The Journal of International Advanced Otology

J Int Adv Otol 2015; 11(3): 229-35 ● DOI: 10.5152/iao.2015.1695

Original Article

# Satisfaction of Children with Auditory Neuropathy and Cochlear Implant

**Guilherme Machado de Carvalho, Thiago M. Zago, Priscila Z. Ramos, Arthur M. Castilho, Alexandre C. Guimarães, Edi L. Sartorato**

Department of Ear Nose Throat, Head and Neck Surgery, Campinas University, Campinas, São Paulo, Brazil (GMC, TMZ, AMC, ACG)
Center for Molecular Biology and Genetic Engineering, Campinas University, Campinas, São Paulo, Brazil (PZR, ELS)

**OBJECTIVE:** In auditory neuropathy (AN) a dyssynchrony in the nerve conduction of the auditory nerve fibers is observed. Typically, patients with AN exhibit moderate to profound sensorineural hearing loss, and treatment using cochlear implants (CIs) or hearing aids should be performed as early as possible for a better hearing rehabilitation. The aim of this study is to evaluate the satisfaction level of patients with AN spectrum disorder treated using CIs. The Satisfaction with Amplification in Daily Life questionnaire was selected to evaluate 10 patients with AN treated using CIs.

**MATERIAL and METHODS:** Clinical study of patients with AN spectrum disorder submitted to CI. A retrospective data analysis, genetic and clinical evaluation in a tertiary referral center was done.

**RESULTS:** The means of the subscales for positive effects, services and costs, negative factors, and personal image were 6.15, 4.6, 3.26, and 3.33, respectively.

**CONCLUSIONS:** Patients with AN treated using CIs consider themselves satisfied.

**KEYWORDS:** Auditory neuropathy spectrum disorder, evoked auditory brainstem response, otoacoustic emissions, GJB2, hearing loss

## INTRODUCTION

Hearing Loss (HL) is one of the most common disorders that affect newborns in developed societies, with an incidence of 1:1000 births [1]. Normal speech development is a desirable goal for the family of these patients [2].

Currently, cochlear implants (CIs) are widely accepted for the treatment of severe to profound sensorineural hearing loss (SNHL), and since its approval in 1990 by the Food and Drug Administration for the treatment of deafness in children above 2 years of age, the number of implants in children has been growing tremendously [3]. The indications of cochlear implantation in patients are divided into pre- and postlingual deafness.

For children under 6 years, the indications are as follows: bilateral severe to profound SNHL, no benefits from conventional hearing aids (HA), and adequate family motivation [4, 5].

For children between 7–12 years of age, the following indications in addition to the above criteria are considered: sentence recognition result ≤50% in the open format using HA, with worse hearing and sentence recognition result <60% with better hearing and the presence of linguistic code set [4, 5].

Auditory neuropathy (AN) is one of the many causes of deafness. It is a hearing disorder caused by a change in the function of the inner hair cells and/or the involvement of the auditory nerve fibers with dyssynchrony in this nerve conduction [4, 5].

Auditory neuropathy is considered as a spectrum of disorders affecting the auditory pathway. The knowledge about their actual pathophysiological origins is limited [6, 7].

A study by Manchaiah et al. [8], which looked into the causes of auditory neuropathy spectrum disorders (ANSD), showed that in 42% of the patients the disorder was associated with hereditary neurological disorders, in 10% of the patients it was associated with toxic, metabolic, immunological, and infectious causes, and in 48% of the patients the cause was unknown [8].

**Presented in:** This study was presented at the 13th International Conference on Cochlear Implants and Other Implantable Auditory Technologies, 18-21 June 2014, Munich, Germany.

**Corresponding Address:** Guilherme Machado de Carvalho, E-mail: guimachadocarvalho@gmail.com

**Submitted:** 23.10.2015 **Accepted:** 04.01.2016

Patients with AN may present several degrees of HL and changes in speech discrimination. Otoacoustic emissions (OAEs) are usually normal with the absence of Brainstem Evoked Response Auditory/Auditory BrainStem Response (BERA/ABR), which is the most frequent clinical findings/phenotypes. The cochlear microphonic may be present and acoustic reflexes absent [9]. Typically, patients with AN exhibit moderate to profound SNHL, present worse speech discrimination, and have severe difficulties in speech perception in a noisy environment.

The treatment of patients with AN using CIs or HAs should be performed as early as possible to achieve better hearing rehabilitation [10].

Speech perception testing has become the gold standard for objectively measuring CI outcomes in adults. There are two basic ways to measure speech perception in individuals who have already learned to speak: (A) word recognition tests and (B) sentence recognition tests [11].

For children who are too young to speak, observations of the child's hearing-related behavior are made and quantified. For example, a commonly used test, the Infant-Toddler Meaningful Auditory Integration Scale (IT-MAIS), uses a structured parent interview to assess auditory behaviors, such as the child's behavior while using an HA or CI, the child's response to his or her name, and the child's awareness of environmental sounds [12, 13].

