

Cortical Auditory Evoked Potentials with Simple (Tone Burst) and Complex (Speech) Stimuli in Children with Cochlear Implant

Kelly Vasconcelos Chaves Martins¹ Daniela Gil¹

¹Department of Speech-Language Pathology and Audiology, Universidade Federal de São Paulo – UNIFESP, São Paulo, Brazil

Address for correspondence Kelly Vasconcelos Chaves Martins, MSc, Rua Botucatu, 802 – Vila Clementino, São Paulo – SP CEP 04023-062, Brazil (e-mail: kellyvcm@hotmail.com).

Int Arch Otorhinolaryngol 2017;21:351–357.

Abstract

Introduction The registry of the component P1 of the cortical auditory evoked potential has been widely used to analyze the behavior of auditory pathways in response to cochlear implant stimulation.

Objective To determine the influence of aural rehabilitation in the parameters of latency and amplitude of the P1 cortical auditory evoked potential component elicited by simple auditory stimuli (tone burst) and complex stimuli (speech) in children with cochlear implants.

Method The study included six individuals of both genders aged 5 to 10 years old who have been cochlear implant users for at least 12 months, and who attended auditory rehabilitation with an aural rehabilitation therapy approach. Participants were submitted to research of the cortical auditory evoked potential at the beginning of the study and after 3 months of aural rehabilitation. To elicit the responses, simple stimuli (tone burst) and complex stimuli (speech) were used and presented in free field at 70 dB HL. The results were statistically analyzed, and both evaluations were compared.

Results There was no significant difference between the type of eliciting stimulus of the cortical auditory evoked potential for the latency and the amplitude of P1. There was a statistically significant difference in the P1 latency between the evaluations for both stimuli, with reduction of the latency in the second evaluation after 3 months of auditory rehabilitation. There was no statistically significant difference regarding the amplitude of P1 under the two types of stimuli or in the two evaluations.

Conclusion A decrease in latency of the P1 component elicited by both simple and complex stimuli was observed within a three-month interval in children with cochlear implant undergoing aural rehabilitation.

Keywords

- ▶ cochlear implant
- ▶ auditory evoked potentials
- ▶ neuronal plasticity
- ▶ aural rehabilitation
- ▶ hearing
- ▶ child

Introduction

The Cochlear Implant (CI) has become a very effective alternative in the treatment of patients with sensorineural severe to profound hearing loss who do not benefit from the use of conventional amplification. This electronic device is capable of performing the function of damaged or missing hair cells by transforming the sound energy into low level electrical

current to directly stimulate the remaining auditory nerve fibers.^{1,2} However, only the adaptation of electronic devices does not guarantee a good prognosis. The hearing rehabilitation becomes essential in the process of development of listening skills and, among the proposed work, the aural rehabilitation approach would be the most appropriate one. It aims to help children learn to use their hearing residue for the development of the hearing function, thus facilitating the

received
July 3, 2016
accepted after revision
January 2, 2017
published online
March 15, 2017

DOI <https://doi.org/10.1055/s-0037-1600122>.
ISSN 1809-9777.

Copyright © 2017 by Thieme Revinter
Publicações Ltda, Rio de Janeiro, Brazil

License terms



construction and the use of oral language, enabling the children to interact with their social environment.³

To analyze the behavior of the auditory pathways resulting from stimulation by CI, the recording of auditory evoked potentials (AEP) has been widely used.⁴⁻⁹ The long latency auditory evoked potentials (LLAEP), or cortical auditory evoked potentials (CAEP), are electrical responses from the peripheral and central auditory systems resulting from acoustic and electric stimuli,¹⁰ and among the sound stimuli used are tone burst (TB) and speech.

Due to the plasticity of the central nervous system, with sensory deprivation, the adjacent regions are designated to perform new functions. With the restoration of hearing by the CI, there is a reorganization of the nervous structures, and the auditory cortex resumes its primary function, even after the previous redirection caused by sensory deprivation.^{7,8}

However, according to Sharma et al¹¹, the plasticity is most evident in the first years of life, and it decreases with age. The P1 component of the CAEP has been considered a biomarker of the development of the central auditory system that shows reduced latency over the years.¹²⁻¹⁴ The comparison between P1 latency in implanted children and their peers and normal hearing thresholds showed that the children submitted to the CI at 3.5 years of age can reach CAEP latencies appropriate for their age 6 months after the beginning of the stimulation.

