Critical Review: Speech perception outcomes following cochlear implantation in children with non-syndromic Auditory Neuropathy Spectrum Disorder as compared to children with sensorineural hearing loss?

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This critical review examines the speech perception abilities of cochlear implanted children diagnosed with Auditory Neuropathy Spectrum Disorder (ANSD) as compared to implanted children with sensorineural hearing loss (SNHL). Study designs included: between subjects non-randomized intervention studies and mixed (between & within) non-randomized intervention studies. Overall, research suggests that cochlear implantation provides speech perception benefit in some children with ANSD who have demonstrated a lack of success with traditional amplification. However, a definitive statement regarding the post-implant performance of ANSD children relative to SNHL children cannot be made due to research limitations including small sample sizes, variations in design and methodology across studies and poor descriptions of patient selection criteria. Large scale studies using standardized research designs and methods are warranted.

Introduction

Auditory Neuropathy Spectrum Disorder (ANSD) is a form of hearing impairment in which outer hair cells remain intact while synchronous activity in the auditory nerve and central auditory pathways is impaired. The clinical manifestations of ANSD tend to be an absent or abnormal auditory brainstem response (ABR) in the presence of otoacoustic emissions (OAE) and/or a cochlear microphonic (CM). Individuals with ANSD may have varying degrees of hearing loss and their speech discrimination abilities tend to be worse than one would predict based on audiometric data alone. Children with pre-lingual ANSD may have particular difficulty developing auditory and oral communication skills resulting in poor school performance. Possible sites that may be affected in cases of ANSD include the inner hair cells (IHC), the synapse between the hair cells and the auditory nerve, and/or the auditory nerve fibers (Jeong et. al., 2007).

Individual differences in the etiology and severity of ANSD have resulted in controversy regarding its appropriate treatment. Traditional amplification and the use of FM systems are of limited benefit in improving speech perception abilities in many children with ANSD. This finding may be understandable given that amplification cannot restore neural encoding of the speech signal (Peterson et. al., 2003). Cochlear implantation has been recommended as an alternative treatment for children with ANSD who do not respond well to traditional amplification. However, the irreversible nature of cochlear implantation and the spontaneous improvement in some ANSD children have stimulated debate regarding its use as a treatment option for this population.

The literature tends to support the use of cochlear implants as a clinical option for ANSD children; however, study outcomes vary considerably and conflicting results have been reported (Jeong et. al., 2007). This wide range of outcomes is consistent with the proposition of multiple etiologies responsible for the symptoms of ANSD. It has been suggested that electrical stimulation of the auditory nerve via cochlear implantation may only be successful when ANSD is caused by damage to the IHCs or the synapse between the hair cells and the spiral ganglion because, in such cases, the site of lesion is bypassed completely. However, the value of electrical stimulation may be limited when the pathology exists in the auditory nerve itself because the signal cannot be transmitted optimally. Although positive outcomes have been reported, difficulties in determining the status of the auditory nerve in children with ANSD has led many clinicians to be cautious in recommending cochlear implants for this population (Buss et. al., 2002).

There are few published reports on speech perception outcomes in implanted children with ANSD. Due to the permanency of this treatment and the limited success of other options, it is essential that the appropriateness of cochlear implantation for ANSD children of varying etiologies be determined. Children with profound SNHL have been shown to benefit from cochlear implants (Buss et. al., 2002). Therefore, comparing speech perception outcomes of implanted ANSD children to implanted SNHL children is important to establish whether ANSD children receive a similar degree of functional benefit from cochlear implantation and to guide future treatment recommendations for this population.

Objectives

The primary objective of this paper was to outline and critically evaluate the current body of research on speech perception outcomes in implanted ANSD children as compared to implanted SNHL children.

Methods

Search Strategy

Computerized databases, including PubMed, Medline and CINAHL were searched using the following search strategy: (auditory neuropathy) OR

(auditory dys-synchrony) AND (cochlear implant). The search was limited to peer-reviewed articles written in English and involving human participants.

