

# An Update on Auditory Neuropathy Spectrum Disorder in Children

Gary Rance, Ph.D.

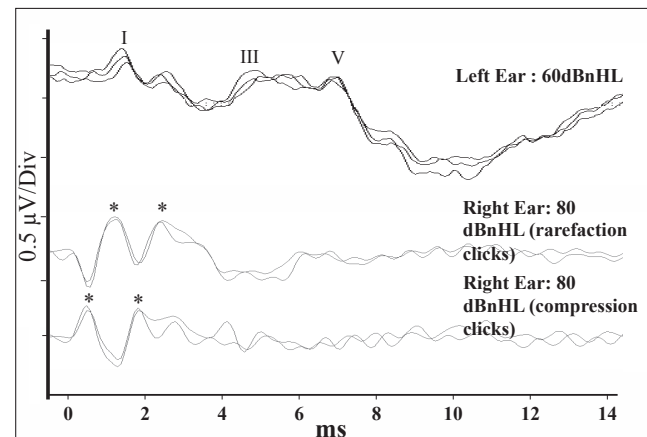
## Abstract

*Auditory neuropathy spectrum disorder (ANSD) is a form of hearing impairment in which cochlear (outer hair cell) function appears normal but afferent neural activity in the auditory pathway is disordered. It is now over 20 years since the first paediatric ANSD cases appeared in the literature and over 15 years since the disorder was identified in infant populations. In the ensuing period our understanding of ANSD's causes, perceptual consequences and associated management challenges has developed considerably. This article provides an overview of the current literature and presents longitudinal outcome data for a group of affected children tracked from infancy through to early adulthood.*

The term “auditory neuropathy” was coined in the mid-1990’s to describe a form of hearing impairment in which cochlear (outer hair cell) function appeared normal, but afferent neural activity in the VIIIth nerve and brainstem was disordered (Starr, Picton, Sininger, Hood, Berlin, 1996). However, the authors of this paper were not the first to show a mismatch between audiologic and electrophysiologic results. Kraus, Ozdamar, Stein, & Reed (1984), for example, had previously described a group of children for whom the auditory brainstem response (ABR) was mysteriously absent despite relatively normal sound detection. The Starr et al. study was, however, significant in that it was amongst the first to explore the nexus between neurology and audiology, presenting possible pathologic mechanisms and providing a template for evaluation of affected patients.

The clinical findings that distinguish “auditory neuropathy” from sensory-type hearing loss are the demonstration of pre-neural, cochlear activity, in conjunction with an inability to record evoked neural responses from

the auditory pathway. Cochlear outer hair cell function in such cases is reflected by the presence of otoacoustic emissions (the acoustic by-product of the cochlear mechanical processes [Kemp, 1978]) and cochlear microphonics (the receptor potentials produced mainly by the polarization and depolarization of the cochlear outer hair cells [Dallos & Cheatham, 1976]). The auditory pathway disorder is suggested by the absence (or severe distortion) of electrical potentials from the auditory nerve and auditory brainstem (ABR). An example of this electrophysiologic result pattern is shown in Figure 1.



**Figure 1.** Averaged EEG tracings for a 2 month old child with unilateral ANSD. The top tracing shows a normal ABR waveform for the left ear. The middle and lower tracings show cochlear microphonic responses but absent ABRs to unipolar stimuli at 80 dBnHL for the right ear. Asterisks denote the positive peaks in the CM waveform.

In the period since 1996, a number of alternative terminologies have been proposed to describe what Starr et al. referred to as “auditory neuropathy”. The most

commonly used include auditory neuropathy/dys-synchrony (Berlin, Hood & Rose, 2001), auditory synaptopathy (Moser, Strenke, Meyer et al. 2006) and presynaptic and postsynaptic nerve disorder (Starr, Sininger & Pratt, 2000). The development of these descriptors reflects the fact that multiple pathological mechanisms may produce a common pattern of physiologic results. For example, the phenotype may result from specific loss of cochlear inner hair cells (Amatuzzi, Liberman & Northrop, 2001), disordered release of neurotransmitter by inner hair cell ribbon synapses (Wynne, Zeng, Bhatt, et al. 2013), differentiation accompanying loss of auditory nerve fibres (Starr, Michalewski, Zeng et al., 2003), neural dys-synchrony or conduction block as a result of demyelination of nerve fibres (Rance, Ryan, Bayliss et al. 2012a) and auditory nerve hypoplasia (Buchman, Roush, Teagle et al. 2006). As a result, the term *auditory neuropathy spectrum disorder (ANSD)* was developed to acknowledge this heterogeneity (Guidelines Development Conference, 2008).

