



Auditory Neuropathy Spectrum Disorder: Diagnosis, Treatment & Long-Term Outcomes

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ANZCED Conference, July 2011

Auditory Neuropathy Spectrum Disorder (ANSD)

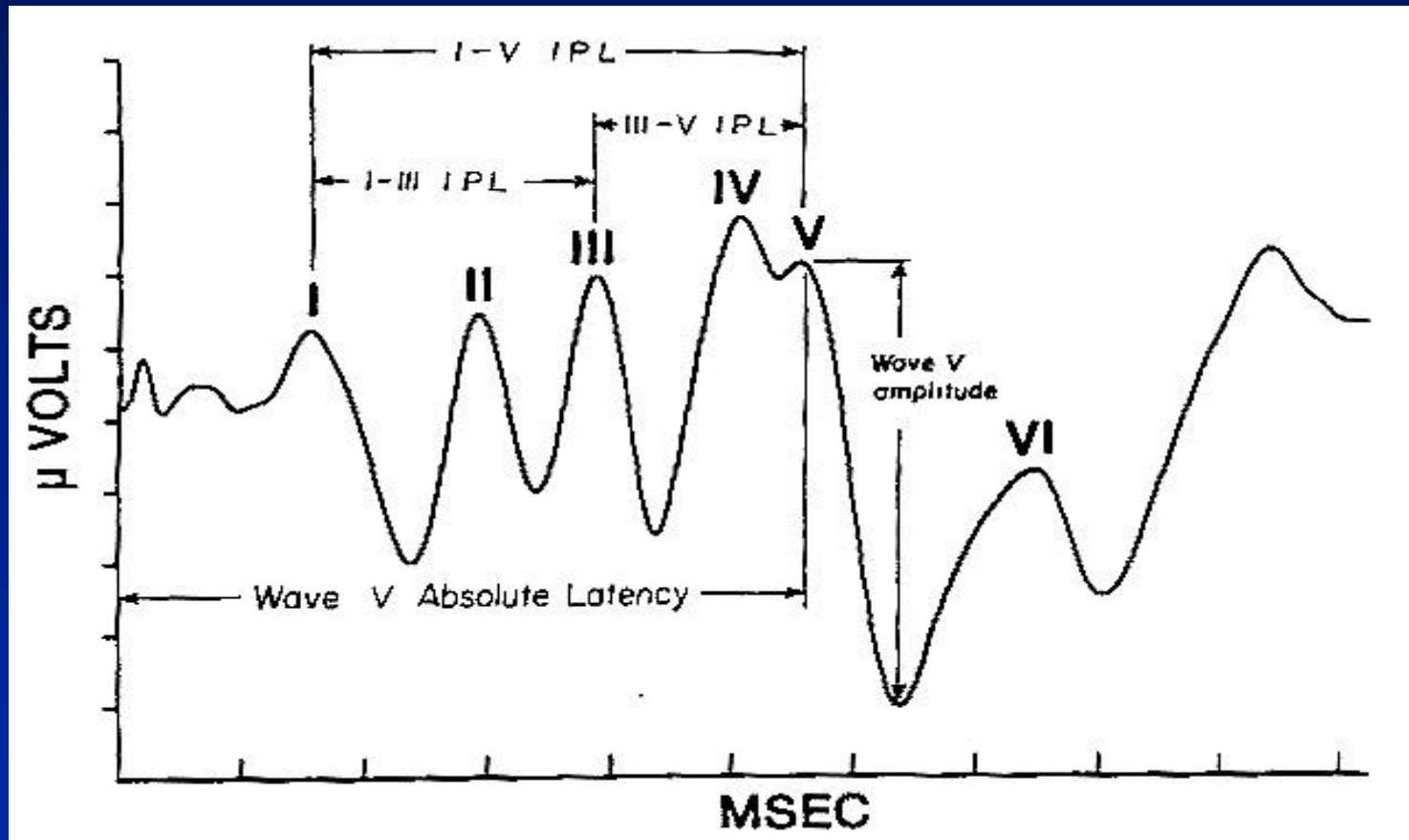
- ◆ Also referred to as: auditory neuropathy, auditory dys-synchrony, auditory synaptopathy...
- ◆ Hearing impairment in which cochlear outer hair cell function is normal but afferent neural transmission is disordered
- ◆ Indicated by the presence of pre-neural responses (OAE / CM) in the absence of auditory neural responses (ABR)

Auditory Brainstem Response (ABR)

- ◆ **Electrophysiologic** response generated in the auditory pathway
 - Cochlear (VIIIth cranial) nerve
 - Neural activity from the auditory brainstem
- ◆ Response occurs in the 10-15 ms following the presentation of an **audible stimulus**

