ANSD
Auditory Neuropathy Spectrum Disorder:

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Arnold Starr, M.D.
University of California - Irvine
• Starr et al. (1991) identified auditory neuropathy (AN) as a timing disorder.

• Zeng et al. (1999) demonstrated temporal processing problems in adults with auditory neuropathy.
Auditory Nerve from AN subject with HSMN due to Myelin protein zero mutation.

Note mark drop out of fibers compared to age matched control.
Model of ANSD Types

Pre-Synapse Type I

Inner hair cell

synaptic ribbon

Auditory Nerve

Synapse Type II

Outer Hair Cells

PS Remember Spoendlin 1972?
BACKGROUND INFORMATION

- Hearing relies on faithful synaptic transmission at the ribbon synapse of cochlear inner hair cells. These synaptic ribbons are essential for synchronous auditory signals.
- Darina Khimich\textsuperscript{1}, Régis Nouvia\textsuperscript{1,2}, Remy Pujol\textsuperscript{2}, Susanne Dieck\textsuperscript{3,5}, Alexander Egner\textsuperscript{4}, Eckart Gundelfinger\textsuperscript{3} and Tobais Moser\textsuperscript{1}.
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- 3. Magdeburg, Germany, 4. Max Planck Institute for Biophysical Chemistry, Goettingen Germany, 5. Max Planck Institute for Brain Research, Frankfurt/M, Germany
- Nature 434 889-894 April 2005
Morphology of synaptic ribbon

✓ Cochlear inner hair cell ribbon synapses from an 8 week old mouse (A B & C).
(D) Saccular hair cell and
(E) color reconstruction.

Nouvian, Beutner, Parsons & Moser,
University of Goettingen, University of Pennsylvania & University of Koeln
Lessons Learned

Speech recognition is very dependant on the ability to make fine timing discriminations in the speech signal which has small temporal “gaps”
Temporal and speech processing deficits in auditory neuropathy

Auditory neuropathy affects the normal synchronous activity in the auditory nerve, without affecting the amplification function in the inner ear. Patients with auditory neuropathy often complain that they can hear sounds, but cannot understand speech. Here we report psychophysical tests indicating that these patients’ poor

Key words: Acoustic simulation; Auditory neuropathy; Hearing disorder; Human; Neural synchronization; Speech perception; Temporal processing

CA Corresponding Author
The characteristics of Hearing Loss in ANSD


- Average of 10 ANSD Adults
- Average normal hearing

Variabile Hearing Levels
BACKGROUND INFORMATION


• Subjective deafness in case of peri-synaptic audiopathy. Isolated defects of the inner haircells?

• “Hypoxia, carboplatin, ototoxicity and metabolic disorders are possible etiologies for damage to the inner hair cells or synapsis.”
BACKGROUND INFORMATION


- Unidad de Genetica Molecular, Hospital Ramon y Cajal, Madrid, Spain.

- Auditory neuropathy in patients carrying mutations in the otoferlin gene (OTOF).


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Background Information

- Berlin et al. (2001), and Hood (2002) proposed auditory dys-synchrony as a more descriptive term. Typical findings include:
  - abnormal evoked potentials
  - otoacoustic emissions (usually present)
  - absent middle ear reflexes
  - lack of benefit from amplification
Audiograms from various testing over 20 years
Prevalence

A conservative estimate of 10% for ANSD (Uus and Bamford, 2005) can be argued which suggests that more than 5,000 children with cochlear implants worldwide are likely to have ANSD as a component of their hearing loss etiology.
Table 2: Prevalence of ANSD in children with permanent hearing loss.

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>No. of Cases</th>
<th>No. of AN/AD</th>
<th>% of Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kraus et al.</td>
<td>Hg. impaired children</td>
<td>48</td>
<td>7</td>
<td>14.58</td>
</tr>
<tr>
<td>(1984)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Park &amp; Lee</td>
<td>Hg. impaired children</td>
<td>139</td>
<td>7</td>
<td>5.04</td>
</tr>
<tr>
<td>(1998)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Vohr et al.</td>
<td>Universal screening</td>
<td>111</td>
<td>2</td>
<td>1.80</td>
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<tr>
<td>(1998)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rance et al.</td>
<td>“at-risk” infants</td>
<td>109</td>
<td>12</td>
<td>11.01</td>
</tr>
<tr>
<td>(1999)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Berlin et al.</td>
<td>Hg. impaired</td>
<td>1000</td>
<td>87</td>
<td>8.70</td>
</tr>
</tbody>
</table>

Rance 2005 AN/AD and it’s Perceptual Consequences

16
In general, various physical, sensory or cognitive issues can be observed in addition to hearing loss and all of these will be educationally significant.

