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Diagnosis and Management of Auditory Neuropathy in Children

Sound for a Young Generation Conference

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Outline



- Overview and Definitions
- Variations in Presentation
- Protocol for Diagnosis and Management
- Counseling Families

Auditory Neuropathy: A Definition

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

Audiologic Findings

- Normal outer hair cell function as measured by present otoacoustic emissions (OAEs) or the presence of a cochlear microphonic (CM).
 - OAEs may be present initially but disappear over time, or be absent at time of diagnosis
(Starr et al, 1996)
- Abnormal auditory nerve response as observed by absent or markedly abnormal ABR
- Acoustic reflexes are absent in most cases
(Berlin et al 2005, 2010)

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
- **Not all individuals diagnosed with ANSD experience the same problems or to the same degree**

Prevalence

- Disorder initially thought to be rare
- Many published reports since late 90' s describing patients with similar audiologic test findings (absent ABR with present CM and/or OAEs)
- Estimates range from 7-10% of children diagnosed with permanent hearing loss

(Rance 2005)

Possible Etiologies and Associations

➤ Genetic Etiologies:

» Syndromic:

- Charcot-Marie-Tooth disease; Friedrich's Ataxia; Hereditary motor and sensory neuropathy (HSMN)

» Non-syndromic:

- Recessive genetic mutations: Otoferlin (OTOF), Pejvakin (PJKV)
- Autosomal dominant mutations: AUNA1 (onset of auditory symptoms in late teens)

➤ Perinatal Conditions:

- » Hyperbilirubinemia
- » Hypoxia
- » Low birth weight
- » More common in premature infants

Rance (2005); Rapin & Gravel (2003); Starr et al. (2003); Hayes 2011

Possible Etiologies and Associations

- **Congenital Conditions:**
 - » Cochlear Nerve Deficiency
- **Infectious Processes**
 - Viral Infections (e.g. mumps, meningitis)
- **Head injury**
 - » e.g. Shaken baby syndrome

Rance (2005);Rapin & Gravel (2003);Starr et al. (2003); Hayes 2011

*Guidelines Development Conference:
Identification of Infants and Children with
Auditory Neuropathy*

Lake Como, Italy, June 19-21, 2008

Guidelines available at:

<http://www.thechildrenshospital.org/pdf/Guidelines%20for%20Auditory%20Neuropathy%20-%20BDCCH.pdf>

(Denver Children's Hospital Website)

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

**Guidelines Development Conference:
Identification of Infants and Children with Auditory Neuropathy
Lake Como, Italy, June 19-21, 2008**

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 (ANSD)



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DIAGNOSIS OF AUDITORY NEUROPATHY

Recommended Audiologic Test Battery

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

Auditory Steady State Response (ASSR)

- ASSR responses can be obtained to high signal levels (>80dBHL) with ANSD but responses are elevated even in children who later show normal behavioral audiograms
- Therefore, ASSR cannot be used to predict behavioral thresholds in ANSD

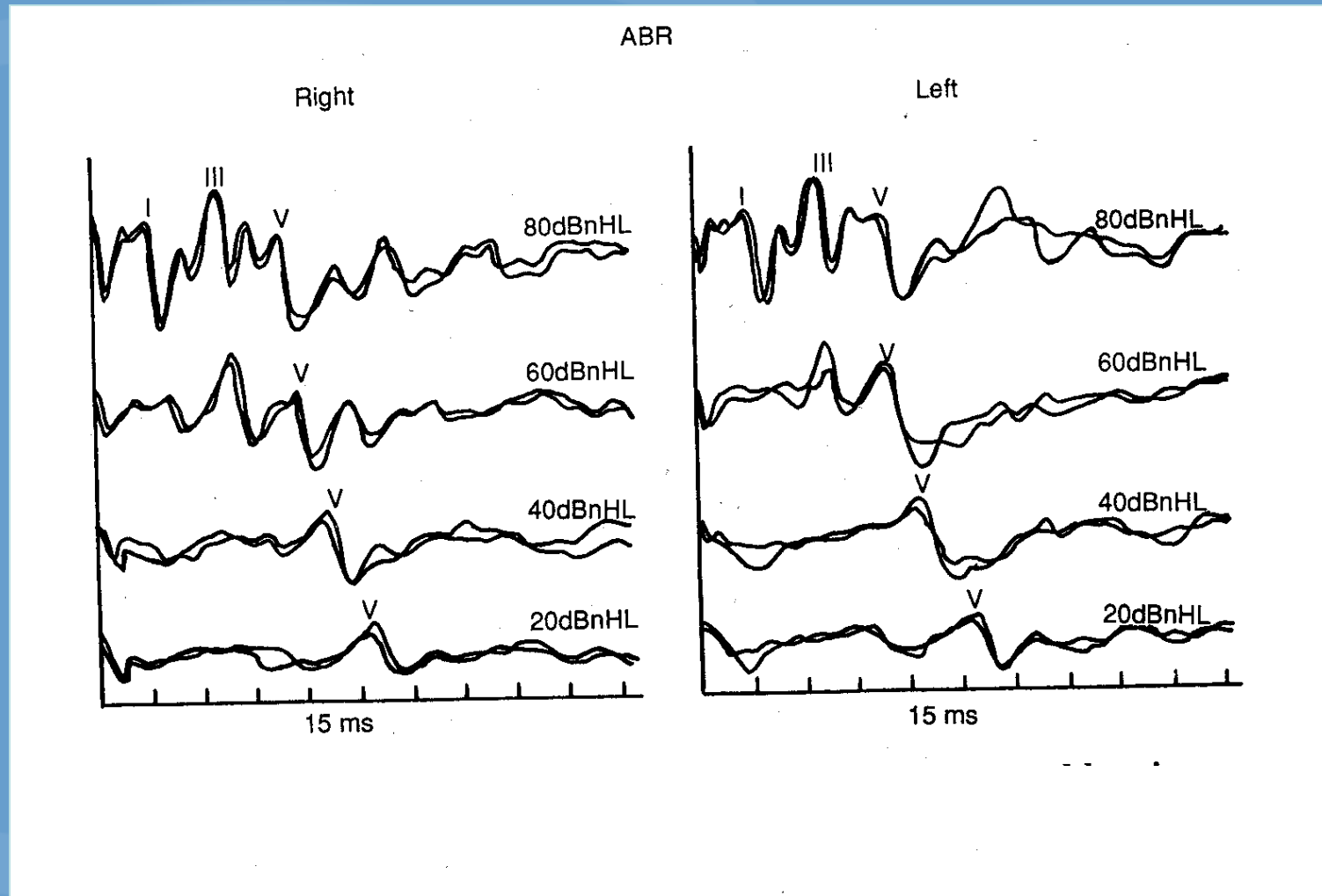
(Attias et al 2006, Rance et al 1998, Rance & Briggs, 2002)

Recommended Audiologic Test Battery

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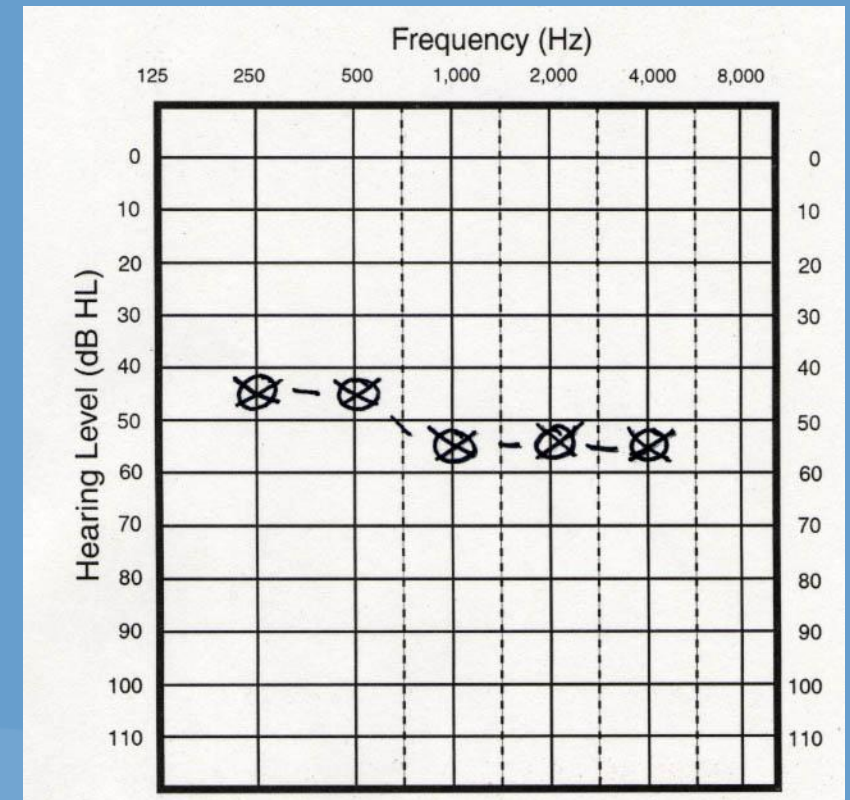
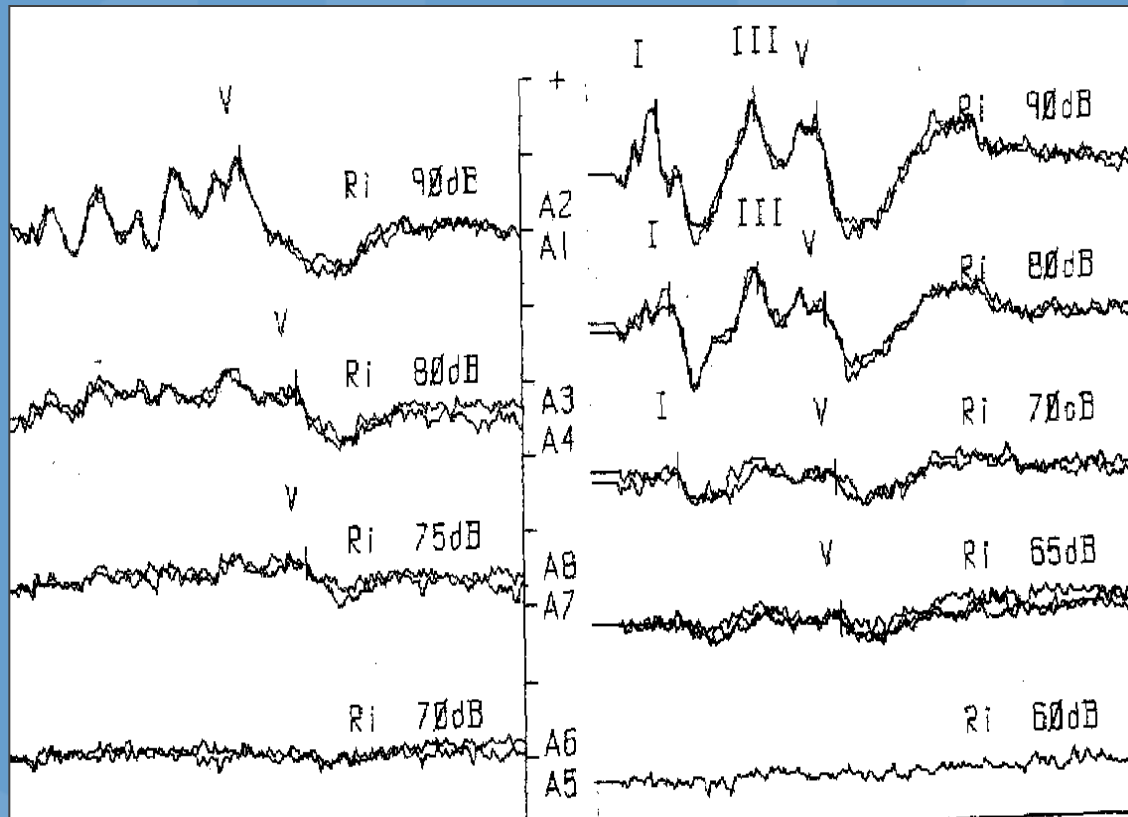