## Etiology of ANSD

While ANSD can occur in the absence of obvious health problems, the majority of reported cases (>70%) have presented with specific medical risk factors (for a review see Rance & Starr, 2011). Over the past decades numerous different aetiologies have been linked with the disorder. In children, ANSD is most commonly associated with transient neonatal insults such as hyperbilirubinaemia (Rance, Beer, Cone-Wesson et al., 1999; Shapiro, 2003) and oxygen deprivation (Rance et al. 1999; Sininger & Oba, 2001). In addition, greater awareness of the potential for auditory deficit in genetic, neurodegenerative conditions such as Charcot-Marie-Tooth disease and the mitochondrial disorders Friedreich ataxia and Leber's Hereditary Optic Neuropathy, is also leading to an increase in early childhood diagnoses in these populations. Interestingly, it is becoming clear that the susceptibility of the auditory system to neural changes means that hearing deficits in individuals with these generalized neuropathic diseases often precede the onset of motor and other sensory symptoms (Starr et al. 1996; Rance et al. 2012a).

Other, less common, causes of paediatric ANSD include infectious processes (such as mumps and meningitis), inflammation (eg. siderosis), neoplasms (eg. acoustic neuroma), autoimmune disorders (such as Guillain Barre syndrome), nutritional disorders and genetic mutations affecting the optic/vestibular nerves and rib-

bon synapse function (for reviews see Rance, 2005; Starr et al., 2003; Starr & Rance, In Press).

## Audiometric Presentation

Sound detection thresholds in children with ANSD vary across the audiometric range. For youngsters with congenital/perinatal aetiologies, average hearing levels are reasonably evenly distributed, with approximately 10% of cases enjoying sound detection within the normal range and a similar proportion presenting with profound hearing loss (Rance & Starr, 2011). Hearing levels in this congenital/perinatal population appear to be independent of whether or not the ABR is present (in distorted form) or absent. In children with ANSD due to neurodegenerative conditions, sound detection thresholds tend to be less affected with around 75% presenting with hearing levels in the normal range, and the remaining typically showing mild/moderate loss (Rance et al. 2012a; 2012c).

Fluctuating hearing levels have been consistently reported since the earliest reports involving children with ANSD (Rance et al. 1999; Sininger & Oba, 2001). While many cases describing day-to-day fluctuations have appeared in the literature, our experience suggests that significant hearing threshold variability is reasonably rare. Only around 5% of the children in the Australian cohort have shown consistent fluctuations in either audiometric levels or functional hearing ability over time.

In some instances, hearing level variability can be attributed to specific clinical changes. Starr, Sininger, Winter et al. (1998) for example, described a family group with mutations in the otoferlin gene which caused disruption of ribbon synaptic release with changes in core body temperature. These individuals showed dramatic ABR changes and temporary shifts in detection threshold when febrile. In most ANSD cases however, the mechanisms underlying hearing level fluctuation are unknown.

## Auditory Processing

Disruption of the neural representation of sound in the VIIIth nerve and central pathways of ANSD listeners results in auditory processing deficits. Psychophysical studies investigating the ways in which this abnormality manifests have found a pattern of effects consistent with the physiologic profile of the disorder. For example, frequency resolution (the ability to separate frequency components in a complex sound) and intensity discrimin-

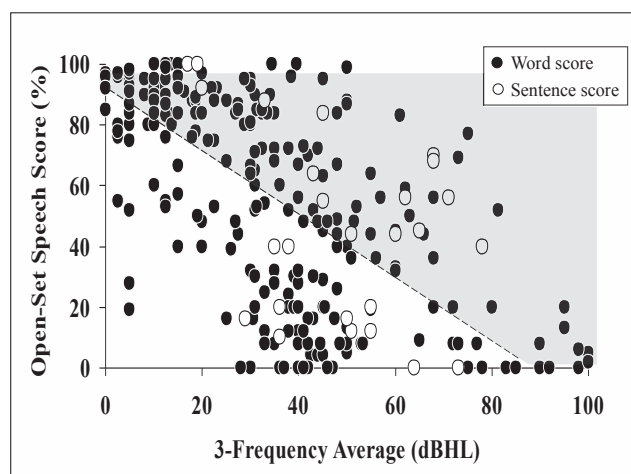
ation (the capacity to detect level differences) are largely dependent on cochlear-level processing and are typically unimpaired in children with ANSD (Rance, McKay & Grayden, 2004; 2012b; Kraus, Bradlow, Cheatham et al. 2000). In contrast, distortion of neural firing patterns in ANSD results in impaired temporal resolution (the ability to perceive brief signal changes over time) and disruption of the temporal aspects of pitch discrimination (Rance et al. 2004; Rance et al. 2012c; Zeng, Kong, Michalewski, Starr, 2005).