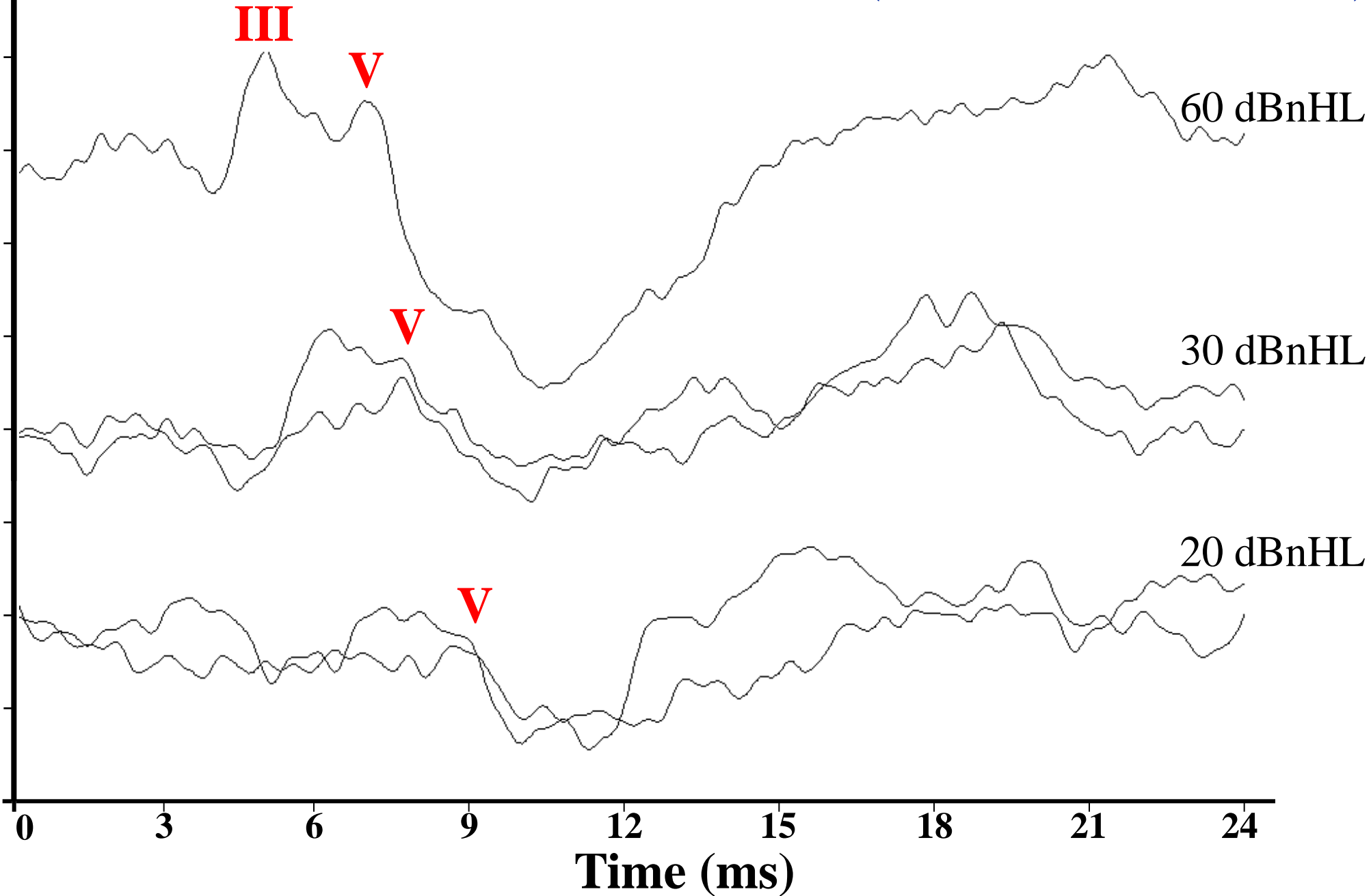
ABR Morphology

- ◆ Adult ABR has five main peaks (I-V)



Click-ABR (normal infant: 1 month)

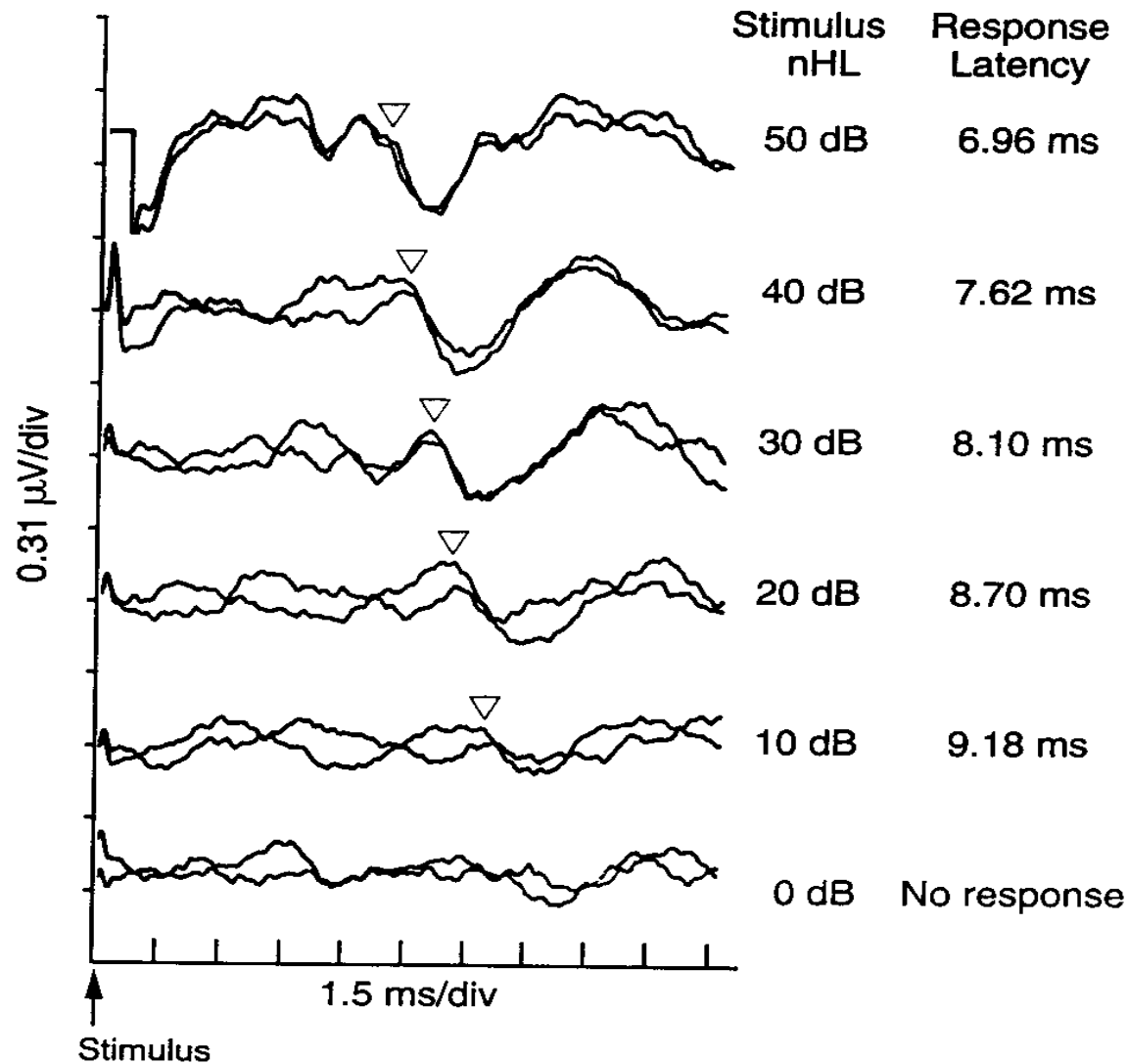
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ABRs in Clinical Testing

