Auditory Neuropathy Spectrum Disorder (ANSD): No Simple Solutions

Improving Outcomes for Children with Hearing Loss: Challenges and Solutions

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Topics

- Background
- Guidelines on AN developed at Lake Como
- Variability in presentation of AN
- Review of outcomes obtained from UNC study on AN
- Implications for Management
Auditory Neuropathy

Clinical syndrome characterized by electrophysiological evidence of normal or near normal cochlear function and absent or abnormal auditory pathway transduction
Audiologic Findings

- Absent or grossly abnormal ABR with presence of normal evoked otoacoustic emissions and/or a cochlear microphonic
- Otoacoustic emissions may be present initially but may disappear over time
- Absent acoustic reflexes in most cases
Normal ABR

![Graph showing Normal ABR waveforms for right and left ears at different sound levels (20dBnHL, 40dBnHL, 60dBnHL, 80dBnHL).]](image)
Estimated Audiogram from ABR
Absent ABR: No Cochlear Microphonic
Child with profound hearing loss
Abnormal ABR with Present Cochlear Microphonic
CM vs stimulus artifact

Bilateral auditory neuropathy/dys-synchrony

CM vs. stimulus artifact

Courtesy of John Grose
ABR Protocol for Evaluating CM

- Must have adequate recording conditions
  - Infant ready to sleep
  - Avoid electrodes positioned over transducer
- **Single polarity** clicks at 80 & 90dBnHL with rarefaction and condensation polarities
- Must use insert earphones
- No-sound run with sound tube disconnected or clamped to check for stimulus artifact
What’s Different?
ANSD vs “typical” SNHL

- Not possible to obtain threshold estimates with ABR in cases of ANSD
- Difficult to predict severity of disorder at time of diagnosis in infants using currently available tests
- If infant is identified early with ANSD it may be several months before child’s detection thresholds can be adequately measured
Clinical Characteristics Reported

- Pure tone thresholds ranging from normal to profound
- Disproportionately poor speech recognition abilities for the degree of hearing loss
- Difficulty hearing in noise
- Impaired temporal processing
- Hearing fluctuation
- Some individuals with AN have little or no communication difficulties while others are functionally deaf

Auditory Neuropathy: Not a New Disorder

- Term “Auditory Neuropathy” first introduced by Starr et al in 1996

- Not a new disorder
  - Early reports of children with absent ABRs responding to sound
    - Davis and Hirsch, 1979
    - Worthington and Peters, 1980
    - Kraus et al, 1984

- Newer technologies and procedures made it possible to conduct differential diagnosis of sensori-neural hearing loss
Starr et al Report 1996

- 10 patients with absent or abnormal ABR with evidence of normal cochlear outer hair cell function
  - Present cochlear microphonic and otoacoustic emissions
- Patients ranged in age from 4-49
- Presented without neurologic involvement at time HL identified
- 8/10 patients subsequently diagnose with other peripheral neuropathies including 3 with Charcot Marie Tooth disease
- Speech recognition scores were poorer than expected for degree of hearing loss
- Results obtained seemed to be characteristic of a “neural hearing loss”
Controversy

Exists in almost every aspect of disorder:

- Terminology
- Etiology
- Possible Mechanisms
- Treatment
Terminology

- **Starr et al 1996:**
  - Auditory neuropathy
- **Berlin et al 2001:**
  - Auditory neuropathy/dys-synchrony
- **Starr et al 2004:**
  - Pre-synaptic (Type I):
    - When evidence of hair cell involvement exists
  - Post-synaptic (Type II):
    - When patient has evidence of auditory nerve involvement
Terminology

- **Gravel and Rapin 2006**:  
  - Sensory hearing loss (hair cells)
  - Auditory neuropathy (pathology of spiral ganglion cells and VIIIth nerve axons)
  - Central hearing loss (central auditory pathway)
  - Neural conduction disorder (when differentiation cannot be made)

- **Gibson et al 2008**:  
  - Imaging, genetic and electrophysiologic testing should allow us to identify pathologic entities according to site of lesion
  - Blanket terms such as AN/AD may be more misleading then helpful
Possible Etiologies and Associations

- Prematurity
- Neonatal insult
  - Hyperbilirubinemia
  - Perinatal asphyxia
  - Artificial ventilation
- Genetic abnormalities
  - OTOF, PMP22, MPZ, NDRGI
  - Charcot-Marie-Tooth syndrome, Guillain-Barre syndrome, Friedrich’s Ataxia
- Infectious Processes
  - Viral Infections (e.g. mumps, meningitis)
- Ototoxic drug exposure
- Head injury