After this optimum period, significant changes in relation to synaptic plasticity may occur, resulting in the abnormal connectivity of neuronal cells, functional disintegration, and the immaturity of auditory cortical areas, as well as the possibility of some areas not developing auditory functions, which leads to abnormalities of restructuring cognitive function.¹⁵ In contrast, implanting the device within the sensitive period enables the cortical maturation to be more appropriate, resulting in the development of speech perception and oral language acquisition.^{16,17}

Cortical auditory evoked potentials stand out as a very important tool in the evaluation of patients undergoing CI, providing valuable information about the maturation and development of the central auditory system, allowing inferences about aspects related to proper adaptation and to the performance that the device may provide to each individual.

By making use of the CAEP, it is possible to objectively measure the development and plasticity of the central auditory system through the analysis of the changes in morphology and latency of the P1 component. Therefore, it is possible to observe the appropriate stimulation and the reestablishment of central auditory pathways^{8,18,19}, as well as the effectiveness of the aural rehabilitation.²⁰

Because of the lack of research on this theme in the dedicated literature, this study could provide important information about the central auditory system behavior caused by electrical stimulation from the CI, together with the aural rehabilitation. It is expected that there is a reduced latency and improvement of amplitude and morphology as the auditory pathways are adequately stimulated by the CI and the effective aural rehabilitation.

Thus, this study aimed to compare the parameters of latency and amplitude of the P1 component of the CAEP elicited by simple (TB) and complex (speech) stimuli in children with CI undergoing aural rehabilitation in a three-month interval.

Method

This is a longitudinal study, and it was approved by the Research Ethics Committee of the institution under the report number 1.093.827, and followed resolution n^o 466/12 of the Brazilian National Health Council, in which participants agreed to their inclusion in the study by signing the free and informed consent form.

Casuistry

The study included individuals from 5 to 10 years old with sensorineural severe to profound hearing loss. The participants were attending aural rehabilitation in the hearing rehabilitation clinic of the institution.

As inclusion criteria, participants of both genders should be CI users for at least 12 months and attend aural rehabilitation at the institution.

As exclusion criteria, participants who had syndromes, cognitive impairment or refused to sign the free and informed consent form were excluded from the study.

Thus, the sample consisted of 6 individuals, 3 female and 3 male, aged 5 to 10 years old, with a mean age of 6.7 years. The average age of the participants at the time of the CI activation was 3.3 years old.

Aural Rehabilitation

The selected individuals were undergoing weekly aural rehabilitation at the institution. The frequency ranged from 1 to 2 sessions per week, and each session lasted 45 minutes.

The approach used was aural with activities for listening skills development (detection, discrimination, recognition and comprehension).

During the data collection period, the predicted number of therapeutic sessions was 24 for patients treated twice a week, and 12 sessions for patients treated once a week.

In order for the variable frequency in the aural rehabilitation to be considered in the analysis of the CAEP, the presence in therapy was computed as a percentage.

In ► **Table 1**, we can observe the sample characterization for sex, age, hearing impairment etiology, age at CI activation, CI usage time and frequency of aural rehabilitation.

Cortical Auditory Evoked Potential (CAEP)

The participants were submitted to CAEP at the beginning of the study and after three months of aural rehabilitation. Simple stimulus, TB, and complex stimulus speech (syllable /ba/) were used to elicit the responses. The research of the CAEP was held on the map in use by the individual at the time of the assessment and, in the case of patients with bimodal stimulation, removal of the contralateral hearing aid was requested.

Table 1 Sample characterization

Participant	Sex	Age (years)	Etiology of deafness	CI activation age (years)	Frequency in rehabilitation (%)
1	M	5	Unknown	2.9	33
2	F	5	Unknown	2.10	100
3	M	6	Unknown	2.2	100
4	F	7	Unknown	4.3	79
5	F	7	Unknown	3.2	75
6	M	10	Unknown	4.6	83
Average	—	6.7	—	3.3	78.3

Abbreviations: CI, cochlear implant; F, female; M, male.

