement does not require a surgical procedure. It can be utilized with any age range and at any place, even beside the patient's bed. ABER is not affected by the subject's state such as waking, sleeping or under general anaesthesia (Starr and Achor, 1975), so it can be

utilized with comatosed patients and with young children who very often need sedation to prevent excessive movement which interferes with recording. The ABER can be recorded using standard audiological masking rules. The time of recording can be decreased by increasing the click rate per second. It gives a useful index of information of peripheral and lower auditory pathway integrity (Hauslein et al., 1980). The ABER latency, particularly JV, is not interfered with by either the cochlearmicrophonic or the myogenic responses (Davis, 1976). The ABER is sensitive to the auditory nerve damage, for example acoustic neuroma (Rosenhamer, 1977; Selters and Brackmann, 1979).

Although the ABER has all the previous advantages, still there are recognised disadvantages such as the auditory response amplitude is very small in relation to the background noise and it is very sensitive to contamination by subject movement such as coughing, yawning, eye movement etc. This requires complete relaxation of the patient to avoid masking with these undesirable potentials (Davis, 1976). It is well recognised that the ABER does not give information concerning the auditory processing at the cortical level (Hauslein et al., 1980). ABER is known to be little influenced by the inner ear lesions (Rosenhamer, 1977; Selters and Brackmann, 1979). The patient with cochlear hearing loss does not meet the criteria as accurately as those with retrocochlear disorders (Bergenus et al., 1982). ABER recording requires sedation in some patients such as young children. In addition to the above mentioned disadvantages there are major problems with ABER; the time and the financial factors. It takes a long time to be recorded and the equipment involved is very expensive.

In spite of the fact that the ABER has been used extensively during the last few years and has come to play an increasingly important role as a diagnostic tool in otoloty, audiology and neurology (Starr and Achor, 1975;

Mogen and Kjaer, 1979; Shanon et al., 1981; Selters and Brackmann, 1977; Maurer et al., 1982; Rosenhall, 1981; Clemis and McGall, 1979; Robinson and Rudge, 1977; Chiappa et al., 1977; Stockard and Rossiter, 1977a; Maurer et al., 1980), but unfortunately the use of ABER as a diagnostic tool in patients with hearing disorders due to thyroid dysfunction and diabetic patients, has received very little attention. In this study the ABER will be utilized as a diagnostic tool in patients who are suffering from hypo and hyper dysfunction of the thyroid gland and diabetic patients, to see if there is any hearing impairment and to ascertain changes on the ABER criteria.

# CHAPTER THREE

# RESEARCH PROGRAMME

## 3.1 The Aim of the Research

The hearing impairment is established now to be one of the clinical manifestations of hypothyroidism. This was clear from reviewing and evaluating published reports dealing with hearing associated hypothyroidism (Howarth and Lloyd, 1956; Ritter and Lawrence, 1960; Hilger, 1956; Post, 1964; De Vos, 1963; Rubenstein et al., 1974). The impairment might be conductive, sensorineural or a mixed type. However it is mainly sensorineural and may occur at low, medium and high frequencies (Howarth and Lloyd, 1956; De Vos, 1963; Post, 1964; Bhatra et al., 1977; Debruyn et al., 1983). Hearing impairment associated with acquired hypothyroidism seems to be less severe than that with congenital hypothyroidism (Batsakis and Nishiyama, 1962; Ritter and Lawrence, 1960). There is an agreement about hearing impairment associated with hypothyroidism and its reversibility by replacing treatment with thyroxine. However the percentage of this association in the hypothyroid patient and the state of reversibility out of standardisation. It is well known that hypo-function of the thyroid gland may lead to anatomical and biochemical changes (see section 6.2) in the auditory pathway. However the exact site of lesion and if the anatomical abnormalities which are identified at this site could be responsible for, and explain the hearing impairments, and the effect of thyroxine imbalance on the auditory pathway are not yet universally agreed upon. In order to explore these points about which there are contradictions and discrepancies, a lot of study needs to be done. This study should include anatomical, biochemical, audiological and electrophysiological

points of view, and involve animals and humans under different conditions of hypothyroidism. From literatures reviews, (see section 6.2) one can find a lot of investigators who have performed these sorts of studies in an attempt to find any abnormalities throughout the auditory pathway, as a result of hypothyroidism, and to determine the exact location of these abnormalities and whether it is enough to explain the functional hearing loss. By reviewing the published reports, it is clear that there is a general agreement among them about the aetiology of conductive hearing loss associated hypothyroidism; the thickening and dryness of the tympanic membrane, myxoedematous changes of the middle ear and eustachian tube mucosa, the middle ear ossicular abnormalities and to the partial and complete obstruction of the oval and round windows. However the sensorineural hearing element associated hypothyroidism is not yet fully understood by organic damage (see section 6.2). Some workers attribute the cause of sensorineural hearing loss to the degeneration of spiral ganglion, there are others who impute that the abnormalities in hair cells are due to the immature development of the organ of Corti, to the tectoral membrane, or to the cochlear structure and ultra structural changes. From the literature review one can deduce that there is no general agreement among the authors about the morphological abnormalities of the sensory cells which might be enough to explain the sensorineural element. However the histological experiments revealed an overall agreement about the abnormality of the tectoral membrane. As a result of the histological studies satisfactory explanation of the cause of the sensorineural hearing loss or where the exact location of the lesion are not yet established.

In addition to the histological experiments biochemical studies have been performed on animals and revealed a lot of facts that could help in

explaining the association of sensorineural hearing loss with hypothyroidism; lipid accumulation in the Hensen's cells and deposits in the cochlear duct as well as large intra-cellular space in the stria vascularis. The sodium and potassium level in the perilymph fluid was within normal limits. It revealed also that the basilar membrane was thickened due to an increase of the amount of amorphous substance in it. With reference to the hair cells, the biochemical studies revealed that they were surrounded by oedema which separated them from the supporting cells in the organ of Corti.

In the light of what is mentioned above, the electrophysiological properties of the auditory pathway should be studied carefully and in detail as it is easy to perform on animals as well as on humans, and because it gives very quick and reliable results of any pathological changes in the auditory system. The importance of electrophysiology studies was increased more and more particularly after the findings of Rubenstein et al. (1974) and Hemelfarb et al. (1981) which revealed that the evoked response audiometry was the most important test that gave pertinent and specific abnormalities, and could show dramatic changes more than any other tests.

No studies dealing with hearing in cases of hyperthyroidism were found, except the one performed by Cohonen et al. (1971) who studied the cochlear-microphonic in hyperthyroid guinea pigs. They did not notice any changes from that of normal control guinea pigs. Another study has been done by Himelfarb et al. (1981) and was performed on hyperthyroid patients. They also only stressed the study of brainstem conduction time and they reported a significant prolongation of this time in relation to the normal control subjects. More studies on hyperthyroid patients are required to show if there is any effect on hyperthyroidism on the auditory system and what sort of effect and which site it might affect.

By reviewing the literature review (see section 8.2) it was clear that it is still not completely accepted that there is an association between diabetes mellitus and hearing impairment and there is a very wide gap between the investigators who are dealing with the study of hearing in diabetic patients. Some of them deny any direct or indirect effect of diabetes mellitus on the auditory system, others reported that 41% of their patients had hearing impairment due to diabetes mellitus. There are very few studies using ABER as a diagnostic technique. The results of these studies showed that the changes in ABER may develop as an early manifestation, and before the appearance of any complication. Continuing to study diabetic patients by using ABER is useful to show what is the complete effect of diabetes mellitus on ABER parameters on one hand, and to show if there is any correlation between the diabetic complication and ABER on the other hand, that is the aim of this study.

## 3.2 Research Plan

Research was planned along four major experimental lines. The first line of experimentation was concerned with obtaining normative ABER data and setting up a diagnostic baseline. This involved comparison of two ABER recordings, one obtained from normal control males and the other obtained from normal control females. The recordings were performed in a certain environment and under certain stimulus parameters. This performance condition was intended to be used with the patients. In this line of experimentation, great emphasis was placed on the statistical properties of the ABER peaks and on the effect of age and sex on these properties (see Chapter 5).

The second line of experimentation was concerned with the evaluation of the ABER with hypothyroid patients. This part involved comparison of the

hypothyroid findings with that of the normal ones. Comparison of two ABER recordings, one before starting the treatment, while the other was obtained after the treatment and restored euthyroid state, (see Chapter 6) in order to show the validity of ABER technique as a follow up after the treatment.

The third line of experimentation was concerned with evaluation of ABER with hyperthyroid patients. This involved comparison of hyperthyroid recordings with the normal controls on one hand and with the recordings of hypothyroid patients on the other (see Chapter 7).

The fourth line of experimentation concerned the evaluation of ABER with diabetic patients, to show the effect of diabetes mellitus on ABER and if there is any relationship between diabetic complications and ABER (see Chapter 8).

# CHAPTER FOUR

# INSTRUMENTATION

## 4.1 Sound Generating System

An Amplaid Mk5 evoked potential signal processor was used as a click generator and white noise masker generator, and controls all parameters of amplifiers, stimulators, noise generator as well as printing and storage devices. Appropriate click and noise signals according to the experimental requisites were transduced by shielded TDH49 earphones to the subject, who lay down just beside the equipment.

### 4.1.1 Generation of acoustic click

The AS501 stimulator was used as the click generator providing a wide variety of stimuli from 10 to 1200μs duration. According to the experimental design, it was set to generate a click of 100μs duration at a repetition rate of 21 pulses per second and in alternating polarity, and intensity ranged from 60 dB above subject threshold-sensation level to 80 dBSL in 10 dB steps. The click was transduced through shielded TDH49 earphones and presented monaurally. The click calibration has been performed in peak equivalent sound pressure level (p.e. SPL) taking a reference of 100μs and 1000 Hz pure tone.

### 4.1.2 White noise generator

An AS502 stimulator was used as the white noise generating source. A high pass filter and band pass filter were plugged in the card for the AS502 stimulator to produce a different masker cut-off. The white noise calibration has been performed in p.e. SPL. The continuous white noise was

presented to the contralateral ear at the intensity of 20 dBnHL less than the intensity of the tested ear.

## 4.2 The Response Recording

The auditory brainstem evoked responses (ABER) were recorded using silver/silver chloride disc electrodes placed on the scalp. The response signal was then amplified by a factor of 100,000 and acquired by the MkV computer and displayed on the Tektronics 4006-1 display and keyboard.

### 4.2.1 Electrode attachment

EEG silver/silver chloride cup electrodes were used for the ABER recording. The active electrode was placed on the ipsilateral mastoid process, the reference electrode on the vertex and the ground electrode on the forehead just below the hair line. The sites of electrodes were cleaned first of all with physoderm soap and then abraded by surgical spirit. The cups of the electrodes were filled with Grass $EC_2$ electrode cream. A piece of cotton gauze was placed over each electrode in order to reduce evaporation and subsequent hardness of the cream. Each electrode was fixed to the scalp by a tape of adhesive plaster. The electrode impedance was checked by an impedance meter. The electrode impedance was less than 4 Kohm at 1 kHz. The electrode impedance was set to be the same on both sides in the same subject. The electrodes were connected to the phP pre-amplifier which was placed beside the subject allowing differential amplification of the response.

4.2.2 Response signal amplification

The differential response signal was presented from the phP 601 pre-amplifier which was put beside the subject to the phA 501 situated inside the main cabinet of Mk5 evoked potential signal processor. The signal was amplified in a total gain of 100,000, the band pass was between 100 and 2000 Hz and fed to the averager - the Tektronix 4006-1 display - by timing control of 10 ms - the window. The sensitivity of the amplifier was limited to ±20μV and it gives a visual signal when the input waveform goes over the voltage limit set.

4.2.3 The response acquisition

Using the Tektronix 4006-1 display and keyboard at the analysis time window of 10 ms and norm display of 500 nV full scale. The sum of 2048 sweeps was averaged for each intensity. The process was repeated for various stimulus intensities. The averaged responses were recorded from the memory of the computer and stored in the mini floppy discs for later off line analysis. In the meantime the waveforms were also recorded on special paper, using the x-y plotter connected to the Mk5.

4.3 Experimental Procedure

Each subject underwent one recording session of about 1 1/2 to 2 hours duration. The session starts by telling the subject everything about the experimental steps and that the experiment could be terminated at any time at the subject's request. Details of age, family history, past history of any disease, any audiological or neurological disorders, any head injury and history of medication if any were noted. Having taken this history the otoscopic examination takes place as well. If nothing affecting the hearing was noted from the history, to exclude any peripheral causes of hearing

defects and to remove wax, if any. The pure tone threshold for each ear at frequencies of 250 to 8000 Hz and tone decay test at 4000, 1000 and 500 Hz were determined.

After history and otoscopic examination the electrodes were attached to the scalp of the subject. The impedance of the electrodes were also checked by the impedance meter as previously described. The subject was then asked to lie on a bed beside the Amplaid Mk5 with a pillow under his head and neck to minimise the muscular contractions in a semi-darkened, but not electric or sound-proof, room. Once the subject was lying down comfortably and relaxed, the click threshold for each ear was determined as follows. The click generator was set on the stimulus intensity at 60 dB SPL and presented to the subject's ear through the TDH49 earphone. The subject was asked to raise his finger if he could hear the click. The click intensity was lowered in 20 dB steps until the subject could not hear the click any more; then the intensity was raised again in 5 dB steps till the subject could hear the click again. The procedure was repeated at least three times, the lower intensity at which the subject could hear the click was considered the click threshold and calculated as zero dB sensation level.

As soon as the click threshold was obtained the subject was asked to relax as much as possible. Most of the subjects went to sleep during the recording or at least part of it. No sedation was given to any of the subjects at all. The stimuli were presented monaurally at 80, 70 and 60 dB above the subject's threshold - sensation level - and at a rate of 21 pulses per second. The contralateral ear was masked by continuous white noise at intensity of 20 dBnHL less than that of the tested ear. The sum of 2048 stimuli were averaged for each intensity and stored on mini floppy discs for later analysis. Recording of ABER was always started with the right ear and

then the left ear by the same procedure. At the end of each session the response was recorded by x-y plotter connected to the Amplaid Mk5 on special paper. At the time of analysis all the traces of the recording of wave I to wave V were displayed on the screen of the Tektronix 4006-1 and measured as follows. The peak latency in μs measured from the initiation of the click stimulus pulse to the negative peak of wave I, III and V. The amplitude in nV is measured between each negative peak and the following positive one. The inter-peak interval of I-V, III-V and I-III is measured between the negative peaks of I and V, III and V and I and III respectively. All the measurements were done using the index cursor of the main frame of the Tektronix display.

Following the recording of ABER, the subjects were brought out of bed in order to remove the recording electrodes and to clean their scalp.

# CHAPTER FIVE

## NORMALS

### 5.1 Introduction

In the past fifteen years there has been worldwide interest in using the auditory brainstem evoked response as a clinical diagnostic tool on humans, and in the research centres on experimental animals. This attention to the utilizing of ABER has been paid since the initial report by Jewett and Wilston in 1971 on the possibility of using this technique in the clinical field. More and more attention has been paid after the reports which have shown that the abnormality of ABER properties were indicative of auditory pathway pathologies (Thornton, 1975b; Starr and Achor, 1975; Starr and Hamilton, 1976; Selters and Brackman, 1977).

The validity of ABER is now established as a diagnostic battery test in neurological and audiological disorders of the cochlea and auditory brainstem pathway. From the published reports it is now possible to outline the diagnostic criteria of ABER by which we can judge the abnormal findings from that of normal ones. These criteria were mentioned earlier (see section 2.4). By application of ABER in the audiological field it is now possible to distinguish between conductive hearing loss and sensorineural hearing loss and between hearing loss due to end organ disorders and that due to retrocochlear lesion (see section 2.3.1). In the neurological field, the effect of tumours and structural lesions in the auditory pathway in the region of the brainstem and mid brain on the ABER have been demonstrated by many investigators (Thornton and Hawkes, 1976; Starr and Achor, 1975; Stockard, Stockard and Sharbrough, 1977). The effect of circulatory disturbance in the brainstem was reported by Starr and Achor (1975),

demylenation disorder in the brainstem, Stockard and Rossiter (1977) and Robinson and Rudgi (1978). In the case of suspected neurological disorders using inter-peak intervals criterion I-III, I-V and III-V is more accurate and more reliable than that of using the measurement of absolute latency and amplitude of the ABER components. The abnormality of interwave intervals are indicative of an abnormality of the neurogenic transmission of the auditory pathway (Stockard, Stockard and Sharbrough, 1978; Starr and Achor, 1975). In addition, and to a lesser extent reduction in the ratio amplitude of wave V and that of wave I (I/V), Starr and Achor (1975), is also used as a diagnostic index. Interaural latency difference (IDL) is also used as a diagnostic criteria in the neuro-otologic diagnosis (Selters and Brackman, 1977). Finally the most reliable diagnostic index of an abnormality in the auditory brainstem pathway is complete absence of one or more peaks other than wave II, IV and VII which were reported to be absent even in some normal human subjects (Stockard, Stockard and Sharbrough, 1978).

It is possible now to summarise how to get the use of ABER technique as a diagnostic tool battery in suspected audiological or neurological disorders of the auditory pathway by the following process. Recording of ABER to 60 or 70 dBSL, the absence of all peaks means that the subject suffers from severe audiological disorders. A repeat of recording at higher intensity is required to see whether there is response at higher intensities or not. The presence of some waves and absence of others is useful in determining the site of lesion, e.g. absence of only wave V means that the lesion might be at the level of inferior colliculus - the site of origin of wave V. In a case of presence of all peaks, measurement of all waveform parameters - latency, amplitude and inter-wave intervals - should be obtained and comparison with that of normal age matching controls should be

done. If, for example, wave V was normal and I-V inter-wave interval was normal as well, the neurological disorders are unlikely. If there is a prolongation in wave V, and I-V interval is normal, a hearing loss is likely. If wave I is normal and I-V is prolonged a neurological disorder is suspected. If wave I is prolonged as well as I-V interval, audiological and neurological disorders are likely (Despland and Galambos, 1980).

To be able to use ABER technique as a diagnostic tool, recording of ABER from both controls and patients should be obtained and comparison of the two using the criteria which were mentioned earlier (see section 2.4). The diagnostic information could then be obtained.

The normal mean values of the ABER parameters of latency, amplitude and inter-wave intervals were reported in the literature of many investigators (Thornton, 1975a; Lieberman and Sohmer, 1973; Schulman, Galambos and Galambos, 1975). The published data for these normal subjects are often not comparable because of variation in equipment used and stimulus techniques (Lieberman et al., 1973b; Thornton, 1975b,c; Stockard and Rossiter, 1977). To be more accurate in obtaining the abnormality between normal controls and that of patients, each laboratory should have its own normal mean values of ABER and making them specific for sex, age and stimulus technique parameters (Stockard, Stockard and Sharbrough, 1978).

The aim of the present study is to investigate some normal age and sex matching controls and take the statistical properties of their mean values to be the baseline by which the mean values of patients can be compared and subsequent diagnostic information can be achieved.

## 5.2 Methods

### 5.2.1 Subjects

Auditory brainstem evoked responses (ABER) were recorded in 31 normal healthy subjects with no abnormality on audiological and neurological examinations, and without a general history, past, present and family history of metabolic or other diseases which might affect their hearing. Their ages ranged from 24-76 years (mean 47.9 and standard deviation 16.1). Fourteen women whose ages ranged from 30-76 years (mean 56.4 and standard deviation 13.1), and 17 men whose ages ranged from 24-64 years (mean 41 and standard deviation 15.1). All the normal subjects had a threshold of 20 dB HL or better as limits of normal pure tone threshold at single frequency by air and bone conduction at frequencies from 250 - 8000 Hz (Tables 5.1a and 5.1b). The choice of normal subjects from the Southampton area (from where the patients were expected to come) was taken, from the occupational classes from which the patients were believed to come. That is, they included students, housewives, teachers and so on. Each subject had attended only one recording session. The recordings were obtained from both ears of the subjects except one lady who was only tested in the right ear.

### 5.2.2 Instrumentation

An Amplaid Mk5 evoked potential signal processor was used as a click and white noise generator. It is managed according to the experimental design to deliver a bipolarity click of 100 $\mu$s duration and at a rate of 21 pulses per second with analysis time of 10 ms and sum of 2048 sweeps for each intensity, and cut off frequency of 100-2000 Hz and with norm display of 500 nV. The stimulus delivered monaurally through shielded TDH49 earphones at intensities of 80, 70 and 60 dB above the individual threshold (sensation level). The non test ear was masked by white noise at intensity

of 20 dBnHL less than that of the tested ear. The instrumentation was described in detail in section 4.1, 4.1.1 and 4.1.2.

### 5.2.3 Electrodes attachment

EEG silver/silver chloride cup electrodes were used to pick up the signals from the subject's scalp. Grass EC2 electrode cream was employed as a conductor media. The electrodes were placed on vertex, ipsilateral mastoid process and on the forehead just below the hair line as negative, positive and earth respectively. The procedure of electrodes attachment was described in detail earlier in section 4.2.1.

### 5.2.4 Recording of ABER

Each normal subject underwent one recording session of about 1 1/2 - 2 hours duration. It started by taking detailed, general, past, present, family and audiological history in order to exclude anyone who might have any metabolic diseases or any disease which may affect his or her hearing, followed by otoscopic examination and pure tone audiometry and tone decay tests. The subject then laid on the bed beside the Amplaid to start the recording with the same procedure which was described earlier in section 4.2.

## 5.3 Results

Auditory brainstem evoked responses (ABER) were recorded in 31 normal control subjects whose ages ranged from 24-76 years (mean 47.9 and S.D. 16.1). Fourteen females whose ages ranged from 30-76 (mean 56.4 and S.D. 13.1) and 17 males whose ages ranged from 24-64 (mean 41 and S.D. 15.1). Figures 5.1 and 5.2 show some of these recordings at intensities of 80, 70

and 60 dB sensation level (above the subjective threshold) for males and females and for both right and left ears. These waveforms represent the average of 2048 click stimulus presentations. The latencies, amplitudes and interwave intervals of all normal controls (male and female) individuals with mean and standard deviations are shown in Tables 5.2 to 5.13.

The pattern of ABER recordings was characterised by the presence of wave I, III and V in all recordings. Wave II was missed in some recordings at 60 dB SL and sometimes even at 70 dB SL. Wave IV was frequently fused with wave V to make IV/V complex. Wave II had the smallest amplitude among the other waves. Wave V was the most consistently observable and the largest component at all intensities. Wave III came after wave V in these properties, which was followed by wave I. The amplitude of wave V was always larger than wave I amplitude.

The amplitude measurements showed a great deal of difference between subjects and sometimes between right and left ear in the same subject. This variation occurred more frequently with wave II than any other wave amplitude.

The amplitude of all waves showed an increase with increasing stimulus intensity and vice versa. The latencies of all components showed a decrease with increasing stimulus intensity, but in a more consistent manner than that of amplitude. The inter-wave intervals were independent of stimulus intensity. The interaural latency difference (IDL) i.e. the difference between wave V latency of right and left ear in the same subject was less than 0.3 ms for both males and females.

By calculating the 95% confidence limit (see Tables 5.17 and 5.18) the lower limit of amplitude was very low for both males and females for both right and left ears, particularly for wave I and III. This limit sometimes encompasses zero.

### 5.3.1 Effect of age and sex on ABER parameters

The data on the peak latency, amplitudes and inter-wave intervals showed normal distribution (Thornton, 1975c). This allows the use of 't' test to compare the means of these values between a group of males and females (see Tables 5.14, 5.15 and 5.16). Both males and females were divided into groups according to their ages, 20-29, 30-39 and so on.

One way of analysis of variance was also done to show if there is any effect of age and sex on the ABER parameters - latency, amplitude and inter-wave intervals.

Females had shorter latency than males for all ABER components and at all intensities. However this difference between males and females did not reach to the significanat level. Females had higher amplitudes for all peaks and at all intensities than males, but the difference between the two was not significant. Interwave intervals showed no difference between males and females.

The results of this study did not show any significant effect of age on latency, amplitude or inter-wave intervals in any age group for males and females.

## 5.4 Discussion

For using the auditory brainstem evoked response (ABER) as a diagnostic technique, the responses from normal hearing subjects should be obtained and the statistical properties of these responses should be known, so that an accurate comparison between these data and pathological data obtained from patients can be made (Thornton, 1975a). In this study ABERs were recorded from 31 normally hearing subjects, both males and females of different ages. The results of these recordings were statistically analysed in an attempt to

be the baseline with which the responses of metabolic disorder patients could be compared. By considering the mean principal findings in this study against the earlier reports announced in relevant study the comment will be on: wave JV was found to be the largest and most reliable component of ABER followed by wave III and wave I. The mean value of absolute amplitude and latency of these waves depended on the stimulus intensity. The mean latency values are well ordered and showed a decrease of about 0.1 - 0.2 ms as the stimulus intensity increased by 10 dB. The mean value of absolute amplitude showed an increase by increasing the stimulus intensity but in a less ordered manner than that of the latency (see Tables 5.2 to 5.10). These findings are in agreement with those reported by Thornton (1975c); Liebermal et al. (1973); Terkeldsen et al. (1973); Hecox and Galambos (1974). The absolute amplitude showed marked variation between subjects and even in the same subject, this variance might be "attributed to the remaining variance of the background noise process" (Thornton, 1975b). The increased latency with decreasing stimulus intensity "could be caused mainly by the accumulating excitation of hair cells and the transduction times from the excitation of hair cells to the first order neuron" (Yamada, Kodera and Yagi, 1979). The absolute amplitude found here to be markedly variable between the subjects and even between right and left ear in the same subject, this variability was more marked with wave II and IV. Furthermore, wave II was missing in some recordings even in high intensity and wave IV is frequently fused together with wave V to make one wave. For this reason the evaluation of ABER in this study was only through its component I, III and V and their inter-wave latency.

In all normal subjects wave V was always larger than wave I. This is in agreement with the findings of Starr and Achor (1975). From the statistical analysis of data in this study it was found that the standard

deviation of the amplitude to its mean is relatively bigger than the standard deviation of the latency to its mean. This makes the absolute latency as a diagnostic criteria, more reliable than that of the absolute amplitude. Furthermore the big variance of the absolute amplitude between subjects, and in the same subject, made the using of absolute amplitude as a diagnostic criteria less reliable than the relative amplitude, i.e. V/I ratio. This observation is supported by Starr and Achor (1975) and Rowe (1978).

The inter-peak intervals were independent on the stimulus intensity. This finding was in agreement with previous published reports (Tekildsen et al., 1973; Rowe, 1978; Sohmer and Student, 1978; Giroux and Pratt, 1983). The importance of the inter-peak intervals is that they provide information about the integrity of the central auditory pathway. Any prolongation in these intervals means abnormality in the central auditory pathway, so the interval between peaks was suggested to be dependent on the normal propagation of the neural impulse (Starr and Achor, 1975; Groûx and Pratt, 1983).

The effect of sex on ABER in this study was; females had shorter latencies than males in all waves and at all intensities. However this difference did not reach a significant level. Patterson et al. (1981) reported that females had shorter latencies than males at waves IV and V. Michalewski et al. (1980) observed that females had shorter latencies than males at wave V. Mogan Kjer (1979) found the latency shortage in females at all waves but being highly significant for wave IV to wave VII. Stockard et al. (1978) reported that females had shorter latency than males at wave V and suggested it was due to the anatomical shortness of the auditory pathway in females. Females had higher amplitudes than males in all waves and at

all intensities. This difference was the same as the latency and did not reach any significant level. Females had significantly higher amplitudes than males reported in the literature (Mogan Kjer, 1979, 1983; Michalewski et al., 1980; Patterson et al., 1981). The difference in the amplitude between males and females could be possibly attributed to the differences in the skull and soft tissue thickness (Michalewski et al., 1980). There is no difference in inter-peak intervals between males and females. This finding is in disagreement with Stockard et al. (1978) who reported that females had significantly shorter inter-peak intervals III-V and I-V.

There is no effect of age on the ABER latency, amplitude or inter-peak intervals in this study. This was in agreement with Beagley and Sheldrake (1978) who found no significant age differences in ABER latencies. Rowe (1978) found that the younger had significantly shorter inter-peak latency I-III than the older. Patterson et al. (1981) reported that "older adults had longer latencies at wave III than either middle aged or young adults".

There is inconsistency about the effect of age and sex on the ABER parameters between this study and others. Other variables involved, rather than the age and sex may be responsible instead. Patterson et al. (1981) for instance, have reported age/sex/stimulus intensity/stimulus rate/ and route of presentation interaction. There is difference in two factors between this study and that of Patterson et al. The stimulation rate and the route of presentation. They use binaural presentation. It is hard to compare the effect of age and sex in a proper way with the fixation of all other factors. To be more accurate, in comprison the pathological data, and to avoid any false positive, or any false negative results, it is planned to compare the male pathological findings with the normal male and the female pathological findings with that of normal females.

All parameters used in the investigation of normal controls were fixed

and employed. This made sure that any change in the ABER recordings of the patients would be related to the disease and not to anything else.

As waves I, III and V were the most identifable and reproducable in all recordings of normal controls and at all intensities, the evaluation of ABER would be only through these peaks and their inter-peak intervals and waves IV and II would be excluded.

From the statistical analysis of normal control recordings it seemed that using the ratio amplitude criteria i.e. (V/I ratio) is a more reliable diagnostic criteria than the absolute amplitude. The latency criteria is more reliable than the amplitude one. This is because of the big variation of the amplitude between subjects and even in the same subject. By the calculation of 95% confidence limit it was found that the amplitude was as low as zero and for some components may encompass zero.

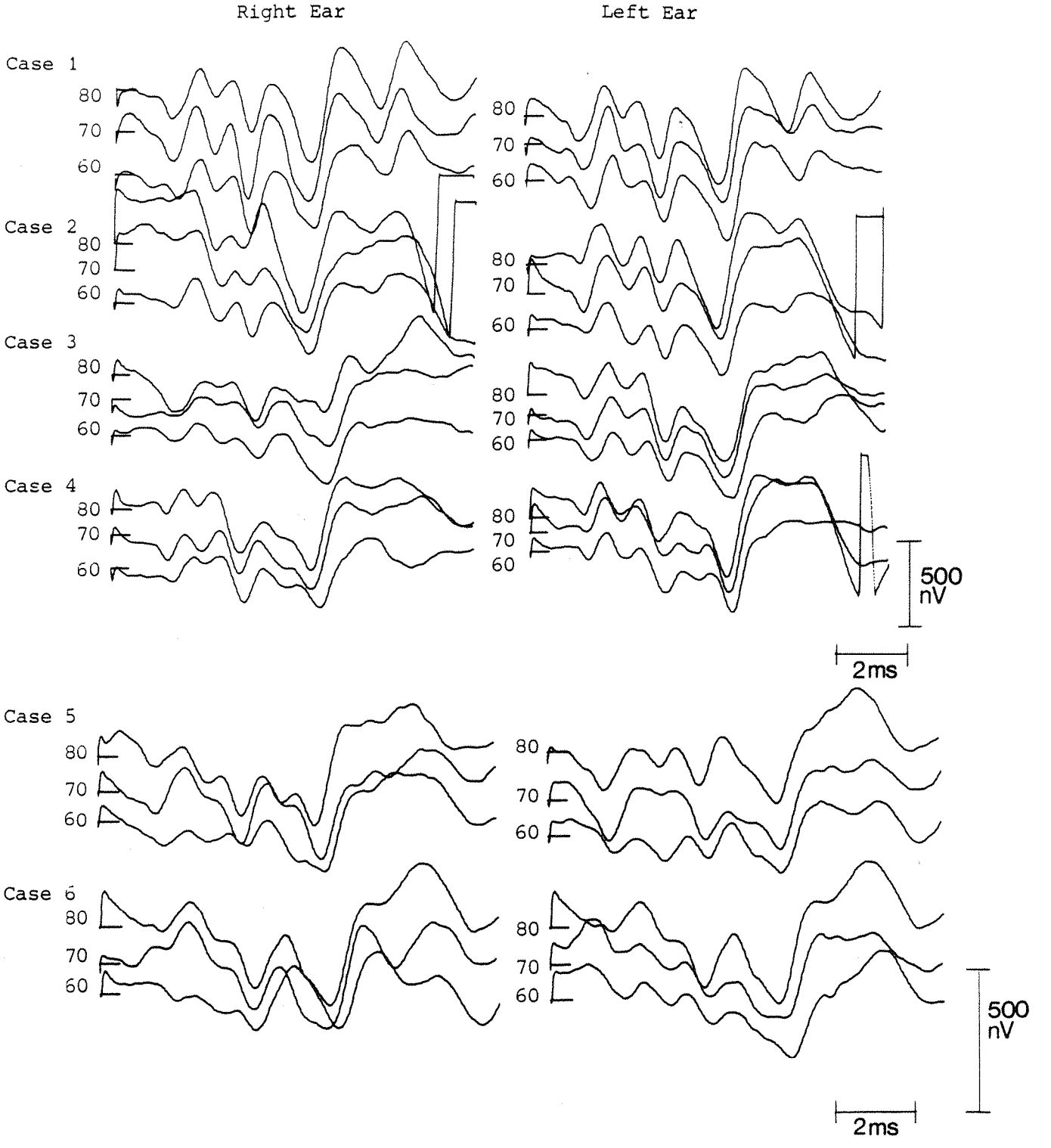


Figure 5.1 Responses from normal control females at intensities of 80, 70 and 60 dBSL for both right and left ears.