The hearing rehabilitation of patients with AN should be held as earlier as possible so that they can achieve the best possible outcomes that can be achieved using speech therapy, CIs, or HAs [6].

In most cases of AN with severe to profound HL, benefits has been demonstrated when treated with early cochlear implantation. However, in AN with mild to moderate HL, these benefits are uncertain, and the management of these cases remains a challenge [7, 14]. The outcomes of CI are conflicting, and the most plausible explanation for this is the heterogeneity of the AN etiology [15].

The improvement of speech development in children with AN using CIs was evaluated by a recent systematic review that showed favorable results after the cochlear implantation; however, it concluded that the evidence in the favor of CIs is weak and more studies are needed to clarify the best situations to perform cochlear implantation in patients with AN [16].

It is not surprising that the auditory performance of cochlear implantation in patients with AN is variable, considering the AN etiological heterogeneity. Therefore, the use of CIs for patients with AN has been reported to be relatively controversial [17].

The aim of this retrospective study was to evaluate the satisfaction levels of patients with AN treated using CIs.

We believe that these findings are of great importance to all professionals who work with patients with AN, such as pediatricians, otolaryngologists, audiologists, geneticists, and researchers.

The underlying causes and treatment options of AN are very discussed in the literature and remain uncertain; therefore, the study of satisfaction levels of patients with AN with CI can help to guide new studies, new discoveries and the interface of these disease with new discoveries.

## MATERIAL and METHODS

We conducted a cross, retrospective, observational study through the analysis of medical records of patients with bilateral HL and clinical diagnosis of AN, accompanied in the auditory health care service of a tertiary care university hospital which undertook a CI surgery.

The analyzed variables were age, gender, HL onset (congenital, childhood, adolescent, or adult), previous pregnancies, perinatal and genetic data, and electrophysiological test results [ABR, transient and distortion product OAEs, and the search of cochlear microphonism (CMs)].

Perinatal and pregnancy history or any other situation such as prematurity, jaundice, kernicterus, admission to neonatal intensive care unit, meningitis, severe neonatal infections (such as pneumonia and sepsis), genetic syndromes, concomitant neurological diseases, infectious diseases (such as measles and toxoplasmosis), clinical systemic comorbidities (such as hypertension and diabetes), and a family history of deafness were described in the background of these patients.

Age groups, based on the age reported at the early onset of symptoms, were defined as follows: congenital (up to 1 year old), childhood (between 1 and 10 years old), adolescent (between 11 and 18 years of life), and adult (over 18 years of life).

The clinical diagnosis of AN was established as follows: absent or abnormal ABR with the preservation of OAEs and/or CMs. All patients had no acoustic reflex, and the presence of the cochlear nerve was assessed using nuclear magnetic resonance (MRI) and computed tomography (CT).

### Inclusion and Exclusion Criteria

Inclusion criteria were as follows: patients with AN who underwent to CI, with bilateral SNHL, normal otoscopy, absence of middle ear disease, and no acoustic reflex.

Clinical spectrum of AN was considered when audiological tests were compatible with either of the following:

A) OAE present and ABR absent
B) OAE absent, ABR absent, and CMs present
C) OAE absent, ABR absent, hearing thresholds present, and a clinical suspicion of AN.

Imaging (MRI/CT) showing the presence of cranial nerve VIII and excluding retrocochlear alterations.

Patients who did not fulfill these criteria were excluded from the study.

Sample: Patients with a clinical diagnosis of AN who presented to the auditory health care service of a tertiary care university hospital in the last 3 years submitted to CIs.

Only patients who underwent audiological and electrophysiological testing with with the same professionals, with the same equipment were included in the sample.

**Audiological Evaluation**

Audiological tests including impedanciometry, speech and pure tone audiometry were performed. The tests were performed using an audiometer AC30-SD25 (Interacoustics; Copenhagen, Denmark), calibrated according to ISO 389 standards/64.

The OAEs distortion products were performed at frequencies of 700–8000 Hz, a stimulus of 65–55 dB SPL, and a frequency ratio of 1.22. OEA was considered to be present when the signal/noise ratio was >6 dB and with a reproducibility ≥70%.

The tests from the ABR and CM were performed with insert earphones. A stimulus of 100 dB HL was used for the ABR covered with frequencies between 250 and 8,000 Hz, with a duration of 100 microseconds, and condensed and rarefied polarities. The abnormality of ABR was defined as the absence of wave formation or severe changes in morphology of the same with up to 100 dB HL stimulus.

Cochlear microphonism was evaluated in ABR tests, with the feature of inverting the polarity (condensed and rarefied). When CM was positive with stimuli of 100 dB HL electrophysiological thresholds, in decreasing order was researched.

For ABR, which was repeated at least twice, the device AT-235 (Interacoustics) was used.

Hearing loss impairment was classified through audiometry stratification in mild, moderate, severe/severe, or profound HL [18].