The procedure was performed at the electrophysiology laboratory of the institution in an acoustically treated room to minimize interference during the registry of the responses. The equipment Smart EP (Intelligent Hearing Systems, Miami, FL, USA) was used, with two recording channels. Channel A aimed to record the auditory evoked potentials in the right ear, and channel B, in the left ear. For both records, the active electrode was placed in Cz, connected to the input (+) of the preamplifier. The reference electrode was placed on the earlobe contralateral to the CI (A1/A2) and connected to the input (-). The ground electrode was positioned in Fpz and connected to the ground input of the preamplifier.

To record the responses, the electrodes were placed with Ten 20 (Weaver and Company, Aurora, CO, USA) conductive paste for the electroencephalogram (EEG), after proper skin preparation with Nuprep (Weaver and Company, Aurora, CO, USA) abrasive paste for the EEG/ECG to eliminate waste. The impedance was maintained between 1 and 3 kohms for the electrodes.

The stimuli were presented in free field, calibrated in dB HL (hearing level), with the loud speaker positioned at an angle of 90 azimuth and 40 cm away from the implanted ear side. The children remained alert, sitting comfortably in a reclining chair, and they were told to watch a silent video on a tablet during the procedure.

To obtain the CAEP with TB, the frequency of 1,000 Hz was used, and to obtain the CAEP with speech stimuli, the syllable /ba/ was used,¹² with interstimulus intervals of 500 ms. As input parameters, alternating polarity was used with

bandpass filter from 1 to 30 Hz, gain of 100,000 with a stimulation rate of 1.9 stimuli per second, and the response analysis window ranged from 100 ms pre-stimulus to 500 ms post-stimulus. Two promediations of 150 stimuli were presented at the intensity of 70 dB HL to confirm the reproducibility of the response.

To analyze the results, the P1 component was identified considering the first positive peak of greater amplitude found in the registry.^{11,21} The latency and amplitude values of P1 were analyzed and compared considering the type of stimulus and the two moments of evaluation.

Data were arranged in Microsoft Excel spreadsheets for statistical analysis with the support of an expert professional in the area. The Pearson correlation coefficient was calculated, and the significance level for all hypothesis tests was of 0.05 (5%). The confidence intervals were built with 95% of statistical confidence.

Results

► **Table 2** shows the behavior of the variable P1 latency (ms) of the CAEP elicited by simple TB and complex speech stimuli of the participants in the two evaluations performed.

The average behavior of the variable P1 latency in the two evaluations was the same for both groups, as shown in ► **Table 2**. There was no evidence of difference between the average of the the variable P1 latency comparing the two types of stimuli used in the CAEP, with no significant *p*-value (0.658).

Table 2 Descriptive statistics for the variable P1 latency (ms) with TB and speech stimuli in each evaluation

CAEP	Evaluation	n	Average	SD	Minimum	Median	Maximum	<i>p</i> -value
TB	1 st evaluation	6	113.7	25.50	92	107.0	162	0.023*
	2 nd evaluation	6	100.7	22.73	82	92.5	143	
Speech	1 st evaluation	6	120.3	15.47	104	116.5	150	0.023*
	2 nd evaluation	6	105.5	14.84	84	108.5	122	
TB x Speech								0.658

Abbreviations: CAEP, cortical auditory evoked potentials; n, number of individuals; SD, standard deviation; TB, tone burst.

Note: * *p*-value statistically significant.

Table 3 Descriptive statistics for the variable P1 (μV) amplitude with TB and speech stimuli in each evaluation

CAEP	Evaluation	n	Average	SD	Minimum	Median	Maximum	p-value
TB	1 st evaluation	6	5.4	2.09	2.56	5.30	8.25	0.423
	2 nd evaluation	6	6.5	3.39	3.57	5.17	12.27	
Speech	1 st evaluation	6	6.2	4.71	2.09	4.09	13.42	0.423
	2 nd evaluation	6	5.7	3.96	2.38	3.83	12.10	
TB x Speech								0.981

Abbreviations: CAEP, cortical auditory evoked potentials; n, number of individuals; SD, standard deviation; TB, tone burst.

