

Neural Recovery Function of the Auditory Nerve in Cochlear Implant Surgery: Comparison between Prelingual and Postlingual Patients

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Abstract

Keywords

- ▶ cochlear implants
- ▶ prelingual hearing loss
- ▶ postlingual hearing loss
- ▶ neural response telemetry

Introduction Cochlear implants (CIs) enable objective measures of the neural function in implanted patients through the measurements of the neural response telemetry (NRT) and of the Auditory nerve Recovery Function (REC). These measurements help in programming the speech processor and understanding the auditory system.

Objective To compare the NRT and the REC in prelingual and postlingual implanted patients.

Methods An observational, descriptive and prospective study was carried out. The NRT and the REC (through the T0, A, and tau parameters) were evaluated in individuals submitted to CI surgery, who were divided into two groups: prelingual and postlingual patients.

Results In total, 46 patients were evaluated. Data analysis showed no statistically significant difference between the NRT measurements and the T0, A, and Tau of the REC in the comparison between the two groups, except for the NRT in the basal cochlear region.

Conclusion There was no statistically significant difference in the REC in pre- and postlingual patients.

Introduction

The age at the onset of deafness is one of the most important factors in the evaluation of a patient with hearing loss (HL). Regarding this aspect, HL can be classified according to the period of language acquisition as prelingual or postlingual. It is said to be prelingual when it occurs before the acquisition of the bases of oral language, and it is postlingual when it occurs after the acquisition of language, when the patient already has an established linguistic code.¹

Auditory deprivation in prelingual HL may affect the development of the auditory neural pathways, since the maturation of these pathways depends on stimulation. This deprivation compromises the maturation of the central auditory pathways,

as well as the development of speech and language skills². In postlingual HL, the neural pathways are already formed, and there is an auditory memory, so, in general, there is no regression of the language due to hearing deprivation.

The development of speech perception and language acquisition, as well as the success of the CI rehabilitation, both in children with prelingual HL and in adults with pre- or postlingual HL, depends on some determinant factors,³ but since the ganglion cells of the auditory nerve are considered the elements that effectively respond to the electrical stimulus released by the CI, the participation of the ganglion cells is the differential factor in the individual's ability to achieve success with the use of the CI.⁴

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Both the neural function of the cochlear nerve as well as the number, distribution, and functionality of the remaining neural cells must be in sufficient quantity to enable the electrical stimulation to be transmitted to the cerebral cortex⁵. This functionality can be evaluated through speech performance or electrophysiological tests.

Initial studies⁶⁻⁸ compared the performance with the CI between postlingual and prelingual adult patients. They observed worse responses in the performance of prelingual patients. Other studies^{9,10} have shown that only prelingual children who are implanted early (before 6 years of age) have achieved full speech recognition in an open set, with an even better performance than the postlingual patients. In the first 6 years of age, a period of high neuronal plasticity^{9,10} was reached with CI stimulation, close to that of a normal listener.

Ching et al¹¹ showed the benefit of early intervention for language development, helping to ensure early amplification and enable cochlear implantation after the diagnosis.

The possibility of performing CI in small children makes it necessary to use objective measurements to aid in the programming of the speech processor. One of them is neural response telemetry (NRT), through which the electrically-evoked compound action potential (ECAP) is obtained using the implant itself to elicit the stimulus and record the responses to study the remaining neural properties¹² without the need to sedate the patient.¹³ The refractory recovery function (REC) can be extracted from the action potential of the neural fibers in response to the use of a pulse with a gap between the main stimulus and the masker.¹⁴

The REC is measured by an exponential function with three parameters: 'T0', 'A' and 'tau'. T0 is the absolute refractory period (in μs); A is the maximum amplitude of the neural response at the maximum saturation level (in μV); and tau is the recovery time constant during the relative refractory period (in μs). It is important to consider the interaction between the three parameters.¹⁴⁻¹⁶

The objective of the present study was to evaluate and compare the NRT and the REC of pre- and postlingual implanted patients.

Methods

An observational, prospective and descriptive study was carried out, with the approval of the institutional Ethics Committee on Research in Human Beings under the CAAE: 69604917.2.0000.5529, registered under CEP 185/2017.

Our institution is an ear, nose and throat (ENT) specific hospital, and the study took place from January to November 2017.

The study included participants undergoing CI surgery, who were divided into two groups:

1. Prelingual: congenital HL or HL that occurred before the acquisition of language;
2. Postlingual: HL that occurred after the acquisition of language.

