Cochlear Implantation versus Hearing Amplification in Patients with Auditory Neuropathy Spectrum Disorder

Stanley Pelosi, MD¹, George Wanna, MD¹, Cathrine Hayes, AuD², Linsey Sunderhaus, AuD², David S. Haynes, MD¹, Marc L. Bennett, MD¹, Robert F. Labadie, MD, PhD¹, and Alejandro Rivas, MD¹

Abstract

Objective. Patients with auditory neuropathy spectrum disorder (ANSD) exhibit altered neural synchrony in response to auditory stimuli. Cochlear implantation (CI) is thought to improve neural synchrony in response to auditory stimuli and improve speech perception relative to conventional hearing amplification (HA).

Study Design. Retrospective review.

Setting. Tertiary otologic practice.

Subjects and Methods. Subjects included patients with ANSD treated at Vanderbilt University from 1999 to 2011. Sixteen patients underwent CI, and 10 received binaural HAs. Pretreatment performance was assessed through speech reception thresholds and parent questionnaire (Infant-Toddler Meaningful Auditory Integration Scale [IT-MAIS]). Posttreatment outcomes were assessed using IT-MAIS and closed-/open-set speech perception scores.

Results. Two HA users underwent neuromaturation and were excluded from further analysis. For the remaining patients, median duration of device use was 48 months. All CI patients had a prior binaural HA trial with failure of auditory skills development. Median available pretreatment IT-MAIS score was 13 and 30 for CI and HA groups, respectively (rank sum test, P = .32). Posttreatment, 6 of 16 CI patients and 4 of 8 HA patients achieved open-set speech perception scores ≥60%. No differences between groups were found in posttreatment IT-MAIS scores (rank sum test, P = .11) or the percentage of patients achieving the above levels of open-set speech perception (Fisher exact test, P = .67).

Conclusions. A wide range of speech perception outcomes are observed in ANSD patients. In our ANSD population, patients who exhibited failure of auditory skills development with HAs were able to achieve comparable overall speech perception outcomes after CI relative to those who continued to make appropriate auditory progress with HAs alone.

Keywords

auditory neuropathy spectrum disorder, cochlear implant, hearing aid, auditory development

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Patients with auditory neuropathy spectrum disorder (ANSD) exhibit altered neural synchrony in response to auditory stimuli. Speech perception impairments in this condition are usually disproportionately worse than would be predicted by the pure-tone audiogram.¹ Several potential sites of dysfunction in ANSD have been proposed, including inner hair cells, the auditory nerve, or synapses between these structures.¹ As such, a substantial heterogeneity exists in the severity of clinical manifestations and benefit from aural rehabilitative options in ANSD patients.

The presence of residual auditory function was a considerable factor limiting early enthusiasm for cochlear implantation (CI) in the ANSD population. Many such patients exhibit pure-tone audiometric thresholds in the mild-moderate range, and by definition, the presence of otoacoustic emissions in ANSD suggests normal cochlear outer hair cell function. Moreover, a subset of ANSD patients may exhibit neuromaturation, whereby auditory brainstem response (ABR) responses develop with age.² For these reasons, hearing aids (HAs) were initially recommended as a primary management strategy in this population. A review of the literature has indicated that some ANSD patients...
will benefit from the improved aided sound detection levels provided by HAs. However, for those who demonstrate limited auditory skills development despite appropriate amplification, CIs have increasingly been pursued. Numerous series have been published on ANSD patients who undergo CIs, and although some early reports have not shown auditory benefit, larger and more recent studies have demonstrated that CI does improve hearing performance in this population. The proposed mechanism by which CIs are accomplishing this improvement is through the high neural synchrony provided by electrical stimulation, which overcomes the processing abnormalities inherent to the disorder.

While CI has been shown to benefit patients with ANSD, the indications for when to pursue implantation over HA are not always clear. Moreover, few studies have directly compared outcomes between ANSD patients with HAs and those who undergo CI. We aim to assess auditory performance in ANSD patients undergoing CI and compare these outcomes to those receiving conventional amplification only. Our hypothesis is that CI will facilitate auditory development in ANSD patients who do not benefit from HAs.

