Intraoperative Neural Response Telemetry and Neural Recovery Function: a Comparative Study between Adults and Children

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Abstract

Introduction Neural response telemetry (NRT) is a method of capturing the action potential of the distal portion of the auditory nerve in cochlear implant (CI) users, using the CI itself to elicit and record the answers. In addition, it can also measure the recovery function of the auditory nerve (REC), that is, the refractory properties of the nerve. It is not clear in the literature whether the responses from adults are the same as those from children.

Objective To compare the results of NRT and REC between adults and children undergoing CI surgery.

Methods Cross-sectional, descriptive, and retrospective study of the results of NRT and REC for patients undergoing IC at our service. The NRT is assessed by the level of amplitude (microvolts) and REC as a function of three parameters: A (saturation level, in microvolts), t0 (absolute refractory period, in seconds), and tau (curve of the model function), measured in three electrodes (apical, medial, and basal).

Results Fifty-two patients were evaluated with intraoperative NRT (26 adults and 26 children), and 24 with REC (12 adults and 12 children). No statistically significant difference was found between intraoperative responses of adults and children for NRT or for REC's three parameters, except for parameter A of the basal electrode.

Conclusion The results of intraoperative NRT and REC were not different between adults and children, except for parameter A of the basal electrode.

Keywords
- telemetry
- cochlear implants
- deafness

Introduction

The cochlear implant (CI) is the treatment of choice for the (re)habilitation of individuals with severe and profound sensorineural deafness.[1] The CI partially replaces the function of the cochlea, transforming sound energy into electrical signals. Its function depends on the integrity of the cochlear nerve to conduct electrical stimuli to the cerebral cortex.[2]

The ganglion cells of the auditory nerve effectively respond to electrical stimuli released by the CI. Therefore, the number, distribution, and function of these neural cells represent determinant factors in relation to successful use of the CI.[3] Therefore, the possibility to obtain information related to the permeability of the cochlear nerve to electrical stimulation data and the way in which some parameters of electrical stimulation interact with the neural structures are very important for research involving the CI, cochlear nerve, and causes of hearing loss.[2]

Neural response telemetry (NRT) captures the action potential of the distal portion of the auditory nerve (ECAP)

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in patients with CI (Nucleus CI, Cochlear Corporation, Australia), using the CI itself to generate stimuli and to record responses.[3] The ECAP wave is typically formed by a negative peak (N1), with ~0.2- to 0.4-millisecond latency, followed by a positive peak (P2), with 0.5- to 0.7-millisecond latency. The response amplitude (measured between N1 and P2) varies with increasing stimulus intensity and is measured in microvolts (ranging between 40 and 2,000 μV).[1]

One way to assess the temporal processing capacity of a CI user is to measure the refractory properties of the auditory nerve, that is, the recovery function of the auditory nerve (REC). RECs are extracted from the neural response amplitude as a function of the interval between the stimulus and the masker stimulus (interpulse interval) and can be measured with NRT using the subtraction technique.[4,5]

The routine clinical applications of NRT are: (1) to confirm correct implant function and electrode array insertion by obtaining the ECAPs; (2) to track implant function over time; (3) to assist the fitting process by using the ECAP thresholds as estimation of audible stimulus levels and loudness.[6] Other implications are estimating channel interaction, degree of neural refractoriness, and auditory system status. The telemetry method has several advantages over other methods, such as obtaining larger amplitudes and prevention of muscle artifacts, and it can be done quickly and effectively.[2]

Studies have shown variation in the threshold and growth curve of the ECAP wave amplitude between individuals and between different etiologies of deafness.[1,7] It is not clear in the literature, though, whether the responses from adults are the same as or differ from children. It is assumed that one should find differences in assessments of children compared with adults due to several factors such as duration of deafness, the maturation of the auditory pathways, and others.

It has been suggested that the human auditory system reaches maturity between 1 and 3 years of age. In this scenario, children with implants would undergo electrical stimulation on immature auditory pathways, and adults, in already mature pathways. Children with implants would therefore have their maturation influenced by electrical stimulation of the CI. On the other hand, adults may have long periods of deafness in relation to children, being subject to varying degrees of nerve degeneration in the auditory pathways from lack of stimulation.[8]

Therefore, the objective of this study is to compare the results of NRT and REC between adults and children undergoing CI surgery intraoperatively.

