Updates on Auditory Neuropathy Spectrum Disorder

By Dennis A. Colucci, AuD, MA, ABA

Auditory neuropathy was first described in 1996 by Arnold Starr, MD, and colleagues as a "hearing impairment that, by behavioral and physiological testing, were compatible with a disorder of the auditory portion of the eighth cranial nerve."[1] Since then, research has found notable hallmarks of normal outer hair cell function in the presence of severely abnormal or absent auditory brainstem evoked potentials. When measurable, speech discrimination scores are proportionally lower than expected for the degree of hearing loss, complementing a patient's hearing difficulty (e.g., "I can hear sound but can't understand speech, especially in noise"). Also, a host of neurological, audiological, and clinical features and findings reveals a variety of causes, genotypes and phenotypes, comorbidities, and auditory consequences. The desynchrony created by auditory neuropathy impairs neural processing, thereby resulting in a series of perceptual disadvantages and compromise—and to various degrees, disabling communication and auditory scene analysis. Whether occuring from a peripheral or a central site, the effects of temporal discord are universal: "Auditory temporal processing determines our understanding of speech, our appreciation of music, being able to localize a sound source, and to listen to a person in a noisy crowd."[2]

Since the discovery of auditory neuropathy, researchers have described various sites of the lesion along the neural pathway. Auditory neuropathy is a condition of abnormal neural encoding of acoustic signals in the presence of normal sensory transduction and amplification properties of the outer hair cells.[3] Potential disorders and sites of lesions include (1) presynaptic disorders affecting inner hair cells and ribbon synapses; (2) postsynaptic disorders affecting unmyelinated auditory nerve dendrites; (3) postsynaptic disorders affecting auditory ganglion cells and their myelinated axons and dendrites; and (4) central neural pathway disorders affecting the auditory brainstem.[4] In some cases, auditory neuropathy may include brainstem connections such as those reported in individuals with multiple brainstem neuropathies.[5] These structures are divided into three primary partitions responsible for encoding sound: sensory, synaptic, and neural (Fig. 1).[6]

Fortunately, advancements in auditory electrophysiology and psychophysical tests have made the identification of the site of lesion and functionality more available to clinical practice. These tools have greatly improved diagnosis, treatment selection, and outcome prediction. Having a basic understanding of this complex topic is useful for audiologists and ENT physicians because auditory neuropathy spectrum disorders (ANSDs) occur in children, adults, and seniors due to aging, noise exposure, trauma, and disease. Take note of these pearls of wisdom that will aid in evaluating, diagnosing, and discussing hearing loss and treatments with patients of all ages.

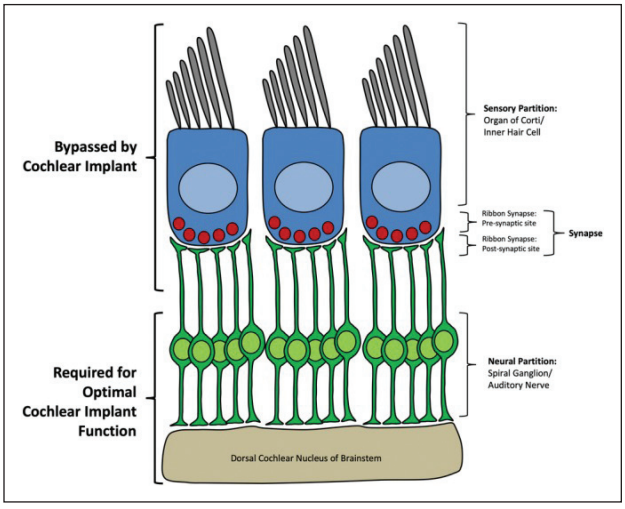


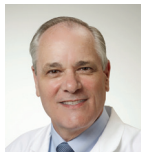
Figure 1. Auditory system delineating the inner hair cells (sensory), pre- and postsynaptic portions (synapse), and the spiral ganglion and auditory nerve (neural). Cochlear implantation bypasses the sensory and synaptic portions providing a time-locked signal to the neural partition.[6]

KEY FACTS & PEARLS OF WISDOM

Research highlights relevant to audiology practices include notable information on ANSD prevalence, causations, symptoms, evaluation, testing, and treatments.

PREVALENCE. One in 7,000 neonates evaluated through newborn hearing screening has been found to have an abnormal auditory nerve function.[4] ANSD is estimated to occur in one in 10 children with permanent hearing loss.[7] Studies suggest that a considerable number of cases may occur in the well-baby population since newborn hearing screenings are typically based on otoacoustic emissions (OAEs)[8] rather than auditory brainstem response (ABR)[7] or simultaneous testing.

The incidence of patients with auditory neuropathy or cochlear synaptopathy[9] in the general population is unknown.



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However, 10 percent of patients seen at Massachusetts Eye and Ear complain of hearing difficulty in the presence of clinically normal hearing,[10] suggesting that ANSD and central auditory processing disorder (CAPD) evaluations should be considered for this population.