**Methods**

A retrospective chart review was performed of patients treated in a tertiary medical center over a 14-year period. Approval was obtained from the Vanderbilt University institutional review board prior to chart review. Forty patients at Vanderbilt University Medical Center were identified with ANSD in the years 1998 to 2011. Each patient underwent audiology with determination of pure tone average (PTA) and speech perception thresholds (SRT), immittance testing, and age-appropriate speech perception measures. They also underwent evaluation for distortion product otoacoustic emissions and ABR. A diagnosis of ANSD was made if patients exhibited absent ABR waveforms but had evidence of a cochlear microphonic with measurable otoacoustic emissions.

Patients were determined to be CI candidates if they had failure of auditory skills development as assessed by speech perception testing and/or parent questionnaire, together with minimal to no benefit from conventional amplification. Both the duration of a hearing aid trial and timing of the decision to place a cochlear implant varied from patient to patient and were dependent on multidisciplinary input from audiology, speech language pathology, and otolaryngology. If the speech pathologist determined that progress in auditory development was not being made at the same rate as the patient’s motor and cognitive development (ie, 3 months of auditory development in 3 months of time), this suggested they were not receiving appropriate benefit from their hearing aid, and placement of a CI was recommended. Similarly, the decision for bilateral cochlear implantation was also based on multidisciplinary evaluation and input, as well as patient/parent motivation. In general, a unilateral CI recipient who was meeting developmental goals using a single implant (ie, auditory development was progressing at the same rate as the patient’s cognitive and motor development) but had poor aided speech perception scores in the nonimplanted ear was considered a good candidate for a second CI.

For all ANSD patients, the presence or absence of known risk factors for auditory neuropathy were assessed, including history of prematurity, hyperbilirubinemia, admission to the neonatal intensive care unit (NICU), mechanical ventilation, exposure to ototoxic medications, multiple births, sepsis, intraventricular hemorrhage, and motor/cognitive developmental delay. In CI recipients, data were collected on preoperative computerized tomography (CT) results, age at implantation, type of implant, electrode insertion approach (cochleostomy vs round window), duration of CI use, and whether the patient used bilateral implants or a contralateral hearing aid.

Posttreatment speech perception outcomes were assessed using several measures depending on the patient’s level of auditory and cognitive development. Parent questionnaires were used, including the Infant-Toddler Meaningful Auditory Integration Scale (IT-MAIS), Parents’ Evaluation of Aural/Oral Performance of Children scale, and LittlEARS Auditory Questionnaire. In older children who could participate, closed-set speech perception testing was performed using the Northwestern University–Children’s Perception of Speech (NU-CHIPS). Several open-set measures were administered for children with sufficient auditory development, including sentence recognition using Hearing in Noise Test sentences for children (HINT-C), Consonant-Nucleus-Consonant words, Lexical Neighborhood Test words, Phonetically Balanced Kindergarten (PBK) words, Northwestern University Auditory Test No. 6 (NU-6), and a version of the AzBio sentence test adapted for children (BabyBio sentences). All closed- and open-set speech perception testing was administered in a sound-treated booth with live voice or recorded stimuli.

To better present developmental trajectories over time with each device, we used as a model the SRI-Q, a hierarchical speech recognition index developed by the authors of the Childhood Development after Cochlear Implantation study. Our index was unique in that it contained the most common audiologic tests used at Vanderbilt University to assess auditory performance from age at device fitting to most recent follow-up. A scale was used to determine the hierarchy of testing measures contained in the index: 0 to 100 parent questionnaire (IT-MAIS), 101 to 200 closed-set testing (NU-CHIPS), 201 to 300 open-set word testing (NU-6, PBK), and 301 to 400 open-set sentence testing (HINT-C).

