Diagnosis And Management Of Auditory Neuropathy Spectrum Disorder (ANSD)

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Physiology of Normal Hearing
The Cochlea

- Contains the organ of hearing
- Encased in the temporal bone of the skull
- “Snail-shaped”

Physiology Of Normal Hearing

Low Frequencies

High Frequencies

Physiology Of Normal Hearing
Diagnosis And Management Of Auditory Neuropathy Spectrum Disorder (ANSD)

Physiology Of Normal Hearing

Physiology Of Normal Hearing

Auditory Pathway Interrupted
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What’s The Site Of Lesion (SOL)?

- Inner hair cells
- Synapse/neurotransmitters
- Auditory nerve-can involve myelin, spiral ganglion, and/or axons

**Routine clinical test findings do not readily identify the specific SOL**

“Conventional Wisdom” re: ANSD

- Audiogram is not really useful in planning remediation/management
- Hearing aids are rarely, if ever, effective
- Cochlear implants are the “go to” treatment
- Label of ANSD characterizes a patient’s auditory performance

About Conventional Wisdom...

“What gets us into trouble is not what we don’t know, it’s what we know for sure that just ain’t so”...Mark Twain
**Heterogeneity & Complexity**

- Auditory Neuropathy *Spectrum* Disorder
- Avoid generalizations from single case examples
- Are conclusions based on systematic studies?
- View every case individually and comprehensively

**ANSD: Different From SNHL?**

- Impaired auditory function
  - May have elevated auditory thresholds
  - May have poorer than expected speech perception, especially in noise
- Impaired auditory neural function
  - Abnormal/absent ABR (not reliable predictor)
  - Absent/elevated middle ear muscle reflex (MEMR)
- Evidence of normal OHC function
  - Normal otoacoustic emissions (OAEs)
  - Present cochlear microphonic

**A Brief History**

- Newly identified, but not a newly emergent
- “Paradoxical” cases in early ABR literature
- Advent of OAEs helped clarify new diagnostic category
- First labeled auditory neuropathy in mid 1990’s (Sinninger et al., 1995; Starr et al., 1996)
Incorrectly Named?

- Is “Auditory Neuropathy” inaccurate?
  - Only 30% - 40% of reported cases have additional neural abnormalities
  - Berlin (2001) proposed name change to auditory dys-synchrony
- Auditory neuropathy/auditory dys-synchrony (AN/AD)

ANSD: It’s Settled Then...

- Auditory Neuropathy Spectrum Disorder
  - Reflects the heterogeneity of individuals with the same clinical findings
  - Recognizes the limitations of current tests to readily identify site of lesion
- Still seems to routinely be shortened to “Auditory Neuropathy”

What Causes ANSD?

- Hyperbilirubinemia
- Hypoxia/anoxia
- Infectious disease
- Genetic
  - Syndromic
  - Nonsyndromic
  - Recessive
  - Dominant

>50% of pediatric ANSD cases have one of these factors in the birth history
Etiology: Genetic Causes

- Syndromic “non-isolated” forms w/ peripheral neuropathy (more than 20)
  - Charcot-Marie-Tooth
  - Mohr-Tranebjaerg syndrome
  - Friedreich Ataxia
  - Poorer outcomes???
- Non-syndromic forms
  - Mostly in families identified with NSRA
  - Several genetic mutations being associated with “isolated” ANSD

Prevalence/Incidence?

- Estimates have ranged from .5% to 15% of all hearing loss
- Accuracy confounded by populations studied (NICU, all HL, at risk, deaf schools)
- 7% to 10% (Rance, 2005)
- 10% would mean:
  - 1 to 2 per 10,000 births
  - .01 to .02% of all births

Accurate Diagnosis of ANSD

- Impaired auditory function
  - Behavioral audiometry
  - Speech perception
- Abnormal auditory nerve function
  - Absent or significantly abnormal ABR
  - Absent acoustic reflexes
- Normal cochlear outer hair cells (OHC)
  - Present otoacoustic emissions (OAEs)
  - Cochlear microphonic on ABR
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Diagnostic Test Battery

- Tympanometry
- Otoacoustic emissions (OAEs) for OHCs
- Auditory Brainstem Response (ABR)
  - Information about neural function
  - Information about OHCs
- Acoustic Stapedial Reflexes (MEMR)
- Behavioral Audiometry

Tympanometry

- ANSD may have normal or abnormal tympanometry
- Presence of middle ear fluid or negative pressure or TM perforation will influence:
  - OAE / Cochlear microphonic (CM)
  - Ability to measure acoustic reflexes
- Should be the first test in the battery

Tympanogram (“Tymps”)

[Diagram of normal and flat tympanograms]
Otoacoustic Emissions (OAE)

- Acoustic response from outer hair cells (OHC), reflective of normal function
- Typically present in patients with ANSD, at least in early childhood
- Sometimes reported as very robust

What does it test?
The function of the sensory hair cells in the cochlea
Otoacoustic Emissions (OAE)

Otoacoustic Emissions (OAE)

Otoacoustic Emissions

Emission not clearly present above noise floor

Emission not clearly present above noise floor
OAEs Test Outer Hair Cells

OAEs: Keep In Mind...