Speech perception tests: During preoperative evaluation, all patients underwent a speech perception test on the day of their surgery. The speech perception test is based on several studies in the English language adapted and developed for the Portuguese language by Bevilacqua et al. [19]. Patients performed the tests using HAs, in a quiet place (best aided condition).

Postoperatively, all subjects repeated the speech perception test at least one year experience with CI. The tests were performed using CI. The same audiologist performed all tests (pre-and postoperative).

Three protocols were used to evaluate the patients' speaking and hearing performance because most of them were children and pre-lingual developed. The scales used were as follows: IT-MAIS, a questionnaire assessing auditory outcomes, the Meaningful Use of Speech Scale (MUSS), a questionnaire for assessing oral language, and Glendonald Auditory Screening Procedure (GASP), which reviews speech perception in profound deaf children ≥5 years old [20-23].

Such scales are widely used in this age group of patients and are adapted to the Portuguese language. IT-MAIS and MUSS are questionnaires that are answered by the parents, but the evaluator determines the score based on the examples that the parents give for each question. It is a way of assessing patients in the first year of implant because they are still in receptive language and has no spoken language, pointing out that the IT-MAIS has a greater focus on hearing and the MUSS score on language acquisition [19-22]. The GASP has been used in patients with more than five years.

Subjective evaluations: After the postoperative speech tests, patients were asked to rate the quality of their experience with CI compared with the experience prior to the implantation on a Likert scale ranging from 0 to 10, similar to the visual analog scale. A score of 0 indicates that the user regretted the implantation and does not recommend it to others and that he/she had been better before the implantation, with their HAs. A score of 10 indicates that the user was completely satisfied with the work and highly recommends it to others.

**Satisfaction with Amplification in Daily Life (SADL)**

The SADL questionnaire was selected to evaluate the study sample. It was translated into Portuguese and adapted to our cultural aspects by Mondelli et al. [23]; it was validated by Danieli et al. [24]. The questionnaire results in an overall satisfaction score and a profile of subscales that address positive effects, service and value, negative characteristics, and personal image.

Satisfaction with Amplification in Daily Life questionnaire was prepared to assess overall patient satisfaction with the use of HA. By identifying the factors that contribute to satisfaction and to try to confirm these attributes to the processes involved, this test has the potential to qualify and analyze the quality of health services [13, 24, 25].

The SADL questionnaire has 15 questions, divided into four subscales, reflecting overall satisfaction. 1) Positive effects: six items related to acoustic and psychological benefit. 2) Service and value: three items related to professional competence, product price, and number of repairs. 3) Negative factors: three items related to environmental noise amplification and phone use. 4) Personal image: four items related to esthetics and the stigma of HA use [25].

Items are rated such that satisfaction is reflected by the high score. A score is generated for each of the four subscales and each subscale score is computed from the average of the answers to the questions.

To answer the 15 questions, a scale of 7 points from the same period that corresponded to a categorical scale from "not at all" to "very much" satisfied was used. For 11 questions, "very much" indicated total satisfaction and was scored 7, whereas "not at all" indicated complete dissatisfaction and was scored 1. The other four questions were inverted, where "very much" indicated complete dissatisfaction and scored 1, whereas "not at all" indicated overall satisfaction and scored 7 [13, 25, 26].

**Molecular Study**

Genomic DNA was extracted from patients' peripheral venous blood according to standard protocols. GJB2 gene mutations were screened by direct sequencing of the gene coding region [13, 14, 27, 28] and the exon 1 and flanking splice donor site [29, 30].

Genomic DNA was extracted from the peripheral blood of patients, according to standard protocols. All samples were tested for mutations in the GJB2 gene, including deletions del(GJB6-D13S1830) and del(GJB6-D13S1854), mitochondrial mutation m.A1555A>G in the MTRNR1 gene, and p.Q829X mutation in the OTOF gene.

Mutations in the GJB2 gene were screened by direct sequencing of the coding region of the gene [13, 14, 29, 31]. Multiplex-PCR method-

ology was used to detect the del (GJB6-D13S1830) and del (GJB6-D13S1854) in the GJB6 gene [29, 30]. The investigation of mutations m.1555A>G and p.Q829X was performed using PCR amplification followed by digestion with BsmAI and BfaI restriction endonucleases, respectively [13, 14, 29, 31].

**Statistical Analysis**

The data were analyzed using descriptive analysis, with the production of means, medians, standard deviation tabs. The software SIGMA XL was used to perform all statistical analysis (SigmaXL Inc.; Kitchener, Ontario, Canada)

The Chi-square text was used to compare the groups of our sample. Because of the small size of some of the variables analyzed, Fisher's Exact test was also used to check the correlation between the groups.

The confidence Interval was of 95%, and a p value of <0.05 was considered statistically significant.

**Ethical Considerations**

This study was approved by the Ethics Research Committee of the Campinas University (FCM–UNICAMP, Report number 396/2006).

## RESULTS

Nineteen subjects were initially selected for the study, but only 10 (seven males and 3 females) passed all the inclusion and exclusion criteria.

