DOI: 10.7860/JCDR/2020/44891.14071

Original Article

Ear, Nose and Throat Section

Investigating the Recovery Properties of Auditory Nerve Fibres at Different Cochlear Regions using Electrically Evoked Compound Action Potential

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ABSTRACT

Introduction: Investigating the recovery function and refractory properties of auditory nerve is essential for us to understand the physiology at neural level, not many tools are available to carry out research in humans. Electrically Evoked Compound Action Potential (ECAP) helps us to record the action potential and also provides us with an option of varying the Interpulse Interval (IPI), hence there is a need to carry out research in Cochlear Implant (CI) users with the help of ECAP.

Aim: To investigate the refractory property of the neurons and the response characteristics at different cochlear regions.

Materials and Methods: Fifty CI users from age 3-10 years with a minimum hearing experience of three months underwent ECAP measures at various IPI. The data were further statistically analysed using SPSS software version 20.0, descriptive and inferential statistics were carried out using ANOVA.

Results: It was found that a high ECAP threshold (648 cu) could be found at the basal region of cochlea when compared to medial (658 cu) and apical region (785 cu) at 300 μs and similar higher thresholds at different IPI, thus attributing to the fact that with increase in population of nerve fibres, a better threshold could be achieved. Another finding revealed that with very low IPI, the ECAP thresholds were elevated, with neural recruitment being a contributing factor.

Conclusion: There was a difference in neural population amongst individuals, even with better auditory performance. ECAP is one of the objective tool to measure neural function and outcomes in CI individuals.

Keywords: Auditory nerve, Cochlea, Cochlear implant, Recruitment, Refractory period

INTRODUCTION

Cochlear implant is an implantable advance medical device that restores auditory function and provides auditory perception to individuals who have severe to profound hearing loss. The CI works on the electrical mode of stimulation in which the electrode array of the implant sends electrical impulses directly to the auditory nerve. There is depolarisation of spiral ganglion cells by the extracellular current provided by the CI [1,2].

The inner hair cells play an essential role in sound encoding with the help of a Ca^{2+} mediated exocytosis at the ribbon synapse between hair cells and type I Spiral Ganglion Neurons (SGNs) which are responsible for the high variability of SGN firing rates in acoustic stimulation [3-5]. Synaptic input are received from inner hair cells and are channelled to various cells in the brainstem. In contrast with acoustic stimulation, electrical stimulation creates better firing and better phase locking but SGNs have a greater dynamic range on acoustic stimulation. Physiological contribution of auditory neuron is that it acts as the bridge that connect the peripheral cochlea and the central nervous system. These neurons crucially contribute to the auditory system as they are serving as the initial layer of auditory neurons which encodes afferent spiking information. These ganglion cells of the auditory nerve effectively respond to the electrical stimuli released by the CI; in other words the number of distribution and function of these normal cells represents determined factor in relation to successful use of CI [6].

The electrically ECAP is a direct measurement of the neural responses from the auditory nerve fibres, which makes it easier for us to understand the physiological status of the nerve fibres. The current CI technology makes it feasible for us to get a near field recording from the intracochlear electrodes. In normal hearing individuals, it makes it difficult for us to record an ECAP as it creates a stimulus artefact. The test procedure done in CI recipients requires no special equipment, except for the programming interface and also has an added advantage of not requiring arousal for the test procedure [7].

The ECAP consists of a time locked negative peak (N1) and positive peak (P1) with in a time window frame of 0.2-0.4 ms and 0.6-0.8 ms, respectively after the stimulus onset. The clinical application of ECAP include intraoperative monitoring during CI surgery, creating map levels during programming and measuring the outcomes in CI users [8,9].

There have been studies published by several authors related to ECAP in CI users [10-15]. An ECAP recording of intracochlear electrodes typically shows a biphasic morphology. Around 80% of CI users get peaks of N1 and P1, but a scarce 20% get two positive peaks (P1 and P2) [10] along with the negative N1, the P2 peak appears around a latency of 0.6-0.8 ms. Authors attribute responses from the axonal and dendritic process respectively to be responsible for the two peak formation [10,11].

