HHS Public Access

Author manuscript

Otol Neurotol. Author manuscript; available in PMC 2016 September 01.

Published in final edited form as:

Otol Neurotol. 2015 September ; 36(8): e121–e128. doi:10.1097/MAO.0000000000000757.

Cochlear Implantation in Children with Autism Spectrum Disorder

Adrien A. Eshraghi, M.D., **Ronen Nazarian, M.D.**, **Fred F. Telischi, M.D.**, **Diane Martinez, Au.D.**, **Annelle Hodges, Ph.D**, **Sandra Velandia, Au.D.**, **Ivette Cejas-Cruz, Ph.D**, **Thomas J. Balkany, M.D.**, **Kaming Lo, M.P.H.**, and **Dustin Lang, M.S.**

Department of Otolaryngology, University of Miami Miller School of Medicine, Miami, FL

Abstract

Objective—To assess the outcome of cochlear implantation in children with Autism Spectrum Disorder

Study Design—Retrospective case review and survey

Setting—Tertiary referral center

Patients—Children who meet criteria for cochlear implantation and diagnosis of Autism Spectrum Disorder

Main Outcome Measures—Receptive and expressive language scores and parental survey data.

Results—15 patients with history of ASD and cochlear implantation were analyzed and compared to 15 patients who received cochlear implant and have no other disability. Post-operatively, more than 67% of children with ASD significantly improved their speech perception skills and 60% significantly improved their speech expression skills while all patients in the control group showed significant improvement in both aspects. The top three reported improvements after cochlear implantation were name recognition, response to verbal requests, and enjoyment of music. Of all behavioral aspects, the use of eye contact was the least improved. Survey results in regards to improvements in patient interaction were more subtle when compared to those related to sound and speech perception. The most improved aspects in the ASD patients' lives after cochlear implantation appeared to be attending to other people's requests and conforming to family routines. Of note, awareness of the child's environment is the most highly ranked improvement attributed to the cochlear implant.

Conclusions—Cochlear implants are effective and beneficial for hearing impaired members of the ASD population even though development of language may lag behind that of implanted children with no additional disabilities. Significant speech perception and overall behavior improvement are noted.

All correspondence should be directed to: Adrien A. Eshraghi M.D., University of Miami Ear Institute, Clinical Research Building, 1120 N.W. 14 St., Fifth Floor, Miami, FL 33136, Phone: 305-243-1413, AEshraghi@med.miami.edu.

Introduction

Despite evidence that cochlear implants are beneficial in the pediatric population,[1–3] a great deal of variability in performance continues to be reported. One reason for the variability in outcomes is the presence of co-morbid diagnoses such as Autism Spectrum Disorder (ASD), and little is known regarding the benefit of implantation in these children. ASD is characterized by deficits in social communication and interaction along with restricted, repetitive patterns of behavior, interests, or activities.

The prevalence of ASD in children has increased considerably over the past few decades from 2–5 in 10,000 (between 1960 and 1980)[4] to 1 in 150 (2002) to 1 in 125 (2004) to 1 in 110 (2006) and finally 1 in 88 (2008), according to the most recent Centers for Disease Control (CDC) estimate provided by the Autism and Developmental Disabilities Monitoring (ADDM) Network[5]. However, some argue that the recent increase is not directly due to an increased prevalence of the disorder, but is due to an increased awareness of the disorder and broadening of its diagnostic criteria[6]. Children who receive intervention by 2–3 years of age generally have more positive outcomes, specifically in terms of language development and school placement[7]. Parents often report autism symptom recognition by the time their child is 18 months[8,9]. However, in many cases, children develop appropriately until 18–24 months and then regress, thus children may not be given a clinical diagnosis of autism until after they reach age 3[5]. Prevalence estimates of hearing impairment in those with ASD vary and are currently a subject of debate. There is currently no conclusive evidence that hearing impairment occurs more frequently in the ASD population than in the general population[10]. However, the difficulties with communication and language as well as central auditory processing issues that are inherent characteristics of ASD present a unique clinical challenge for evaluation of this population with regards to CI candidacy as well as for assessment of outcomes. Hearing problems may be missed because of diagnostic overshadowing; that is, behaviors resulting from hearing problems may be considered part of the symptoms of autism, such as lack of attention, speech problems, lack of eye contact or shading of the eyes, and clumsiness. To date, few studies have evaluated the benefits of cochlear implantation in children with ASD[11–17]. The current study will add to this small body of literature by assessing receptive and expressive language skills in children with ASD post-implantation and surveying the parents in regard to the benefits of implantation.

Methods

Patients

This is a retrospective review comparing both pre- and post-implantation speech perception and expression scores in children with ASD and CIs to those of typically developing children with CIs. All ASD patients in the current study were diagnosed under the DSM-IV criteria, and are reported as such. A survey, which asked about the effect of CI on behaviors closely associated to ASD as well as overall device satisfaction, was also administered to parents of children in the ASD group.