Methods

This study was approved by the Ethics Committee on Human Research of our hospital under CAAE: 13157113.4.0000.5529. This is a cross-sectional and descriptive study of the results of telemetry patients receiving CIs in our hospital in the year 2012. The sample included patients undergoing CI surgery who underwent intraoperative NRT, without limits of age, of both sexes. Exclusion criteria were patients who underwent surgery but did not undergo intraoperative NRT or who failed (had no response) in assessment of impedance telemetry or in obtaining intraoperative ECAP.

Measurements were obtained during CI surgery through computer software NRT Custom Sound EP 3.2 (3.2.3855), connected to the portable programming unit and speech processor and the transmission antenna of the CI (software developed by Cochlear Corporation). We used apical, medial, and basal electrodes (1, 11, and 22) for the telemetry response measures and the t0 (absolute refractory period, in seconds), A (saturation level, in microvolts), and tau (curve of the model function) measures for the calculation of the exponential function of neural recovery for groups of children (0 to 18 years) and adults (>18 years). The NRT measurements consisted of ECAP threshold and ECAP recovery function measurements. ECAP thresholds were measured automatically using AutoNRT.

The current level used for the recordings of REC was 15 to 20 units of current above the current level at which the NRT

Table 1 Demographic data for neural response telemetry patients: adults

Patient	Age (y)	Cause of deafness	Duration of deafness
1	39	Idiopathic	10 y
2	21	Congenital rubella	Lifetime
3	30	Idiopathic	11 y
4	26	Idiopathic	9 y
5	42	Congenital rubella	Lifetime
6	30	Idiopathic	10 y
7	22	Idiopathic	8 y
8	46	Idiopathic	12 y
9	31	Idiopathic	11 y
10	65	Idiopathic	12 y
11	24	Genetic	8 y
12	32	Congenital rubella	Lifetime
13	46	Meningitis	25 y
14	19	Idiopathic	8 y
15	34	Idiopathic	10 y
16	41	Idiopathic	11 y
17	69	Meniere syndrome	10 y
18	39	Idiopathic	9 y
19	83	Presbycusis	5 y
20	22	Idiopathic	8 y
21	37	Idiopathic	9 y
22	18	Idiopathic	8 y
23	51	Idiopathic	11 y
24	21	Idiopathic	9 y
25	46	Idiopathic	12 y
26	32	Idiopathic	11 y

Table 2 Demographic data for neural response telemetry patients: children

Patient	Age	Cause of deafness	Duration of deafness
1	11 y	Idiopathic	Lifetime
2	1 y	Idiopathic	Lifetime
3	4 y	Idiopathic	Lifetime
4	1 y	Idiopathic	Lifetime
5	1 y	Idiopathic	Lifetime
6	4 y	Idiopathic	Lifetime
7	2 y	Idiopathic	Lifetime
8	4 y	Idiopathic	Lifetime
9	3 y	Genetic	Lifetime
10	9 y	Genetic	Lifetime
11	10 y	Idiopathic	Lifetime
12 (bilateral)	2 y	Genetic	Lifetime
13	3 y	Genetic	Lifetime
14 (bilateral)	2 y	Genetic	Lifetime
15	5 y	Idiopathic	Lifetime
16	5 y	Idiopathic	Lifetime
17	9 y	Idiopathic	Lifetime
18	2 y	Idiopathic	Lifetime
19	4 y	Meningitis	2 y
20	3 y	Idiopathic	Lifetime
21	5 y	Idiopathic	Lifetime
22	9 mo	Genetic	Lifetime
23	4 y	Encephalitis	1 y
24	8 y	Idiopathic	Lifetime

was obtained in each stimulated electrode (apical, medial, and basal), only 20 units being used if there was need for higher current to obtain the neural response and not cause saturation of the amplifier. The parameters of the amplifier gain and delay used for this study were the same as determined by the series of optimization of the electrode stimulation frequency of 80 Hz according to Lai.[9] The probe rate was 80 Hz between stimuli, and 20 MPI (masker probe interval) measurements were performed from 100 to 10,000 µs. In some cases, it was necessary to perform manual corrections of the measurement of N1/P2; in others, the calculations given by the software were used.