In addition to suffering these monaural processing limitations, listeners with ANSD also show reduced ability to integrate binaural cues. That is, the temporally distorted signals conducted through the left and right auditory nerves cannot be effectively combined at the level of the superior olivary complex (lower brainstem) (Reidel & Kollmeier, 2002). One important consequence of this deficit is impaired localization ability. While localization based on inter-aural level differences (as required for high frequency sounds) is typically normal in ANSD listeners, sound direction judgements based on inter-aural timing differences (as for low-frequency stimuli) may be greatly affected (Starr et al. 1991; Zeng et al. 2005).

### Functional Hearing (Speech Perception)

Speech understanding difficulties are the major functional consequence of ANSD. Most adults with the disorder have shown perceptual deficits greater than predicted from their behavioural audiogram (Rance, Fava, Baldock et al., 2008; Starr et al., 1996; Starr et al., 2000). Results in children are more variable. At best, young ANSD listeners show speech perception abilities equivalent to those of their peers with sensory hearing loss. At worst, they may demonstrate no functional ability at all despite, in many cases, enjoying complete access to the normal speech signal. Figure 2 shows this broad range of abilities and reflects the lack of relationship between open-set speech perception score and signal audibility in listeners with ANSD. As can be seen from this data, a high proportion of individuals (approximately 40%) show perceptual ability considerably poorer than the expected minimum for sensory hearing loss. It is worth noting, however, (given the generally pessimistic expectations that have developed for this population over the past few decades) that for listening in quiet at least, many children with ANSD do show significant functional hearing abilities.

The mismatch between audibility and speech understanding in listeners with ANSD suggests that distortion



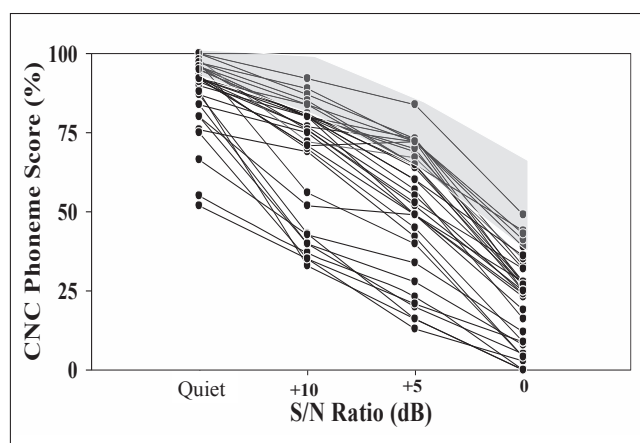
**Figure 2.** Open-set speech perception scores (in quiet) plotted against average hearing level for listeners with ANSD. Data represents a meta-analysis of published findings as of December 2013. The filled data points are results from word-level assessment and the open points show sentence test findings. The grey area represents the 95% performance range for ears with sensory hearing loss (Yellin et al., 1989).

of supra-threshold cues is the limiting factor in perceptual performance (Rance et al., 1999; 2002; 2012a; Starr et al., 1996; 2000). Speech perception ability for this population, in fact, appears more closely related to the level of neural disruption in the central auditory pathways and the resulting degree of temporal processing deficit (Kraus et al., 2000; Zeng et al., 2005).

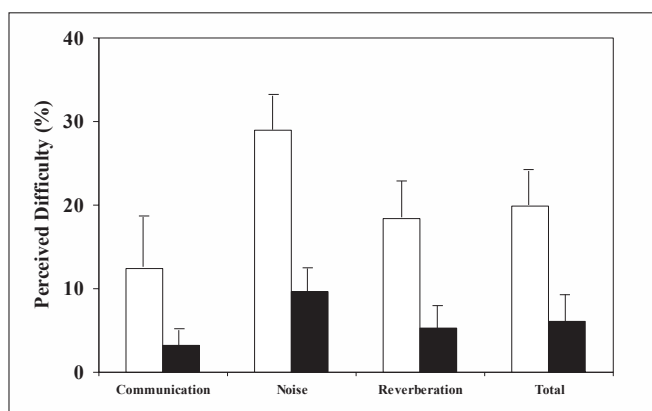
Accurate neural representation of timing cues is a pre-requisite for speech understanding. In order to discriminate phonemes in running speech or even in single words, the listener must be able to identify the characteristic spectral shapes of individual phonemes, and importantly, be able to rapidly update this perception to track the flow of speech sounds. Recent work from our laboratory (Rance et al. 2008; 2010) has used transmission analysis techniques to identify speech perception error patterns in ANSD listeners and found that discrimination of temporal-based speech cues is a particular problem. Where individuals with sensory loss struggle to discriminate phonemes differing in frequency content (e.g., /s/ and /f/), ANSD listeners consistently mistake speech sounds differing in their temporal characteristics such as the consonants /p/ and /b/ or /t/ and /d/ where voice-onset-time (VOT) is the major acoustic marker and vowels such as /i/ and /I/ where duration is the primary cue.

