

## **Auditory Neuropathy/Dys-synchrony with Secondary Loss of Otoacoustic Emissions in a Child with Autism**

**Patrick N. Plyler, Ph.D.**

**Erin L. Plyler, Au.D.**

Department of Audiology & Speech Pathology  
*University of Tennessee*  
*Knoxville, TN*

**John P. Little, M.D.**

Pediatric Otolaryngology Head and Neck Surgery, PLLC  
*University of Tennessee Medical Center*  
*Knoxville, TN*

**Otoacoustic emissions are commonly present in cases of auditory neuropathy/dys-synchrony; however, otoacoustic emissions are absent or disappear in approximately one-third of patients with the disorder. Failure to identify AN/AD patients with absent otoacoustic emissions may result in improper diagnosis and management. The purpose of this article is to present findings from a case of auditory neuropathy/dys-synchrony with secondary loss of otoacoustic emissions to increase clinician awareness regarding the relationship between otoacoustic emissions and the disorder.**

---

### **Introduction**

Auditory neuropathy/dys-synchrony (AN/AD) describes a set of auditory characteristics in patients with normal outer hair cell (OHC) function and abnormal inner hair cell and/or neural function. Normal OHC function is indicated by the presence of otoacoustic emissions (OAEs); the presence of cochlear microphonics (CMs) indicates both residual outer as well as inner hair cells (Starr et al., 2003). Abnormal neural function is indicated by the absence of middle-ear muscle reflexes (MEMRs) despite normal tympanograms and auditory brainstem responses (ABRs) that demonstrate a lack of synchrony to click stimuli (Berlin et al., 1998; Hood, Berlin, Bordelon, & Rose, 2003; Starr, McPherson, & Patterson, 1991).

Possible mechanisms for AN/AD include abnormal mechanical transduction or functional characteristics of the inner hair cells (IHCs), affected synaptic juncture between the IHCs and the cochlear branch of the VIIIth nerve, or abnormal axons or cell bodies of the VIIIth nerve (Berlin et al., 1998; Hood, 1998; Starr et al., 1991). AN/AD patients range in age from infants to adults and demonstrate significant hearing difficulty, particularly in the presence of background noise. Pure-tone thresholds vary from normal sensitivity to the severe or profound hearing loss range (Berlin, Hood, Cecola, Jackson, & Szabo, 1993; Berlin, Hood, Hurley, & Wen, 1994; Starr et al., 1991; Starr, Picton, & Sininger,

1996) and speech recognition performance, especially in noise, is typically poorer than expected based on audiometric results (Hood et al., 2003).

Although OAEs are commonly present in cases of AN/AD, present OAEs are not a prerequisite for the disorder (Berlin, Morlet, & Hood, 2003; Deltenre et al., 1999; Rance et al., 1999). In fact, research has demonstrated that OAEs may be absent or may disappear in as many as one-third of AN/AD cases (Berlin et al., 2003; Deltenre et al., 1999; Starr et al., 2003). Emission loss in AN/AD cases may be attributed to middle ear disease, cochlear dysfunction, and/or hearing aid use (Berlin et al., 2003, Starr et al., 2003). In addition, the loss of emissions could be part of the extension of the *Otoferlin* gene activity which first compromises the inner hair cells (Varga et al., 2003).

AN/AD patients with absent OAEs are indistinguishable from patients with more commonly recognized sensorineural hearing loss. For example, diagnostic results from a patient with severe to profound inner ear loss would reveal normal tympanograms, absent MEMRs and absent OAEs; however, diagnostic results from an AN/AD patient with absent otoacoustic emissions might suggest these same findings (Berlin et al., 2002). Therefore, electrophysiological assessment, consisting of separate responses to negative and to positive polarity clicks to differentiate cochlear and neural responses, must be conducted to distinguish between cases of commonly understood sensorineural hearing

loss and cases of AN/AD with absent OAEs (Berlin et al., 1998). Failure to identify AN/AD patients with absent OAEs may result in improper diagnosis and management, and may have serious ramifications regarding speech and language development as well as the educational services rendered. Therefore, the purpose of this article is to present findings from a case of AN/AD with secondary loss of OAEs to increase clinician awareness regarding the relationship between OAEs and AN/AD.