We included patients who were submitted to the CI and to the intraoperative assessments that are part of our routine (► **Table 1**). The indications for the CI are well known in the literature.

There was no randomization of the patients, because the groups were based on preexisting conditions (age of acquisition of language). No patients were lost to follow-up.

The CI used was the Freedom Implant Contour Advance CI24RE (CA) (Cochlear Ltd, Sidney, Australia), and, to record the impedances, the ECAP and the REC, we used the Custom Sound EP 4.4 software (Cochlear Ltd.), which controls the parameters of stimulation and recording, and is installed in a computer coupled to the portable programming interface (portable programming system) and the speech processor CP810 Sound Processor (Cochlear Ltd.).

During the surgery, shortly after the insertion of the electrodes into the cochlea, impedance telemetry (IT) was performed to evaluate the integrity and functionality of the electrodes. Then, the measurement of the Threshold NRT (T-NRT), Automatic NRT (autoNRT) was performed using 5 or 9 electrodes corresponding to the frequency bands, according to cochlear tonotopy. The current level (CL) at each electrode started at 170 current units (cu), with a range of 6 cu between one stimulus and the other, until the maximum stimulation of 255 cu, or until the T-NRT was found. The parameters were the software's default settings.

The REC was the next measurement. We used advanced NRT to create a new series 'Recovery,' and chose 3 electrodes obeying cochlear tonotopy. The electrodes were divided according to their position within the cochlea in the apical (22-16), medial (15-8) and basal (7-1) regions.

The masking level was set at 10 cu above the CL used for pacing (probe level). The interpulse interval was set at 500 μs , and the pacing rate was 80 Hz in a series of 25 μs per phase. The REC uses 20 interval values between the triggering of the stimulus on the masking electrode and the triggering of the stimulus on the electrode tested (between 100 μs and 10,000 μs). Other parameters, such as amplification gain, time interval between stimulus end and response recording (defined as the number of artifacts to enable a better visualization of the N1 wave), and the distance between MP1 and MP2, were adjusted and modified according to the proposition made by Abbas et al¹³ and Lai.¹⁷ The level of the stimulus used for the REC recordings was an average of 20 cu

Table 1 Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Patients (male and female children and adults) submitted to cochlear implants and intraoperative assessments.	Neurological or cognitive deficit.

above the level at which the NRT was obtained in each stimulated electrode (apical, medial and basal), with attention to obtain a neural response, and not to cause saturation of the amplifier.

The software automatically transforms REC measurements into an exponential function, a mathematical model proposed by Müller-Deile et al,¹⁸ which defines that: F Masker Probe Interval (MPI) = $A(1 - \exp[-\alpha(MPI - T_0)])$.

We performed a descriptive analysis of the data through frequencies, measurements of central tendency (mean and median) and dispersion (standard deviation, minimum and maximum) of variables. Neural recovery parameters T_0 , A and τ , as well as the CL for the REC, were recorded for the apical, medial and basal electrodes in both groups. The results of the quantitative variables were described by means and standard deviations, medians and amplitudes. For the categorical variables, frequencies and percentages were presented. The comparison between the groups in relation to the NRT and the REC measurements (T_0 , A and τ) was performed using the Student t -test for independent samples. The normality of the variables was evaluated by the Kolmogorov-Smirnov test. Values of $p < 0.05$ indicated statistical significance. The data were analyzed using the Stata/SE (StataCorp LLC, College Station, TX, US) software, version 14.1.

Results

In the prelingual group, 22 patients were included, 4 of which were bilateral, resulting in 26 ears, aged between 10 and 46 years. In the postlingual group, there were 24 patients, 4 of whom were bilateral, resulting 28 ears, aged between 22 and 62 years. In total, 54 ears were evaluated.

The age of the sample ranged from 10 to 62 years. The mean age of the prelingual patients was 28.3 years, and the mean duration of the HL was 27.7 years. For the postlingual patients, the mean age was 44.1 years, and the mean duration of the HL was 11.1 years.

The causes of HL for all patients are included in ► **Table 2**.

For all patients, the CI presented IT of the electrodes within normal values during surgery, showing that the electrodes were capable of being activated. The results of the intraoperative NRT for the apical, medial and basal electrodes are shown in **table 3**. There was no difference between groups for the apical and medial NRT, but there was a difference for the basal NRT.