## Speech Perception in Background Noise

All forms of permanent hearing loss impair figure/ground perception (Rance, Barker, Mok et al 2007). Speech perception in noise problems for ANSD listeners with impaired sound detection thresholds are likely to be severe, but the underlying mechanisms may be difficult to tease out in such cases. More obvious are the deficits caused by ANSD in cases with normal or near normal hearing levels. As demonstrated in Figure 3, which shows speech perception findings for a group of ANSD



**Figure 3.** Open set speech perception scores for ANSD children with 4-frequency average hearing thresholds <30 dBHL. Shown are scores for CNC-words presented in quiet and at +10 dB, +5 dB and 0 dB signal-to-noise ratios. The shaded area represents the 95% performance range for age-matched controls.



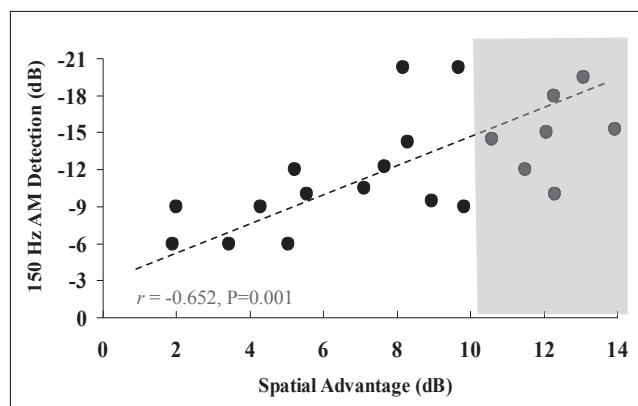
**Figure 4.** Hearing disability survey results for 26 school-aged children with ANSD and average hearing levels <30 dBHL (unfilled bars) and matched control subjects (filled bars). Individuals with ANSD reported significantly higher degrees of everyday listening and communication difficulty than healthy counterparts. “Perceived difficulty”, is the proportion of situations in which the subject struggled to hear/communicate.

children with relatively normal sound detection shows that even those individuals with reasonable perception in quiet can struggle to discriminate speech in noise at levels consistent with real-life listening conditions (0-5 dB SNR). The consequent effects on everyday listening and general communication are reflected in Figure 4 which shows self-reported hearing disability ratings from the Abbreviated Profile of Hearing Aid Benefit (APHAB) questionnaire.

The mechanisms underlying figure/ground deficits in individuals with ANSD are not completely understood, but psychophysical studies have shown similarly exaggerated noise effects in both simultaneous (where the signal is presented within the noise) and non-simultaneous (where the noise occurs immediately before or after the signal) masking experiments (Kraus et al., 2000; Vinay & Moore, 2007; Zeng et al., 2005). As such, it appears that affected listeners are less able to separate sounds occurring both concurrently and successively. In an everyday listening context, where the level of background noise fluctuates, this temporal processing deficit might impair the listener’s ability to use brief gaps in the noise to access the speech signal and optimize understanding.

Another way in which listening in noise may be affected by ANSD involves spatial listening. In everyday circumstances where auditory signals emanate from multiple directions, sound localization cues may be used to separate a target signal (such as speech) from the competing noise (Michey, Carlyon, Gotshal et al., 2007). ANSD disrupts the ability to selectively attend to a particular voice based on its location and as a result, affected listeners typically require much lower noise levels than their normal peers to understand speech and communicate effectively (Rance et al, 2012b). This effect can be seen in Figure 5 which shows Spatial Advantage levels (dB) obtained using the Listening in Spatialized Noise Test (LiSN-S). Spatial advantage in this context is the difference in speech reception threshold (SRT) obtained when speech and noise stimuli are presented from different directions (90 apart) compared to when the speech and noise emanate from the same direction. As such, the advantage is a reflection of the listener’s ability to use inter-aural difference cues to localize the sound sources, and hence, improve perception. Not surprisingly, most of the ANSD children represented showed impaired spatial ability. Normal children, are typically afforded a 10-14 dB release from masking when signal and noise are spatially separated. Amongst children with ANSD, in contrast, spatial advantage varied considerably (de-

pending on the degree of temporal processing deficit), but on average, youngsters with the disorder obtained only  $\approx 6$  dB improvement from separation of signal and noise sources. In real-world listening, this deficit may pose a significant threat to communication competence.