## Methods and Results

### Background Information

A 26-month-old boy was evaluated to rule out hearing loss as a possible cause for developmental delays and abnormal behaviors before being diagnosed as autistic. He is a quadruplet who was born at 26 weeks gestation and remained in the Neonatal Intensive Care Unit (NICU) for approximately 3 1/2 months. Results of his initial distortion product otoacoustic emission (DPOAE) screening in the NICU indicated a pass at the left ear and a fail at the right ear; however, a subsequent DPOAE screening revealed a passing result binaurally. He has a significant visual impairment at the left eye, fair vision at the right eye, and was receiving speech therapy and occupational therapy at the time of the initial appointment.

### Initial Test Session

Initial testing included immittance measures, visual reinforcement audiometry (VRA), DPOAEs, and ABRs. Immittance measures revealed normal tympanograms at each ear; however, MEMR testing could not be completed due to the child's activity level. He would not accept insert or supra-aural earphones; therefore, behavioral testing was completed in the soundfield utilizing VRA. Audiometric results indicated a moderate hearing loss at the better ear; however, a speech awareness threshold (45 dB HL) was in poor agreement with the pure-tone average (63 dB HL), suggesting poor test reliability. As a result, sedated physiologic testing (chloral hydrate) was recommended in order to obtain ear specific information and to further investigate site of dysfunction.

DPOAE and ABR testing were conducted following sedation. DPOAE testing was initiated using a 65/55 tone pair with two points per octave ranging from 1000-6000 Hz. Responses were absent at each ear, suggesting OHC dysfunction bilaterally. ABR testing then was completed with air-conducted clicks presented to each ear through insert earphones at a rate of 27.7 per second. Testing at the limits of the equipment (90 dBnHL) indicated a possible Wave I bilaterally; however, no responses were obtained to unmasked bone-conducted clicks (65 dBnHL) or air-conducted 500-Hz tonebursts (90 dBnHL).

Results from the initial test session revealed conflicting behavioral and neurophysiological findings. DPOAEs were consistent with behavioral results obtained via VRA; however, results of ABR testing were not consistent with behavioral results and suggested a profound sensorineural hearing loss bilaterally. Therefore, follow-up behavioral and neurophysiological testing was recommended in order to investigate the degree and nature of

the hearing loss further. A trial amplification period with loaner hearing aids was initiated and an aural/oral evaluation was scheduled in order to assess his auditory and oral communication skills for the purpose of developing treatment plans.

### Radiographic & Laboratory Evaluations

A computed tomography (CT) scan was performed and revealed normal temporal bone structural anatomy. A magnetic resonance image (MRI) also was performed and revealed no abnormalities. Etiologic testing for sensorineural hearing loss was performed with normal findings on each of the following tests: Cytomegalovirus titers, RPR/MHATP, Free T4 level, TSH level, Connexin 26 assay, erythrocyte sedimentation rate (ESR), and urinalysis.

### Subsequent Behavioral Evaluations

Three separate occasions were used to confirm the behavioral results obtained during the initial test session. Initial audiometric results as well as subsequent audiometric findings are displayed in Table 1. Audiometric results obtained from the subsequent behavioral evaluations were consistent with the initial behavioral results and suggested a moderate hearing loss in at least the better ear. Furthermore, the child's mother reported that he had accepted his loaner hearing aids readily, however, no significant differences in listening and auditory behaviors had been observed.

**Table 1. Soundfield thresholds (dB HL) obtained via VRA for the initial audiometric evaluation and three subsequent behavioral evaluations.**

Test Item	Initial Test	Test 2	Test 3	Test 4
500 Hz	55	60	40	70
1000 Hz	60	50	50	70
2000 Hz	75	50	60	60
4000 Hz	60	65	70	70
Pure Tone Average	63	53	50	67
Speech Awareness	45	45	45	50
Tympanometry	Normal-AU	Normal-AU	Normal-AU	Normal-AU