Data analysis was performed using STATA software. Frequency and proportion calculations were made for categorical variables, while continuous variables were reported as median and interquartile range (IQR). Auditory performance between HA and CI groups before and after treatment intervention were compared using several methods. Median IT-MAIS score and SRT differences were assessed using a Wilcoxon rank sum test ($P < .05$), while the percentages of patients with closed-/open-set speech perception
scores >60% were compared using Fisher exact test (2-tailed, \( P < .05 \)).

**Results**

Forty patients were identified with ANSD. Twenty-six patients managed with HAs and/or CIs and with at least 1 year of posttreatment follow-up were included for further analysis. The study population included 14 males and 12 females, and the median age at diagnosis was 6 months (IQR, 4-23 months). The most frequent historical features were prematurity and NICU admission, present in 81% and 85% of patients, respectively. Other findings included a history of mechanical ventilation (n = 16), otoxic medication exposure (n = 15), motor/cognitive developmental delay (n = 13), multiple births (n = 8), hyperbilirubinemia (n = 7), intraventricular hemorrhage (n = 3), and sepsis (n = 3).

Figure 1 summarizes the management strategy. All 26 ANSD patients underwent an HA trial. Sixteen patients who demonstrated limited HA benefit underwent CI (CI group), and 8 patients made developmentally appropriate auditory progress with HA use alone (HA group). Two patients exhibited neuromaturation with normalization of ABR waveforms on repeat testing 12 and 16 months after diagnosis; these patients were not included in further analysis.

**Tables 1 and 2 summarize auditory performance outcomes for each patient group.** The median duration of device use for HA users was 42 months (IQR, 24-84 months), and for CI users it was 52 months (IQR, 28-52 months). Six (75%) HA patients and 14 (88%) CI patients were able to achieve at least closed speech perception scores >60% in 1 ear. Open-set speech perception scores >60% were achieved in 4 (50%) HA patients and 7 (44%) CI patients. The most common open-set measure tested postoperatively was HINT-C (n = 10), and the median score in the better-performing ear was 84% (67%-98%). No differences between HA and CI groups were found in the percentage of patients achieving at least closed-set speech perception scores >60% (Fisher exact test, \( P = .57 \)) or the percentage of patients with open-set scores >60% (Fisher exact test, \( P = .1 \)). Of the 7 patients who received bilateral implants, 4 (57%) achieved open-set abilities, while only 2 of 9 (22%) unilaterally implanted patients achieved open-set abilities (difference nonsignificant, Fisher exact text, \( P = .3 \)).

We examined whether a significant difference in pretreatment SRT or IT-MAIS scores existed between patients who developed open-set speech perception abilities and those who did not. Although the median pretreatment SRT was 55 in patients who developed closed- or open-set speech perception abilities and 75 in those who did not, this difference did not reach significance (rank sum test, \( P = .08 \)). In addition, we did not observe a difference in pretreatment IT-MAIS scores between patients who did and did not achieve speech perception abilities (rank sum test, \( P = .13 \)).
We assessed for a potential relationship between development of speech perception abilities in all patients (both HA and CI groups) and other variables including age at device fitting, duration of device use, and age at most recent follow-up. While the median duration of device use and age at last follow-up were greater for patients who developed speech perception abilities compared with those who did not (49 vs 36 and 8 vs 4, respectively), these differences did not reach significance (rank sum test, $P = .53$ and $P = .16$, respectively). Developmental trajectories from the time of device fitting for CI recipients and HA users are summarized in Figures 2 and 3, respectively. In general, a trend