Normal ABR



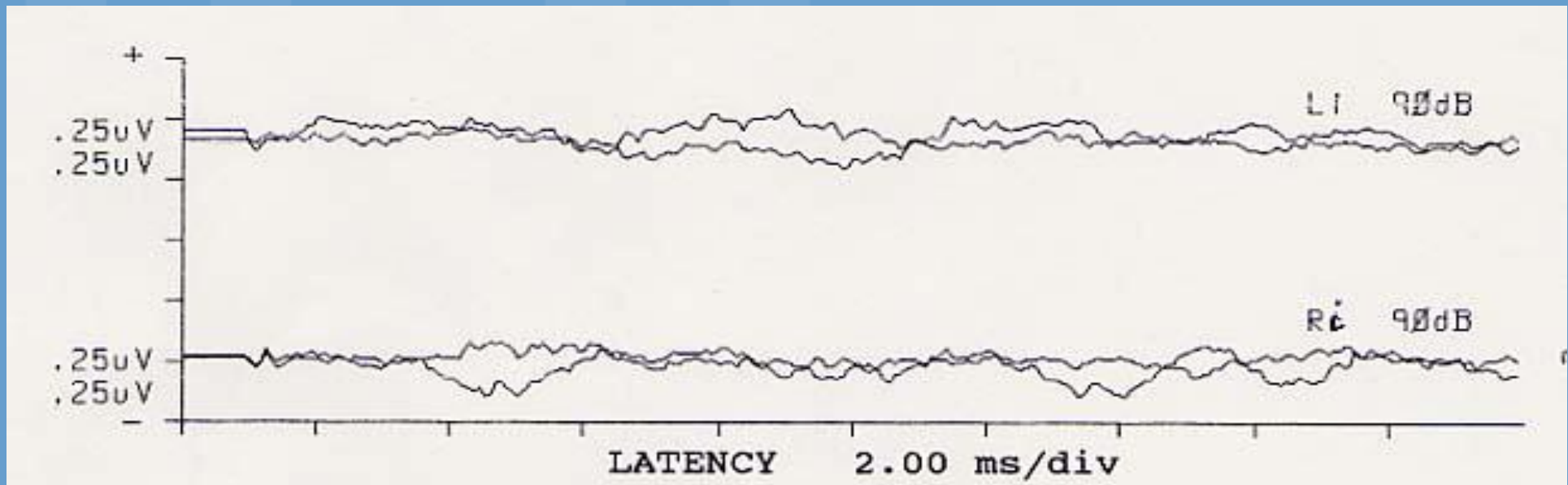


Estimating the Audiogram from Tone Burst ABR in Non-AN type hearing loss



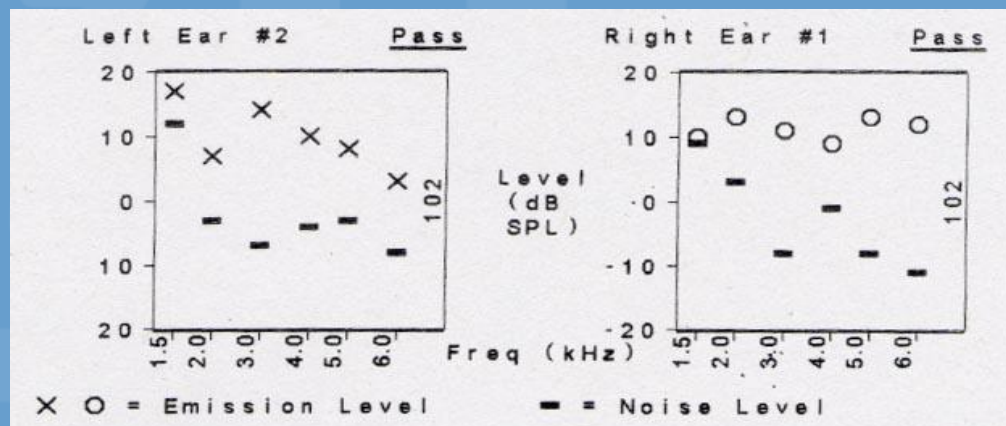
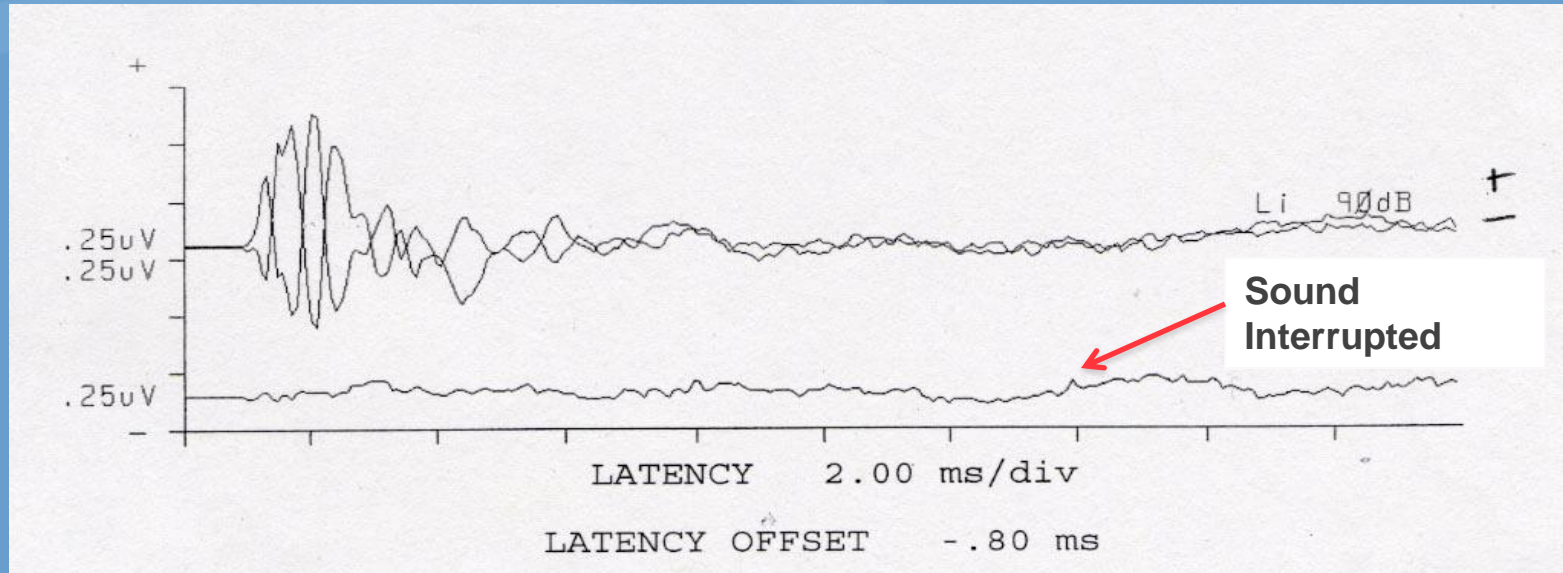


Absent ABR with No Cochlear Microphonic: Child with profound hearing loss



Typical Pattern of ANSD

Abnormal ABR with Present CM



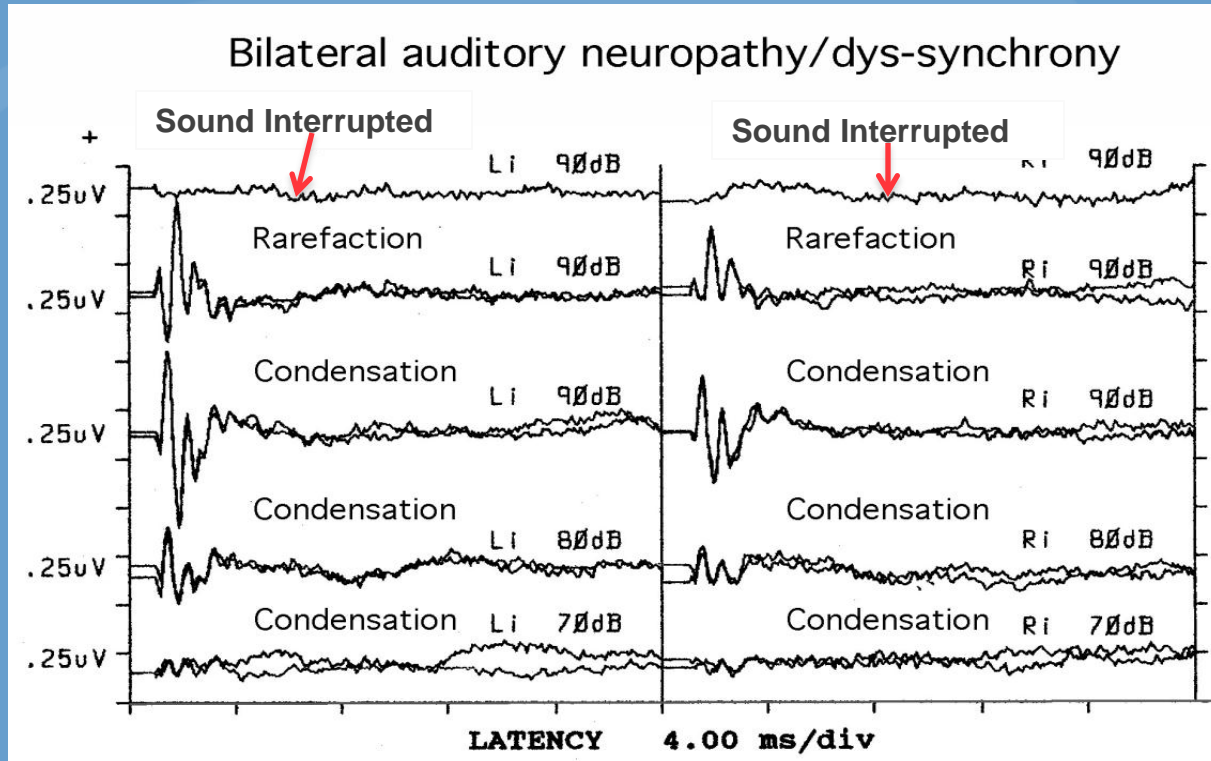
What is a Cochlear Microphonic (CM)?

- Pre-neural response (occurs before Wave I in the ABR)
- Unlike the ABR, the CM shows a direct phase relationship to the acoustic wave form. When the polarity of the stimulus is changed there is a reversal of CM waveform
- Considered to have limited clinical use in past; renewed interest in diagnosis of ANSD
- CM can be recorded in normal ears, ears with “typical SNHL” and ears with ANSD
- Significance in ANSD is when CM is present when neural response is absent or markedly abnormal

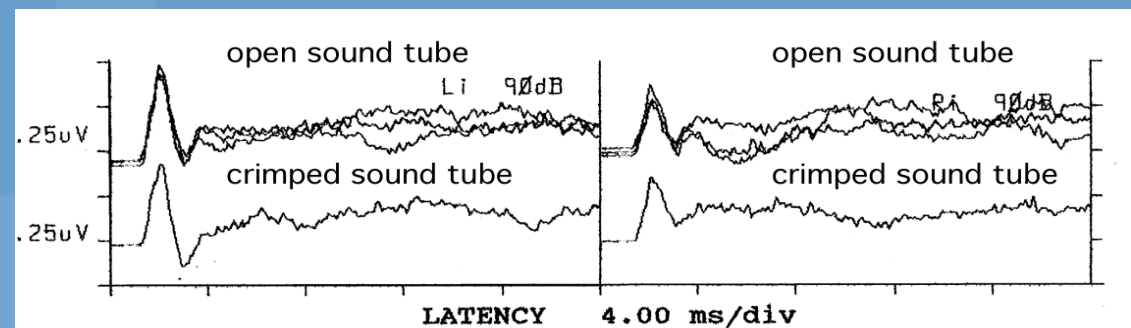
ABR Protocol for Evaluating CM

- Must have adequate recording conditions
 - Infant ready to sleep (natural or sedated sleep)
 - Avoid electrodes positioned over transducer
- *Single polarity* clicks at 90dBnHL with rarefaction and condensation polarities
- Must use insert earphones
 - Excessive stimulus artifact with standard headphones obscures cochlear microphonic
- Sound interrupted run with stimulus on but sound tube disconnected or clamped to check for stimulus artifact

CM vs stimulus artifact



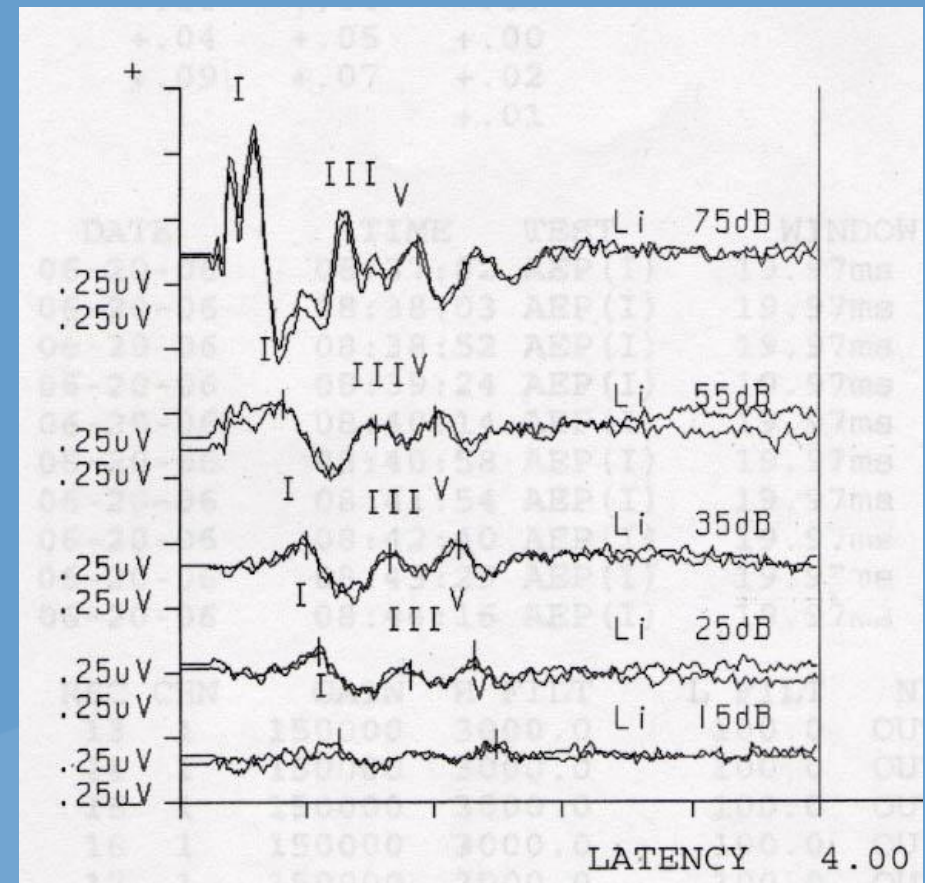
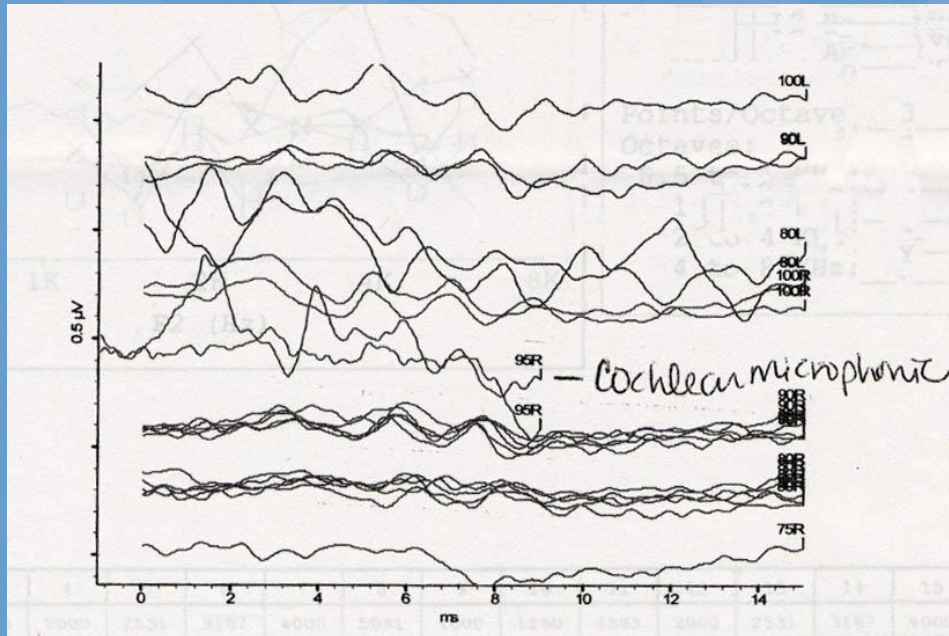
If response remains with sound tube disconnected from transducer, response obtained is stimulus artifact and not CM as in case below