### Subsequent Neurophysiological Evaluation

Immittance, DPOAE, and ABR testing were conducted following sedation (chloral hydrate). Immittance measures revealed normal tympanograms at each ear; however, ipsilateral MEMRs were absent at 500 Hz, 1000 Hz and 2000 Hz bilaterally. DPOAE testing was repeated using a 65/55 tone pair with two points per octave ranging from 1000-6000 Hz. Responses remained absent at each ear, confirming OHC dysfunction bilaterally (Table 2). These results were consistent with the DPOAE results from the initial test session and with all behavioral results obtained via VRA. However, the triage of normal tympanograms, absent MEMRs, and absent OAEs suggested either severe to profound inner ear loss or AN/AD with concomitant loss of otoacoustic emissions (Berlin et al., 2002).

**Table 2. Distortion product otoacoustic emission results (distortion product-to-noise floor ratio) for the initial test session and the subsequent neurophysiological evaluation**

Geometric Mean	Initial Session		Subsequent Session	
	Left Ear	Right Ear	Left Ear	Right Ear
1750	3.7	-2.9	-1	5.9
2100	8.4	1.5	7	-0.2
2708	1.5	-5.3	-1.5	-2.5
3336	4.4	3.9	-8.3	5.2
4269	-11.1	1.2	-5.4	4.8
5343	9.1	12.9	1.8	15.2
Overall Result	Refer	Refer	Refer	Refer

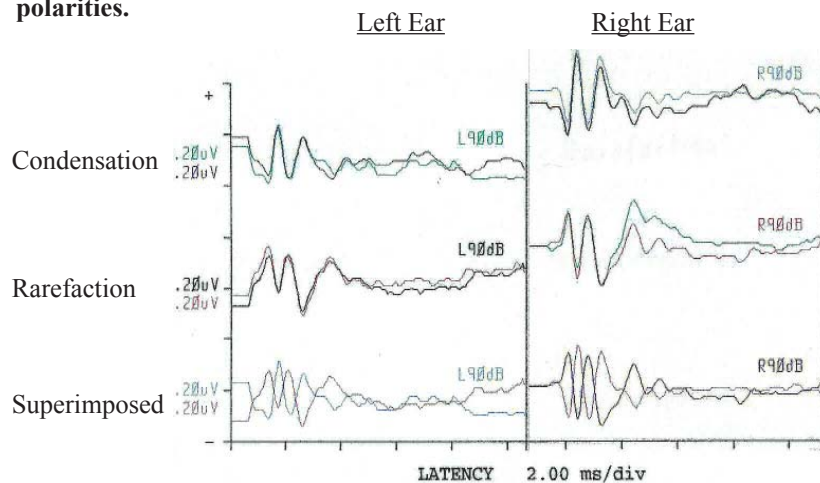
ABR testing was completed with air-conducted clicks presented to each ear through insert earphones at a rate of 27.7 per second. Testing at the limits of the equipment (90 dBnHL) indicated a possible Wave I bilaterally; however, no responses were obtained to unmasked bone-conducted clicks (65 dBnHL) or air-conducted 500-Hz tonebursts (90 dBnHL). These results were consistent with the ABR results from the initial test session and with the MEMR results from the current test session, both of which suggested a profound sensorineural hearing loss bilaterally or AN/AD with loss of emissions.

ABR testing was then repeated to examine the nature of the apparent Wave I bilaterally. Reversing the polarity of the stimulus differentiates cochlear and neural responses because a cochlear microphonic (CM) response will invert with polarity inversion while a neural response will not (Berlin et al., 1998). Therefore, air-conducted click stimuli were presented at 90 dBnHL using the opposite stimulus polarity to determine if the ABR waveform inverted in phase. Results demonstrated that the ABR waveform did invert in phase when the stimulus polarity was reversed (Figure 1). These findings revealed that the apparent Wave I was a cochlear response and not a neural response. Stated differently, the apparent Wave I reflected a CM response rather than the compound action potential of the VIIIth nerve. These results demonstrate that electrophysiological assessment, consisting of separate responses to negative and to positive polarity clicks to differentiate cochlear and neural responses, must be conducted to distinguish between cases of commonly understood sensorineural hearing loss and cases of AN/AD with absent OAEs (Berlin et al., 1998).