Rance (2005); Rapin & Gravel (2003); Starr et al. (2003)
Prevalence

- Estimates range from 7-10% of children diagnosed with permanent hearing loss (Rance 2005)
Auditory Neuropathy: Challenges/Questions

- What should we call this disorder?
- How do we accurately diagnose it?
- What should we tell a family to expect following initial diagnosis of AN when infant is only a few weeks of age?
- Do all children who present with audiological findings of AN have the same disorder or to the same degree?
- Can treatment protocols be generalized or should they be individualized?
- Are there clinically available diagnostic tools that allow us to predict benefit from a particular technology?
Auditory Neuropathy: Challenges/Questions

- Will hearing aids be helpful for the short term or the long term?
- What constitutes an adequate trial period with amplification?
- How do we determine who will benefit from hearing aids or cochlear implants?
- Will alternative hearing aid processing strategies result in better performance?
- What communication approach is best?
Guidelines Development Conference: Identification of Infants and Children with Auditory Neuropathy

Lake Como, Italy, June 19-21, 2008
Panel Members

- Charles Berlin
- Barbara Cone
- Deborah Hayes
- Gary Rance

- Pat Roush
- Jon Shallop
- Yvonne Sininger
- Arne Starr
- Kai Uus
Guidelines: Identification and Management of Infants and Young Children with Auditory Neuropathy Spectrum Disorder

- Terminology
- Diagnostic Criteria
- Comprehensive Assessments
- Audiological Test Battery
- Amplification Strategies
- Considerations for Cochlear Implantation
- Habilitation for Communication Development
- Screening
- Monitoring Infants with “Transient” ANSD
- Counseling Families of Infants with ANSD
Terminology Considerations

- Same constellation of findings with different sites of lesion:
  - Auditory nerve
  - Synaptic dysfunction at junction of inner hair cell/auditory nerve
  - Myelin disorder
  - Cochlear nerve deficiency (small or absent 8th nerve)

- Panel sought to identify simplified terminology to reflect an auditory disorder with a range of presentations secondary to variety of etiologies

- **AUDITORY NEUROPATHY SPECTRUM DISORDER**
Diagnostic Criteria

● Minimum Test Battery Required for Diagnosis:
  – Tests of cochlear hair cell (sensory) function:
    • Otoacoustic emissions and/or
    • Cochlear microphonics

● Tests of auditory nerve function:
  – Click-evoked auditory brainstem response (ABR) to high-level click stimuli
Recommended Audiologic Test Battery

- Otoscopic Examination
- Auditory Brainstem Response (ABR)
- Acoustic Immittance Measures
  - Tympanometry
  - Acoustic Reflex Testing
- Otoacoustic Emissions Testing
- Behavioral Audiometry
  - VRA, BOA, play audiometry
- Speech Recognition Testing
ASSR responses can be obtained to high signal levels (>80dBHL) but responses are elevated even in children who later show normal behavioral audiograms (Attias et al 2006, Rance et al 1998, Rance & Briggs, 2002).

Therefore, ASSR cannot be used to determine thresholds in ANSD.
Cortical Evoked Potentials (CAEPs)

- CAEPs not as reliant on timing as earlier evoked potentials and may be present when ABR is not
- Unlike ABR must be completed in awake (but quiet) infants
  - Cone Wesson and Wunderlich, 2003
- CAEP may be useful tool for some difficult to test patients
- Further CAEP research needed with normal infants and infants with SNHL and ANSD
Comprehensive Evaluations Following Diagnosis with ANSD

- Otologic
- Radiologic imaging (MRI/CT)
- Neurologic
- Medical Genetics
- Ophthalmologic
- Pediatric and Developmental Evaluations
- Communication Assessment
Behavioral Audiometry: Guidelines for ANSD

- Behavioral assessment of pure tone threshold using developmentally appropriate, conditioned test procedures such as VRA
  - Begin at developmental age of 6-7 months
  - Goal should be to obtain individual ear measures and bone conduction thresholds by 8-9 months of age

- For very young or developmentally-delayed infants, behavioral observation audiometry (BOA) may be used to observe infant’s reflexive response to sound but should not be interpreted as representing behavioral thresholds or minimum response levels
Method Used Depends on Child’s Developmental Age