Selection Criteria

Studies selected for inclusion in this critical review were required to investigate the speech perception abilities of implanted ANSD children (< 18 yrs) as compared to implanted SNHL children. The studies were limited to those including children with non-syndromic ANSD without associated medical disorders. No limits were set on the age of implantation or the research methods used.

Data Collection

Results of the literature search yielded six articles that were congruent with the selection criteria above: 3 between-groups and 3 mixed groups non-randomized intervention studies. In accordance with the level of evidence hierarchy for high-quality standards (Cox, 2005), all six studies provided a level 3(-) of evidence.

Results

Between Groups Non-Randomized Intervention Studies

Study 1. Buss et. al. (2002) used a prospective design to compare speech production outcomes in children with ANSD (n=4) and children with SNHL (n=33) following unilateral cochlear implantation. Two of the ANSD participants (S1 and S2) were approximately 2 years old at the time of implant and were matched with a group of SNHL children implanted between 2 and 4 years of age (n=13). The other two participants (S3 and S4) were approximately 5.5 years old at the time of implant and matched with a group of SNHL children implanted between 4 and 6 years of age (n=13).

Speech production was assessed at 1 year post-implantation by a speech language pathologist (SLP) according to nine categories of possible errors using the Paden-Brown test. Neural integrity was evaluated by measuring electrically evoked auditory brainstem responses (EABR).

Individual ANSD participant test scores were compared to the mean score of the matched control group. This comparison revealed that participants S1, S2, and S4 had post-implant scores that fell within or above one standard deviation of the control group mean on all nine test categories. Participant S3 had speech production scores that fell more than one standard deviation below the mean of the control group on two of the nine test categories. This result was associated with S3's continued use of manual communication post-implantation. The EABR measure revealed an identifiable wave V for all four implanted ANSD children. The results were interpreted as evidence that cochlear implantation in ANSD children can produce a synchronized neural response and that this can be used to develop speech perception and production abilities similar to those found in implanted SNHL children.

The non-significant differences in speech production between groups may have been the result of an insufficient sample of ANSD children (n=4). It is unknown if experimenters were blinded to participant condition. Pre-operative speech measures were not reported for either group limiting comparisons to baseline conditions. The effects of speech production and vocabulary limitations on test outcomes were not accounted for. Also, the ANSD and SNHL groups were not matched for other variables, besides age at implantation and duration of use, which could have affected speech production outcomes post-implantation (i.e. pre-implant mode of communication, hearing thresholds, type of implant and programming strategy, post-implant auditory training etc.).

Study 2. Gibson & Sanli (2007) completed a prospective, longitudinal study to investigate post-implant speech perception outcomes in three groups of children: (1) ANSD and normal EABRs (Group A, n=41); (2) ANSD and abnormal EABRs (Group B, n=15); (3) SNHL and normal EABRs (Group C, n=46). The ANSD group was divided according to EABR test results in order separate cases of ANSD associated with inner hair cell and/or synaptic dysfunction (i.e. normal EABR) from those associated with damage to the auditory nerve (i.e. abnormal EABR).

Speech perception was assessed using the Melbourne speech perception categories at 1 and 2 years post-implantation. For this test, participants were rated on seven categories of speech perception.

A one-way analysis of variance (ANOVA) revealed significant differences between groups in speech perception at 1 and 2 years post-implantation ($p < 0.0005$). A multiple comparison t-test revealed that ANSD children with normal EABRs (group A) performed significantly better than those with abnormal EABRs (group B) or SNHL (group C). Also, group C performed significantly better than group B ($p < 0.0005$). Power calculations for comparing group means revealed that the statistical results were valid despite the significantly reduced sample size of group B (n=15) ($p < 0.05$). These findings suggest that post-implant speech perception of children with ANSD caused by a peripheral site of lesion are as good as, or better than, those found in children with SNHL or ANSD caused by auditory nerve damage.

Pre-operative speech perception outcome measures were not reported. The effects of speech production and vocabulary limitations on test outcomes were not accounted for. There was no information given regarding who administered the test or whether they were blinded to participant condition. There was no matching of participant groups on any of the factors known to affect test outcomes, making it difficult to

attribute group differences in speech perception to differences in hearing disorder and site of lesion alone.