The Custom Sound EP software automatically converts measurement of the recovery function (REC) in an exponential function:

$$\text{Recovery of function} = A(1 - \exp((-1/\text{tau})(\text{MPI} - t0)))$$

The comparison between NRT and REC averages between the two groups (children versus adults) and statistical analysis was performed using Student *t* test and Mann-Whitney test, with $p < 0.05$ considered significant.

Results

Fifty-two patients were assessed (26 children and 26 adults) for NRT and 24 patients (12 children and 12 adults) for the REC. The minimum age was 9 months, and the maximum 83 years. The mean age of children was 4.15 $\pm$ 2.92 years and for adults, 37.12 $\pm$ 16.22 years.

Causes of impairment in the NRT adults (26 patients) included one case of genetic cause, three causes of congenital rubella, one case of presbycusis, one case of meningitis, and one case of late stage Meniere syndrome, and all the other causes were idiopathic. On the other hand, the children (26 patients) included six cases of genetic cause, one case of meningitis, and one case of encephalitis, and all the others were of idiopathic cause (►**Tables 1** and **2**).

In the REC adults (12 patients), there was one case of genetic cause, two cases of late-stage otosclerosis, and one case of congenital rubella. The children (12 patients) included four cases of genetic cause and the others were idiopathic causes (►**Tables 3** and**4**).

No patient failed in obtaining impedance response during the surgery, showing that the electrodes were positioned correctly.

The results of intraoperative NRT are shown in ►**Table 5**, for the apical, medial, and basal electrodes. There was no significant difference between the NRT results between adults and children.

The results of the REC were evaluated for t0, A, and tau for the apical, medial, and basal electrodes and are show in ►**Tables 6**, **7**, and **8**. For the three parameters, there was no significant difference, except for the level of saturation of the basal electrode.

Table 3 Demographic data for recovery function of the auditory nerve: adults

Patients	Age (y)	Cause of deafness	Duration of deafness (years)
1	41	Idiopathic	11
2	46	Idiopathic	12
3	46	Idiopathic	12
4	41	Otosclerosis	8
5	30	Idiopathic	10
6	39	Idiopathic	10
7	19	Idiopathic	8
8	39	Idiopathic	9
9	43	Otosclerosis	8 y
10	22	Idiopathic	8
11	24	Congenital rubella	Lifetime
12	30	Genetic	5 y

Table 4 Demographic data for recovery function of the auditory nerve: children

Patients	Age (y)	Cause of deafness	Duration of deafness
1	1	Genetic	Lifetime
2	2	Genetic	Lifetime
3	3	Idiopathic	Lifetime
4	13	Idiopathic	Lifetime
5	5	Idiopathic	Lifetime
6	2	Idiopathic	Lifetime
7	3	Idiopathic	Lifetime
8	1	Genetic	Lifetime
9	10	Idiopathic	Lifetime
10	3	Genetic	Lifetime
11	8	Idiopathic	Lifetime
12	2	Idiopathic	Lifetime

Discussion

A CI for severe to profound sensorineural hearing loss unresponsive to hearing aids may be indicated for both children and adults, according to the criteria proposed in the guidelines. There is a great variability among the candidates for CI in relation to age, type of deafness, hearing deprivation, speech production, and communication skills. Speech perception and word recognition tests assess the subjective result of the implant, which is the ability to enable communication skills. However, there is no standardization of these tests in our country, making it difficult to compare results among research centers.[10] In this scenario, an objective test, characteristic of the CI model such as NRT, has great value in the evaluation and comparison of data among individuals, and it is easy to standardize analysis and interpretation among research centers.[11]

Because it does not require external electrodes, the NRT is less susceptible to myogenic interference and needs fewer stimuli to trigger the ECAP. Assessment during surgery with either general or local anesthesia with sedation allows better evaluation of the responses without causing discomfort to the patient by increasing the current units needed to unleash the potential.[1] Furthermore, the NRT through the ECAP is a direct way to evaluate in vivo the functional characteristics of ganglion cells and other auditory neural structures. Knowledge of the function of these structures is essential for the development of improved technologies and increasing knowledge of the different etiologies of deafness.[3] Yet there are not many studies on the cochlear nerve function, especially in comparison between adults and children.