The neural adaptation studied in individuals with CI reveals that with increase in rate of stimulation (pulse per second), the ECAP amplitude reduces, amount of amplitude reduced is calculated by comparing amplitudes of ECAP elicited by pulses occurring later in the pulse train to that of the amplitude of ECAP occurring earlier in the pulse train [12,13].

Polarity sensitivity has been studied using ECAP, with the aid of cathodic and anodic pulse, authors postulate that at a higher level cathodic pulse activate peripheral process and anodic pulse activate central axons. Hence concluding that cathodic leading pulses can be used, but if there is no response, an anodic pulse can be utilised as an alternate [14,15].

The recovery function of auditory nerve can be recorded using electrical mode of stimulation. ECAPs play a major impact in affecting the refractory properties of the auditory nerve that are extracted from the amplitude of the neural response as a function of the interval between the stimulus (i.e., the IPI). ECAPs allow variation in IPI. This helps in evaluating the duration that neural fibres remain in refractory period by varying IPI [11]. There are only few studies focusing the response characteristics at different regions in cochlea with variable results of these studies, which could be due to both stimulus and response properties of neurons. The present study investigated the refractory property of the neurons and the response characteristics at different cochlear regions with the objectives of measuring the refractory period of neurons at different cochlear region by measuring the ECAP at different IPI of 300 μs, 500 μs, 750 μs, 1500 μs, 2000 μs, 2500 μs, 3000 μs, 5000 μs, 6000 μs and 8000 μs and comparing the ECAP measures at different regions of the cochlea (basal, medial and apical)

MATERIALS AND METHODS

The cross-sectional study begun in the month of June 2018 and data collection went on until May 2019.

Participants

The study included a total of 50 children from the age range of 3-10 years. All the participants had experienced the CI for the minimum period of three months. These participants had intra operative ECAP measure done. Participants with syndromes, anomalies in the cochlea, auditory neuropathy, other neurologically associated damage, and partial insertion of electrode and absence of intraoperative ECAP were excluded from the study. An informed consent was taken from the parents prior to testing.

Instruments Used

Dell laptop with Maestro version 6 with Max programming system, telemetry cable and programming cable were used.

Test Procedure

The participants included in the current study had undergone impedance field telemetry measures and ECAP measure using the amplitude growth function method (with the default IPI of 500 μs), with that ECAP threshold was obtained based on the minimum amplitude.

The Recovery function method of measuring ECAP was incorporated with different IPI such as 300 μs, 500 μs, 750 μs, 1500 μs, 2000 μs, 2500 μs, 3000 μs, 5000 μs, 6000 μs and 8000 μs. Electrodes 1-4 were considered as apical elctrodes, electrodes 5-8 were considered as medial electrodes and elctrodes 9-12 were considered as basal electrodes. The basal electrodes were tested first followed by medial electrodes and apical electrodes. IPI of 300 μs was considered the least and 8000 μs was considered the highest. The IPI were increased in the order from low to high.

The recorded ECAP measures was visually detected with the presence of N and P peaks (Amplitude level and IPI).

STATISTICAL ANALYSIS

The collected samples were subjected to statistical analysis using Statistical Package for Social Science (SPSS version 20), descriptive statistics was done to extract mean, standard deviation and inferential statistics such as ANOVA was done to extract nature of significance between the groups of samples.

RESULTS

Out of the 50 children included in the study, 30 were males, and 20 were females with a mean age range of 4.6 years. The usage of the device varied from six months to 4.5 years amongst the 50 children.

ECAP Threshold at Different Interpulse Interval (IPI) at Different Regions (Basal, Medial and Apical)

The ECAP threshold at different IPI was subjected to the descriptive statistics (Mean, SD and Range) for the different region in the cochlea, it was observed that the mean threshold is better at the basal and medial region than apical region irrespective of its IPI [Table/Fig-1]. However, the distribution was more in the Rosenthal canal, hence this could be one of the reason to have better mean threshold at the basal region as well medial region and also noted that the amplitude of the ECAP was increased with the use of the CI. On undergoing repeated measures ANOVA across different IPIs, a high significance value (<0.05) was obtained across all the IPIs.