- Methods used vary according to the age and developmental level of the child
- If child premature, age is adjusted for prematurity and test choice depends on “adjusted age”
- If child has developmental delays, knowledge of child’s developmental age is helpful
- Parents can help when documentation unavailable
Recommended Audiologic Test Battery

- Otoscopic Examination
- Auditory Brainstem Response (ABR)
- Acoustic Immittance Measures
  - Tympanometry
  - Acoustic Reflex Testing
- Otoacoustic Emissions Testing
- Behavioral Audiometry
  - VRA, BOA, play audiometry
- Speech Recognition Testing
Speech Perception Test Battery

- Early Speech Perception Test battery (ESP) (Moog and Geers, 1990)
  - Standard
  - Low Verbal

- MLNT/LNT words and phonemes (Kirk, et al, 1995)

- PB-k words and phonemes (Haskins, 1949)

- C-HINT sentences in quiet and noise conditions

- Functional Assessment Tools:
  - ELF
ANSD Guidelines: 
Recommended Amplification Strategies

- If infant or young child with ANSD demonstrates elevated pure-tone and speech detection thresholds with consistent test-retest reliability, hearing aid fitting should be considered and trial use of hearing aids should be offered to families.
ANSD Guidelines:
Recommended Amplification Strategies

- Hearing aid fitting strategies...should follow established guidelines for the fitting of amplification in infants and toddlers
  - Pediatric Working Group of the Conference on Amplification for Children with Auditory Deficits, 2001
ANSD Guidelines:
Recommended Amplification Strategies

- Amplification should be fitted as soon as ear specific elevated pure-tone and speech detection thresholds are demonstrated by conditioned test procedures (VRA, COR)
- Since Improvement in auditory function has been reported in some cases, careful monitoring needed to adjust and modify amplification as needed.
ANSD Guidelines: Recommended Amplification Strategies

- Strategies to improve signal-to-noise ratio for children with ANSD should, theoretically improve speech recognition and language learning (Hood et al 2003)
- Trial use of an FM system, especially in structured and spontaneous language-learning activities should be considered.
ANSD Guidelines
Special Considerations for Cochlear Implantation
ANSD Guidelines: Special Considerations for Cochlear Implantation

- Significant improvement including “recovery” has been reported in a subset of infants with ANSD.
- Families should be informed that spontaneous improvement in auditory function has been reported up to two years.
- Cochlear implantation should not be considered until auditory test results stable and demonstrate unequivocal evidence of permanent ANSD.
- Deferring decision to two years of age may be appropriate.
ANSD Guidelines:
Special Considerations for Cochlear Implantation

Evidence of auditory nerve sufficiency should be obtained prior to surgery using appropriate imaging technology

(Buchman et al., 2006)
ANSD Guidelines:
Special Considerations for Cochlear Implantation

Children with ANSD who do not demonstrate good progress in speech recognition and language development should be considered candidates for cochlear implantation regardless of audiometric thresholds. Children in this category with elevated pure tone and speech detection thresholds should receive a trial of amplification fitted using pediatric amplification guidelines prior to consideration for implantation.
Variable Presentations of ANSD
Variable Presentation of ANSD Case #1
Present CM and OAEs

- 24 week preemie
- Intensive care nursery
- 4 months
- Ventilated 2 months
- ABR repeated at 18 months-no change
Variable Presentation of ANSD Case #1
Normal thresholds, present CM and OAEs

Audiogram at 14 months
Audiogram at 18 months
Variable Presentation of ANSD Case #2
Child with Profound Bilateral HL
Present CM and OAEs
Variable Presentation of ANSD #3
Child with “moderate loss”
CM present, absent OAEs
Variable Presentation of ANSD Case #4
Large CM, present OAEs but distal waveforms

Is this normal hearing??