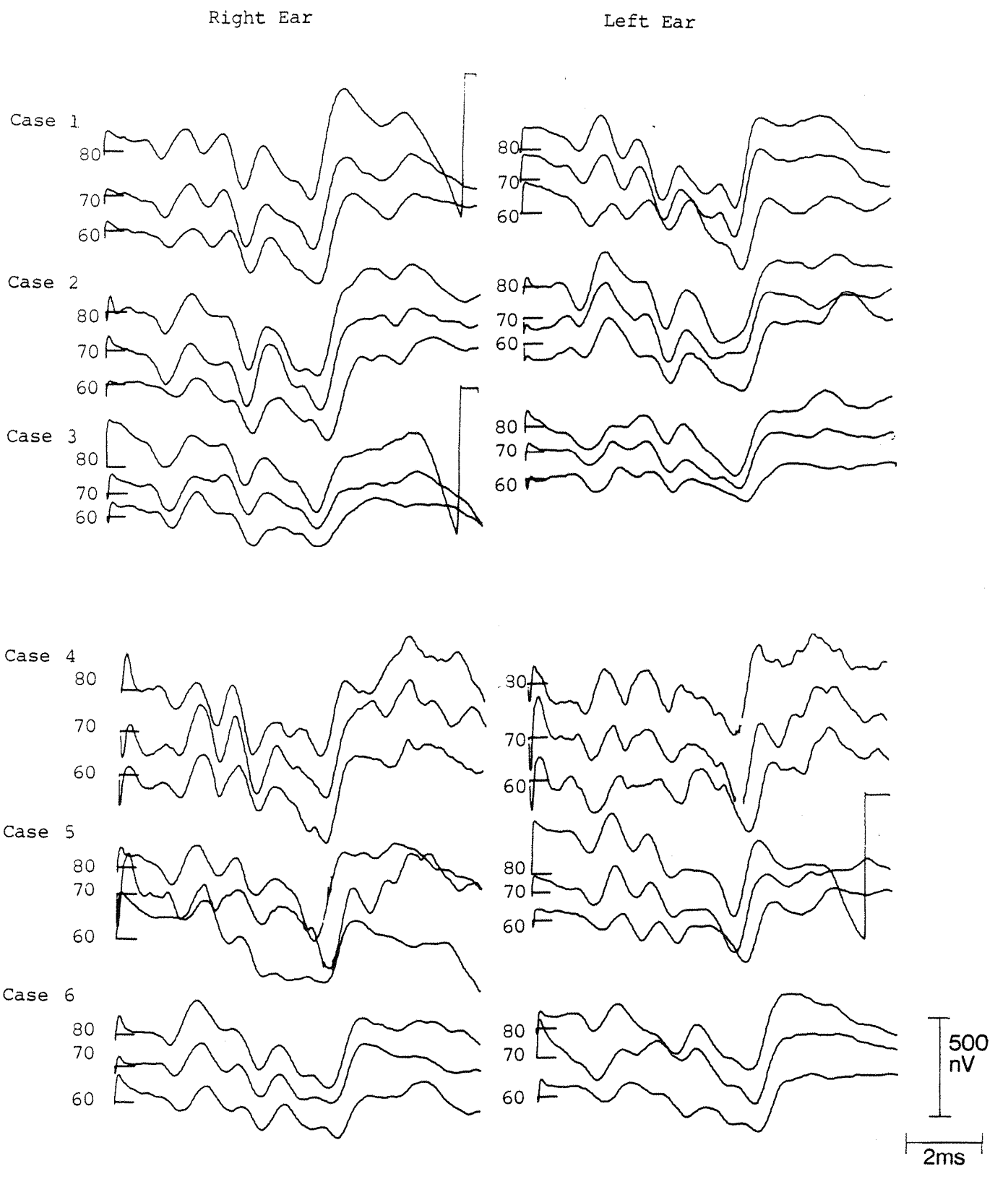


Figure 5.2 Responses from normal control males at intensities of 80, 70 and 60 dBSL for both right and left ears.

| Subject | Age Years | | 250 Hz | 500 Hz | 1000 Hz | 2000 Hz | 3000 Hz | 4000 Hz | 8000 Hz |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 24 | R | 20 | 20 | 15 | 5 | 5 | 5 | 10 |
| | | L | 20 | 25 | 20 | 10 | 10 | 10 | 15 |
| 2 | 25 | R | 15 | 15 | 10 | 0 | 0 | 0 | 0 |
| | | L | 20 | 20 | 10 | 0 | 10 | 10 | 0 |
| 3 | 25 | R | 15 | 15 | 10 | 0 | 5 | 5 | 20 |
| | | L | 15 | 15 | 10 | 0 | 5 | 10 | 20 |
| 4 | 25 | R | 20 | 20 | 15 | 5 | 10 | 10 | 5 |
| | | L | 20 | 20 | 15 | 10 | 10 | 10 | 5 |
| 5 | 26 | R | 15 | 15 | 15 | 5 | 0 | 0 | 10 |
| | | L | 20 | 15 | 15 | 5 | 10 | 5 | 15 |
| 6 | 30 | R | 20 | 20 | 15 | 5 | 10 | 15 | 15 |
| | | L | 25 | 20 | 15 | 10 | 15 | 10 | 10 |
| 7 | 30 | R | 15 | 20 | 10 | 15 | 15 | 10 | 10 |
| | | L | 15 | 15 | 10 | 15 | 10 | 10 | 20 |
| 8 | 31 | R | 20 | 20 | 10 | 5 | 0 | 0 | 5 |
| | | L | 20 | 20 | 10 | 5 | 5 | 0 | 10 |
| 9 | 34 | R | 20 | 20 | 10 | 5 | 15 | 15 | 10 |
| | | L | 20 | 20 | 5 | 10 | 15 | 10 | 10 |
| 10 | 37 | R | 15 | 15 | 10 | 0 | 0 | 0 | 10 |
| | | L | 20 | 20 | 15 | 0 | 0 | 0 | 10 |
| 11 | 40 | R | 15 | 15 | 10 | 20 | 10 | 20 | 20 |
| | | L | 15 | 15 | 10 | 20 | 10 | 15 | 20 |
| 12 | 42 | R | 20 | 20 | 10 | 10 | 10 | 15 | 15 |
| | | L | - | - | - | - | - | - | - |
| 13 | 42 | R | 15 | 15 | 20 | 10 | 0 | 10 | 15 |
| | | L | 15 | 15 | 20 | 5 | 5 | 10 | 10 |
| 14 | 45 | R | 20 | 15 | 15 | 15 | 5 | 5 | 20 |
| | | L | 20 | 20 | 15 | 15 | 15 | 10 | 15 |
| 15 | 48 | R | 20 | 15 | 10 | 0 | 15 | 10 | 20 |
| | | L | 20 | 15 | 0 | 5 | 0 | 0 | 15 |
| 16 | 48 | R | 25 | 20 | 15 | 10 | 10 | 15 | 10 |
| | | L | 20 | 20 | 15 | 10 | 10 | 15 | 5 |

TABLE 5.1a Pure tone audiograms of normal control subjects. Threshold in dB (ISO).

| Subject | Age Years | | 250 Hz | 500 Hz | 1000 Hz | 2000 Hz | 3000 Hz | 4000 Hz | 8000 Hz |
|---|---|---|---|---|---|---|---|---|---|
| 17 | 52 | R | 25 | 20 | 15 | 10 | 15 | 10 | 10 |
| | | L | 25 | 20 | 20 | 10 | 15 | 20 | 10 |
| 18 | 53 | R | 20 | 20 | 10 | 5 | 5 | 10 | 10 |
| | | L | 20 | 20 | 15 | 10 | 5 | 5 | 10 |
| 19 | 54 | R | 20 | 20 | 20 | 10 | 10 | 10 | 25 |
| | | L | 20 | 20 | 10 | 15 | 15 | 15 | 20 |
| 20 | 56 | R | 25 | 25 | 20 | 10 | 15 | 10 | 20 |
| | | L | 25 | 25 | 15 | 15 | 10 | 10 | 25 |
| 21 | 56 | R | 25 | 25 | 20 | 10 | 15 | 10 | 15 |
| | | L | 25 | 25 | 20 | 15 | 20 | 15 | 10 |
| 22 | 61 | R | 25 | 25 | 15 | 10 | 10 | 15 | 20 |
| | | L | 25 | 25 | 20 | 10 | 15 | 10 | 25 |
| 23 | 63 | R | 25 | 25 | 15 | 15 | 10 | 20 | 25 |
| | | L | 25 | 20 | 20 | 10 | 10 | 20 | 15 |
| 24 | 63 | R | 30 | 25 | 20 | 10 | 10 | 25 | 25 |
| | | L | 30 | 30 | 20 | 15 | 10 | 25 | 25 |
| 25 | 63 | R | 25 | 25 | 20 | 25 | 20 | 15 | 25 |
| | | L | 25 | 25 | 15 | 20 | 15 | 20 | 20 |
| 26 | 64 | R | 25 | 20 | 20 | 15 | 25 | 25 | 20 |
| | | L | 25 | 30 | 25 | 15 | 20 | 25 | 25 |
| 27 | 64 | R | 25 | 25 | 20 | 10 | 25 | 15 | 25 |
| | | L | 30 | 25 | 25 | 20 | 20 | 15 | 25 |
| 28 | 68 | R | 30 | 30 | 30 | 15 | 20 | 20 | 15 |
| | | L | 25 | 25 | 25 | 20 | 15 | 20 | 20 |
| 29 | 69 | R | 25 | 25 | 20 | 20 | 25 | 25 | 30 |
| | | L | 30 | 25 | 25 | 20 | 25 | 20 | 25 |
| 30 | 72 | R | 25 | 25 | 20 | 15 | 20 | 25 | 30 |
| | | L | 30 | 25 | 25 | 20 | 25 | 25 | 25 |
| 31 | 76 | R | 30 | 30 | 20 | 25 | 25 | 30 | 30 |
| | | L | 30 | 30 | 25 | 25 | 20 | 25 | 30 |

TABLE 5.1b Pure tone audiograms of normal control subjects. Threshold in dB (ISO).

| CASE | AGE YEARS | AMPLITUDE | | | LATENCY | | |
|---|---|---|---|---|---|---|---|
| | | I | III | V | I | III | V |
| 1 | 30 | R 234 | 621 | 836 | 1.54 | 3.42 | 5.26 |
| | | L 228 | 508 | 641 | 1.48 | 3.40 | 5.40 |
| 2 | 42 | R 484 | 270 | 543 | 1.52 | 3.78 | 5.50 |
| | | L — | — | — | — | — | — |
| 3 | 45 | R 109 | 486 | 541 | 1.50 | 3.94 | 5.54 |
| | | L 96 | 403 | 560 | 1.62 | 3.94 | 5.48 |
| 4 | 48 | R 176 | 373 | 529 | 1.46 | 3.64 | 5.24 |
| | | L 145 | 141 | 387 | 1.74 | 3.74 | 5.52 |
| 5 | 48 | R 98 | 306 | 500 | 1.52 | 3.58 | 5.38 |
| | | L 90 | 352 | 691 | 1.48 | 3.72 | 5.74 |
| 6 | 52 | R 176 | 223 | 449 | 1.56 | 3.80 | 5.64 |
| | | L 258 | 297 | 535 | 1.50 | 3.78 | 5.64 |
| 7 | 56 | R 109 | 488 | 547 | 1.50 | 3.94 | 5.54 |
| | | L 98 | 402 | 566 | 1.62 | 3.94 | 5.48 |
| 8 | 56 | R 211 | 86 | 188 | 1.54 | 3.70 | 5.64 |
| | | L 238 | 90 | 500 | 1.54 | 3.70 | 5.50 |
| 9 | 63 | R 129 | 395 | 496 | 1.42 | 3.74 | 5.78 |
| | | L 184 | 391 | 625 | 1.64 | 3.78 | 5.80 |
| 10 | 64 | R 437 | 195 | 586 | 1.50 | 3.90 | 5.76 |
| | | L 450 | 207 | 488 | 1.52 | 3.92 | 5.84 |
| 11 | 68 | R 172 | 242 | 387 | 1.62 | 3.86 | 5.94 |
| | | L 50 | 305 | 370 | 1.58 | 3.84 | 5.84 |
| 12 | 69 | R 115 | 380 | 438 | 1.58 | 3.76 | 5.70 |
| | | L 98 | 305 | 500 | 1.56 | 3.70 | 5.64 |
| 13 | 72 | R 94 | 176 | 320 | 1.60 | 3.72 | 5.70 |
| | | L 101 | 183 | 251 | 1.62 | 3.76 | 5.78 |
| 14 | 76 | R 93 | 180 | 390 | 1.56 | 3.66 | 5.52 |
| | | L 130 | 230 | 350 | 1.54 | 3.88 | 5.58 |
| **Mean** | 56.36 | R 188 | 316 | 482 | 1.53 | 3.75 | 5.58 |
| | | L 167 | 293 | 497 | 1.57 | 3.78 | 5.63 |
| S.D. | 13.06 | R 124 | 149 | 148 | 0.05 | 0.15 | 0.20 |
| | | L 107 | 120 | 128 | 0.07 | 0.14 | 0.15 |

TABLE 5.2 Values of peak-to-peak amplitude (nV) and latency (msec) for normal control females at 80 dBSL for right and left ears.

| CASE | AGE | AMPLITUDE | | | LATENCY | | |
|---|---|---|---|---|---|---|---|
| | YEARS | I | III | V | I | III | V |
| 1 | 30 | R 240 | 473 | 560 | 1.58 | 3.50 | 5.40 |
| | | L 241 | 471 | 561 | 1.58 | 3.50 | 5.45 |
| 2 | 42 | R 457 | 184 | 375 | 1.58 | 3.84 | 5.66 |
| | | L — | — | — | — | — | — |
| 3 | 45 | R 176 | 158 | 480 | 1.72 | 3.98 | 5.76 |
| | | L 176 | 160 | 490 | 1.58 | 3.96 | 5.74 |
| 4 | 48 | R 120 | 301 | 477 | 1.31 | 3.62 | 5.36 |
| | | L 109 | 141 | 387 | 1.80 | 3.86 | 5.60 |
| 5 | 48 | R 99 | 430 | 582 | 1.35 | 3.66 | 5.42 |
| | | L 85 | 238 | 656 | 1.74 | 3.82 | 5.82 |
| 6 | 52 | R 176 | 156 | 480 | 1.72 | 3.98 | 5.76 |
| | | L 176 | 160 | 488 | 1.58 | 3.96 | 5.74 |
| 7 | 56 | R 164 | 340 | 508 | 1.70 | 4.04 | 5.76 |
| | | L 164 | 340 | 516 | 1.70 | 4.02 | 5.76 |
| 8 | 56 | R 191 | 98 | 313 | 1.76 | 3.76 | 5.86 |
| | | L 156 | 39 | 402 | 1.66 | 3.80 | 5.60 |
| 9 | 63 | R 168 | 367 | 480 | 1.60 | 3.74 | 5.80 |
| | | L 156 | 250 | 430 | 1.72 | 3.84 | 5.84 |
| 10 | 64 | R 407 | 180 | 527 | 1.54 | 3.98 | 5.87 |
| | | L 411 | 280 | 390 | 1.64 | 4.02 | 5.94 |
| 11 | 68 | R 121 | 219 | 340 | 1.72 | 4.00 | 6.08 |
| | | L 43 | 273 | 250 | 1.70 | 3.98 | 5.98 |
| 12 | 69 | R 110 | 359 | 407 | 1.64 | 3.82 | 5.76 |
| | | L 89 | 299 | 368 | 1.64 | 3.78 | 5.68 |
| 13 | 72 | R 63 | 160 | 258 | 1.72 | 3.78 | 5.88 |
| | | L 93 | 129 | 195 | 1.70 | 3.82 | 5.88 |
| 14 | 76 | R 85 | 145 | 340 | 1.73 | 3.71 | 5.57 |
| | | L 105 | 125 | 250 | 1.81 | 3.86 | 5.64 |
| Mean | 56.36 | R 184 | 255 | 437.6 | 1.62 | 3.82 | 5.70 |
| | | L154.2 | 223 | 414 | 1.68 | 3.86 | 5.74 |
| S.D. | 13.06 | R 116 | 120 | 99 | 0.14 | 0.16 | 0.20 |
| | | L 93.2 | 114 | 131 | 0.08 | 0.14 | 0.15 |

TABLE 5.3 Values of peak-to-peak amplitude (nV) and latency (msec) for normal control females at 70 dBSL for right and left ears.

| CASE | AGE YEARS | AMPLITUDE | | | LATENCY | | |
|---|---|---|---|---|---|---|---|
| | | I | III | V | I | III | V |
| 1 | 30 | R 215 | 531 | 598 | 1.70 | 3.54 | 5.86 |
| | | L 180 | 406 | 586 | 1.64 | 3.52 | 5.98 |
| 2 | 42 | R 371 | 250 | 426 | 1.68 | 3.86 | 5.74 |
| | | L -- | -- | -- | -- | -- | -- |
| 3 | 45 | R 103 | 290 | 440 | 1.882 | 4.04 | 5.88 |
| | | L 96 | 251 | 520 | 1.70 | 3.98 | 5.84 |
| 4 | 48 | R 109 | 141 | 477 | 1.82 | 3.68 | 5.40 |
| | | L 31 | 109 | 461 | 1.90 | 3.96 | 5.70 |
| 5 | 48 | R 98 | 316 | 516 | 1.58 | 3.68 | 5.58 |
| | | L 129 | 227 | 559 | 1.62 | 3.88 | 5.90 |
| 6 | 52 | R 43 | 133 | 465 | 2.02 | 4.12 | 6.00 |
| | | L 98 | 250 | 517 | 1.70 | 3.98 | 5.84 |
| 7 | 56 | R 102 | 289 | 441 | 1.82 | 4.04 | 5.88 |
| | | L 148 | 258 | 434 | 1.78 | 4.10 | 5.82 |
| 8 | 56 | R 55 | 82 | 152 | 2.00 | 4.08 | 6.08 |
| | | L 148 | 121 | 367 | 1.72 | 3.90 | 5.80 |
| 9 | 63 | R 86 | 191 | 441 | 1.80 | 3.76 | 6.00 |
| | | L 63 | 207 | 492 | 1.80 | 3.92 | 5.88 |
| 10 | 64 | R 390 | 74 | 516 | 1.68 | 4.08 | 6.00 |
| | | L 328 | 266 | 247 | 1.74 | 4.04 | 6.08 |
| 11 | 68 | R 70 | 150 | 250 | 1.94 | 4.16 | 6.42 |
| | | L 38 | 212 | 187 | 1.82 | 4.14 | 6.28 |
| 12 | 69 | R 97 | 250 | 367 | 1.72 | 3.92 | 5.82 |
| | | L 83 | 218 | 273 | 1.78 | 3.88 | 5.82 |
| 13 | 72 | R 55 | 148 | 215 | 1.84 | 3.90 | 5.94 |
| | | L 65 | 113 | 177 | 1.78 | 3.90 | 5.98 |
| 14 | 76 | R 77 | 143 | 238 | 1.92 | 3.88 | 5.68 |
| | | L 70 | 94 | 185 | 1.87 | 3.91 | 5.73 |
| Mean | 56.36 | R 134 | 213 | 396 | 1.81 | 3.91 | 5.88 |
| | | L113.6 | 202.5 | 389 | 1.76 | 3.93 | 5.86 |
| S.D. | 13.06 | R 112 | 121 | 132 | 0.13 | 0.19 | 0.24 |
| | | L 78.4 | 85.7 | 150 | 0.08 | 0.15 | 0.19 |

TABLE 5.4 Values of peak-to-peak amplitude (nV) and latency (msec) for normal control females at 60 dBSL for right and left ears.

| CASE | AGE YEARS | | INTERWAVE INTERVAL | | |
|---|---|---|---|---|---|
| | | | I - III | III - V | I - V |
| 1 | 30 | R | 1.88 | 1.84 | 3.72 |
| | | L | 1.92 | 2.00 | 3.92 |
| 2 | 42 | R | 2.26 | 1.72 | 3.98 |
| | | L | — | — | — |
| 3 | 45 | R | 2.44 | 1.60 | 4.04 |
| | | L | 2.32 | 1.54 | 3.86 |
| 4 | 48 | R | 2.18 | 1.60 | 3.78 |
| | | L | 2.10 | 1.78 | 3.88 |
| 5 | 48 | R | 2.06 | 1.80 | 3.86 |
| | | L | 2.28 | 2.02 | 4.30 |
| 6 | 52 | R | 2.24 | 1.84 | 4.08 |
| | | L | 2.28 | 1.86 | 4.14 |
| 7 | 56 | R | 2.44 | 1.60 | 4.04 |
| | | L | 2.32 | 1.54 | 3.86 |
| 8 | 56 | R | 2.16 | 1.94 | 4.10 |
| | | L | 2.16 | 1.80 | 3.96 |
| 9 | 63 | R | 2.32 | 2.04 | 4.36 |
| | | L | 2.14 | 2.02 | 4.16 |
| 10 | 64 | R | 2.40 | 1.86 | 4.26 |
| | | L | 2.40 | 1.92 | 4.32 |
| 11 | 68 | R | 2.24 | 2.08 | 4.32 |
| | | L | 2.26 | 2.00 | 4.26 |
| 12 | 69 | R | 2.18 | 1.94 | 4.12 |
| | | L | 2.14 | 1.94 | 4.08 |
| 13 | 72 | R | 2.12 | 1.98 | 4.10 |
| | | L | 2.14 | 2.02 | 4.16 |
| 14 | 76 | R | 2.10 | 1.86 | 3.96 |
| | | L | 2.34 | 1.70 | 4.04 |
| Mean | 56.36 | R | 2.22 | 1.84 | 4.05 |
| | | L | 2.22 | 1.86 | 4.07 |
| S.D. | 13.06 | R | 0.16 | 0.16 | 0.19 |
| | | L | 0.13 | 0.16 | 0.17 |

TABLE 5.5 Values of peak-to-peak interwave intervals (msec) for normal females at 80 dBSL.

| CASE | AGE YEARS | | INTERWAVE INTERVAL | | |
|---|---|---|---|---|---|
| | | | I - III | III - V | I - V |
| 1 | 30 | R | 1.92 | 1.90 | 3.82 |
| | | L | 1.92 | 1.95 | 3.87 |
| 2 | 42 | R | 2.22 | 1.82 | 3.94 |
| | | L | — | — | — |
| 3 | 45 | R | 2.26 | 1.78 | 4.04 |
| | | L | 2.38 | 1.78 | 4.16 |
| 4 | 48 | R | 2.31 | 1.74 | 4.05 |
| | | L | 2.06 | 1.74 | 3.80 |
| 5 | 48 | R | 2.31 | 1.76 | 4.07 |
| | | L | 2.08 | 2.00 | 4.08 |
| 6 | 52 | R | 2.26 | 1.78 | 4.04 |
| | | L | 2.38 | 1.78 | 4.16 |
| 7 | 56 | R | 2.34 | 1.78 | 4.06 |
| | | L | 2.32 | 1.74 | 4.06 |
| 8 | 56 | R | 2.00 | 2.10 | 4.10 |
| | | L | 2.14 | 1.80 | 3.94 |
| 9 | 63 | R | 2.14 | 2.06 | 4.20 |
| | | L | 2.12 | 2.00 | 4.12 |
| 10 | 64 | R | 2.44 | 1.86 | 4.30 |
| | | L | 2.38 | 1.92 | 4.30 |
| 11 | 68 | R | 2.28 | 2.08 | 4.36 |
| | | L | 2.28 | 2.00 | 4.28 |
| 12 | 69 | R | 2.18 | 1.94 | 4.12 |
| | | L | 2.14 | 1.90 | 4.04 |
| 13 | 72 | R | 2.06 | 2.02 | 4.08 |
| | | L | 2.12 | 2.06 | 4.18 |
| 14 | 76 | R | 1.98 | 1.86 | 3.84 |
| | | L | 2.05 | 1.78 | 3.83 |
| Mean | 56.36 | R | 2.19 | 1.89 | 4.07 |
| | | L | 2.18 | 1.88 | 4.06 |
| S.D. | 13.06 | R | 0.15 | 0.13 | 0.15 |
| | | L | 0.15 | 0.12 | 0.16 |

TABLE 5.6 Values of peak-to-peak interwave intervals (msec) for normal females at 70 dBSL.

| CASE | AGE YEARS | | INTERWAVE INTERVAL | | |
|---|---|---|---|---|---|
| | | | I - III | III - V | I - V |
| 1 | 30 | R | 1.84 | 1.82 | 3.66 |
| | | L | 1.88 | 1.96 | 3.84 |
| 2 | 42 | R | 2.18 | 1.88 | 4.06 |
| | | L | — | — | — |
| 3 | 45 | R | 2.26 | 1.80 | 4.06 |
| | | L | 2.28 | 1.86 | 4.14 |
| 4 | 48 | R | 2.02 | 1.72 | 3.74 |
| | | L | 2.06 | 1.74 | 3.80 |
| 5 | 48 | R | 2.10 | 1.90 | 4.00 |
| | | L | 2.26 | 2.02 | 4.28 |
| 6 | 52 | R | 2.10 | 1.88 | 3.98 |
| | | L | 2.28 | 1.86 | 4.14 |
| 7 | 56 | R | 2.26 | 1.80 | 4.06 |
| | | L | 2.32 | 1.78 | 4.04 |
| 8 | 56 | R | 2.08 | 2.00 | 4.08 |
| | | L | 2.18 | 1.90 | 4.08 |
| 9 | 63 | R | 1.96 | 2.24 | 4.20 |
| | | L | 2.12 | 1.96 | 4.08 |
| 10 | 64 | R | 2.40 | 1.92 | 4.32 |
| | | L | 2.30 | 2.04 | 4.34 |
| 11 | 68 | R | 2.22 | 2.26 | 4.48 |
| | | L | 2.32 | 2.14 | 4.46 |
| 12 | 69 | R | 2.20 | 1.90 | 4.10 |
| | | L | 2.10 | 1.94 | 4.04 |
| 13 | 72 | R | 2.06 | 2.04 | 4.10 |
| | | L | 2.12 | 2.08 | 4.20 |
| 14 | 76 | R | 1.96 | 1.80 | 3.76 |
| | | L | 2.04 | 1.82 | 3.86 |
| Mean | 56.36 | R | 2.12 | 1.93 | 4.04 |
| | | L | 2.17 | 1.93 | 4.10 |
| S.D. | 13.06 | R | 0.15 | 0.16 | 0.22 |
| | | L | 0.14 | 0.12 | 0.20 |

TABLE 5.7 Values of peak-to-peak interwave intervals (msec) for normal females at 60 dBSL.

| CASE | AGE | AMPLITUDE | | | LATENCY | | |
|---|---|---|---|---|---|---|---|
| | YEARS | I | III | V | I | III | V |
| 1 | 24 | R 98 | 203 | 539 | 1.48 | 3.82 | 5.56 |
| | | L 43 | 164 | 508 | 1.54 | 4.06 | 5.66 |
| 2 | 25 | R 199 | 289 | 750 | 1.52 | 3.72 | 5.46 |
| | | L 191 | 207 | 594 | 1.68 | 3.84 | 5.70 |
| 3 | 25 | R 59 | 90 | 500 | 1.54 | 3.10 | 5.48 |
| | | L 203 | 199 | 375 | 1.68 | 3.76 | 5.48 |
| 4 | 25 | R 270 | 105 | 605 | 1.46 | 3.74 | 5.32 |
| | | L 270 | 55 | 520 | 1.54 | 3.78 | 5.52 |
| 5 | 26 | R 199 | 289 | 640 | 1.52 | 3.72 | 5.46 |
| | | L 201 | 200 | 375 | 1.64 | 3.80 | 5.50 |
| 6 | 30 | R 95 | 133 | 430 | 1.76 | 3.74 | 5.56 |
| | | L 152 | 184 | 359 | 1.46 | 3.72 | 5.44 |
| 7 | 31 | R 266 | 285 | 574 | 1.50 | 3.74 | 5.54 |
| | | L 395 | 217 | 504 | 1.48 | 3.76 | 5.34 |
| 8 | 34 | R 186 | 227 | 527 | 1.48 | 3.58 | 5.44 |
| | | L 316 | 207 | 625 | 1.54 | 3.84 | 5.62 |
| 9 | 37 | R 141 | 105 | 285 | 1.50 | 3.82 | 5.88 |
| | | L 242 | 219 | 262 | 1.56 | 3.94 | 5.96 |
| 10 | 40 | R 95 | 172 | 211 | 1.68 | 3.88 | 5.68 |
| | | L 125 | 117 | 227 | 1.54 | 3.94 | 5.84 |
| 11 | 42 | R 156 | 223 | 547 | 1.50 | 3.88 | 5.80 |
| | | L 176 | 177 | 520 | 1.50 | 3.82 | 5.76 |
| 12 | 53 | R 137 | 137 | 492 | 1.58 | 3.94 | 5.78 |
| | | L 176 | 168 | 520 | 1.50 | 3.82 | 5.76 |
| 13 | 54 | R 66 | 270 | 270 | 1.78 | 4.16 | 6.10 |
| | | L 139 | 194 | 266 | 1.71 | 4.04 | 5.80 |
| 14 | 61 | R 211 | 180 | 355 | 1.52 | 3.66 | 5.58 |
| | | L 140 | 129 | 414 | 1.60 | 3.80 | 5.58 |
| 15 | 63 | R 43 | 199 | 535 | 1.58 | 3.90 | 5.84 |
| | | L 76 | 359 | 535 | 1.54 | 3.88 | 5.70 |
| 16 | 63 | R 98 | 250 | 676 | 1.54 | 3.92 | 5.54 |
| | | L 74 | 74 | 668 | 1.60 | 3.84 | 5.56 |
| 17 | 64 | R 266 | 287 | 579 | 1.50 | 3.74 | 5.55 |
| | | L 75 | 74 | 665 | 1.58 | 3.82 | 5.54 |
| Mean | 41 | R 152 | 203 | 501 | 1.56 | 3.77 | 5.62 |
| | | L 170 | 167 | 467 | 1.57 | 3.86 | 5.64 |
| S.D. | 15.1 | R 75 | 70 | 128 | 0.10 | 0.22 | 0.20 |
| | | L 98 | 74 | 138 | 0.08 | 0.11 | 0.17 |

TABLE 5.8 Values of peak-to-peak amplitude (nV) and latency (msec) for normal control males at 80 dBSL for right and left ears.

| CASE | AGE | | AMPLITUDE | | | LATENCY | | |
|---|---|---|---|---|---|---|---|---|
| | YEARS | | I | III | V | I | III | V |
| 1 | 24 | R | 82 | 223 | 550 | 1.50 | 3.94 | 5.58 |
| | | L | 35 | 152 | 488 | 1.74 | 4.16 | 5.78 |
| 2 | 25 | R | 234 | 285 | 617 | 1.62 | 3.74 | 5.62 |
| | | L | 184 | 152 | 371 | 1.70 | 3.80 | 5.54 |
| 3 | 25 | R | 42 | 234 | 340 | 1.68 | 3.68 | 5.70 |
| | | L | 191 | 207 | 594 | 1.68 | 3.84 | 5.70 |
| 4 | 25 | R | 203 | 242 | 506 | 1.66 | 3.76 | 5.50 |
| | | L | 273 | 74 | 520 | 1.70 | 3.92 | 5.54 |
| 5 | 26 | R | 82 | 220 | 563 | 1.58 | 3.80 | 5.58 |
| | | L | 190 | 200 | 390 | 1.68 | 3.84 | 5.70 |
| 6 | 30 | R | 121 | 180 | 363 | 1.60 | 3.84 | 5.66 |
| | | L | 164 | 176 | 348 | 1.58 | 3.76 | 5.64 |
| 7 | 31 | R | 266 | 402 | 535 | 1.64 | 3.74 | 5.68 |
| | | L | 277 | 207 | 383 | 1.52 | 3.84 | 5.88 |
| 8 | 34 | R | 355 | 332 | 613 | 1.56 | 3.68 | 5.58 |
| | | L | 227 | 125 | 570 | 1.72 | 3.90 | 5.66 |
| 9 | 37 | R | 148 | 215 | 145 | 1.72 | 3.88 | 5.98 |
| | | L | 74 | 238 | 441 | 1.76 | 3.96 | 6.00 |
| 10 | 40 | R | 203 | 258 | 336 | 1.62 | 3.92 | 5.82 |
| | | L | 195 | 254 | 305 | 1.64 | 3.94 | 5.90 |
| 11 | 42 | R | 309 | 160 | 473 | 1.52 | 3.92 | 5.82 |
| | | L | 191 | 175 | 496 | 1.54 | 3.90 | 5.84 |
| 12 | 53 | R | 39 | 94 | 480 | 1.58 | 4.08 | 5.94 |
| | | L | 191 | 180 | 396 | 1.54 | 3.90 | 5.84 |
| 13 | 54 | R | 39 | 94 | 480 | 1.58 | 4.08 | 5.90 |
| | | L | 160 | 160 | 379 | 1.78 | 4.14 | 5.92 |
| 14 | 61 | R | 223 | 145 | 250 | 1.64 | 3.74 | 5.64 |
| | | L | 160 | 82 | 344 | 1.64 | 3.90 | 5.64 |
| 15 | 63 | R | 82 | 90 | 355 | 1.64 | 3.98 | 5.94 |
| | | L | 63 | 184 | 457 | 1.64 | 3.98 | 5.80 |
| 16 | 63 | R | 184 | 515 | 707 | 1.70 | 4.00 | 5.76 |
| | | L | 125 | 74 | 586 | 1.72 | 3.90 | 5.64 |
| 17 | 64 | R | 147 | 216 | 146 | 1.70 | 3.90 | 5.96 |
| | | L | 124 | 74 | 584 | 1.73 | 3.91 | 5.65 |
| Mean | 41 | R | 162 | 230 | 438 | 1.62 | 3.86 | 5.75 |
| | | L | 166 | 160 | 450 | 1.67 | 3.93 | 5.76 |
| S.D. | 15.1 | R | 96 | 111 | 102 | 0.06 | 0.13 | 0.16 |
| | | L | 67 | 57 | 95 | 0.08 | 0.13 | 0.17 |

TABLE 5.9 Values of peak-to-peak amplitude (nV) and latency (msec) for normal control males at 70 dBSL for right and left ears.

| CASE | AGE | AMPLITUDE | | | LATENCY | | |
|---|---|---|---|---|---|---|---|
| | YEARS | I | III | V | I | III | V |
| 1 | 24 | R 125 | 117 | 523 | 1.96 | 4.10 | 5.84 |
| | | L 97 | 141 | 520 | 1.78 | 4.26 | 5.98 |
| 2 | 25 | R 129 | 238 | 589 | 1.72 | 3.88 | 5.64 |
| | | L 156 | 199 | 480 | 1.80 | 3.92 | 5.84 |
| 3 | 25 | R 47 | 145 | 285 | 1.72 | 3.74 | 5.80 |
| | | L 133 | 117 | 277 | 1.84 | 3.92 | 5.80 |
| 4 | 25 | R 133 | 27 | 418 | 1.82 | 3.96 | 5.64 |
| | | L 105 | 109 | 395 | 1.88 | 3.96 | 5.76 |
| 5 | 26 | R 129 | 238 | 591 | 1.72 | 3.88 | 5.64 |
| | | L 131 | 118 | 277 | 1.85 | 3.93 | 5.81 |
| 6 | 30 | R 102 | 31 | 418 | 1.86 | 3.96 | 5.84 |
| | | L 102 | 83 | 316 | 1.84 | 3.90 | 5.84 |
| 7 | 31 | R 121 | 211 | 535 | 1.88 | 3.98 | 5.90 |
| | | L 262 | 191 | 430 | 1.64 | 3.94 | 5.92 |
| 8 | 34 | R 301 | 164 | 195 | 1.64 | 3.78 | 5.64 |
| | | L 246 | 234 | 461 | 1.78 | 4.16 | 5.96 |
| 9 | 37 | R 211 | 121 | 199 | 1.82 | 4.00 | 6.06 |
| | | L 207 | 137 | 344 | 1.82 | 4.04 | 6.04 |
| 10 | 40 | R 74 | 109 | 313 | 1.90 | 4.12 | 6.02 |
| | | L 82 | 180 | 383 | 1.66 | 4.10 | 5.94 |
| 11 | 42 | R 227 | 156 | 402 | 1.60 | 3.94 | 5.86 |
| | | L 199 | 82 | 441 | 1.66 | 3.98 | 5.94 |
| 12 | 53 | R 66 | 270 | 270 | 1.78 | 4.16 | 6.10 |
| | | L 66 | 63 | 441 | 1.84 | 4.06 | 5.96 |
| 13 | 54 | R 66 | 270 | 270 | 1.80 | 4.18 | 6.12 |
| | | L 94 | 85 | 164 | 1.90 | 4.25 | 6.04 |
| 14 | 61 | R 246 | 109 | 215 | 1.70 | 3.86 | 5.70 |
| | | L 152 | 82 | 160 | 1.76 | 3.90 | 5.76 |
| 15 | 63 | R 80 | 156 | 289 | 1.82 | 4.20 | 6.16 |
| | | L 63 | 82 | 402 | 1.78 | 4.08 | 5.96 |
| 16 | 63 | R 130 | 220 | 457 | 1.75 | 3.95 | 5.90 |
| | | L 109 | 83 | 438 | 1.78 | 4.20 | 5.94 |
| 17 | 64 | R 245 | 110 | 213 | 1.70 | 3.86 | 5.10 |
| | | L 198 | 83 | 442 | 1.80 | 3.99 | 5.95 |
| Mean | 41 | R 143 | 143 | 394 | 1.78 | 3.97 | 5.82 |
| | | L 141 | 122 | 375 | 1.79 | 4.04 | 5.93 |
| S.D. | 15.1 | R 75 | 75 | 138 | 0.10 | 0.14 | 0.26 |
| | | L 62 | 51 | 105 | 0.08 | 0.13 | 0.18 |