Example of child with normal hearing incorrectly diagnosed with ANSD

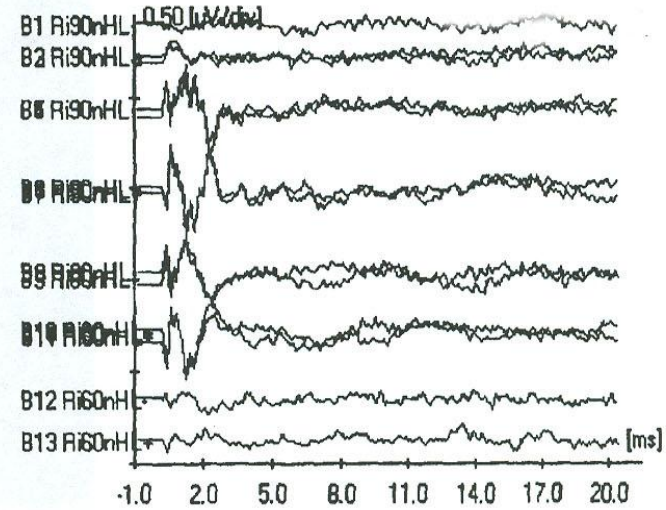
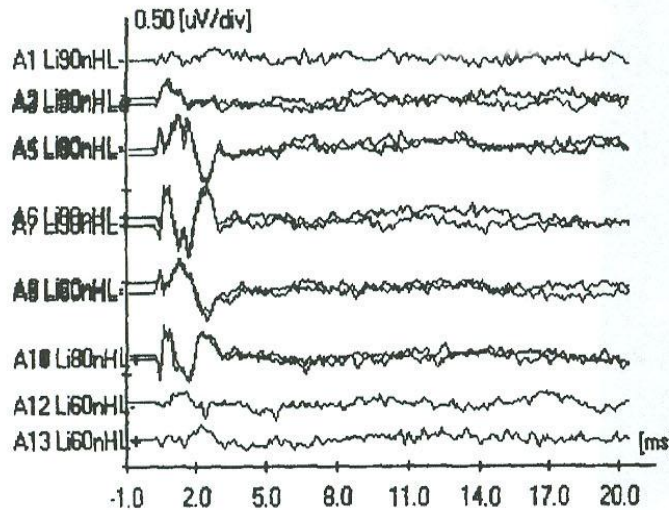
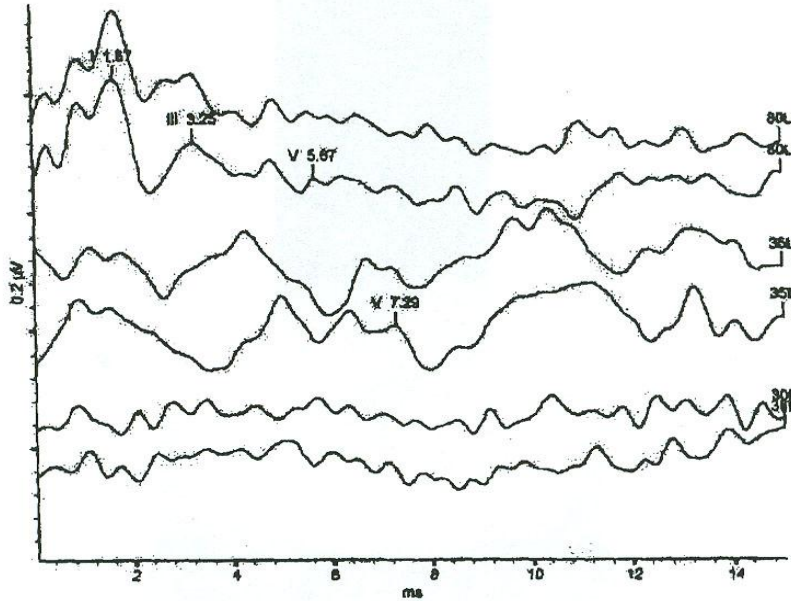
~Note poor quality of ABR on left compared to right





Example of child with ANSD
incorrectly diagnosed with
normal hearing

~Note incorrect identification
of waveforms on left



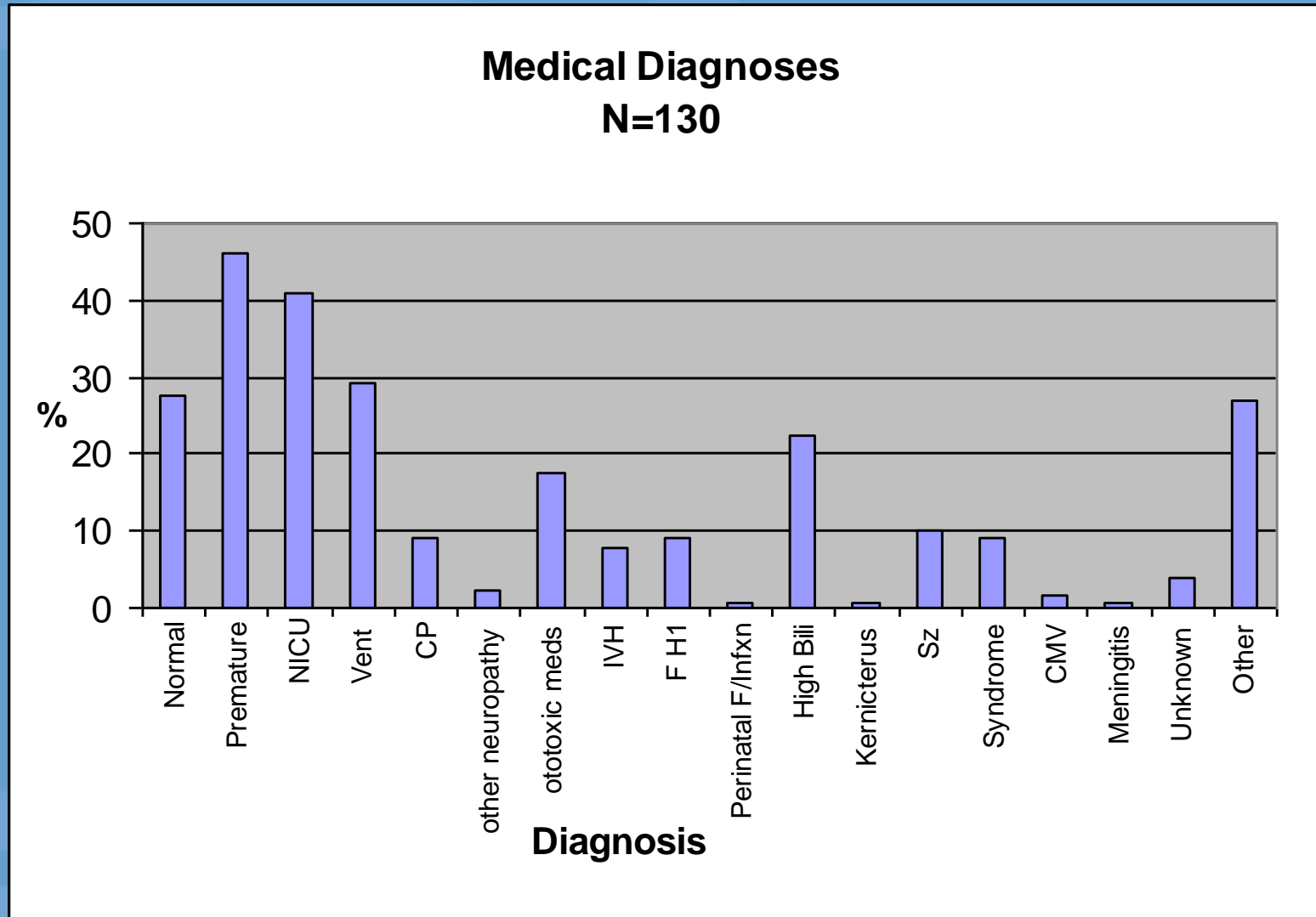
Otologic Examination

- Medical History
- Ear Exam
- Etiology
- Evaluate for other associated problems
 - » Seizures
 - » Motor delays
 - » Visual problems
 - » Ear canal problems
 - » Otitis media
- Radiologic Studies (MRI/CT)
 - » Inner ear malformations
 - » Cochlear nerve integrity
- Other studies as needed



Medical Diagnosis in 130 Children with ANSD at University of North Carolina

72% have positive history of other medical diagnoses

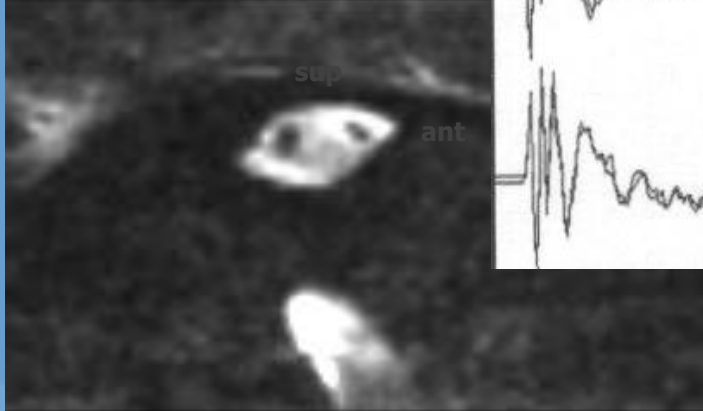
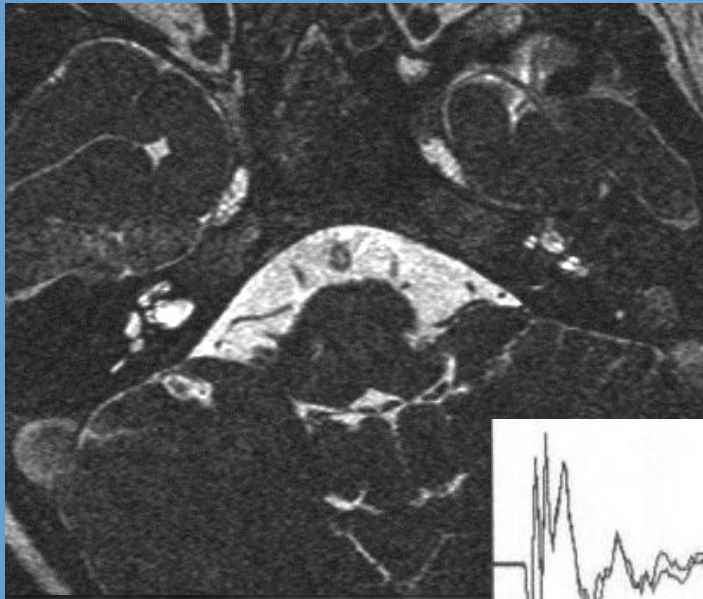


Cochlear Nerve Deficiency (CND) (May present with ANSD pattern)

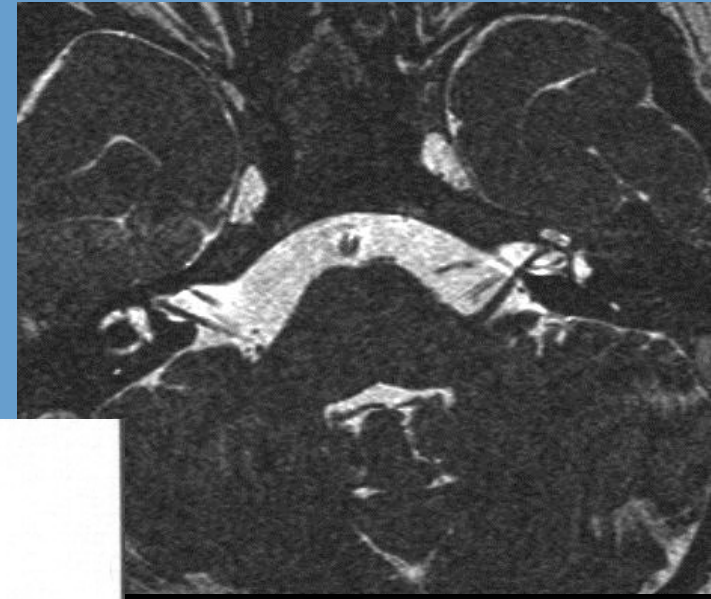
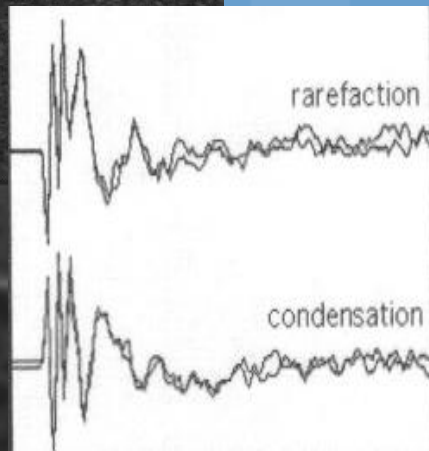
- Small or absent VIII nerve
- Must perform MRI to determine if VIII nerve is small or absent
- CT may show normal internal auditory canal when cochlear nerve is absent
- In cases when there is question of CND both CT and MRI imaging may be needed
- Imaging is especially important when behavioral audiometry shows profound hearing loss

Child with bilateral deafness

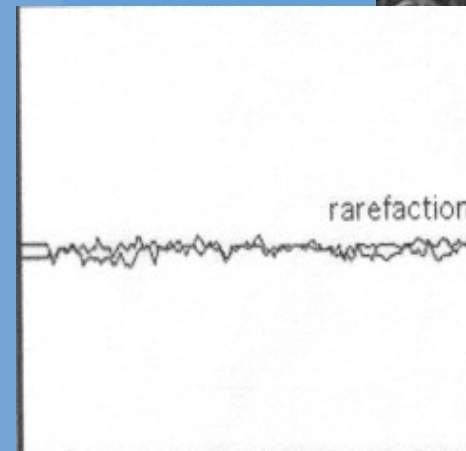
No VIIIth nerve on right



Right Ear



Left Ear



UNC Children with Characteristics of ANSD and Available MRI (2009)

N=140

- 35/140 (25%) Cochlear Nerve Deficiency (CND)
(absent or small cochlear nerve) in one or both ears
 - » Unilateral (n=24; 69%)
 - » Bilateral (n=11; 31%)

Buchman, C, Roush P, Teagle H, Brown C, Zdanski C, Grose J.
Auditory neuropathy characteristics in children with cochlear
nerve deficiency. *Ear Hear.* 2006 Aug;27(4):399-408

Recommended Audiologic Test Battery

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ANSD Protocol for Infants: Behavioral Audiometry

- Behavioral assessment with VRA beginning at 6-7 months (developmental age) with goal of obtaining individual ear measures and bone conduction thresholds by 8-9 months of age
 - » May be difficult (or impossible) with children who have additional developmental or medical challenges
 - » Behavioral Observation may be needed