[Graphs and waveforms depicting auditory function tests]
Behavioral Audiometry Case #4
VRA with insert earphones
Age 14 months
Variable Presentation of ANSD Case #6
Child with CHARGE
Right: Moderate loss
Left: Absent cochlear nerve
Variable Presentation of ANSD Case #7
Child with bilateral deafness
No VIII\textsuperscript{th} nerve on right
Variable Presentation of ANSD Case #7
Child with bilateral deafness
No VIII\textsuperscript{th} nerve on right
UNC Children with Auditory Neuropathy Characteristics and Cochlear Nerve Deficiency (small/absent) VIIIth Nerve

- 2006-Retrospective review of 65 children with characteristics of ANSD
- 51/65 had MRI data available
- 9/51 (18%) had small or absent 8th nerves
  - Small (n=2); 4%
  - Absent (n=7); 14%

Buchman, Roush, Teagle, Brown, Zdanski and Grose
Ear and Hearing 2006 Aug 27(4): 399-408
37 (31%) Cochlear Nerve Deficiency (CND) in one or both ears

- Unilateral (n=24; 20%)
- Bilateral (n=13; 11%)
UNC Children with Cochlear Nerve Deficiency (Small or Absent) VIII<sup>th</sup> nerve  
N=57

- 37 (65%) have absent ABR with present CM

- Radiographic studies not always clear or 100% accurate, difficult to know how to advise families
  - 5 ears in 4 kids were implanted
  - Have no electrical response at surgery
  - Stimulate but have no open set abilities
Take Home

- Absent 8\textsuperscript{th} Nerve
  - not uncommon
  - can result in auditory neuropathy phenotype
  - commonly has normal internal auditory canal (IAC) morphology
  - commonly has normal labyrinth

- Need MRI instead of CT in all kids
  - with profound hearing loss
  - with auditory neuropathy phenotype

- Audiological, educational, and medical recommendations will be influenced by these findings e.g. CI or HA candidacy
University of North Carolina-Chapel Hill
ANSD Study

- 134 infants and children with ANSD
- 10 year prospective study underway to determine characteristics of children with ANSD and benefit from assistive devices
- All patients evaluated by pediatric audiologist and otologist
- Neurology, genetics, opthalmology consults recommended
- Many in study are very young and we are just beginning to be able to evaluate outcomes
Universal NB screening in NC began in 1999

- 160,000 births/year
- 300 diagnostic ABRs/year
- 100 hearing aid fittings/year
- ~75 cochlear implants/year
- Total 1350 infants and children
  - 750 using amplification
  - 600 with cochlear implants
- 134 children with characteristics of ANSD
UNC-Chapel Hill AN/AD Children
Medical Diagnosis N=112
81/112 (72%) have some positive history

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<th>Condition</th>
<th>Count</th>
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<td>Unknown</td>
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<td>Other</td>
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UNC Children with ANSD
Radiologic Findings

- 66% of ANSD children in our program have abnormal finding on MRI
  - White matter problems
  - Developmental brain abnormalities, e.g. Dandy Walker malformation
  - Cochlear nerve deficiency

- Medical disorder with audiological manifestations
  - Important to involve medical colleagues
UNC Unilateral vs Bilateral ANSD
N=134

Unilateral vs Bilateral AN
N = 131

- Unilateral: 22%
- Bilateral: 78%

Unilateral
N=30

Bilateral
N=104
UNC AN No Assistive Device
N=34

- 17  NAD unilateral normal hearing contralateral ear
-  7  NAD normal hearing
-  3  NAD no nerves
-  6  NAD no BEA/too young or too impaired
-  1  NAD refused
UNC AN Children with CI
N=49

CI in AN EAR

- 37% <6 months CI use/CNT N=11
- 22% Closed Set Data Only N=13
- 27% Limited Open Set N=7
- 14% Open Set Performers N=18
UNC AN Children with CI
Open Set Performance N=25

OPEN SET PERFORMANCE
N = 25

Percent Correct (%)

0 10 20 30 40 50 60 70 80 90 100

Subject #
60 42 47 9 3 23 25 24 94 37 45 15 13 16 17 58 18 41 48 33 35 5 51 68

Words
Phonemes
UNC-Chapel Hill CI Users with AN Performance/Duration of Use

OPEN SET PERFORMANCE
N = 25

Percent Correct (%)

Length of Use (months)

Words
Phonemes
UNC AN Children with HA

Hearing Aid Users
N = 33

- HA progress (12)
- Too Young (8)
- Multiple Medical Problems CNT (5)
- Lost to F/U or transferred (8)
## UNC AN Hearing Aid Users
### Able to Evaluate

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age (Months)</th>
<th>Gestational Age</th>
<th>Aided Word Recognition</th>
<th>Test Used</th>
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<td>80%</td>
<td>PBK</td>
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<td>69</td>
<td>24</td>
<td>68%</td>
<td>WIPI</td>
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<td>39</td>
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<td>ESP Mono</td>
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<td>126</td>
<td>34</td>
<td>60%</td>
<td>W-22</td>
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UNC-Chapel Hill ANSD Children
Unaided vs Aided PTA

