INTRODUCTION

CHAPTER 1
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1. The brain functions both to perceive and to translate sensation into action. We gain information about the environment through the sensory system which transduces, transmits and processes the information about the physical world around us. There are two ways to study the living brain:

(a) the study of the regional anatomy of the living brain by means of imaging techniques,

(b) the study of physiological events i.e. the study of various sensory events that alter the activity of the brain and generate specific perceptions.

1.1 Study of Anatomy

There are three imaging techniques:

(a) computerized tomography,

(b) positron emission tomography and

(c) magnetic resonance imaging.

Each of these methods allows the structure of the human brain to be visualized in details. As a result, neural scientists can examine the brain while people think, perceive and initiate voluntary actions; and clinicians can now localise lesions of the brain with remarkable accuracy, without invasive procedures that interfere with normal function and even endanger life.

Computerized tomography allows us to explore the regional anatomy of the brain in living patients suffering from neurological disease. The CT Scan is an image of a single plane. The image produced is a computerized reconstruction of the degree to which different tissues absorb transmitted X-rays. Positron
emission tomography scanning combines CT with radioisotopic imaging and makes it possible to probe function as well as structure. A powerful application of PET scanning is the mapping of the sugar metabolism of neurons (1).

Magnetic resonance imaging explores function as does PET, but it has better resolution. This technique can distinguish different body tissues because of their individual chemical compositions.

1.2. Study of Physiology

The physiological aspect of the brain can be studied through various sensory systems, such as visual, auditory, tactile. The sensory neurons show remarkable specificity for a stimulus (1). Specificity is important for encoding within the nervous system, some of the critical attributes of sensations. The function of the cerebral cortex depends on the complex and dynamic activity of many neurons. Recordings of electrical responses from neuronal ensembles may be obtained in humans when the cortical surface is, exposed during surgery, electrocorticogram (ECOG) or even from the surface of the scalp, electroencephalogram (EEG).

Both types of recordings are based on a theory called 'volume conduction' which describes the flow of ionic current generated by nerve cells through the extracellular space under various conditions of cellular activity (2).
Potential changes recorded from the scalp, as with EEG, are generated by the summed ionic currents of many thousands of neurons located under the recording electrode. The net ionic current can be recorded as a voltage across the resistance of the extracellular space (1, 2). The EEG is a record of the extracellular current flow associated with the summed activity of the individual cells underlying the electrode. The most obvious source for these extracellular potential is the action potential, largest signal generated by neurons, (1). The synchronous activity recorded from the scalp results from extracellular current flow associated with summated postsynaptic potentials (1). The exact configuration of the gross potential is related in a complex way to the site and the sign of postsynaptic potentials (1, 2).

1.3. **Evoked Potential**

The clinically interesting potential recorded from the scalp is the sensory evoked potential. This potential is a specific change in the ongoing EEG resulting from stimulation of a sensory pathway (3, 4). Sensory evoked potentials are time-locked to the stimulus and are specific for the sensory system that evokes them (3). The study of event related potential facilitates to record the contribution of noncortical structures to the evoked potential and thereby to learn something about the role of these regions in processing stimuli; e.g. in the auditory system one can assess the contribution of each relay station.
i.e. nucleus in the auditory pathway in terms of its contribution to the recording from the scalp.

1.4. **Auditory Evoked Potential**

Development of any sensory modality can be measured and studied using an event related potential tool, such as auditory evoked potential, visual evoked potential and somatosensory evoked potential. The auditory pathway, especially may give more information regarding signal to noise processing, information modulation and lateralisation processes at different nuclei (5). Manuel Don et al (6) have stated that the major determinants of ABR morphology are:

(a) refractory periods of neural elements,
(b) changes in synaptic transmission,
(c) receptor adaptation and fatigue.

It is also possible that both a reduction in neural activity and a change in synchronization of the neurons may be responsible for the latency shift (6). Loss of hair cells may have been one of many factors contributing to the observed change in ABR morphology (7).

The generators of various peaks have been considered as the nuclei situated on the auditory pathway. The latency does not project only the status of the nuclei, since any altered event related waveform is a combination of slowing of nerve conduction velocity, selective loss of fast conductive element and alterations of synaptic efficiency (9). Any sensory system
requires a finite period of time following an adequate stimulus for full recovery of their responsiveness. If subsequent stimuli occur before recovery is completed, the system's response will be altered. The shift of latency of the brainstem response components with rapid stimulated rates is considered as a manifestation of incomplete recovery (5). Hence measurement of only latency or amplitude is not sufficient to assess the altered AEP waveform. It is essential to study:

(a) synchronization of neurons within any nuclei,
(b) relative strength of the excitatory and inhibitory input of neurons, which ultimately defines the peak.