Study 3. Leigh et. al. (2009) compared post-operative speech perception in implanted ANSD children (n=7) to previously reported outcomes from implanted SNHL children (n= 102). The ANSD group ranged in age from 3.5 to 8.5 years and varied in duration of implant use from 2 to 4 years. Mean age at implantation ranged from 6 months to 4.5 years. Participant data was collected retrospectively from patient medical records. All SNHL children received implants prior to 4 years of age but no other information was provided for this group.

Post-implant speech perception was assessed by an experienced audiologist using one of two equivalent tests of open-set monosyllabic word perception: the Phonetically Balanced Kindergarten (PBK) and/or the Consonant-Nucleus-Consonant (CNC) word lists. Neural integrity was assessed intra-or post-operatively with Neural Response Telemetry (NRT) and/or EABR measures.

NRT and EABR measures revealed post-implant neural synchrony in 6 of 7 ANSD children. Participant 7 had an absent post-implant EABR. The mean post-implant speech perception score for the ANSD group was 71.6% (range from 10 to 93%). When Participant 7 was removed from the analysis, the score was 81.8% (range from 60 to 93%). The ANSD scores were plotted against the mean score (79%) of the implanted SNHL group. The six ANSD children demonstrating post-implant neural synchrony and assumed to have a peripheral site of lesion, had speech perception scores that were similar to implanted SNHL children. This was interpreted as evidence that the success of cochlear implantation depends upon site of lesion and its relationship to post-implant neural synchrony.

Statistical analysis of speech perception outcomes was not carried out. It is unknown if examiners were blinded to participant condition and the small number of ANSD children (n=7) most likely resulted in an unrepresentative sampling of this group. The between groups comparison only included ANSD children demonstrating neural synchrony and the one child who performed poorly was omitted from the analysis. This may have biased the results in a positive direction. The ANSD and SNHL groups were not matched on any of the variables known to affect post-implant speech perception, limiting the validity of comparisons between these groups.

Mixed Non-Randomized Intervention Studies

Study 1. Peterson et. al. (2003) investigated pre-and post-implant speech perception abilities in ANSD children (n=10) as compared SNHL children (n=10). All data was collected retrospectively from patient medical records.

The ANSD and SNHL groups were matched for average age at assessment, duration of pre-implant deafness and age at implantation. Children in both groups varied significantly in duration of implant use. Most participants used oral communication and participated in educational programs that enforced this strategy. One child from each group used American Sign Language (ASL) as their primary mode of communication.

Neural integrity was assessed intra-and post-operatively with NRT, EABR and visual electrical acoustic reflex (VESR). Pre- and post-implant speech perception was assessed by an experienced audiologist using the Early Speech Perception (ESP) test. The ESP is a closed-set, picture pointing task containing three sub-tests: pattern perception, spondee identification and monosyllable identification. This test reduced the confounding influence of speech production and vocabulary limitations on speech perception outcomes.

The Wilcoxen Rank Sums test ($p < 0.05$) revealed no significant differences between implanted ANSD and SNHL groups in pre-operative hearing loss, SATs and/or SRTs. All participants showed evidence of intra- and post-operative neural synchrony. Eighteen of 20 children from both groups demonstrated an improvement in speech perception post-operatively. Both the ANSD and SNHL groups performed equally following implantation.

Individual scores were not reported and statistical analysis of speech perception outcomes was not carried out. Two children failed to make improvements in speech perception following implantation; however, test scores were not reported for these children and there was no mention of which participant group they belonged to.

Study 2. Rance & Barker (2008) used a prospective design to compare speech perception outcomes for three groups of children: (1) implanted ANSD children (n=10) (mean age at implantation =33.3 +/- 16.9 months; mean age at testing = 89.6 +/- 42.1 months) (2) aided ANSD(n=10) children demonstrating progress with amplification (matched for mean age at assessment =94.2 +/- 57 months); (3) implanted SNHL children (n=37) (matched for mean age at implantation = 30.2 +/- 15.5 months; mean age at testing= 92.6 +/- 34.6 months).