VRA Six Month Old



Hearing Aid Fitting in Infants with ANSD

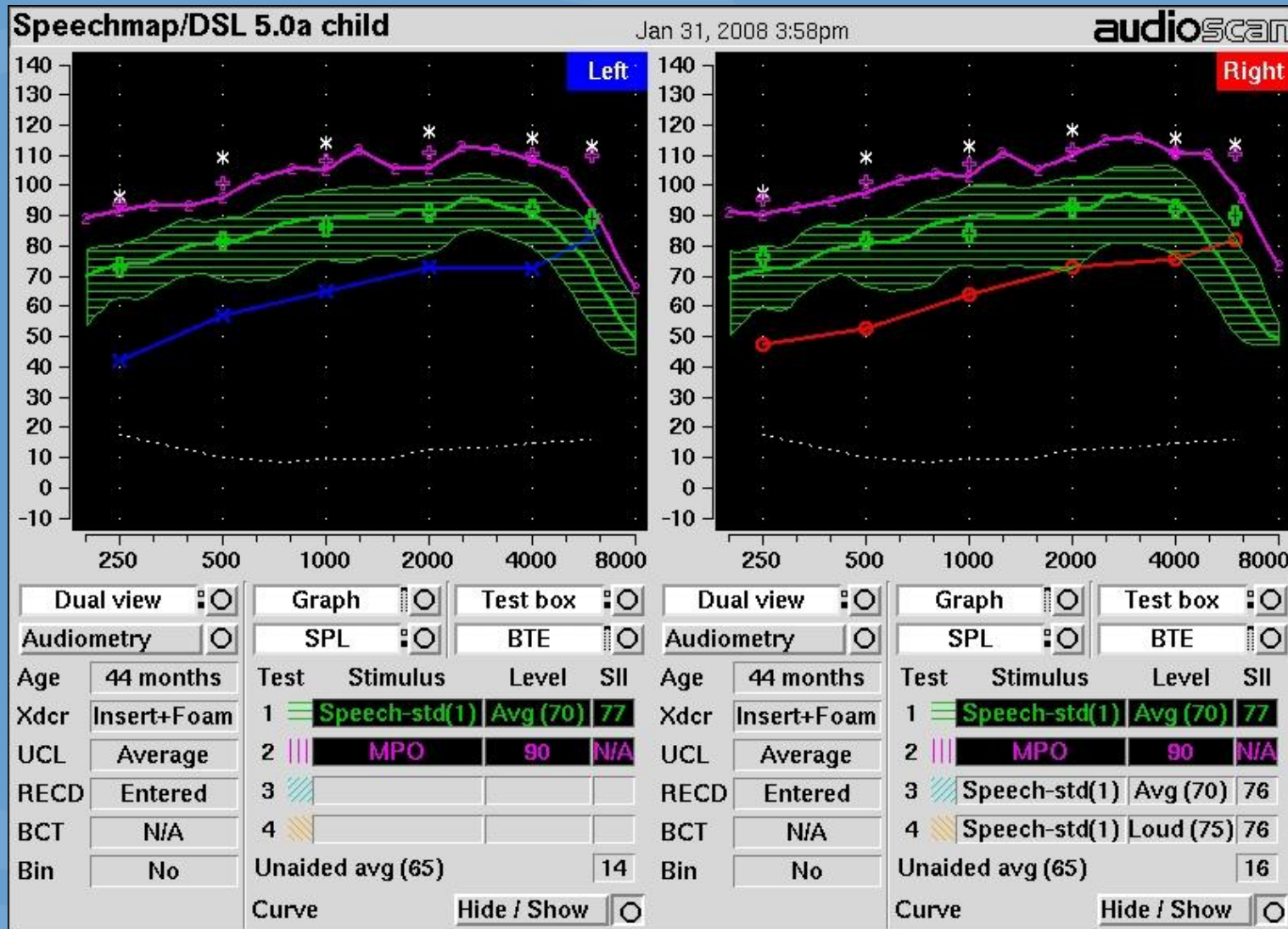
- Behavioral thresholds cannot be predicted from ABR or ASSR
- Determination of hearing thresholds is delayed until infant developmentally able to perform task (6-9 months of age for most typically developing infants)
- Many children with ANSD are at risk for cognitive impairments resulting in a lengthier and more complicated process of threshold determination
- This results in delays in hearing aid fitting and greater amount of time without adequate audibility of speech signal

ANSD Guidelines (Como 2008): 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
- Hearing aid fitting strategies...should follow established guidelines for the fitting of amplification in infants and toddlers
 - » e.g. American Academy of Audiology Pediatric Amplification Protocol, 2003
- Since improvement in auditory function has been reported in some cases, careful monitoring needed to adjust and modify amplification as needed.



Verifying Audibility of Speech Spectrum



Evaluation of Speech Perception Following Hearing Aid Fitting or Cochlear Implantation

- Parent Questionnaires (e.g. PEACH, IT-MAIS or MAIS) (Zimmerman-Phillips, et al., 2000; Robbins, et al.,1991)
- 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)
- HINT sentences in quiet and noise conditions

Early Speech Perception Test (ESP)





Factors that may affect outcomes

For all children benefit from a particular technology will depend on several factors including:

- » Age at diagnosis and treatment
- » Appropriateness of device fitting
- » Consistency of use
- » Quality of intervention
- » Extent of family involvement
- » Cognitive abilities of child
- » Presence of other medical conditions



ANSD Guidelines (Como 2008): Special Considerations for Cochlear Implantation

- Evidence of auditory nerve sufficiency should be obtained prior to surgery using appropriate imaging technology (Buchman et al., 2006)
- 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*.
- Families should be informed that spontaneous improvement in has been reported. CI should not be considered until test results are stable and demonstrate unequivocal evidence of permanent ANSD...

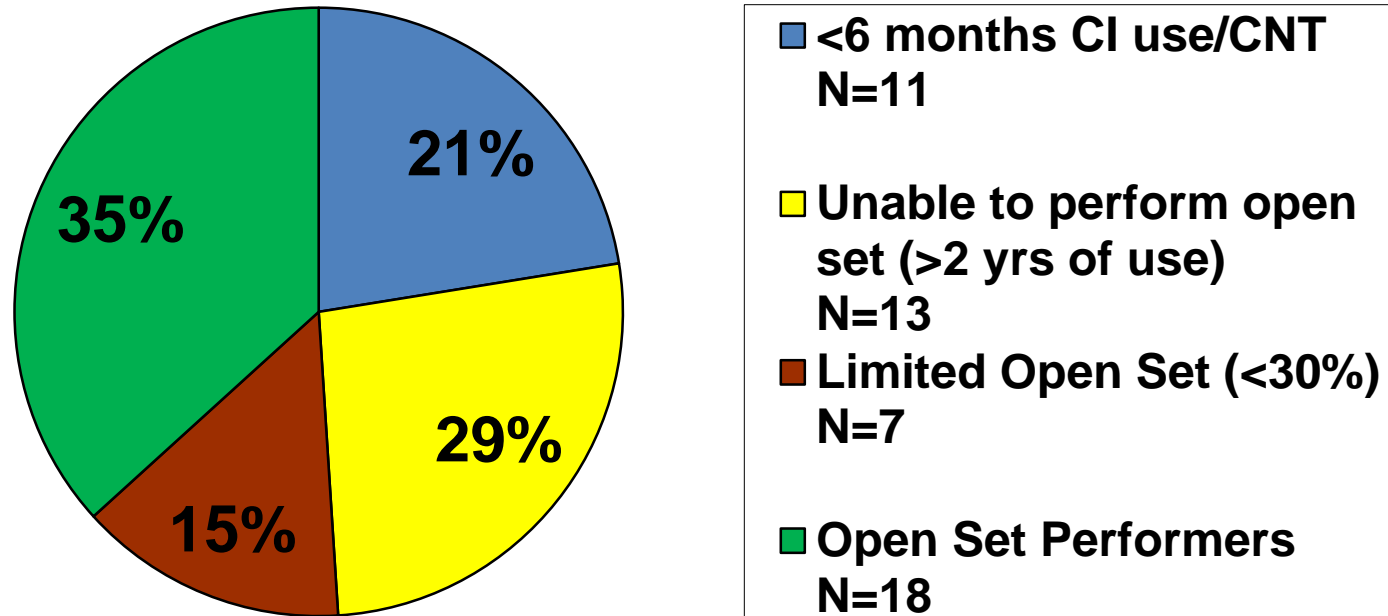


CI Criteria-Children

- **Advanced Bionics**
 - Children-age 4 or less:
 - **Failure to reach auditory milestones or <20% on MLNT at 70 dB SPL**
 - Children > 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