**Figure 5.** Spatial advantage scores (LiSN-S) plotted against AM detection threshold (temporal resolution ability) for children with ANSD and average hearing levels  $<30$  dBHL. The shaded area represents the 95% performance range for matched controls.

## Management of Children with ANSD Using Hearing Aids and Cochlear Implants

In the period since ANSD was first identified in children, opinion has fluctuated as to the efficacy of acoustic amplification and cochlear implantation as management options. As more data has become available there has been general (if not universal) acceptance that some children will derive most benefit from hearing aids and some will be best served by cochlear implantation. For a thorough review see Roush, Frymark, Venediktov, & Wang (2011).

### Hearing Aid Amplification

As the basic function of conventional hearing aids is to amplify acoustic signals, they can make environmental sounds and speech louder (allowing improved access to ANSD listeners with impaired sound detection), but they cannot dramatically improve the clarity of a temporally distorted signal. Amplification outcomes have been mixed with some children (typically those with lesser degrees of temporal disruption) responding well and showing aided speech perception abilities consistent

with their sensorineural counterparts (Rance et al., 2002; Roush et al., 2011). In many youngsters (and almost all reported adults), however, conventional amplification has been of little or no benefit (Berlin, Hood, Morlet et al., 2010; Rance, 2005; Starr et al., 1996). As a result, Digital Signal Processing (DSP) hearing aids with strategies designed to accentuate temporal cues in the acoustic signal have been considered (Narne & Vanaja, 2008; Zeng, Oba & Starr, 2001) and may, in the future, improve outcomes in some cases.

### Cochlear Implantation

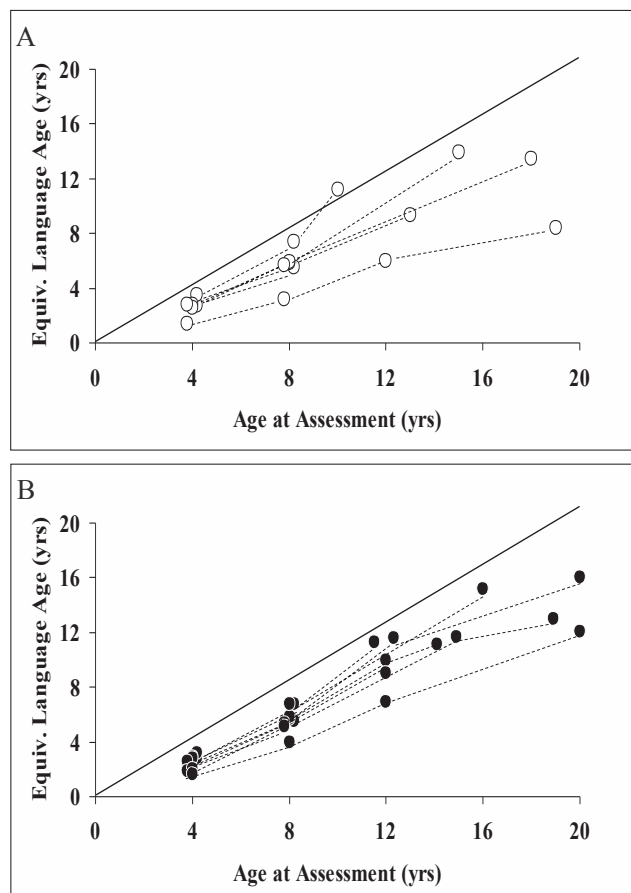
The literature regarding CI outcomes in ANSD children has followed an interesting course of the past 15 years. Early reports (Miyamoto, Iler-Kirk, Renshaw, Hussain et al., 1999; Rance et al. 1999) described poor CI outcomes in a (small) number of cases and advised against implantation arguing that perception would likely be impaired as the signal provided by the device must still pass through a disordered neural system. Then followed a period (in the 2000's) in which CI results were almost universally positive with a series of publications showing speech perception benefits in ANSD cases consistent with those of young implantees with sensory loss (Madden, Rutter, Hilbert, Greinwald, Choo, 2002; Mason, DeMichele, Stevens, Ruth, Hashisaki, 2003; Shallop, 2002; Teagle, Roush, Woodward et al., 2010; Trautwein, Shallop, Fabry, Friedman, 2001; Zeng & Liu, 2006). More recently, however, expectations have been tempered slightly with a number of studies reporting poorer than anticipated speech perception results (Neary & Lightfoot, 2012; Roush et al. 2011), again raising the possibility that some forms of ANSD can affect the neural integrity of the CI-elicited signal and highlighting the need for diagnostic procedures that can better differentiate between sites of lesion. While cochlear implantation remains the intervention option of choice for most children with ANSD, clinicians and particularly families need to be aware of the possibility of unexpected outcomes in this population.