The action potential measured by NRT reflects the synchronized firing of many auditory nerve fibers and consists of the sum of the electrical activity of hundreds of neurons. As

Table 5 Comparison of neural response telemetry results between adults and children according to electrode

	Patients	*n*	Average current units			
			Min–max	Average	SD	*p* value (*t* test)
Apical electrode	Adults	26	84–225	181.12	34.54	0.28
	Children	26	90–218	171.15	30.40	
Medial electrode	Adults	26	146–236	191.69	18.56	0.51
	Children	26	112–225	195.54	22.69	
Basal electrode	Adults	26	104–243	193.96	32.67	0.17
	Children	26	121–220	182.54	25.76	

Abbreviations: Min, minimum; max, maximum; SD, standard deviation.

Table 6 Comparison of mean absolute refractory period between adults and children

	Patients	*n*	Mean absolute refractory period (μs)			
			Min–max	Average	SD	*p* value (Mann-Whitney test)
Apical electrode	Adults	12	184.43–1011.02	498.64	262.89	0.40
	Children	12	131.21–1667.18	527.28	409.29	
Medial electrode	Adults	11	333.38–1040.90	636.06	252.93	0.44
	Children	12	270.38–1471.89	598.56	305.04	
Basal electrode	Adults	12	31.97–770.51	477.99	225.74	0.20
	Children	12	73.59–666.89	428.20	171.34	

Abbreviations: Min, minimum; max, maximum; SD, standard deviation.

Table 7 Comparison of mean saturation level between adults and children

	Patients	*n*	Mean saturation level (μV)			
			Min–max	Average	SD	*p* value (Mann-Whitney test)
Apical electrode	Adults	12	13.72–229.84	101.50	68.35	0.27
	Children	12	26.37–278.98	136.50	93.22	
Medial electrode	Adults	11	20.83–193.02	83.96	55.02	0.16
	Children	12	29.92–509.37	131.66	125.57	
Basal electrode	Adults	12	16.17–216.40	57.07	53.46	0.02
	Children	12	38.41–146.25	76.98	34.35	

Abbreviations: Min, minimum; max, maximum; SD, standard deviation.

Table 8 Comparison of the curvature parameter of the model function (μs) between adults and children

	Patients	*n*	Curvature parameter of the model function (μs)			
			Min–max	Average	SD	*p* value (Mann-Whitney test)
Apical electrode	Adults	12	16.60–1967.28	853.68	609.84	0.14
	Children	12	430.79–1856.67	1086.15	432.02	
Medial electrode	Adults	11	24.43–1846.94	1073.66	653.96	0.14
	Children	12	1076.69–1956.13	1464.97	233.58	
Basal electrode	Adults	12	11.64–1870.72	607.35	595.07	0.06
	Children	12	246.48–1623.40	929.38	516.12	

Abbreviations: min, minimum; max, maximum; SD, standard deviation.

ECAP occurs immediately after stimulus presentation, it is not affected by the maturation of the auditory system.

Gordon et al found higher amplitudes of the ECAP and lower latency in children compared with postlingual adults.[12] These differences were attributed to auditory deprivation time or number of stimulated neurons. In our study, we found a secluded difference between the amplitudes of the saturation level between children and adults only in the basal electrode.

Studies have shown that periods of slower recovery and lower amplitudes were found in basal electrodes. These changes were attributed to the fact that the electrodes stimulate a smaller population of neurons, due to the greater distance of the cells or to a smaller number of surviving cells in this portion because of the neurosensory deafness itself.[7,12] On the other hand, a more recent study found that slower ECAP recovery, at equal loudness, is associated with larger neural populations.[5]

The importance of determining thresholds, amplitude, and refractory properties of the responses of the action potential of the VIII nerve may indicate differences in the neural population of individuals, and even on the auditory perception performance.[1] But conflicts in results among studies show that there is still a need for more research regarding this subject. Measures of both the NRT and the REC in combination may be important indicators of success with the CI.[7] Therefore, more studies about them and their correlation to clinical data are indispensable.

Conclusion

No differences were found in measures of NRT and REC intraoperatively between adults and children, except for the level of saturation at the basal electrode.

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