TABLE 5.10 Values of peak-to-peak amplitude (nV) and latency (msec) for normal control males at 60 dBSL for right and left ears.

| CASE | AGE YEARS | INTERWAVE INTERVAL | | | |
|---|---|---|---|---|---|
| | | | I - III | III - V | I - V |
| 1 | 24 | R | 2.34 | 1.74 | 4.08 |
| | | L | 2.52 | 1.60 | 4.12 |
| 2 | 25 | R | 2.20 | 1.74 | 3.94 |
| | | L | 2.16 | 1.86 | 4.02 |
| 3 | 25 | R | 2.10 | 1.84 | 3.94 |
| | | L | 2.08 | 1.72 | 3.80 |
| 4 | 25 | R | 2.28 | 1.64 | 3.92 |
| | | L | 2.24 | 1.74 | 3.90 |
| 5 | 26 | R | 2.20 | 1.74 | 3.94 |
| | | L | 2.16 | 1.70 | 3.86 |
| 6 | 30 | R | 1.98 | 1.82 | 3.80 |
| | | L | 2.26 | 1.72 | 3.98 |
| 7 | 31 | R | 2.24 | 1.80 | 4.04 |
| | | L | 2.28 | 1.58 | 3.86 |
| 8 | 34 | R | 2.10 | 1.86 | 3.96 |
| | | L | 2.30 | 1.78 | 4.08 |
| 9 | 37 | R | 2.24 | 2.06 | 4.30 |
| | | L | 2.02 | 2.36 | 4.38 |
| 10 | 40 | R | 2.20 | 1.80 | 4.00 |
| | | L | 2.40 | 1.90 | 4.30 |
| 11 | 42 | R | 2.38 | 1.96 | 4.30 |
| | | L | 2.32 | 1.94 | 4.26 |
| 12 | 53 | R | 2.36 | 1.84 | 4.20 |
| | | L | 2.32 | 1.94 | 4.26 |
| 13 | 54 | R | 2.38 | 1.94 | 4.32 |
| | | L | 2.33 | 1.76 | 4.09 |
| 14 | 61 | R | 2.14 | 1.92 | 4.06 |
| | | L | 2.20 | 1.78 | 3.98 |
| 15 | 63 | R | 2.32 | 1.94 | 4.26 |
| | | L | 2.34 | 1.82 | 4.16 |
| 16 | 63 | R | 2.38 | 1.62 | 4.00 |
| | | L | 2.24 | 1.72 | 3.96 |
| 17 | 64 | R | 2.24 | 1.81 | 4.05 |
| | | L | 2.24 | 1.72 | 3.96 |
| Mean | 41 | R | 2.24 | 1.83 | 4.07 |
| | | L | 2.26 | 1.80 | 4.06 |
| S.D. | 15.1 | R | 0.12 | 0.12 | 0.16 |
| | | L | 0.12 | 0.18 | 0.17 |

TABLE 5.11 Values of peak-to-peak interwave intervals (msec) for normal control males at 80 dBSL for right and left ears.

| CASE | AGE YEARS | INTERWAVE INTERVAL | | | |
|---|---|---|---|---|---|
| | | | I - III | III - V | I - V |
| 1 | 24 | R | 2.44 | 1.64 | 4.08 |
| | | L | 2.42 | 1.62 | 4.04 |
| 2 | 25 | R | 2.12 | 1.88 | 4.00 |
| | | L | 2.10 | 1.74 | 3.84 |
| 3 | 25 | R | 2.00 | 2.02 | 4.02 |
| | | L | 2.16 | 1.86 | 4.02 |
| 4 | 25 | R | 2.10 | 1.74 | 3.84 |
| | | L | 2.22 | 1.62 | 3.84 |
| 5 | 26 | R | 2.22 | 1.78 | 4.00 |
| | | L | 2.16 | 1.68 | 4.02 |
| 6 | 30 | R | 2.24 | 1.82 | 4.06 |
| | | L | 2.18 | 1.82 | 4.06 |
| 7 | 31 | R | 2.10 | 1.94 | 4.04 |
| | | L | 2.32 | 2.04 | 4.36 |
| 8 | 34 | R | 2.12 | 1.90 | 4.02 |
| | | L | 2.18 | 1.76 | 3.94 |
| 9 | 37 | R | 2.16 | 2.10 | 4.26 |
| | | L | 2.20 | 2.04 | 4.24 |
| 10 | 40 | R | 2.30 | 1.90 | 4.20 |
| | | L | 2.30 | 1.96 | 4.26 |
| 11 | 42 | R | 2.40 | 1.90 | 4.30 |
| | | L | 2.36 | 1.94 | 4.30 |
| 12 | 53 | R | 2.50 | 1.86 | 4.36 |
| | | L | 2.36 | 1.94 | 4.30 |
| 13 | 54 | R | 2.46 | 1.82 | 4.32 |
| | | L | 2.36 | 1.78 | 4.14 |
| 14 | 61 | R | 2.10 | 1.90 | 4.00 |
| | | L | 2.26 | 1.74 | 4.00 |
| 15 | 63 | R | 2.34 | 1.96 | 4.30 |
| | | L | 2.34 | 1.82 | 4.16 |
| 16 | 63 | R | 2.30 | 1.76 | 4.06 |
| | | L | 2.18 | 1.74 | 3.92 |
| 17 | 64 | R | 2.16 | 2.10 | 4.26 |
| | | L | 2.18 | 1.74 | 3.92 |
| Mean | 41 | R | 2.24 | 1.88 | 4.13 |
| | | L | 2.26 | 1.82 | 4.10 |
| S.D. | 15.1 | R | 0.15 | 0.12 | 0.15 |
| | | L | 0.11 | 0.13 | 0.18 |

TABLE 5.12 Values of peak-to-peak interwave intervals (msec) for normal control males at 70 dBSL for right and left ears.

| CASE | AGE YEARS | INTERWAVE INTERVAL | | |
|---|---|---|---|---|
| | | I - III | III - V | I - V |
| 1 | 24 | R 2.14 | 1.74 | 3.88 |
| | | L 2.48 | 1.72 | 4.20 |
| 2 | 25 | R 2.16 | 1.76 | 3.92 |
| | | L 2.12 | 1.92 | 4.04 |
| 3 | 25 | R 2.02 | 2.06 | 4.08 |
| | | L 2.08 | 1.88 | 3.96 |
| 4 | 25 | R 2.14 | 1.68 | 3.82 |
| | | L 2.08 | 1.80 | 3.88 |
| 5 | 26 | R 2.16 | 1.76 | 3.92 |
| | | L 2.08 | 1.88 | 3.96 |
| 6 | 30 | R 2.10 | 1.88 | 3.98 |
| | | L 2.06 | 1.94 | 4.00 |
| 7 | 31 | R 2.04 | 1.98 | 4.02 |
| | | L 2.30 | 1.98 | 4.28 |
| 8 | 34 | R 2.14 | 1.86 | 4.00 |
| | | L 2.38 | 1.80 | 4.18 |
| 9 | 37 | R 2.18 | 2.06 | 4.24 |
| | | L 2.22 | 2.00 | 4.22 |
| 10 | 40 | R 2.22 | 1.90 | 4.12 |
| | | L 2.54 | 1.84 | 4.28 |
| 11 | 42 | R 2.34 | 1.92 | 4.26 |
| | | L 2.32 | 1.96 | 4.28 |
| 12 | 53 | R 2.38 | 1.94 | 4.32 |
| | | L 2.22 | 1.82 | 3.92 |
| 13 | 54 | R 2.38 | 1.94 | 4.32 |
| | | L 2.35 | 1.79 | 4.14 |
| 14 | 61 | R 2.16 | 1.84 | 4.00 |
| | | L 2.14 | 1.86 | 4.00 |
| 15 | 63 | R 2.38 | 1.96 | 4.34 |
| | | L 2.30 | 1.88 | 4.18 |
| 16 | 63 | R 2.20 | 1.95 | 4.15 |
| | | L 2.42 | 1.74 | 4.16 |
| 17 | 64 | R 2.16 | 1.84 | 4.00 |
| | | L 2.19 | 1.96 | 4.15 |
| Mean | 41 | R 2.19 | 1.89 | 4.08 |
| | | L 2.25 | 1.95 | 4.13 |
| S.D. | 15.1 | R 0.11 | 0.11 | 0.17 |
| | | L 0.15 | 0.25 | 0.17 |

TABLE 5.13 Values of peak-to-peak interwave intervals (msec) for normal control males at 60 dBSL for right and left ears.

| PARAMETERS | | Female | | Male | | T-test (dF=29) | |
|---|---|---|---|---|---|---|---|
| | Wave | Mean | S.D. | Mean | S.D. | t | p |
| 80 dBSL | I | 188 | 124 | 152 | 75 | 0.10 | N.S. |
| | III | 316 | 149 | 203 | 70 | 3.01 | 0.005 |
| | V | 482 | 148 | 501 | 128 | 1.06 | N.S. |
| 70 dBSL | I | 184 | 116 | 162 | 96 | 0.98 | N.S. |
| | III | 255 | 120 | 230 | 111 | 0.01 | N.S. |
| | V | 437 | 99 | 438 | 102 | 0.593 | N.S. |
| 60 dBSL | I | 134 | 112 | 143 | 75 | 1.42 | N.S. |
| | III | 213 | 122 | 143 | 75 | 1.96 | 0.05 |
| | V | 396 | 132 | 364 | 138 | 0.66 | N.S. |

TABLE 5.14 Summary of statistical analysis t-test of amplitude of normal females-males at 80, 70 and 60 dBSL, where NS = not significant.

| PARAMETERS | | Female | | Male | | T-test (df 20) | |
|---|---|---|---|---|---|---|---|
| | Wave | Mean | S.D. | Mean | S.D. | t | p |
| 80 dBSL | I | 1.53 | 0.05 | 1.56 | 0.10 | 0.900 | N.S. |
| | III | 3.75 | 0.15 | 3.77 | 0.22 | 1.150 | N.S. |
| | V | 5.58 | 0.20 | 5.62 | 0.20 | 1.526 | N.S. |
| 70 dBSL | I | 1.62 | 0.14 | 1.62 | 0.06 | 0.250 | N.S. |
| | III | 3.82 | 0.16 | 3.86 | 0.13 | 1.863 | 0.05 |
| | V | 5.70 | 0.20 | 5.75 | 0.16 | 1.793 | 0.05 |
| 60 dBSL | I | 1.81 | 0.13 | 1.78 | 0.10 | 0.989 | N.S. |
| | III | 3.91 | 0.19 | 3.97 | 0.14 | 1.642 | N.S. |
| | V | 5.88 | 0.24 | 5.8 | 0.26 | 0.88 | N.S. |

TABLE 5.15 Summary of statistical analysis t-test of latency of normal females-males at 80, 70 and 60 dBSL, where NS = not significant.

| PARAMETERS | | Female | | Male | | T-test (dF=38) | |
|---|---|---|---|---|---|---|---|
| | Wave | Mean | S.D. | Mean | S.D. | t | p |
| 80 dBSL | I-III | 2.22 | 0.16 | 2.24 | 0.12 | 1.42 | N.S. |
| | III-V | 1.84 | 0.16 | 1.83 | 0.12 | 1.31 | N.S. |
| | I-V | 4.05 | 0.19 | 4.07 | 0.16 | 1.38 | N.S. |
| 70 dBSL | I-III | 2.19 | 0.15 | 2.24 | 0.15 | 1.51 | N.S. |
| | III-V | 1.89 | 0.13 | 1.88 | 0.12 | 1.23 | N.S. |
| | I-V | 4.07 | 0.15 | 4.13 | 0.15 | 1.58 | N.S. |
| 60 dBSL | I-III | 2.12 | 0.15 | 2.19 | 0.11 | 1.55 | N.S. |
| | III-V | 1.93 | 0.16 | 1.89 | 0.11 | 0.82 | N.S. |
| | I-V | 4.04 | 0.22 | 4.08 | 0.17 | 0.57 | N.S. |

TABLE 5.16 Summary of statistical analysis t-test of interwave intervals of normal females-males at 80, 70 and 60 dBSL, where NS - not significant.

| PARAMETERS | | 80 dB SL | | 70 dB SL | | 60 dB SL | |
|---|---|---|---|---|---|---|---|
| | Confidence Limit | Male | Female | Male | Female | Male | Female |
| AMPLITUDE | | | | | | | |
| I | Upper | 299 | 431 | 350 | 411 | 290 | 353 |
| | Lower | 5 | -55 | -26 | -43 | -4 | 85 |
| III | Upper | 340 | 608 | 448 | 490 | 290 | 237 |
| | Lower | 66 | 24 | 12 | 20 | -4 | 189 |
| V | Upper | 752 | 772 | 638 | 632 | 303 | 655 |
| | Lower | 250 | 192 | 238 | 243 | 13 | 137 |
| LATENCY | | | | | | | |
| I | Upper | 1.76 | 1.63 | 1.74 | 1.89 | 1.98 | 2.06 |
| | Lower | 1.36 | 1.73 | 1.50 | 1.35 | 1.58 | 1.56 |
| III | Upper | 4.20 | 4.04 | 4.11 | 4.13 | 4.24 | 4.28 |
| | Lower | 3.34 | 3.46 | 3.61 | 3.51 | 3.70 | 3.54 |
| V | Upper | 6.01 | 5.97 | 6.06 | 6.09 | 6.33 | 6.35 |
| | Lower | 5.23 | 5.19 | 5.44 | 5.31 | 5.31 | 5.41 |
| INTERWAVE INTERVAL I - III | Upper | 2.48 | 2.53 | 2.53 | 2.48 | 2.41 | 2.41 |
| | Lower | 2.00 | 1.91 | 1.95 | 1.90 | 1.97 | 1.83 |
| III - V | Upper | 2.07 | 2.15 | 2.12 | 2.14 | 2.11 | 2.24 |
| | Lower | 1.59 | 1.53 | 1.64 | 1.64 | 1.67 | 1.62 |
| I - V | Upper | 4.38 | 4.42 | 4.42 | 4.36 | 4.41 | 4.47 |
| | Lower | 3.76 | 3.68 | 3.84 | 3.78 | 3.75 | 3.61 |

TABLE 5.17 95% confidence limits for right ears of normal male and female controls at 80, 70 and 60 dBSL.

| PARAMETERS | | 80 dB SL | | 70 dB SL | | 60 dB SL | |
|---|---|---|---|---|---|---|---|
| | Confidence Limit | Male | Female | Male | Female | Male | Female |
| AMPLITUDE | | | | | | | |
| I | Upper | 362 | 377 | 297 | 336 | 263 | 266 |
| | Lower | -22 | -43 | 35 | -28 | -19 | -40 |
| III | Upper | 312 | 528 | 272 | 446 | 222 | 369 |
| | Lower | 22 | 58 | 48 | -0.44 | 22 | 35 |
| V | Upper | 737 | 748 | 636 | 671 | 581 | 683 |
| | Lower | 197 | 246 | 264 | 157 | 169 | 95 |
| LATENCY | | | | | | | |
| I | Upper | 1.73 | 1.71 | 1.83 | 1.84 | 1.95 | 1.92 |
| | Lower | 1.41 | 1.43 | 1.51 | 1.52 | 1.63 | 1.53 |
| III | Upper | 4.08 | 4.05 | 4.18 | 4.13 | 4.29 | 4.22 |
| | Lower | 3.64 | 3.51 | 3.68 | 3.59 | 3.79 | 3.64 |
| V | Upper | 5.97 | 5.92 | 6.09 | 6.03 | 6.28 | 6.23 |
| | Lower | 5.31 | 5.34 | 5.43 | 5.45 | 5.58 | 5.49 |
| INTERWAVE INTERVAL I - III | Upper | 2.50 | 2.47 | 2.48 | 2.47 | 2.54 | 2.44 |
| | Lower | 2.02 | 1.97 | 2.04 | 1.89 | 1.96 | 1.90 |
| III - V | Upper | 2.15 | 2.17 | 2.07 | 2.12 | 2.44 | 2.17 |
| | Lower | 1.45 | 1.55 | 1.57 | 1.64 | 1.46 | 1.69 |
| I - V | Upper | 4.39 | 4.40 | 4.45 | 4.37 | 4.46 | 4.49 |
| | Lower | 3.73 | 3.74 | 3.74 | 3.75 | 3.80 | 3.71 |

TABLE 5.18 95% confidence limits for left ears of normal male and female controls at 80, 70 and 60 dBSL.

# CHAPTER SIX

# HYPO-THYROIDISM

## 6.1 Introduction

Many reports in the literature showed considerable interest in using evoked potential properties of the auditory system to study the effect of hypothyroidism on hearing. A great deal of information might be obained due to changes in amplitude, latency and interwave interval latency from the normal controls.

In 1971, Cohonen et. al. studied cochlear evoked potentials. They reported a significant reduction in cochlear microphonic in guinea pigs made hypothyroid by intra peritoneal injections of radioiodine. More recently, Uziel et. al. (1980) reported a delay of cochlear potential at the round window in rats treated with propyl-thio-uracel. Meyerhoff (1979) stated the elevation of threshold of $N_1$ and $N_2$ and brainstem evoked response in hypo-thyroid guinea pigs. The auditory nerve action potential has been studied by Rubenstein et. al. (1975). They reported changes in the shape, amplitude and latency of this potential in comparison with the normal guinea pigs. In the meanwhile they stated that these changes were reversible after treatment with thyroid hormone. Rubenstein et. al. (1974) reported prolongation of the latency period of evoked response audiometry and abnormal prolonged nerve conduction time in four congenital sporadic hypothyroid patients.

In addition to the use of evoked potentials in studying hypo-thyroidism, Mendel and Robinson (1978) reported only the presence of wave I and II of ABER in a two year old hypothyroid child. After the treatment the late waves, that is wave III, IV and V reappeared. More recently, Himelfarb et. al. (1981) used the auditory brainstem evoked response technique in

studying hypothyroid patients. They reported a significant prolongation of brainstem conduction time.

## 6.2 Literature Review

Hypothyroidism, congenital and acquired may be associated with hearing impairment. Although hypothyroidism has been recognized for a long time, the association of impairment of hearing due to this condition has only been appreciated and stressed since the end of the nineteenth century. The Myxoedema Committee of the Clinical Society of London reported in 1888, hearing impairment in 38 patients out of 69 suffering from myxoedema (cited in De Vos, 1963). Hearing impairment associated with hypothyroidism occurs in only a certain percentage: it might be conductive, sensorineural or mixed; it might be reversible by replacement thyroxine therapy; it occurs at any age. De Vos (1963) in his study on 32 hypothyroid patients found just 17 patients who suffered from hearing impairment. They had a variable degree of sensorineural deafness. In ten patients the loss was slight, while in three it was moderate, and severe in four patients. None of his patients had a conductive or mixed type of deafness. Post (1964) reported in an investigation of 42 hypothyroid patients that only four were found to have sensorineural impairmennt. They improved by treatment of hypothyroidism. Moehlig (1927) cited a hearing loss in 24 hypothyroid patients. He mentioned nothing about the type of loss, but the hearing improved after the treatment of hypothyroidism. Barnes (1947) reported the occurrence of hearing impairment in 45 patients. This impairment was conductive in all the patients.

McMahon (1947) stated that the hearing impairment associated with hypothyroidism could be conductive or sensorineural. He thought that the

sensorineural loss may not entirely return to normal by the thyroxine supplement therapy. McMahon noted with his patient that after medication the audiogram remained unchanged although the thyroid was in an euthyroid state and the patient felt that his hearing was improved.

Howarth and Lloyd (1956) in their study of hearing impairment associated hypothyroidism, observed that five out of seven patients had sensorineural deafness. This deafness occurred more with high frequencies. The other two patients had mixed deafness. Only two of the sensorineural deafness patients have been cured by the treatment of hypothyroidism. Just one of the two patients with mixed deafness showed an improvement of hearing with the thyroxine replacement therapy, the other showed no change. Hilger (1956) was the first who documented audiologically the degree of hearing loss in cases of acquired hypothyroidism. He studied acquired hypothyroid in three patients. He found that all of these patients had a flat bilateral sensorineural hearing loss. The hearing loss improved with the treatment. In a study of 72 patients with acquired and congenital hypothyroidism, Bhatia et. al. (1977) stated the occurrence of hearing impairment in 31 patients (43.0%), being conductive in 8.3% and sensorineural in 34.7%. The pure tone audiogram was flat in all the patients with sensorineural deafness.

Debruyne et. al. (1983) described 45 patients with congenital hypothyroidism. They stated that 80% of these patients had normal hearing and 20% had sensorineural hearing loss, most of them at high frequencies. Furthermore they noted that the deafness was serious in 11% of patients to a degree that they needed rehabilitation with the use of hearing aids. Kemp (1907) reported the occurrence of hearing loss in a 53 year old hypothyroid woman. In the same manner, King (1907) described a 56 year old hypothyroid man. This man had normal hearing prior to being hypothyroid: the hearing

was improved following thyroid therapy. McLaurin (1945) also reported hearing impairment in a 47 year old hypothyroid man. Ritter and Lawrence (1960) observed that the hearing impairment in their two hypothyroid patients was of the sensorineural type. It was reversible by the replacement therapy. In a study of congenital sporadic hypothyroidism in 21 patients, Rubenstein et. al. (1974) found that only 13 patients were suffering from hearing impairment, being sensorineural in eight, conductive in two and a mixed deafness in three patients.

Hearing impairment associated with acquired hypothyroidism seems to be less severe than that associated with congenital hypothyroidism (Batsakis and Nisheyama, 1962; Ritter and Larwence, 1960).

It is well known that there is a general agreement about the occurrence of hearing impairment associated with hypothyroidism. However the pathogenesis, the degree, the audiological characteristics and the site of lesion of this impairment are not yet universally agreed upon. The conductive hearing impairment element was attributed to the thickening and dryness of the tympanic membrane, and to myxoedematous changes of middle ear and eustachian tube mucosa (McMahon, 1947; Ritter, 1967; Howarth and Lloyd, 1956 and Kemp, 1907), and to the ossicular abnormalities, partial and complete obstruction of the oval and round windows (Meyerhoff, 1979).

The sensorineural hearing element in acquired hypothyroidism is not fully explained by organic damage to the labyrinth yet. A lot of histological experiments have been carried out on different kinds of animals in an attempt to explore the effect of hypothyroidism on the auditory pathway. Ritter and Lawrence (1960) in a study on chicken embryos rendered hypothyroidism by injection of thio-urea at the fourth, ninth and fourteenth day of incubation. Nothing abnormal was noted with embryos injected at the

ninth and fourteenth day. The fourth day injected embryos showed: delay in hatching; under-development; oedema in the nerve cells region in the organ of corti at acoustic papilla. The middle ear showed delay in ossification of the stapes but no sign of hypertrophy of the middle ear mucous membrane. Round and oval windows were normal. Ritter (1967) in another study on rats showed no damage in the sensory cells. De Vos (1963) in his study on mice reported that no morphological changes had been found in the organ of corti in a state of acquired hypothyroidism and the only anatomical abnormality was slight degeneration of the spiral ganglion. This degeneration was general and not always present. Degeneration of spiral ganglion with the absence of any pathological changes in the cochlear structures and presence of sensorineural deafness was found in some hypothyroid patients. All these findings carried him to presume that the site of lesion would be retro-cochclear rather than cochlear. Kohonen et. al. (1971) revealed, by histological study performed on guinea pigs, that there is slight to moderate outer hair cells loss. This was mostly in the apical half of the organ of corti. The remainder of the organ of corti was normal. They noted that this finding could occur even in the normal guinea pigs and was not significant to produce hearing loss. They attribute their failing to demonstrate that definite morphological changes correlate with functional hearing loss, to the lack of histological methods. Myerhoff (1979) confirmed that the site of lesion is the cochlea in a study on guinea pigs. He stated the presence of degeneration of outer and inner hair cells as well as the supporting cells, furthermore he found some abnormality in stria vascularis, the large intra cellular space; and the tectorial membrane was irregular. For the Hensen's cells he found the accumulation of lipid in them and debris in the cochlear duct. Myerhoff, in the light of these results, emphasized that the cochlea is the site of lesion. Debruyne et.

al. (1983) in their investigative study on 45 congenital hypothyroid patients concluded that the pathological basis of sensorineural deafness was due to an immature development of the organ of corti. Anniko and Rosenkvist (1982) were in agreement with the findings of Meyerhoff about the tectorial membrane. The tectorial membrane was retracted from the surface of the organ of corti and lying in the inner sulcus region. Also it lost its normal structure and stiffness. Anniko and his associates disagreed with Meyerhoff about the inner and outer hair cells. They found the preservation of these cells without any change. Anniko et. al. (1982) stated that the basilar membrane was thickened due to the precipitation of the amorphous substance in it. Anniko et. al. achieved these findings as a result of the study on rats made hypothyroid by adding mithemazole to their drinking water for six weeks.

In another study on mice, hypothyroidism was caused by adding propyl-thio-uracil to their drinking water. Deol (1973b) found that the mice had severe hearing loss. By histological study Deol could find that the tectorial membrane was grossly distorted and out of contact with the hair cells. The hair cells were malformed. Deol stated that the hearing and the organ of corti of the offspring were normal after adding L-thyroxine to their drinking water. He summarized that "The loss of hearing can be fully accounted for by the cochlear abnormalities".

Uziel et. al. (1981) attributed the sensorineural hearing loss element in the case of hypothyroidism to the immaturity of the cochlear structures and ultra structure changes. They achieved this result from the investigating study on rat pups made hypothyroidic by propyl-thio-uracil during the first 35 days after birth. They reported some morphological changes in the cochlea and the tectorial membrane. In the cochlea they

found the persistance of Kolleker's organ, marked signs of immaturity of the sensory epithelium. The tunnel of corti had not opened yet, and the sensory and supporting cells were immature with abnormal persistance of Kinocilium. The tectorial membrane was markedly distorted.

Besides the anatomical studies which I mentioned previously, there were some electro-physiological studies in order to show the effect of hypothyroidism on the sensory evoked potential properties of the auditory system, and an attempt to study hearing impairment in the case of hypothyroidism by another method. Kohonen et. al. (1971) in a study of the cochlear microphonic in guinea pigs made hypothyroidism by an intra peritoneal injection of radioiodine. They demonstrated a reduction in cochlear microphonic evoked potentials. This reduction was more significant at low frequencies, that is to say 500 and 1000 Hz. Kohenen, and his associates could find in the same study, slight to moderate sensory cell loss in the third and fourth coils of the cochlea. These findings go with the fact that low frequencies are represented in the apical area of the cochlea. Rubenstein et. al. (1975) reported in their study on guinea pigs, the presence of abnormality in the shape of auditory nerve action potential, reduction in the amplitude and prolonged latency. These changes were reversed after the treatment with thyroid hormone.

In a study of congenital sporadic hypothyroidism, Rubenstein et. al. (1974), recorded a prolonged latency of the evoked response and abnormal prolonged nerve conduction time in four patients. Mendel and Robinson (1978) reported that only wave I and II of ABER were recorded in a two year old girl with congenital hypothyroidism. After the treatment with the thyroid hormone, the ABER recording had appeared to be similar to the normal one, that is to say the later waves had appeared as the serum thyroxine reached the normal level. By using the ABER technique in the study of

thyroid dysfunction, Himelfarb et. al. (1981) found a significant prolonged brainstem conduction time, diminished amplitude, poor synchronization and flattened peaks of waveforms in cases of hypothyroid patients. Himelfarb et. al. reported that these changes were more pronounced in elderly hypothyroid patients than in younger ones, and by treatment, the brainstem conduction time returned to normal when the euthyroid state had been reached. Himelfarb and his associates in this study concluded that the ABER could show dramatic changes in brainstem conduction time of all the patients, while the conventional audiometry detected hearing impairment in only three elderly patients. Consequently the ABER technique might be used to follow up the treatment in case of hypo-thyroid patients. Uziel et. al. (1980) reported a delay of cochlear microphonic potential at the round window in rats treated with propyl-thio-uracil.

In the study of the effect of hypothyroidism on other kinds of potentials, Lolas et. al. (1977) recorded reduction in amplitude of visual response of slow brain potential. Ladenson et. al. (1984) reported prolonged latency and reduction in amplitude of visual evoked potential in hypothyroid patients. These changes returned to normal after treatment. Abbott et. al. (1983) found prolonged latency and reduction in amplitude of visual evoked response in hypothyroid patients but these changes were not significant and were reversible by hypothyroidism treatment.

Causes of Hearing Loss

From the previous review, it would be possible to summarize the causes of hearing impairment in the case of hypothyroidism as follows:

1) Conductive hearing loss

In this case the cause might be: thickening and dryness of the tympanic membrane; Myxoedematous changes in the middle ear and eustachian tube mucosa (McMahon, 1947; Kemp, 1907; Howarth and Lloyd, 1956 and Ritter, 1967); ossicular and ligaments of the middle ear abnormalities; partial and complete obstruction of the oval and round windows (Meyerhoff, 1979).

2) Sensorineural hearing loss

Oedema in the nerve cells region in the organ of corti (Ritter and Lawrence, 1960); oedema in the spiral ganglion cells (Ritter, 1967); slight degeneration of the spiral ganglion (De Vos, 1963); degeneration of outer and inner hair cells as well as of the supporting cells; large intra cellular space in the stria vascularis (Meyerhoff, 1979); irregularity of the tectorial membrane and lipid accumulation in the Hensen's cells and debris in the cochlear duct (Meyerhoff, 1979); immature development of the organ of corti (Debruyne, 1983); retraction of the tectorial membrane from the surface of the organ of corti, the tectorial membrane also lost its normal structure and stiffness. Thickness of the basilar membrane due to the increase of the amount of amorphous substance in it (Anniko et. al., 1982); distortion of the tectorial membrane and its non contact with hair cells and malformation of hair cells (Deol, 1973b); retardation of the maturation of cochlear structure and ultra structural changes (Uziel et. al., 1981); slight to moderate outer hair cells loss, this was mainly in the apical half of the organ of corti (Kohonen et. al., 1971). De Vos (1963) suggested that hearing impairment in the case of hypothyroidism was not only due to thyroid hormone deficiency but also might be due to harmful substances circulating in the blood and have an enzymatic reaction on the auditory system and thyroid gland.

All experimental studies which are mentioned above showed the effect of hypothyroidism on different parts of the auditory pathway and the study of auditory evoked potentials in hypothyroid patients could be useful in adding something new to the diagnostic tests. In the present study an attempt was made to establish the validity of the ABER technique as a routine clinical diagnostic tool with hypothyroid patients.

## 6.3 Methods

### 6.3.1 Subjects

Auditory brainstem evoked responses (ABER) were recorded in 14 untreated hypothyroid patients. Thirteen were female and one male. The age of the women ranged from 26-78 years (mean 60.07, standard deviation 14.90) and the man was aged 78 years. Two patients underwent subtotal thyroidectomy due to severe thyroiditis. The remainder of the patients had simultaneous hypothyroidism. All the patients have been chosen from those who came to the laboratory of Nuclear Medicine for routine blood testing for suspected thyroid dysfunction. The diagnosis of hypothyroidism is based mainly on the clinical manifestations and on the radioimmune assay of serum free thyroxine [$FT_4$]. It was in the range from 1 to 7.3 p.Mol/L in all patients (normal range 8 to 24 p.Mol/L). The patients agreed to attend the recording session twice, once before starting the treatment and again within two to four months after the treatment and when an euthyroid state had been achieved.

### 6.3.2 Instrumentation

An Amplaid MK5 evoked potential signal processor was used as click and white noise generator. It controlled the amplifiers, stimulation, printing and storage devices. This was described earlier (see section 4.1, 4.1.1 and

4.1.2). Appropriate click and noise signals were transduced to the patient's ear through shielded TDH49 earphones as he was lying down on a bed beside the equipment.

### 6.3.3 Electrode attachment

In order to record the cochlear action potential and the subsequent brainstem responses, the electrodes were placed on the mastoid process ipsilateral to the stimulation (active), on the vertex (reference) and on the forehead just below the hair line (ground). The procedure of the electrode attachment was described earlier (see section 4.2.1).

### 6.3.4 Recording of ABER

Each patient underwent two recording sessions of about one and a half to two hours duration. One before the treatment and the other one after the treatment. At the beginning of the recording session, detailed, general and audiological histories were taken followed by pulse and temperature and otoscopic examination. Then the recording started with the same procedures which were described in section 4.3. Each intensity of recording was repeated twice and the average was taken.

## 6.4 Results

Untreated hypothyroid patients who were chosen from the laboratory of Nuclear Medicine after routine blood testing for suspected thyroid dysfunction were investigated. Of the 14 patients, thirteen were female and one male. The age of the women ranged from 26 to 78 years, the mean being 60.07 and standard deviation 14.89, and the man was aged 78 years. Two patients underwent subtotal thyroidectomy due to severe thyroiditis. The

remainder of the patients had simultaneous hypothyroidism. The diagnosis of hypothyroidism depended mainly on the clinical manifestations and on the level of the serum free thyroxine ($FT_4$). $FT_4$ was in the range from 1 to 7.3 p.mol/L in all patients (normal 8 to 24 p.mol/L). Otoscopic examination showed normal appearance of the tympanic membrane as well as the eustachian tube function. The tuning fork tests showed Rhinne's test to be positive and reduced in five patients. The pure tone audiograms showed a reduction in hearing in both air and bone conduction in five out of the fourteen patients (36%). The hearing impairment ranged from 5 to 16 dB at four frequencies average [FFA] 500, 1000, 2000 and 4000 Hz. In other words the hearing was slightly diminished in four patients and mildly diminished in one (see Table 6.3). It can be seen that 8 kHz, for which the audiometer limit was 80 dB, is the most affected frequency among the other frequencies (see Table 6.1). The hearing impairment was most probably due to hypothyroidism alone, as a careful and detailed medical history was taken from each patient, as well as an otoscopic examination being performed. Any patient whose hearing impairment seemed to be due to causes other than hypothyroidism was excluded. The tuning fork tests and pure tone audiogram revealed that bilateral, symmetrical and sensorineural hearing impairment was approximately equal in both sides in five patients (see Table 6.1). There was no significant hearing loss in the other nine patients. None of the patients showed an abnormal fatigue, that is to say the Cahart's tone decay test was negative.

Auditory brainstem evoked response waveforms for all hypothyroid patients at intensities 80, 70 and 60 dB sensation level (dBSL) for both right and left ears are shown in Figure 6.1. Tables 6.7 - 6.12 outline each waveform which represents an average of 2048 stimulus presentations measured at negative peak latency and peak-to-peak amplitude - from negative peak to

the following positive one - as well as the interwave interval latency of I-V, I-III and III-V.