**Autism Diagnosis**

As previously mentioned, this child was referred to rule out hearing loss as a possible cause for developmental delays and abnormal behaviors before being diagnosed as autistic. Evaluations were conducted by a psychologist and a neurologist following the diagnosis of AN/AD. Results of these evaluations confirmed the diagnosis of autism. It should be noted that, unlike many children with autism, this child does not seem to be hypersensi-

**Figure 1. ABRs recorded during the subsequent physiological evaluation using air-conduction click stimuli with opposite polarities.**



**Case Management**

Management of this case has been particularly challenging given the fact that this child has AN/AD in addition to loss of emissions, visual impairment, and autism. AN/AD patients do not typically benefit from standard amplification because their inner hair cells and/or nerve fibers do not respond synchronously (Berlin et al., 1999; Miyamoto, Kirk, Renshaw, & Hussain, 1999). However, conventional amplification has been reported to be beneficial in pre-lingual AN/AD cases when OAEs are absent (Deltenre et al., 1999; Rance et al., 1999). Therefore, this child was fit with personal binaural hearing aids to facilitate speech and language development.

AN/AD patients also may benefit from frequency modulation (FM) systems due to an improved signal-to-noise ratio (Hood, 1998). Consequently, this child was fit with an FM system to be used in conjunction with his personal hearing aids. Although visual communication systems have been recommended for typical AN/AD patients to assist the facilitation of language development (Hood, 1998), a total communication approach was recommended in this case due to the presence of visual and hearing impairments that may both deteriorate over time.

This child has been attending aural rehabilitation therapy for two hours a week for approximately 14 months. His mother reports minimum hearing-aid usage outside of therapy; however, she notes significant changes in his behavior when he utilizes his amplification. Although the hearing aids have been beneficial, they have not allowed him to develop adequate speech and language through auditory means alone. Therefore, a Picture Exchange Communication System (PECS) was initiated to augment his communication. He uses the PECS card to request and identify an object and is beginning to initiate communication via picture exchange and vocalizations spontaneously. His play skills have improved and are more appropriate. Occupational therapy is provided on a weekly basis. He continues to be followed by his pediatric ophthalmologist for his vision impairment. Educational assistance is provided currently by a combination of several state agencies.

The use of cochlear implants also may be a viable option for selected children with AN/AD (Peterson et al., 2003). Therefore, the idea of cochlear implantation was discussed among the team of professionals involved in this case. These individuals include his pediatric otolaryngologist, pediatric psychologist, pediatric ophthalmologist, audiologists and speech-language pathologists with extensive pediatric experience, and his parents. Of primary concern was that with the diagnosis of autism, the increased sensory input provided by the cochlear implant may be over-stimulating for this child, and may be more of a detriment than an asset in his daily functioning and communication. However, the child does not seem to be hypersensitive to visual stimuli or the currently used hearing aids.

Furthermore, recent research suggests that cochlear implantation can be beneficial for hearing-impaired children with autism. Parents of autistic children reported positive benefits of implantation that included changes in behavior, changes in communication, and increased awareness of the environment. Parents also reported an increased reaction to music and sound, vocalization, eye contact, use of sign language, and response to requests. Unfortunately, implantation did not impact other behaviors commonly associated with autism such as poor compliance to family routine and reduced interaction with siblings and other children (Donaldson, Heavner, & Zwolan, 2004). The family of this child continues to be interested in implantation; however, they have not reached a final decision regarding this issue.

## Conclusion

Findings from the present case provide further evidence that AN/AD may exist with concomitant loss of otoacoustic emissions. Clinicians must be aware that AN/AD cases may be misinterpreted as cases of severe to profound inner ear loss when OAEs are absent or disappear prior to the initial evaluation if electrophysiological measures are not obtained. Therefore, the use of a test battery approach that includes tympanometry, MEMRS, OAEs, and ABRs with a positive and negative polarity click (Berlin et al., 1998) is essential in identifying AN/AD patients. Failure to identify AN/AD patients in the earliest stages may result in improper diagnosis and management, and may have serious ramifications regarding speech and language development as well as the educational services rendered.