The ways in which perception is improved by the CI in individuals with ANSD are currently under investigation. Significantly, most subjects with cochlear implants show normal ABRs to electrical stimulation suggesting either an increase in the number of neural elements contributing to the evoked response (perhaps as a result of by-passing peripheral abnormality when stimulating the spiral ganglion directly) or an improvement in the synchrony of neural firing (perhaps reflecting the fact

that the electrical stimuli produced by CIs is in the form of discrete pulse trains which more efficiently generate synchronous activity).

## Long-Term Outcomes

While the relative benefits of amplification and cochlear implantation on speech perception ability have been reasonably well documented, the effects of these interventions on oral language development, has been underexplored (Roush et al. 2011). In 2009 we published cross-sectional language data for a (small) group of school-aged children which suggested no difference in pronunciation abilities (Diagnostic Evaluation of Articulation and Phonology [DEAP]) and receptive vocabulary (Peabody Picture Vocabulary Test [PPVT]) (Rance & Barker 2009) between aided and CI groups. More recently, Ching, Day, Dillon et al. (2013) has shown similar results in a larger cohort of children tested at 3 yrs of age. In our clinic (University of Melbourne) we manage a cohort of children diagnosed with ANSD in the early 1990's and have longitudinal data across a number of domains (auditory processing, speech perception, hearing disability, educational progress etc) from infancy to (in some cases) early adulthood. Figure 6 shows long-term receptive language outcomes for ANSD children managed with cochlear implants (panel A) and hearing aids fit according to the NAL procedure (Byrne & Dillon, 1986) (panel B). Mean rates of language growth for the two intervention categories were equivalent ( $P > 0.05$ ) and children in both groups showed a developmental course only mildly delayed relative to that of normally hearing youngsters. As such, the findings suggest that good long-term oral language development is a realistic expectation for many children with ANSD – provided they are offered the management option most appropriate to their abilities. The aided participants in Figure 6 represent a biased sample. Many of the ANSD children in our clinical cohort who were originally fit with hearing aids, were subsequently referred for CI when it became clear that they were not showing adequate progress with amplification. As such, the children who remained hearing aid users reflect the subset that was able to use their audition to develop good oral language. A significant research challenge for the future is to develop clinically applicable procedures that can measure a child's auditory capacity at a young age so that management decisions can be made in a timely fashion.



**Figures 6A & 6B.** Receptive language development (PPVT) for children with ANSD. Data points represent the child's equivalent language age plotted against chronological age at each assessment point. Panel A shows findings for 5 children managed with either monaural or binaural cochlear implants. Panel B shows findings for 6 children managed with conventional hearing aids. The diagonal line represents the expected rate of language growth for normally hearing/developing children.

## Summary

Our understanding of ANSD, its causes, and particular perceptual consequences has improved considerably over the past two decades. The variability of presentation continues, however, to raise clinical questions and it is clear that a “one size fits all” approach is not appropriate for this population. Development of a knowledge-base that can underpin management decision-making remains a significant goal for the future.