The ASD group consisted of 15 children who were implanted at the THIS UNIVERSITY between the years of 1992 and 2011. Eleven patients were diagnosed with autistic disorder

and 4 were diagnosed with PDD-NOS. Nine of these children were diagnosed post-implantation. The ASD group was compared with a control group of 15 CI patients with no additional disabilities who were similar by age at first implantation and years of implant usage. This study was approved by the University of BLANK IRB. All children were implanted with no complications and appropriate CI function was verified.

Speech perception and speech expression evaluation

All of the children in both ASD and control groups participated in a standard CI evaluation. Pediatric CI candidacy is determined based on the following criteria: 1) age 12 months to 17 years; 2) profound sensorineural hearing loss (unaided pure tone average thresholds of ≥ 90 dB HL); 3) minimal benefit from hearing aids, defined as less than 30% on single-syllable word tests; 4) no evidence of central auditory lesions, lack of auditory nerve, or Michel deformity; and 5) no contraindications to surgery. Specific methods of audiologic assessment are chosen which are developmentally appropriate for age, language level, and auditory ability. Furthermore, an auditory brainstem response (ABR) test is performed as an objective measure of auditory function[18]. For the children in this study, pure tone audiometry was performed in both aided and non-aided conditions and speech discrimination was evaluated in quiet using standardized methods such as the Early Speech Perception (ESP) test, Multisyllabic Lexical Neighborhood Test (MLNT), or the Phonetically Balanced Kindergarten (PBK) test. For the purpose of this study, a categorical scoring approach of functional speech perception skills and expression vocabulary skills was used (Table 1a and 1b). This approach provides us a practical estimate of the subjects' communication abilities. The scoring was done at the most recent post-implant visit and is done based on CI evaluation and agreement between 3 audiologists and 1 speech pathologist familiar with the patients at our institution.

Parental survey

A parental survey consisting of 39 questions evaluating subjective impression of CI benefits was also administered to parents of children in the ASD group by telephone interview. To be consistent with the small body of literature available, we utilized an identical survey which was described by Donaldson et al[19]. The questionnaire focuses on three core characteristics of ASD: 1) communication skills, 2) behavior, and 3) interaction with others.

Statistical analysis

Sign tests were used to evaluate whether the ordinal outcome had improved in a significant amount of pairs in each of the groups after implantation. Furthermore, Fisher's exact tests were used to test whether the proportions of significant improvement (defined as an improvement of at least 2 scores in the outcome) is different between control and ASD. All statistical analyses were performed using SAS (v.9.2, SAS institute, Cary, NC) and a type I error rate of 0.05 was used for hypothesis testing.

Results

Average age at implantation in the ASD group was 3 years (Range 18 months to 5.5 years) and average CI use was 8.3 years (Table 2). Average age at implantation in the control group was 3.5 years (Range 1.5 – 15 years) and average CI use was 8.2 years (Table 3).

Speech perception data

Table 4 summarizes the speech perception data for both the control and ASD groups. Fourteen out of 15 patients in the ASD group had pre-operative records that enabled assessment of their pre-implant speech perception ability. Pre-operatively, none of the patients in either the control group or the ASD group attained a speech perception category above 2. In the control group 93.3% (14 out of 15) children were in the lowest categories (0–1) and in the ASD group, 85.7% (12 out of 14) of the children were in the lowest categories (0–1). Post-operatively, 93.3% (14 out of 15) of the children in the control group improved to a speech perception category 4 and the remaining child improved to category 3. Most children with ASD also significantly improved their speech perception skills. Specifically, 67% (10 out of 15) attained a speech perception category of 3 or 4 while 33% (4 out of 15) were rated category 1, and none of the ASD patients remained in category 0. Results from sign test revealed that the improvement within both control ($p<0.0001$) and ASD ($p=0.0001$) was significant after implantation (Table 5).

Speech expression data

Table 6 summarizes the results of the expressive vocabulary data. Fourteen out of 15 patients in the ASD group had pre-operative records which assessed their speech abilities, with 93% (13 out of 14) of the children in the lowest categories (0–1), However, one child in the ASD group was able to communicate using words, likely to due to appropriate amplification use prior to complete deterioration of hearing. Pre-operatively, 93.3% (14 of 15) of the children in the control group were in the lowest speech expression categories (0 or 1) with the remaining child in category 2. Post-operatively, 93.3% (14 of 15) of the children in the control group improved to speech expression category 4 and the remaining child improved to category 3. Children in the ASD group also improved their expressive vocabulary, as 60% (9 out of 15) improved to a category of 3 or 4, indicating that they were able to communicate using simple phrases and some sentences. Further, 33% (5 out of 15) remained in category 1 and none of the patients remained in category 0. Results from sign test revealed that the improvement within both control ($p<0.0001$) and ASD ($p=0.0010$) was significant after implantation (Table 5).