Table 3 Neural response telemetry (NRT) results

Variables	Group	n	Mean	Median	Minimum	Maximum	Standard deviation	p-value*
NRT - apical	Postlingual	28	179.9	183	84	228	27.2	0.585
	Prelingual	26	183.6	185	144	222	21.5	
NRT - medial	Postlingual	28	195.9	197	156	240	17.3	0.755
	Prelingual	26	194.6	196.5	170	220	13.0	
NRT - basal	Postlingual	28	191.2	190.5	145	225	22.5	0.005
	Prelingual	26	172.3	169	136	226	24.8	

Note: * Student t -test for independent samples; $p < 0.05$.

Table 2 Patients according to the etiology of the hearing loss

Etiology	Group	
	Postlingual	Prelingual
Idiopathic	14 (50%)	1 (3.8%)
Genetic	8 (28.6%)	7 (26.9%)
Ménière syndrome	1 (3.6%)	
Parry-Romberg syndrome	2 (7.1%)	
Traumatic brain injury	1 (3.6%)	
Otosclerosis	2 (7.1%)	
Prematurity		2 (7.7%)
Neonatal jaundice		1 (3.8%)
Rubella		9 (34.6%)
Meningitis		1 (3.8%)
Uscher syndrome		1 (3.8%)
Congenital		1 (3.8%)
Measles		1 (3.8%)
Cytomegalovirus		2 (7.7%)
Total	28	26

The REC results are shown in **table 4**. No differences were found in any of the three parameters for each electrode.

Discussion

It is suggested that auditory maturation of the brainstem, measured through neural potentials, occurs between 1 and 3 years of age in hearing people. For implanted patients, however, it is not so clear, given that the characteristics of the auditory system in adults using the CI may be different from those of children using the CI. Many adults have postlingual deafness, acquired after the normal development of the auditory system in childhood, promoted by binaural hearing, while many children receiving implants have bilateral congenital deafness. In prelingual children, the lack of auditory input during the primary stages of development may alter the normal maturation of the central auditory system. On the other hand, adults may experience long periods of deafness, during which varying degrees of neural degeneration may occur in the auditory pathways.¹⁹

Table 4 Neural recovery function (REC) results

Variables	Region	Group	N	Mean	Median	Minimum	Maximum	Standard deviation	p-value *
T0	Apical	Postlingual	28	534.8	496	186	1108	240.4	
		Prelingual	26	467.8	452	131	1071	218.1	0.290
	Medial	Postlingual	28	611.8	604	233	1189	255.7	
		Prelingual	26	694.9	638.5	32	1599	343.2	0.315
A	Basal	Postlingual	28	482.1	456.5	128	855	184.0	
		Prelingual	26	457.7	514	31	810	201.2	0.643
	Apical	Postlingual	28	113.6	96	19	376	75.2	
		Prelingual	26	114.0	105.5	11	250	65.8	0.984
Tau	Medial	Postlingual	28	124.5	112	24	403	81.3	
		Prelingual	26	139.2	96.5	20	509	119.1	0.596
	Basal	Postlingual	28	80.8	69.5	20	238	52.9	
		Prelingual	26	66.9	60	16	183	40.9	0.289
Tau	Apical	Postlingual	28	834.1	792.5	11	1870	558.7	
		Prelingual	26	680.2	706	35	1499	460.1	0.276
	Medial	Postlingual	28	1046.5	1062.5	11	1967	423.9	
		Prelingual	26	1222.7	1427	24	1865	546.5	0.190
Basal	Postlingual	28	923.1	994.5	12	1827	443.9		
	Prelingual	26	1115.6	1122	16	1967	538.8	0.157	

Note: * Student t-test for independent samples; $p < 0.05$.

Previous studies that compared pre- and postlingual implanted patients observed their performance through speech tests. Hinderink et al²⁰ compared 19 pre- and postlingual adult patients who received CI through discrimination tests and concluded that the group of postlingual patients had a performance in the closed-set and tests of auditory perception superior to that of the prelingual ones. Results similar to those are found in the literature^{7,21}.

Kraaijenga et al²² retrospectively studied the factors that influenced outcomes in 428 adult implanted patients. They used consonant-vowel-consonant scores before and after implantation as a measure, dividing the sample into pre- and postlingual patients. They observed that in postlingual patients the preimplantation speech perception score and age at onset of the HL were positive predictive factors, and meningitis and otosclerosis as etiology are negative factors for postimplant speech perception. In prelingual patients, the only strong positive predictive factor was the perception of preimplant speech. The age at implant was not a significant factor in either group.