However, it was observed that the average of latencies in the second evaluation for the two types of stimuli was considerably lower than in the first evaluation, showing a statistically significant difference ($p = 0.023$) for both TB and speech (→ **Table 2**).

Regarding the amplitude of the P1 component of the CAEP, → **Table 3** shows the behavior of the variable P1 amplitude (μV) in the CAEP elicited by the simple stimulus, TB, and the complex stimulus, speech, in each evaluation performed.

An opposite behavior of the variable P1 amplitude according to each stimulus was observed. With the use of the TB stimulus, there was an increase in the amplitude of the P1 component in the second evaluation in relation to the first; however, with the use of the speech stimulus, there was a decrease in the amplitude of P1 when comparing both evaluations. Nonetheless, there was no evidence of a significant difference between the average of the variable P1 amplitude considering the two types of stimuli ($p = 0.981$) and the two evaluations ($p = 0.423$).

→ **Table 4** shows the values of the Pearson correlation coefficient between the variables P1 latency versus TB (ms), P1 latency versus speech (ms), P1 amplitude versus TB (μV), P1 amplitude versus speech (μV), and the variable frequency in the aural rehabilitation.

→ **Table 4** also shows the p -values associated with the test in which the correlation linear coefficient of population is zero. In none of the four variables there was evidence of a linear association with the variable frequency in the aural rehabilitation ($p \geq 0.148$). It is worth highlighting, however, that the value of the Pearson correlation coefficient among the variables P1 latency with TB (ms) and frequency in aural rehabilitation was equal to 0.667, showing an increased

linear association. In other words, the higher the number of absences, the higher the value of P1 latency with TB. However, this association was not considered significant ($p = 0.148$), most likely due to the small sample size.

Discussion

This study aimed to verify the influence of aural rehabilitation in the parameters of latency and amplitude of the P1 component of the CAEP elicited by simple stimulus (TB) and complex stimulus (speech) in children with CIs attending aural rehabilitation at the institution.

The results found in the study were discussed and compared with the specialized literature. Due to the lack of a control group, the findings were analyzed according to studies that proposed normal standards for the latency and amplitude of the CAEP P1 component, in addition to providing data on the maturity of this component, which made it possible to differentiate the maturation effects from the stimulation effects provided by the aural rehabilitation in the children selected for this study.

→ **Table 1** shows the characteristics and specifications of each participant. According to Sharma et al (2002),¹¹ the plasticity of the central nervous system is most evident in the first years of life, and it decreases with age. The development of the central auditory pathways occurs gradually and linearly, and the maturational process is complete around the second decade of life, from 15 to 20 years old.^{13,14,22} The age group of this study ranged from 5 to 10 years old; therefore, in this period, the maturation is still occurring.

However, according to Sharma et al (1997),¹³ the ideal period for intervention in children with congenital hearing loss is up to 3.5 years old, because implanting the CI within

Table 4 Values of Pearson correlation coefficient associated to the test of non-linear association hypothesis between each variable and frequency in rehabilitation

Variables	Pearson correlation coefficient	p-value
Latency P1 TB (ms) x frequency in rehabilitation	0.667	0.148
Latency P1 Speech (ms) x frequency in rehabilitation	-0.029	0.957
Amplitude P1 TB (μV) x frequency in rehabilitation	0.406	0.425
Amplitude P1 Speech (μV) x frequency in rehabilitation	-0.029	0.957

this sensitive period allows more appropriate cortical maturation, resulting in the development of speech perception and oral language acquisition.^{16,17}

The same authors also affirmed that children implanted between 3.5 and 7 years old showed very different cortical responses and P1 latencies from those shown by children who were implanted after 7 years old, who remained late even after years of stimulation. It can be seen in ► **Table 1** that the average age of activation of the patients in this study was 3.3 years old; however, two participants (4 and 6 years old) implanted the CI after that ideal period, at 4.3 and 4.6 years old respectively.