Control vs ASD in outcomes

In addition to the observation of the improvements in speech perception and expression within each of the groups, comparisons using Fisher's exact test was performed to test whether the proportions of significant improvements were different between the two groups for each outcome. A significant improvement was defined as an increase of at least 2 scores after the implantation. Results showed that more significant improvement is observed in the control group than in ASD group in both speech perception (100% vs 66.7%, $p=0.0421$) and speech expression (100% vs 60%, $p=0.0169$) (Table 7).

Parental Survey

All 15 parents of children in the ASD group were contacted to complete the survey, with 13 families agreeing to participate. The results with regard to behavior and communication are illustrated in table 8. The top three reported improvements after CI were name recognition, response to verbal requests, and enjoyment of music. Of all behavioral aspects, the use of eye contact was the least improved. Table 9 displays survey results with regard to interaction before and after cochlear implantation. The most improved aspects after CI were attending to other people's requests and conforming to family routines.

Parental ranking of behaviors most affected by the implant is summarized in table 10. Awareness of the child's environment is the most highly ranked improvement attributed to the CI. In addition, high rankings were obtained for improvements in communication and educational potential. Overall, social interaction and improvement in the emotional needs of the child were the least improved post-implantation. Finally, 12 out of 13 surveyed parents responded that the child's overall success level with implant was better than they expected. All of them reported that they would recommend the CI to another family in a similar situation.

Discussion

Consistent with prior research, improvements in speech perception and expressive vocabulary was demonstrated. Children with bilateral implants in the current study improved the most and obtained a category score of 4 with regards to speech perception. This is consistent with outcome studies on bilateral implants showing an improvement in localization of sound and speech perception in a noise. However, given that these children were implanted sequentially, it could be that the ones who were performing particularly well with their first implant were more likely to go ahead with the second. Similar to the Donaldson study, the top improvements reported by parents in the current study were name recognition, response to verbal requests, and reaction to music. Parents in the Donaldson study indicated that communication was the most impacted by the implant, while the top ranked improvement in the current study was awareness of the environment[19]. In addition, improvement in education ability was the third highest ranked improvement in our study, which only played a minor role in the Donaldson study. Survey results from the Donaldson study indicated that 5 of 7 families would recommend CIs to another family in the same situation. In our study, all of the families would recommend CIs. The prevalence of ASD among the CI population at their center was reported to be 1.7% and the average age at diagnosis was 4.7 years, which is later than 3.4 years for children without hearing loss. The prevalence in our center is 2.6%.

Cruz et al. reported that oral language scores were lower for children with ASD than for typically developing children after 3 years of follow-up[11]. Our study confirmed these findings. However, 9 of 15 children in our ASD group are in category 3 or 4 for expressive language following implantation meaning that they can express their basic needs and carry on basic conversation. Five out of the 15 children in our ASD group were placed in category 1 for expressive vocabulary, indicating that they did not develop speech. Interestingly, 4 of 5 of these had additional disabilities. Furthermore, this is not surprising considering estimates

that 50% of children with ASD do not acquire speech as a primary mode of communication[20].

In contrast to the conclusions of Donaldson et al., we found that implantation did have some positive effect on the features most closely associated with ASD[19]. However, this effect is not large enough to change the child's diagnosis. These results imply that CIs can be beneficial in children with ASD even though they may not exhibit immediate gains in language and communication skills like their typically developing implanted peers, as shown in our control group. An additional factor that we must keep in mind when evaluating outcomes is that ASD is a spectrum that varies widely so that, all things being equal, one child with autistic disorder may not possess the ability to develop language and communication to the same extent as another. Therefore, the appropriateness of implantation should be evaluated by a multidisciplinary team on a case-by-case basis. Further, an interesting observation of positive outcomes of implantation in ASD is found in witnessing the bond that the child forms with the device. Our CI audiologists who work closely with these kids say that the children with device failure are unhappy and behavior is better with the implant. This is in contrast to the finding of Cruz et al. which stated that children with ASD had higher rates of externalizing behavior problems following implantation[11]. The findings of these authors may have been due to the fact that the children in their study were too young to exhibit any behavior problems at all prior to the time of implantation and that the development of behavior problems was a function of their developmental disorder rather than a function of the cochlear implant.

Limitations of the current study include difficulty in composing a control group that is exactly matching on all criteria with our ASD group. There is also the possibility for parental bias in the survey responses. While useful, the insight provided by grouping the outcomes of implanted individuals with ASD and comparing them to a group of neuro-typically developing peers with CIs is limited. This is because one child with ASD can be very different from another, thus outcomes can be expected to vary within the group. It should be noted that we also did not separately analyze the effect of bilateral implantation. The majority of the participants (10 out of 15) in the ASD group were not diagnosed with autism until months to years after cochlear implantation. The average time between implantation and diagnosis of autism was 19 months. This is a significant amount of time that needs to be shortened, as we know that the prognosis of ASD is linked to early intervention. Thus, this emphasizes the need for the development of gold standards for evaluation of autism in children with hearing loss. Evaluation for dual diagnosis should be prompted if, after implantation, the child is not developing language appropriately, is displaying self-stimulating or hyperactive behaviors, is not making eye contact or not pointing, and has symptoms of sensory processing disorders. Once diagnosed, children with autism using cochlear implants can start appropriate management and intervention for both disorders.