The average age of the patients at the CI surgery was 4 years and 4 months, ranging from 2 years and 6 months to 6 years and 1 month. The average CI use was for 5 years and 3 months. AN was identified in 50% of the cases because patients had OAE present with ABR being abnormal or absent. The others 50% of patients have CM present with ABR being abnormal or absent.

Pathogenic variants that accounted for HL were detected in three patients (30%), all of them homozygous for the c.35delG mutation, at conexin 26 (GJB2) gene.

In all cases, the onset of symptoms appeared at birth. The past history of those subjects was as follows: 60% were premature (average, 33 weeks of pregnancy), 60% ate Neonatal Intensive Care Unity (average, 25 days), 10% had neonatal jaundice, 10% had cardio respiratory failure, 10% had family history of SNHL (brother with SNHL). No cases had meningitis.

The overall satisfaction score (Likert scale, ranging 0–10) was 8 (average). The median and mode were both 8, and the standard deviation was ±1. The minimum score was 7 and the maximum score was 9, one patient at each score (Tables 1, 2).

The SADL results are shown in Figure 1.

## DISCUSSION

This is an important topic given the ambiguity of the current outcome data and clinical guidelines, the invasiveness of the therapy combined with significant potential, and the fact that it is generally the proxy decision-makers who decide whether to perform a cochlear implantation on children.

**Table 1.** Distribution of the mean results to the SADL questionnaire subscales

| Subscale | Mean | Median | Standard deviation | Percentile 20 | Percentile 80 |
|---|---|---|---|---|---|
| Positive effects | 6.15 | 7 | 1.09 | 5 | 7 |
| Services and costs | 4.6 | 5 | 2.16 | 2.8 | 7 |
| Negative factors | 3.26 | 3 | 1.50 | 2 | 5 |
| Personal Image | 3.33 | 2.5 | 2.41 | 1 | 6 |

SADL: satisfaction with amplification in daily life

**Table 2.** Distribution of the mean value results between the first and the second application of each question in the SADL questionnaire as to the mean/average, media, minimum value, maximum value, and standard deviation

| SADL question | n (s) | Mean | Median | Min | Max | SD |
|---|---|---|---|---|---|---|
| 1 | 10 | 6.4 | 7 | 4 | 7 | 1.26 |
| 2 | 10 | 3.8 | 2 | 2 | 6 | 1.68 |
| 3 | 10 | 6.6 | 7 | 5 | 7 | 0.84 |
| 4 | 10 | 3 | 2.5 | 1 | 7 | 2.26 |
| 5 | 10 | 6 | 6 | 5 | 7 | 0.94 |
| 6 | 10 | 6.3 | 7 | 4 | 7 | 1.05 |
| 7 | 10 | 2.9 | 3 | 2 | 3 | 0.31 |
| 8 | 10 | 4.9 | 6 | 1 | 6 | 2.07 |
| 9 | 10 | 6.3 | 7 | 4 | 7 | 1.25 |
| 10 | 10 | 5.3 | 6 | 4 | 6 | 0.94 |
| 11 | 10 | 3.1 | 2 | 1 | 7 | 2.02 |
| 12 | 10 | 6.7 | 7 | 6 | 7 | 0.48 |
| 13 | 10 | 2.1 | 1 | 1 | 7 | 2.33 |
| 14 | 10 | 2.3 | 1.5 | 1 | 4 | 1.49 |
| 15 | 10 | 4.8 | 5 | 3 | 7 | 1.54 |

s: subjects; min: minimum; max: maximum; SD: standard deviation; SADL: satisfaction with amplification in daily life

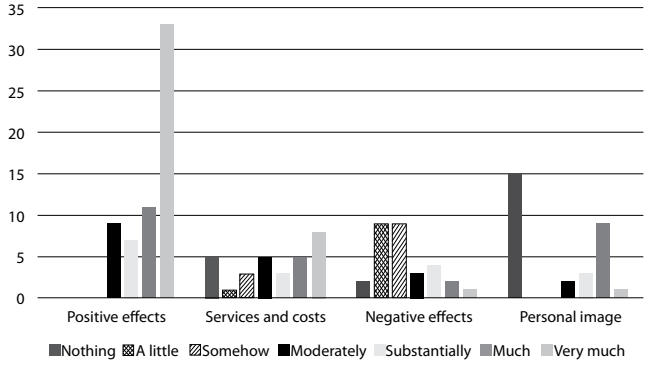


**Figure 1.** Illustration of the mean results to the SADL Questionnaire subscales
SADL: Satisfaction with Amplification in Daily Life

Satisfaction with Amplification in Daily Life is a questionnaire that was developed to evaluate the degree of satisfaction attributed to a hearing device for people with hearing disorders. This questionnaire evaluates several factors and is very useful to define how satisfied the patient is in daily life situations after the use of a hearing device.