Although both had exceeded the optimal period for intervention, the capture of the CAEP was quite different for the two participants, confirming variable results in children between 3.5 and 7 years old. The evaluation of the participant who was implanted at 4 years old was much faster, around 30 minutes, showing responses with great morphology and large amplitude of the P1 component. The participant who was implanted at 6, however, took twice as long to capture responses with better morphology, that is, responses that make it possible to clearly identify the P1 component of the CAEP.

Some authors^{12-14,18,23-25} elected the use of CAEP, mainly the P1 component, as the central auditory system maturation biomarker over the years, since several studies showed a reduction in the P1 latency according to age increase.^{12,13,23,25}

In a study by Sharma et al (1997),¹³ the P1 component in adults was less robust than in children, with latency around 50 ms. In contrast, in children, the P1 latency had a more robust peak, around 100 ms, with an average of 87 ms at 6 years old, reaching 74 ms at 10 years old.

Ponton et al (2000)²⁵ also found similar latency values for the component P1. At the age of 6, latency values were on average 85 ms, reducing to 64 ms at 10 years old. The latency values decreased following a more gradual pattern, while more abrupt decreases were observed in relation to the amplitude of the P1 component.

The study by Ventura et al (2009)²⁶ also aimed to characterize the maturation of the central auditory system in children with normal hearing thresholds. With age increase, there was an improvement in the morphology and a decrease in the values of latency and amplitude of the P1 component. Still, in relation to latency values, there was a statistically significant association between age and the P1 component, with an expected decrease in the latency value of 1.6 ms per year.

In this study, despite shorter latencies for the simple stimulus (TB), the average behavior of the variable P1 latency in the two evaluations was the same for both the CAEP elicited by TB and by speech, as noted in ► **Table 2**. Thus, there was no statistically significant difference between the stimuli, that is to say, independently of the eliciting stimulus, the variable P1 latency showed the same behavior pattern, with latency reduction in the second evaluation.

Regarding the values of the variable P1 latency, also in ► **Table 2**, for the CAEP with TB, the latency average of the P1 component was of 113.7 ms in the first evaluation, and

of 100.7 ms in the second evaluation, while for the speech stimulus, the latency average of P1 proved to be increased, with an average of 120.3 ms and 105.5 ms respectively. Thus, when comparing the P1 component latencies between the two evaluations with each eliciting stimulus alone, there was a statistically significant difference, with the variable P1 latency significantly lower in the second evaluation for both TB stimulus and for speech, with an average reduction of 13 ms and 14.8 ms respectively (► **Table 2**).

According to the obtained values, the differences between the two evaluations could not be justified only by maturation, as evidences from national and international studies show,^{13,25,26} demonstrating that the aural rehabilitation performed in the interval during the evaluations provided considerable changes in the P1 component of the CAEP, objectively reflecting in the neural plasticity. As observed before, according to the study by Ventura et al²⁶, a reduction of 1.6 ms per year can be expected for the P1 latency value; however, in this study, there was a change about ten times higher than expected from the natural maturation referred in the study by Ventura et al.²⁶ Therefore, we must consider the possibility that this reduction in latency may have been promoted as a result of the aural rehabilitation stimulation, plus the incidental use of hearing and language. However, to confirm this statement, further studies with larger samples and a control group are necessary.

In relation to the amplitude of the P1 component of the CAEP, the authors^{13,25,26} also showed a decrease over the years, as the central auditory pathways age. According to the study by Ventura et al²⁶, there was a reduction of 0.02 mV per year in the amplitude values of the P1 component.

In this study, the average of the variable P1 amplitude in the two evaluations was different, as shown in ► **Table 3**. There was an increase of variable P1 amplitude in the second evaluation of the CAEP TB, and a decrease in the variable P1 amplitude in the second evaluation of the CAEP speech.

However, there was no statistically significant difference in the amplitude of the variable P1 when comparing the results of the stimuli used in the CAEP in two evaluations (► **Table 3**). Thus, for TB, the behavior of variable amplitude did not corroborate the findings of these studies, and the same was observed for the speech stimuli. However, despite these concordant and discordant results in the literature, the comparison between the two stimuli showed no difference.