UNC ANSD Children with CI N=52

CI in AN EAR

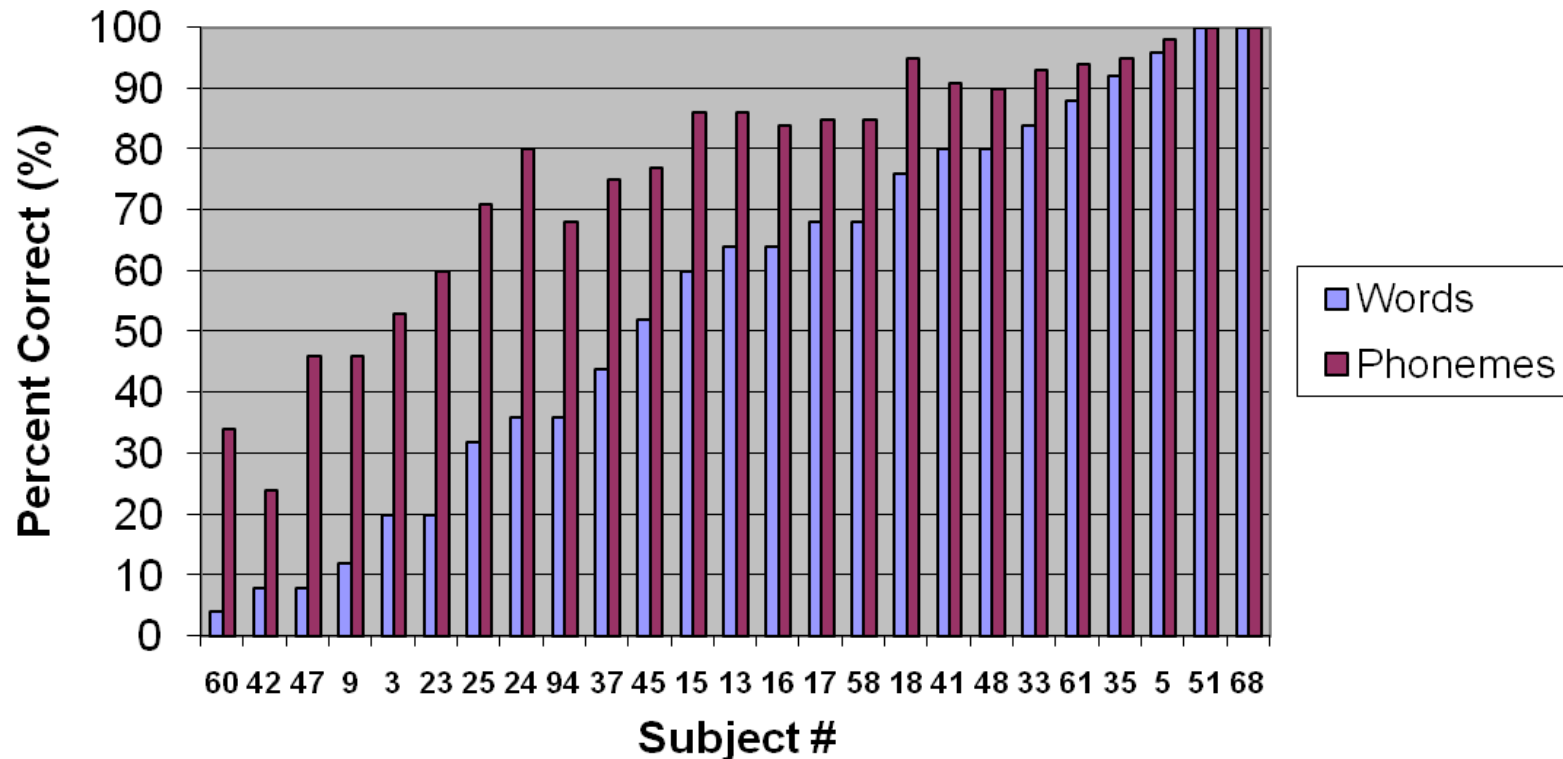


UNC ANSD Children with CI



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OPEN SET PERFORMANCE N = 25

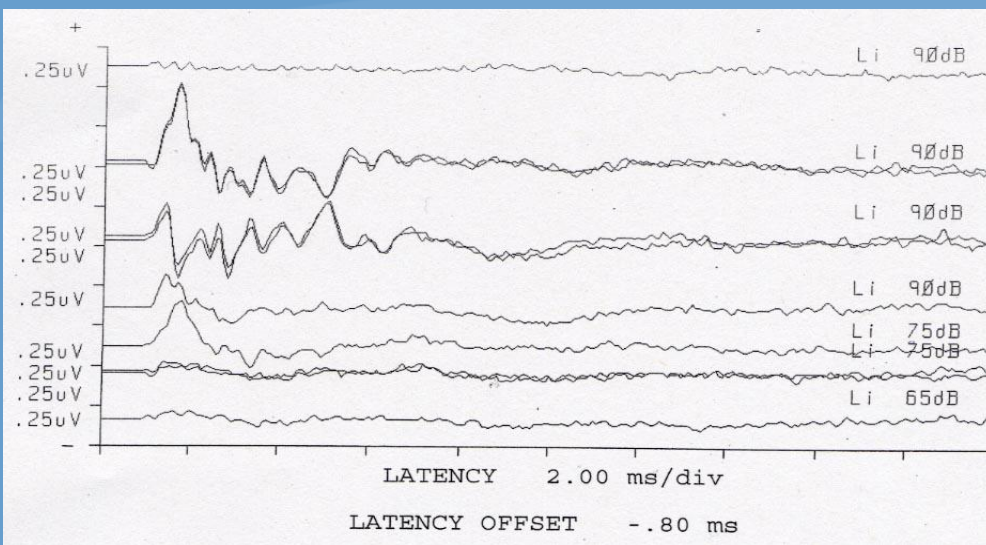




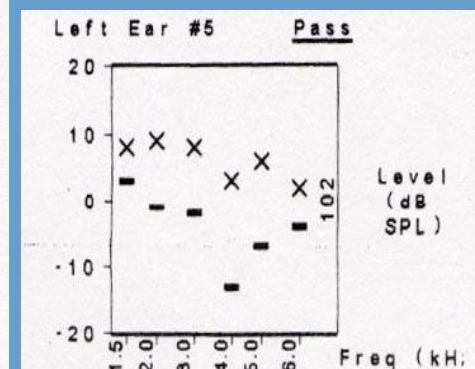
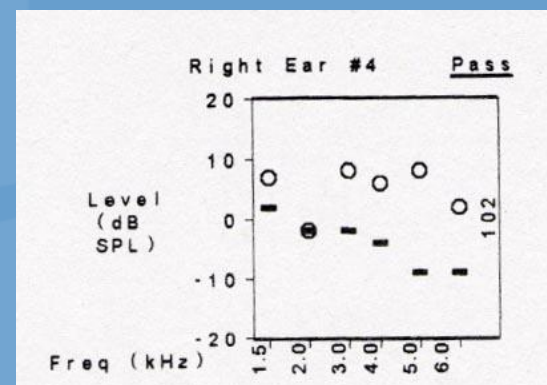
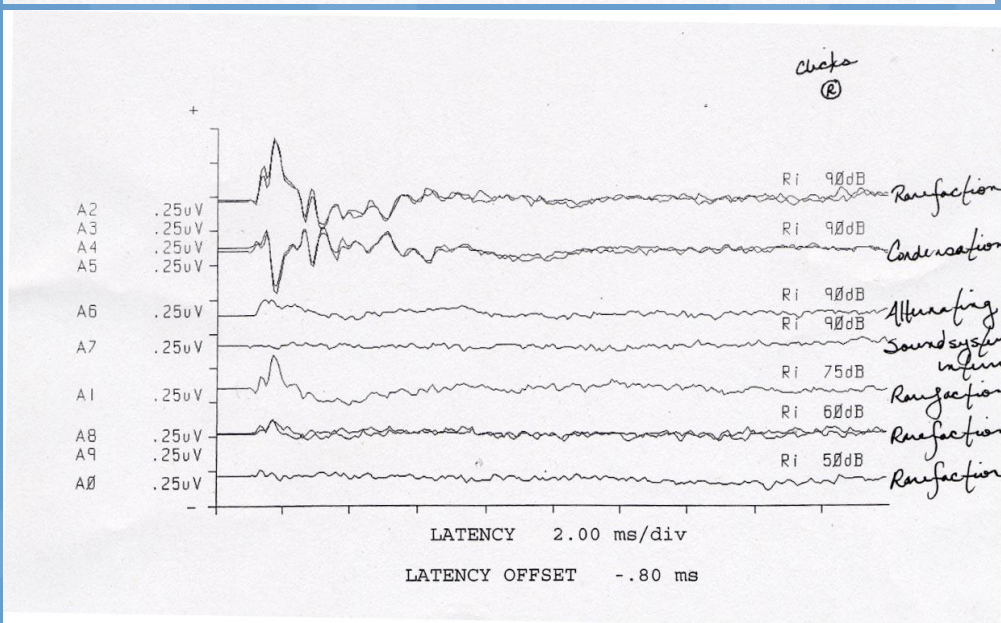
Variable Presentations of ANSD

Case Examples

Case #1: Present CM and OAEs



- 24 wk preemie, 940 grams
- NICU 4 months, ventilated
- ABR at 4 and 5 months of age abnormal
- ABR repeated at 18 months-no change

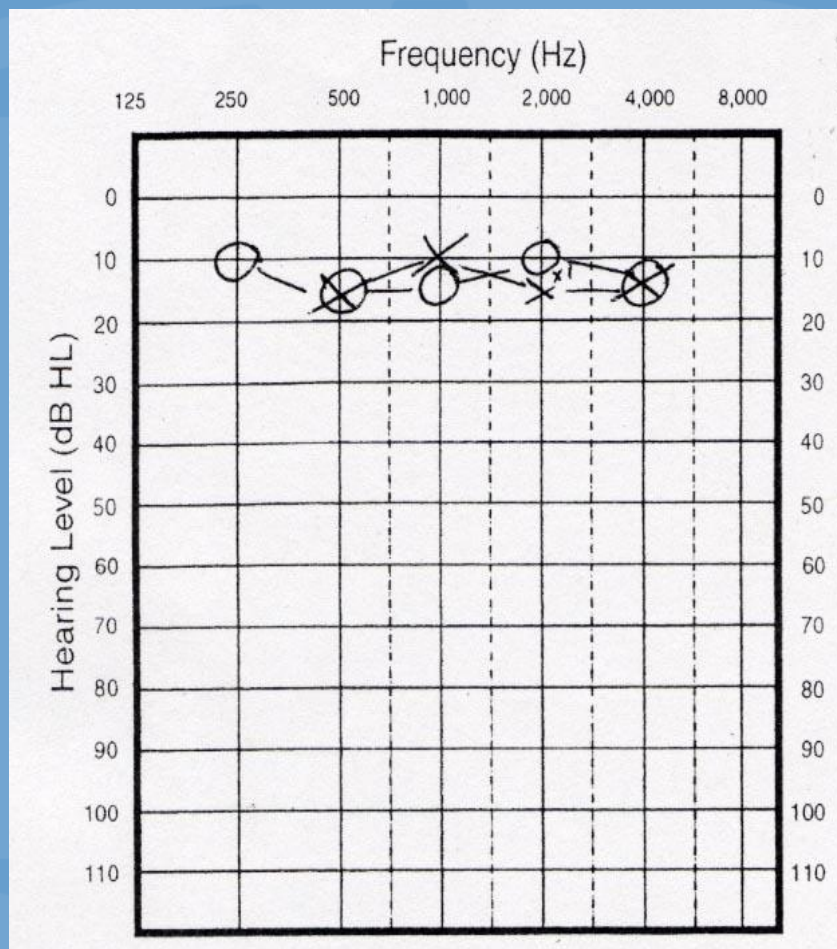


Case #1

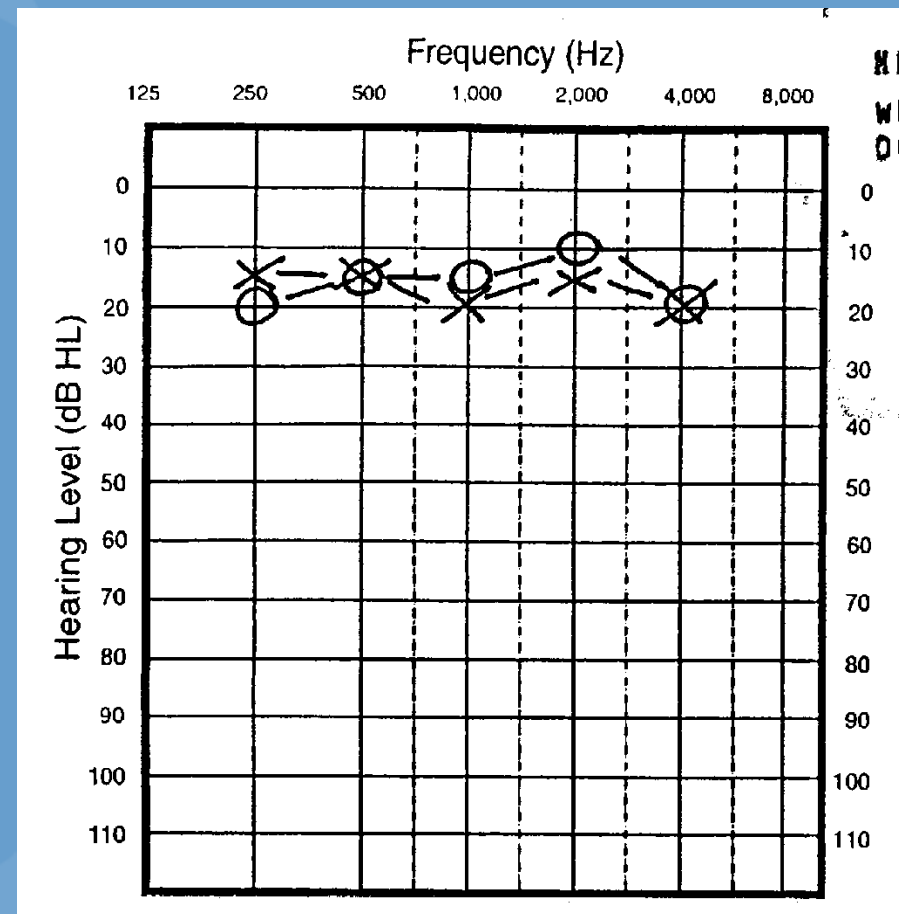
Normal thresholds, Present CM and OAEs



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Audiogram at 14 months



Audiogram at 18 months

Case #1

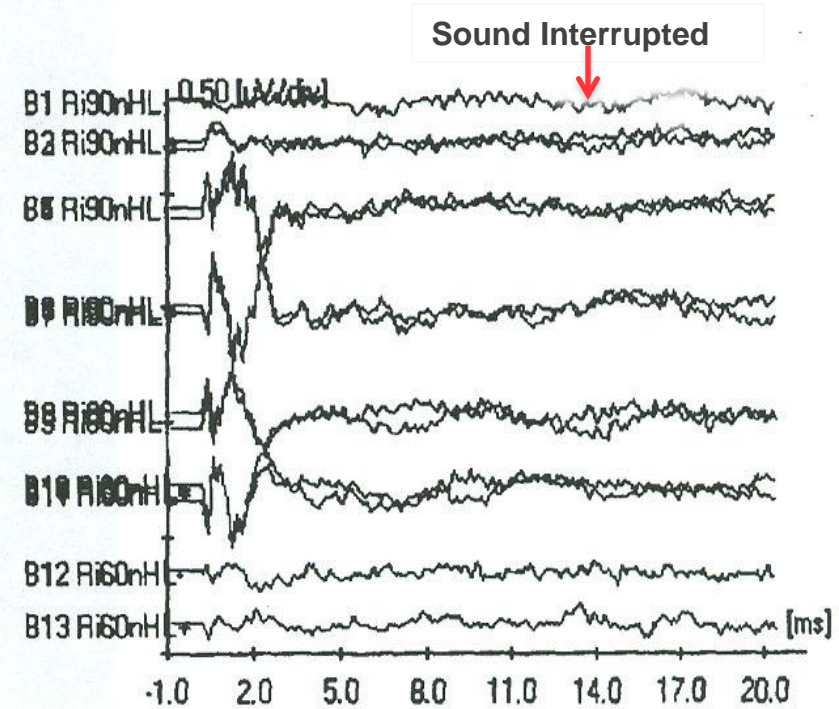
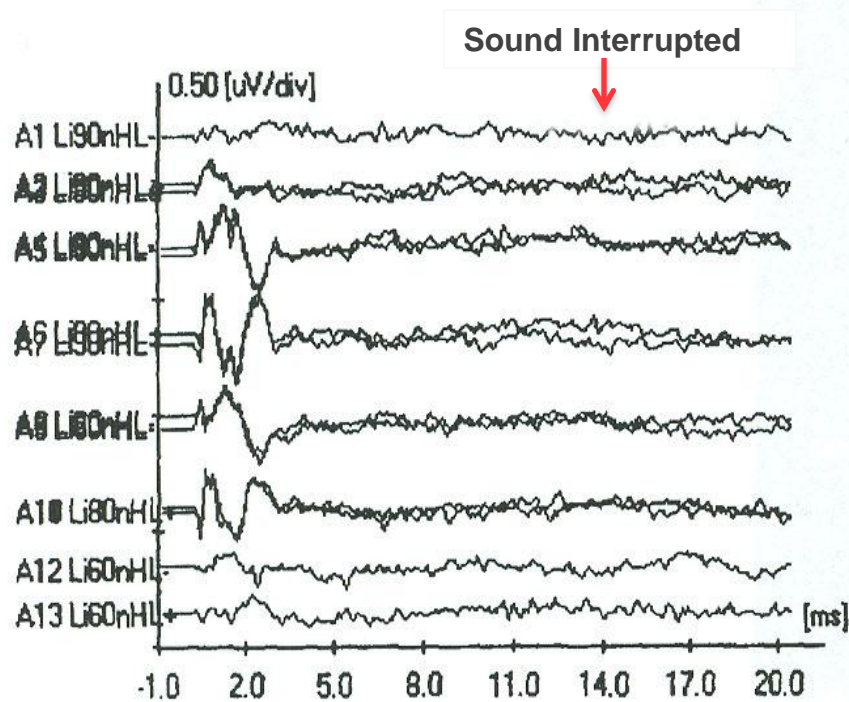
Speech Perception Test Results

- Age 2 yrs-11 months:
 - ESP monosyllabic word test (closed set test of speech perception):
 - 12/12 correct for each ear at 50dBHL
- Age 5 years:
 - PBK words: 80% and 84% at 60dBHL for right and left ears