The pattern of ABER was generally characterized by the fact that waves I, III and V were identified in virtually all subjects at all intensities with more flatness and broadness of their peaks and lack of synchronization than in the normal control subjects, as shown in Figure 6.1. Wave II was not identified in all patients and wave IV fused with wave V to make IV/V complex in most cases. There was a reduction of amplitude and prolonged latency of wave I of both ears as shown in Tables 6.7 - 6.9, but it was not statistically significant in relation to the normal control subjects. A significant reduction in amplitude of wave III and V ($p < 0.005$) and prolonged latency of wave III and wave V ($p < 0.01$) of both the left and right ear were found. No significant delay in the interwave I-III and III-V interval was present, but there was significant delay in I-V interwave interval ($p < 0.05$) as shown in Tables 6.10 - 6.12 for both sides.

The hypo-thyorid patient had a subnormal body temperature (35.99 ± 0.5°C) at the onset of the experimental test. Figure 6.3 shows the change of I-V interval plotted against oral temperature of 35.2 - 37°C in 21 patients. The interwave latency demonstrated prolongation differs from one patient to another, this prolongation was to an increase of wave V because wave I was within the normal range.

The best fit linear regression relating I-V interval and temperature is I-V interval = 13.23 - 0.25 × temperature. This had a correlation coefficient of .62. Rosenblum found a slope of -0.28 ms/°C, Stockard and Kusakari obtained slope values of -0.18 ms/°C and -0.42 ms∃°C respectively compared to the value of -.25 ms/°C found here.

6.4.1 Statistical analysis

State parameters of ABER at peaks of waves I, III and V at intensities of 80, 70 and 60 dB SL were obtained from both right and left ears for both normal control subjects and hypothyroid patients in relation to amplitude latency and inter-wave intervals of I-III, I-V and III-V. The null hypothesis to be tested:

$$HO: \quad U_1 > U_2$$

where $U_1$ = the mean of hypothyroid patients
$U_2$ = the mean of the normal control subjects

Student t-test has been used to test the above mentioned hypothesis under the level of significance $\alpha = < 0.05$. Significance differences are presented in Table 6.4. This implies that the 't' lies inside the critical region and the difference is significant. We say that there is evidence to accept the null hypothesis.

Re-test

Ten patients were re-tested up to four to five months later when they were clinically and biochemically euthyroid after the treatment with thyroxine. Figure 6.2 shows ABER for all re-test patients at 80, 70 and 60 dB SL for both right and left ears. The pattern of the peaks of the responses seems to be sharper than before the treatment. There are no significant changes in the latency and amplitude of wave I, marginal changes in wave III and maximal in wave V as shown in Table 6.6. There was change in the I-V interval but it was not statistically significant, however it seems now to be within normal levels.

The peaks of waveforms after treatment showed more synchronization than before the treatment. The pure tone audiograms showed changes between 5 - 15 dB mainly in the low frequencies (see Table 6.2). After the course of treatment the temperature of all the patients was raised to normal levels.

Statistical Analysis

The state parameters in relation to latency, amplitude and interwave intervals were obtained at waves I-III and V and I-III, I-V and III-V from hypothyroid patients before and after the treatment. The null hypothesis to be tested is:

$$HO: \quad U_1 - U_2 = 0$$

where $U_1$ is the mean of patients after the treatment
$U_2$ is the mean of patients before the treatment

Paired t-test has been investigated to test the above mentioned hypothesis under the level of significance $\alpha = 0.05$. Data are presented in Table 6.6. The 't' lies inside the critical region and the difference was significant, so there is no evidence to acept the null hypothesis.

A correlation was calculated between each ABER parameter and the following factors: the duration of hypothyroidism, $FT_4$, the hearing loss and the pulse rate for each patient. However there is no clear overall effect of these factors on any of the ABER parameters.

## 6.5 Discussion

The purpose of this experimental study was an attempt to establish the validity of using the ABER technique as a routine diagnostic investigatory tool to ascertain whether or not hearing impairment has occurred in hypothyroid patients. This study arose from research which found: firstly, that the evoked potential is one of the most important audiological test battery which shows pertinent and specific abnormalities in hypothyroid patients (Rubenstein et. al., 1974). Secondly, the ABER technique could show dramatic changes in hypothyroid patients to a far greater extent than conventional audiometric tests. Consequently, the ABER technique has great importance in monitoring and following up the effect of the treatment (Himelfarb et. al., 1981). Thirdly, the ABER technique can play an

important role in finding different types of information which might be helpful to interpret the mechanism by which the hypothyroidism affects the auditory pathway; in locating the site of the lesion; in determining the type of hearing loss and in showing the effect of thyroxine imbalance on the hearing process particularly after anatomical, audiological and biochemical studies have failed to get a universal agreement on these points. Fourthly, there is a lack of literature on studies of hypothyroidism using all ABER diagnostic criteria on human patients.

Fourteen patients, twelve with spontaneous and two with induced hypothyroidism by subtotal thyroidectomy were studied using the ABER technique. Occupational noise, which might have induced hearing loss, was not present. No presbyacusis or other local or systemic causes of hearing loss which might have had an effect on ABER were experienced in all the patients. All the patients were proved to have hypothyroidism from clinical manifestations and from biochemical tests which depended mainly on the level of serum-free thyroxine ($FT_4$). This was less than 7.3 p.mol/L (normal range 8-24 p.mol/L).

Five patients showed sensorineural hearing impairment which graduated from a slight to a mild hearing loss (36%). The hearing impairment happened at low, middle and high frequencies in four patients and at high frequency in just one patient (No. 14).

From Table 6.3 it can be seen that normal hearing was present in some patients with more severe hypothyroidism and slight hearing impairment in patients with milder hypothyroidism. This finding is consistent with those of Post (1964) and Raman and Beirwalter (1954).

From Table 6.4 it can be seen that there was a significant reduction in the mean amplitude and prolongation of the mean latency of wave III and V ($p < 0.01$) and the delay of I-V interwave interval ($p < 0.05$), and that the

prolonged latency and reduction in amplitude of wave I, but the fact that these were not statistically signficant suggests that the effect of hypothyroidism is most probably located in the region of the superior olivary complex, and medially, and has little effect on the peripheral auditory system (auditory nerve and cochlea)(Stockard and Rossiter, 1977; Thornton, 1975; Thornton and Hawkes, 1976; Star and Archer, 1975; Star and Hamilton, 1976). The prolonged I-V interwave interval with the presence of wave I at a nearly normal range found in this study indicates neurological disorders (Despland and Galambos, 1980). From Tables 6.7 - 6.12, it can be seen that when both wave I and V were prolonged and the I-V interval was delayed as well, this indicated the probability of both audiological and neurological disorders (Despland and Galambos, 1980), which are retro-cochlear in location (Sohmer, 1984). This was found to be the case in some patients. The location of the lesion is mainly retro-cochlear and the findings of this study were in agreement with Kohonen et. al. (1971) and De Vos (1963). To support this idea De Vos pointed out the absence of any notable interference with the vestibular function and mentioned that "This in itself, is against the lesion being located in the peripheral part of the VIII nerve" (De Vos, 1963) and Kohonen et. al. (1971).

The mechanism by which the thyroid hormone affects hearing is not as yet well understood. However, the interpretation of the data derived from this study, the reduction of amplitude and prolonged latency of wave III and wave V as well as the conduction delay in the hypothyroid patients was mainly due to low body temperature, as the body temperature of hypothyroid patients is often subnormal (O'Malley et. al., 1980; Abbott et. al., 1983) and it has been established that the results of the ABER are influenced by temperature alteration. Stockard et al., 1978 reported the effect of

hypothermia on ABER, they found that I-V interwave interval prolonged about 0.166 ms/°C in relation to the normal control subjects. Rosenblum et al. (1985) demonstrated a pronounced effect of hypothermia on the ABER, they found that the interwave I-V interval prolonged from 4 ms at 37°C to 9.2 ms at 15°C when wave V was difficult to be identified below this degree. Rosenblum et al. found minimal changes in wave I. They suggested that hypothermia does not affect auditory nerve function the same as that on the central auditory pathway. Koskari et al. (1984) reported that the effect of hypothermia was on wave I, III and V, 0.12, 0.25 and 0.53 ms/°C respectively and wave III and V disappeared earlier at cooling and reappeared later at rewarming than wave I. They explained this phenomenon; that the peripheral nerve (wave I) is less sensitive to hypothermia than the brainstem (wave III and V). Marshall and Donchin (1981) found that a reduction of 1°C in oral temperature is associated with an increase of 0.200 ms in the latency of wave V and 0.160 ms in I-V interval. Samra and Lilly (1983) reported that the latency of wave V increased linearly with decreasing temperature over the range of 35 to 29°C. In this study the major latency changes were found in the absolute latency wave V, then wave III and interwave latency I-V and the smallest changes were in the latency of wave I and interwave I-III. These results are similar to the findings of Gold et. al. (1985), Stockard et. al. (1978), Kanga et. al. (1979) and Marshall and Donchin (1981). This phenomenon could possibly be explained as Marshall and Donchin (1981) have suggested by the presence of a greater number of synapses at more levels of the brainstem auditory pathway than at that of the peripheral auditory pathway.

The other mechanisms by which the data could be explained are that it is now well known that the deficiency of thyroid hormones may induce

biochemical and morphological changes in the auditory pathway such as the accumulation of amorphous substances and oedema at the organ of corti (Meyerhoff, 1979; Cohonen, 1971), the separation of tectorial membrane from sensory hair cells and the loss of its stiffness and flexibility (Uziel et. al. 1981; Deol, 1973a; Anniko, 1982). Furthermore thyroxine plays an important role in the development of the organ of corti (Uziel et. al., 1980) and hypothyroidism may result in an overall retardation of the maturation of the cochlear structure and ultra structural changes (Uziel et. al., 1981). Thyroid hormones may influence the synthesis of nervous system proteins (Caldoff, 1977). They may also influence the production of enzymes and brain lipids (Bass et. al., 1977). The effect of hypothyroidism mainly on the rostal part of the auditory pathway which was found in this study, was supported by the results of the work of Mendel and Robinson (1978) who reported the absence of wave III and V in a two year old hypothyroid child with normal wave I and wave II, and the appearance of wave III and wave V after hypothyroid treatment. Mendel and Robinson suggested as did Rubenstein et. al. (1975) that the thyroxine is necessary in man for the development of normal midbrain function.

The above interpretations might be true as after the treatment and euthyroid status has been achieved, the temperature raised to the normal range, the absolute latency decreased and the amplitude increased to approach nearly to normal level, the transmission time also decreased and comes to almost normal range (see Tables 6.19 - 6.24). This proves that hypothyroidism may act on human hearing through causing changes in the body temperature, through its biochemical and morphological changes and through the necessity of thyroxine for the development of the auditory pathway.

There was no evidence of cochlear manifestations - which conflicted with the results of some earlier histological and biochemical studies. This

might be due to the fact that cochlear manifestations take a long time to appear in the case of acquired hypothyroidism and the test applied to the patients in this experiment came just a couple of months after the diagnosis of hypothyroidism (see Table 6.3) or the hypothermia does not affect the peripheral auditory pathway function the same as it does on the central one, (Rosenblum et al., 1985), or the peripheral auditory system is less sensitive to the temperature changes than the brainstem region (Rosakari et al., 1984). On the other hand, the appearance of retro-cochlear manifestations in this short time was because in the central auditory pathway there are more synapses than in the peripheral auditory pathway and the effect of the changes of temperature is greater in the synaptic region than in the non synaptic one (De Jesus et. al., 1973; Marshall and Donchin, 1981).

The results of this study indicated that the effect of hypothyroidism was mainly retro-cochlear and through the changes of body temperature. However, this mechanism could not completely explain the finding of this study. Histological studies on the brainstem auditory pathway are needed to determine if there are changes along the central auditory pathway and its location. These studies might reveal findings which could contribute an interpretation of the effect of hypothyroidism on the auditory system and its location.

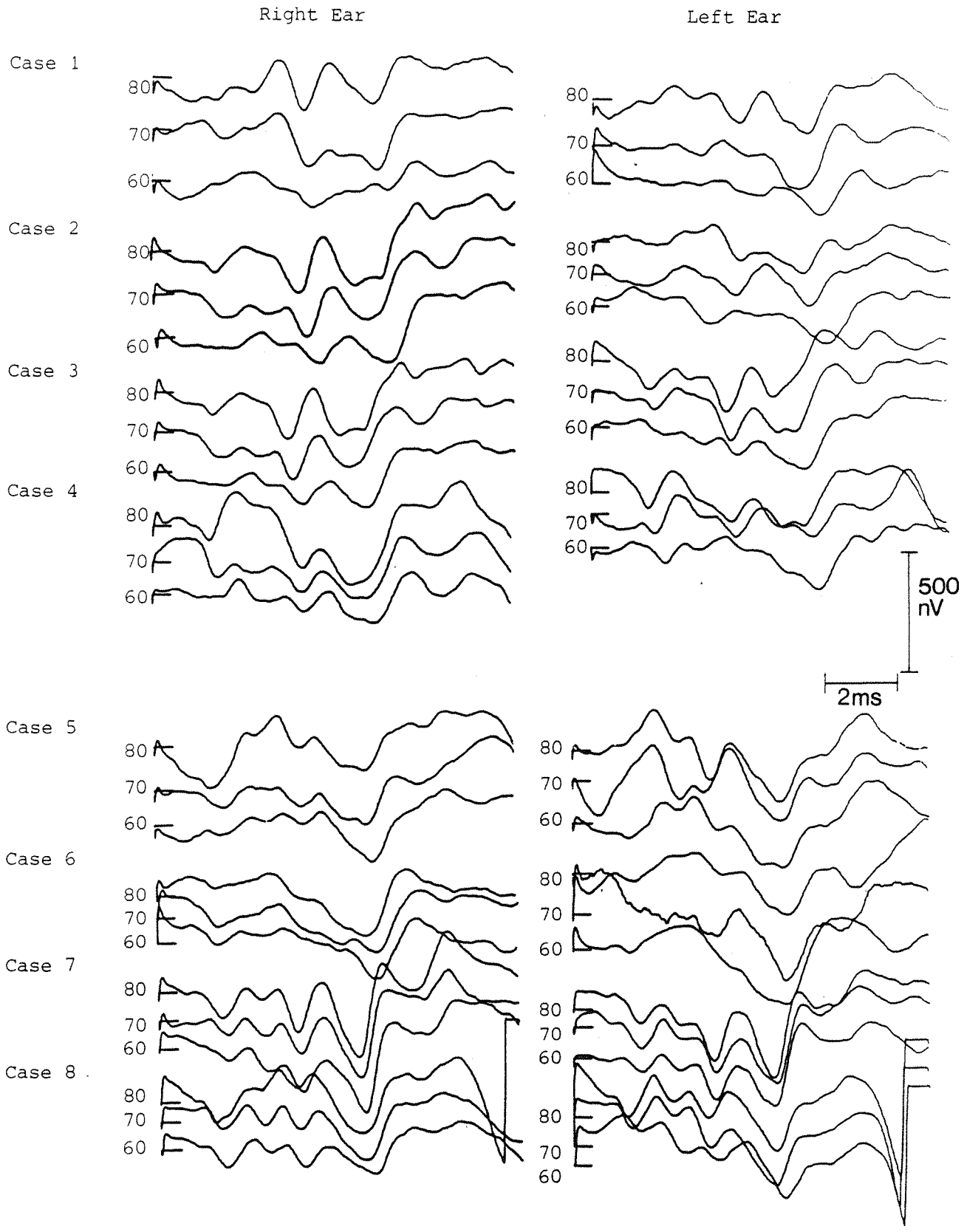


Figure 6.1 Response of hypothyroid patients before treatment at intensities of 80, 70 and 60 dBSL for both right and left ears.

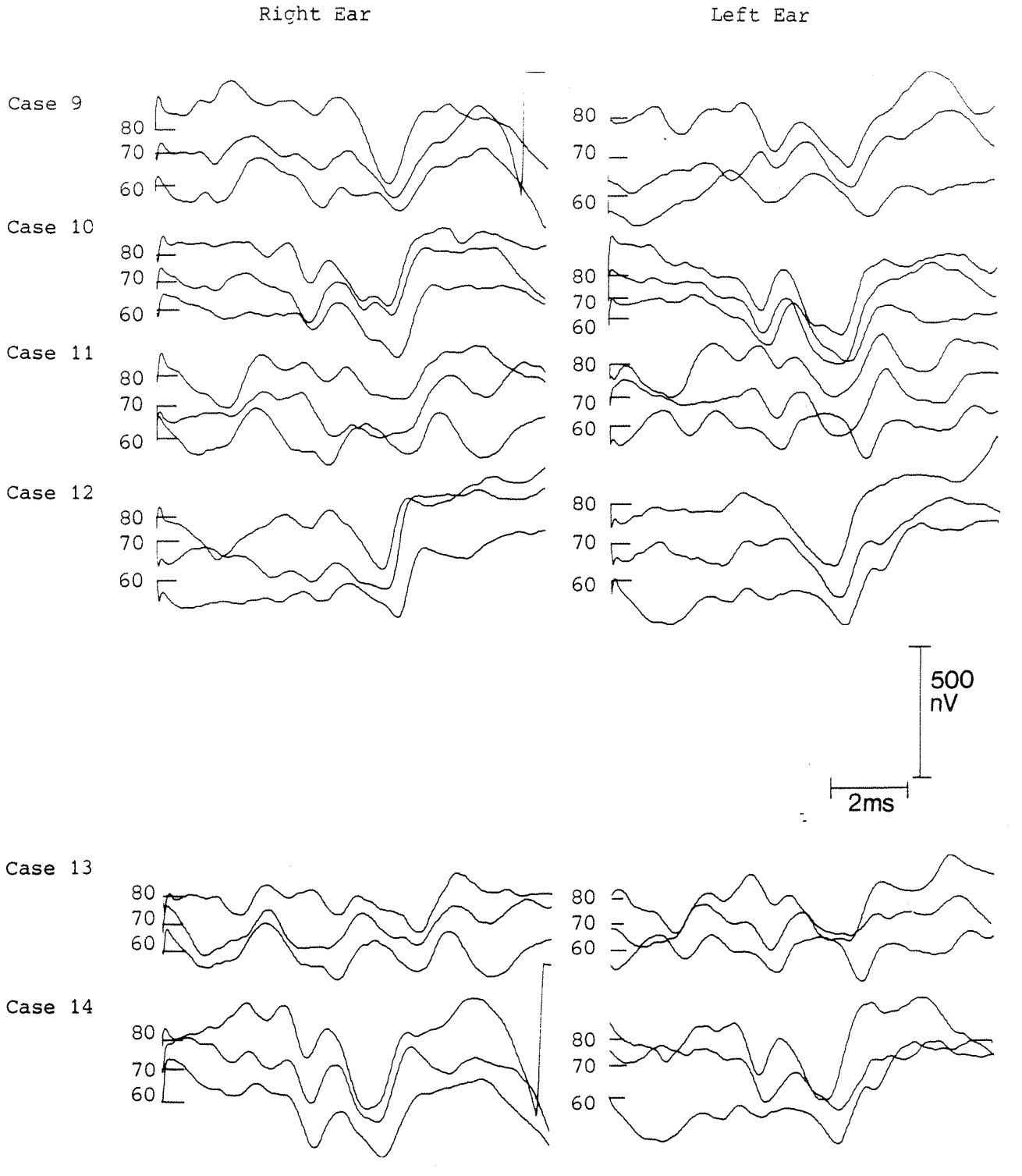


Figure 6.1 (Continued) Response of hypothyroid patients before treatment at intensities of 80, 70 and 60 dBSL for both right and left ears.

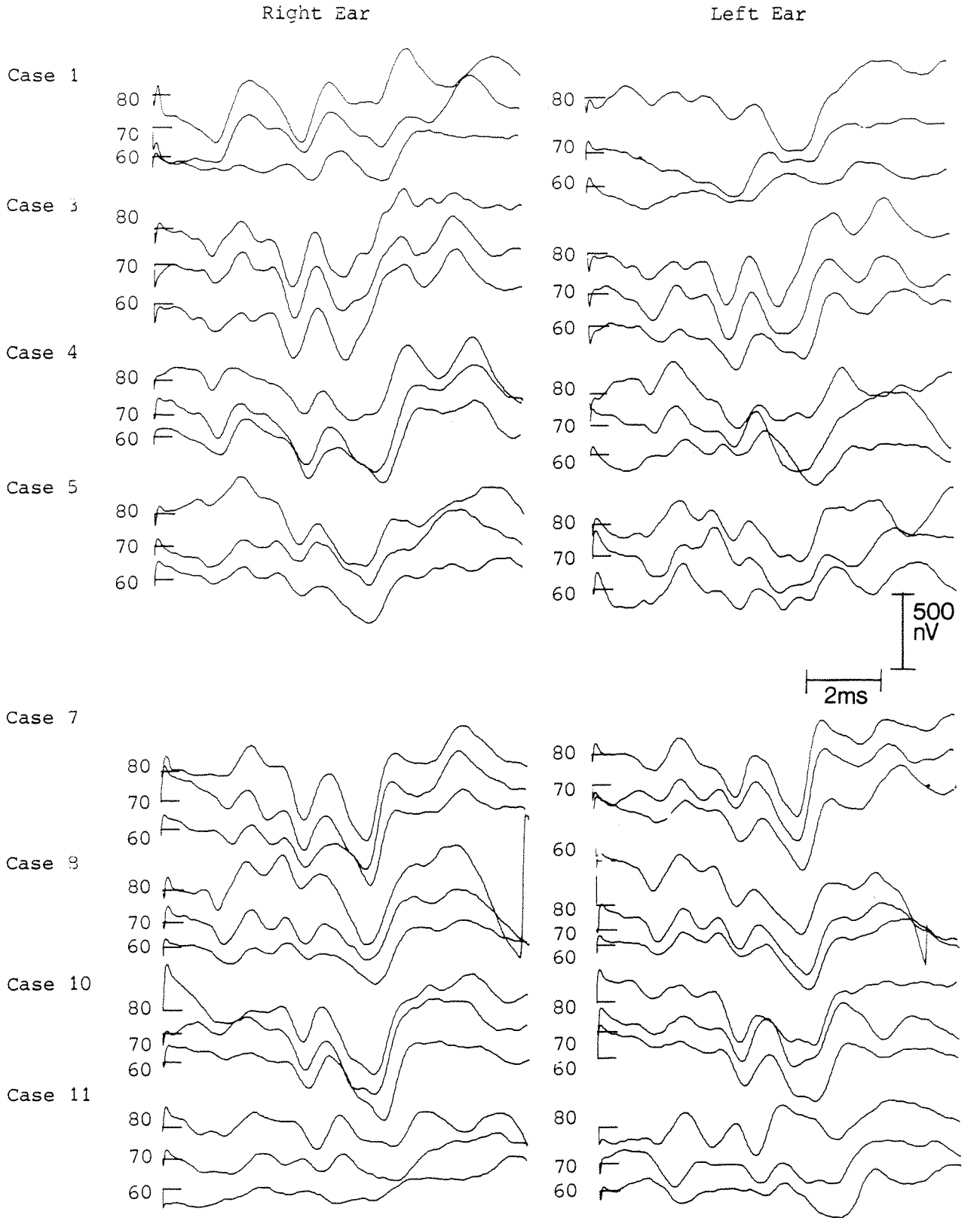


Figure 6.2 Responses of hypothyroid patients after treatment at intensities of 80, 70 and 60 dBSL for both right and left ears.

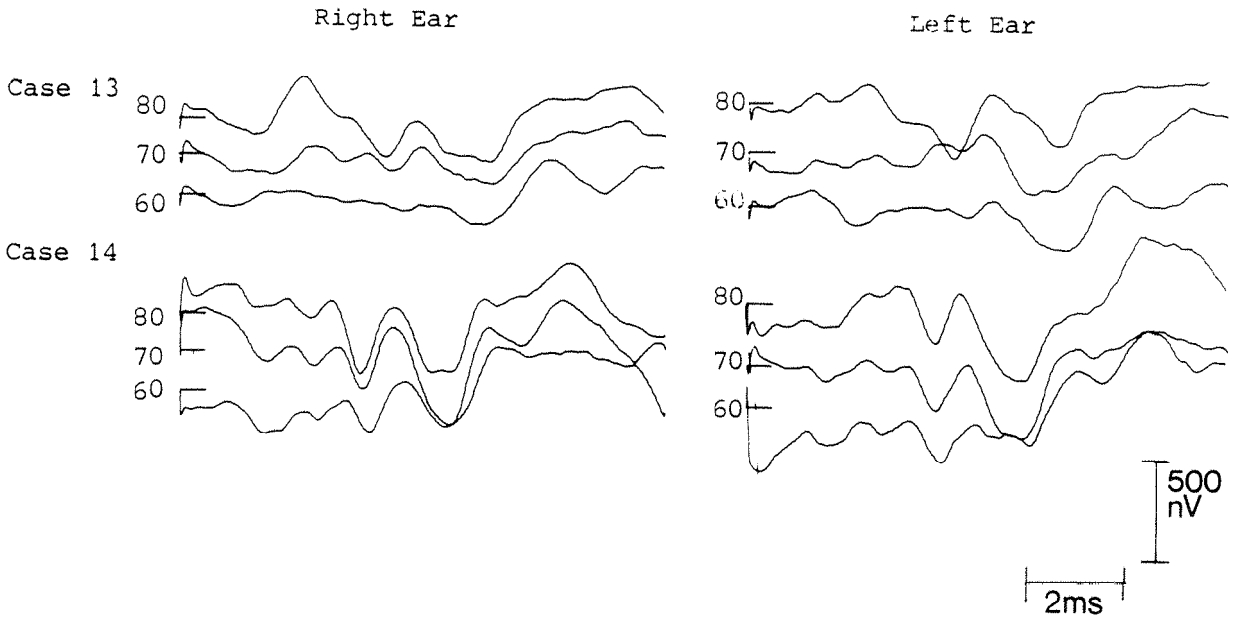


Figure 6.2 (Continued) Responses of hypothyroid patients after treatment at intensities of 80, 70 and 60 dBSL for both right and left ears.

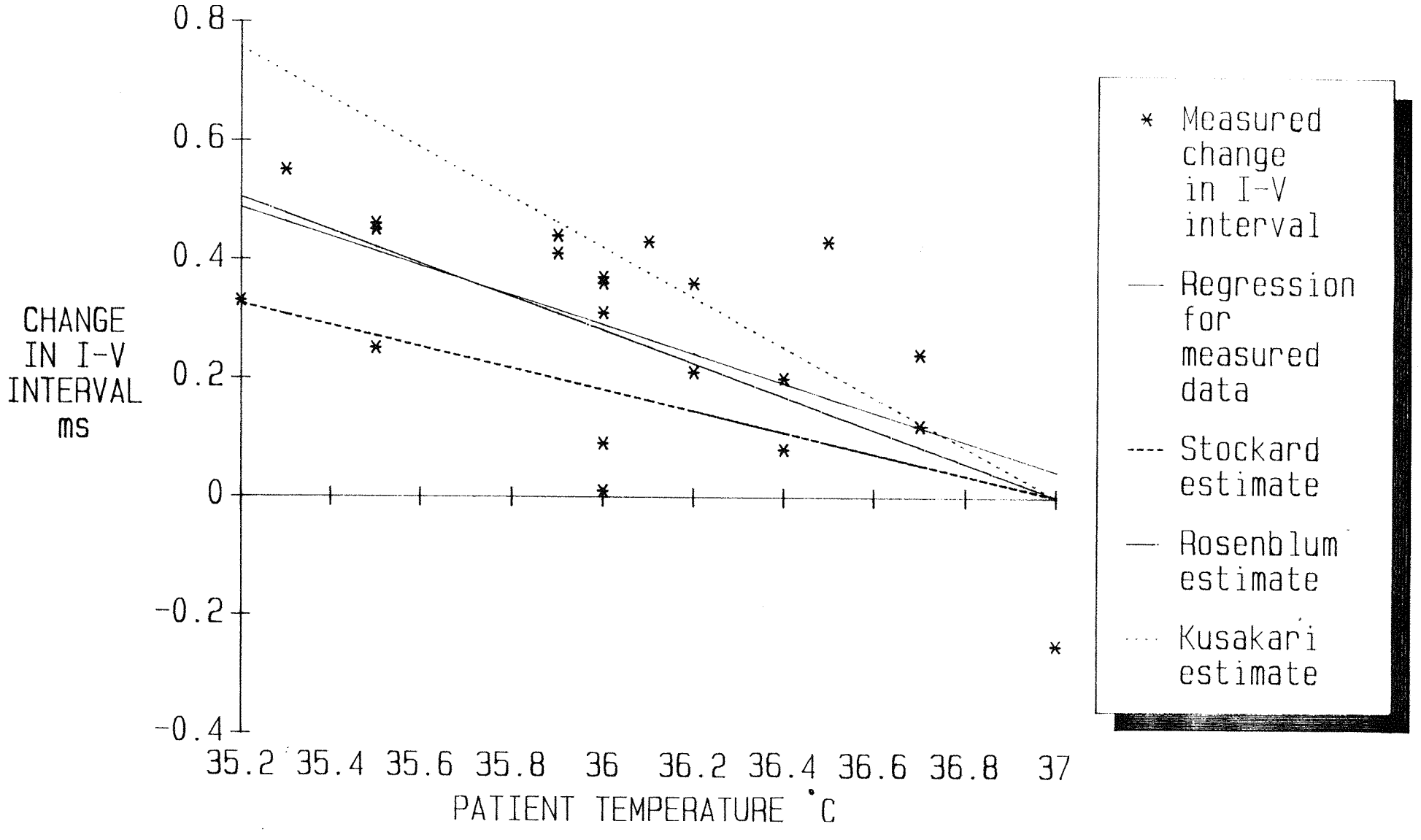


Figure 6.3 Change in I-V interval with change of temperature.

| Subject | Age Years | | 250 Hz | 500 Hz | 1000 Hz | 2000 Hz | 3000 Hz | 4000 Hz | 8000 Hz |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 60 | R | 35 | 40 | 30 | 25 | 40 | 70 | 70 |
| | | L | 40 | 40 | 30 | 30 | 60 | 55 | 70 |
| 2 | 67 | R | 30 | 25 | 15 | 10 | 15 | 15 | 70 |
| | | L | 35 | 25 | 15 | 15 | 15 | 10 | 60 |
| 3 | 32 | R | 20 | 20 | 10 | 10 | 10 | 15 | 0 |
| | | L | 20 | 20 | 10 | 0 | 15 | 5 | 10 |
| 4 | 60 | R | 25 | 20 | 15 | 20 | 10 | 10 | 10 |
| | | L | 25 | 20 | 20 | 15 | 15 | 20 | 15 |
| 5 | 64 | R | 35 | 35 | 25 | 20 | 35 | 45 | 65 |
| | | L | 35 | 40 | 30 | 25 | 30 | 45 | 75 |
| 6 | 78 | R | 25 | 25 | 15 | 15 | 25 | 25 | 50 |
| | | L | 25 | 30 | 20 | 25 | 20 | 25 | 70 |
| 7 | 61 | R | 30 | 35 | 35 | 35 | 45 | 45 | 65 |
| | | L | 25 | 30 | 25 | 30 | 35 | 45 | 65 |
| 8 | 26 | R | 20 | 20 | 15 | 5 | 10 | 15 | 10 |
| | | L | 25 | 20 | 15 | 15 | 20 | 25 | 25 |
| 9 | 60 | R | 25 | 30 | 20 | 15 | 20 | 35 | 50 |
| | | L | 25 | 25 | 20 | 10 | 15 | 25 | 40 |
| 10 | 72 | R | 30 | 30 | 25 | 30 | 45 | 40 | 45 |
| | | L | 30 | 35 | 20 | 30 | 45 | 45 | 60 |
| 11 | 64 | R | 25 | 25 | 15 | 15 | 20 | 20 | 45 |
| | | L | 25 | 20 | 15 | 10 | 15 | 25 | 30 |
| 12 | 53 | R | 30 | 25 | 15 | 10 | 15 | 15 | 15 |
| | | L | 30 | 25 | 15 | 10 | 15 | 10 | 15 |
| 13 | 64 | R | 25 | 25 | 15 | 15 | 20 | 20 | 45 |
| | | L | 25 | 20 | 15 | 10 | 15 | 25 | 30 |
| 14 | 78 | R | 35 | 35 | 25 | 25 | 30 | 30 | 50 |
| | | L | 25 | 25 | 20 | 30 | 30 | 30 | 60 |

TABLE 6.1 Pure tone audiogram for hypothyroid patients
Threshold in dB (ISO).

| Subject | Age Years | | 250 Hz | 500 Hz | 1000 Hz | 2000 Hz | 3000 Hz | 4000 Hz | 8000 Hz |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 62 | R | 35 | 30 | 15 | 25 | 25 | 55 | 75 |
| | | L | 30 | 30 | 25 | 25 | 45 | 65 | 75 |
| 2 | | | | | | | | | |
| 3 | 72 | R | 15 | 15 | 15 | 0 | 15 | 10 | 5 |
| | | L | 20 | 15 | 10 | 5 | 10 | 5 | 5 |
| 4 | 60 | R | 35 | 30 | 20 | 15 | 15 | 10 | 10 |
| | | L | 25 | 25 | 15 | 10 | 10 | 10 | 15 |
| 5 | 64 | R | 30 | 20 | 20 | 10 | 20 | 30 | 40 |
| | | L | 30 | 30 | 20 | 10 | 25 | 35 | 70 |
| 6 | | | | | | | | | |
| 7 | 61 | R | 35 | 45 | 45 | 30 | 40 | 45 | 60 |
| | | L | 25 | 30 | 20 | 25 | 30 | 35 | 60 |
| 8 | 26 | R | 20 | 20 | 15 | 5 | 15 | 15 | 10 |
| | | L | 20 | 20 | 15 | 15 | 15 | 15 | 25 |
| 9 | | | | | | | | | |
| 10 | 72 | R | 25 | 25 | 20 | 25 | 30 | 35 | 35 |
| | | L | 25 | 25 | 15 | 20 | 40 | 35 | 40 |
| 11 | 64 | R | 25 | 20 | 15 | 10 | 15 | 25 | 30 |
| | | L | 30 | 25 | 20 | 15 | 15 | 10 | 30 |
| 12 | | | | | | | | | |
| 13 | 64 | R | 25 | 20 | 15 | 10 | 15 | 25 | 30 |
| | | L | 30 | 25 | 20 | 15 | 15 | 10 | 30 |
| 14 | 78 | R | 30 | 25 | 35 | 25 | 35 | 35 | 45 |
| | | L | 30 | 30 | 20 | 35 | 35 | 40 | 60 |

TABLE 6.2 Pure tone audiogram for Hypothyroid patients after replacement therapy. Threshold in dB (ISO).

| Case | Name | Age YEARS | Duration | $FT_4$ | Pulse P/M | Hearing Loss R | L | Comments |
|---|---|---|---|---|---|---|---|---|
| 1 | K.V. | 62 | 8 M | < 1 | 60 | 41 | 39 | Mild hearing impairment |
| 2 | G.B. | 67 | 8 M | < 1 | 55 | 16 | 16 | Normal |
| 3 | B.P. | 32 | 11 M | 1.6 | 68 | 15 | 12 | Normal |
| 4 | B.G. | 60 | 9 M | 1.8 | 50 | 16 | 19 | Normal |
| 5 | D.R. | 64 | 9 M | 1.9 | 70 | 31 | 35 | Slight hearing impairment |
| 6 | A.M. | 78 | 10 M | 2.8 | 68 | 20 | 25 | Normal |
| 7 | D.B. | 61 | 20 Y | 3.7 | 48 | 37 | 33 | Slight hearing impairment |
| 8 | S.H. | 26 | 2 Y | 4.4 | 75 | 14 | 19 | Normal |
| 9 | D.C | 60 | 11 M | 4.5 | 68 | 25 | 20 | Normal |
| 10 | C.M. | 72 | 11 M | 4.5 | 60 | 31 | 32 | Slight hearing impairment |
| 11 | B.R. | 64 | 11 M | 5.7 | 67 | 19 | 18 | Normal |
| 12 | C.T. | 53 | 11 M | 5.8 | 76 | 16 | 15 | Normal |
| 13 | B.R. | 64 | 17 M | 6.0 | 58 | 19 | 18 | Normal |
| 14 | B.M. | 78 | 10 M | 7.3 | 72 | 29 | 26 | Slight hearing impairment |