Our post-op management includes weekly 1 hour AVT sessions incorporating other means of communication used with the child. The initial stimulation takes place 3 weeks following implantation surgery. Subsequent follow-up occurs at 1 week following initial stimulation, then 2 weeks later, then 1 month later, then every 3 months after that. Electrical stapedial

reflex thresholds (ESRT), neural response telemetry (NRT), neural response imaging (NRI), and automated response telemetry (ART) may be used for programming when a behavioral response is not obtainable. However, programming should proceed conservatively since children with ASD may be prone to hyperacusis[21]. We did not find this to be a particularly troublesome issue with our patients. There was only one ASD subject (patient # 11) for which the level of stimulation had to be limited due to discomfort in order to facilitate acceptance of the new equipment.

Parent involvement is capital for the success of these children with ASD. Patient #12 illustrates that well. While initially the hearing deficit masked a diagnosis of underlying autism, this patient was implanted at 3 years of age, expression scores did not improve over the following 6 years. Once autism was diagnosed, special instructional courses were pursued by the parents. The child exhibited marked learning improvement with the implant and was even implanted bilaterally at age 12. Today, this patient is high functioning and attending college with a major in chemistry. Having the full support of the parents in the whole process includes also being able to address their concerns with regard to vaccination before CI. The risk of meningitis is known to be higher in those with hearing impairment, as well as those undergoing CI surgery[22–25]. For this reason, the CDC has published guidelines for pneumococcal vaccination for CI recipients and this is now the standard of care, as it should be. However, this issue must be addressed using special care when dealing with parents of children with ASD. Many parents of children with ASD report significant side effects from previous vaccinations that their child has received, with some cases reporting severe developmental regression[26,27]. This fact was also shared by many parents during our survey. The fear of regression caused many parents of children with ASD to alter their vaccination practices[28]. According to Bazzano et al., half of parents of children with ASD discontinued or changed their vaccination practices for this reason[29]. While there is an obvious genetic component in cases of ASD, recent findings are in favor of interaction with some yet unknown specific environmental factors that may trigger the regressive form of autism in many cases and may explain the increase in prevalence in recent years[30]. Recent findings have also shown that the many children with ASD display some form of immune dysregulation and neuro-inflammation[31,32].

According to these studies, most of the individuals with Autism have high levels of oxidative stress[33], low glutathione levels which impair the ability to detoxify heavy metals[34], impaired methylation[35], gastrointestinal distress and mitochondrial dysfunction[36,37]. All these conditions do interplay and exacerbate one another’s ill functioning and many of these conditions may be negatively affected by further immune stimulation such as vaccination. Chez et al. reviewed immunization in this population and also discusses the history of autoimmunity as another possible predisposing factor for autism[38]. Therefore, we should be sensitive to parental concerns and individual factors such as regressive form of autism and family history of autoimmunity. However, meningitis after cochlear implantation remains a concern and we should keep in mind its main risk factors: abnormal cochlea, history of meningitis, CSF leak during cochleostomy, and previously used dual component electrode. In the presence of any of these risk factors the family should be strongly recommended to accept the anti-pneumococcal vaccine.

Realistic expectations should be discussed with parents prior to implantation and children with autism using CIs should receive auditory training via auditory verbal therapy (AVT). However, this should be combined with ABA, an evidenced based treatment for children with autism that uses positive reinforcement techniques. Easterbrooks et al. presented a case in which ABA was successfully used to reduce self-stimulating behaviors in a child with CIs and ASD[39]. The possibility of other problems must be recognized, such as sensory hyper or hyposensitivity or central processing disorder. Sensory integration therapy may also be employed as necessary.

Counseling should specifically focus on discussing with the family factors associated with a favorable prognosis, such as less severe form of ASD (previously Asperger syndrome or PPD-NOS), no comorbid mental retardation or neurological problems, early implantation, and the importance of family support. Parents should be aware that the implant may not substantially affect behaviors inherent to ASD and will not likely change their child's diagnosis. Furthermore, given that children are being implanted at younger ages, the possibility of underlying developmental disorders becoming apparent following implantation and the effect that those disorders may have on outcomes should be discussed with families.

Conclusions

This new data suggests that CIs improve expressive and receptive language for hearing impaired children with ASD. Furthermore, children with ASD and CIs have a bond with their device and benefit from it even if they do not develop language to the same extent as children with no additional disability. Overall, families are satisfied with the outcomes post-implantation. However, they should be counseled adequately on realistic expectations. If an implanted child does not develop language appropriately, an evaluation for comorbidities, such as ASD, should be recommended.