### Table 1. Cochlear Implant Recipients with Auditory Neuropathy Spectrum Disorder

<table>
<thead>
<tr>
<th>Patient</th>
<th>Comorbidities</th>
<th>SRT</th>
<th>IT-MAIS before CI</th>
<th>Age at CI</th>
<th>Months of CI Use</th>
<th>Age at Last Follow-up, y</th>
<th>Highest NU-CHIPS Score, %</th>
<th>Highest HINT-C Score, %</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>Motor ataxia</td>
<td>60</td>
<td>N/A</td>
<td>2.5</td>
<td>90</td>
<td>10.5</td>
<td>90</td>
<td>64</td>
</tr>
<tr>
<td>2</td>
<td>Motor/cognitive developmental delay</td>
<td>55</td>
<td>N/A</td>
<td>10.5</td>
<td>85</td>
<td>19.5</td>
<td>N/A</td>
<td>98</td>
</tr>
<tr>
<td>3</td>
<td>Motor ataxia</td>
<td>90</td>
<td>35</td>
<td>1.5</td>
<td>48</td>
<td>5.5</td>
<td>90</td>
<td>63</td>
</tr>
<tr>
<td>4</td>
<td>Motor ataxia</td>
<td>N/A</td>
<td>42.5</td>
<td>1.5</td>
<td>57</td>
<td>6</td>
<td>92</td>
<td>84</td>
</tr>
<tr>
<td>5</td>
<td>Motor ataxia</td>
<td>N/A</td>
<td>N/A</td>
<td>3</td>
<td>95</td>
<td>11</td>
<td>100</td>
<td>98</td>
</tr>
<tr>
<td>6</td>
<td>Motor ataxia</td>
<td>50</td>
<td>15</td>
<td>4.5</td>
<td>22</td>
<td>7.5</td>
<td>88</td>
<td>84</td>
</tr>
<tr>
<td>7</td>
<td>Motor ataxia</td>
<td>50</td>
<td>N/A</td>
<td>3.5</td>
<td>17</td>
<td>4.5</td>
<td>100</td>
<td>76</td>
</tr>
<tr>
<td>8</td>
<td>Motor ataxia</td>
<td>30</td>
<td>65</td>
<td>1.5</td>
<td>28</td>
<td>4</td>
<td>60</td>
<td>DNT</td>
</tr>
<tr>
<td>9</td>
<td>Motor ataxia</td>
<td>80</td>
<td>27.5</td>
<td>2.5</td>
<td>75</td>
<td>9</td>
<td>80</td>
<td>DNT</td>
</tr>
<tr>
<td>10</td>
<td>Motor ataxia</td>
<td>N/A</td>
<td>N/A</td>
<td>4.5</td>
<td>84</td>
<td>11.5</td>
<td>68</td>
<td>DNT</td>
</tr>
<tr>
<td>11</td>
<td>Motor ataxia</td>
<td>70</td>
<td>57.5</td>
<td>1.5</td>
<td>17</td>
<td>3</td>
<td>60</td>
<td>DNT</td>
</tr>
<tr>
<td>12</td>
<td>Motor ataxia</td>
<td>45</td>
<td>13.5</td>
<td>8</td>
<td>55</td>
<td>12.5</td>
<td>92</td>
<td>DNT</td>
</tr>
<tr>
<td>13</td>
<td>Motor ataxia</td>
<td>70</td>
<td>60</td>
<td>3.5</td>
<td>16</td>
<td>5</td>
<td>80</td>
<td>DNT</td>
</tr>
</tbody>
</table>