This can be achieved with the study of amplitude, amplitude ratio, 1/2 width and area of the peak along with latency and interpeak latency. Fria, J.J. (10) has pointed out that no characteristic auditory evoked potential abnormality for specific neurologic lesions, or diseases has been documented. Hecox et al. (11) and Stockard et al. (12) have also shown that the latency function can not be the single parameter to be used to measure neurological sequelae. Stockard (12) has also demonstrated the need to use Gaussian curve fitting analysis to evaluate auditory evoked potential response. Hecox (13) has shown that asphyxia is the most common etiology resulting in abnormal amplitude ratio. Similarly it has been documented that absence of a response at a particular intensity in a premature infant may be due to conductive hearing loss, immaturity and
or pathology of cochlea and brainstem (14). Nakamura, Hajime (15) have documented that neonatal hyperbilirubinemia is associated with transient aberrations of auditory brainstem response and contribute to delayed waveform. Similarly, low birth weight and preterm cases demonstrated delayed waveform which can be attributed to high incidence of middle ear effusions and myelination status of the auditory nerve (12, 16).

Eggermont et al (17) have shown that a combination of ABR parameters provide a more reliable test rather than any one measure used in isolation; however, there are still no universally accepted normal limits for these measures.

1.5. **The objectives**

The above introduction makes it clear that there is a strong need to develop multi parameter approach to study event related potential. These parameters are (i) latency, (ii) interpeak latency (IPL), (iii) Amplitude (A), (iv) Amplitude ratio (AR), (v) 1/2 width of a peak (HW), (vi) Area (AP) of the peak.

This approach will throw a light upon:

1. Synchronization of neurons within any nucleus,
2. Relative strength of the excitatory and inhibitory input of neurons, which ultimately defines the peak.
3. Asynchronization of neurons along with slowing of transmission velocity.
The present study is focused on the auditory channel and the objective of this study is to evaluate the various neurological conditions in the high risk conditions of neonates and infants. Brainstem evoked response is being measured using Neuromatic 2000C, a microprocessor based instrument which consists of amplifiers, averagers, chart recorder, and auditory stimulator, (Please ref. to Appendix 'A') 10 control and 53 infants around six months of corrected age are tested under various pathological conditions.

1. Preterm and low birth weight,
2. hyperbilirubinemia,
3. convulsive disorders,
4. respiratory distress.

The collected data from 10 normal and 53 pathological cases will be correlated in the following manner:

1. To record AEP waveform in normal neonates using a 81 dB SPL click stimulus and compare the latency and amplitude parameters with reported normal values.
2. To record AEP waveform in neonates and in infants in high risk conditions and measure L, IPL, A, AR, HW, AP.
3. To compare AEP parameters in different pathological subgroups.
4. Follow-up recording of AEP in certain pathologies and comparison of AEP waveforms.
5. Fourier analysis and curve fitting of AEP waveforms in 10 cases, representing two cases from each group.
The chapters are distributed as follows:

CHAPTER I : INTRODUCTION

CHAPTER II : OVERVIEW AND LITERATURE SURVEY

Literature survey of evoked potential with special reference to auditory evoked potential. The objectives and hypothesis of the problem have been stated and put forward in this chapter.

CHAPTER III : ANATOMY & PHYSIOLOGY OF AUDITORY PATHWAY.

This chapter is focused on anatomy and physiology of auditory pathway. Definitions of high risk conditions and the role of neurotransmitters of the auditory systems are given and discussed in detail.

CHAPTER IV : MATERIAL AND METHODS

In this chapter, the plan of the pilot study and experimental study have been given. Acquisition of data is also covered in this chapter.
CHAPTER V: DATA ANALYSIS

Critical data analysis with various parameters and possible inferences are discussed. The application of curve fitting and the Fourier analysis procedure have been also discussed in this chapter.

CHAPTER VI: CONCLUSIONS AND FUTURE DEVELOPMENT

This chapter deals with the final conclusion, and possible future development.
REFERENCES