In this study the SADL questionnaire was used to evaluate the satisfaction of children with AN after at least one year of cochlear implantation, the results showed that the positive effects were very high, with very low negative factors, costs or negative effects on personal image of the patients, indicating that cochlear implantation proved to be good for these patients.

Modern CI systems have become highly effective in helping patients to perceive and understand speech. Compared with other disabled people, those with severe to profound deafness have historically the lowest median education achievement level, the lowest median annual family income, the lowest rate of participation in the labor force, the lowest rate of persons in professional and technical jobs, and the poorest self-rated general health [30].

There is clear evidence that children who undergo cochlear implantation at a younger age have significantly better hearing outcomes than those undergoing at an older age. It is thought there is a window of time in the first few years of life during which implantation is critical to achieve maximum benefit. Beyond which the child's brain becomes less plastic or adaptable, and it begins to lose its ability to develop new neural pathways in response to the new auditory input that a CI provides [32].

Cochlear implantation has dramatically changed the outcomes for these patients because it provides auditory information that was available through conventional HA technology. In a study conducted by Geers et al. [33] comparing both technologies, a large percentage of young patients who have underwent cochlear implantation had auditory characteristics within the normal range [34].

Treatment CI not only improves the ability to hear but also improves the ability to acquire speech and language skills; it brings about greater success within the education system, better employment status, and improves the patient's quality of life. In addition, CIs provide benefits to the society in terms of decreased educational costs and restoration of work productivity potential [35].

A positive impact on a deaf child's quality of life is profoundly related to CI, with benefits seen more clearly in the preteen and teenage years. Quality of life (QOL) is defined as an individual's contentment or satisfaction with life [34].

Despite the first disappointing results of CI in children with AN, lately there has been an increasing number of studies showing a promising outcome of CI in such patients. Children with AN without any benefits from HAs seem to achieve significant benefits from CI. A reasonable explanation would be that CI provides adequate stimulation of the auditory pathway to overcome the existing dyssynchrony [36, 37].

It seems that in many cases acoustic stimulation, even when amplified by a conventional HA, will not be sufficient to overcome the auditory dyssynchrony. Thus, some of these children's speech perception will be very poor, resulting in disappointing language development skills. On the other hand, most of these children will achieve satisfactory speech perception and development following CI probably because the electric stimulation through the CI overcomes the existing auditory dyssynchrony [38].

Altogether, hearing rehabilitation with electronic devices such as HA, CI is beyond the HA performance, showing benefits to the patient's perceptions in everyday communication, self-esteem improvement, social life activities, and overall health [39-42].

Mutations in the connexin 26 (GJB2) gene are a common cause of genetic SNHL in many populations [29, 31]. However, there is no scientific evidence to support the real relationship between AN and mutations in the connexin 26 gene. Two studies detected mutations in this gene among patients with AN [43-45].

The auditory performance of cochlear implanted patients with mutations in the GJB2 gene is controversial in literature. Some studies report better results for GJB2-related HL, whereas others find no difference when compared to other causes [46, 47].

Genetic testing combined with clinical and audiological exams allows an accurate diagnosis, as well as the development of specific treatments and genetic counseling for patients and/or families.

Many subjective and psychosocial factors are related to the adaptation of HAs and CIs. The professionals involved need to know how to evaluate and validate them to make the adaptation easier and faster for the patients. Patients and their families must be informed that the device will not restore normal hearing, but it will support the acquisition of more acoustic information. Furthermore, hearing rehabilitation activities should be introduced when the patient starts using the device.

Although the benefits of CIs are well stablished and demonstrated, its cost-effectiveness must be considered. This device is more expensive than other forms of hearing rehabilitation devices, which can limit its use at the public health system. In some cases, patients who could benefit from this technology have to wait for a considerable time to undergo surgery if they cannot afford the procedure in a non-public hospital. We hope that in the near future, with the spread of this technology, CIs become less expensive and more accessible [48, 49].

Cochlear implants can positively impact the life of hearing impaired subjects, which has been demonstrated in multiple reports. Satisfaction surveys through questionnaires have been performed for evaluating these positive effects [50-53].

It can be considered a challenge to evaluated this topic using developing methodologies to systematically assess outcomes, particularly for moderate AN in young children. The small sample size of this study does not render the results insignificant, the bias of this study is the limited number of patients (n=10) which needs to be pointed out when analizing the results and conclusions.

Another difficult of these results is that the measurements used, particularly on the young children, it is a combination of objective measures and parental observation reports. This may a cause a bias because it is difficult to make a safe way of how integrated these information, and particularly about the parental observation can be very subjective.

This study concludes that the assessed patients with AN were satisfied with the CI intervention as analyzed using the SADL questionnaire .

**Ethics Committee Approval:** Ethics committee approval was received for this study from the ethics committee of School of Medical Sciences of Campinas University (UNICAMP, São Paulo, Brazil) /Report number 396/2006.