- OAEs may over time:
  - Decrease in level
  - Disappear
- Sensitive to changes in middle ear status
- Absent OAEs are not enough to eliminate ANSD as a potential diagnosis

Auditory Brainstem Response (ABR)
Example – ABR Waveform

ABR In ANSD

- ANSD – Absent or abnormal
  - Absent is obvious
  - What is “abnormal”?
- ABR thresholds not predictive of behavioral sensitivity threshold, i.e. poor correlation between the two

Cochlear Microphonic

- Considered OHC response
- Bio-electric analog of the stimulus signal
- Reverses polarity with changes in stimulus polarity (rare/cond)
- Finding in ANSD is present CM with absent/abnormal ABR
**Cochlear Microphonic (CM)**

No measurable neural response

**ABR Tests Auditory Nerve Function**

Can ALSO Tell About OHC Function
**Middle Ear Muscle Reflexes**

- a.k.a. Acoustic reflex or stapedial reflex
- Absent or elevated in cases of ANSD
- Berlin et al. (2005)
  - None had normal AR pattern
  - None had reflexes at both 1000 and 2000 Hz

**Acoustic Reflexes: Keep In Mind**

- Abnormal acoustic reflexes can result from a number of causes
- By itself not sufficient to make a diagnosis of ANSD
- Results abnormal or inconsistent with what is expected = consider referral for ABR

**Acoustic Reflex Tests Nerve Function**
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Audiogram

- Can vary from normal to profound
- Rising configuration in some cases
- May be progressive/fluctuating
- Not a reliable indicator of speech perception ability
  - May be poorer than similar degree of SNHL
  - May be the comparable to similar degree of SNHL
- “Audiogram tells you nothing...”?

Test Battery For ANSD

- Normal middle ear function
- Normal OAEs
- Abnormal ABR
  - Absent waveform
  - Presence of cochlear microphonics for high amplitude test stimulus
- Absent acoustic reflex thresholds
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### ANSD Or Not?
- Flat tympanograms/abnormal middle ear function
- OAEs absent
- ABR abnormal
  - Absent waveform
  - Absent cochlear microphonics

### AN 15 Background
- Male, 4 years of age, speech-lang. Concerns
- Clinic contacted with inquiries about testing for CAPD
- No particular concerns for hearing
- Scheduled for speech-lang. evaluation and hearing screening

### Previous Findings (Age 2)

![Audiogram Chart]

- 125 250 500 1000 2000 4000 6000 8000 10000 Hz
- Frequency in kHz (Hz)
- 120 110 100 90 80 70 60 50 40 30 20 10 dB
- 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 dB
Audiological Testing

- No particular concerns for hearing
- Very active and difficult to condition to testing task
- Proceeded with SLE, but rescheduled audio testing

Risk Factor History

- Premature: 27 weeks G.A., 1 lb. 3 oz.
- Ventilator dependent for 2 ½ months
- Ototoxic medications
  - Gentamycin
  - Vancomycin
- Numerous bradycardic and apnic episodes
- Passed newborn hearing screen at discharge
- Language concerns from an early age

Distortion Product OAEs (Age 4)

- Right Ear
- Left Ear
**Pre-ABR Audiogram (Age 4)**

SAT: 30 dB HL
Could identify spondees at 75-80 dB HL with visual cues but not without

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**ABR results**

No neural responses at 90 dB HL, AU, but cochlear microphonic present

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**ABR Results**

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Following diagnosis

- Enrolled in auditory/oral school program
- Consistent use of binaural BTEs and wireless FM system
- Aided results: 88% correct at 55 dB HL for NU-CHIPS (closed set)
- Recommendation to supplement auditory input with sign language

Recovery From ANSD

- “Growing out” of the disorder
- Neuromaturation?
- Association with hyperbilirubinemia
- Seems to occur within age 12-16 months
  - Not likely after 24 months
- Implications for cochlear implantation?
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Recovery From ANSD?