Acknowledgments

The project described was supported by Grant Number 1UL1TR000460, University of Miami Clinical and Translational Science Institute, from the National Center for Advancing Translational Sciences and the National Institute on Minority Health and Health Disparities. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH.

References

1. Niparko JK, Tobey EA, Thal DJ, et al. Spoken language development in children following cochlear implantation. JAMA. 2010; 303(15):1498–1506. [PubMed: 20407059]
2. Baldassari CM, Schmidt C, Schubert CM, Srinivasan P, Dodson KM, Sismanis A. Receptive language outcomes in children after cochlear implantation. Otolaryngol Head Neck Surg. 2009; 140(1):114–119. [PubMed: 19130973]
3. Forli F, Arslan E, Bellelli S, et al. Systematic review of the literature on the clinical effectiveness of the cochlear implant procedure in paediatric patients. Acta Otorhinolaryngol Ital. 2011; 31(5):281–298. [PubMed: 22287820]
4. Duchan E, Patel DR. Epidemiology of autism spectrum disorders. Pediatr Clin North Am. 2012; 59(1):27–43. ix–x. [PubMed: 22284791]

5. Baio J. Prevalence of autism spectrum disorders – autism and developmental disabiilties monitoring network, 14 sites, united states, 2008. Morbidity and Mortality Weekly Report (MMWR). 2012; 61(SS03):1-2-19.
6. Johnson CP, Myers SM, American Academy of Pediatrics Council on Children With Disabilities. Identification and evaluation of children with autism spectrum disorders. Pediatrics. 2007; 120(5): 1183–1215. [PubMed: 17967920]
7. Rogers SJ. Brief report: Early intervention in autism. J Autism Dev Disord. 1996; 26(2):243–246. [PubMed: 8744493]
8. Chakrabarti S, Fombonne E. Pervasive developmental disorders in preschool children: Confirmation of high prevalence. Am J Psychiatry. 2005; 162(6):1133–1141. [PubMed: 15930062]
9. Spitzer RL, Siegel B. The DSM-III-R field trial of pervasive developmental disorders. J Am Acad Child Adolesc Psychiatry. 1990; 29(6):855–862. [PubMed: 2273011]
10. Beers AN, McBoyle M, Kakande E, Dar Santos RC, Kozak FK. Autism and peripheral hearing loss: A systematic review. Int J Pediatr Otorhinolaryngol. 2014; 78(1):96–101. [PubMed: 24300947]
11. Cruz I, Vicaria I, Wang NY, Niparko J, Quittner AL, CDaCI Investigative Team. Language and behavioral outcomes in children with developmental disabilities using cochlear implants. Otol Neurotol. 2012; 33(5):751–760. [PubMed: 22699986]
12. Daneshi A, Hassanzadeh S. Cochlear implantation in prelingually deaf persons with additional disability. J Laryngol Otol. 2007; 121(7):635–638. [PubMed: 17147840]
13. Edwards LC. Children with cochlear implants and complex needs: A review of outcome research and psychological practice. J Deaf Stud Deaf Educ. 2007; 12(3):258–268. [PubMed: 17493953]
14. Filipo R, Bosco E, Mancini P, Ballantyne D. Cochlear implants in special cases: Deafness in the presence of disabilities and/or associated problems. Acta Otolaryngol Suppl. 2004; (552):74–80. [PubMed: 15219052]
15. Hamzavi J, Baumgartner WD, Egelierler B, Franz P, Schenk B, Gstoettner W. Follow up of cochlear implanted handicapped children. Int J Pediatr Otorhinolaryngol. 2000; 56(3):169–174. [PubMed: 11137590]
16. Meinzen-Derr J, Wiley S, Grether S, Choo DI. Children with cochlear implants and developmental disabilities: A language skills study with developmentally matched hearing peers. Res Dev Disabil. 2011; 32(2):757–767. [PubMed: 21129916]
17. Wiley S, Meinzen-Derr J, Choo D. Auditory skills development among children with developmental delays and cochlear implants. Ann Otol Rhinol Laryngol. 2008; 117(10):711–718. [PubMed: 18998496]
18. Wackym, AP.; Runge-Samuelson, CL. Chapter 158: Cochlear implantation: Patient evaluation and device selection. In: Flint, PW.; Haughey, BH.; Lund, VJ., et al., editors. Cummings otolaryngology – head and neck surgery. Fifth. Philidelphia, PA: Mosby, Elsevier; 2010.
19. Donaldson AI, Heavner KS, Zwolan TA. Measuring progress in children with autism spectrum disorder who have cochlear implants. Arch Otolaryngol Head Neck Surg. 2004; 130(5):666–671. [PubMed: 15148195]
20. Prizant BM. Brief report: Communication, language, social, and emotional development. J Autism Dev Disord. 1996; 26(2):173–178. [PubMed: 8744480]
21. Gomes E, Pedroso FS, Wagner MB. Auditory hypersensitivity in the autistic spectrum disorder. Pro Fono. 2008; 20(4):279–284. [PubMed: 19142473]
22. Reefhuis J, Whitney CG, Mann EA. A public health perspective on cochlear implants and meningitis in children. Otol Neurotol. 2010; 31(8):1329–1330. [PubMed: 20802368]
23. Heman-Ackah SE, Roland JT Jr, Haynes DS, Waltzman SB. Pediatric cochlear implantation: Candidacy evaluation, medical and surgical considerations, and expanding criteria. Otolaryngol Clin North Am. 2012; 45(1):41–67. [PubMed: 22115681]
24. Cohen NL, Hirsch BE. Current status of bacterial meningitis after cochlear implantation. Otol Neurotol. 2010; 31(8):1325–1328. [PubMed: 20818287]
25. Lalwani AK, Cohen NL. Does meningitis after cochlear implantation remain a concern in 2011? Otol Neurotol. 2012; 33(1):93–95. [PubMed: 22143298]