## References

- Amatuzzi M, Liberman M.C. & Northrop C. (2001). Selective inner hair cell loss in prematurity: a temporal bone study of infants from a neonatal intensive care unit. *Journal of the Association for Research in Otolaryngology*, 12(5), 595-604.
- Berlin, C.I., Hood, L.J., Morlet, T. et al. (2010). Multi-site diagnosis and management of 260 patients with auditory neuropathy/dys-synchrony (auditory neuropathy spectrum disorder). *International Journal of Audiology*, 49, 30-43.
- Berlin, C. I., Hood, L. J. & Rose, K. (2001). On renaming auditory neuropathy as auditory dys-synchrony. *Audiology Today*, 13, 15-17.
- Buchman, C.A., Roush, P.A., Teagle, H.F.B., Brown, C., Zdanski, C.J., Grose J.H. (2006). Auditory neuropathy characteristics in children with cochlear nerve deficiency. *Ear and Hearing*, 27, 399-408.
- Byrne, D. & Dillon, H. (1986). The National Acoustics Laboratories (N.A.L.) new procedure for selecting the gain and frequency response of a hearing aid. *Ear and Hearing*, 7, 257-265.
- Ching, T., Day, J., Dillon, H. et al. (2013). Impact of the presence of auditory neuropathy spectrum disorder (ANSD) on outcomes of children at 3 years of age. *International Journal Audiology*, 52, 55-64.
- Dallos, P. & Cheatham, M. A. (1976). Production of cochlear potentials by inner and outer hair cells. *Journal of the Acoustical Society of America*, 60, 510-512.
- Guidelines Development Conference on the Identification and Management of Infants with Auditory Neuropathy*. (2008). [www.thechildrenshospital.org/conditions/speech/danielscenter/ANSD-Guidelines.aspx](http://www.thechildrenshospital.org/conditions/speech/danielscenter/ANSD-Guidelines.aspx).
- Kemp, D. T. (1978). Stimulated acoustic emission from the human auditory system. *Journal of the Acoustical Society of America*, 64, 1386-1391.
- Kraus N., Ozdamar O., Stein L. & Reed N. (1984). Absent auditory brain stem response: peripheral hearing loss or brain stem dysfunction. *Laryngoscope*, 94(3), 400-406.
- Kraus, N., Bradlow, A.R., Cheatham, J., Cunningham, C.D., King, D.B., Koch, T.G., Nicol, T.J., McGee, L.K., Stein, L.K., Wright, B.A. (2000). Consequences of neural asynchrony: A case of auditory neuropathy. *Journal of the Association for Research in Otolaryngology*, 1(1), 33-45.
- Madden, C., Rutter, M., Hilbert, L., Greinwald, J., Choo, D. (2002). Clinical and audiological features in auditory neuropathy. *Archives of Otolaryngology-Head and Neck Surgery*, 128, 1026-1030.
- Mason, J. C., De Michele, A., Stevens, C., Ruth, R., Hashisaki, G. (2003). Cochlear implantation in patients with auditory neuropathy of varied etiologies. *Laryngoscope*, 113(1), 45-49.
- Micheyl C., Carlyon R.P., Gutshalk A. et al. (2007). The role of auditory cortex in the formation of auditory streams. *Hearing Research*, 229, 116-131.
- Miyamoto, R. T., Iler Kirk, K., Renshaw, J., Hussain, D. (1999). Cochlear implantation in auditory neuropathy. *Laryngoscope*, 109, 181-185.
- Moser T., Strenke N., Meyer A. et al. (2006). Diagnosis and therapy of auditory synaptopathy/neuropathy. *Hals-Nasen-Ohrenheikunde*, 54(11), 833-839.
- Narne, V. K. & Vanaja, C. S. (2008). Effect of envelope enhancement on speech perception in individuals with auditory neuropathy. *Ear and Hearing*, 29, 45-53.
- Neary W. & Lightfoot G. (2012). Auditory neuropathy spectrum disorder: Examples of poor progress following cochlear implantation. *Audiological Medicine*, 10, 143-150.
- Rance, G. (2005). Auditory neuropathy spectrum disorder and its perceptual consequences. *Trends in Amplification*, 9(1), 1-43.
- Rance G. & Barker E. (2009). Speech and language outcomes in children with auditory neuropathy/dys-synchrony managed with either cochlear implants or hearing aids. *International Journal of Audiology*, 48, 313-320.
- Rance, G., Barker, E., Mok, M., Dowell, R., Rincon, A., Garratt, R. (2007). Speech perception in noise for children with auditory neuropathy/dys-synchrony type hearing loss. *Ear and Hearing*, 28(3), 351-360.
- Rance, G., Beer, D.E., Cone-Wesson, B., Shepherd R.K., Dowell, R.C., King, A.K., 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.
- Rance, G., Cone-Wesson, B., Wunderlich, J., Dowell, R.C. (2002). Speech perception and cortical event related potentials in children with auditory neuropathy. *Ear and Hearing*, 23, 239-253.
- Rance, G., Corben, L., Barker, E., Carew, P., Chisari, D., Rogers, M., Dowell, R., Jamaluddin, S., Bryson, R., Delatycki, M. (2010). Auditory perception in individuals with Friedreich Ataxia. *Audiology & Neurotology*, 15, 229-240.
- Rance, G., Fava, R., Baldock, H., Chong, A., Barker, E., Corben, L., Delatycki, M. (2008). Speech perception