Interpulse interval	Apical region	Medial region	Basal region
300 μs	785 cu	658 cu	648 cu
500 μs	728 cu	652 cu	620 cu
750 μs	722 cu	652 cu	612 cu
1500 μs	712 cu	600 cu	612 cu
2000 μs	710 cu	600 cu	595 cu
2500 μs	710 cu	597 cu	582 cu
3000 μs	710 cu	597 cu	580 cu
5000 μs	710 cu	592 cu	562 cu
6000 μs	700 cu	592 cu	560 cu
8000 μs	700 cu	592 cu	560 cu

[Table/Fig-1]: Mean threshold values obtained at different Interpulse Intervals (IPI) across different regions of Cochlea. Electrodes 1 to 4 were considered apical electrodes, electrodes 5 to 8 were considered medial electrodes and electrodes 9 to 12 were considered basal electrodes.

Comparison of ECAP Threshold Across Different Interpulse Interval (IPI) and Different Regions in the Cochlea

The comparison across the different IPI and the regions of the same subject was analysed using the repeated measure ANOVA, the results revealed that there was no significant difference across the regions for the ECAP (p-value >0.005) threshold amplitude however the presence of ECAP threshold amplitude was noted at very low IPI (300 μs).

DISCUSSION

The present study was conducted to assess the recovery function at different regions of Cochlea. Thresholds were observed to be less at basal region, which could be due to stiffness of the basilar membrane which is more towards the base compared to apex [16], so the electrical stimulation gives a force to the basilar membrane, but due to elasticity of the basilar membrane the duration of stimulation is required less at base, than at the apex. Another reason for higher threshold in the apical region could be due to the reduced number of spiral ganglion cells in the apical region as it has more of afferent peripheral axons and diameter of apical end being small, the apical electrode is more proximal to the modiolar wall thus, affecting the response [11].

Cochlea is tonotopically organised, that is the high frequency at the base and low frequency at the apex. Neurons at the base of the cochlea have to fire more rapidly than the neurons at the apex to code the incoming stimulus, i.e., high frequency at the base and low frequency at the apex. So, the neurons at the base should have lesser recovery time compared to the neurons at the apex. In this study, the ECAP threshold were lesser at the base compared to apex, so from the above data we could predict that the characteristics of the neurons vary depending on the place of stimulation in the cochlea.

Similar to this study, the research carried out by Botros A and Psarros C found shorter recovery function time constant, with increasing duration of hearing loss [17]. Larger neural population was associated with slower ECAP recovery function. Slower ECAP recovery is associated with greater temporal responsiveness to increasing stimulation rate, and it is suggested that greater neural recruitment is responsible for somewhat counter intuitive observation.

This could be due to the fact that lower IPI induces a neural recruitment that hence elevate the ECAP threshold. Although it can be assumed that the basal electrodes exhibit a higher degree of degradation than the apical ones reported by Gordon KA et al., [18].

In support with the present findings reported by Tanamati LF et al., showed that basal electrodes have slower recovery period and lower amplitudes [6] and attribute to the fact that electrodes stimulate a smaller portions of nerve fibres, this could be because of more distance between the cells or presence of less number of surviving cells in this portion because of neurosensory deafness [19]. On the other hand, a more recent study found that slower ECAP recovery, at equal loudness, is associated with larger neural populations [20].

Limitation(s)

A comparison between early implantees and late implantees could have been carried out to understand the correlation between age at implantation and recovery properties. The experiment can also be tried on anomalous Cochlea and hypoplastic nerves to understand the recovery properties in such kind of individuals.

CONCLUSION(S)

The amplitude of ECAP and recovery of ECAP varied significantly at basal, middle and apical region in the cochlea, as the ECAP recovery was faster in basal region and slower in apical region, with stimulation amplitude being constant.

Better outcomes of CI can be measured with the help of a combination of both ECAP and recovery function. It also must be understood that the recovery properties of auditory nerve fibres can only be carried on animal subjects and not normal human subjects. With the help of CI subjects, it will be able to understand the recovery properties at human level.

Further research on recovery function must be performed at a larger sample size and a relationship must be identified between neural refractoriness and CI experience.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: May 07, 2020
- Manual Googling: Jul 17, 2020
- iThenticate Software: Sep 15, 2020 (14%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? No
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **May 03, 2020**
Date of Peer Review: **Jun 09, 2020**
Date of Acceptance: **Jul 23, 2020**
Date of Publishing: **Oct 01, 2020**