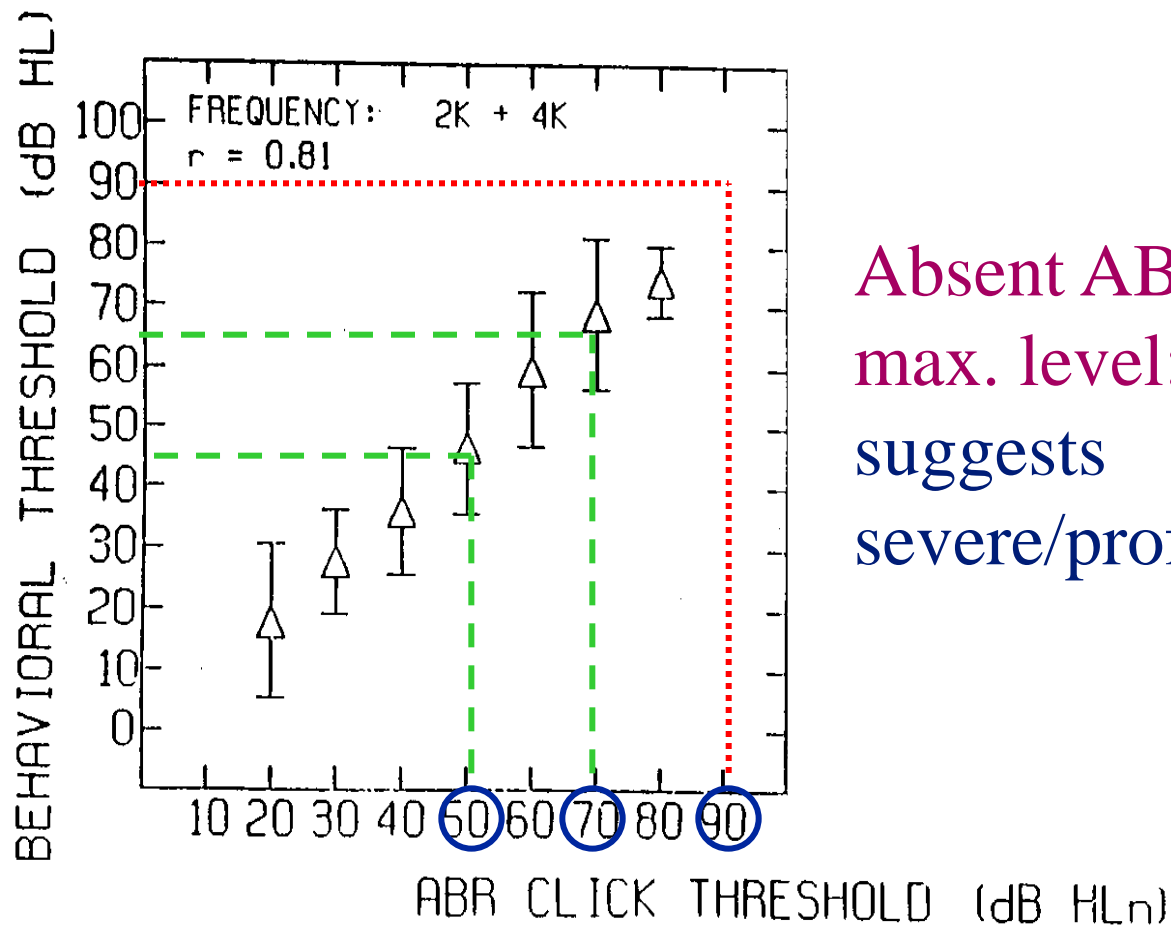
- ◆ Adults: neurodiagnosis (acoustic neuroma)
 - Tumor slows neural conduction
(increased latency between peaks)
- ◆ Children: test of hearing (sound detection)
 - Response only present if stimulus is above hearing threshold
 - Vary level of stimulus
 - » ABR threshold – correlates with the audiogram

Click-ABR Threshold (normal subject)