Average Unaided vs Aided PTA

- Avg Unaided PTA R/L
- Aided PTA

Subject: 1, 2, 3, 4, 5, 6
UNC-Chapel Hill ANSD Children with Hearing Aids
Unaided vs Aided SRT

Unaided vs Aided SRT

<table>
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<th>3</th>
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<tr>
<td>Avg Unaided SRT</td>
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<tr>
<td>Aided SRT</td>
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SRT dBHL

0 10 20 30 40 50 60 70
CI Criteria-Children

- **Advanced Bionics**
  - Children-age 4 or less:
  - Failure to reach auditory milestones or <20% on MLNT at 70 dB SPL
  - Children older than age 4: <12% on PBK words or < 30% on open set sentences at 70 dB SPL

- **Cochlear Corporation**
  - Children-12 months though 17 years
  - Bilateral profound SNHL in children 12 months to 2 years
  - Bilateral severe to profound SNHL in children 2 years and older
  - 30% or less on open set MLNT or LNT
  - 3-month trial with HA if not previously amplified

- **Med El**
  - Children- 12 months to 17:11 (17 years, 11 months)
  - Profound SNHL specified as 90 at 1K Hz
  - Lack of progress in auditory skills with habilitation and amplification provided for at least 3 months
  - Less than 20% on MLNT or LNT
  - 3-6 month HA trial without previous fitting; waived if ossification
Counseling in ANSD: What Do We Say to Families?

- Important that information we provide to families is based on current evidence and not “hearsay”
- More difficult than with typical sensory hearing loss to provide “prognosis” for family
  - With sensory hearing loss, pure tone audiogram allows us to make reasonable predictions of expected outcomes for many children
  - Lack of clinical tools available to determine degree of impairment in cases of ANSD makes counseling families difficult
Counseling in ANSD: What Do We Say to Families?

- Child has an auditory disorder
- Difficult to know prognosis
- Degree of deficit may be mild or severe
- Results of behavioral testing are necessary before specific recommendations can be made
- Hearing aid use helpful in some cases not in others but we will only know if child is fit appropriately and has consistent use
- Cochlear implantation may be a better option if adequate benefit from HA not received
Counseling in ANSD: What Do We Say to Families?

- Frequent follow up visits will be necessary
- Child should be enrolled in early intervention as soon as family is ready
- Most effective communication strategy will need to be determined with input from family, teachers, therapists, and audiologist
- We’ll work together as a team to find a solution for their child’s hearing disorder
Summary

- **Diagnosis of ANSD:**
  - Consequences of incorrect diagnosis are significant:
    - Identifying child with normal hearing or mild problem as deaf
  - Must have good recording conditions
  - Use insert earphones
  - Avoid “alternating” polarity clicks, complete rarefaction and condensation runs.
  - Complete “no sound run” to rule out stimulus artifact

- **Behavioral Audiometry**
  - Experience in evaluating infant and young children essential
  - Use established protocols such as those described by Judy Gravel and Judith Widen
  - Important to remember that severity of functional deficit may not be related to level of pure tone thresholds
  - Accuracy of hearing aid fitting is only as good as our ability to determine the infant’s auditory capacity

- **Speech Recognition Testing**
  - Critical to use developmentally appropriate measures as early as possible
Conclusions

- ANSD is more complicated than originally thought and population more heterogeneous.
- It’s unlikely that a single approach to management will meet the needs of all children.
- Some children will benefit from hearing aids either in the short term or the long term, others will require cochlear implantation.
- Visual methods to support communication may be required for some children even those who have received cochlear implants.
Conclusions

- The available clinical evidence does not support withholding audibility from infants with ANSD. Although audibility does not ensure good speech recognition, lack of audibility is certain to result in poor speech recognition.
- Important to consider the needs of the whole child, not only the auditory neuropathy diagnosis.
- Important to use team approach to carefully monitor child’s progress in meeting communication goals.
Research Needs

- Better clinical tools to help determine site of lesion
- Better ways to predict who will benefit from amplification vs cochlear implantation
- Continued research needed into the role of CAEP and other electrophysiologic tests in evaluation and management
- Research into signal processing strategies that target temporal vs spectral disruptions
THANK YOU!