Pre-and post-implant speech perception was assessed using a list of pre-recorded CNC words and participant responses were scored as a percentage correct. Speech production skills were assessed with the Diagnostic Evaluation of Articulation Phonology test and all participants scored over 80%, suggesting that speech production limitations were not likely to confound test outcomes.

A one-way analysis of variance (ANOVA) revealed significant differences in post-implant speech perception scores between groups and a post hoc Tukey analysis demonstrated that the implanted SNHL children performed significantly better than either of the ANSD groups ($F_{2,28}$= 8.07; p = 0.002). There were no significant differences between aided and implanted ANSD groups. The implanted ANSD children showed an improvement in speech perception scores following implantation. Regression analysis revealed no relationship between test outcomes and average hearing loss, age at assessment, age at implantation or duration of use for any of the groups. The authors concluded that cochlear implantation improves speech perception in children with ANSD, however, the improvement is not as great as that seen in implanted SNHL children and is not superior to that seen in aided ANSD children.

Pre-implant test scores were not reported to support the claim of an improvement in speech perception for ANSD children following implantation. Eight out of 10 implanted ANSD children had neonatal risk factors that may have contributed to their poorer performance. The non-significant differences between implanted and aided ANSD groups may have been due to sampling bias as the aided children tended to do well with amplification and may not represent how all ANSD children will perform with hearing aids.

Study 3. Jeong et. al. (2009) compared pre- and post-implant speech perception and intra-operative auditory nerve status in implanted ANSD children (n=6) and implanted SNHL children (n=12). All participant data was collected retrospectively from previous medical records.

The implanted ANSD group had a mean age at diagnosis of 1 year 7 months (range of 5 months to 5 years) and they received their implants at an average of 4 years (range of 1 year 9 months to 11 years 5 months). A control group of implanted SNHL children were selected to match the ANSD group for duration of deafness, age at implantation, mode of communication and type of cochlear implant. The groups varied significantly in duration of implant use.

Pre- and post-implant speech perception was assessed with the Categories of Auditory Performance (CAP), the Monosyllabic Word (MW) test and the Common Phrases (CP) test. Both the MW and CP are tests of open-set speech perception. Neural synchrony was assessed intra-operatively by comparing the slopes of the evoked compound action potentials (ECAPs) amplitude growth functions from three regions of the cochlea.

There were no significant differences between groups in the slopes of their ECAPs suggesting similar spiral ganglion populations. Mann-Whitney U tests revealed no significant differences between ANSD and SNHL groups on any of the matched variables. Repeated-measures analysis of variance (RW-ANOVA) revealed no significant differences in post-implant speech perception scores between groups on any of the tests. The RW-ANOVA also revealed that both ANSD and SNHL groups improved over time ($p < 0.00001$). The findings of this study suggest that cochlear implantation may produce similar speech perception outcomes in ANSD and SNHL children.

The non-significant differences in speech perception between groups may have been the result of insufficient sample sizes. The effects of speech production and vocabulary limitations on test outcomes were not accounted for. It is unknown if the tests were administered by the same examiner and whether the examiner was blinded to participant condition. The groups were not matched for duration of implant use at the time of assessment which may have had an effect on test results.

Discussion

These results must be interpreted with caution as most included small sample sizes and none used random selection to form participant groups. Five out of six studies had samples of 10 or fewer participants. This is somewhat understandable given the limited number of ANSD children receiving cochlear implants in the general population and the ethical issues involved in withholding proper treatment. The majority of studies found no differences between implanted ANSD and SNHL children and this finding was interpreted as evidence supporting the use of cochlear implants as a treatment option for ANSD children. One must be cautious in accepting such conclusions as it is unclear whether the failure to find differences between implanted ANSD and SNHL children was the result of insufficient sample sizes or a true lack of differences between these groups. However, Gibson & Sanli (2007) demonstrated superior speech perception in some implanted ANSD children, using a larger sample of 56 subjects sub-divided into two groups based on the presence or absence of a synchronous post-implant neural response. This study had sufficient power to support the conclusion that children with ANSD caused by a peripheral site of lesion demonstrate speech perception outcomes that are as good as, or better than, those found in SNHL children or cases of ANSD caused by auditory nerve damage.