### Table 2. HA Users with Auditory Neuropathy Spectrum Disorder

<table>
<thead>
<tr>
<th>Patient</th>
<th>Comorbidities</th>
<th>SRT</th>
<th>IT-MAIS before HA</th>
<th>Age at HA Fitting, y</th>
<th>Months of HA Use</th>
<th>Age at Last Follow-up, y</th>
<th>Highest NU-CHIPS Score, %</th>
<th>Highest Open-Set Score, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Developmental delay</td>
<td>30</td>
<td>N/A</td>
<td>6</td>
<td>48</td>
<td>9</td>
<td>76</td>
<td>NU-6, 68</td>
</tr>
<tr>
<td>2</td>
<td>Developmental delay</td>
<td>40</td>
<td>N/A</td>
<td>3.5</td>
<td>50</td>
<td>9</td>
<td>88</td>
<td>HINT-C, 98</td>
</tr>
<tr>
<td>3</td>
<td>Developmental delay</td>
<td>40</td>
<td>N/A</td>
<td>4</td>
<td>57</td>
<td>8.5</td>
<td>N/A</td>
<td>HINT-C, 96</td>
</tr>
<tr>
<td>4</td>
<td>Developmental delay</td>
<td>N/A</td>
<td>N/A</td>
<td>4.5</td>
<td>63</td>
<td>10</td>
<td>N/A</td>
<td>PBK, 100</td>
</tr>
<tr>
<td>5</td>
<td>Developmental delay</td>
<td>50</td>
<td>72</td>
<td>3</td>
<td>36</td>
<td>6</td>
<td>70</td>
<td>DNT</td>
</tr>
<tr>
<td>6</td>
<td>Cerebral palsy, severe developmental delay</td>
<td>70</td>
<td>34</td>
<td>1</td>
<td>19</td>
<td>2.5</td>
<td>80</td>
<td>DNT</td>
</tr>
<tr>
<td>7</td>
<td>Cerebral palsy, severe developmental delay</td>
<td>70</td>
<td>34</td>
<td>1</td>
<td>31</td>
<td>3.5</td>
<td>DNT</td>
<td>DNT</td>
</tr>
<tr>
<td>8</td>
<td>Cerebral palsy, severe developmental delay</td>
<td>70</td>
<td>34</td>
<td>3</td>
<td>12</td>
<td>4.5</td>
<td>DNT</td>
<td>DNT</td>
</tr>
</tbody>
</table>

Abbreviations: CI, cochlear implantation; DNT, not tested; HINT-C, Hearing in Noise Test sentences for children; IT-MAIS, Infant-Toddler Meaningful Auditory Integration Scale; N/A, not available; NU-CHIPS, Northwestern University–Children’s Perception of Speech; SRT, speech reception threshold.
toward improved speech index score was seen with advancing age in both HA users and CI recipients, although the result interpretation is limited by relatively few data points for most patients. In addition, both figures illustrate the substantial variability in age at the time of different testing measures.

Discussion

The purpose of this study was to compare auditory performance outcomes in ANSD patients who underwent CI versus those receiving conventional amplification. Our results support the work of other authors in demonstrating that CI will facilitate auditory development in ANSD patients who do not benefit from HAs. Comparison of pre-treatment hearing status showed CI recipients to have higher median SRTs and lower IT-MAIS scores than HA users. Moreover, following treatment, 88% of CI recipients had at least closed-set abilities in comparison to 75% of HA users. These results suggest that in our ANSD population, CI recipients with comparable or worse pretreatment hearing impairment can achieve auditory development that is similar to that of successful HA users with ANSD.

Consistent with other series involving ANSD patients was the substantial clinical heterogeneity of our study population. On initial evaluation, there was a large range of SRTs (mild-profound) and IT-MAIS scores (0%-72%) for the ANSD group as a whole (Tables 1 and 2). Moreover, the response to hearing amplification was highly variable. While a significant percentage of patients in the HA group developed closed- or even open-set abilities over time, all patients who ultimately received CIs demonstrated minimal benefit from amplification even after an extended period of use (median, 11 months).

Also consistent with other series involving ANSD patients was the variability in post-CI outcomes. Following implantation, open-set speech discrimination scores >60% were achieved in 6 of 16 (38%) of our patients. Peterson et al reported that only 3 of 10 ANSD patients achieved some level of open-set speech perception after cochlear implantation. Similarly, Teagle et al reviewed 52 patients with ANSD who underwent CI and found that 50% developed open-set speech discrimination abilities. Again, however, a wide range of clinical outcomes was observed, as 27% with at least 2 years of CI experience still scored <30% on open-set testing measures. With advancing age and increased time spent using their CIs, it would be expected that a progressively higher percentage of our patients will ultimately achieve open-set speech perception abilities. Breneman et al described their long-term outcomes (mean follow-up 71 months) in ANSD patients undergoing CI and found that 28 of 35 ANSD patients exhibited open-set speech perception scores of at least 80%.