There was a large inter-subject variation in the responses of the CAEPs, leading to the conclusion that the clinical application of CAEP is most effective when the individual is compared with himself, in other words, the individual as his control.

Although the literature suggests an ideal period for intervention in congenital deaf children, the CI alone does not guarantee a satisfactory outcome; other factors, such as family involvement in the intervention process, contribute to the proper development of hearing and language skills.

Thabet and Said²⁰ observed in their study that an effective aural rehabilitation caused changes in the CAEP. The P1 component presented with significantly earlier latencies in individuals with adequate aural rehabilitation. Thus, the

component P1 can be regarded as a clinical tool to guide the choice of the intervention and its effectiveness, monitoring the results of aural rehabilitation. Moreover, it can be used for counseling the families of deaf children whose attendance in the aural rehabilitation program is inadequate.

A similar result occurred in the present study. Although it showed no correlation between the variables latency and amplitude of the P1 component and frequency in the aural rehabilitation (► **Table 4**), it found that there was a positive linear association for P1 latency with TB stimulus, that is, it was observed that the lower the attendance, the greater the value of the P1 latency with TB.

In face of the evidence found, the aural rehabilitation is an essential component to support the proper development of hearing and language skills. Family participation also becomes very important in the evolution process, as it is essential to bring to the child's daily life what was trained in rehabilitation, to talk about the achievements and difficulties, and to collaborate in the development of effective communication for the success of the process intervention.^{27,28}

Despite the CAEP being a type of procedure that requires more time to be performed, when properly registered in ideal conditions, it is a very efficient tool to monitor the behavior of the central auditory pathways in response to stimuli from the electronic devices and aural rehabilitation.

It is true that the performance of electrophysiological tests in children demands more time to suit the conditions of evaluation due to behavioral issues; however, the use of silent video in a tablet proved to be very effective to help controlling these individuals during the procedure, making it possible to add another important data to the study of hearing impaired subjects.

The topic discussed is still scarce; therefore, further studies with a larger sample and a longer longitudinal follow-up, including a control group of children with normal hearing thresholds and different therapeutic strategies can considerably contribute to provide important information regarding the maturation and the influence of stimulation through the CI and the effective aural rehabilitation in the CAEP of hearing impaired individuals.

Conclusion

According to the analysis of the results, a decrease in latency of the P1 component of the CAEP elicited by both simple stimulus (TB) and complex stimulus (speech) was observed within a three-month interval in children with CI undergoing aural rehabilitation.

Financial Support

Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - CAPES

Conflict of Interest

There are no conflicts of interest to declare.