TABLE 6.3 Duration of the disease, $FT_4$ amount in the serum in pmol/L, pulse and hearing loss in hypothyroid patients

| PARAMETERS | 60 dB SL | | 70 dB SL | | 80 dB SL | |
|---|---|---|---|---|---|---|
| | Right | Left | Right | Left | Right | Left |
| **AMPLITUDE** | | | | | | |
| I | -- | -- | P < 0.022 | -- | -- | -- |
| III | P < 0.011 | P < 0.006 | P < 0.012 | -- | P < 0.005 | P < 0.015 |
| V | P < 0.002 | P < 0.0006 | P < 0.008 | P < 0.0005 | P < 0.017 | P < 0.005 |
| **LATENCY** | | | | | | |
| I | -- | P < 0.023 | -- | -- | P < 0.0034 | -- |
| III | P < 0.005 | P < 0.0034 | P < 0.011 | P < 0.020 | P < 0.018 | P < 0.023 |
| V | P < 0.0011 | P < 0.0005 | P < 0.0031 | P < 0.0014 | P < 0.008 | P < 0.0018 |
| **INTER-PEAK INTERVAL** | | | | | | |
| V-I | P < 0.013 | P < 0.024 | P < 0.011 | P < 0.022 | P < 0.009 | P < 0.029 |
| V-III | -- | P < 0.024 | -- | -- | P < 0.030 | -- |
| III-I | P < 0.014 | -- | -- | -- | -- | P < 0.036 |

TABLE 6.4 Summary of statistical analysis - t-test of amplitude, latency and interwave intervals of hypothyroid - normal controls (where -- = not significant)

| PARAMETERS | 60 dB SL | | 70 dB SL | | 80 dB SL | |
|---|---|---|---|---|---|---|
| | Right | Left | Right | Left | Right | Left |
| AMPLITUDE<br>I | -- | -- | -- | -- | -- | -- |
| III | -- | -- | -- | -- | P < 0.029 | P < 0.046 |
| V | P < 0.03 | P < 0.0001 | P < 0.018 | P < 0.008 | P < 0.006 | P < 0.0022 |
| LATENCY<br>I | -- | P < 0.023 | -- | -- | P < 0.034 | -- |
| III | P < 0.027 | P < 0.032 | P < 0.033 | P < 0.031 | P < 0.016 | P < 0.013 |
| V | P < 0.0018 | P < 0.0003 | P < 0.009 | P < 0.003 | P < 0.0012 | P < 0.0066 |
| INTER-PEAK INTERVAL<br>V-I | P < 0.023 | P < 0.042 | P < 0.029 | -- | P < 0.006 | -- |
| V-III | -- | P < 0.039 | -- | -- | -- | -- |
| III-I | -- | -- | P < 0.015 | -- | P < 0.014 | -- |

TABLE 6.5 Summary of statistical analysis - t-test of amplitude, latency and interwave intervals of hypothyroid - hyperthyroid patients (where -- = not significant)

| PARAMETERS | 60 dB SL | | 70 dB SL | | 80 dB SL | |
|---|---|---|---|---|---|---|
| | Right | Left | Right | Left | Right | Left |
| AMPLITUDE<br>I | -- | -- | P < 0.009 | -- | -- | -- |
| III | P < 0.022 | -- | P < 0.008 | -- | P < 0.0045 | -- |
| V | P < 0.011 | -- | P < 0.012 | P < 0.012 | -- | -- |
| LATENCY<br>I | -- | P < 0.018 | P < 0.016 | -- | -- | -- |
| III | P < 0.007 | P < 0.01 | P < 0.049 | -- | -- | P < 0.016 |
| V | P < 0.004 | P < 0.0003 | P < 0.009 | P < 0.017 | P < 0.0012 | P < 0.0066 |
| INTER-PEAK INTERVAL<br>V-I | -- | -- | -- | -- | -- | -- |
| V-III | -- | P < 0.037 | -- | -- | -- | -- |
| III-I | -- | -- | -- | | -- | -- |

TABLE 6.6 Summary of statistical analysis - paired t-test of amplitude, latency and interwave intervals of hypothyroid - retest hypothyroid patients (where -- = not significant)

| CASE | AGE YEARS | $FT_4$ | AMPLITUDE | | | LATENCY | | |
|---|---|---|---|---|---|---|---|---|
| | | | I | III | V | I | III | V |
| 1 | 62 | < 1 | R 78 | 309 | 300 | 1.74 | 4.18 | 6.14 |
| | | | L 90 | 160 | 289 | 1.68 | 4.02 | 5.98 |
| 2 | 67 | < 1 | R 74 | 105 | 289 | 1.66 | 3.98 | 5.98 |
| | | | L 90 | 43 | 219 | 1.58 | 3.96 | 5.86 |
| 3 | 32 | 1.6 | R 156 | 340 | 332 | 1.55 | 3.70 | 5.71 |
| | | | L 107 | 240 | 420 | 1.57 | 3.70 | 5.88 |
| 4 | 60 | 1.8 | R 219 | 129 | 395 | 1.62 | 4.14 | 6.00 |
| | | | L 277 | 90 | 344 | 1.58 | 3.92 | 6.00 |
| 5 | 64 | 1.9 | R 234 | 63 | 305 | 1.58 | 4.02 | 5.86 |
| | | | L 164 | 211 | 297 | 1.54 | 3.84 | 5.78 |
| 6 | 78 | 2.8 | R 43 | 31 | 316 | 1.64 | 3.82 | 5.70 |
| | | | L 113 | 23 | 382 | 1.50 | 3.96 | 5.58 |
| 7 | 61 | 3.7 | R 148 | 316 | 563 | 1.68 | 3.80 | 5.50 |
| | | | L 145 | 316 | 251 | 1.72 | 3.82 | 5.66 |
| 8 | 26 | 4.4 | R 94 | 90 | 281 | 1.52 | 3.78 | 5.78 |
| | | | L 269 | 105 | 351 | 1.60 | 3.80 | 5.60 |
| 9 | 60 | 4.5 | R 223 | 102 | 211 | 1.42 | 3.98 | 5.86 |
| | | | L 152 | 191 | 293 | 1.64 | 4.14 | 6.00 |
| 10 | 72 | 4.5 | R 33 | 170 | 443 | 1.53 | 3.79 | 5.77 |
| | | | L 12 | 258 | 425 | 1.61 | 3.85 | 5.87 |
| 11 | 64 | 5.7 | R 188 | 168 | 262 | 1.56 | 4.06 | 6.06 |
| | | | L 297 | 207 | 313 | 1.64 | 4.10 | 6.16 |
| 12 | 53 | 5.8 | R 66 | 59 | 473 | 1.58 | 3.74 | 5.66 |
| | | | L 43 | 156 | 438 | 1.56 | 3.86 | 5.66 |
| 13 | 64 | 6.0 | R 230 | 107 | 234 | 1.67 | 4.23 | 6.26 |
| | | | L 254 | 59 | 365 | 1.60 | 4.25 | 5.98 |
| 14 | 78 | 7.3 | R 94 | 188 | 395 | 1.56 | 3.66 | 5.52 |
| | | | L 129 | 223 | 340 | 1.54 | 3.88 | 5.58 |
| Mean | 60.07 | 3.7 | R 134 | 155 | 343 | 1.59 | 3.92 | 5.83 |
| | | | L 153 | 163 | 338 | 1.60 | 3.94 | 5.83 |
| S.D. | 19.89 | 2.0 | R 74 | 100 | 99 | 0.08 | 0.19 | 0.23 |
| | | | L 90 | 88 | 65 | 0.06 | 0.15 | 0.19 |

TABLE 6.7 Values of peak-to-peak amplitude (nV) and latency (msec) for hypothyroid patients at 80 dBSL for right and left ears.

| CASE | AGE YEARS | $FT_4$ | AMPLITUDE | | | LATENCY | | |
|---|---|---|---|---|---|---|---|---|
| | | | I | III | V | I | III | V |
| 1 | 62 | < 1 | R 75 | 82 | 280 | 1.94 | 4.28 | 6.24 |
| | | | L 20 | 63 | 278 | 1.98 | 4.16 | 6.12 |
| 2 | 67 | < 1 | R 46 | 31 | 199 | 1.84 | 4.18 | 6.18 |
| | | | L 74 | 100 | 220 | 1.68 | 4.12 | 6.08 |
| 3 | 32 | 1.6 | R 104 | 295 | 264 | 1.70 | 3.80 | 5.73 |
| | | | L 114 | 213 | 420 | 1.76 | 3.86 | 5.65 |
| 4 | 60 | 1.8 | R 125 | 145 | 387 | 1.72 | 4.22 | 6.10 |
| | | | L 203 | 121 | 164 | 1.72 | 3.98 | 6.18 |
| 5 | 64 | 1.9 | R 86 | 86 | 289 | 1.68 | 4.08 | 5.88 |
| | | | L 156 | 176 | 332 | 1.56 | 3.88 | 5.84 |
| 6 | 78 | 2.8 | R 55 | 63 | 258 | 1.66 | 3.94 | 5.86 |
| | | | L 51 | 86 | 230 | 1.70 | 4.06 | 5.84 |
| 7 | 61 | 3.7 | R 109 | 258 | 375 | 1.80 | 3.82 | 5.58 |
| | | | L 102 | 238 | 398 | 1.78 | 3.88 | 5.80 |
| 8 | 26 | 4.4 | R 90 | 89 | 257 | 1.68 | 3.92 | 5.92 |
| | | | L 260 | 103 | 270 | 1.68 | 3.92 | 5.78 |
| 9 | 60 | 4.5 | R 218 | 51 | 201 | 1.48 | 4.10 | 5.98 |
| | | | L 109 | 125 | 273 | 1.82 | 4.32 | 6.20 |
| 10 | 72 | 4.5 | R 70 | 176 | 471 | 1.60 | 3.86 | 5.91 |
| | | | L 27 | 254 | 381 | 1.53 | 3.90 | 6.04 |
| 11 | 64 | 5.7 | R 137 | 156 | 207 | 1.72 | 4.18 | 6.22 |
| | | | L 254 | 207 | 199 | 1.78 | 4.24 | 6.34 |
| 12 | 53 | 5.8 | R 31 | 60 | 470 | 1.66 | 3.90 | 5.80 |
| | | | L 40 | 60 | 363 | 1.76 | 3.84 | 5.74 |
| 13 | 64 | 6.0 | R 145 | 143 | 240 | 1.87 | 4.27 | 6.42 |
| | | | L 152 | 174 | 248 | 1.77 | 4.26 | 6.24 |
| 14 | 78 | 7.3 | R 91 | 190 | 363 | 1.72 | 3.70 | 5.56 |
| | | | L 33 | 95 | 211 | 1.96 | 4.01 | 5.79 |
| Mean | 60.07 | 3.7 | R 99 | 130 | 304 | 1.72 | 4.02 | 5.96 |
| | | | L 114 | 148 | 285 | 1.75 | 4.03 | 5.97 |
| S.D. | 19.89 | 2.0 | R 48 | 79 | 93 | 0.12 | 0.19 | 0.25 |
| | | | L 81 | 72 | 81 | 0.13 | 0.16 | 0.22 |

TABLE 6.8 Values of peak-to-peak amplitude (nV) and latency (msec) for hypothyroid patients at 70 dBSL for right and left ears.

| CASE | AGE YEARS | $FT_4$ | AMPLITUDE | | | LATENCY | | |
|---|---|---|---|---|---|---|---|---|
| | | | I | III | V | I | III | V |
| 1 | 62 | < 1 | R 35 | 78 | 278 | 2.06 | 4.40 | 6.38 |
| | | | L 15 | 35 | 275 | 2.24 | 4.46 | 6.44 |
| 2 | 67 | < 1 | R 40 | 8 | 90 | 2.08 | 4.54 | 6.52 |
| | | | L 12 | 39 | 218 | 2.00 | 4.18 | 6.32 |
| 3 | 32 | 1.6 | R 53 | 119 | 324 | 1.95 | 3.95 | 5.93 |
| | | | L 14 | 123 | 350 | 1.91 | 4.05 | 6.04 |
| 4 | 60 | 1.8 | R 122 | 126 | 277 | 1.98 | 4.32 | 6.24 |
| | | | L 156 | 45 | 159 | 2.00 | 4.10 | 6.32 |
| 5 | 64 | 1.9 | R 74 | 16 | 266 | 1.86 | 4.16 | 6.08 |
| | | | L 109 | 40 | 250 | 1.92 | 4.02 | 5.98 |
| 6 | 78 | 2.8 | R 54 | 66 | 246 | 1.72 | 4.00 | 6.02 |
| | | | L 31 | 62 | 242 | 1.74 | 4.16 | 6.06 |
| 7 | 61 | 3.7 | R 105 | 176 | 387 | 1.88 | 3.92 | 5.64 |
| | | | L 86 | 191 | 453 | 1.84 | 3.92 | 6.04 |
| 8 | 26 | 4.4 | R 89 | 74 | 226 | 1.84 | 4.06 | 6.00 |
| | | | L 117 | 74 | 267 | 1.84 | 4.04 | 5.92 |
| 9 | 60 | 4.5 | R 164 | 160 | 152 | 1.58 | 4.16 | 6.12 |
| | | | L 105 | 31 | 117 | 2.08 | 4.54 | 6.36 |
| 10 | 72 | 4.5 | R 51 | 133 | 414 | 1.68 | 3.43 | 6.01 |
| | | | L 35 | 219 | 352 | 1.82 | 3.99 | 6.22 |
| 11 | 64 | 5.7 | R 129 | 121 | 203 | 1.80 | 4.34 | 6.48 |
| | | | L 117 | 86 | 158 | 1.90 | 4.42 | 6.42 |
| 12 | 53 | 5.8 | R 31 | 70 | 441 | 1.96 | 4.06 | 6.02 |
| | | | L 50 | 47 | 332 | 1.88 | 4.06 | 5.96 |
| 13 | 64 | 6.0 | R 92 | 47 | 66 | 2.07 | 4.57 | 6.59 |
| | | | L 188 | 195 | 229 | 1.89 | 4.27 | 6.46 |
| 14 | 78 | 7.3 | R 78 | 156 | 238 | 1.92 | 3.88 | 5.68 |
| | | | L 35 | 94 | 184 | 2.02 | 4.06 | 5.88 |
| **Mean** | 60.07 | 3.7 | R 80 | 96 | 258 | 1.93 | 4.16 | 6.12 |
| | | | L 76 | 89 | 256 | 1.93 | 4.16 | 6.17 |
| S.D. | 19.89 | 2.0 | R 40 | 53 | 111 | 0.26 | 0.23 | 0.29 |
| | | | L 57 | 68 | 92 | 0.13 | 0.19 | 0.21 |

TABLE 6.9 Values of peak-to-peak amplitude nV) and latency (msec) for hypothyroid patients at 60 dBSL for right and left ears.

| CASE | AGE YEARS | $FT_4$ | INTERWAVE INTERVAL | | | |
|---|---|---|---|---|---|---|
| | | | | I - III | III - V | I - V |
| 1 | 62 | < 1 | R | 2.44 | 1.96 | 4.40 |
| | | | L | 2.34 | 1.96 | 4.30 |
| 2 | 67 | < 1 | R | 2.32 | 2.00 | 4.32 |
| | | | L | 2.38 | 1.90 | 4.28 |
| 3 | 32 | 1.6 | R | 2.15 | 2.06 | 4.16 |
| | | | L | 2.13 | 1.78 | 3.91 |
| 4 | 60 | 1.8 | R | 2.52 | 1.86 | 4.38 |
| | | | L | 2.34 | 2.08 | 4.42 |
| 5 | 64 | 1.9 | R | 2.44 | 1.84 | 4.28 |
| | | | L | 2.30 | 1.94 | 4.24 |
| 6 | 78 | 2.8 | R | 2.18 | 1.88 | 4.06 |
| | | | L | 2.40 | 1.62 | 4.02 |
| 7 | 61 | 3.7 | R | 2.12 | 1.70 | 3.82 |
| | | | L | 2.10 | 1.84 | 3.94 |
| 8 | 26 | 4.4 | R | 2.26 | 2.00 | 4.26 |
| | | | L | 2.20 | 1.80 | 4.00 |
| 9 | 60 | 4.5 | R | 2.56 | 1.88 | 4.44 |
| | | | L | 2.50 | 1.86 | 4.36 |
| 10 | 72 | 4.5 | R | 2.26 | 1.98 | 4.24 |
| | | | L | 2.24 | 2.02 | 4.26 |
| 11 | 64 | 5.7 | R | 2.50 | 2.00 | 4.53 |
| | | | L | 2.46 | 2.06 | 4.56 |
| 12 | 53 | 5.8 | R | 2.16 | 1.92 | 4.08 |
| | | | L | 2.30 | 1.80 | 4.10 |
| 13 | 64 | 6.0 | R | 2.56 | 2.03 | 4.50 |
| | | | L | 2.65 | 1.73 | 4.38 |
| 14 | 78 | 7.3 | R | 2.10 | 1.86 | 3.96 |
| | | | L | 2.34 | 1.70 | 4.04 |
| Mean | 60.07 | 3.7 | R | 2.33 | 1.92 | 4.25 |
| | | | L | 2.33 | 1.86 | 4.20 |
| S.D. | 19.89 | 2.0 | R | 0.17 | 0.10 | 0.21 |
| | | | L | 0.15 | 0.14 | 0.20 |

TABLE 6.10 Values of peak-to-peak interwave intervals (msec) for hypothyroid patients at 80 dBSL for right and left ears.

| CASE | AGE YEARS | $FT_4$ | | INTERWAVE INTERVAL | | |
|---|---|---|---|---|---|---|
| | | | | I - III | III - V | I - V |
| 1 | 62 | < 1 | R | 2.34 | 1.96 | 4.30 |
| | | | L | 2.18 | 1.96 | 4.14 |
| 2 | 67 | < 1 | R | 2.34 | 2.00 | 4.34 |
| | | | L | 2.44 | 1.96 | 4.40 |
| 3 | 32 | 1.6 | R | 2.10 | 1.93 | 4.03 |
| | | | L | 2.10 | 1.79 | 3.89 |
| 4 | 60 | 1.8 | R | 2.50 | 1.88 | 4.38 |
| | | | L | 2.26 | 2.20 | 4.46 |
| 5 | 64 | 1.9 | R | 2.40 | 1.80 | 4.20 |
| | | | L | 2.32 | 1.96 | 4.28 |
| 6 | 78 | 2.8 | R | 2.28 | 1.92 | 4.20 |
| | | | L | 2.36 | 1.78 | 4.14 |
| 7 | 61 | 3.7 | R | 2.02 | 1.76 | 3.78 |
| | | | L | 2.10 | 1.92 | 4.02 |
| 8 | 26 | 4.4 | R | 2.24 | 2.00 | 4.24 |
| | | | L | 2.24 | 1.86 | 4.10 |
| 9 | 60 | 4.5 | R | 2.62 | 1.88 | 4.50 |
| | | | L | 2.50 | 1.88 | 4.38 |
| 10 | 72 | 4.5 | R | 2.26 | 2.05 | 4.31 |
| | | | L | 2.37 | 2.14 | 4.51 |
| 11 | 64 | 5.7 | R | 2.46 | 2.04 | 4.50 |
| | | | L | 2.46 | 2.10 | 4.56 |
| 12 | 53 | 5.8 | R | 2.24 | 1.90 | 4.14 |
| | | | L | 2.08 | 1.90 | 3.98 |
| 13 | 64 | 6.0 | R | 2.40 | 2.15 | 4.55 |
| | | | L | 2.49 | 1.98 | 4.47 |
| 14 | 78 | 7.3 | R | 1.98 | 1.86 | 3.84 |
| | | | L | 2.05 | 1.78 | 3.83 |
| Mean | 60.07 | 3.7 | R | 2.30 | 1.94 | 4.24 |
| | | | L | 2.28 | 1.94 | 4.23 |
| S.D. | 19.89 | 2.0 | R | 0.18 | 0.10 | 0.23 |
| | | | L | 0.16 | 0.13 | 0.24 |

TABLE 6.11 Values of peak-to-peak interwave intervals (msec) for hypothyroid patients at 70 dBSL for right and left ears.

| CASE | AGE YEARS | $FT_4$ | INTERWAVE INTERVAL | | |
|---|---|---|---|---|---|
| | | | I - III | III - V | I - V |
| 1 | 62 | < 1 | R 2.34 | 1.98 | 4.32 |
| | | | L 2.22 | 1.98 | 4.20 |
| 2 | 67 | < 1 | R 2.46 | 1.98 | 4.44 |
| | | | L 2.18 | 2.14 | 4.32 |
| 3 | 32 | 1.6 | R 2.00 | 1.98 | 3.98 |
| | | | L 2.14 | 1.99 | 4.13 |
| 4 | 60 | 1.8 | R 2.34 | 1.92 | 4.26 |
| | | | L 2.10 | 2.22 | 4.32 |
| 5 | 64 | 1.9 | R 2.30 | 1.92 | 4.22 |
| | | | L 2.10 | 1.96 | 4.06 |
| 6 | 78 | 2.8 | R 2.28 | 2.02 | 4.30 |
| | | | L 2.42 | 1.90 | 4.32 |
| 7 | 61 | 3.7 | R 2.04 | 1.72 | 3.76 |
| | | | L 2.08 | 2.12 | 4.20 |
| 8 | 26 | 4.4 | R 2.22 | 1.94 | 4.16 |
| | | | L 2.20 | 1.88 | 4.08 |
| 9 | 60 | 4.5 | R 2.58 | 1.96 | 4.54 |
| | | | L 2.46 | 1.82 | 4.28 |
| 10 | 72 | 4.5 | R 2.25 | 2.08 | 4.33 |
| | | | L 2.17 | 2.23 | 4.40 |
| 11 | 64 | 5.7 | R 2.54 | 2.14 | 4.68 |
| | | | L 2.52 | 2.19 | 4.57 |
| 12 | 53 | 5.8 | R 2.10 | 1.96 | 4.06 |
| | | | L 2.18 | 1.90 | 4.08 |
| 13 | 64 | 6.0 | R 2.50 | 2.02 | 4.52 |
| | | | L 2.38 | 2.00 | 4.52 |
| 14 | 78 | 7.3 | R 1.96 | 1.80 | 3.76 |
| | | | L 2.04 | 1.82 | 3.86 |
| Mean | 60.07 | 3.7 | R 2.28 | 1.96 | 4.24 |
| | | | L 2.23 | 2.01 | 4.24 |
| S.D. | 19.89 | 2.0 | R 0.20 | 0.11 | 0.28 |
| | | | L 0.15 | 0.14 | 0.19 |

TABLE 6.12 Values of peak-to-peak interwave intervals (msec) for hypothyroid patients at 60 dBSL for right and left ears.

| CASE | AGE YEARS | $FT_4$ | AMPLITUDE | | | LATENCY | | |
|---|---|---|---|---|---|---|---|---|
| | | | I | III | V | I | III | V |
| 1 | 62 | 12.3 | R 219 | 309 | 363 | 1.66 | 3.98 | 6.02 |
| | | | L 90 | 129 | 309 | 1.70 | 4.00 | 5.92 |
| 3 | 32 | 10.4 | R 211 | 343 | 350 | 1.52 | 3.66 | 5.64 |
| | | | L 117 | 344 | 450 | 1.52 | 3.70 | 5.62 |
| 4 | 60 | 20.2 | R 219 | 220 | 480 | 1.52 | 4.00 | 5.96 |
| | | | L 218 | 183 | 308 | 1.56 | 3.88 | 5.90 |
| 5 | -64 | 18.0 | R 280 | 114 | 350 | 1.54 | 4.00 | 5.81 |
| | | | L 171 | 184 | 260 | 1.49 | 3.80 | 5.72 |
| 6 | | | | | | | | |
| 7 | 61 | 26.9 | R 195 | 313 | 601 | 1.68 | 3.84 | 5.52 |
| | | | L 223 | 277 | 656 | 1.74 | 3.86 | 5.58 |
| 8 | 26 | 28.1 | R 270 | 145 | 395 | 1.50 | 3.72 | 5.66 |
| | | | L 255 | 125 | 350 | 1.54 | 3.80 | 5.60 |
| 9 | | | | | | | | |
| 10 | 72 | 28.7 | R 82 | 234 | 480 | 1.52 | 3.80 | 5.66 |
| | | | L 63 | 176 | 383 | 1.54 | 3.90 | 5.66 |
| 11 | 64 | 25.2 | R 192 | 290 | 294 | 1.54 | 3.96 | 5.88 |
| | | | L 320 | 293 | 459 | 1.59 | 3.91 | 5.89 |
| 12 | | | | | | | | |
| 13 | 64 | 25.0 | R 250 | 195 | 340 | 1.57 | 4.13 | 6.16 |
| | | | L 290 | 263 | 387 | 1.55 | 3.76 | 5.76 |
| 14 | 78 | 14.1 | R 117 | 246 | 434 | 1.48 | 3.68 | 5.54 |
| | | | L 121 | 219 | 350 | 1.54 | 3.80 | 5.68 |
| Mean | 58.3 | 20.89 | R 203 | 240 | 408 | 1.55 | 3.87 | 5.78 |
| | | | L 188 | 226 | 398 | 1.58 | 3.84 | 5.72 |
| S.D. | 16.4 | 6.86 | R 62 | 75 | 91 | 0.07 | 0.16 | 0.22 |
| | | | L 87 | 72 | 105 | 0.08 | 0.09 | 0.13 |

TABLE 6.13. Values of peak-to-peak amplitude (nV) and latency (msec) for hypothyroid patients after replacement therapy at 80 dBSL for right and left ears.

| CASE | AGE YEARS | $FT_4$ | AMPLITUDE | | | LATENCY | | |
|---|---|---|---|---|---|---|---|---|
| | | | I | III | V | I | III | V |
| 1 | 62 | 12.3 | R 210 | 234 | 242 | 1.74 | 4.08 | 6.14 |
| | | | L 39 | 120 | 300 | 1.72 | 4.16 | 6.12 |
| 2 | | | | | | | | |
| 3 | 32 | 10.4 | R 160 | 330 | 348 | 1.64 | 3.80 | 5.70 |
| | | | L 110 | 316 | 429 | 1.68 | 3.76 | 5.70 |
| 4 | 60 | 20.2 | R 187 | 210 | 476 | 1.68 | 4.12 | 6.00 |
| | | | L 207 | 152 | 296 | 1.76 | 4.00 | 5.98 |
| 5 | 64 | 18.0 | R 120 | 109 | 319 | 1.65 | 4.05 | 5.85 |
| | | | L 171 | 213 | 326 | 1.53 | 3.82 | 5.69 |
| 6 | | | | | | | | |
| 7 | 61 | 26.9 | R 129 | 234 | 594 | 1.70 | 3.88 | 5.60 |
| | | | L 140 | 180 | 617 | 1.84 | 3.96 | 5.62 |
| 8 | 26 | 28.1 | R 250 | 137 | 348 | 1.62 | 3.84 | 5.68 |
| | | | L 238 | 122 | 345 | 1.62 | 3.86 | 5.68 |
| 9 | | | | | | | | |
| 10 | 72 | 28.7 | R 74 | 203 | 460 | 1.68 | 3.90 | 5.76 |
| | | | L 46 | 170 | 367 | 1.66 | 3.96 | 5.74 |
| 11 | 64 | 25.2 | R 185 | 210 | 280 | 1.58 | 4.00 | 6.00 |
| | | | L 218 | 197 | 397 | 1.70 | 4.18 | 6.25 |
| 12 | | | | | | | | |
| 13 | 64 | 25.0 | R 230 | 183 | 319 | 1.63 | 4.02 | 5.87 |
| | | | L 193 | 199 | 317 | 1.69 | 3.99 | 5.72 |
| 14 | 78 | 14.1 | R 70 | 240 | 430 | 1.66 | 3.72 | 5.66 |
| | | | L 102 | 215 | 330 | 1.62 | 3.40 | 5.76 |
| **Mean** | 58.3 | 20.89 | R 161 | 209 | 382 | 1.66 | 3.94 | 5.83 |
| | | | L 146 | 188 | 372 | 1.68 | 3.97 | 5.82 |
| S.D. | 16.4 | 6.86 | R 62 | 60 | 107 | 0.04 | 0.13 | 0.18 |
| | | | L 70 | 56 | 95 | 0.08 | 0.13 | 0.21 |

TABLE 6.14. Values of peak-to-peak amplitude (mV) and latency (msec) for hypothyroid patients after replacement therapy at 70 dBSL for right and left ears.

| CASE | AGE YEARS | $FT_4$ | AMPLITUDE | | | LATENCY | | |
|---|---|---|---|---|---|---|---|---|
| | | | I | III | V | I | III | V |
| 1 | 62 | 12.3 | R 35 | 82 | 208 | 2.00 | 4.20 | 6.36 |
| | | | L 30 | 118 | 140 | 1.86 | 4.22 | 6.34 |
| 2 | | | | | | | | |
| 3 | 32 | 10.4 | R 86 | 242 | 340 | 1.78 | 3,94 | 5.86 |
| | | | L 86 | 223 | 375 | 1.82 | 3.96 | 5.86 |
| 4 | 60 | 20.2 | R 180 | 190 | 470 | 1.72 | 4.14 | 6.18 |
| | | | L 60 | 150 | 210 | 1.90 | 4.16 | 6.10 |
| 5 | 64 | 18.0 | R 74 | 88 | 265 | 1.80 | 4.10 | 6.00 |
| | | | L 140 | 169 | 258 | 1.83 | 3.93 | 5.86 |
| 6 | | | | | | | | |
| 7 | 61 | 26.9 | R 125 | 152 | 515 | 1.86 | 3.90 | 5.70 |
| | | | L 136 | 160 | 478 | 1.94 | 4.00 | 5.68 |
| 8 | 26 | 28.1 | R 94 | 45 | 350 | 1.70 | 3.90 | 5.84 |
| | | | L 117 | 70 | 343 | 1.72 | 3.96 | 5.80 |
| 9 | | | | | | | | |
| 10 | 72 | 28.7 | R 55 | 160 | 449 | 1.80 | 3.98 | 5.90 |
| | | | L 45 | 160 | 360 | 1.78 | 4.08 | 6.00 |
| 11 | 64 | 25.2 | R 140 | 210 | 290 | 1.75 | 3.97 | 5.87 |
| | | | L 135 | 170 | 129 | 1.81 | 4.30 | 6.32 |
| 12 | | | | | | | | |
| 13 | 64 | 25.0 | R 139 | 159 | 208 | 1.74 | 4.07 | 6.10 |
| | | | L 68 | 103 | 249 | 1.79 | 4.07 | 5.99 |
| 14 | 78 | 14.1 | R 68 | 238 | 371 | 1.70 | 3.84 | 5.70 |
| | | | L 80 | 200 | 300 | 1.72 | 4.00 | 5.80 |
| Mean | 58.3 | 20.89 | R 99 | 156 | 347 | 1.91 | 4.00 | 5.95 |
| | | | L 89 | 152 | 284 | 1.82 | 4.06 | 5.97 |
| S.D. | 16.4 | 6.86 | R 45 | 67 | 107 | 0.14 | 0.12 | 0.21 |
| | | | L 40 | 45 | 109 | 0.07 | 0.12 | 0.22 |

TABLE 6.15 Values of peak-to-peak amplitude (mV) and latency (msec) for hypothyroid patients after replacement therapy at 60 dBSL for right and left ears.

| CASE | AGE YEARS | $FT_4$ | INTERWAVE INTERVAL | | |
|---|---|---|---|---|---|
| | | | I - III | III - V | I - V |
| 1 | 62 | 12.3 | R 2.32 | 2.04 | 4.36 |
| | | | L 2.30 | 1.92 | 4.22 |
| 2 | | | | | |
| | | | L | | |
| 3 | 32 | 10.4 | R 2.14 | 1.98 | 4.12 |
| | | | L 2.18 | 1.92 | 4.10 |
| 4 | 60 | 20.2 | R 2.48 | 1.96 | 4.44 |
| | | | L 2.32 | 2.02 | 4.34 |
| 5 | 64 | 18.0 | R 2.46 | 1.81 | 4.27 |
| | | | L 2.31 | 1.92 | 4.23 |
| 6 | | | | | |
| | | | L | | |
| 7 | 61 | 26.9 | R 2.16 | 1.68 | 3.84 |
| | | | L 2.12 | 1.72 | 3.84 |
| 8 | 26 | 28.1 | R 2.22 | 1.94 | 4.16 |
| | | | L 2.26 | 1.80 | 4.06 |
| 9 | | | | | |
| | | | L | | |
| 10 | 72 | 28.7 | R 2.28 | 1.86 | 4.14 |
| | | | L 2.36 | 1.76 | 4.12 |
| 11 | 64 | 25.2 | R 2.42 | 1.92 | 4.34 |
| | | | L 2.32 | 1.98 | 4.30 |
| 12 | | | | | |
| 13 | 64 | 25.0 | R 2.46 | 1.93 | 4.43 |
| | | | L 2.21 | 1.88 | 4.09 |
| 14 | 78 | 14.1 | R 2.20 | 1.86 | 4.06 |
| | | | L 2.26 | 1.88 | 4.14 |
| **Mean** | 58.3 | 20.89 | R 2.31 | 1.90 | 4.22 |
| | | | L 2.26 | 1.88 | 4.14 |
| S.D. | 16.4 | 6.86 | R 0.13 | 0.10 | 0.19 |
| | | | L 0.07 | 0.09 | 0.14 |

TABLE 6.16 Values of peak-to-peak interwave intervals (msec) for hypothyroid patients after replacement therapy at 80 dBSL for right and left ears.

| CASE | AGE YEARS | $FT_4$ | INTERWAVE INTERVAL | | |
|---|---|---|---|---|---|
| | | | I - III | III - V | I - V |
| 1 | 62 | 12.3 | R 2.34 | 2.06 | 4.40 |
| | | | L 2.44 | 1.96 | 4.40 |
| 2 | | | | | |
| 3 | 32 | 10.4 | R 2.16 | 1.90 | 4.06 |
| | | | L 2.08 | 1.94 | 4.02 |
| 4 | 60 | 20.2 | R 2.44 | 1.88 | 4.32 |
| | | | L 2.24 | 1.98 | 4.22 |
| 5 | 64 | 18.0 | R 2.40 | 1.80 | 4.20 |
| | | | L 2.27 | 1.87 | 4.16 |
| 6 | | | | | |
| 7 | 61 | 26.9 | R 2.18 | 1.72 | 3.90 |
| | | | L 2.12 | 1.66 | 3.78 |
| 8 | 26 | 28.1 | R 2.22 | 1.84 | 4.06 |
| | | | L 2.24 | 1.82 | 4.06 |
| 9 | | | | | |
| 10 | 72 | 28.7 | R 2.22 | 1.86 | 4.08 |
| | | | L 2.30 | 1.78 | 4.08 |
| 11 | 64 | 25.2 | R 2.42 | 2.00 | 4.42 |
| | | | L 2.48 | 2.07 | 4.55 |
| 12 | | | | | |
| 13 | 64 | 25.0 | R 2.39 | 1.85 | 4.24 |
| | | | L 2.30 | 1.73 | 3.93 |
| 14 | 78 | 14.1 | R 2.06 | 1.94 | 4.00 |
| | | | L 2.28 | 1.86 | 4.14 |
| **Mean** | 58.3 | 20.89 | R 2.28 | 1.89 | 4.17 |
| | | | L 2.27 | 1.87 | 4.13 |
| S.D. | 16.4 | 6.86 | R 0.13 | 0.10 | 0.18 |
| | | | L 0.12 | 0.12 | 0.22 |