Further discussion is needed regarding those patients with failed auditory progress using either device. Two HA users in our series did not develop speech perception abilities despite at least 1 year of use, and 2 CI recipients with more than 2 years of use had no level of speech perception abilities. We did not find significant differences in SRT, IT-MAIS score, age, or duration of device use between patients who did and did not develop speech perception abilities, likely due in part to the small sample of poor performers. Hence, individualized explanations are necessary for failed auditory development in each poorly performing patient. Both HA users had developmental delay. One of these HA users (patient 8 in Table 2) was determined to be making auditory progress appropriate for their level of motor and cognitive development despite not developing speech perception abilities after 12 months of HA use. The second HA user (patient 7 in Table 2) had such severe delays that a multidisciplinary decision was made to withhold CI because of minimal expected benefit. Of the CI recipients without speech perception abilities, 1 did not consistently wear their device and had inconsistent follow-up for programming
adjustments (patient 16 in Table 1), providing an unambiguous explanation for limited auditory progress with the implant. In the other CI recipient, once again coexisting motor/cognitive delays were assumed to account for the failure to exhibit auditory progress (patient 15 in Table 1). While a significant percentage of our overall ANSD study population (50%) had some level of motor/cognitive delay, the extent of developmental delay was highly variable between patients, thus limiting the ability to associate its presence with failure to develop speech perception abilities.

Although not reaching statistical significance, there was a trend toward improved performance in bilaterally implanted patients relative to those undergoing unilateral CI. This observation may be accounted for by one of two factors: (1) the second implant enhanced auditory development or (2) a selection bias existed in which patients exhibiting favorable auditory development with one implant were more likely to be implanted with a second. We suspect the latter finding is true, as all 4 patients who were sequentially implanted had been making progress in auditory development at the time of their second implant.

All CI recipients in our series underwent cochleostomy. Data on hearing preservation were limited in our population, as only 4 patients had recorded postimplantation unaided audiogram test results. Of these, 2 had residual hearing preoperatively (PTAs of 53 and 68), but after implantation, neither maintained PTAs within 30 dB of preoperative values. It is unclear as to whether hearing preservation techniques would benefit ANSD patients undergoing CI, as the presence of residual hearing and its associated temporal processing abnormalities might interfere with the speech perception gains otherwise provided by CIs. Because of similar concerns, contralateral amplification has traditionally not been recommended for ANSD patients with CIs until auditory development has reached a point at which aided speech perception testing in noise can be completed with a HA in the contralateral ear and benefit is demonstrated. In our series, 2 of 13 patients with a unilateral CI were fitted with a HA (patients 10 and 16 in Table 1). At last follow-up, patient 10 had achieved closed-set speech perception abilities, while patient 16 still had not. A recent study found auditory benefits in CI recipients with ANSD when also using a contralateral HA compared with CI alone.21 Looking forward, both hearing preservation techniques and contralateral amplification may play a greater role in promoting auditory development for ANSD patients undergoing CI.

Conclusions
A wide range of speech perception outcomes are observed in ANSD patients. For patients with ANSD who demonstrate limited auditory skills development with conventional amplification, cochlear implants can facilitate development of closed- and even open-set speech perception abilities.

Author Contributions
Stanley Pelosi, acquisition of data, analysis and interpretation, drafting article, revising critically, final approval; George Wanna, conception and design, analysis and interpretation, revising critically, final approval; Cathrine Haynes, analysis and interpretation, revising critically, final approval; Linsey Sunderhaus, analysis and interpretation, revising critically, final approval; David S. Haynes, analysis and interpretation, revising critically, final approval; Marc L. Bennett, analysis and interpretation, revising critically, final approval; Robert F. Labadie, analysis and interpretation, revising critically, final approval; Alejandro Rivas, conception and design, acquisition of data, analysis and interpretation, revising critically, final approval.

Disclosures
Competing interests: David S. Haynes, advisory board for Cochlear, Advanced Bionics, and Ansphach and consultant for Grace Medical; Robert F. Labadie, advisory board for Med-El and Ototronix and consultant for Cochlear.

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