- ability in individuals with Friedreich Ataxia. *Brain*, 131, 2002-2012.
- Rance, G., McKay, C. & Grayden, D. (2004). Perceptual characterisation of children with auditory neuropathy. *Ear and Hearing*, 25, 34-46.
- Rance G., Ryan M.M., Bayliss K., Gill K., O'Sullivan C. & Whitechurch M. (2012a). Auditory function in children with Charcot-Marie-Tooth Disease. *Brain*, 135, 1412-1422.
- Rance G., Ryan M.M., Carew P., Corben L.A., Yiu E., Tan J. and Delatycki M.B. (2012b). Binaural speech processing in individuals with auditory neuropathy. *Neuroscience*, 226: 227-235.
- Rance G., Corben L.A. & Delatycki M.D. (2012c). Auditory processing deficits in children with Friedreich ataxia. *Journal of Childhood Neurology*, 27(9), 1197-1203.
- Rance, G. & Starr, A. (2011). Auditory neuropathy/dys-synchrony. In *Comprehensive Handbook of Pediatric Audiology*. R.C. Seewald & M.A. Tharpe (Eds.), Chapter 13, (pp. 225-242). Plural Publishing, San Diego.
- Riedel H. & Kollmeier B. (2002). Auditory brain stem responses evoked by lateralized clicks: is lateralization extracted from the human brain stem? *Hearing Research*, 163, 12-26.
- Roush, P., Frymark, T., Venediktov, R. & Wang, B. (2011). Audiologic management of auditory neuropathy spectrum disorder in children: A systematic review of the literature. *American Journal of Audiology*, 20, 159-170.
- Shallop, J. K. 2002. Auditory neuropathy spectrum disorder in adults and children. *Seminars in Hearing*, 23(3): 215-223.
- Shapiro S.M. 2003. Bilirubin toxicity in the developing nervous system. *Pediatr Neurol* 29(5):410-21
- Sininger, Y.S. and Oba, S. 2001. Patients with auditory neuropathy: Who are they and what can they hear? In Y.S. Sininger & A. Starr (Eds.), *Auditory Neuropathy* (pp. 15-36). San Diego: Singular Publishing.
- Starr, A., McPherson, D., Patterson, J., Don, M., Luxford, W., Shannon, R., Sininger, Y., Tonakawa, L. and Waring, M. 1991. Absence of both auditory evoked potentials and auditory percepts dependent on timing cues. *Brain*, 114: 1157-1180.
- Starr, A., Michalewski, H. J., Zeng, F. G., Fujikawa-Brooks, S., Linthicum, F., Kim, C. S., et al. 2003. Pathology and physiology of auditory neuropathy with a novel mutation in the MPZ gene. *Brain*, 126: 1604-1619.
- Starr, A., Picton, T.W., Sininger, Y.S., Hood, L.J. and Berlin, C.I. 1996. Auditory Neuropathy. *Brain*, 119 (3): 741-753.
- Starr A. and Rance G. (*In Press*). Auditory Neuropathy. In Human Auditory System. GG Celesia, G Hickok (Eds). Elsevier Publishing.
- Starr, A., Sininger, Y.S. and Pratt, H. 2000. The varieties of auditory neuropathy. *J Basic & Clin Physiol Pharmacol*, 11(3): 215-230.
- Starr, A., Sininger, Y. S., Winter, M., Derebery, M. J., Oba, S. and Michalewski, H. J. 1998. Transient deafness due to temperature-sensitive auditory neuropathy. *Ear and Hearing*, 19: 169-179.
- Teagle, H., Roush, P., Woodward, J. S. et al. 2010. Cochlear implantation in children with auditory neuropathy spectrum disorder. *American Journal of Audiology*, 20: 159-170.
- Trautwein, P., Shallop, J., Fabry, L. and Friedman, R. 2001. Cochlear implantation of patients with auditory neuropathy. In Y. S. Sininger, & A. Starr (Eds.), *Auditory neuropathy* (pp. 203-232). San Diego, CA: Singular Publishing.
- Vinay and Moore, B.C.J. 2007. Ten(HL)-test results and psychophysical tuning curves for subjects with auditory neuropathy. *International Journal of Audiology*, 46(1): 39-46.
- Wynne D.P., Zeng F.G., Bhatt S., Michalewski H.J., Dimitrijevic A. and Starr A. 2013. Loudness adaptation accompanying ribbon synapse and auditory nerve disorders. *Brain*, 136( 5): 1626-38.
- Yellin, M.W., Jerger, J. and Fifer, R.C. 1989. Norms for disproportionate loss in speech intelligibility. *Ear Hear* 10(4): 231-234.
- Zeng, F.-G., Kong, Y.,-Y., Michalewski, H.J. and Starr, A. 2005. Perceptual consequences of disrupted auditory nerve activity. *J Neurophysiol*, 93: 3050-3063.
- Zeng, F.-G. and Liu, S. 2006. Speech perception in individuals with auditory neuropathy. *J Speech Lang Hear Res*, 49: 36.
- Zeng, F.-G., Oba, S. and Starr, A. 2001. Supra threshold processing deficits due to desynchronous neural activities in auditory neuropathy. In *Physiological and Psychophysical bases of Auditory Function*, pp. 365-372. D.J. Breebaart, A.J.M. Houtma, A. Kohlrausch, V.F. Prijs & R. Schoonhoven (Eds.), Shaker Publishing BV, Maastricht, Netherlands.