TABLE 6.17 Values of peak-to-peak interwave intervals (msec) for hypothyroid patients after replacement therapy at 70 dBSL for right and left ears.

| CASE | AGE YEARS | $FT_4$ | INTERWAVE INTERVAL | | |
|---|---|---|---|---|---|
| | | | I - III | III - V | I - V |
| 1 | 62 | 12.3 | R 2.20 | 2.16 | 4.36 |
| | | | L 2.36 | 2.12 | 4.48 |
| 2 | | | | | |
| 3 | 32 | 10.4 | R 2.16 | 1.92 | 4.08 |
| | | | L 2.14 | 1.90 | 4.04 |
| 4 | 60 | 20.2 | R 2.42 | 2.04 | 4.46 |
| | | | L 2.26 | 1.94 | 4.20 |
| 5 | 64 | 18.0 | R 2.30 | 1.92 | 4.22 |
| | | | L 2.10 | 1.93 | 4.03 |
| 6 | | | | | |
| 7 | 61 | 26.9 | R 2.04 | 1.80 | 3.84 |
| | | | L 2.06 | 1.68 | 3.74 |
| 8 | 26 | 28.1 | R 2.20 | 1.94 | 4.14 |
| | | | L 2.24 | 1.84 | 4.08 |
| 9 | | | | | |
| 10 | 72 | 28.7 | R 2.18 | 1.92 | 4.10 |
| | | | L 2.26 | 1.96 | 4.22 |
| 11 | 64 | 25.2 | R 2.22 | 2.04 | 4.12 |
| | | | L 2.49 | 2.02 | 4.51 |
| 12 | | | | | |
| 13 | 64 | 25.0 | R 2.33 | 2.03 | 4.36 |
| | | | L 2.28 | 1.92 | 4.20 |
| 14 | 78 | 14.1 | R 2.14 | 1.86 | 4.00 |
| | | | L 2.28 | 1.80 | 4.08 |
| Mean | 58.3 | 20.89 | R 2.22 | 1.96 | 4.17 |
| | | | L 2.24 | 1.91 | 4.16 |
| S.D. | 16.4 | 6.86 | R 0.11 | 0.11 | 0.18 |
| | | | L 0.12 | 0.12 | 0.22 |

TABLE 6.18 Values of peak to peak interwave intervals (msec) for hypothyroid patients after replacement therapy at 60 dBSL for right and left ears.

| | | | AMPLITUDE | | | LATENCY | | |
|---|---|---|---|---|---|---|---|---|
| | | | I | III | V | I | III | V |
| RETEST | MEAN | R | 203 | 240 | 408 | 1.55 | 3.87 | 5.78 |
| | | L | 188 | 226 | 398 | 1.58 | 3.84 | 5.72 |
| | S.D. | R | 62 | 75 | 91 | 0.07 | 0.16 | 0.22 |
| | | L | 87 | 72 | 105 | 0.08 | 0.09 | 0.13 |
| NORMAL | MEAN | R | 188 | 316 | 482 | 1.53 | 3.75 | 5.58 |
| | | L | 167 | 293 | 497 | 1.57 | 3.78 | 5.63 |
| | S.D. | R | 124 | 149 | 148 | 0.05 | 0.15 | 0.20 |
| | | L | 107 | 120 | 128 | 0.07 | 0.14 | 0.15 |
| HYPO-THYROID | MEAN | R | 134 | 155 | 343 | 1.59 | 3.92 | 5.83 |
| | | L | 153 | 163 | 338 | 1.60 | 3.94 | 5.83 |
| | S.D. | R | 74 | 100 | 99 | 0.08 | 0.19 | 0.23 |
| | | L | 90 | 88 | 65 | 0.06 | 0.15 | 0.19 |

TABLE 6.19 Mean values and standard deviation of peak-to-peak amplitude (nV) and latency (msec) of hypothyroid patients after treatment-retest, normal controls and hypothyroid patients at 80 dBSL for right and left ears.

| | | | AMPLITUDE | | | LATENCY | | |
|---|---|---|---|---|---|---|---|---|
| | | | I | III | V | I | III | V |
| RETEST | MEAN | R | 161 | 209 | 382 | 1.66 | 3.94 | 5.83 |
| | | L | 146 | 188 | 372 | 1.68 | 3.97 | 5.82 |
| | S.D. | R | 62 | 60 | 107 | 0.04 | 0.13 | 0.18 |
| | | L | 70 | 56 | 95 | 0.08 | 0.13 | 0.21 |
| NORMAL | MEAN | R | 184 | 255 | 437 | 1.62 | 3.82 | 5.70 |
| | | L | 154 | 223 | 414 | 1.68 | 3.86 | 5.74 |
| | S.D. | R | 116 | 120 | 99 | 0.14 | 0.16 | 0.20 |
| | | L | 93 | 114 | 131 | 0.08 | 0.14 | 0.15 |
| HYPO-THYROID | MEAN | R | 99 | 130 | 304 | 1.72 | 4.02 | 5.96 |
| | | L | 114 | 148 | 285 | 1.75 | 4.03 | 5.97 |
| | S.D. | R | 48 | 79 | 93 | 0.12 | 0.19 | 0.25 |
| | | L | 81 | 72 | 81 | 0.13 | 0.16 | 0.22 |

TABLE 6.20 Mean values and standard deviation of peak-to-peak amplitude (nV) and latency (msec) of hypothyroid patients after treatment-retest, normal controls and hypothyroid patients at 70 dBSL for right and left ears.

| | | | AMPLITUDE | | | LATENCY | | |
|---|---|---|---|---|---|---|---|---|
| | | | I | III | V | I | III | V |
| RETEST | MEAN | R | 99 | 156 | 347 | 1.91 | 4.00 | 5.95 |
| | | L | 89 | 152 | 284 | 1.82 | 4.06 | 5.97 |
| | S.D. | R | 45 | 67 | 107 | 0.14 | 0.12 | 0.21 |
| | | L | 40 | 45 | 109 | 0.07 | 0.12 | 0.22 |
| NORMAL | MEAN | R | 134 | 213 | 396 | 1.81 | 3.91 | 5.88 |
| | | L | 113 | 202 | 389 | 1.76 | 3.93 | 5.86 |
| | S.D. | R | 112 | 12 | 132 | 0.13 | 0.19 | 0.24 |
| | | L | 78 | 85 | 150 | 0.08 | 0.15 | 0.19 |
| HYPO-THYROID | MEAN | R | 80 | 96 | 258 | 1.93 | 4.16 | 6.12 |
| | | L | 76 | 89 | 256 | 1.93 | 4.16 | 6.17 |
| | S.D. | R | 40 | 53 | 111 | 0.26 | 0.23 | 0.29 |
| | | L | 57 | 68 | 92 | 0.13 | 0.19 | 0.21 |

TABLE 6.21 Mean values and standard deviation of peak-to-peak amplitude (nV) and latency (msec) of hypothyroid patients after treatment-retest, normal controls and hypothyroid patients at 60 dBSL for right and left ears.

| | | INTERWAVE INTERVAL | | |
|---|---|---|---|---|
| | | I - III | III - V | I - V |
| RETEST | MEAN | R 2.31 | 1.90 | 4.22 |
| | | L 2.26 | 1.88 | 4.14 |
| | S.D. | R 0.13 | 0.10 | 0.19 |
| | | L 0.07 | 0.09 | 0.14 |
| NORMAL | MEAN | R 2.22 | 1.84 | 4.05 |
| | | L 2.22 | 1.86 | 4.07 |
| | S.D. | R 0.16 | 0.16 | 0.19 |
| | | L 0.13 | 0.16 | 0.17 |
| HYPO-THYROID | MEAN | R 2.33 | 1.92 | 4.25 |
| | | L 2.33 | 1.86 | 4.20 |
| | S.D. | R 0.17 | 0.10 | 0.21 |
| | | L 0.15 | 0.14 | 0.20 |

TABLE 6.22 Mean values and standard deviation of peak-to-peak interwave interval (msec) of hypothyroid patients of replacement therapy-retest, normal controls and hypothyroid patients at 80 dBSL for right and left ears.

| | | INTERWAVE INTERVAL | | |
|---|---|---|---|---|
| | | I - III | III - V | I - V |
| RETEST | MEAN | R 2.28 | 1.89 | 4.17 |
| | | L 2.27 | 1.87 | 4.13 |
| | S.D. | R 0.13 | 0.10 | 0.18 |
| | | L 0.12 | 0.12 | 0.22 |
| NORMAL | MEAN | R 2.19 | 1.89 | 4.07 |
| | | L 2.18 | 1.88 | 4.06 |
| | S.D. | R 0.15 | 0.13 | 0.15 |
| | | L 0.15 | 0.12 | 0.16 |
| HYPO-THYROID | MEAN | R 2.30 | 1.94 | 4.24 |
| | | L 2.28 | 1.94 | 4.23 |
| | S.D. | R 0.25 | 0.18 | 0.23 |
| | | L 0.16 | 0.13 | 0.24 |

TABLE 6.23 Mean values and standard deviation of peak-to-peak interwave interval (msec) of hypothyroid patients of replacement therapy-retest, normal controls and hypothyroid patients at 70 dBSL for right and left ears.

| | | INTERWAVE INTERVAL | | |
|---|---|---|---|---|
| | | I - III | III - V | I - V |
| RETEST | MEAN | R 2.22 | 1.96 | 4.17 |
| | | L 2.24 | 1.91 | 4.16 |
| | S.D. | R 0.11 | 0.11 | 0.18 |
| | | L 0.12 | 0.12 | 0.22 |
| NORMAL | MEAN | R 2.12 | 1.93 | 4.04 |
| | | L 2.17 | 1.93 | 4.10 |
| | S.D. | R 0.24 | 0.15 | 0.22 |
| | | L 0.14 | 0.12 | 0.20 |
| HYPO-THYROID | MEAN | R 2.28 | 1.96 | 4.24 |
| | | L 2.23 | 2.01 | 4.24 |
| | S.D. | R 0.29 | 0.20 | 0.28 |
| | | L 0.15 | 0.14 | 0.19 |

TABLE 6.24 Mean values and standard deviation of peak-to-peak interwave interval (msec) of hypothyroid patients of replacement therapy-retest, normal controls and hypothyroid patients at 60 dBSL for right and left ears.

# CHAPTER SEVEN

# HYPER-THYROIDISM

## 7.1 Introduction

Although theere are many reports in the literature showing the effect of hypothyroidism on hearing and on the properties of the auditory evoked potentials in hypothyroid patients, I am not aware of any report on hearing disorders in the case of hyperthyroid patients at the time of undertaking this investigatory study. There have been as yet few reports on the effect of hyperthyroidism on auditory evoked potentials.

Kohonen et al. (1971) studied cochlear microphonic in guniea pigs with hyperthyroidism. They stated that there was no difference in the cochlear activity between the hyperthyroid guinea pigs and that of normal control ones. In a recent study, Himelfarb et al. (1981) reported a significant decrease in brainstem conduction time and the peaks were of more sharp and high amplitude than that of the controls in some patients. They found that the brainstem evoked response technique is more sensitive and more reliable than the conventional audiometry. The conventional detected hearing loss only was found in some elderly patients who were suffering thyroid dysfunction; the auditory brainstem evoked response recording showed abnormality of auditory brainstem conduction time in all the patients. Abbott et al. (1983) observed no abnormalities in the visual evoked potentials in hyperthyroid patients. In contrast Vitava et al. (1976) reported high voltage response and significant latency decrease of both early and late components of cerebral evoked potentials.

From the review of studies mentioned above it is clear that there is discrepancy and disagreement among the investigators about the effect of

hyperthyroidism on adult patients, besides which there is only one study which used the ABER on humans in the case of hyperthyroidism (Himelfarb et al., 1981).

The study of ABER in hyperthyroid patients could be useful in adding to the audiological battery tests as a diagnostic test as well as a follow up to the treatment.

In this study an attempt was made to establish whether or not hyperthyroidism has an effect on the ABER parameters in oder to use this technique as a diagnostic tool and as a follow up in the treatment of this sort of patient.

## 7.2 Literature Review

I am not aware of reports on hearing disorders in over-activity of the thyroid gland. However many investigators have studied whether congenital and acquired hypothyroidism causes deafness in both humans and experimental animals as shown in section 6.2. The literature review in the case of hyperthyroidism is inclusive only in some reports achieved as subsequent for results of studies using auditory evoked responses in both humans and experimental animals. In guinea pigs made hyperthyroidism by administration of tri-iodothyronine, Kohonen et al. (1971) reported no changes in the cochlear microphonic. Furthermore Kohonen and his associates did not find any pathological abnormalities by histological examination of these animals' cochlea. In human study and by using the auditory brainstem evoked response technique, Himelfarb et al. (1981) reported a significant decrease of brainstem conduction time, high amplitude and sharp peaks in some cases in relation to the normal control subjects. They noticed that all these changes were reversible by the treatment of hyperthyroidism. Abbott et al.

(1983) have studied the effect of hyperthyroidism on the visual evoked potential and on the peripheral nerve conduction. They reported no changes either in the latencies of the visual evoked responses or in peripheral nerve conduction in comparison with normal age matching controls.

In neonatal rats given daily injections of thyroxine starting from birth to the 20th day, Hebert and Dussault (1984) reported that the rats showed hyperthyroidism, were precocious and showed accelerated maturation of cochlear-evoked potentials. Using cerebral-evoked response Vitova et al. (1976) in a study of 22 hyperthyroid children observed high voltage response pattern and significant latency decrease of both early and late cerebral evoked potential components in some patients in comparison with age matching controls.

## 7.3 Methods

### 7.3.1 Subjects

Auditory brainstem evoked responses were recorded in 12 untreated hyperthyroid patients whose ages ranged from 36-74 years (mean 53.92, standard deviation 11.66). Nine were females whose ages ranged from 36-74 years (mean 54.89, standard deviation 12.7) and three males whose ages ranged from 37-59 years (mean 51, standard deviation 12.17). The diagnosis of hyperthyroidism was based on the clinical manifestations, and on the radioimmune assay of the serum free thyroxine ($FT_4$) in the range from 28.2 - 74.1 p.mol/L (normal range 8-24 p.mol/L). All the patients have been chosen from those patients who come to the laboratory of nuclear medicine for routine blood testing for suspected hyperthyroid function. All the patients agreed to attend for recording sessions twice, once before starting the treatment and again after the treatment when euthyroid state has been achieved.

### 7.3.2 Instrumentation

An Amplaid Mk5 evoked potential signal processor was used as the click and white noise generator. The experiment was designed to achieve clicks from the Mk5 equipment at 80, 70 and 60 dB sensation level for each ear and white noise which was used as masking and delivered to the contralateral ear at intensity of 20 dBnHL less than that of the click intensity. The Mk5, besides its function as a click and white noise generator, is designed to control the amplifiers, printing and storage devices, this was described earlier (see section 4.1, 4.1.1 and 4.1.2). The clicks and white noise signals were transmitted to the patient's ears, who was lying down on a bed beside the equipment, through shielded TDH49 earphones.

### 7.3.3 Electrodes attachment

In order to achieve better cochlear action potential and brainstem responses, the electrodes were placed on the mastoid process of the testing ear as active, on the vertex as negative and on the forehead just below the hair line as earth. The procedure of the electrode attachment was described earlier (see section 4.2.1).

### 7.3.4 Recording of ABERs

Each patient has attended one recording session of about 1 1/2 - 2 hours duration. Before starting the recording detailed general history, family history, present and past history as well as audiological history were taken followed by pulse and temperature recording and otoscopic examination for both right and left ears. The patient then lay on a bed beside the Amplaid to start recording the ABER with the same procedure which

was described earlier (see section 4.2). Each intensity recording was repeated twice and the average was taken.

## 7.4 Results

Untreated hyperthyroid patients were those attending the laboratory of nuclear medicine for their blood test for suspicion of hyperthyroid activity. Investigated were twelve patients whose ages ranged from 36-74 years (mean 53.92, standard deviation 11.66). Nine were females whose ages ranged from 36-74 years (mean 54.89, standard deviation 12.07) and three were males who ages ranged from 37-59 years (mean 51, standard deviation 12.17). The diagnosis of hyperthyroidism was based mainly on the clinical manifestations and on the radioimmuno assay of the serum free thyroxine ($FT_4$). It was in the range from 28.2-74.1 p.mol/L (normal range 8-24 p.mol/L). Otoscopic examination for both ears showed normal appearance of tympanic membrane as well as the middle ear and eustachian tube function. Tuning fork tests showed the Rinne test to be positive in one patient (No. 4 in Table 7.1). The pure tone audiogram showed a reduction in hearing in both air and bone conduction in two patients, the hearing impairment was 5 and 13 dB respectively according to the four frequency average (FFA) at 500, 1000, 2000 and 4000 Hz. As shown in Table 7.2 it can be seen that there is a small elevation in the threshold in low frequencies with some patients. None of the patients showed an abnormal fatigue, that is to say the Cahart's tone decay test was negative.

ABER recordings for all hyperthyroid patients at intensities 80, 70 and 60 dB sensation level for both right and left ear are shown in Figure 7.1. Tables 7.4 to 7.9 outline each waveform which represents an average of 2048 stimuli presentations measured at negative peak latency and peak to peak amplitude, from negative peak to the following positive one, as well as the

inter-wave interval latency of I-V, I-III and III-V.

The pattern of ABER recording was characterised by the presence of wave I, III and V, similar in their broadness and sharpness of peaks more or less to that of the normal control subjects. Wave II was missing in some recordings almost the same as in the control ones. Wave IV fused with wave V to make IV/V complex in a lot of recordings and this had been noticed in normal control subject recordings. There was no significant difference in ABER parameters (latency, amplitude and inter-wave interval latency) between hyperthyroid patients and normal control subject (see Table 7.3). However there was significant difference ($p < 0.05$) in these parameters between hyper and hypothyroid patients. The amplitude was bigger and latencies short for waves III and V in hyper-thyroid patients (see Table 6.5).

### 7.4.1 Statistical analysis

a) Hyperthyroid-Normals

State parameters of ABER at peaks of wave I, III and V at intensities of 80, 70 and 60 dB SL were obtained for both right and left ears for normal and hyperthyroid patients in relation to amplitude, latency and inter-wave intervals of I-III, I-V and III-V. The null hypothesis to be tested:

$$HO : \mu_1 > \mu_2$$

where: $\mu_1$ = the mean of hyperthyroid patients

$\mu_2$ = the mean of normal control subjects

Student t-test has been investigated to test the above mentioned hypothesis under the level of significance $\alpha = 0.05$. Significant differences are presented in Table 7.3. This implies that the 't' lies outside the critical region and the difference is not significant. We say

that there is no evidence to accept the null hypothesis and it is rejected.

b) Hyperthyroid-Hypothyroid

The ABER parameters of hyperthyroid and hypothyroid patients were statistically analysed in the same manner as that of hyperthyroidism and normal controls were done. The null hypothesis is:

$$HO : \mu_1 > \mu_2$$

where: $\mu_1$ is the mean of hyperthyroid patients

$\mu_2$ is the mean of hypothyroid patients

$\alpha < 0.05$

where: $\alpha$ is the level of significance at 5%.

The data are presented in Table 6.5. This implies that 't' lies inside the critical region and the difference is significant so we say that there is evidence to accept the null hypothesis.

These results were not encouraging enough to repeat the brainstem recordings in hyperthyroid patients after the treatment.

## 7.5 Discussion

The aim of this experimental study was an attempt to establish the validity of using the ABER technique as a routine diagnostic tool to ascertain whether or not hearing impairment has occurred in thyrotoxic patients. This hypothesis arose out of previous work which proved that the ABER might be a good diagnostic tool in distinguishing between the normal control subjects and hypothyroid patients on one hand and between hypo-thyroid and hyperthyroid on the other hand, and also from other researches which found that this technique might be helpful as an index to follow up

treatment for hypo and hyperthyroidism. The ABER technique could show dramatic changes in the auditory pathways to a far greater extent than conventional audiometry. Himelfarb et al. (1981) reported in a study on patients suffering from thyroid dysfunction that conventional audiometry could detect hearing loss only in some elderly patients, while ABER recording showed dramatic abnormal changes related to the thyroid function state in all patients. Furthermore the ABER technique can play an important role in finding some information which might be helpful in exploring the mechanism by which the excess thyroxine affects the auditory pathway and in localising the lesion of thyroxosis, if any, in the auditory system.

Twelve patients with hyperthyroidism were studied using the ABER technique. All local and systemic causes of hearing loss which might have had an effect on the ABER were excluded in all patients. The patients were proved to have hyperthyroidism based on clinical manifestations as well as on radioimmuno assay of serum free thyroxine ($FT_4$).

The results of this study showed no significant difference in ABER parameters between normal subject controls and hyperthyroid patients. However, it showed a significant difference between hypo and hyperthyroid patients. These results simply mean that there is no effect of excess thyroxine at least on the auditory pathway of the adult persons. If this is true we have to prove that excess thyroxine has no effect on the adult CNS in general and on the auditory system in particular. It is well established that the excess of thyroid hormones has an effect on the central nervous system as well as on the peripheral nervous system of adults and neonatals. In adult life the effect of thyroxine on the CNS is irritability and restlessness. This action of the thyroid hormones is probably due to increased responsiveness of catecalamines with consequent activation of the

reticular activating system, as the blood/brain barrier does not allow thyroxine to enter the CNS except in traces in the case of adults (Gangon, 1981). Thyroxine is known to be necessary for the development of the CNS and for the peripheral sensory structures. Thyroid dysfunction interfers with this development, prenatal hypothyroidism impairs the mechanisms underlying the CNS development, that is to say myelonogenesis, neural cell formation, migration, maturation and synaptogenesis (Morreale de Escobar et al., 1980). An excess of thyroxine in the neonatal life has been shown to increase protein lipid and nucleic acid metabolism in the developing brain (Gelbar et al., 1964). An administration of excess thyroxine to neonatal rats was found to markedly increase the spontaneous locomotor activity (Rostagi and Singhal, 1976). In neonatal life the blood/brain barrier is not well developed and thyroid hormones had marked effects on the brain. It is clear that in the case of hypothyroid infants there are synapses developing abnormality, defective myelination and mental retardation. These changes are reversible only if thyroxine replacement therapy begins soon after birth (Ganong, 1981). Thyroxine seems to affect the CNS only in early life. Neonatal hyperthyroidism is characterised by intial hasting neuronal process differentiation followed rapidly by an abrupt interruption of migration and maturation process of the CNS (Legrand, 1979). Furthermore, thyroid hormones have a calorigenic action on the body tissue. This action is produced by an increasing $O_2$ consumption of almost all metabolically active tissue, the exceptions being the adult brain, testes, lymph nodes, uterus, spleen and anterior pituritry gland (Ganong, 1981).

Thyroxine exerts an effect on the peripheral nervous system. It is now established that the reflexes, e.g. knee cap reflex and ankle jerk (Achilles) reflex are used to assess the thyroid function. The reflexes are slow in hypothyroidism and rapid in hyperthyroidism. This being true,

however, these reflexes are affected by factors other than the level of thyroid hormones circulating in the blood stream.

In the auditory system it was proved that thyroxine plays an important role in the development of the organ of corti (Uziel et al., 1980), and it is necessary for the development of mid-brain auditory function (Rubenstein et al., 1975; Mendel and Robinson, 1978). Thyroxine deficiency leads to biochemical, anatomical and electrophysiological changes in the auditory pathway (see section 6.2.), (Bragman and Gardner, 1967; Deol, 1973, 1976; Uziel et al., 1980, 1981; Kohonen et al., 1971; Meyerhoff, 1979; Van middlesworth and Norris, 1980). Neonatal administration of thyroxine showed acceleration and maturation of cochlear activity (Herbert and Dussaut, 1984). This acceleration might be explained in part, as Bernard et al. (1982) suggested, that the role of thyroxine is to accelerate the development of the external auditory meatus, by quicker resorbtion of middle ear mesenchyma as well as by an acceleration and maturation of the hair cells and afferent synapses of the inner ear. Thyroxine seems to have an effect on the auditory system only in early life and for a certain limited time. In an experimental study on rats made hyperthyroid on the first day of birth, Herbert and Dussault (1984) reported the acceleration and maturation of cochlear activity. The wave I was high in amplitude and short in latency in neonatal hyperthyroid rats in comparison to the control group. However, this difference vanished on the 16th day after birth. Mendel and Robinson (1978) noticed the appearance of only wave I and II in the hypothyroid child. The administration of thyroxine therapy helped in the appearance of the rest of the ABER waves to the normal without any change in the amplitude and the latency of wave I and II which were in the normal range. An excess of thyroxine has no effects on the other kinds of evoked

potentials in adults. Kohonen et al. (1971) found no change in the cochlear microphonic potentials in adult guinea pigs made hyperthyroid by administration of triodo thyronine. In addition they could not find any pathohistological changes by histologic examination of these animals' cochleas. Abbott et al. (1983) did not notice any difference either in the latency of the visual evoked responses or in the peripheral nerve conduction in thyrotoxic patients compared to the control groups.

Now it is possible to conclude that thyroxine is necessary for the development of the auditory system and might have a direct effect on it in neonatal life. There was no effect of thyroxine on the adult auditory system. The abnormality in ABER parameters due to hypothyroidism which is mentioned in Chapter 6 was due mainly to the direct effect of thyroxine deficiency on the body temperature of hypothyroid patients and is always subnormal. If we take the body temperature changes into account, all the hyperthyroid patients in this study were within normal range. Although the skin of hyperthyroid patients is smooth, warm and moist, the body temperature is usually normal (Larsen, 1985).

ABER technique appears to be a useful test to distinguish between hypothyroidism and normal subjects on the one hand and between hypo and hyperthyroidism on the other, but it is unhelpful in distinguishing between hyperthyroidism and that of normal ones.

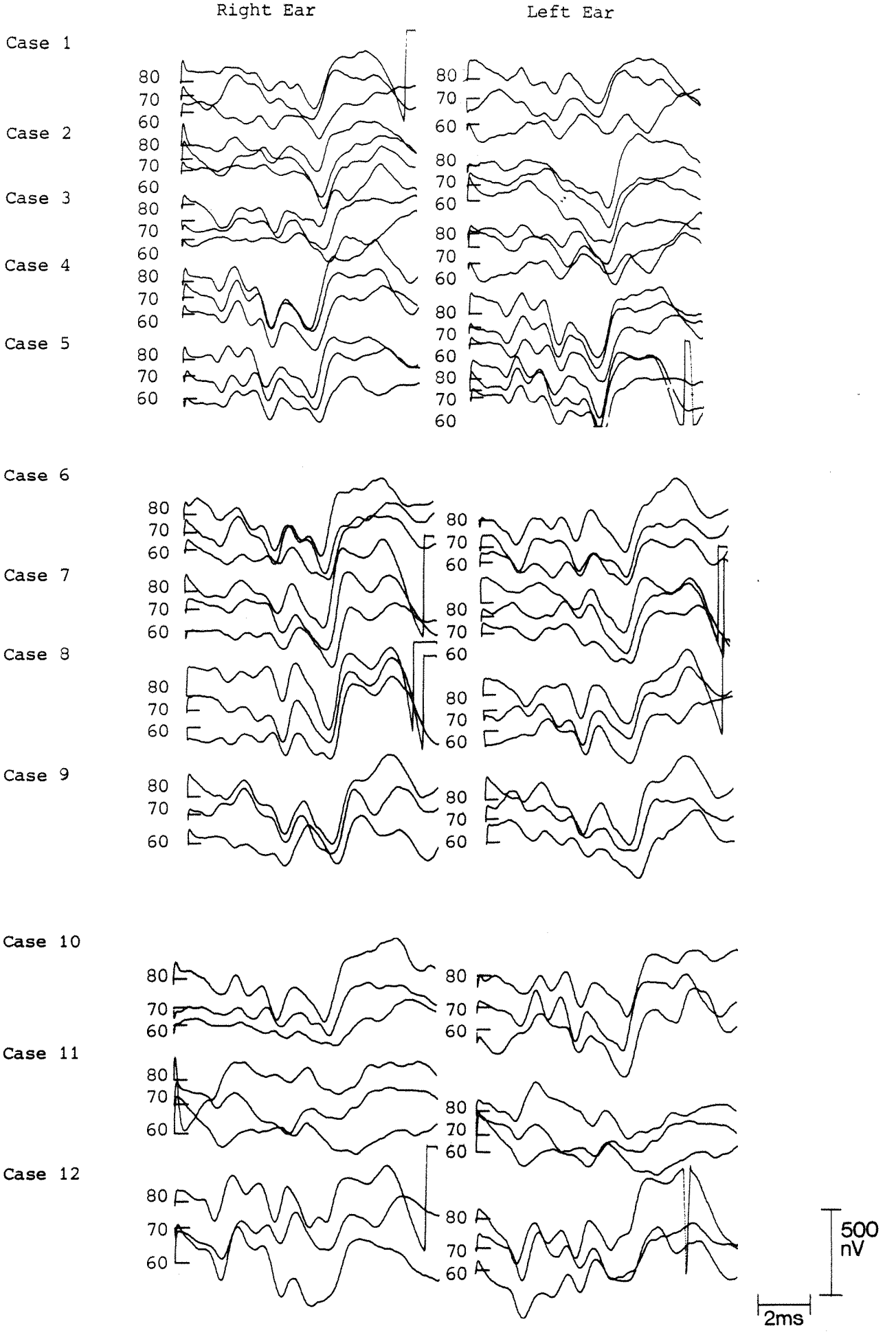


Figure 7.1 Responses of hyperthyroid patients at intensities of 80, 70 and 60 dBSL for both right and left ears.

| Subject | Age Years | | 250 Hz | 500 Hz | 1000 Hz | 2000 Hz | 3000 Hz | 4000 Hz | 8000 Hz |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 62 | R | 25 | 25 | 20 | 5 | 10 | 10 | 15 |
| | | L | 25 | 20 | 20 | 5 | 10 | 15 | 5 |
| 2 | 49 | R | 35 | 30 | 20 | 15 | 10 | 15 | 45 |
| | | L | 35 | 30 | 20 | 10 | 15 | 15 | 30 |
| 3 | 65 | R | 30 | 35 | 30 | 25 | 35 | 30 | 55 |
| | | L | 25 | 35 | 25 | 25 | 35 | 25 | 55 |
| 4 | 74 | R | 35 | 25 | 20 | 35 | 45 | 30 | 80 |
| | | L | 25 | 25 | 20 | 40 | 50 | 45 | ∞ |
| 5 | 53 | R | 20 | 25 | 20 | 10 | 5 | 10 | 10 |
| | | L | 25 | 20 | 20 | 15 | 10 | 10 | 15 |
| 6 | 57 | R | 30 | 35 | 25 | 10 | 10 | 15 | 30 |
| | | L | 25 | 25 | 20 | 5 | 15 | 30 | 30 |
| 7 | 36 | R | 20 | 15 | 15 | 0 | 10 | 0 | 10 |
| | | L | 15 | 15 | 15 | 5 | 5 | 5 | 5 |
| 8 | 37 | R | 10 | 10 | 5 | 15 | 15 | 15 | 0 |
| | | L | 20 | 20 | 10 | 15 | 10 | 10 | 0 |
| 9 | 62 | R | 25 | 25 | 15 | 15 | 15 | 10 | 30 |
| | | L | 30 | 20 | 20 | 20 | 25 | 30 | 10 |
| 10 | 59 | R | 35 | 30 | 15 | 15 | 20 | 20 | 40 |
| | | L | 25 | 25 | 15 | 20 | 20 | 25 | 40 |
| 11 | 52 | R | 35 | 35 | 30 | 15 | 10 | 10 | 25 |
| | | L | 30 | 25 | 20 | 5 | 15 | 20 | 25 |
| 12 | 41 | R | 25 | 25 | 15 | 10 | 10 | 10 | 15 |
| | | L | 25 | 25 | 20 | 15 | 10 | 15 | 15 |

TABLE 7.1 Pure tone audiometry of hyperthyroid patients. Threshold in dB (ISO).

| Case | Name | Age Years | Duration Months | $FT_4$ | Pulse Rate /m | Hearing Loss dB (ISO) R | L | Comments |
|---|---|---|---|---|---|---|---|---|
| 1 | V.P. | 62 | 11 | 28.2 | 80 | 15 | 15 | Normal |
| 2 | P.W. | 49 | 10 | 29.0 | 85 | 20 | 19 | Normal |
| 3 | I.J. | 65 | 10 | 32.3 | 78 | 30 | 28 | Slight Hearing Impairment |
| 4 | C.J. | 74 | 10 | 32.7 | 68 | 28 | 33 | Slight Hearing Impairment |
| 5 | W.S. | 53 | 9 | 33.4 | 84 | 16 | 16 | Normal |
| 6 | E.S. | 57 | 9 | 46.5 | 84 | 21 | 20 | Normal |
| 7 | C.H. | 36 | 9 | 47.8 | 92 | 15 | 10 | Normal |
| 8 | D.W. | 37 | 10 | 48.0 | 72 | 11 | 14 | Normal |
| 9 | S.H. | 62 | 9 | 54.3 | 82 | 16 | 23 | Normal |
| 10 | P.K. | 59 | 9 | 58.5 | 102 | 20 | 20 | Normal |
| 11 | S.I. | 52 | 9 | 71.0 | 100 | 23 | 18 | Normal |
| 12 | P.G. | 41 | 8 | 74.1 | 82 | 15 | 19 | Normal |

TABLE 7.2 The duration of the disease, $FT_4$ amount in the serum in p.mol/L, pulse and hearing loss in hyperthyroid patients.

| PARAMETERS | 60 dB SL | | 70 dB SL | | 80 dB SL | |
|---|---|---|---|---|---|---|
| | Right | Left | Right | Left | Right | Left |
| AMPLITUDE<br>I | -- | -- | -- | -- | -- | P = 0.22 |
| III | -- | P = 0.001 | -- | P = 0.01 | -- | -- |
| V | -- | -- | -- | -- | -- | -- |
| LATENCY<br>I | -- | -- | -- | -- | -- | -- |
| III | -- | -- | -- | -- | -- | -- |
| V | -- | P = 0.05 | -- | -- | -- | -- |
| INTER-PEAK INTERVAL<br>V-I | -- | P = 0.05 | -- | -- | -- | -- |
| V-III | -- | -- | -- | -- | -- | -- |
| III-I | -- | -- | -- | -- | -- | -- |

TABLE 7.3 Summary of statistical analysis t-test of amplitude, latency and interwave intervals of hyperthyroid - normal controls, where -- = not significant.