Case #2

Abnormal ABR with Present CM

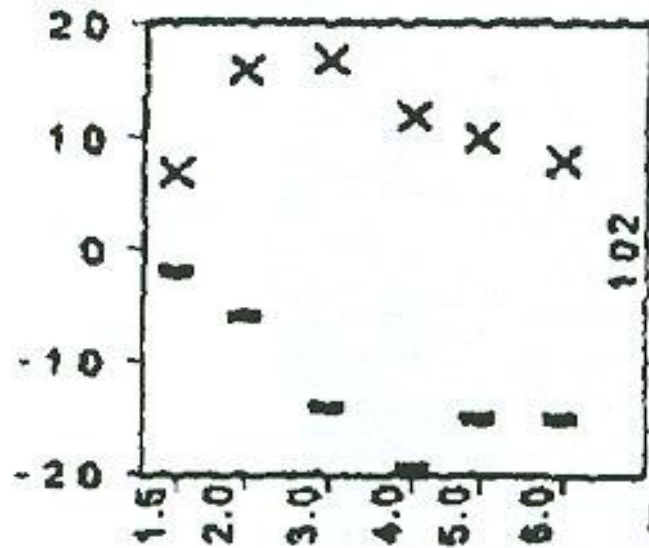




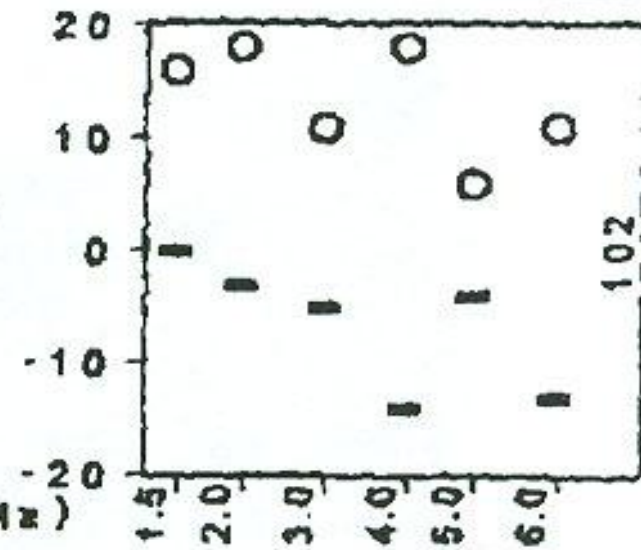
Case #2

Present OAEs

Left Ear #2 Pass

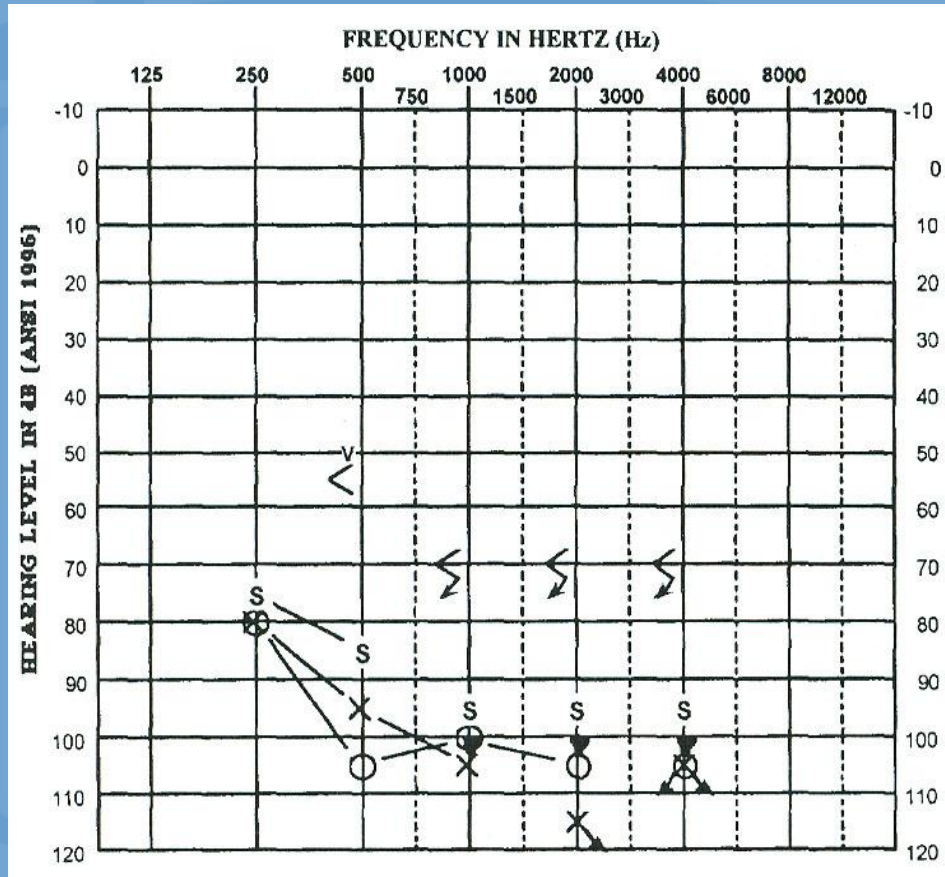


Right Ear #1 Pass



Case #2

Child with Profound Bilateral HL
Present CM and OAEs



Ear exam: *Normal*

EKG: *Normal*

MRI: *Normal*

Connexin test: *Negative*

Otoferlin test: **POSITIVE**

Received CI at 24
months of age

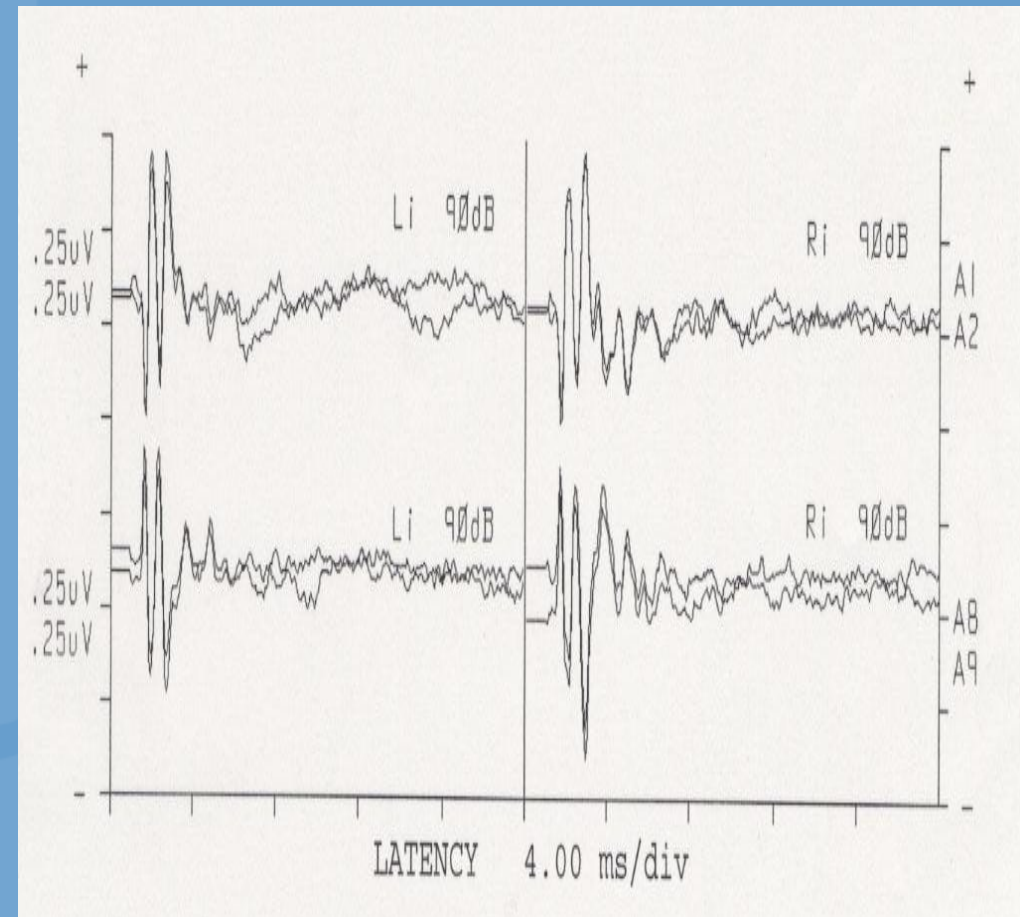
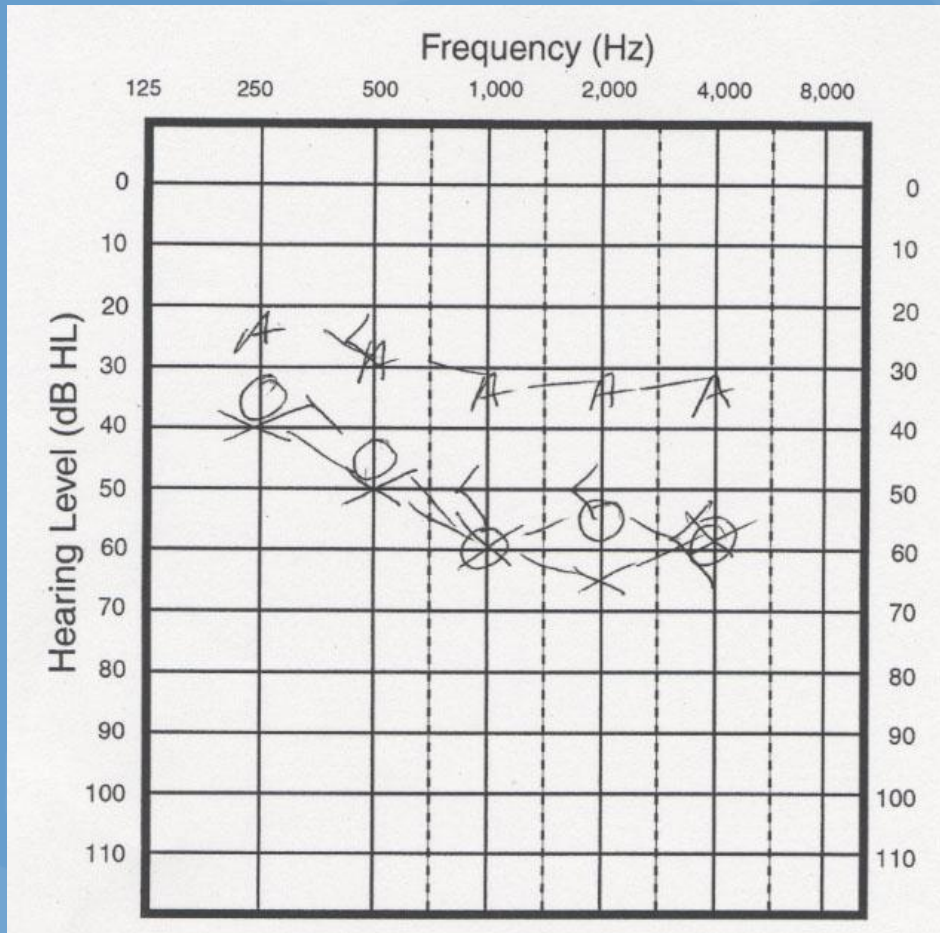
Case # 3 Background

- 25 weeks gestation
- Ventilated for 6 weeks
- Oxygen 3 ½ months
- Hyperbilirubinemia
 - » Treated with lights, exchange transfusion
- Treated with antibiotics and diuretics
- Hospitalized 4 ½ months
- No family history of hearing loss
- Did not pass newborn hearing screen at hospital discharge
- Initially diagnosed with profound bilateral SNHL at an outside clinic and fitted with high gain hearing aids



Case #3

Child with “moderate loss” CM present, absent OAEs



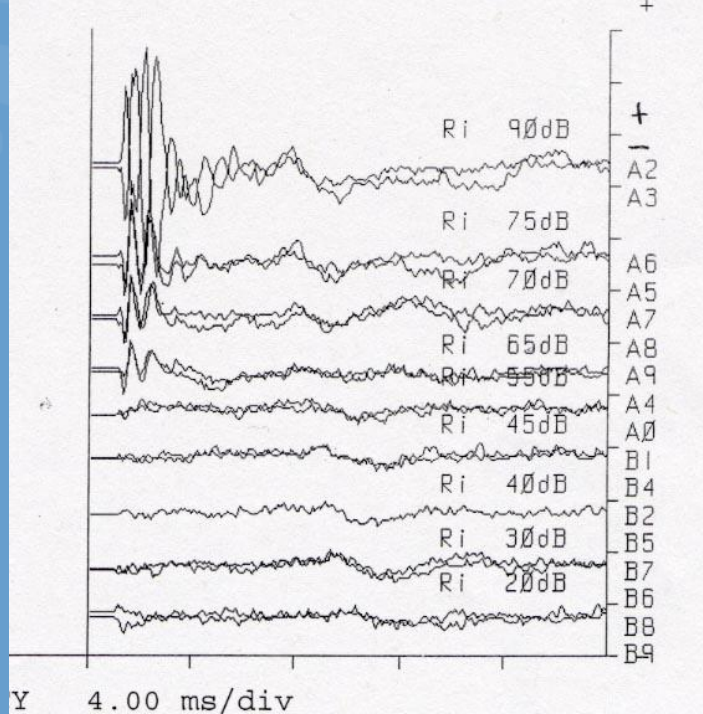
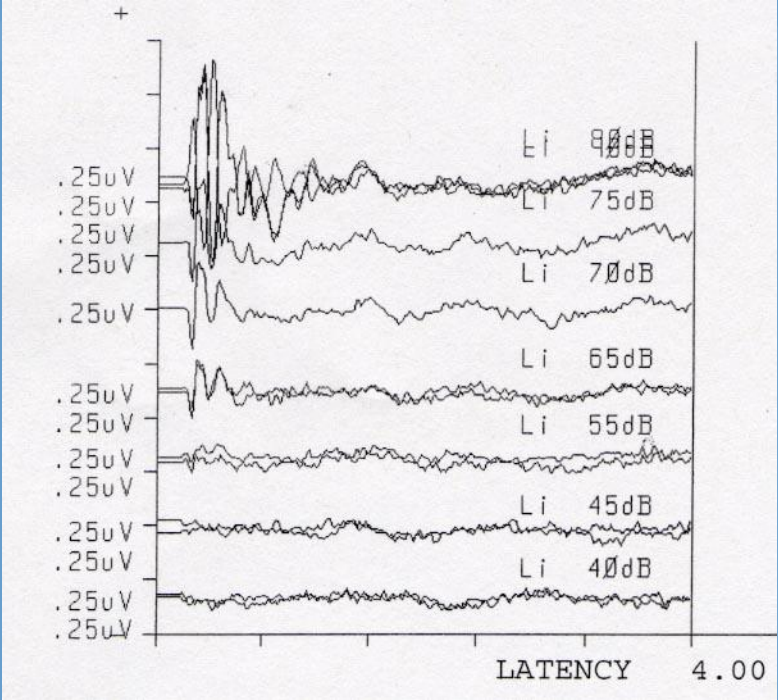
Case #3

Age 8 years

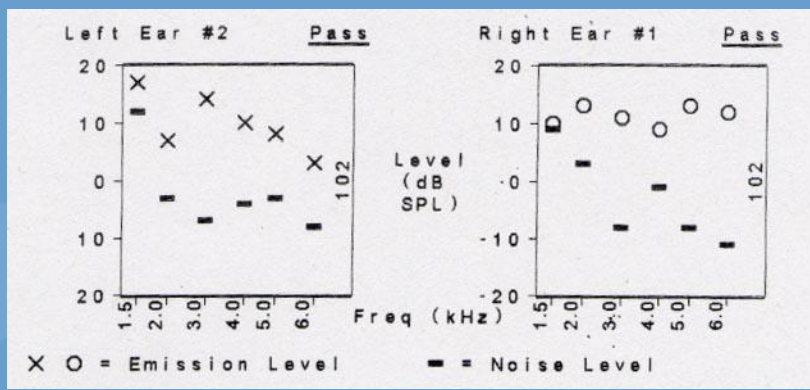
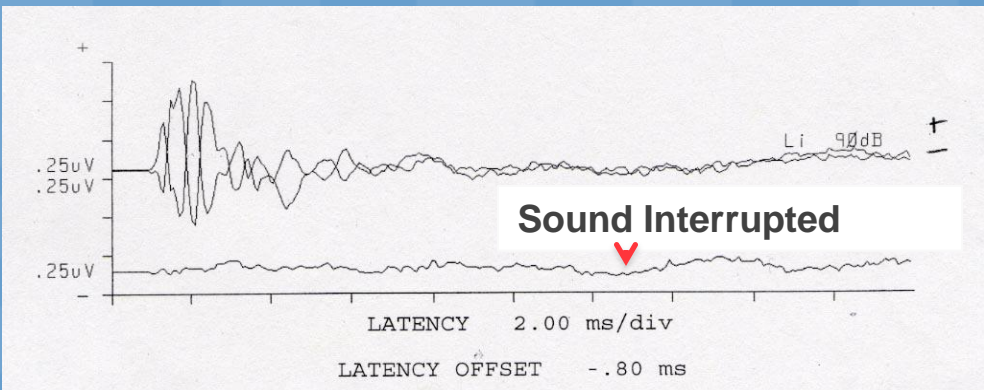