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - G.M.C.; Design - G.M.C.; Supervision - A.M.C., E.L.S.; Resources - G.M.C., P.Z.R.; Materials - G.M.C.; Data Collection and/or Processing - G.M.C., T.M.Z., P.Z.R.; Analysis and/or Interpretation - G.M.C., A.C.G.; Literature Search - G.M.C., T.M.Z., P.R., A.C.G.; Writing Manuscript - G.M.C., T.Z., P.R., A.C.G.; Critical Review - G.M.C., A.C.G., E.L.S.; Other - G.M.C.

**Acknowledgements:** We would like to thank all patients and their families for entitle the possibility of this study. We would also like to mention all members of our department, such as professors, medical assistants, ENT resident (special to Dr. Fernando L. Fernandes), audiologists, speech therapists, geneticists, nurses, assistants, administrative and everyone who helped directly and indirectly the execution of our projects. The present study, including the protocols for subject recruitment and assessment, the informed consent for participants, and the overall analysis plan were reviewed and approved by the Faculty of Medical Sciences-UNICAMP and the Center for Molecular Biology and Engineering (CBMEG), São Paulo, Brazil, by their doctoral programs and research ethics committees. The authors would also like to thank their University, their Department, their patients and every person who supported them in performing their research. This article is part of a doctoral project that is funded by CAPES (Higher Education Personnel Improvement Coordination, Ministry of Health, Brazil). The authors would like to thank to the Institutional Support from CNPq (National Council for Scientific and Technological Development).

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study has received no financial support. This article is part of a doctoral project that is fomented by CAPES (Higher Education Personnel Improvement Coordination - Ministry of Health - Brazil).