- Madden et al., 2002: 9/18 improved
- Psarommatis et al., 2006: 13/20 from NICU
- Raveh et al., 2007: 4/19 improved
- Attias & Raveh, 2007: Case reports for 5 children with partial or full recovery

Recovery Example 1: Initial ABR

Recovery Example 1: ABR 1 Yr. Later
Remediation Options For ANSD

- Amplification/ hearing aids
- Cochlear Implantation

Big Assumptions In ANSD?

- Audiogram is not useful in treatment
- Label of ANSD means poor speech perception skills
- Hearing aids are not effective remediation
- Cochlear implants are the best treatment option

Management And Intervention

- Heterogeneity
  - Audiometry
  - Speech recognition
  - Etiology/S.O.L.
- One management approach is unlikely to be successful for all patients with ANSD
Children with ANSD

- Mean speech recognition score is 48%
  - Normal hearing (96%)
  - SNHL (84%)

Conclusion?
- Children with ANSD have poorer than expected word recognition.

Mean Scores Can Be Mean

- Controversial topic
- Assumption of poor speech perception abilities
- Several studies report limited or no hearing aid benefit
  - Few studies have evaluated this issue systematically
  - Adult patients with ANSD tend to not perform well with amplification.

Hearing Aids With ANSD

Low Speech Perception? (Rance, 2005)

- Word Rec. scores from 10 studies of ANSD
- Compared to minimum expected score from Yellin et al., 1989
CNC Scores In Quiet

![Graph showing CNC scores in quiet](image1)

Rance, Barker, Mok, Dowell, Rincon, & Garrett (2007)

Poorer Speech Perception In Noise?

![Graphs showing speech perception in noise](image2)

Rance et al., (2007)

Does Amplification Seldom Help?

- **Rance et al. (2002)**
  - aided vs. unaided scores
  - 7 subjects - no improvement
  - 8 subjects - mean difference score of 56.8%
  - Not correlated with the audiogram.

![Graph showing aided vs. unaided scores](image3)
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Aided CNC Scores

Rance & Barker, 2007

Language Quotient & Articulation

Hearing aid users with ANSD compared to matched SNHL

Rance, Barker, Sarant, & Ching (2007)

Language Quotient
**Data from BTNRH Patient**

![Graph showing speech perception at sentence level with different conditions: CI Alone, HA Alone, and Bimodal (CI + HA).]

<table>
<thead>
<tr>
<th>% Correct</th>
<th>CI Alone</th>
<th>HA Alone</th>
<th>Bimodal (CI + HA)</th>
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**Arguments Supporting HA Trial**

- Sensitivity loss not explained by dys-synchrony alone
- Some studies show benefit with amplification
  - Particularly with early intervention
  - Difficult to predict who will benefit
- “Treat the patient, but don’t ignore the audiogram”
  - Audibility, audibility, audibility...
  - Consider “limited” benefit vs. no benefit/decrement

**Summary: Amplification In ANSD**

- Data show mixed results
- Assumption of poor aided speech perception is overgeneralization
- Physiological results and detection thresholds alone do not predict who will benefit
- Further research is needed to determine if the means exist to help predict benefit
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Cochlear Implants And ANSD

• Initially assumed to be poor candidates
  – Site of lesion = auditory (VIIIth) nerve
  – CI directly stimulates VIIIth nerve

• Earliest published reports were not promising
  – Miyamoto et al. (1999)
  – Rance et al. (1999)

Changin Ideas About CI

• Restored synchronous activity of VIIIth nerve
  – Fabry, 2000
  – Trautwein et al, 2000

• Mayo Clinic experience
  – Shallop et al., 2001
  – Peterson et al., 2003

• Numerous case reports and studies emerged

Outcomes With CI

Leigh et al. (2009)
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Language Development

Why Does CI Work?

- Bypasses site of lesion just as in recipients with SNHL
  - Inner Hair Cell (IHC) disorder
  - IHC/VIIIth nerve synapse disorder
- Improved neural responses due to either:
  - Improved synchrony of neural firing
  - Increased number of neural elements recruited
- CI can address multiple sites of lesion

The Silver Bullet For ANSD?