- Re-fitted with appropriate hearing aids at 9 months of age
- Now mainstreamed in 2nd grade
 - » Using personal FM in classroom
- Receiving services from auditory verbal therapist and speech and language pathologist
- Aided monosyllabic word score 88% at 57dBHL.
- Functioning in average range in receptive and expressive language development
- Working on articulation errors

Case #4: Large CM; Present OAEs; Distal Waveforms Present



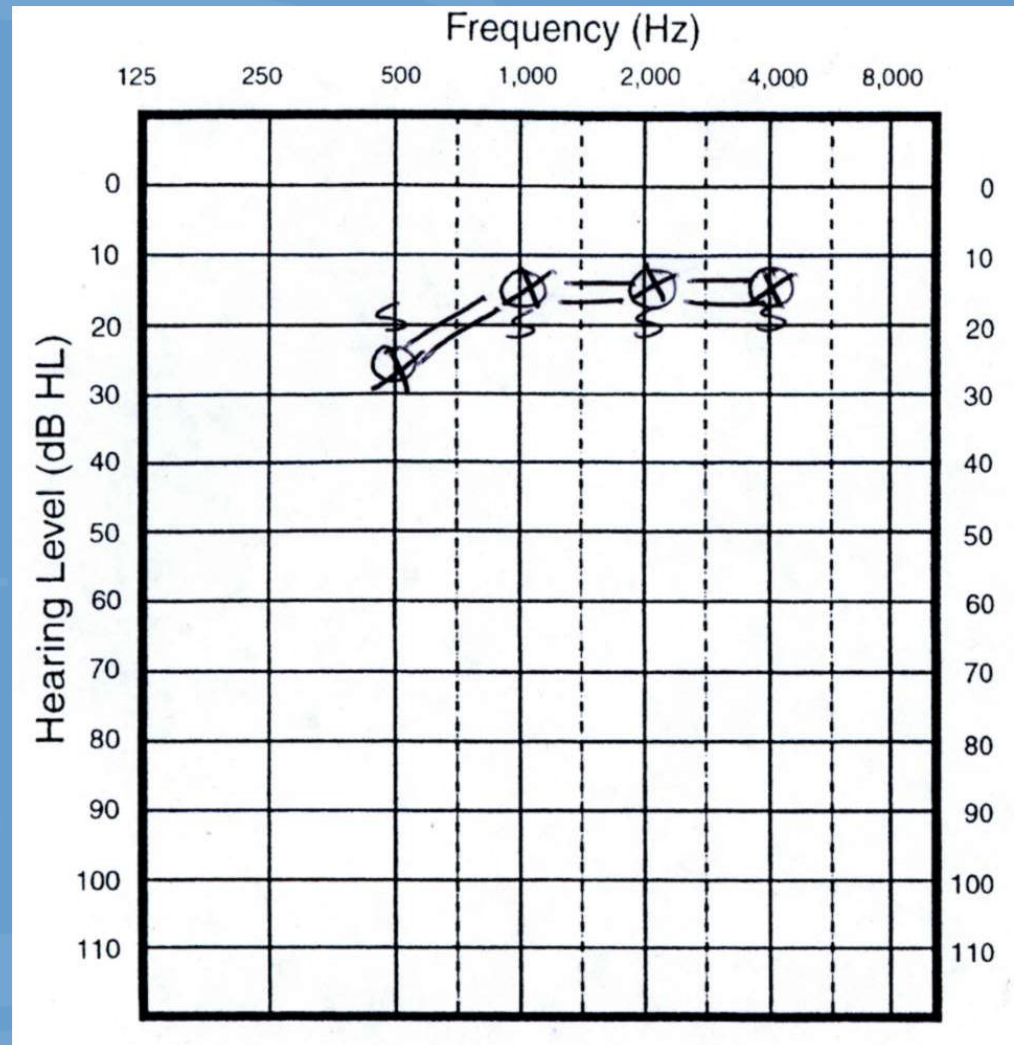
Caution needed when interpreting ABRs that show abnormal waveform morphology at high intensity levels



Case #4 (continued)

VRA with insert earphones

Age 14 months



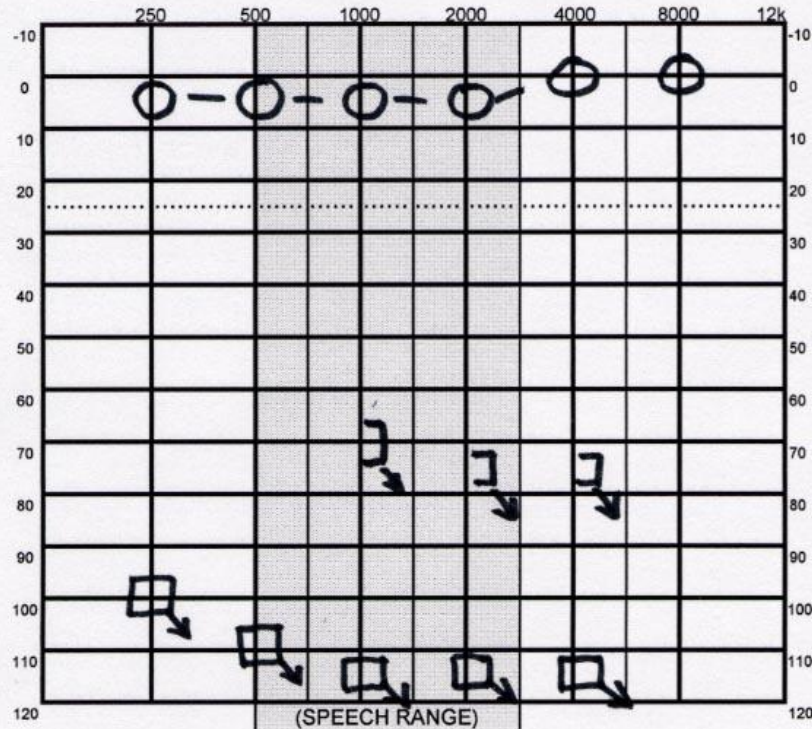
Case #5

- Child born at full term
- No family history of hearing loss
- Presented to clinic with left profound unilateral hearing loss at 4 years of age.
- Passed newborn hearing screen using OAEs

Case # 5



PURE TONE AUDIOMETRY (RE: ANSI 1969)



	RIGHT (RED)	LEFT (BLUE)
LEGEND		
AR	O	X
AR (OPP. EAR MASKED)	Δ	□
BOHE	<	>
BONE (OPP. EAR MASKED)	[]
NO RESPONSE	↓	↓
SOUND FIELD	S	
AIDED	R	L

TEST	
STANDARD	
PLAY	
COR/VRA	
BOA	

SITE	
BOOTH	
OTHER	

RELIABILITY	
EXCELLENT	
GOOD	
FAIR	
POOR	

TYMPANOMETRY

CONTRA (Phone Ear)	.5k Hz	1k Hz	2k Hz	4k Hz
RIGHT (AD)				
LEFT (AS)				

IPSI (Probe Ear)	.5k Hz	1k Hz	2k Hz	4k Hz
RIGHT (AD)	85	85	85	
LEFT (AS)	NR	NR	NR	

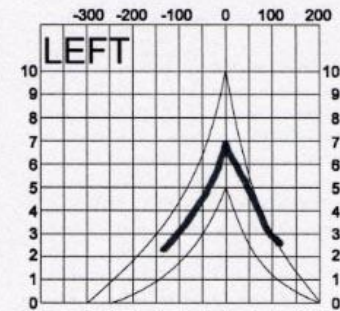
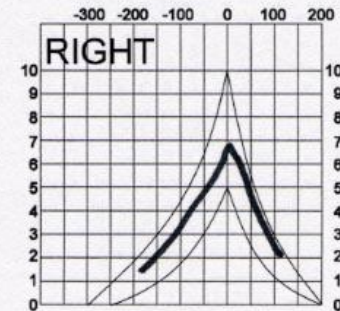
REFLEX DECAY @ 1k Hz STATIC COMPLIANCE

RIGHT (AD)		
LEFT (AS)		

MODE

STANDARD EARPHONES	
INSERT EARPHONES	
SOUND FIELD TESTING	
ASSISTED EVALUATION	

TYMPANOMETER: _____



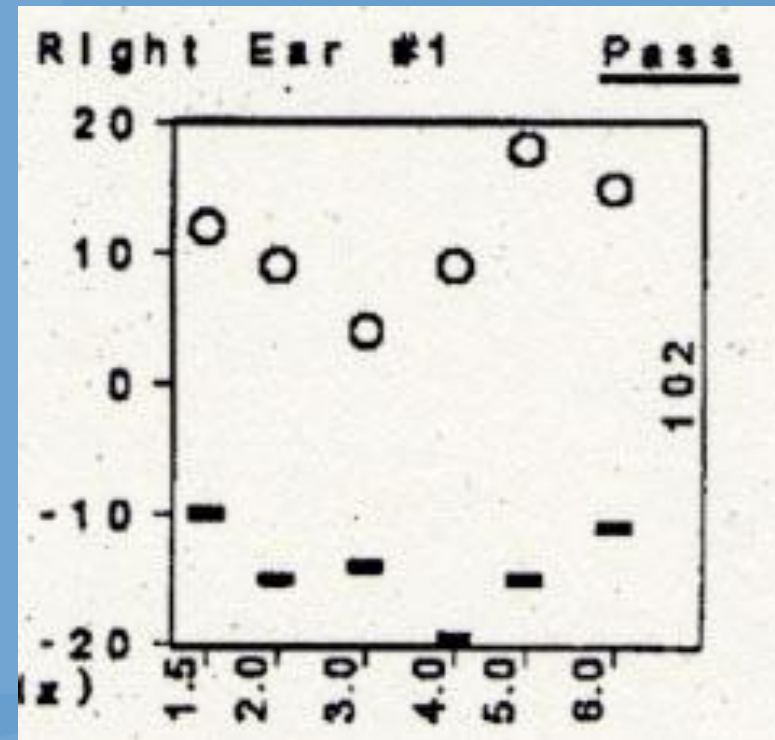
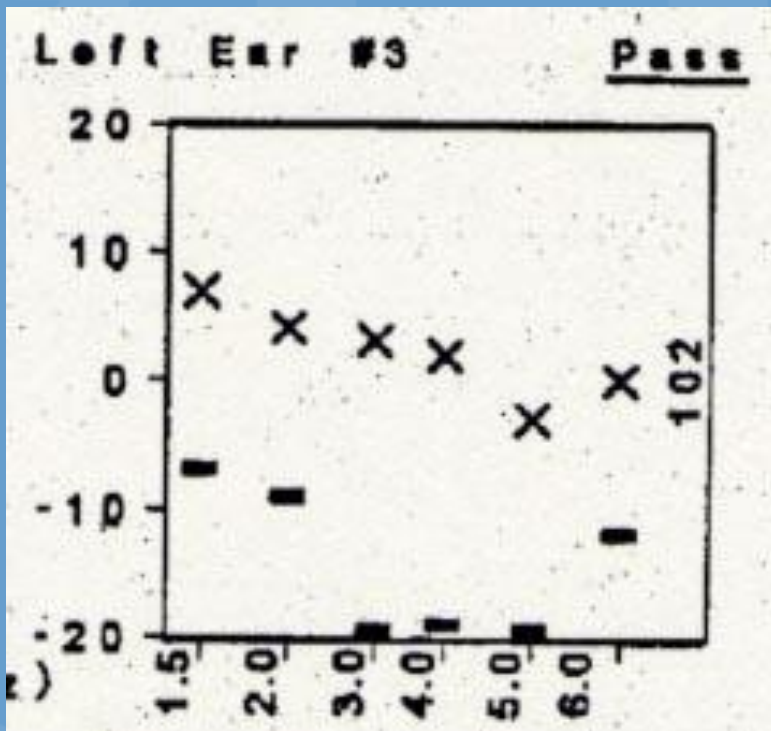
SPEECH AUDIOMETRY

	PTA	SRT/SAT	SPEECH RECOGNITION		SPEECH RECOGNITION		MCL	UCL
			%	dB HL	%	dB HL		
RIGHT (AD)		0	100	50				
masking								
LEFT (AS)		NR	CNT					
masking								