CAUSATION. Syndromic and nonsyndromic disorders cause auditory neuropathy through synaptic and neural pathways. Auditory neuropathy varies by etiology, onset age, site of lesion, auditory behavior, and the presence or absence of other peripheral neuropathies.[11] Prematurity, low birth weight, hyperbilirubinemia, anoxia, otoferlin gene mutations, Waardenburg's syndrome, Charcot-Marie-Tooth disease (hereditary motor and sensory neuropathy), ototoxic drugs, infection, and cranial nerve hypoplasia, among others, have been reported as risk factors. Genetic disorders account for most cases, especially in children. A mild head injury can cause cranial nerve injury, including an injury to the eighth nerve, although this is less frequent.[12]

Auditory synaptopathy impairs sound encoding at the synapses between inner hair cells and spiral ganglion neurons.[3] Should discrimination difficulty accompany normal hearing sensitivity by standard audiometry (some with ultra-high-frequency hearing loss) and a history of noise exposure or advanced aging, the patient may have cochlear synaptopathy or hidden hearing loss.[13]

SYMPTOM. Psychophysical testing reveals auditory neuropathy results in perceptual consequences that impair speech discrimination and auditory scene analysis. Unlike cochlear impairments, this condition has a minor effect on loudness, high-frequency pitch discrimination, or localization based on level differences. On the other hand, auditory neuropathy patients have deficiencies in time-based perceptions such as pitch discrimination at low frequencies, temporal integration and modulation detection, binaural beats, masking paradigms, hearing signals in noise, gap detection, and localization using interaural timing.[14]

Children with this condition may have excellent visual cognition but exhibit poor auditory skills.[15] Speech may develop normally or be delayed. Speech discrimination may range from no difficulty in quiet with issues hearing in noise to profound hearing loss in quiet.[7]

Adults who acquire auditory neuropathy complain of difficulty understanding speech and deafness in background noise. They have difficulty with music perception, sound fading, and localization, and often dislike noise. They may be unemployable for certain jobs, cannot hear well on the telephone, and prefer online jobs and email for communication.

Patients with auditory neuropathy may have constant low-frequency bilateral tinnitus ($\leq$ 1,000 Hz) with pitch matching at the greatest degree of hearing loss, typically 10 to 15 dB SL.[16]

In cases of comorbid peripheral neuropathy or a diagnosis of Charcot-Marie-Tooth disease (the most common inherited neurological disease), hearing loss occurs several years before the onset of other symptoms.[3]

Auditory neuropathy may be progressive as a result of several conditions. These include genetic mutations, mitochondrial disorders, autoimmune anomalies, degenerative changes from aging and noise trauma, toxic metabolic disorders, and nutritional deficits.[3]

Mutations of the OTOF gene (otoferlin) can express as a transient temperature-sensitive auditory neuropathy, which resolves once the increased body temperature is resolved.[17,18] A gene responsible for autosomal dominant auditory neuropathy (AUNA1) was found in a family of European ancestry. The average age of symptom onset was 19 years old.[19]

EVALUATION. Audiological testing may cover a wide variety of evaluations depending on the patient's age. These may include testing of pure tones, hearing in noise, otoacoustic emissions with and without crossed suppression, acoustic reflexes, cochlear microphonics, summating potentials, ABR, and cortical auditory-evoked potential (CAEP), as well as tympanometry and electrocochleography (ECochG).

Medical evaluation includes an MRI of the inner ears, retrocochlear and brainstem structures, a complete history and genetic analysis, and a physical examination. Audiometric configurations can be downsloping, flat, or high frequency. Low-frequency or reverse curve loss is more prominent, potentially as a result of phase-locking difficulty caused by desynchrony compared to higher frequencies at approximately 2,000 Hz.[1]

In some cases of auditory neuropathy, patients may have abnormalities in the cochlear microphonic, low amplitude wave V without a wave I, and absent TEOAEs.[20] Despite compromised ABRs, CAEPs can often be recorded in ANSD patients. Emerging research highlights the application of CAEP in estimating the behavioral thresholds in this population.[21] A slower time constant and recovery allow for better synchrony and reliability.

Vestibular neuropathy may accompany findings of auditory and peripheral neuropathies. Some patients with abnormal caloric responses may be asymptomatic in the presence of peripheral neuropathy.[22] The prevalence of at least one vestibular complaint with auditory neuropathy is 20 percent.[23] Using the Dizziness Handicap Inventory, the severity of balance complaints is reported as moderate.[24]

The British Society of Audiology has published comprehensive recommendations for testing young infants who fail newborn screening or considered at risk for ANSD. Testing for this cohort starts with a 4kHz tpABR, followed by another test to identify sensorineural or mixed hearing loss or ANSD, such as a bone conduction ABR, 1 kHz or 0.5 kHz ABR, click ABR, OAE, and/or cochlear microphonics, tympanometry, or stapedial reflexes testing.[7] In premature babies, ABR retesting over weeks and months should be conducted to identify those with delayed maturation.

TREATMENT. Goals for newborns with suspected ANSD are to provide appropriate treatment and begin rehabilitation within the first six months. Visual cueing is important in the early stages until the infant's hearing level and diagnosis can be established. Hearing aids, cochlear implants (CI), and rehabilitation options are guided by the locus of the lesion, the severity of synaptic degeneration, concomitant sensory loss, neural competency, and behavioral responses.

Hearing aids are not effective in many cases, although some studies suggest that a trial with amplification, which may include wireless communication, may be recommended based on the patient's degree of hearing loss, age, comor-

bidities, and behavioral factors. Amplification is typically fit to standard formulas. Enhanced spectral cues and low-pass filtering in the hearing aid prescription are suggested in some cases.[7]

Regarding CIs, assessment of spiral ganglion health using intraoperative ECochG measurements has become one of the best predictors of CI outcomes. Cochlear implantation results are better when the site of lesion is sensory or synaptic since the CI bypasses these regions to simulate the neural partition (Fig. 1).[6] A new hypothesis suggests that "binaural cues improve perception in noise. Screening for residual binaural sensitivity might be important when evaluating a patient with AN's candidacy for hearing aids and/or cochlear implants."[25]

Based on CAEP testing, children more likely show maturation effects within six months and age-appropriate responses when CIs are fitted under the age of two.[26]

References for this article can be found at http://bit.ly/HJcurrent.