## REFERENCES

1. JCIH - Joint committee on infant hearing: principles and guidelines for early hearing detection and intervention programs (position statement). Pediatrics 2007; 120: 898-921.
2. Vohr B, Jodoin-Krauzyk J, Tucker R, Johnson MJ, Topol D, Ahlgren M. Early language outcomes of early-identified infants with permanent hearing loss at 12 to 16 months of age. Pediatrics 2008; 122: 535-44. [CrossRef]
3. Peixoto MC, Spratley J, Oliveira G, Martins J, Bastos J, Ribeiro C. Effectiveness of cochlear implants in children: Long term results. Int J Pediatr Otorhinolaryngol 2013; 77: 462-8. [CrossRef]
4. Sutton Gravel J, Hood LJ, Lightfoot G, Mason S, Sirimanna T, Stevens J, et al. Assessment and management of auditory neuropathy/auditory dyssynchrony. NHSP AN/AD Protocol 2008; 1(Pt 1).
5. El-Badry MM, McFadden SL. Evaluation of inner hair cell and nerve fiber loss as sufficiently pathologies underlying auditory neuropathy. Hear Res 2009; 255: 84-90. [CrossRef]
6. Berlin CI, Hood LJ, Morlet T, Wilensky D, Li L, Mattingly KR, et al. Multi-site diagnosis and management of 260 patients with auditory neuropathy/dys-synchrony (auditory neuropathy spectrum disorder). Int J Audiol 2010; 49: 30-43. [CrossRef]
7. Nikolopoulos TP. Auditory dyssynchrony or auditory neuropathy: Understanding the pathophysiology and exploring methods of treatment. Int J Pediatr Otorhinolaryngol 2014; 78: 171-3. [CrossRef]
8. Manchaiah VK, Zhao F, Danesh AA, Duprey R. The genetic basis of auditory neuropathy spectrum disorder (ANSD). Int J Pediatr Otorhinolaryngol 2011; 75: 151-8. [CrossRef]
9. Berlin CI, Hood LJ, Morlet T, Wilensky D, John P, Montgomery E, et al. Absent or elevated middle ear muscle reflexes in the presence of normal otoacoustic emissions: a universal finding in 136 cases of auditory neuropathy/dys-synchrony. J Am Acad Audiol. 2005; 16: 546-53. [CrossRef]
10. Roush P, Frymark T, Venediktov R, Wang B. Audiologic management of auditory neuropathy spectrum disorder in children: a systematic review of the literature. Am J Audiol 2011; 20: 159-70. [CrossRef]
11. Wilson BS, Dorman MF. The design of cochlear implants. In: Niparko JK, editor. Cochlear implants: principles & practice. 2nd edition. Philadelphia: Lippincott Williams & Wilkins; 2009. p. 95-135.
12. Robins AM, Rensaw JJ, Berry SW. Evaluating meaningful auditory integration in profoundly hearing-impaired children. Am J Otol 1991; 12 (Suppl): 144-50.
13. McLeod B, Upfold L, Broadbent C. An investigation of the applicability of the inventory, satisfaction with amplification in daily life, at 2 weeks post hearing aid fitting. Ear Hear 2001; 22: 342-7. [CrossRef]
14. Prezant TR, Agapian JV, Bohlman MC. Mitochondrial ribosomal RNA mutation associated with both antibiotic-induced and non-syndromic deafness. Nat Genet. 1993; 4: 289-94. [CrossRef]
15. Migliosi V, Modamio-Hoybjor S, Moreno-Pelayo MA. Q829X, a novel mutation in the gene encoding otoferlin (OTOF), is frequently found in Spanish patients with prelingual non-syndromic hearing loss. J Med Genet 2002; 39: 502-6. [CrossRef]
16. Jeon JH, Bae MR, Song MH, Noh SH, Choi KH, Choi JY. Relationship between electrically evoked auditory brainstem response and auditory performance after cochlear implant in patients with auditory neuropathy spectrum disorder. Otol Neurotol 2013; 34: 1261-6. [CrossRef]
17. Hayes D, Sininger YS, Northern J. Guidelines for identification and management of infants and young children with auditory neuropathy spectrum disorder. Conference NHS 2008, Como, Italy.
18. Goodman A. Reference zero levels for pure-tone audiometers. ASHA 1965; 7: 262-73.
19. Bevilacqua MC, Banhara MR, Da Costa EA, Vignoly AB, Alvarenga KF. The Brazilian Portuguese hearing in noise test. Int J Audiol 2008; 47: 364-5. [CrossRef]
20. Nascimento LT. Uma proposta de avaliação da linguagem oral [monografia]. Bauru: Hospital de Pesquisa e Reabilitação de Lesões lábio-Palatais, 1997. Adaptado de: Robbins AM, Osberger MJ. Meaningful use of speech scales. Indianápolis: University of Indiana School of Medicine, 1990.
21. Bevilacqua MC, Tech EA. Elaboração de um procedimento de avaliação de percepção de fala em crianças deficientes auditivas profundas a partir de cinco anos de idade. In: Marchesan IQ, Zorzi JL, Gomes ICD, editores. Tópicos em Fonoaudiologia. São Paulo: Lovise; 1996. P. 411-33. Adaptado de Erber N. Glendonald auditory screening procedure. Auditory training 1982; 47: 71.
22. Castiquini EAT. Escala de integração auditiva significativa: procedimento adaptado para a avaliação da percepção da fala [dissertação]. São Paulo: Pontifícia Universidade Católica; 1998. Adaptado de: Zimmerman-Phillips S; Osberger MJ; Robbins AM. Infant-Toddler: Meaningful Auditory Integration Scale (IT-MAIS). Sylmar, Advanced Bionics Corporation, 1997.
23. Mondelli MF, Magalhães FF, Lauris JR. Cultural Adaptation of the SADL (Satisfaction with Amplification in Daily Life) questionaire for Brazilian Portuguese. Braz J Otorhinolaryngol 2011; 77: 563-72. [CrossRef]
24. Danieli F, Castiquini EA, Zambonatto TC, Bevilacqua MC. Avaliação do nível de satisfação de usuários de aparelhos de amplificação sonora individuais dispensados pelo Sistema Único de Saúde. Rev Soc Bras Fonoaudiol. 2011; 16: 152-9. [CrossRef]
25. Cox RM, Alexander GC. Measuring Satisfaction with Amplification in Daily Life: the SADL scale. Ear Hear 1999; 20: 306-20. [CrossRef]
26. Cook JA, Hawkins DB. Outcome measurement for patients receiving hearing aid services. Laryngoscope 2007; 117: 610-3. [CrossRef]
27. Denoyelle F, Weil D, Wilcox AS. Prelingual deafness: high prevalence of a 30delG mutation in the connexin 26 gene. Hum Molec Genet 1997; 6: 2173-7. [CrossRef]
28. Kelsell DP, Dunlop J, Stevens HP, Lench NJ, Liang JN, Parry G, et al. Connexin 26 mutations in hereditary non-syndromic sensorineural deafness. Nature 1997; 387: 80-3. [CrossRef]