On the other hand, correlations between speech perception and nerve cell count are probably complicated by several factors: it is unlikely that speech perception scores and spiral ganglion counts have a direct and linear correlation; the processed speech provided by the CI may contain redundant information that could effectively mask the functional changes that may occur at the peripheral level; in many implant users, there are large variations in ECAP measurements, such as limiting and tilting the growth function through electrodes within an individual implant

user, because speech perception is usually measured using the entire set of electrodes, and these variations can affect correlations with performance; and speech perception may be influenced by changes in central nervous system plasticity or by additional patient (cognitive) variables not related to the auditory periphery²³.

Some authors evaluated brain function comparing pre- and postlingual implanted patients. Naito et al²⁴ evaluated changes in regional cerebral blood flow in the auditory cortex induced by sound stimulation. They concluded that the neural networks for speech processing in the area of auditory association in postlingual deaf subjects are similar to those of normal hearing subjects, whereas in prelingual deaf patients who received the CI after the acquisition of language, this area may not develop completely. Okazawa et al²⁵ evaluated brain scanning through positron-emission tomography (PET) and magnetic resonance imaging (MRI) scans. Their findings suggest that the cortical representation of language is not dependent on prior auditory experience, whereas processing in the primary auditory cortex is dependent on experience.

With respect to the NRT and the REC, few studies performed evaluations based on the differences between pre and postlingual patients. Carvalho et al²⁶ compared the values of the NRT in children (aged between 9 months and 11 years) and adults (age range: 18 to 83 years), and showed no difference in the comparison of these two groups except for the saturation level 'A' in the basal cochlear region. The patients who were children were mostly prelingual, and the adults were mostly postlingual.

In the present study, we showed that in the same NRT comparison between postlingual and prelingual patients, there was a statistically significant difference in the same basal cochlear region. This may have been due to the fact that the studied groups were similar: children and adults, and prelingual and postlingual groups, even though our mean age was higher for the prelingual group (28.3 years). In addition, we believe that these differences may have occurred because the apical T0 values for the prelingual group were lower than the apical T0 values for the postlingual group. The same was true for baseline A values for the postlingual group, which were lower than those of the prelingual group.

In a retrospective study, Kutscher et al²⁷ evaluated children and adults regarding REC measurements and their correlation with etiology, the duration of the HL, and the duration of the use of hearing aids before the CI. There was no statistically significant correlation between the analyzed factors and the REC. However, the authors found that there may be a trend: the shorter the duration of the HL, the faster the REC.

Even though software to collect data from the CI manufacturers are highly sophisticated, they are not perfect. The influence of artifacts and the quality of recorded potentials may vary between patients and with the selection of stimulation parameters. Even with certain pathologies, such as ossification of the cochlear lumen in otosclerosis, ECAPs may be difficult to collect.²³

The fact that there was no statistical correlation between the preoperative data and the REC measurements leads us to question whether recording the NRT and the REC with the methodology proposed by Abbas et al¹³ is sensitive and specific, even considering that the authors evaluated only postlingual patients, and that the purpose of their investigation was to enable the recording of the ECAP in the majority of patients with CI.

Other studies, such as the one by Miller et al,²⁸ report new research on ECAP measurements, as well as possible methods, interpretations, and implications on neural functions.

Alvarez et al²⁹ analyzed the use of ECAP recordings to aid in the activation of the electrodes in the map of implanted patients, comparing pre- and postlingual patients. They found no statistically significant differences between the two groups regarding ECAP thresholds. But there was a difference in the C levels measured by the audiologist. These were greater in prelingual than in postlingual patients. So the authors came up with different equations to estimate C levels based on ECAP responses.

We believe that future studies can clarify these doubts and bring new uses for the objective measurements of neural function.

Conclusion

No statistically significant difference in the values of the measurements of the REC, comparing prelingual and postlingual patients, was found. There were only differences in the basal region of the cochlea in the evaluation of the NRT between the groups, and in the evaluation of the T0, A and tau measurements individually for each group.

We suggest that new studies should compare REC measurements to speech perception performance tests or patient preferences in the choice of parameters to be used in programming the CI.

Conflict of Interests

The authors have none conflict of interests to declare.

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