26. Jyonouchi H, Sun S, Le H. Proinflammatory and regulatory cytokine production associated with innate and adaptive immune responses in children with autism spectrum disorders and developmental regression. J Neuroimmunol. 2001; 120(1–2):170–179. [PubMed: 11694332]
27. Poling JS, Frye RE, Shoffner J, Zimmerman AW. Developmental regression and mitochondrial dysfunction in a child with autism. J Child Neurol. 2006; 21(2):170–172. [PubMed: 16566887]
28. Holler K, Scalzo A. “I’ve heard some things that scare me”. responding with empathy to parents’ fears of vaccinations. Mo Med. 2012; 109(1):10–3. 16–8. [PubMed: 22428439]
29. Bazzano A, Zeldin A, Schuster E, Barrett C, Lehrer D. Vaccine-related beliefs and practices of parents of children with autism spectrum disorders. Am J Intellect Dev Disabil. 2012; 117(3):233–242. [PubMed: 22716265]
30. Grabrucker AM. Environmental factors in autism. Front Psychiatry. 2012; 3:118. [PubMed: 23346059]
31. Vargas DL, Nascimbene C, Krishnan C, Zimmerman AW, Pardo CA. Neuroglial activation and neuroinflammation in the brain of patients with autism. Ann Neurol. 2005; 57(1):67–81. [PubMed: 15546155]
32. Cohly HH, Panja A. Immunological findings in autism. Int Rev Neurobiol. 2005; 71:317–341. [PubMed: 16512356]
33. Chauhan A, Chauhan V. Oxidative stress in autism. Pathophysiology. 2006; 13(3):171–181. [PubMed: 16766163]
34. Rose S, Melnyk S, Pavliv O, et al. Evidence of oxidative damage and inflammation associated with low glutathione redox status in the autism brain. Transl Psychiatry. 2012; 2:e134. [PubMed: 22781167]
35. James SJ, Cutler P, Melnyk S, et al. Metabolic biomarkers of increased oxidative stress and impaired methylation capacity in children with autism. Am J Clin Nutr. 2004; 80(6):1611–1617. [PubMed: 15585776]
36. Dhillon S, Hellings JA, Butler MG. Genetics and mitochondrial abnormalities in autism spectrum disorders: A review. Curr Genomics. 2011; 12(5):322–332. [PubMed: 22294875]
37. Sharpe MA, Livingston AD, Baskin DS. Thimerosal-derived ethylmercury is a mitochondrial toxin in human astrocytes: Possible role of fenton chemistry in the oxidation and breakage of mtDNA. J Toxicol. 2012; 2012:373678. [PubMed: 22811707]
38. Chez MG, Chin K, Hung PC. Immunizations, immunology, and autism. Semin Pediatr Neurol. 2004; 11(3):214–217. [PubMed: 15575416]
39. Easterbrooks SR, Handley CM. Behavior change in a student with a dual diagnosis of deafness and pervasive developmental disorder: A case study. Am Ann Deaf. 2005; 150(5):401–407. [PubMed: 16610472]

Table 1

a: Speech Perception Categories	
Category	**Perception Criteria**
0	No awareness of environment
1	Awareness, detection or localization of sound
2	Identification/recognition of words
3	Identification/recognition of simple phrases (2 words) and commands
4	Understands conversations

b: Speech Expression Categories	
Category	**Expression Criteria**
0	No vocalization
1	Some vocalization (consonants, vowels, nasal sounds)
2	Words only
3	Simple Phrases and Commands (Where is X, lets go, etc)
4	Able to produce sentences

Table 2

Clinical Characteristics of the Patients in ASD group (AD = Autistic Disorder)