29. Del Castillo FJ, Rodríguez-Ballasteros M, Alvares A. A novel deletion involving the connexin 30 gene del(GJB6-D13S1854), found in trans with mutations in the GJB2 gene (connexin 26) in subjects with DFNB1 nonsyndromic hearing impairment. J Med Genet 2005; 42: 588-94. [CrossRef]
30. Baldassari CM, Schmidt C, Schubert CM, Srinivasan P, Dodsan KM, Sismanis A. Receptive language outcomes in children after cochlear implantation. Otolaryngol Head Neck Surg 2009; 140: 114-9. [CrossRef]
31. Del Castillo I, Moreno-Pelayo MA, Del Castillo FJ. Prevalence and evolutionary origins of the del(GJB6-D13S1830) mutation in the DFNB1 locus in hearing impairment subjects: a multicenter study. Am F Hum Genet 2003; 73: 1452-8. [CrossRef]
32. Cosetti MK, Waltzman SB. Outcomes in cochlear implantation: variables affecting performance in adults and children. Otolaryngol Clin North Am 2012; 45: 155-71. [CrossRef]
33. Geers A, Brenner C, Nicholas J, Uchanski R, Tye-Murray N, Tobey E. Rehabilitation factors contributing to implant benefit in children. Ann Otol Rhinol Laryngol Suppl 2002; 189: 127-30.
34. Kant AR, Patadia R, Govale P, Rangasayee R, Kirtane M. Acoustic analysis of speech of cochlear implantees and its implications. Clin Exp Otorhinolaryngol 2012; 5: S14-8. [CrossRef]
35. Russell JL, Pine HS, Young DL. Pediatric cochlear implantation: expanding applications and outcomes. Pediatr Clin N Am 2013; 60: 841-63. [CrossRef]
36. Lin FR, Niparko JK. Measuring health-related quality of life after pediatric cochlear implantation: a systematic review. Int J Pediatr Otorhinolaryngol 2006; 70: 1695-706. [CrossRef]
37. Kontorinis G, Lloyd SK, Henderson L, Jayewardene-Aston D, Milward K, Bruce IA, et al. Cochlear implantation in children with auditory neuropathy spectrum disorders Cochlear Implants Int 2014; 15(Suppl 1): S51-4. [CrossRef]
38. Teagle HFB, Roush PA, Woodard JS, Hatch DR, Zdanski CJ, Buss E, et al. Cochlear implantation in children with auditory neuropathy spectrum disorder. Ear and Hear 2010; 31: 325-35. [CrossRef]
39. Hosford-Dunn H, Halpern J. Clinical application of the satisfaction with amplification in daily life scale in private practice I: statistical, content, and factorial validity. J Am Acad Audiol 2000; 11: 523-39.
40. Hosford-Dunn H, Halpern J. Clinical application of the SADL scale in private practice II: predictive validity of fitting variables. Satisfaction with amplification in daily life. J Am Acad Audiol 2001; 12: 15-36.
41. Veiga LR, Merlo, ARC, Mengue SS. Satisfaction level with hearing aid in the daily life of Army Healthcare System users. Braz J Otorhinolaryngol 2005; 71: 67-73. [CrossRef]
42. Humphriss R, Hall A, Maddocks J, Macleod J, Sawaya K, Midgley E. Does cochlear implantation improve speech recognition in children with auditory neuropathy spectrum disorder? A systematic review. Int J Audiol 2013; 52: 442-54. [CrossRef]
43. Cheng X, Li L, Brashears S, Morlet T, Ng SS, Berlin C, et al. Connexin 26 variants and auditory neuropathy/dys-synchrony among children in schools for the deaf. Am J Med Genet. 2005; 139A: 13-8. [CrossRef]
44. Santarelli R, Cama E, Scimemi P, Dal Monte E, Genovese E, Arslan E. Audiological and electrocochleography findings in hearing-impaired children with connexin 26 mutations and otoacoustic emissions. Eur Arch Otorhinolaryngol 2008; 265: 43-51. [CrossRef]
45. Del Castillo FJ, Del Castillo I. Genetics of isolated auditory neuropathies. Frontiers in Bioscience 2012; 17: 1251-65. [CrossRef]
46. Reinert J, Honegger F, Gürtler N. High homogeneity in auditory outcome of pediatric CI-patients with mutations in Gap-Junction-Protein Beta2. Int J Pediatr Otorhinolaryngol 2010; 74: 791-5. [CrossRef]
47. El Bakkouri W, Loundon N, Thierry B, Nevoux J, Marlin S, Rouillon I, et al. Cochlear implantation and congenital deafness: perceptive and lexical results in 2 genetically pediatric identified population. Otol Neurotol 2012; 33: 539-44. [CrossRef]
48. UK. Criteria of candidacy for unilateral cochlear implantation in post lingually deafened adults II: cost-effectiveness analysis. Ear Hear 2004; 25: 336-60. [CrossRef]
49. Bond M, Elston J, Mealing S, Anderson R, Weiner G, Taylor RS, et al. Systematic reviews of the effectiveness and cost-effectiveness of multi-channel unilateral cochlear implants for adults. Clin Otolaryngol 2010; 35: 87-96. [CrossRef]
50. Olze H, Grabel S, Forster U, Zirke N, Huhnd LE, Haupt H. Elderly patients benefit from cochlear implantation regarding auditory rehabilitation, quality of life, tinnitus, and stress. Laryngoscope 2012; 122: 196-203. [CrossRef]
51. Orabi AA, Mawman D, Al-Zoubi F, Saeed SR, Ramsden RT. Cochlear implant outcomes and quality of life in the elderly: Manchester experience over 13 years. Clin Otolaryngol 2006; 31: 116-22. [CrossRef]
52. Vermeire K, Brokx JP, Wuyts FL, Cochet E, Hofkens A, Van de Heyning PH. Quality-of-life benefit from cochlear implantation in the elderly. Otol Neurotol 2005; 26: 188-95. [CrossRef]
53. Chung J, Chueng K, Shipp D, Friesen L, Chen JM, Nedzelski JM, et al. Unilateral Multi-Channel Cochlear Implantation Results in Significant Improvement in Quality of Life. Otol Neurotol 2012; 33: 566-71. [CrossRef]