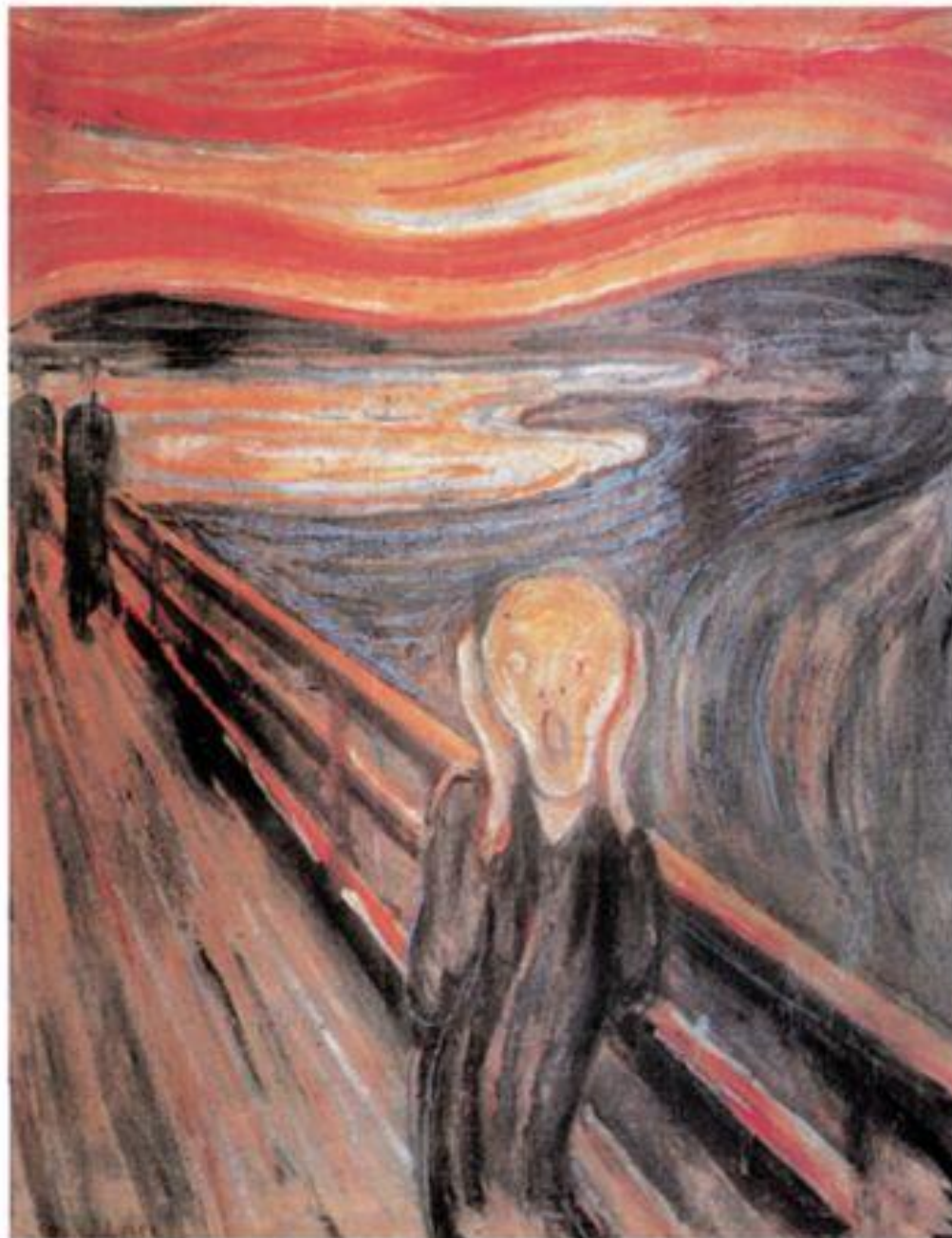
ABR threshold & sensorineural hearing loss

- ◆ ABR elevated by the degree of the loss



Absent ABR at
max. level:
suggests
severe/prof. loss

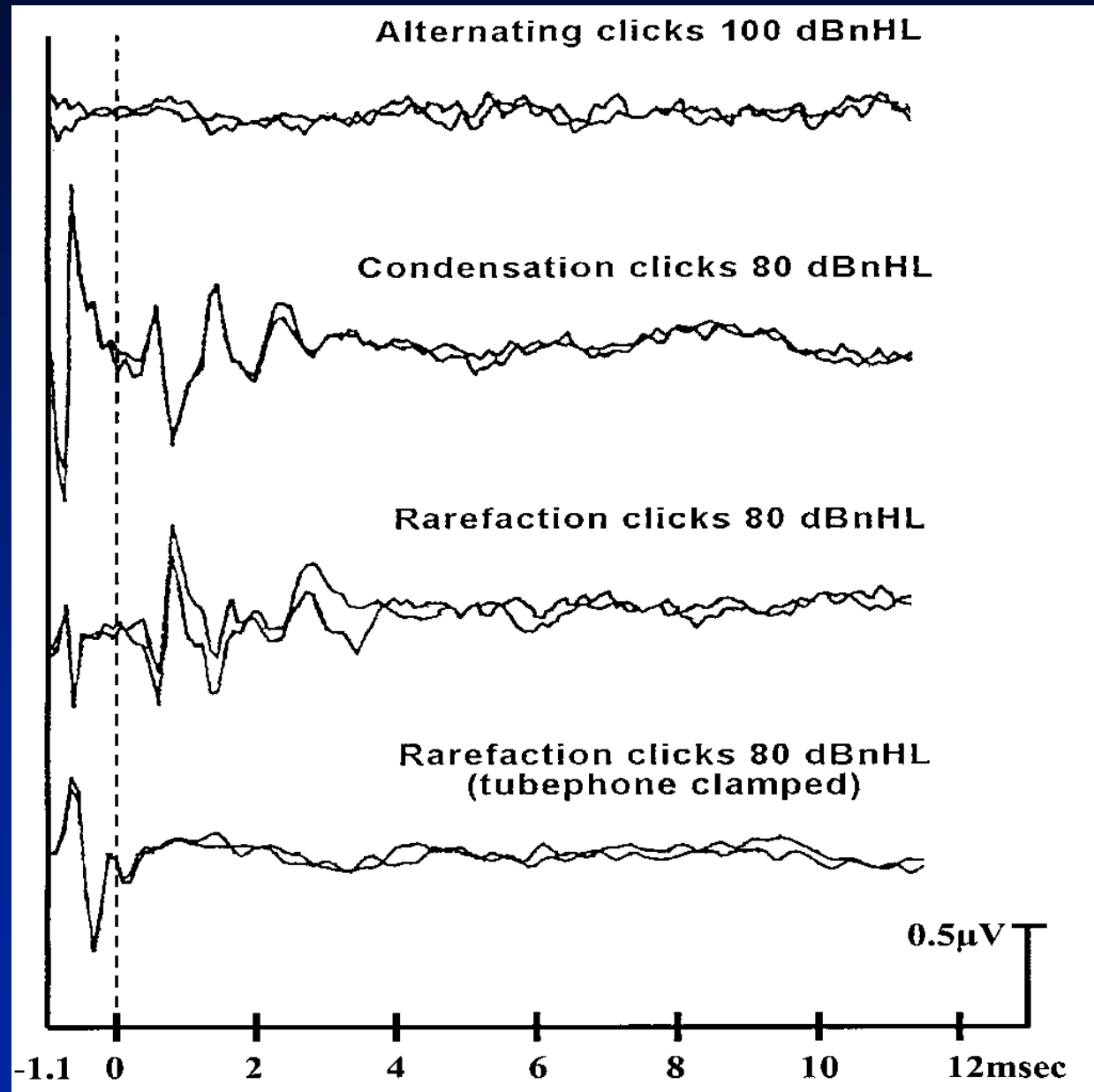
However...