Patient	Current Age (years)	Autism Spectrum (DSM-IV)	Bilateral Implant	Age at Implant (years)	Years with Implant	Associated Disability	Continues to use implant?
1	8.5	AD	No	1.75	6.5	Rumination, GERD, Strabismus	Intermittent
2	15	AD	No	5.5	9.5	Gross motor delay, Strabismus	Yes
3	6	AD	No	4.5	1.5	Prematurity, encephalopathy, gross motor delay	Yes
4	13.5	AD	No	3.5	10	polymicrogyria, gliosis, developmental delay	Yes
5	7	PDD-NOS	No	2	5	ADHD	Yes
6	14	AD	Yes	4 (1st) 10 (2nd)	10	None	Yes
7	12	AD	Yes	1.5 (1st) 6 (2nd)	10.5	None	Yes
8	14	AD	No	3	11	None	Yes
9	15.5	AD	Yes	4 (1st) 15 (2nd)	11	None	Yes
10	11.5	PDD-NOS	No	1.67	9.5	None	Yes
11	9	AD	No	4	5	Ushers	Yes
12	22	AD	Yes	3 (1st) 12 (2nd)	19	meningitis at 18 months	Yes
13	10	PDD-NOS	No	4	6	None	Yes
14	5	PDD-NOS	No	2	3	None	Yes
15	9	AD	Yes	1.5 (1st) 2 (2nd)	7.5	None	Yes

Table 3

Clinical Characteristics of the patients in control group

Patient	Current Age (years)	Bilateral Implant	Age at Implant (years)	Years with Implant	Associated Disability	Continues to use implant?
1	9	No	2	7	No	Yes
2	15	No	9	6	No	Yes
3	6	Yes	5 (1st) 5 (2nd)	1.5 (1st) 1.5 (2nd)	No	Yes
4	13	Yes	3 (1st) 4 (2nd)	10 (1st) 9 (2nd)	No	Yes
5	7.5	No	1.5	6	No	Yes
6	13	Yes	4 (1st) 7 (2nd)	7 (1st) 4 (2nd)	No	Yes
7	13	Yes	7 (1st) 11 (2nd)	7(1st) 3 (2nd)	No	Yes
8	14	No	3	11	No	Yes
9	15	No	3.5	11.5	No	Yes
10	12	Yes	1.5 (1st) 6.5 (2nd)	10.5 (1st) 5.5 (2nd)	No	Yes
11	9	No	3	6	Yes	Yes
12	24	Yes	4 (1st) 21 (2nd)	20 (1st) 3 (2nd)	No	Yes
13	10	No	3.5	6.5	No	Yes
14	7	No	2	5	Yes	Yes
15	9	Yes	1.5 (1st) 3.5 (2nd)	7.5 (1st) 5.5 (2nd)	No	Yes

Table 4

Speech Perception Scores. Refer to table 1 for score key.

	Speech Perception Pre-Implant		Speech Perception Post-Implant	
Patient	**Control**	**ASD**	**Control**	**ASD**
1	0	1	4	1
2	2	0	4	2
3	1	0	4	1
4	1	0	4	1
5	0	1	4	4
6	1	0	4	3
7	1	0	4	4
8	0	0	4	4
9	1	2	4	4
10	0	0	4	4
11	0	0	4	1
12	1	0	4	4
13	0	2	4	3
14	0	0	3	3
15	0	n/a	4	4
Avg.	**0.5**	**0.4**	**3.9**	**2.9**

Table 5

Sign test was used to test for the difference between pre-implant and post-implant on perception and expression score within each group. The perception and expression scores significantly improved after implantation in a significant amount of pairs in both the control (p-value<0.0001) and ASD (p-value<0.0001) groups.

	Control		ASD	
	Median	**Range**	**Median**	**Range**
Speech Perception				
Pre-Implant	0	0–2	0	0–2
Post Implant	4	3–4	3	1–4
Speech Expression				
Pre-Implant	0	0–2	0	0–2
Post Implant	4	3–4	3	1–4

Table 6

Speech Expression Scores. Refer to table 1 for score key.

	Speech Expression Pre-Implant		Speech Expression Post-Implant	
Patient	**Control**	**ASD**	**Control**	**ASD**
1	0	1	4	1
2	2	1	4	1
3	0	1	4	1
4	1	0	4	1
5	0	0	4	4
6	1	0	4	3
7	1	0	4	3
8	0	1	4	3
9	1	0	4	4
10	0	0	4	4
11	0	0	4	1
12	1	1	4	4
13	0	2	4	2
14	0	0	3	3
15	0	n/a	4	4
Avg.	**0.5**	**0.5**	**3.9**	**2.6**

Table 7

Fisher's exact tests were used to determine whether the proportions of significant improvement (defined as an improvement of at least 2 scores in the outcome) are different between control and ASD groups. More significant improvement is observed in the control group than in ASD group in both speech perception and speech expression.