## References

- Berlin, C.I., Bordelon, J., St. John, P., Wilensky, D., Hurley, A., Kluka, E., & Hood, L.J. (1998). Reversing click polarity may uncover auditory neuropathy in infants. *Ear and Hearing, 19*, 37-47.
- Berlin, C.I., Hood, L.J., Cecola, R.P., Jackson, D.F., & Szabo, P. (1993). Does Type I afferent neuron dysfunction reveal itself through lack of efferent suppression? *Hearing Research, 65*, 40-50.
- Berlin, C.I., Hood, L.J., Hurley A., & Wen H. (1994). Contralateral suppression of otoacoustic emissions: An index of the function of the medial olivocochlear system. *Otolaryngology Head and Neck Surgery, 100*, 3-21.
- Berlin, C.I., Hood, L.J., Jeanfreau, J., Morlet, T., Brashears, S., & Keats, B.B. (2002). The physiological bases of audiological management. In: C.I. Berlin, L.J. Hood, & A. Ricci (Eds). *Hair Cell Micromechanics and Otoacoustic Emissions* (pp. 139-154). Clifton Park, NY: Thomson Delmar Learning.
- Berlin, C.I., Morlet, T., & Hood, L.J. (2003). Auditory neuropathy/dyssynchrony: Its diagnosis and management. *Pediatric Clinics of North America, 50*, 331-340.
- Deltenre, P., Mansbach, A.L., Bozet, C., Christiaens, F., Barthelemy, P., Paulissen, D., & Renglet, T. (1999). Auditory neuropathy with preserved cochlear microphonics and secondary loss of otoacoustic emissions. *Audiology, 38*, 187-195.
- Donaldson, A.I., Heavner, K.S., Zwolan, T.A. (2004). Measuring progress in children with autism spectrum disorder who have cochlear implants. *Archives of Otolaryngology Head and Neck Surgery, 130*, 666-671.
- Hood, L.J. (1998). *Clinical applications of the auditory brainstem response*. San Diego: Singular Publishing Group, Inc.
- Hood, L.J., Berlin, C.I., Bordelon, J., & Rose, K. (2003). Patients with auditory neuropathy/dys-synchrony lack efferent suppression of transient evoked otoacoustic emissions. *Journal of the American Academy of Audiology 14*, 302-313.
- Miyamoto, R.T., Kirk, K.I., Renshaw, J., & Hussain, D. (1999). Cochlear implantation in auditory neuropathy. *Laryngoscope, 109* (2, Pt. 1), 181-185.
- Peterson, A., Shallop, J., Driscoll, C., Breneman, A., Babb, J., Stoeckel, R., & Fabry, L. (2003). Outcomes of cochlear implantation in children with auditory neuropathy. *Journal of the American Academy of Audiology, 4*, 188-201.
- Rance, G., Beer, D., Cone-Wesson, B., Shepherd, R., Dowell, R.C., King, A.M., Rickards, F.W., & Clark, G.M. (1999). Clinical findings for a group of infants and young children with auditory neuropathy. *Ear and Hearing, 20*, 238-252.
- Starr, A., McPherson, D., & Patterson, J. (1991). Absences of both auditory evoked potentials and auditory percepts depending on timing cues. *Brain, 114*:1157-1180.
- Starr, A., Picton, T.W., & Sininger, Y. (1996). Auditory neuropathy. *Brain, 119*, 741-753.
- Starr, A., Sininger, Y., Nguyen, T., Michalewski, H.J., Oba, S., & Adbala, C. (2003). Cochlear receptor (microphonic and summing potentials, otoacoustic emissions) and auditory pathway (auditory brain stem potentials) activity in auditory neuropathy. *Ear and Hearing, 22*, 91:99.
- Trautwein, P., Sininger, Y.S., & Nelson, R. (2000). Cochlear implantation of auditory neuropathy. *Journal of the American Academy of Audiology, 11*, 309-315
- Varga, R., Kelley, P.M., Keats, B.J., Starr, A., Leal, S.M., Cohn, E., & Kimberling, W.J. (2003). Non-syndromic recessive auditory neuropathy is the result of mutations in the otoferlin (OTOF) gene. *Journal of Medical Genetics, 40*, 45-50.