Threshold estimation

- ◆ Hearing level prediction based upon the ABR assumes the problem is “peripheral”
(middle ear/ cochlea)
- ◆ i.e. ABR absent because stimulus is not loud enough
- ◆ Another possibility:
 - ABR disrupted by abnormal transmission in the neural pathway
(auditory neuropathy spectrum disorder)

CM /ABR assessment for a 3 mo old with ANSD



Possible mechanisms producing the ANSD result pattern

- ◆ Cochlear damage restricted to the inner hair cells (IHC)
- ◆ IHC/auditory nerve synapse
- ◆ Auditory nerve abnormality
 - reduced neuronal population
 - disruption of neural synchrony
 - cochlear nerve deficiency

Presentation of ANSD

◆ Infancy

- Perinatal risk factors
 - » Anoxia
 - » Hyperbilirubinaemia

◆ Later onset

- Typically associated with neurodegenerative disease
 - » Demyelinating conditions (eg CMT1)
 - » Axonal degeneration (eg Friedreich ataxia)
 - » Mitochondrial disorders

Prevalence of ANSD

- ◆ Difficult to determine in adults
 - Pre-neural tests not routinely carried out
- ◆ Also unclear in well-baby populations
- ◆ Hearing impaired children

Prevalence of ANSD in children with permanent hg. loss

| Study | Population | # Permanent Hg. loss | # AN/AD cases | % |
|---------------------------------|---------------------|-----------------------------|----------------------|----------|
| Kraus et al (1984) | Hg. Imp. Children | 48 | 7 | 14.6 |
| Park & Lee (1998) | Hg. Imp. Children | 139 | 7 | 5.0 |
| Vohr et al (1998) | Universal screening | 111 | 2 | 1.8 |
| Rance et al (1999) | “at-risk” infants | 109 | 12 | 11.0 |
| Berlin et al (2000) | Hg. Imp. Children | 1000 | 87 | 8.7 |
| Cone-Wesson et al (2000) | Universal screening | 56 | 3 | 5.4 |
| Lee et al (2001) | Hg. Imp. Children | 67 | 2 | 3.0 |
| Madden et al (2002) | Hg. Imp. Children | 428 | 22 | 5.1 |
| Tang et al (2004) | Hg. Imp. Children | 56 | 1 | 1.8 |
| Rance et al (2005) | “at risk” infants | 290 | 19 | 6.6 |

ANSD: Clinical Profile

- ◆ Behavioural audiogram
 - Level: normal hearing to profound loss
 - Configuration: $\approx 30\%$ low frequency emphasis
 - Fluctuating hearing
- ◆ Auditory evoked potentials
 - Middle latency/cortical responses
 - » variable: presence/absence correlated with perceptual ability
- ◆ Impaired speech perception