Another limitation in interpreting the findings of this research involves differences in research design and methodology across studies. Studies varied in the measurement tools used to assess speech perception. In addition, most studies provided limited information regarding who administered these tools and whether these individuals were blinded to participant condition. This could have reduced the reliability of test results. Also, the influences of speech production and vocabulary limitations on test outcomes were accounted

for in some studies (Rance & Barker, 2008; Peterson et. al., 2003) but not others (Buss et. al., 2002; Gibson & Sanli, 2007; Jeong et. al., 2009; Leigh et. al., 2009). Finally, the studies varied in their tendency to control for differences between participant groups on variables known to affect speech perception test results, such as age at implantation, duration of implant use, age at assessment, type of implant, mode of communication and post-implant auditory training. Two of the reviewed studies made no attempt to match participant groups on any of these variables (Gibson & Sanli, 2007; Leigh et. al., 2009). These differences in research design and methodology limit the validity of comparisons across studies.

Based on the aforementioned study limitations, there is not a strong degree of evidence to support the use of cochlear implants as a treatment option for children with ANSD. In fact, Rance & Barker (2008) found that implanted ANSD children performed worse on post-operative speech perception measures than implanted SNHL children. This study had some advantages over the others as the ANSD participants were sub-divided based on degree of benefit from amplification. This study also provided a better description of participant selection by specifying the criteria used to indicate lack of hearing aid benefit and they accounted for the influence of vocabulary and speech production limitations on test outcomes. However, it is possible that the subject selection criteria introduced experimental bias causing the implanted ANSD participants to perform worse than the SNHL group. Specifically, the higher functioning ANSD subjects, less disordered by their condition, were successful with hearing aids and therefore did not receive a cochlear implant. Conversely, those with more disabling ANSD, who did not benefit from amplification, formed the implanted ANSD group. It is unknown whether the aided ANSD participants would have performed better with cochlear implants and, therefore, whether the results were biased in a negative direction.

In contrast, Gibson & Sanli (2007) found that ANSD children demonstrating post-implant neural synchrony performed significantly better than those with abnormal neural responses and children with SNHL. The findings of this study support the notion that the success of cochlear implantation may depend upon underlying pathology. By failing to separate ANSD participants according to post-implant neural status, the other studies included in this review may have used a group of ANSD children that were heterogeneous in underlying pathology. This may have resulted in a large variance in speech perception outcomes and the failure to find significant differences between groups.

Clinical Recommendations

Regardless of the performance of implanted ANSD children relative to implanted SNHL children, studies employing a pre-and post-implant repeated measures design found significant improvements in speech perception abilities of ANSD children following implantation (Jeong et. al., 2009; Rance & Barker, 2008). This finding, along with the results of the study by Gibson & Sanli(2009), suggest that cochlear implantation may be beneficial for some ANSD children, especially those with a peripheral rather than retrocochlear site of lesion. However, given the available research, it remains difficult to predict the success of this treatment for individual ANSD children. This uncertainty, along with the permanent nature of cochlear implantation, means that a strong recommendation for its use as a standard treatment for all ANSD children cannot be made.

The assumption that ANSD children will not benefit from traditional amplification has resulted in the use of cochlear implantation as the default treatment strategy for this population. However, it has been demonstrated that hearing aids may be a viable option in some cases of ANSD (Rance & Barker, 2008). Therefore, all ANSD children should undergo a rigorous trial period with simultaneous amplification and intensive auditory-oral habilitation similar to that provided for cochlear implant recipients. In addition, clinical practice guidelines outlining the parameters of such hearing aid trials, as well as clear criteria for determining success with amplification should be established. Cochlear implant candidacy should only be considered in cases of ANSD demonstrating a lack of perceptual benefit from hearing aids and habilitation.

Further research is needed to more clearly understand the effects of cochlear implantation on speech perception in children with ANSD. This research would require larger sample sizes, appropriate statistical analyses and the use of standardized measures of speech perception. Research should also focus on determining the relationship between speech perception outcomes and underlying pathology. The development of reliable methods for identifying the status of the auditory nerve prior to implantation is also warranted to improve the prognostic information available to ANSD patients and their families

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