As these “issues” arise, there is an increase in the probability of auditory neuropathy / dys-synchrony as an additional problem.
The characteristics and co-morbidities of ANSD

• Developmental delays
• Learning disabilities, ADD, ADHD
• Autism spectrum disorders
• Emotional or behavioral problems
• Uncorrected visual problems, blindness
The characteristics and co-morbidities of ANSD

• Other health impairment
• Cerebral palsy, motor disorders
• Apraxia
• Inner ear malformations, Atretic or absent auditory nerve
• Seizures
• Syndromes
The characteristics and co-morbidities of ANSD

- Hearing is usually abnormal in these children
- However they may exhibit good sound “detection”
- And very poor speech recognition in most cases
- But some will benefit from hearing aids
- .... And why? Sound demonstration
Case Study

Absent Auditory Nerve Right

If this child had been “screened” for hearing loss he would have

Passed OAE screening
Absent ABR
Otoacoustic Emissions Present In Both Ears

REMARKS:
Earphone: Inset
Transient otoacoustic emissions (TEOAE’s) were obtained for frequencies 1.5 through 4.0 KHz in the left and right ear.

Contra-lateral acoustic reflexes present: sound in LEFT ear
Remember, the RIGHT ear shows no sound detection.
Normal Example MR Cisternography of the IAC and Labyrinth

VII - facial

VIII - Balance Superior Vestibular

VIII - Balance Inferior Vestibular

Anterior

Normal IAC

Cochlear Nerve in anteroinferior quadrant
AA01: MR Cisternography of the IAC and Labyrinth

Small IAC with FN present – Vest Nerve not present
Cochlear Nerve not present in anteroinferior quadrant
Lessons Learned

A profound unilateral hearing loss can be caused by the absence of an auditory nerve and cochlear function could be normal in such cases.
Lessons Learned

- **ALL** children being considered for a cochlear implant should have MRI of the brain and auditory nerve cross section to visualize the 4 nerves within the internal auditory canal and verification of brain structures.
Case Study
ANSD Child 01 MCR

• Normal birth history
• Negative family history
• Passed OAE birth hearing screen
• Delayed speech-language
• Referred at 17 mo to Mayo Clinic
• Normal OAEs
• Abnormal ABR with ++ CM
• CI24 in 1998 now 11 years post implant
Pre-operative transient otoacoustic emissions (Right ear) for ANSD 01

**Strong OAEs**

- Stimulus: +0.5 mPa (28 dB)
- Response Waveform
- Power Analysis Stim, Echo, Noise
- Noise level: 41.1 dB
- Rejection: 47.3 dB
- Equivalent Pa: 4.6 mPa
- Quiet eN: 123 = 38%
- Noisy XN: 195
- A&B mean: 16.0 dB
- A-B diff: 11.2 dB
- Response: 15.4 dB
- Wave repro: 72%
- Band repro/SNR dB: 0.8 1.6 2.4 3.2 4.0 kHz
- 00 75 95 94 92 %
- Snr: 5.13 13 11 dB
- Stimulus 83 dBpk
- Stability: 91%
- Test time: 1 min 17 sec
- Save directory
Intra-operative Cochlear Potentials ANSD C01
CM & SP for a 4000 Hz toneburst (2-10-2 msec)
at 80 dB nHL

Note the very large cochlear microphonics and summing potentials.

M7
SP
M4
Condensation
M8
R + C
Rarefaction
Base

6 µV/div
0 20 ms
Case ANC 01
Normal EABR

E20
CL 204
81/S
@ 60 mo

Pre-operative ABR

Lat 3.85(2)
Amp .22(2)
8-2006  8 year eval

Audiogram

CI24M Right
ANSD: C1 - 8 year test results
60 dBA SPL

- CNC words: 60% correct for words & 78% phonemes
- Sentences in quiet: 97% correct
- BKB-SIN 4 list average: 10.25 dB SNR for 50% correct
- She performs at the average speech recognition levels as our adults.
Summary Points

• Hearing loss is typically a loss of **sensitivity** in hearing levels as demonstrated on an audiogram.

• But hearing loss can also be a loss of the ability to make fine **temporal** and **frequency** discriminations.

• These factors will reduce the ability of children to “understand” spoken language.
Thank you!