- Some reports of limited benefit from CI
  - Miyamoto et al, 1999; Rance et al, 1999; Gibson & Sanli, 2007; Leigh et al, 2009; Teagle et al, 2010
- Additional neuropathies/medical complications
  - Charcot-Marie-Tooth disease, Friedreich ataxia, Mohr-Tranebjaerg syndrome, etc.
  - May be present in as many as 30-40% of patients with ANSD
Cochlear Nerve Deficiency (CND)

- Condition in which auditory nerve is abnormally small or even absent
- May only be identifiable through MRI
- Buchman et al., 2006; Adunka et al., 2006; Bradley et al., 2008; Walton et al., 2008
- Consideration for CI candidacy?
  - Possible poor/limited CI outcomes
  - MRI for all patients with ANSD (CT may be normal)

Outcomes In Abnormal MRI

CI & ANSD Data (Gibson & Sanli, 2007)

- 60 of 435 CI recipients (13.8%) diagnosed with ANSD
- Abnormal EABR after CI in 15 (25%)
  - Significantly poorer speech perception than SNHL with CI controls
  - Significantly poorer than other ANSD with CI
  - Assumed to have true “auditory neuropathy” (AN) or “brainstem auditory neuropathy” (BAN)
Recent Data (Teagle et al. 2010)

• 52 CI Recipients
  – 27% have limited speech recognition
  – Significant variability
• Predictive factors include
  – Normal MRI
  – Normal ECAP

Abnormal VIIIth Nerve Potentials

ECAP – Evoked Compound Action Potential

CI Candidate?
**Diagnosis And Management Of Auditory Neuropathy Spectrum Disorder (ANSD)**

**CI Candidate?**

![Graphs showing Unaided Word Recognition and Aided Sentence Recognition](image)

- **Unaided Word Recognition**
  - NU-6 Words
  - Left: 48, Right: 32

- **Aided Sentence Recognition**
  - Left Aid: 46, Right Aid: 41

**CI in ANSD With Milder Hearing Loss**

- 2007 JCIH
- 2008 Guidelines and Development Conf. on the Identification and Management of Children with Auditory Neuropathy
- Rationale is to restore synchronous function in the auditory nerve
- Few reports in the literature & more evidence is warranted

**CI In Milder Degrees Of Hearing Loss**

- Cautious and methodical approach
  - Trial with amplification
  - Assessment of speech perception
  - Assessment of speech-language skills development
- Delay implant beyond 12-18 month range
- Can child benefit from less invasive intervention than CI?
Summary Of CI In ANSD

• No difference compared to SNHL?
  – Speech perception and language development
  – ECAP and EABR in normal range

• Sometimes poorer for ANSD
  – Related to etiology or site of lesion
    • Demyelinating or axonal disorder – true AN/BAN
    • Cochlear nerve deficiency
  – Limited speech perception benefit

• May be appropriate in milder degrees of loss when amplification is not satisfactory

Key Points

• Cochlear implantation may be an option for individuals with ANSD
• Hearing aids can be of benefit in some individuals with ANSD
• BUT, behavioral results are needed in order to appropriately fit amplification
• Dx of ANSD should not mean an immediate referral for CI
• Don’t automatically discard any intervention options

Auditory Neuropathy Spectrum Disorder (ANSD) Case Studies
### Erber's Hierarchy Of Auditory Skills

<table>
<thead>
<tr>
<th>Comprehension</th>
<th>Identification</th>
<th>Discrimination</th>
<th>Detection</th>
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*Erber (1982)*

### Variety Of Tests Over Time

- What is child’s level of auditory development?
- Detection...presence vs. absence
- Pattern Perception
- Closed-set words
- Open-set words
- Open-set phrases
- Paragraph/narrative comprehension

### Auditory Tests

- **Behavioral Audiogram with Hearing Aid or Cochlear Implant**
  - Detection task
  - For monitoring over time
  - Overall picture of potential for audibility and perception of speech
- **Speech Perception Testing**
  - Skills develop over time
### Pattern Perception

- Blank lines

### Closed-Set Words

- Blank lines

### Closed-Set

- Blank lines
### Open-Set Words

- From an effectively “infinite” set
- Can vary in vocabulary level
- Lexical Neighborhood Test (LNT)
- Multi-syllable Lexical Neighborhood Test (MLNT)
- PBK-50 Words
- CNC Words

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### Open-Set Words

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### Open-Set Words

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### Open-Set Words

**STUDENT #1**
15 years old

**Consonant Nucleus Consonant Test (CNC)**
### Open-Set Phrases/Sentences

- Levels of linguistic complexity
- In quiet or in varying levels of noise
- Commons Phrases
- Hearing in Noise Test (HINT)
  - Children’s version (HINT-C)
  - Standard version
- AZ Bio Sentences
Narrative Comprehension

- Varying length and linguistic complexity
- Test of Auditory Comprehension
- Subtests from speech-language protocols
  - Paragraph Comprehension (from CASL)
  - The Listening Comprehension Test-2
  - Test of Auditory Processing Skills-3 (TAPS-3)
  - Understanding Spoken Paragraphs (from CELF-4)
- Comprehension of passages from books or of stories

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