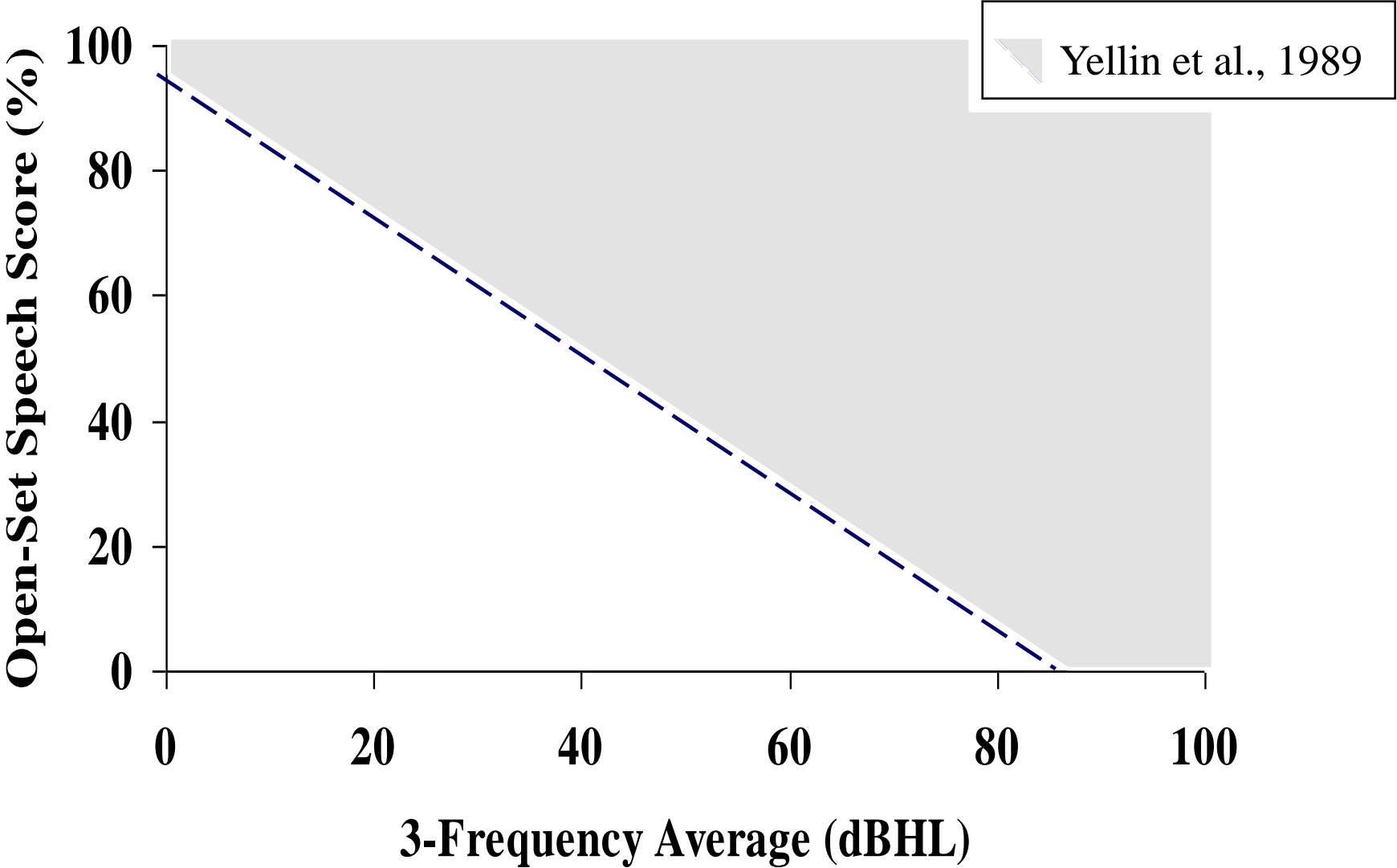


Speech Understanding

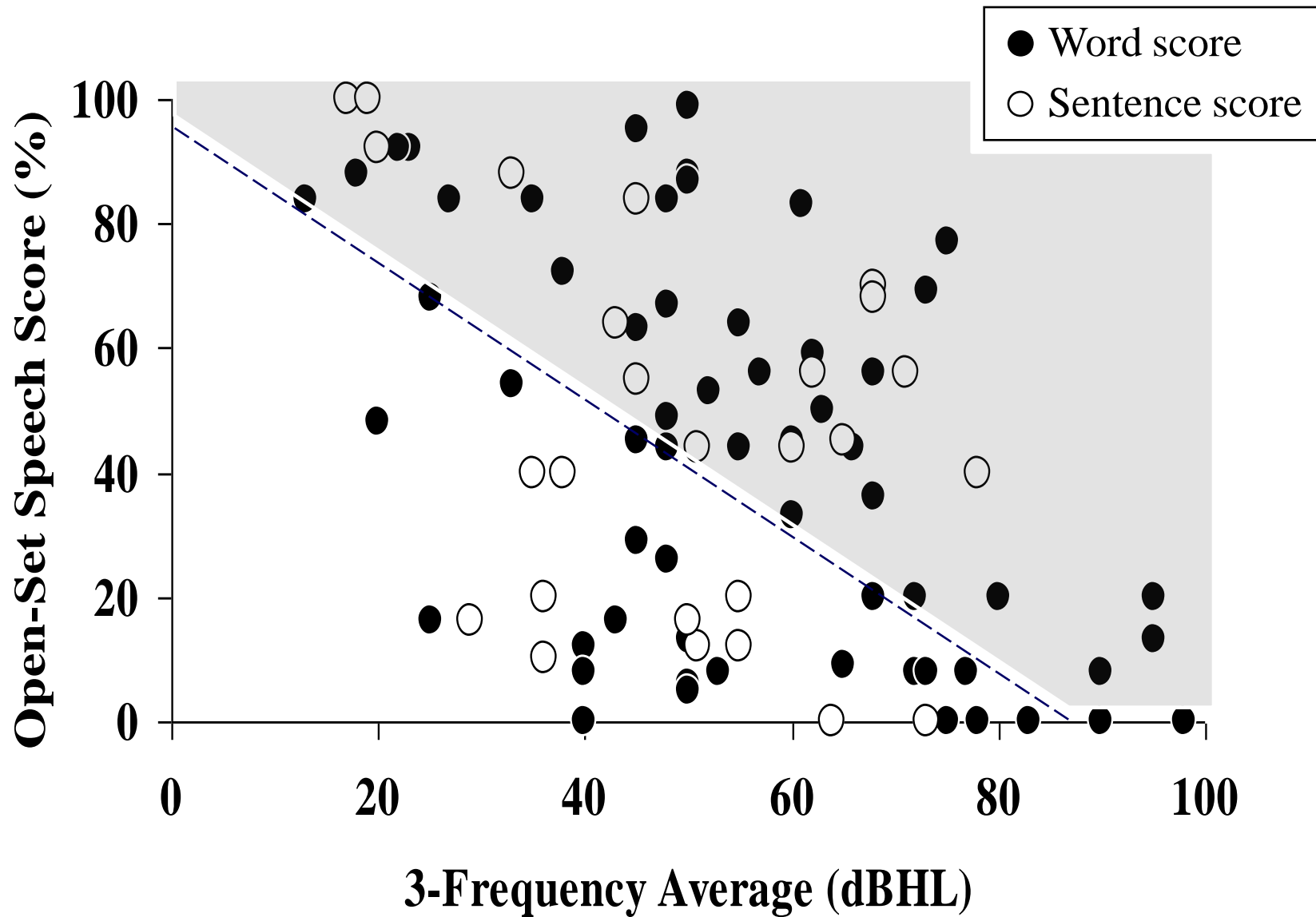
Speech Understanding

- ◆ Consistently reported problem in both adults and children with ANSD
- ◆ Difficulties out of proportion with the behavioural audiogram
 - Abnormal speech perception in subjects with “normal hearing”
 - Subjects with abnormal hearing thresholds show speech perception poorer than for SN loss of equivalent degree