| CASE | AGE YEARS | $FT_4$ | AMPLITUDE | | | LATENCY | | |
|---|---|---|---|---|---|---|---|---|
| | | | I | III | V | I | III | V |
| 1 | 62 | 28.2 | R 221 | 285 | 652 | 1.50 | 3.80 | 5.64 |
| | | | L 207 | 270 | 640 | 1.48 | 3.76 | 5.60 |
| 2 | 49 | 29.0 | R 160 | 254 | 574 | 1.60 | 3.88 | 5.68 |
| | | | L 230 | 531 | 402 | 1.50 | 3.66 | 5.46 |
| 3 | 65 | 32.3 | R 164 | 125 | 383 | 1.50 | 3.78 | 5.74 |
| | | | L 94 | 277 | 629 | 1.56 | 4.00 | 5.86 |
| 4 | 74 | 32.7 | R 121 | 277 | 695 | 1.52 | 3.66 | 5.52 |
| | | | L 140 | 129 | 484 | 1.52 | 3.76 | 5.72 |
| 5 | 53 | 33.4 | R 156 | 253 | 652 | 1.46 | 3.42 | 5.40 |
| | | | L 242 | 145 | 680 | 1.48 | 3.52 | 5.38 |
| 6 | 57 | 46.5 | R 191 | 203 | 387 | 1.54 | 3.86 | 5.72 |
| | | | L 102 | 184 | 387 | 1.50 | 3.72 | 5.60 |
| 7 | 36 | 47.8 | R 250 | 277 | 691 | 1.50 | 3.66 | 5.40 |
| | | | L 203 | 285 | 547 | 1.48 | 3.74 | 5.48 |
| 8 | 37 | 48.0 | R 61 | 314 | 645 | 1.52 | 3.59 | 5.46 |
| | | | L 234 | 292 | 469 | 1.46 | 3.80 | 5.74 |
| 9 | 62 | 54.3 | R 109 | 383 | 648 | 1.52 | 3.78 | 5.54 |
| | | | L 152 | 387 | 457 | 1.60 | 3.86 | 5.62 |
| 10 | 59 | 58.5 | R 230 | 117 | 254 | 1.48 | 3.48 | 5.62 |
| | | | L 277 | 160 | 285 | 1.52 | 3.80 | 5.68 |
| 11 | 52 | 71.0 | R 74 | 89 | 543 | 1.54 | 3.60 | 5.48 |
| | | | L 117 | 195 | 250 | 1.56 | 3.64 | 5.56 |
| 12 | 41 | 74.1 | R 408 | 356 | 459 | 1.51 | 3.74 | 5.69 |
| | | | L 574 | 191 | 257 | 1.52 | 3.85 | 5.86 |
| Mean | 53.92 | 46.3 | R 178 | 244 | 549 | 1.52 | 3.69 | 5.58 |
| | | | L 214 | 251 | 457 | 1.51 | 3.76 | 5.63 |
| S.D. | 11.66 | 15.9 | R 93 | 94 | 145 | 0.04 | 0.15 | 0.13 |
| | | | L 128 | 118 | 148 | 0.05 | 0.12 | 0.15 |

**TABLE 7.4** Values of peak-to-peak amplitude (nV) and latency (msec) for hyperthyroid patients at 80 dBSL for right and left ear

| CASE | AGE YEARS | $FT_4$ | AMPLITUDE | | | LATENCY | | |
|---|---|---|---|---|---|---|---|---|
| | | | I | III | V | I | III | V |
| 1 | 62 | 28.2 | R 117 | 230 | 593 | 1.60 | 3.90 | 5.74 |
| | | | L 102 | 86 | 527 | 1.54 | 3.88 | 5.82 |
| 2 | 49 | 29.0 | R 70 | 98 | 430 | 1.88 | 4.00 | 5.82 |
| | | | L 332 | 296 | 598 | 1.66 | 3.76 | 5.56 |
| 3 | 65 | 32.3 | R 148 | 31 | 348 | 1.60 | 3.84 | 5.86 |
| | | | L 66 | 82 | 398 | 1.60 | 4.10 | 5.92 |
| 4 | 74 | 32.7 | R 82 | 207 | 658 | 1.70 | 3.76 | 5.54 |
| | | | L 160 | 172 | 516 | 1.68 | 3.88 | 5.76 |
| 5 | 53 | 33.4 | R 133 | 246 | 586 | 1.54 | 3.46 | 5.44 |
| | | | L 203 | 117 | 656 | 1.54 | 3.60 | 5.42 |
| 6 | 57 | 46.5 | R 43 | 195 | 281 | 1.60 | 3.92 | 5.98 |
| | | | L 74 | 180 | 293 | 1.60 | 3.96 | 5.86 |
| 7 | 36 | 47.8 | R 248 | 277 | 613 | 1.60 | 3.72 | 5.50 |
| | | | L 201 | 242 | 545 | 1.68 | 3.78 | 5.56 |
| 8 | 37 | 48.0 | R 236 | 301 | 482 | 1.58 | 3.63 | 5.56 |
| | | | L 270 | 195 | 461 | 1.50 | 3.86 | 5.78 |
| 9 | 62 | 54.3 | R 86 | 371 | 629 | 1.70 | 3.82 | 5.64 |
| | | | L 180 | 289 | 438 | 1.72 | 3.92 | 5.72 |
| 10 | 59 | 58.5 | R 141 | 145 | 66 | 1.56 | 4.24 | 5.72 |
| | | | L 136 | 140 | 370 | 1.54 | 4.20 | 5.68 |
| 11 | 52 | 71.0 | R 132 | 66 | 445 | 1.60 | 3.78 | 5.66 |
| | | | L 78 | 219 | 410 | 1.66 | 3.68 | 5.62 |
| 12 | 41 | 74.1 | R 455 | 285 | 320 | 1.56 | 3.83 | 5.70 |
| | | | L 470 | 174 | 334 | 1.72 | 3.95 | 5.98 |
| Mean | 53.92 | 46.3 | R 158 | 204 | 454 | 1.63 | 3.85 | 5.60 |
| | | | L 189 | 183 | 462 | 1.62 | 3.88 | 5.72 |
| S.D. | 11.66 | 15.9 | R 112 | 102 | 177 | 0.09 | 0.19 | 0.37 |
| | | | L 120 | 71 | 109 | 0.08 | 0.17 | 0.16 |

**TABLE 7.5** Values of peak-to-peak amplitude (nV) and latency (msec) for hyperthyroid patients at 70 dBSL for right and left ears

| CASE | AGE YEARS | $FT_4$ | AMPLITUDE | | | LATENCY | | |
|---|---|---|---|---|---|---|---|---|
| | | | I | III | V | I | III | V |
| 1 | 62 | 28.2 | R 23 | 190 | 449 | 1.76 | 3.98 | 5.88 |
| | | | L 66 | 74 | 383 | 1.64 | 4.00 | 5.88 |
| 2 | 49 | 29.0 | R 80 | 86 | 227 | 1.98 | 4.22 | 6.04 |
| | | | L 179 | 262 | 508 | 1.78 | 3.80 | 5.58 |
| 3 | 65 | 32.3 | R 12 | 43 | 337 | 1.88 | 4.04 | 6.00 |
| | | | L 55 | 47 | 344 | 1.86 | 4.14 | 6.02 |
| 4 | 74 | 32.7 | R 105 | 156 | 598 | 1.82 | 3.86 | 5.72 |
| | | | L 133 | 27 | 414 | 1.86 | 4.02 | 5.98 |
| 5 | 53 | 33.4 | R 121 | 234 | 359 | 1.62 | 3.60 | 5.60 |
| | | | L 164 | 115 | 480 | 1.60 | 3.64 | 5.58 |
| 6 | 57 | 46.5 | R 35 | 39 | 238 | 1.82 | 4.08 | 6.08 |
| | | | L 70 | 170 | 275 | 1.86 | 4.16 | 6.00 |
| 7 | 36 | 47.8 | R 207 | 219 | 516 | 1.84 | 3.80 | 5.64 |
| | | | L 188 | 199 | 535 | 1.78 | 3.88 | 5.66 |
| 8 | 37 | 48.0 | R 84 | 137 | 484 | 1.80 | 3.77 | 5.66 |
| | | | L 129 | 234 | 395 | 1.66 | 4.04 | 5.82 |
| 9 | 62 | 54.3 | R 102 | 270 | 590 | 1.78 | 3.86 | 5.68 |
| | | | L 102 | 262 | 418 | 1.86 | 4.00 | 5.80 |
| 10 | 59 | 58.5 | R 125 | 86 | 109 | 1.72 | 4.44 | 6.04 |
| | | | L 130 | 90 | 360 | 1.70 | 4.30 | 5.98 |
| 11 | 52 | 71.0 | R 23 | 117 | 313 | 1.82 | 3.84 | 5.80 |
| | | | L 43 | 125 | 234 | 1.72 | 3.94 | 5.88 |
| 12 | 41 | 74.1 | R 275 | 293 | 352 | 1.72 | 3.93 | 5.87 |
| | | | L 225 | 156 | 311 | 1.86 | 4.07 | 6.09 |
| Mean | 53.92 | 46.3 | R 99 | 156 | 381 | 1.80 | 3.95 | 5.67 |
| | | | L 124 | 147 | 388 | 1.77 | 4.00 | 5.86 |
| S.D. | 11.66 | 15.9 | R 78 | 86 | 151 | 0.08 | 0.22 | 0.53 |
| | | | L 58 | 81 | 91 | 0.10 | 0.17 | 0.17 |

**TABLE 7.6** Values of peak-to-peak amplitude (nV) and latency (msec) for hyperthyroid patients at 60 dBSL for right and left ear

| CASE | AGE YEARS | $FT_4$ | INTERWAVE INTERVAL | | |
|---|---|---|---|---|---|
| | | | I - III | III - V | I - V |
| 1 | 62 | 28.2 | R 2.30 | 1.84 | 4.14 |
| | | | L 2.28 | 1.84 | 4.12 |
| 2 | 49 | 29.0 | R 2.28 | 1.80 | 4.08 |
| | | | L 2.16 | 1.80 | 3.96 |
| 3 | 65 | 32.3 | R 2.28 | 1.96 | 4.24 |
| | | | L 2.44 | 1.86 | 4.30 |
| 4 | 74 | 32.7 | R 2.14 | 1.86 | 4.00 |
| | | | L 2.24 | 1.96 | 4.20 |
| 5 | 53 | 33.4 | R 1.96 | 1.98 | 3.94 |
| | | | L 2.04 | 1.86 | 3.90 |
| 6 | 57 | 46.5 | R 2.32 | 1.86 | 4.10 |
| | | | L 2.36 | 1.74 | 4.10 |
| 7 | 36 | 47.8 | R 2.16 | 1.74 | 3.90 |
| | | | L 2.26 | 1.74 | 4.00 |
| 8 | 37 | 48.0 | R 2.07 | 1.67 | 3.94 |
| | | | L 2.34 | 1.92 | 4.28 |
| 9 | 62 | 54.3 | R 2.26 | 1.76 | 4.02 |
| | | | L 2.26 | 1.76 | 4.02 |
| 10 | 59 | 58.5 | R 2.00 | 2.14 | 4.14 |
| | | | L 2.28 | 1.88 | 4.16 |
| 11 | 52 | 71.0 | R 2.06 | 1.88 | 3.94 |
| | | | L 2.08 | 1.92 | 4.00 |
| 12 | 41 | 74.1 | R 2.23 | 1.94 | 4.17 |
| | | | L 2.33 | 2.01 | 4.34 |
| Mean | 53.92 | 46.3 | R 2.17 | 1.87 | 4.05 |
| | | | L 2.26 | 1.86 | 4.12 |
| S.D. | 11.66 | 15.9 | R 0.13 | 0.12 | 0.11 |
| | | | L 0.12 | 0.09 | 0.14 |

**TABLE 7.7** Values of peak-to-peak interwave intervals (msec) for hyperthyroid patients at 80 dBSL for right and left ears.

| CASE | AGE YEARS | $FT_4$ | INTERWAVE INTERVAL | | |
|---|---|---|---|---|---|
| | | | I - III | III - V | I - V |
| 1 | 62 | 28.2 | R 2.30 | 1.84 | 4.14 |
| | | | L 2.34 | 1.94 | 4.28 |
| 2 | 49 | 29.0 | R 2.12 | 1.82 | 3.94 |
| | | | L 2.10 | 1.80 | 3.90 |
| 3 | 65 | 32.3 | R 2.24 | 2.02 | 4.26 |
| | | | L 2.50 | 1.82 | 4.32 |
| 4 | 74 | 32.7 | R 2.06 | 1.78 | 3.84 |
| | | | L 2.20 | 1.88 | 4.08 |
| 5 | 53 | 33.4 | R 1.92 | 1.98 | 3.90 |
| | | | L 2.06 | 1.82 | 3.88 |
| 6 | 57 | 46.5 | R 2.32 | 2.06 | 4.38 |
| | | | L 2.36 | 1.90 | 4.26 |
| 7 | 36 | 47.8 | R 2.12 | 1.78 | 3.90 |
| | | | L 2.10 | 1.78 | 3.88 |
| 8 | 37 | 48.0 | R 2.05 | 1.93 | 3.99 |
| | | | L 2.36 | 1.92 | 4.28 |
| 9 | 62 | 54.3 | R 2.12 | 1.82 | 3.94 |
| | | | L 2.20 | 1.80 | 4.00 |
| 10 | 59 | 58.5 | R 1.76 | 1.48 | 4.16 |
| | | | L 1.76 | 1.50 | 4.16 |
| 11 | 52 | 71.0 | R 2.18 | 1.88 | 4.06 |
| | | | L 2.02 | 1.94 | 3.96 |
| 12 | 41 | 74.1 | R 2.27 | 1.87 | 4.14 |
| | | | L 2.23 | 2.03 | 4.26 |
| Mean | 53.92 | 46.3 | R 2.12 | 1.86 | 4.05 |
| | | | L 2.19 | 1.84 | 4.11 |
| S.D. | 11.66 | 15.9 | R 0.16 | 0.15 | 0.17 |
| | | | L 0.20 | 0.13 | 0.17 |

**TABLE 7.8** Values of peak-to-peak interwave intervals (msec) for hyperthyroid patients at 70 dBSL for right and left ears.

| CASE | AGE YEARS | $FT_4$ | INTERWAVE INTERVAL | | |
|---|---|---|---|---|---|
| | | | I - III | III - V | I - V |
| 1 | 62 | 28.2 | R 2.22 | 1.90 | 4.12 |
| | | | L 2.36 | 1.88 | 4.24 |
| 2 | 49 | 29.0 | R 2.24 | 1.82 | 4.06 |
| | | | L 2.12 | 1.78 | 3.90 |
| 3 | 65 | 32.3 | R 2.16 | 1.96 | 4.12 |
| | | | L 2.28 | 1.88 | 4.16 |
| 4 | 74 | 32.7 | R 2.04 | 1.86 | 3.90 |
| | | | L 2.16 | 1.96 | 4.12 |
| 5 | 53 | 33.4 | R 1.98 | 2.00 | 3.98 |
| | | | L 2.04 | 1.94 | 3.98 |
| 6 | 57 | 46.5 | R 2.26 | 2.00 | 4.26 |
| | | | L 2.30 | 1.84 | 4.14 |
| 7 | 36 | 47.8 | R 1.96 | 1.84 | 3.80 |
| | | | L 2.10 | 1.78 | 3.88 |
| 8 | 37 | 48.0 | R 1.97 | 1.89 | 3.66 |
| | | | L 2.38 | 1.78 | 4.16 |
| 9 | 62 | 54.3 | R 2.08 | 1.82 | 3.90 |
| | | | L 2.14 | 1.80 | 3.94 |
| 10 | 59 | 58.5 | R 2.72 | 1.60 | 4.32 |
| | | | L 2.60 | 1.68 | 4.28 |
| 11 | 52 | 71.0 | R 2.02 | 1.96 | 3.98 |
| | | | L 2.22 | 1.94 | 4.16 |
| 12 | 41 | 74.1 | R 2.21 | 1.94 | 4.15 |
| | | | L 2.21 | 2.02 | 4.23 |
| Mean | 53.92 | 46.3 | R 2.16 | 1.88 | 4.02 |
| | | | L 2.24 | 1.86 | 4.10 |
| S.D. | 11.66 | 15.9 | R 0.21 | 0.11 | 0.20 |
| | | | L 0.15 | 0.10 | 0.14 |

**TABLE 7.9** Values of peak-to-peak interwave intervals (msec) for hyperthyroid patients at 60 dBSL for right and left ears.

# CHAPTER EIGHT

# DIABETES MELLITUS

## 8.1 Introduction

Hearing impairment associated with diabetes mellitus is still contradictory even after investigating studies which involved audiological, histological and neuro-physiological tests. The investigators who studied the diabetic patients audiologically, showed wide variation in the incidence of hearing impairment ranging from 0 - 93% (see literature review section 8.2). Some of them deny effects of diabetes mellitus on the auditory system while others related this variation to the difference of methodology. There is disagreement among the authors regarding the existence of histological abnormality, secondary to diabetes mellitus, while reports have demonstrated the vascular and neuropathy involved the cochlea, auditory nerve and brainstem. There are some authors who deny these changes.

Disagreement has existed, not only among the audiological and histological workers who dealt with hearing impairment and diabetes mellitus, but also among the investigators who used the ABER technique as a tool of investigation, while some authors recorded a reduction in amplitude and an increase of absolute latencies of all waves as well as delay in the interwave interval of the major waves. There are others who did not find any difference between diabetic patients and their matching control subjects - as mentioned in the literature review.

## 8.2 Literature Review

### 8.2.1 Incidence

It is still not completely accepted that there is an association between diabetes mellitus (D.M.) and hearing impairment. Williams and Porte (1974) stated that diabetes mellitus has no direct or indirect effect on the auditory system. This statement comes after discussion on the relationship between diabetes mellitus and hearing impairment which started more than 100 years ago, when Jordao, in 1857, reported for the first time, the existence of hearing impairment in a 41 year old diabetic man, cited in Jorgensen and Buch (1961).

A lot of studies have been undertaken on diabetic patients to show if there is any effect of diabetes mellitus on hearing. The reports published so far were often conflicting. Axelsson and Fagerberg (1968) in a study of 99 diabetic patients using more than one audiological test - pure tone audiometry, speech audiometry and impedance measurements - did not find any significant hearing loss in their patients in pure tone audiometry. However they found minor but definite impairment by using speech audiometry, Bekesy audiometry and directional audiometry. Axelsson et al. (1978) in a review of 205 diabetic patients, reported occasional pure tone loss at higher frequencies with some patients. Osterhammel and Christau (1980) in a study of 61 diabetic patients below 50 years of age who suffered from diabetes mellitus for more tham 10 years duration, used conventional pure tone audiometry, speech audiometry, high frequency audiometry (up to a maximum of 20 kHz) and stapedius reflex thresholds. They found no difference between the patients and normal controls, not even in the patients with severe diabetic retinopathy. In a study of 33 diabetic patients with known diabetic retinopathy; Miller et al. (1983) could not find any abnormality in the hearing acuity in their patients in relation to the normal controls,

when they assessed them by conventional audiometry. However, they found a significant difference in hearing after they used a more subtle filtered speech audiometry. Taylor and Irwin (1978) reported in the study of 38 patients assessing only the pure tone thresholds, the existence of a significant hearing loss in the patients, compared with the normal controls. Taylor and Irwin noted that the conflicting deafness in their patients might be related to the method of investigation variation. They reported that the incidences of deafness ranged from 0 - 95% for their patients. This variation was due to varying the limits of normality. In a study of 60 diabetic patients who had been selected randomly, none of them had complained spontaneously of hearing difficulties. Marullo (personal communication, 1987) reported that 25 of those patients were suffering from hearing impairment; 19 of them had a sensorineural hearing loss, 3 conductive, and 3 patients had a mixed type of hearing loss. Sieger et al. (1983) in a study of 51 insulin dependent diabetic patients aged 8 - 21 years, using pure tone audiometry, speech audiometry and impedance measurements, found no significant difference between the patients and normal controls and between diabetic patients without complications and those with diabetic complications. Gibben and Davis (1981) made a study of 50 diabetic patients whose ages ranged from 18 - 74 years old, selected randomly from those patients who are insulin dependent and non insulin dependent. Gibben and Davis used pure tone audiometry, speech audiometry and tone decay in the evaluation of their patients. They reported that there was no significant difference between the diabetic patients and that of matching age and sex control subjects for the pure tone audiometry or speech audiometry. However they found significant incidence of tone decay in all groups of diabetics. Gibben and Davis related that to the

probability of occurence of early presbyacusis.

In 1915, Edgar (cited in Jorgensen and Buch, 1961), was the first one who performed a systematic investigation on the inner ear function in a study of 52 diabetic patients. He used the whispered and spoken voice and tuning fork tests. Edgar reported that 25 out of the 52 patients had bilateral, sensorineural deafness, mainly with high tones. After a lot of study, it is established that hearing impairment associated with diabetes mellitus is characterized by slowly progressive bilateral symmetrical, mainly sensorineural deafness and occurs mostly at higher frequencies, (Friedman et al. 1975; Jorgensen and Buch, 1961; Neetens and Verschuern 1982). These findings support the results of Edgar's work. Hearing impairment associated with diabetes mellitus might show an acute onset and be accompanied by tinnitus and dizziness, (Jorgensen 1960; Jorgensen and Buch, 1961). Friedman et al. (1975) in a study of 20 diabetic patients with peripheral neuropathy, whose ages ranged from 22 - 70 years, reported that 11 patients (55%) had hearing impairment compared with normal age matched controls. It was of a sensorineural type. This impairment was more prominent in older patients. Jorgensen and Buch (1961) in a study of 69 diabetic patients reported the occurence of hearing impairment in 28 patients. This impairment was, in most cases, bilateral, progressive and symmetrical at high frequencies and more in older patients. However, they found that the impairment had happened in an acute onset in some patients, and there was a marked difference between the two ears. In addition some of their patients showed hearing impairment, not only at higher frequencies but also at the low frequencies. Moreover, Jorgensen and Buch noticed that the hearing impairment was twice as common in diabetic patients with retinopathy than in patients without retinopathy.

Camisasca, 1950 (cited in Jorgensen and Buch, 1960), was the first to

evaluate the hearing impairment audiometrically in diabetic patients. In a study of 81 diabetic patients (29 - 75 years of age), Camisasca reported that 37 patients were suffering from sensorineural hearing loss and 9 patients from conductive hearing loss.

### 8.2.2 Pathogenesis

The pathology of hearing impairment in the case of diabetes mellitus is not yet fully understood. It is presumed that the lesion might be cochlear, retrocochlear or both. Panse (1906) and Wittmaack (1907) (cited in Jorgensen and Buch (1961)), described in histological studies on diabetic patients degeneration in the cochlea, partial absence of hair cells, degeneration of the cochlear nerve, the spiral ganglion and the organ of corti. Jorgensen (1961) in his study of the temporal bones of 32 diabetic patients demonstrated reduction of ganglion cells, thickening of the capillary walls of the basement membrane, and thickening of the wall of the stria vascularis due to precipitation of a periodic acid schiff positive (PAS). Jorgensen noticed that these changes were the same as the changes in the vessels of the retina and kidneys in long standing diabetic patients with complications. Makishima and Tanaka (1971) reported in a study of 4 diabetic temporal bones that very slight atrophy of the stria vascularis, atrophy of the spiralganglion, demyelination and beading of the myeline sheath of the auditory nerve, there was thickening and narrowing of the lumina in the small arteries in the internal auditory canal. Precipitation of PAS positive in the capillaries of the stria vascularis, as well as in the small arteries of the internal auditory canal. The precipitation of PAS positive and thickening in the capillary walls of the stria vascularis, and in the modiolus was also found by Costa (1967). Furthermore, Costa could

demonstrate the thickening of the basement membrane. Kovar (1973) described in his study of 14 diabetic patients with long standing disease, the thickening of the walls of the capillaries of the stria vascularis as well as of the vessels of the auditory nerve. Oliveira et al. (1977) in an experimental study on chinchillas with diabetes mellitus induced by streptozolocin, found narrowing, irregularity or complete closure in the capillaries of the stria vascularis.

Although a number of investigators have shown histologically the evidence of microangiopathy affecting the capillaries of the stria vascularis and other small arteries through the auditory pathway, and the evidence of neuropathy; there are some reports which deny these changes. Schuknech (1974) reported that no changes were observed in 11 sets of human temporal bones of diabetic patients, except those occurring in the small vessels which are specific for diabetes mellitus. Naufal and Schuknecht (1972) in a study of the temporal bone of a diabetic patient suffering from an attack of severe vertigo, found no abnormality except loss of vestibular neurons in the superior region of the vestibular nerve.

### 8.2.3 Auditory brainstem evoked response and diabetes mellitus

The discrepancy and contradictions present are not only between the audiological and histological studies of the effect of diabetes mellitus on hearing, but also between the workers who use the ABER technique as an investigatory tool in this sort of study. Sieger et al. (1983) in a study of 8 insulin dependent diabetes mellitus patients (IDDM) stressed only on I-V interwave interval. They reported that this was normal in comparison with normal control subjects. Verma et al. (1984) recorded ABER in 22 diabetic patients. Their ages ranged from 15 - 65 years and with the mean duration of illness of 5.8 years. No difference was found in the individual wave

latency, interpeak latencies and wave V amplitude between the patients and their matching controls. Wilson et al. (1982) have performed ABER on 5 diabetic patients with idopathic sudden hearing loss. They found that all latencies and interwave latencies were within normal limits in 4 patients who might have been tested afteer recovery with no evidence of auditory dysfunction for both ears. The evidence of a retrocochlear disorder could not be ruled out in the fifth patient.

In contrast to the previous studies there were reports which could demonstrate the abnormalities of ABER in diabetic patients. Goldsher et al. (1986) in their study of 33 IDDM patients aged between 15 - 55 years, selected from subjects who were free from ototoxicity, past history of exposure to high level of noise or previous ear diseases. Some of the patients had diabetic neuropathy and some of them did not. Goldsher et al. reported prolongation of absolute latency of all waves and this prolongation was greater with later waves, besides that they could demonstrate delayed I-V and III-V interwave intervals. The ABER abnormalities were more prominent in patients with neuropathy than the patients without neuropathy. Donald et al. (1981) in their study of ABER in diabetic patients took the age, sex and duration of diabetes into consideration. This study revealed no significant alteration in the absolute latency of wave I and II, and prolongation of latency of wave III and V and delay of the interwave interval of I-III and I-V. These results suggest that there is a delay in the brainstem conduction time and the lesion is higher than the cochlear nucleus possibility at the level of upper brainstem and midbrain. Donald et al. (1984) in the second study investigated a large number of patients and they tried to correlate ABER with age, sex and conduction velocity of some peripheral nerves. They confirmed the results of their previous work and,

in particular, the delay in wave V and I-V interwave interval. They also restate their belief that the delay was most likely to be the central auditory pathway rather than in the acoustic nerve. Khadori et al. (1986) reported in a study of 34 IDDM patients with long-standing disease that 32% had abnormal ABER. These abnormalities resembled the prolongation of absolute latency of wave V and delayed I-V interval in both males and females. Prolongation of wave III latency was only in males and delayed III-V interval only in females, and reduction of wave V amplitude in males. Khadori et al. (1986) did not find any correlation between wave latency, interwave interval and age, duration of diabetes, blood glucose or any diabetic complications. Fedele et al. (1984) investigated 30 IDDM patients aged between 15 - 41 years. They reported the prolongation of absolute latencies of all waves as well as delayed in I-V interval. Fedele and his associates reported that there is no correlation between ABER parameters and blood glucose, duration of the disease or to the presence of any diabetic complications. Harkins et al. (1985) in their study of 10 young IDDM patients using ABER and somatosensory evoked potentials reported significant prolongation of I-V, III-V and I-III intervals.

The present study is designed to evaluate two kinds of audiological battery of tests: the pure tone audiometry and brainstem evoked response audiometry, in an attempt to comapre the results of the two methods. This came after the claim of some authors that the wide variation of an incidence of hearing impairment in diabetic patients might be related to the variation of the methodological technique (Taylor and Irwin, 1978; Miller et al. 1983). Most histological studies proved the existence of pathological changes in the stria vascularis which plays an important role in the electro-physiological properties of the inner ear. Finally, after establishment by many authors, diabetes mellitus has an effect on the

central nerve responsiveness, recorded by ABER as a reduction in amplitude and prolongation of latency of some components. Other workers failed to show these abnormalities.

## 8.3 Methods

### 8.3.1 Subjects

Thirteen patients with type 1-insulin dependent diabetes mellitus were selected for this study from patients attending the diabetic clinic for routine checks at the Royal South Hants Hospital. A general, medical and otological history of each individual was obtained. The patients were selected according to the following criteria: diabetic by WHO criteria; their ages were within the same range as the normal matching controls; none of the female patients were pregnant; and they were audiologically and neurologically free, that is to say no past history of ear disease, head injury, exposure to high noise level and no past history of diseases or taking drugs known to have an effect on the central nervous system.

The age of the patients ranged from 24 - 72 years (mean 42.7 ± 17.5) Seven were males aged between 25 - 72 (mean 45 ± 21) and six were females aged between 28 - 66 (mean 41 ± 15). The known duration of diabetes mellitus ranged from 1 - 26 years (mean 11.80 ± 8.60). Glycocylated haemoglobin (Hb A1c) measurements were 6.8% - 11.9% (mean 9.3 ± 1.6%; normal range 5.2 - 7.3%). Some patients presented with complications, see Table 8.12. An audiological test battery, including air and bone conduction thresholds and a tone decay test was performed for both right and left ears, prior to ABER recording.

### 8.3.2 Instrumentation

An Amplaid Mk5 evoked potential signal processor was used as a click and white noise generator. The ABERs were assessed at 80, 70 and 60 dBSL. Clicks of alternating polarity, i.e. condensation and rarefaction were presented at a rate of 21 per second via TDH-49 headphones. The band pass was between 100 and 2000 Hz and presented monaurally to the test ear. The white noise which was used as masking was delivered to the contralateral ear at an intensity of 20 dBnHL less than that of the click intensity to the test ear. The clicks and white noise were transmitted to the ear of the patient, who was lying on a bed beside the equipment, through shielded TDH-49 earphones in the non shielded sound room. The instrumentation was described in detail (see sections 4.1, 4.1.1 and 4.1.2).

### 8.3.3 Electrode attachment

The ABERs were recorded from vertex as reference, ipsilateral mastoid as active and from the forehead just below the hair line as a ground. The sort of electrodes, the procedure of electrode attachment were described in detail in section 4.2.1.

### 8.3.4 Recording of ABER

Each patient has attended one recording session of about 1 1/2 - 2 hours duration. The session started with detailed general history, family history, past and present history and otologic history. Then the pulse, temperature and blood pressure were recorded. Following otoscopic examination for both ears, the patient then lay on a bed beside the equipment to start the recording with the same procedure which was described earlier in section 4.3. Each intensity recording was repeated twice and the average was taken.

## 8.4 Results

Auditory brainstem evoked responses were recorded in 13 insulin dependent diabetes mellitus (IDDM) patients who were proved, by specialists at the Royal South Hants Hospital, to be diabetic by clinical and metabolic examinations.

From Table 8.1 a typical hearing loss associated with diabetes mellitus, which was described in the literature to be bilateral, symmetrical, sensorineural and with high frequencies was not found in all patients who had a hearing impairment. In this study it was found to be bilateral, symmetrical, sensorineural but just with low frequencies in patients 2 and 9 and with low and high frequencies in patients 10 and 12 and just in high frequencies in patient 13. It was in all frequencies in patient 11 and the hearing was normal in the rest of the patients (7 patients), see Table 8.1.

Figure 8.1 shows ABER of all patients at 80, 70 and 60 dBSL (above the subject threshold) no gross morphological differences were observed between the two ears in any individual. Some patients showed peaks the same as in the normal control subjects. However, some specific peaks could not be easily identified in some patients, particularly the old ones. This reflected the difference in the value of absolute latency and amplitude of the ABER components and subsequently the interwave intervals between the patients themselves on the one hand and between those patients and normal controls on the other hand.

The value of an individual's latency, amplitude and interwave intervals with the mean and standard deviation of tracings of all patients are presented in Tables 8.6, 8.7, 8.8, 8.9, 8.10 and 8.11 and measured in m.sec and nanovolt respectively.

T-test analysis applied to the ABER parameters (amplitude, latency and interwave intervals of patients) gave high significance ($p < 5\%$) as shown in Table 8.4. This significant difference was with wave III and V as well as with the I-V interwave interval. However no significant difference was found in wave I and I-III and III-V interwave intervals except in some patients who showed significant prolongation of latency and reduction of amplitude of wave I.

The female patients showed shorter latencies and higher amplitude of all waves than that of male patients. By analysis the effect of sex on these results there was no significant difference between males and females.

## 8.5 Discussion

This experimental study was undertaken to assess the auditory brainstem evoked response (ABER) technique as a diagnostic tool in an accurate and easy diagnosis, and in an attempt to detect any complications in patients suffering from diabetes mellitus. This aim had arisen from results of the relevant researchers who have dealt with studying the hearing impairment associated with diabetes mellitus and from other researchers who proved the usefulness and reliability of ABER as a non invasive and very sensitive technique to the changes of the auditory system function. Diabetic patients are known to have abnormalities of the central auditory system. These abnormalities were recorded by some investigators as changes in parameters of some components of ABER and an increase of interwave intervals of these components (Donald et al. 1981; Donald et al. 1984; Goldsher et al. 1986; Khardoni et al. 1986; Harkins et al. 19885; Fedele et al. 1984). However some other investigators failed to demonstrate any differences between their diabetic patients and their matching controls using the ABER (Verma et al. 1984; Sieger et al. 1983; Wilson et al.

1982).

Thirteen diabetic patients including both male and female and with diffferent durations were studied. Some of them have had diabetic complications and some not. All patients were chosen to be free from exposure to high level noise or to any local or systemic diseases or medications which might have an effect on hearing. The results of ABER obtained from these patients revealed that there is a prolongation in the absolute latency of wave III and V as well as reduction in their amplitude in comparison with normal control subjects. There is no significant difference in the absolute latency and amplitude of wave I. There is also a delay in the I-V interwave interval. These findings would be suggestive of the evidence of normal peripheral auditory conduction times and a delay in the central conduction time. This delay is most probably at the inferior collicular level and medially (Starr and Achor, 1975; Stockard and Rossiter, 1977). The interwave interval varies with structural and physiological disorders of the auditory pathway of the brainstem (Jones et al. 1974; Starr and Hamilton, 1976; Thornton and Hawks, 1976; Stockard and Rossiter, 1977).

From Table 8.4 there is a significant prolongation of the latency ($p < 0.05$) and a reduction in amplitude ($p < 0.01$) of wave I as well as a delay in I-V interval, which means that the delay implicated the peripheral and central auditory pathway in the same time (for patients 11 and 13).

From Tables 8.2 and 8.3 females had a shorter latency of wave I and V than males. However, the difference between the two did not reach the significant level. The absence of a significant effect of sex in the result of this study rules out the findings of Rosenhamer et al. (1980); Beagly and Sheldrake (1978) and Michalewski et al. (1980) who reported shorter

latencies for wave V in females.