HISTORY: _____



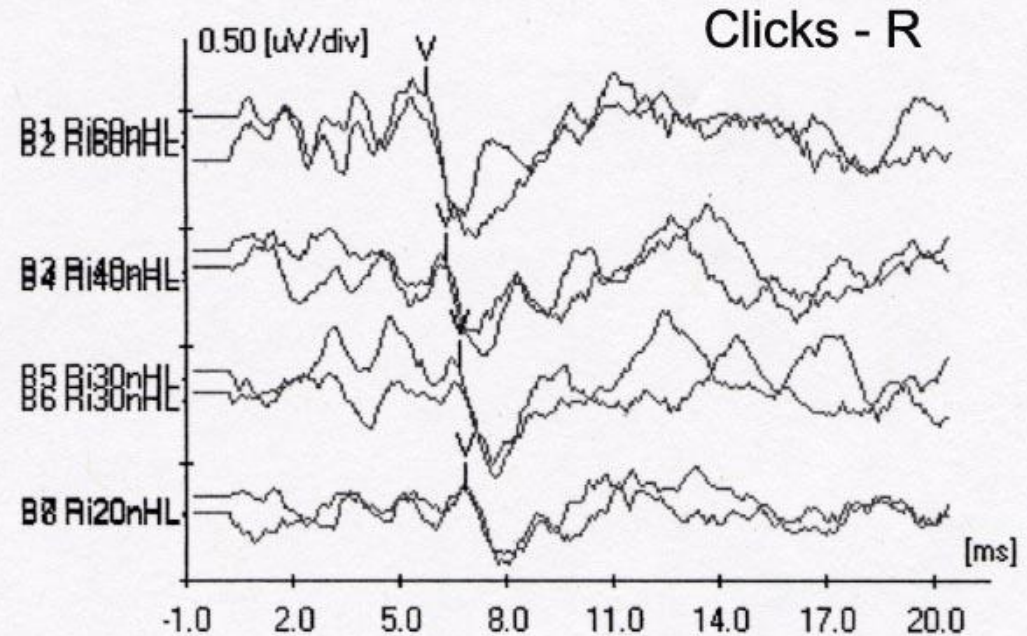
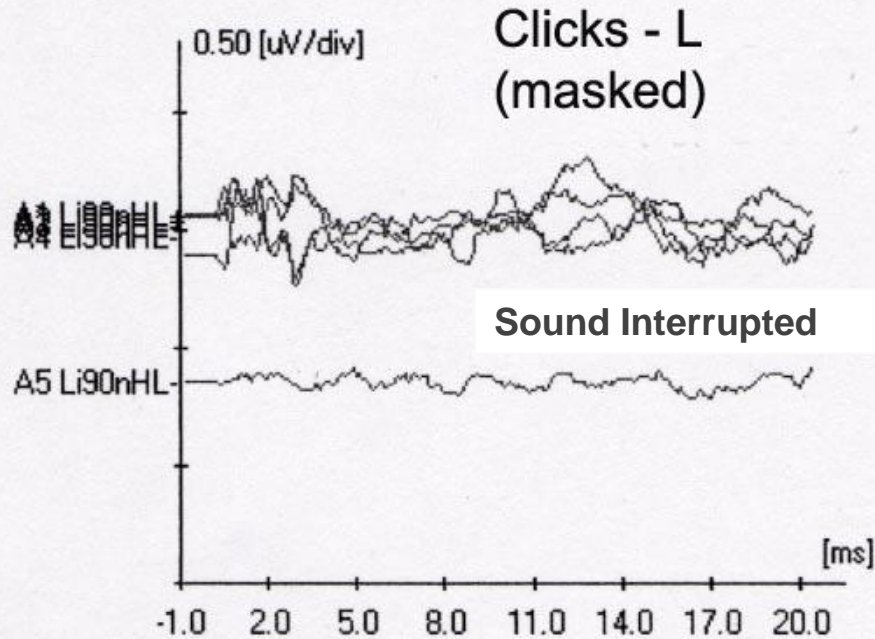
Case #5 OAEs





Case #5

ABR Completed at Age 4 years

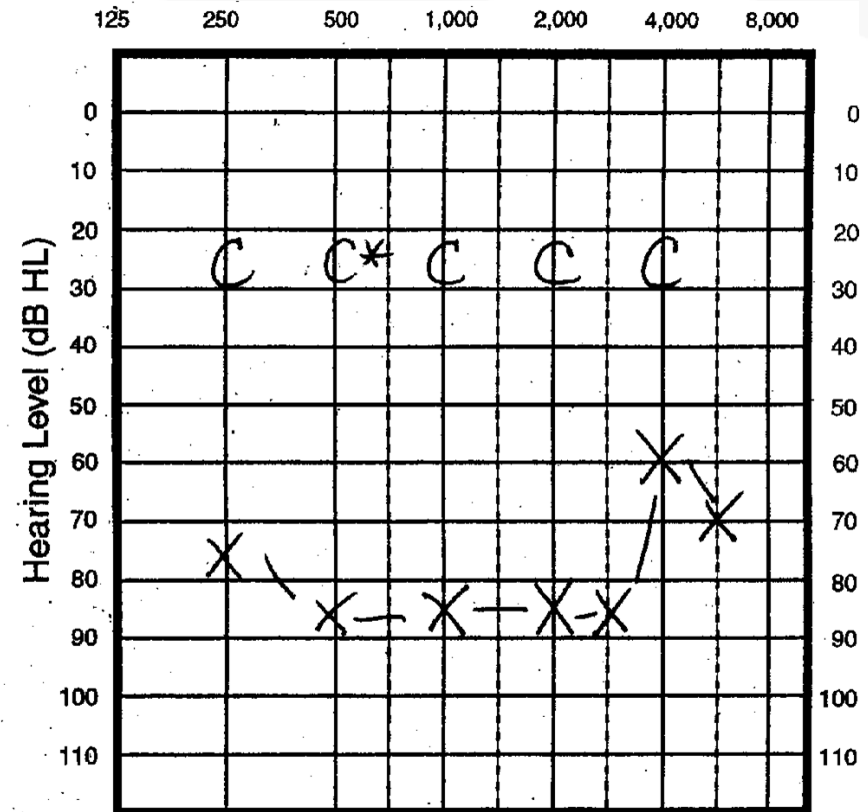


Case #5

- Results of MRI:
 - » Right ear: Normal inner ear anatomy
 - » Left ear: Consistent with small or absent nerve VIII
- At age 7 years child has above average speech and language development, no academic problems
- Managed as we do other cases with profound unilateral hearing loss.

Case #6: 8 year old with ANSD

- Child with progressive neurologic disease
- Speech recognition scores 5 years post CI in right ear:
 - » 6 % words: 38% phonemes
- Recently began wearing HA again in non-CI ear
- Mom reports increased benefit compared to CI alone
- Many additional medical issues:
 - » Ataxic (in wheelchair now)
 - » Optic neuropathy (only sees at close range)
- Probably “true” neuropathy



Six Cases with ANSD pattern on ABR...Six Different Outcomes

1. Normal hearing sensitivity no device needed, limited services required
2. Child with profound bilateral hearing loss; doing well with CI
3. Child with moderate HL benefitting from amplification
4. Child with ANSD pattern on ABR but distal waveforms present; normal hearing sensitivity
5. Child with unilateral profound HL and absent cochlear nerve
6. Child with progressive neurologic disease; limited benefit from either HA or CI alone; child feels best benefit from CI and HA combined

Evidence re Amplification

- Evidence regarding outcomes from amplification is limited
- Few peer-reviewed studies re outcomes with amplification or CI have been published
- Existing literature is based on small number of children
- Many of published reports are anecdotal
- Only a few published studies document use of a prescription-based fitting strategy that ensures audibility of speech signals



Audiological Management of Auditory Neuropathy Spectrum Disorder: A Systematic Review of the Literature

B. Roush, P., Frymark, T., Venedictov, R., and Wang.,

American Journal of Audiology 2011, Sept. 22
(epub ahead of print)

Cortical Evoked Potentials (CAEPs)

- ABR evaluates outer ear to lower brainstem
- CAEP evaluates outer ear to auditory cortex
- CAEPs not as reliant on timing as earlier evoked potentials and may be present when ABR is not
 - » Hood, 1998, Rapin and Gravel, 2003
- Unlike ABR must be completed in awake (but quiet) infants
 - » Cone Wesson and Wunderlich, 2003)
- Further CAEP research needed with normal infants and infants with SNHL and ANSD



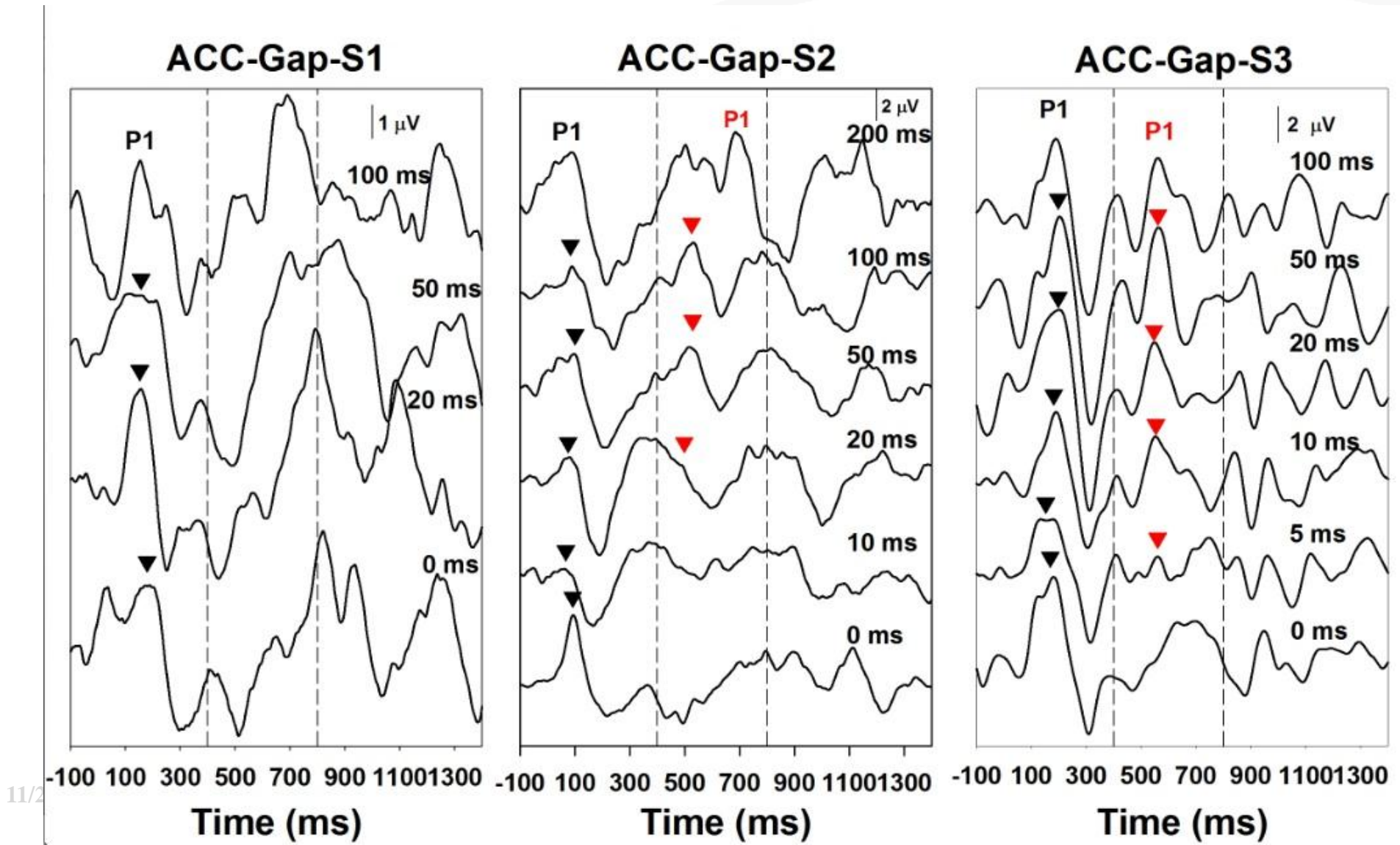
Cortical Evoked Potentials (CAEP)



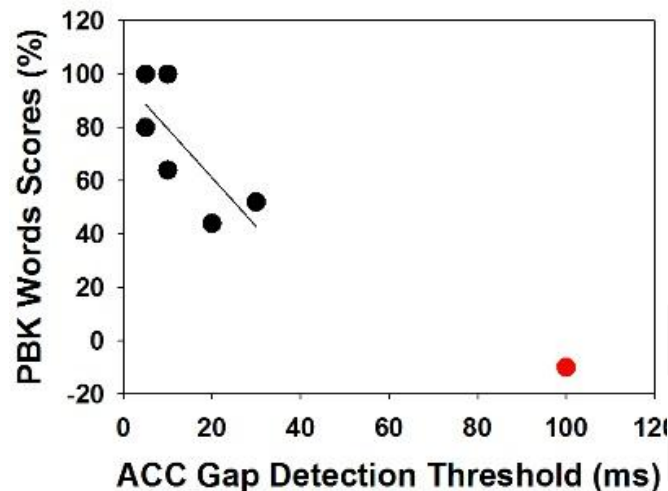
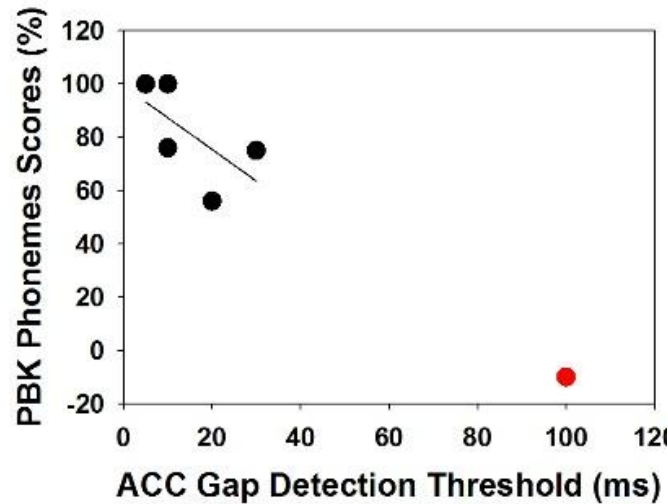


Acoustic Change Complex-Gap Detection
Preliminary Findings
Shuman He, PhD
University of North Carolina at Chapel Hill

Acoustic Change Thresholds (ACC)-Gap Detection



Acoustic Change Complex (ACC) Gap Detection Thresholds and PBK Scores





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Counseling Families

Counseling in ANSD: What Do We Say to Families?

- Child has an auditory disorder; difficult to know prognosis at time of ABR evaluation
- Degree of deficit may be mild or severe
 - a small number have normal hearing sensitivity
- Results of behavioral testing are necessary before specific recommendations can be made
- Hearing aid use is helpful in some cases but not in others; benefit can only be determined with appropriate fitting and consistent use
- Cochlear implantation may be a better option if adequate benefit from amplification not received

Summary of UNC Protocol for Management of Infants with ANSD

- Diagnose ANSD using ABR with single polarity clicks
- Counsel family about recommended steps in first year of life
- Enroll in early intervention
- Complete otologic exam including imaging with MRI (and CT if needed)
- Attempt behavioral audiometry with VRA beginning at 6-7 months developmental age
- Fit child with hearing aids as soon as behavioral thresholds have been established

Summary of UNC Protocol for Management of Infants with ANSD (continued)

- Set hearing aids to match targets for gain and output using prescriptive formula
- Perform hierarchical battery of speech perception tests
- Regularly communicate with early intervention teacher and parent re communication progress
- Consider CI if benefit from amplification insufficient for continued progress in communication skill development
- Use cortical evoked potentials to aid with management when needed
- Refer for comprehensive developmental evaluation when child has complex needs

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

- Evidence regarding clinical management and use of amplification is still limited. More research needed especially with infants and young children
- Studies aimed at evaluating hearing aid outcomes should include evidence-based prescriptive hearing aid fitting methods and real-ear verification methods appropriate for use with infants and children.
- 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



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Muchas Gracias!

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