	Control		ASD		
	Count	**%**	**Count**	**%**	**P-value**
Speech Perception					
No significant improvement	0	0	5	33.33	0.0421
Significant improvement	15	100	10	66.67	
Speech Expression					
No sig. improvement	0	0	6	40	0.0169
Significant improvement	15	100	9	60	

Table 8

Parental Survey-Behavior and Communication Scores: Thirteen of 15 parents answered the survey pertaining to behavior and communication improvement after the implant. Scores are presented as before->after implantation for each question. Average scores for each question are presented in the second to last column. Average difference in score improvement is presented in the last column. Score 1 = never, Score 3 = sometimes, Score 5 = always.

Pre > Post Rating															
Subject	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**Avg**	**Avg Δ**
Reacts to Sound	3>4	2>5	2>4	1>5	2>5	2>4	1>5	2>5	2>5	1>5	1>5	1>5	3>4	**1.7>4.7**	**+3**
Vocalizes	3>4	3>4	2>5	1>3	1>5	1>4	1>5	2>5	1>5	1>5	1>3	3>4	4>5	**1.7>4.3**	**+2.6**
Makes eye contact	2>3	3>5	3>5	1>5	2>3	1>3	1>5	2>4	2>4	1>3	5>3	2>4	2>2	**2.1>4**	**+1.9**
Recognizes name	1>4	1>5	1>4	1>1	1>5	1>5	1>5	1>5	3>5	1>5	1>5	1>5	5>5	**1.2>4.5**	**+3.3**
Enjoys music	2>4	3>5	1>4	1>3	2>5	1>5	1>5	1>5	1>3	1>5	1>5	1>4	1>1	**1.4>4.5**	**+3.1**
Responds to verbal requests	1>3	2>4	1>4	1>3	1>5	1>3	1>5	1>5	1>4	1>5	1>5	1>5	4>2*	**1.1>4.3**	**+3.2**
Uses sign language	1>4	4>5	5>3	1>1	4>3	3>4	1>1	1>5	3>1	3>1	5>3	1>1	1>4*	**2.8>2.8**	**0**

Table 9

Parental Survery- Interaction Scores. Thirteen of 15 parents answered the survey pertaining to patient interaction improvement after the implant. Scores are presented as before->after implantation for each question. Average scores for each question are presented in the second to last column. Average difference in score improvement is presented in the last column. Score 1 = never, Score 3 = sometimes, Score 5 = always.

Pre>Post Rating															
Subject	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**Avg**	**Avg Δ**
Siblings play with Child	3>3	n/a	5>5	n/a	n/a	n/a	3>4	n/a	n/a	n/a	n/a	1>4	5>5	**4.2>4.4**	**+0.2**
Child taken to family gatherings	2>3	3>5	4>4	1>3	5>5	4>4	5>5	5>5	3>5	5>5	5>5	5>5	5>5	**3.7>4.5**	**+0.8**
Other Children play with Child	3>3	2>4	2>4	1>1	4>5	1>5	4>4	1>4	1>3	n/a>5	5>5	1>1	3>3	**2.4>3.8**	**+1.4**
Child conforms to family routine	3>4	1>4	3>5	1>1	n/a>3	3>4	n/a>5	1>5	2>5	n/a>5	1>5	2>4	5>5	**2.1>4.2**	**+2.1**
Comfortable taking child to public places	4>3	2>4	5>5	1>3	2>4	5>4	5>5	2>5	1>5	5>5	3>3	1>4	5>5	**3.1>4.3**	**+1.2**
Attends to people	4>3	2>4	2>4	1>3	1>4	1>4	1>5	1>4	1>4	4>5	1>5	1>4	5>5	**1.8>4.1**	**+2.3**
Others are interested in child's progress	3>4	2>5	5>5	5>5	4>5	5>5	4>4	5>5	2>5	5>5	4>4	1>4	5>5	**3.7>4.7**	**+1**

Table 10

Parental Survey: Ranking of 10 most improved behavioral aspects after cochlear implantation. Parents were asked to rank from 1–10 the most improved to the least improved behavioral ability. Rank of 1 was the behavior most affected by the implant and 10 was the least affected.

Subject	1	2	3	4	5	6	7	8	9	10	11	12	13	Mean
Overall Behavior	9	9	1	5	9	7	10	5	1	3	1	1	1	**6**
Communication	6	10	2	9	1	3	1	1	4	1	3	2	8	**3**
Sibling Interaction	10	6	8	n/a	n/a	n/a	5	n/a	9	7	9	9	4	**6.9**
Overall family interaction	1	5	9	1	4	6	6	6	8	9	5	7	5	**4.9**
Education	3	3	6	7	3	1	4	4	3	5	4	4	2	**3.8**
Attention	5	4	4	8	6	2	3	7	7	2	2	5	10	**4.9**
Awareness of Environment	2	1	5	6	2	4	2	2	2	6	6	6	6	**2.8**
Social Interaction	7	7	10	3	5	5	9	8	5	10	8	10	9	**6.3**
Potential to Succeed	4	8	3	4	7	8	7	3	6	8	7	3	7	**4.7**
Emotional needs of Child	8	2	7	2	10	9	8	9	10	4	10	8	3	**6.3**