References

- Costa OA. Implantes cocleares multicanais no tratamento da surdez em adultos. [Thesis]. Bauru: Faculdade de Odontologia de Bauru, Universidade de São Paulo; 1998
- Yoon PJ. Hearing loss and cochlear implantation in children. *Adv Pediatr* 2011;58(01):277-296
- Bevilacqua MC, Formigoni GMC. *Audiologia educacional: uma opção terapêutica para a criança deficiente auditiva*. Carapicuíba, São Paulo: Pró-fono; 1997
- Beynon AJ, Snik AFM, van den Broek P. Evaluation of cochlear implant benefit with auditory processing in experienced adult cochlear implant users. *Clin Neurophysiol* 2005;116(06):1235-1246
- Pantev C, Ross B, Wollbrink A, et al. Acoustically and electrically evoked responses of the human cortex before and after cochlear implantation. *Hear Res* 2002;171(1-2):191-195
- Kelly AS, Purdy SC, Thorne PR. Electrophysiological and speech perception measures of auditory processing in experienced adult cochlear implant users. *Clin Neurophysiol* 2005;116(06):1235-1246
- Gilley PM, Sharma A, Dorman MF. Cortical reorganization in children with cochlear implants. *Brain Res* 2008;1239:(1239):56-65
- Sharma A, Nash AA, Dorman M. Cortical development, plasticity and re-organization in children with cochlear implants. *J Commun Disord* 2009;42(04):272-279
- McNeill C, Sharma M, Purdy SC. Are cortical auditory evoked potentials useful in the clinical assessment of adults with cochlear implants? *Cochlear Implants Int* 2009;10(Suppl 1):78-84
- Reis ACMB, Frizzo ACF. *Potencial Evocado Auditivo de Longa Latência*. Bevilacqua MC, Martinez MAN, Balen SA, Pupo AC, Reis ACM, Frota S. *Tratado de Audiologia*. 1st ed. São Paulo: Santos; 2011
- Sharma A, Dorman MF, Spahr AJ. A sensitive period for the development of the central auditory system in children with cochlear implants: implications for age of implantation. *Ear Hear* 2002;23(06):532-539
- Ponton CW, Don M, Eggermont JJ, Waring MD, Kwong B, Masuda A. Auditory system plasticity in children after long periods of complete deafness. *Neuroreport* 1996;208(1):61-5
- Sharma A, Kraus N, McGee TJ, Nicol TG. Developmental changes in P1 and N1 central auditory responses elicited by consonant-vowel syllables. *Electroencephalogr Clin Neurophysiol* 1997;104(06):540-545
- Sharma A, Martin K, Roland P, et al. P1 latency as a biomarker for central auditory development in children with hearing impairment. *J Am Acad Audiol* 2005;16(08):564-573
- Kral A, Sharma A. Developmental neuroplasticity after cochlear implantation. *Trends Neurosci* 2012;35(02):111-122
- Kral A, Eggermont JJ. What's to lose and what's to learn: development under auditory deprivation, cochlear implants and limits of cortical plasticity. *Brain Res Rev* 2007;56(01):259-269
- Ganek H, McConkey Robbins A, Niparko JK. Language outcomes after cochlear implantation. *Otolaryngol Clin North Am* 2012;45(01):173-185
- Jang JH, Jang HK, Kim SE, Oh SH, Chang SO, Lee JH. Analysis of p1 latency in normal hearing and profound sensorineural hearing loss. *Clin Exp Otorhinolaryngol* 2010;3(04):194-198
- Nash A, Sharma A, Martin K, Biever A. Clinical applications of the p1 cortical auditory evoked potential (CAEP) biomarker. *Seewald R, Bamford J*. 2007:43-9
- Thabet MT, Said NM. Cortical auditory evoked potential (P1): a potential objective indicator for auditory rehabilitation outcome. *Int J Pediatr Otorhinolaryngol* 2012;76(12):1712-1718
- Sharma A, Dorman MF, Kral A. The influence of a sensitive period on central auditory development in children with unilateral and bilateral cochlear implants. *Hear Res* 2005;203(1-2):134-143
- Ponton CW, Don M, Eggermont JJ, Waring MD, Masuda A. Maturation of human cortical auditory function: differences between

- normal-hearing children and children with cochlear implants. *Ear Hear* 1996;17(05):430–437
- 23 Sharma A, Dorman MF, Spahr AJ. Rapid development of cortical auditory evoked potentials after early cochlear implantation. *Neuroreport* 2002;13(10):1365–1368
- 24 Wunderlich JL, Cone-Wesson BK, Shepherd R. Maturation of the cortical auditory evoked potential in infants and young children. *Hear Res* 2006;212(1-2):185–202
- 25 Ponton CW, Eggermont JJ, Kwong B, Don M. Maturation of human central auditory system activity: evidence from multi-channel evoked potentials. *Clin Neurophysiol* 2000;111(02):220–236
- 26 Ventura LMP, Costa Filho OA, Alvarenga KF. Maturação do sistema auditivo central em crianças ouvintes normais. *Pró-Fono R Atual Cient* 2009;21(02):101–106
- 27 Figueiredo CC, Gil D. Avaliação do grau de envolvimento familiar nos atendimentos de crianças com deficiência auditiva. *Audiol Communic Res* 2013;18(04):303–307
- 28 Fortes PC. Satisfação de pais de crianças deficientes auditivas quanto ao desenvolvimento auditivo e de linguagem: construindo indicadores de qualidade em um serviço de saúde auditiva [Dissertation]. São Paulo: Pontifícia Universidade Católica de São Paulo; 2009