The findings of this study revealed that the abnormality of ABER as well as the pure tone audiometry have happened only with patients with retinopathy, nephropathy and neuropathy, although some other patients had long-standing diabetes mellitus without any complications, those patients did not show any abnormality. The diabetic complications, i.e. retinopathy, nephropathy and neuropathy have attributed to the diabetic angiopathy in these organs (Naufal and Schuknecht, 1972; Miller et al. 1983). This was in agreement with the findings of Goldsher et al. (1986) who found that the incidence of the abnormalities of ABER were more in diabetic patients with neuropathy more than in patients without neuropathy. Also in agreement with Khardori et al. (1986) and Fedele et al. (1984) who were not related to the duration of diabetes mellitus. Jorgensen and Buch (1961) reported that there was a correlation between the presence of retinopathy and the hearing impairment in their diabetic patients.

How can one explain the pathophysiological changes which were found in this study as well as with other studies and not relate them to the effect of age or sex? In fact it is not possible to find one thing to explain the mechanism of these changes. However in the light of the results of this study, that is to say the presence of ABER abnormalities of Wave III, Wave V and of I-V interval only in patients with diabetic complications, these complications were attributed to the micro-angiopathy which takes place in these organs (Naufal and Schrnecht, 1972; Miller et al. 1983). The ABER neuropathy which is responsible for hearing abnormality in diabetic patients should be attributed to the diabetic angiopathy in this area as suggested by Goldsher et al. (1986).

Angiopathy is a common phenomenon in diabetic patients. It is characterized by the thickening of the basement membrane and narrowing of

the lumen of the affected capillaries and small vessels. It occurs in the small arteries and capillaries of the skin, muscles, kidney, retina and peripheral nerves. It was observed in the internal auditory artery (Makishima and Tanaka, 1971). Most histo-pathological reports are in agreement that the abnormal changes in the auditory pathway in diabetic patients are primarily due to the effect of diabetes mellitus on the vascular system. However, Friedman et al. (1975) believe that the neuropathy is the primary lesion to the hearing impairment associated with diabetes mellitus. They do not rule out the cochlear mechanism as a factor for hearing impairment. Makishima and Tanaka (1971) in their study of temporal bones and the central auditory pathway of diabetic patients found that the hearing impairment in those patients might be due to neural degeneration and the vascular lesion might be the most important factor in causing this degeneration.

The diabetic angiopathy is an essential factor in causing hearing impairment. Sieger et al. (1983) failed to demonstrate any hearing abnormality in their 51 patients because none of those patients had advanced forms of micro-angiopathic complications. Marshak (1972) induced diabetes mellitus in experimental animals. He measured the evoked potential of endolymphatic and cochlear microphonic as an index of the function of stria vascularis and the hair cells activity respectively. He found that the function of the inner ear of these animals was normal. Marshak was unable to demonstrate any vascular changes. Marshak himself concluded that the absence of angiopathy in these animals might explain these normal results.

The histopathological studies have shown the presence of micro-vascular lesions in the inner ear as well as in the brainstem auditory pathway (Makishima and Tanaka, 1971; Kam-Hansen and Sorensen, 1978). The question

is why the retrocochlear manifestations are more prominent than that of cochlear ones? It is right to say the answer to this question that Axelson and Fagerberg (1968) have suggested, is that the brain tissues are more susceptible to an anoxia resulting from diabetic angiopathy, than that of the cochlea.

In conclusion the results of this experiment detect that the reduction of the amplitude and prolongation of the latency of some components of the ABER as well as the increase of the interwave interval of I-V proved to be the most reliable effect of diabetes mellitus on the auditory system. The involvement of the peripheral auditory system is not ruled out, as shown in some patients in this study. The retro-cochlear manifestations are more predominant than the cochlear ones. In this study the ABER abnormalities have appeared only in diabetic patients with complications. This might mean that the recording of significant changes in the ABER in any diabetic patient is a good indicative sign of the presence of diabetic complications. The main cause of cochlear hearing impairment in the case of diabetic patients is the angiopathy, i.e. the micro-vascular lesion in the inner ear which was found by a lot of workers. This vascular lesion could have an effect on hearing either by direct effect or by diminution of blood supply to the cochlea. The main cause of retro-cochlear impairment might be due to the neuropathy which is caused by atrophy of the spiral ganglion, demyelination and beading of the myelin sheath of the auditory nerve as well as the neuronal degeneration due to vascular lesions which were found by Makishima and Tanaka (1971) and Kovar (1973).

Further investigation of large numbers of diabetic patients with angiopathic complications is needed to evaluate the possible association between the angiopathic complications and auditory dysfunctions. This study should include more sensitive and accurate measurements of the presence of

the angiopathic complications such as fluorescein angiopathy. Furthermore, consideration should be given to matching those patients with the same age, sex and illness duration but without angiopathic complications.

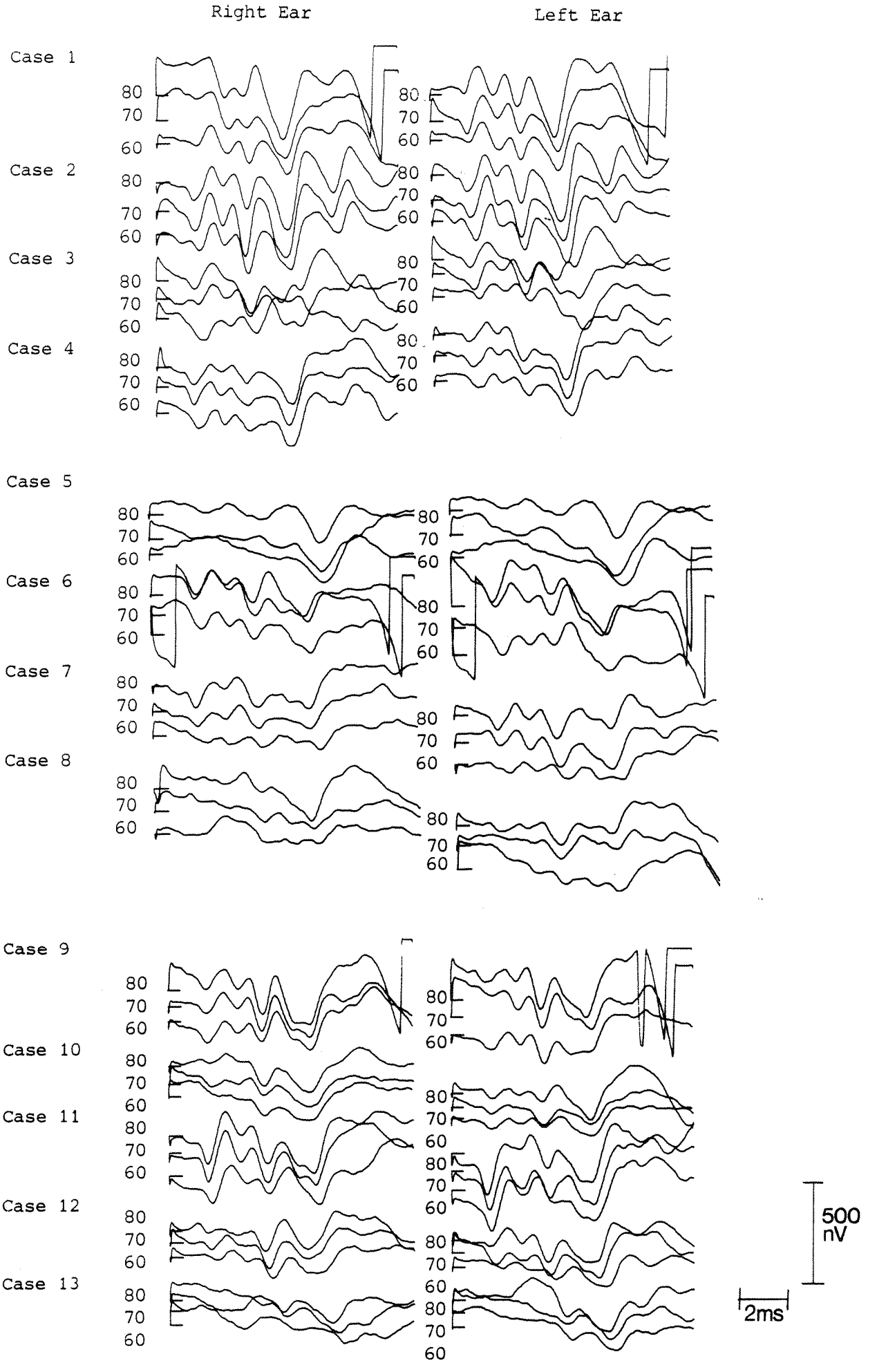


Figure 8.1 Responses of Diabetes Mellitus patients at intensities of 80, 70 and 60 dBSL for both right and left ears.

| Subject | Age Years | | 250 Hz | 500 Hz | 1000 Hz | 2000 Hz | 3000 Hz | 4000 Hz | 8000 Hz |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 25 | R | 25 | 25 | 10 | 15 | 5 | 10 | 10 |
| | | L | 25 | 25 | 15 | 5 | 10 | 10 | 5 |
| 2 | 26 | R | 45 | 30 | 20 | 20 | 20 | 20 | 20 |
| | | L | 35 | 30 | 20 | 20 | 20 | 20 | 25 |
| 3 | 26 | R | 10 | 15 | 10 | 5 | 15 | 10 | 15 |
| | | L | 15 | 10 | 15 | 10 | 20 | 0 | 10 |
| 4 | 28 | R | 20 | 20 | 5 | 20 | 15 | 25 | 15 |
| | | L | 15 | 20 | 10 | 25 | 25 | 25 | 15 |
| 5 | 31 | R | 20 | 15 | 10 | 5 | 15 | 10 | 20 |
| | | L | 20 | 20 | 10 | 5 | 10 | 10 | 10 |
| 6 | 34 | R | 30 | 25 | 15 | 5 | 15 | 10 | 10 |
| | | L | 30 | 30 | 20 | 10 | 15 | 15 | 5 |
| 7 | 35 | R | 5 | 10 | 5 | 10 | 10 | 0 | 10 |
| | | L | 10 | 15 | 10 | 10 | 10 | 0 | 10 |
| 8 | 38 | R | 15 | 20 | 30 | 10 | 10 | 5 | 15 |
| | | L | 15 | 20 | 20 | 10 | 5 | 10 | 15 |
| 9 | 50 | R | 40 | 40 | 25 | 20 | 15 | 15 | 20 |
| | | L | 30 | 30 | 15 | 20 | 20 | 20 | 30 |
| 10 | 56 | R | 25 | 20 | 10 | 20 | 25 | 30 | 55 |
| | | L | 35 | 30 | 15 | 15 | 25 | 35 | 65 |
| 11 | 66 | R | 30 | 40 | 30 | 45 | 60 | 70 | -- |
| | | L | 35 | 30 | 40 | 40 | 70 | 65 | 70 |
| 12 | 68 | R | 20 | 20 | 25 | 5 | 15 | 15 | 40 |
| | | L | 35 | 30 | 25 | 15 | 35 | 35 | 60 |
| 13 | 72 | R | 25 | 30 | 30 | 25 | 55 | 80 | -- |
| | | L | 20 | 20 | 20 | 15 | 55 | 80 | -- |

TABLE 8.1 Pure tone audiograms of diabetes mellitus patients. Threshold in dB (ISO).

| PARAMETERS | | 60 dB SL | | 70 dB SL | | 80 dB SL | |
|---|---|---|---|---|---|---|---|
| | Mean S.D. | Male | Female | Male | Female | Male | Female |
| AMPLITUDE | | | | | | | |
| I | Mean | 62 | 115 | 88 | 128 | 121 | 146 |
| | S.D. | 56 | 73 | 73 | 80 | 88 | 90 |
| III | Mean | 118 | 102 | 164 | 138 | 161 | 181 |
| | S.D. | 58 | 80 | 82 | 77 | 80 | 82 |
| V | Mean | 184 | 208 | 226 | 258 | 284 | 329 |
| | S.D. | 62 | 72 | 100 | 81 | 117 | 107 |
| LATENCY | | | | | | | |
| I | Mean | 1.87 | 1.86 | 1.73 | 1.73 | 1.63 | 1.64 |
| | S.D. | 0.10 | 0.20 | 0.13 | 0.18 | 0.13 | 0.15 |
| III | Mean | 4.20 | 4.12 | 4.06 | 4.03 | 3.97 | 3.89 |
| | S.D. | 0.30 | 0.33 | 0.32 | 0.32 | 0.32 | 0.23 |
| V | Mean | 6.22 | 6.04 | 6.03 | 5.90 | 5.82 | 5.78 |
| | S.D. | 0.26 | 0.44 | 0.25 | 0.39 | 0.42 | 0.37 |
| INTERWAVE INTERVAL I - III | Mean | 2.33 | 2.25 | 2.33 | 2.30 | 2.38 | 2.25 |
| | S.D. | 0.23 | 0.18 | 0.22 | 0.19 | 0.22 | 0.14 |
| III - V | Mean | 2.02 | 1.93 | 1.97 | 1.88 | 1.95 | 1.89 |
| | S.D. | 0.17 | 0.14 | 0.12 | 0.11 | 0.10 | 0.17 |
| I - V | Mean | 4.35 | 4.19 | 4.40 | 4.17 | 4.28 | 4.14 |
| | S.D. | 0.20 | 0.27 | 0.23 | 0.27 | 0.16 | 0.26 |

TABLE 8.2 Mean values and standard deviation of peak-to-peak amplitude (nV), latency (msec) and interwave intervals (msec) of male and female diabetes mellitus patients at 80, 70 and 60 dBSL for right ears.

| PARAMETERS | | 60 dB SL | | 70 dB SL | | 80 dB SL | |
|---|---|---|---|---|---|---|---|
| | Mean<br>S.D. | Male | Female | Male | Female | Male | Female |
| AMPLITUDE | | | | | | | |
| I | Mean | 70 | 123 | 95 | 185 | 110 | 200 |
| | S.D. | 65 | 63 | 79 | 101 | 78 | 97 |
| III | Mean | 135 | 152 | 191 | 173 | 222 | 192 |
| | S.D. | 79 | 88 | 107 | 92 | 106 | 93 |
| V | Mean | 203 | 240 | 241 | 321 | 298 | 345 |
| | S.D. | 91 | 73 | 93 | 55 | 102 | 104 |
| LATENCY | | | | | | | |
| I | Mean | 1.85 | 1.87 | 1.72 | 1.75 | 1.61 | 1.63 |
| | S.D. | 0.10 | 0.18 | 0.06 | 0.14 | 0.05 | 0.13 |
| III | Mean | 4.20 | 4.10 | 4.08 | 4.03 | 3.98 | 3.87 |
| | S.D. | 0.32 | 0.31 | 0.33 | 0.28 | 0.33 | 0.21 |
| V | Mean | 6.26 | 6.07 | 6.10 | 5.92 | 5.99 | 5.81 |
| | S.D. | 0.33 | 0.41 | 0.34 | 0.37 | 0.34 | 0.37 |
| INTERWAVE INTERVAL I - III | Mean | 2.35 | 2.23 | 2.36 | 2.28 | 2.36 | 2.24 |
| | S.D. | 0.30 | 0.15 | 0.30 | 0.17 | 0.29 | 0.13 |
| III - V | Mean | 2.06 | 1.97 | 2.03 | 1.89 | 2.01 | 1.94 |
| | S.D. | 0.08 | 0.14 | 0.05 | 0.12 | 0.04 | (0.18 |
| I - V | Mean | 4.41 | 4.20 | 4.38 | 4.17 | 4.38 | 4.18 |
| | S.D. | 0.30 | 0.27 | 0.30 | 0.25 | 0.30 | 0.26 |

TABLE 8.3 Mean values and standard deviation of peak-to-peak amplitude (nV), latency (msec) and interwave intervals (msec) of male and female diabetes mellitus patients at 80, 70 and 60 dBSL for left ears.

| PARAMETERS | 60 dB SL | | 70 dB SL | | 80 dB SL | |
|---|---|---|---|---|---|---|
| | Right | Left | Right | Left | Right | Left |
| AMPLITUDE | | | | | | |
| I | -- | -- | P < 0.05 | -- | -- | -- |
| III | P < 0.05 | -- | P < 0.001 | -- | P < 0.004 | P < 0.05 |
| V | P < 0.0008 | P < 0.003 | P < 0.008 | P < 0.005 | P < 0.001 | P < 0.0007 |
| LATENCY | | | | | | |
| I | -- | P < 0.04 | -- | -- | P < 0.01 | -- |
| III | P < 0.05 | P < 0.02 | P < 0.03 | P < 0.005 | P < 0.02 | -- |
| V | P < 0.04 | P < 0.02 | -- | P < 0.02 | P < 0.01 | P < 0.02 |
| INTER-PEAK INTERVAL | | | | | | |
| V-I | P < 0.02 | P < 0.04 | P < 0.05 | P < 0.03 | P < 0.05 | P < 0.04 |
| V-III | -- | -- | -- | -- | -- | -- |
| III-I | P < 0.02 | -- | -- | -- | -- | -- |

TABLE 8.4 Summary of sdtatistical analysis - t-test - of amplitude, latency and interwave intervals of diabetes mellitus - normal controls, where -- = not significant.

| PARAMETERS | 60 dB SL | | 70 dB SL | | 80 dB SL | |
|---|---|---|---|---|---|---|
| | Right | Left | Right | Left | Right | Left |
| AMPLITUDE<br>I | 86 | 95 | 107 | 137 | 132 | 151 |
| III | 111 | 143 | 152 | 182 | 171 | 208 |
| V | 195 | 220 | 241 | 276 | 305 | 319 |
| LATENCY<br>I | 1.87 | 1.86 | 173 | 173 | 1.64 | 1.62 |
| III | 4.16 | 4.23 | 4.04 | 4.06 | 3.88 | 3.92 |
| V | 6.14 | 6.17 | 5.97 | 5.97 | 5.80 | 5.90 |
| INTER-PEAK INTERVAL<br>V-I | 4.28 | 4.32 | 4.30 | 4.28 | 4.21 | 4.29 |
| V-III | 1.98 | 2.02 | 1.93 | 1.96 | 1.92 | 1.98 |
| III-I | 2.30 | 2.28 | 2.31 | 2.32 | 2.30 | 2.31 |

TABLE 8.5 Mean values of peak-to-peak amplitude (nV), latency (msec) and interwave intervals (msec) of diabetes mellitus patients for right and left ears at 80, 70 and 60 dBSL.

| CASE | AGE YEARS | AMPLITUDE | | | LATENCY | | |
|---|---|---|---|---|---|---|---|
| | | I | III | V | I | III | V |
| 1 | 25 | R 261 | 212 | 373 | 1.50 | 3.88 | 5.42 |
| | | L 253 | 260 | 390 | 1.56 | 3.94 | 6.00 |
| 2 | 26 | R 175 | 101 | 273 | 1.62 | 3.94 | 5.84 |
| | | L 164 | 234 | 230 | 1.64 | 3.88 | 5.94 |
| 3 | 26 | R 98 | 305 | 500 | 1.56 | 3.70 | 5.00 |
| | | L 115 | 380 | 438 | 1.58 | 3.76 | 5.70 |
| 4 | 28 | R 216 | 270 | 397 | 1.66 | 3.76 | 5.52 |
| | | L 251 | 313 | 398 | 1.62 | 3.74 | 5.56 |
| 5 | 31 | R 199 | 102 | 322 | 1.58 | 3.74 | 5.72 |
| | | L 171 | 114 | 318 | 1.64 | 3.74 | 5.82 |
| 6 | 34 | R 58 | 281 | 346 | 1.54 | 3.68 | 5.46 |
| | | L 222 | 289 | 399 | 1.52 | 3.70 | 5.40 |
| 7 | 35 | R 237 | 195 | 486 | 1.50 | 3.90 | 5.76 |
| | | L 250 | 207 | 488 | 1.52 | 3.92 | 5.84 |
| 8 | 38 | R 172 | 142 | 187 | 1.62 | 3.86 | 5.94 |
| | | L 50 | 305 | 370 | 1.58 | 3.84 | 5.84 |
| 9 | 50 | R 150 | 144 | 218 | 1.64 | 3.96 | 5.72 |
| | | L 286 | 136 | 257 | 1.60 | 3.86 | 5.76 |
| 10 | 57 | R 29 | 62 | 269 | 1.60 | 4.00 | 5.92 |
| | | L 42 | 77 | 251 | 1.62 | 3.96 | 5.96 |
| 11 | 66 | R 16 | 94 | 204 | 1.92 | 4.32 | 6.50 |
| | | L 18 | 91 | 207 | 1.88 | 4.27 | 6.47 |
| 12 | 68 | R 94 | 176 | 220 | 1.60 | 3.72 | 5.70 |
| | | L 101 | 183 | 251 | 1.62 | 3.76 | 5.78 |
| 13 | 72 | R 15 | 132 | 165 | 1.90 | 4.66 | 6.42 |
| | | L 42 | 117 | 156 | 1.70 | 4.70 | 6.72 |
| Mean | 42.7 | R 132 | 170 | 305 | 1.64 | 3.93 | 5.80 |
| | | L 151 | 208 | 319 | 1.62 | 3.92 | 5.90 |
| S.D. | 17.5 | R 86 | 78 | 111 | 0.13 | 0.27 | 0.38 |
| | | L 96 | 97 | 101 | 0.09 | 0.27 | 0.34 |

TABLE 8.6 Values of peak-to-peak amplitude (nV) and latency (msec) for diabetes mellitus patients at 80 dBSL for right and left ears.

| CASE | AGE / EARS | AMPLITUDE | | | LATENCY | | |
|---|---|---|---|---|---|---|---|
| | | I | III | V | I | III | V |
| 1 | 25 | R 226 | 195 | 347 | 1.60 | 3.94 | 6.00 |
| | | L 248 | 241 | 277 | 1.68 | 4.04 | 6.12 |
| 2 | 26 | R 91 | 99 | 266 | 1.70 | 4.02 | 6.08 |
| | | L 121 | 191 | 227 | 1.74 | 4.00 | 6.06 |
| 3 | 26 | R 89 | 299 | 368 | 1.64 | 3.78 | 5.68 |
| | | L 110 | 359 | 407 | 1.64 | 3.82 | 5.76 |
| 4 | 28 | R 198 | 266 | 290 | 1.74 | 3.86 | 5.60 |
| | | L 298 | 273 | 312 | 1.72 | 3.86 | 5.62 |
| 5 | 31 | R 171 | 61 | 310 | 1.66 | 3.86 | 5.88 |
| | | L 151 | 74 | 372 | 1.78 | 3.92 | 5.92 |
| 6 | 34 | R 54 | 109 | 294 | 1.66 | 3.74 | 5.52 |
| | | L 172 | 199 | 329 | 1.64 | 3.84 | 5.56 |
| 7 | 35 | R 207 | 180 | 327 | 1.54 | 3.98 | 5.84 |
| | | L 211 | 280 | 390 | 1.64 | 4.02 | 5.94 |
| 8 | 38 | R 121 | 219 | 140 | 1.72 | 4.00 | 6.08 |
| | | L 43 | 273 | 250 | 1.70 | 3.98 | 5.98 |
| 9 | 50 | R 127 | 143 | 214 | 1.70 | 4.08 | 5.96 |
| | | L 266 | 132 | 242 | 1.70 | 3.96 | 5.88 |
| 10 | 57 | R 20 | 53 | 161 | 1.74 | 4.16 | 6.06 |
| | | L 31 | 69 | 231 | 1.80 | 4.08 | 6.12 |
| 11 | 66 | R 11 | 68 | 114 | 2.08 | 4.64 | 6.62 |
| | | L 14 | 78 | 281 | 2.02 | 4.59 | 6.59 |
| 12 | 68 | R 63 | 160 | 158 | 1.72 | 3.78 | 5.80 |
| | | L 93 | 129 | 195 | 1.70 | 3.82 | 5.88 |
| 13 | 72 | R 8 | 121 | 140 | 1.99 | 4.73 | 6.48 |
| | | L 17 | 78 | 97 | 1.78 | 4.79 | 6.81 |
| Mean | 42.7 | R 107 | 152 | 241 | 1.73 | 4.04 | 5.97 |
| | | L 137 | 182 | 278 | 1.73 | 2.83 | 6.02 |
| S.D. | 17.5 | R 76 | 78 | 89 | 0.15 | 0.31 | 0.32 |
| | | L 98 | 96 | 86 | 0.10 | 1.29 | 0.35 |

TABLE 8.7 Values of peak-to-peak amplitude (nV) and latency (msec) for diabetes mellitus patients at 70 dBSL for right and left ears.

| CASE | AGE | | AMPLITUDE | | | LATENCY | | |
|---|---|---|---|---|---|---|---|---|
| | YEARS | | I | III | V | I | III | V |
| 1 | 25 | R | 171 | 104 | 205 | 1.76 | 4.16 | 6.34 |
| | | L | 202 | 171 | 252 | 1.80 | 4.16 | 6.30 |
| 2 | 26 | R | 30 | 83 | 171 | 1.84 | 4.22 | 6.24 |
| | | L | 62 | 105 | 203 | 2.00 | 4.24 | 6.28 |
| 3 | 26 | R | 83 | 218 | 273 | 1.78 | 3.88 | 5.82 |
| | | L | 97 | 250 | 367 | 1.72 | 3.92 | 5.82 |
| 4 | 28 | R | 177 | 257 | 288 | 1.78 | 3.88 | 5.68 |
| | | L | 176 | 191 | 301 | 1.86 | 3.94 | 5.76 |
| 5 | 31 | R | 152 | 38 | 196 | 1.86 | 3.92 | 6.00 |
| | | L | 96 | 52 | 236 | 1.82 | 4.02 | 6.08 |
| 6 | 34 | R | 50 | 99 | 288 | 1.72 | 3.87 | 5.63 |
| | | L | 167 | 218 | 300 | 1.68 | 3.84 | 5.60 |
| 7 | 35 | R | 190 | 74 | 216 | 1.68 | 4.08 | 6.00 |
| | | L | 128 | 266 | 297 | 1.74 | 4.04 | 6.08 |
| 8 | 38 | R | 70 | 150 | 250 | 1.94 | 4.16 | 6.42 |
| | | L | 38 | 212 | 187 | 1.82 | 4.14 | 6.28 |
| 9 | 50 | R | 112 | 93 | 111 | 1.90 | 4.20 | 6.14 |
| | | L | 160 | 130 | 136 | 1.90 | 4.04 | 6.10 |
| 10 | 57 | R | 18 | 48 | 150 | 1.86 | 4.32 | 6.24 |
| | | L | 14 | 43 | 166 | 1.98 | 4.20 | 6.30 |
| 11 | 66 | R | 6 | 48 | 148 | 2.24 | 4.74 | 6.84 |
| | | L | 10 | 56 | 168 | 2.20 | 4.70 | 6.80 |
| 12 | 68 | R | 55 | 148 | 115 | 1.84 | 3.90 | 5.94 |
| | | L | 65 | 113 | 177 | 1.78 | 3.90 | 5.98 |
| 13 | 72 | R | 6 | 76 | 121 | 2.06 | 4.78 | 6.54 |
| | | L | 13 | 52 | 68 | 1.85 | 4.86 | 6.87 |
| Mean | 42.7 | R | 86 | 110 | 195 | 1.87 | 4.16 | 6.14 |
| | | L | 94 | 143 | 220 | 1.85 | 4.23 | 6.17 |
| S.D. | 17.5 | R | 67 | 66 | 65 | 0.15 | 0.31 | 0.35 |
| | | L | 67 | 80 | 82 | 0.14 | 0.34 | 0.36 |

TABLE 8.8 Values of peak-to-peak amplitude (nV) and latency (msec) for diabetes mellitus patients at 60 dBSL for right and left ears.

| CASE | AGE | | INTERWAVE INTERVAL | | |
|---|---|---|---|---|---|
| | YEARS | | I - III | III - V | I - V |
| 1 | 25 | R | 2.38 | 2.04 | 4.42 |
| | | L | 2.38 | 2.06 | 4.44 |
| 2 | 26 | R | 2.32 | 1.90 | 4.22 |
| | | L | 2.24 | 2.06 | 4.30 |
| 3 | 26 | R | 2.14 | 1.94 | 4.08 |
| | | L | 2.18 | 1.94 | 4.12 |
| 4 | 28 | R | 2.10 | 1.76 | 3.86 |
| | | L | 2.12 | 1.82 | 3.94 |
| 5 | 31 | R | 2.16 | 1.98 | 4.14 |
| | | L | 2.10 | 2.08 | 4.18 |
| 6 | 34 | R | 2.14 | 1.78 | 3.92 |
| | | L | 2.18 | 1.70 | 3.88 |
| 7 | 35 | R | 2.40 | 1.86 | 4.26 |
| | | L | 2.40 | 1.92 | 4.32 |
| 8 | 38 | R | 2.24 | 2.08 | 4.32 |
| | | L | 2.26 | 2.00 | 4.26 |
| 9 | 50 | R | 2.32 | 1.76 | 4.08 |
| | | L | 2.26 | 1.90 | 4.16 |
| 10 | 57 | R | 2.40 | 1.92 | 4.32 |
| | | L | 2.34 | 2.00 | 4.34 |
| 11 | 66 | R | 2.40 | 2.18 | 4.58 |
| | | L | 2.39 | 2.20 | 4.59 |
| 12 | 68 | R | 2.12 | 1.98 | 4.10 |
| | | L | 2.14 | 2.02 | 4.16 |
| 13 | 72 | R | 2.76 | 1.76 | 4.52 |
| | | L | 3.00 | 2.02 | 5.02 |
| Mean | 42.7 | R | 2.30 | 1.92 | 4.22 |
| | | L | 2.30 | 1.97 | 4.28 |
| S.D. | 17.5 | R | 0.18 | 0.14 | 0.22 |
| | | L | 0.23 | 0.12 | 0.29 |

**TABLE 8.9** Values of peak-to-peak interwave intervals (msec) for diabetes mellitus patients at 80 dBSL for right and left ears.

| CASE | AGE YEARS | | INTERWAVE INTERVAL | | |
|---|---|---|---|---|---|
| | | | I - III | III - V | I - V |
| 1 | 25 | R | 2.34 | 2.06 | 4.40 |
| | | L | 2.36 | 2.08 | 4.44 |
| 2 | 26 | R | 2.32 | 2.06 | 4.38 |
| | | L | 2.26 | 2.06 | 4.32 |
| 3 | 26 | R | 2.14 | 1.90 | 4.04 |
| | | L | 2.18 | 1.94 | 4.12 |
| 4 | 28 | R | 2.12 | 1.74 | 3.86 |
| | | L | 2.14 | 1.76 | 3.90 |
| 5 | 31 | R | 2.20 | 2.02 | 4.22 |
| | | L | 2.14 | 2.00 | 4.14 |
| 6 | 34 | R | 2.08 | 1.78 | 3.86 |
| | | L | 2.20 | 1.72 | 3.92 |
| 7 | 35 | R | 2.44 | 1.86 | 4.30 |
| | | L | 2.38 | 1.92 | 4.30 |
| 8 | 38 | R | 2.28 | 2.08 | 4.36 |
| | | L | 2.28 | 2.00 | 4.28 |
| 9 | 50 | R | 2.38 | 1.88 | 4.26 |
| | | L | 2.26 | 1.92 | 4.18 |
| 10 | 57 | R | 2.42 | 1.90 | 4.32 |
| | | L | 2.28 | 2.04 | 4.32 |
| 11 | 66 | R | 2.56 | 1.98 | 4.54 |
| | | L | 2.57 | 2.00 | 4.57 |
| 12 | 68 | R | 2.06 | 2.02 | 4.80 |
| | | L | 2.12 | 2.06 | 4.18 |
| 13 | 72 | R | 2.74 | 1.75 | 4.49 |
| | | L | 3.01 | 2.02 | 5.03 |
| Mean | 42.7 | R | 2.31 | 1.93 | 4.29 |
| | | L | 2.32 | 1.96 | 4.28 |
| S.D. | 17.5 | R | 0.20 | 0.12 | 0.26 |
| | | L | 0.24 | 0.11 | 0.29 |

TABLE 8.10 Values of peak-to-peak interwave intervals (msec) for diabetes mellitus patients at 70 dBSL for right and left ears.

| CASE | AGE | | INTERWAVE INTERVAL | | |
|---|---|---|---|---|---|
| | YEARS | | I - III | III - V | I - V |
| 1 | 25 | R | 2.40 | 2.18 | 4.58 |
| | | L | 2.36 | 2.14 | 4.50 |
| 2 | 26 | R | 2.38 | 2.02 | 4.40 |
| | | L | 2.24 | 2.04 | 4.28 |
| 3 | 26 | R | 2.10 | 1.94 | 4.04 |
| | | L | 2.20 | 1.90 | 4.10 |
| 4 | 28 | R | 2.10 | 1.80 | 3.90 |
| | | L | 2.08 | 1.82 | 3.90 |
| 5 | 31 | R | 2.06 | 2.08 | 4.14 |
| | | L | 2.20 | 2.06 | 4.26 |
| 6 | 34 | R | 2.15 | 1.76 | 3.91 |
| | | L | 2.16 | 1.76 | 3.92 |
| 7 | 35 | R | 2.40 | 1.92 | 4.32 |
| | | L | 2.30 | 2.04 | 4.34 |
| 8 | 38 | R | 2.22 | 2.26 | 4.48 |
| | | L | 2.32 | 2.14 | 4.46 |
| 9 | 50 | R | 2.30 | 1.94 | 4.24 |
| | | L | 2.14 | 2.06 | 4.20 |
| 10 | 57 | R | 2.46 | 1.92 | 4.38 |
| | | L | 2.22 | 2.10 | 4.32 |
| 11 | 66 | R | 2.50 | 2.10 | 4.60 |
| | | L | 2.50 | 2.10 | 4.60 |
| 12 | 68 | R | 2.06 | 2.04 | 4.10 |
| | | L | 2.12 | 2.08 | 4.20 |
| 13 | 72 | R | 2.72 | 1.76 | 4.48 |
| | | L | 3.01 | 2.01 | 5.02 |
| Mean | 42.7 | R | 2.30 | 1.98 | 4.27 |
| | | L | 2.29 | 2.01 | 4.31 |
| S.D. | 17.5 | R | 0.20 | 0.15 | 0.24 |
| | | L | 0.24 | 0.11 | 0.29 |

TABLE 8.11 Values of peak-to-peak interwave intervals (msec) for diabetes mellitus patients at 60 dBSL for right and left ears.

| Case | Age YEARS | Sex | Duration | Complication | Glycocylate Hb A1c |
|---|---|---|---|---|---|
| 1 | 25 | Male | 12 Y | Nephropathy Retinopathy | 8.8% |
| 2 | 26 | Male | 24 Y | Retinopathy | 10.1% |
| 3 | 26 | Male | 6 Y | Nephropathy Retinopathy | 8.7% |
| 4 | 28 | Female | 1 Y | — | 7.3% |
| 5 | 31 | Female | 13 Y | — | 8.1% |
| 6 | 34 | Female | 8 Y | Nephropathy | 11.9% |
| 7 | 35 | Female | 20 Y | Retinopathy | 11.4% |
| 8 | 38 | Male | 26 Y | Reinopathy | 10.0% |
| 9 | 50 | Female | 4 Y | — | 9.5% |
| 10 | 57 | Male | 4 Y | — | 8.3% |
| 11 | 66 | Female | 3 Y | Nephropathy | 11.2% |
| 12 | 68 | Male | 11 Y | Retinopathy Neuropathy Nephropathy | 9.4% |
| 13 | 72 | Male | 22 Y | Nephropathy | 6.8% |
| Mean<br>S.D. | 42.7<br>17.5 | | 11.8 Y<br>8.6 Y | | 9.3%<br>1.6% |

TABLE 8.12 Age, sex, duration, type of complication and Glycocylate Hb A1C for diabetes mellitus patients

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