Open-set Speech Perception (in Quiet) for Children with ANSD



Open-set Speech Perception/Hg. Level for Children with ANSD

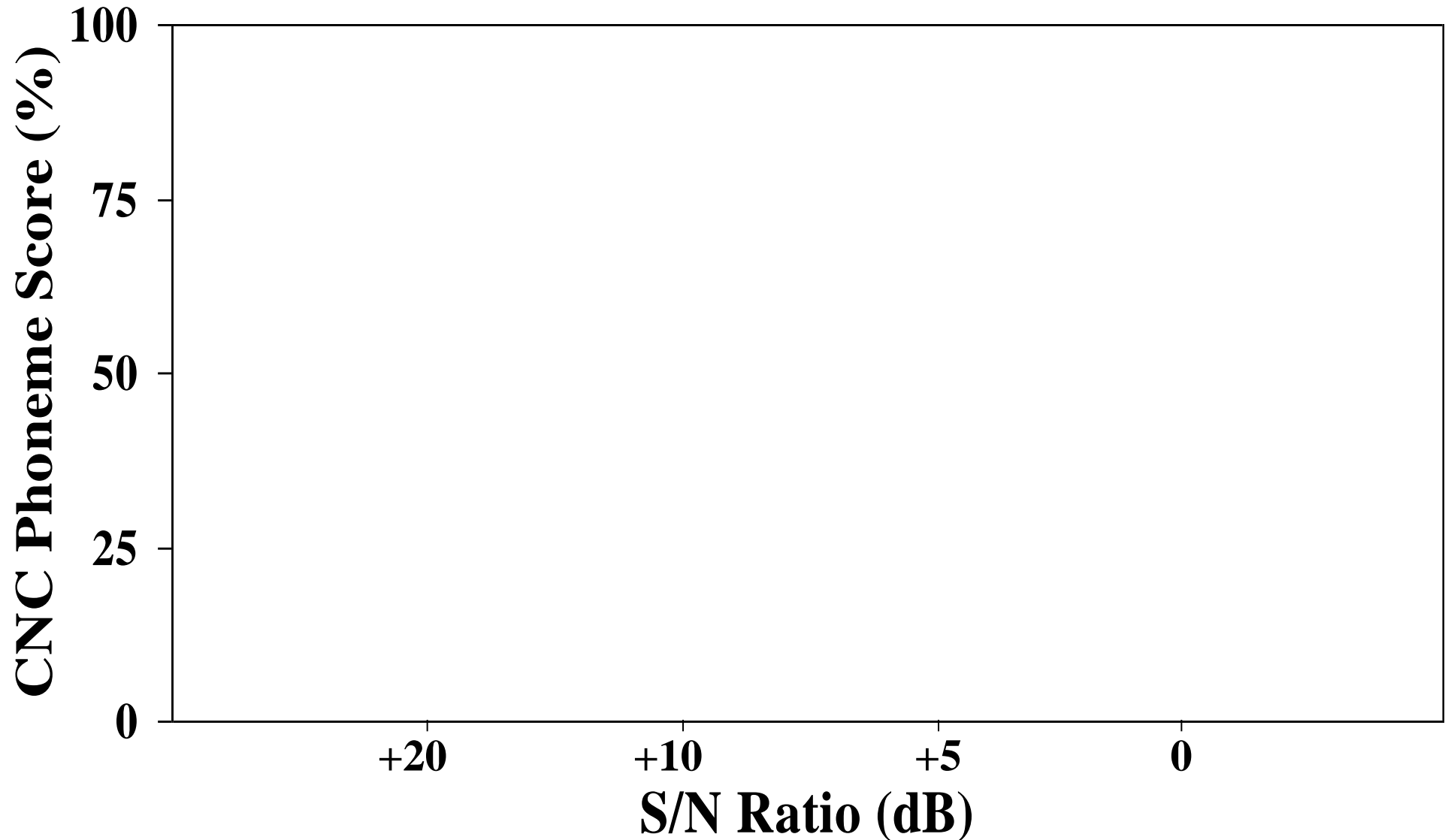


Speech Perception in Noise

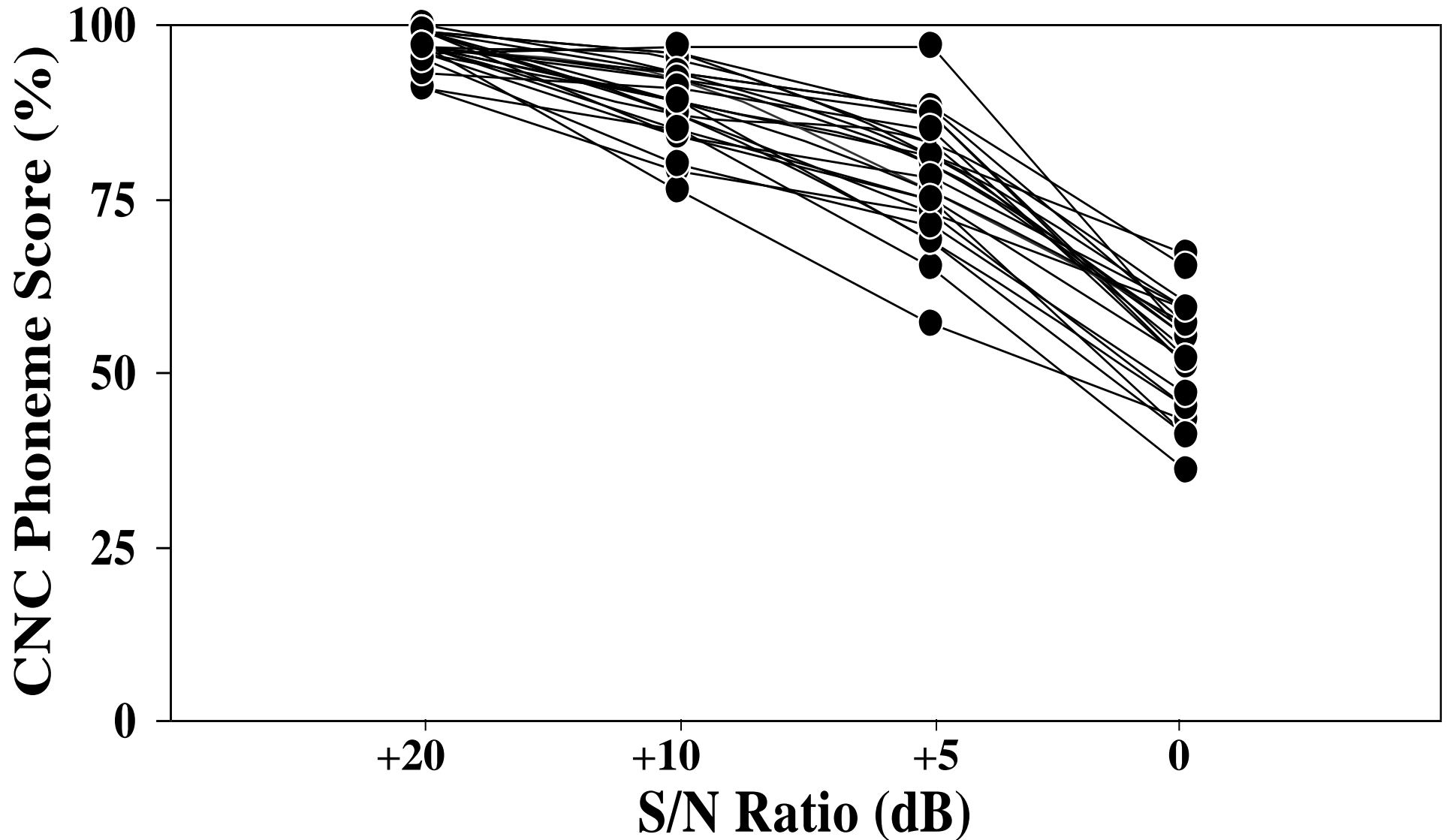


- ◆ Extreme difficulty reported in adults and children with ANSD (Kraus et al., 2000; Rance et al., 2007; Shallop, 2002; Starr et al., 1998)
- ◆ Some cases show normal understanding in quiet and negligible perception in “everyday” listening conditions

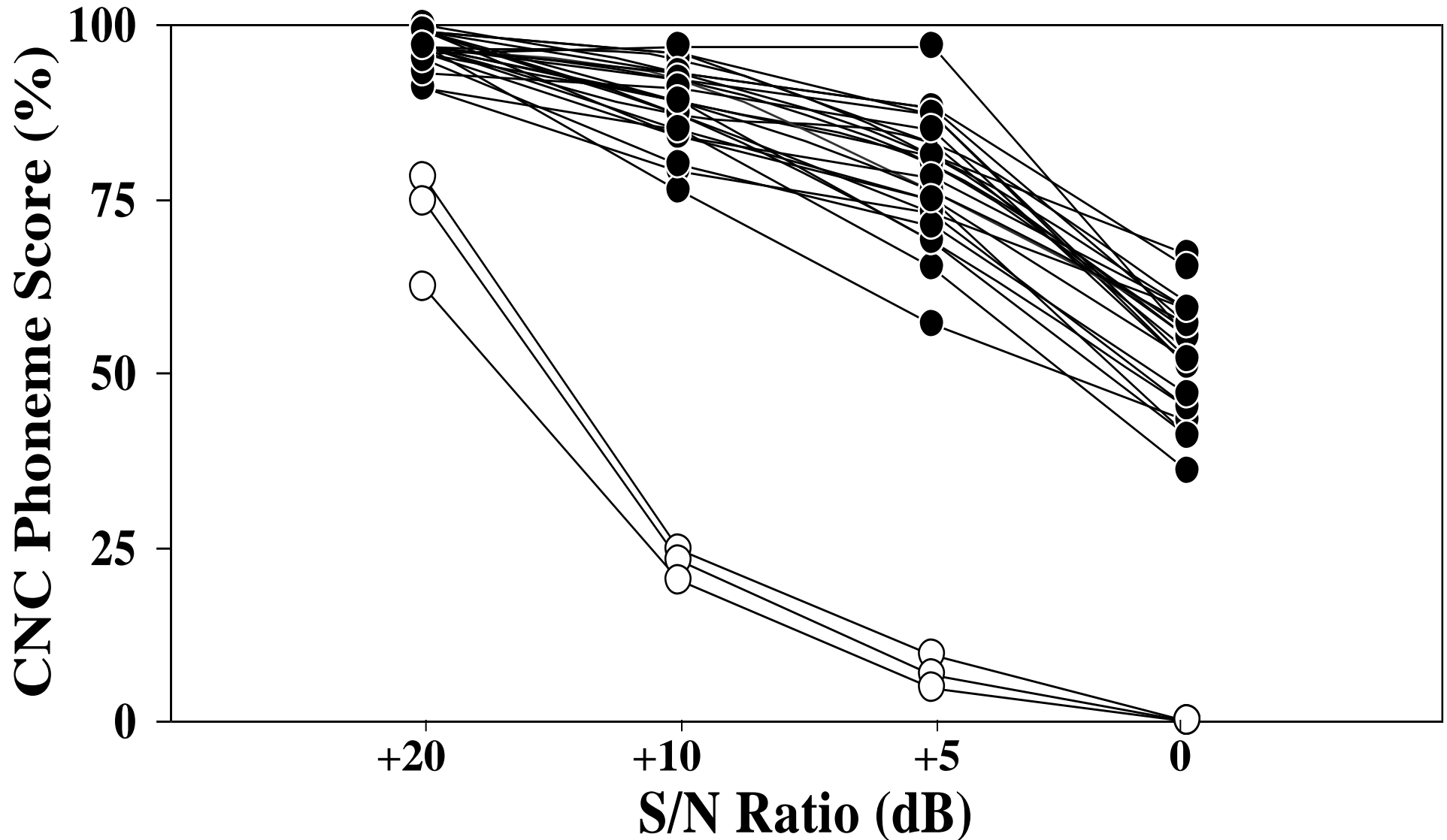
Speech in Noise: normally hearing adult subjects (3 with Friedreich's Ataxia)



Speech in Noise: normally hearing adult subjects (3 with Friedreich's Ataxia)



Speech in Noise: normally hearing adult subjects (3 with Friedreich's Ataxia)





◆ Management of speech in noise problems

Personal FM systems

FM Systems & ANSD

- ◆ Personal listening devices designed to improve listening in background noise (particular problem for ANSD-type loss)
- ◆ Rance et al. 2010 (Neuroscience)
- ◆ Phonak FM systems fit to 10 Friedreich ataxia patients with ANSD

Personal FM Devices



- ◆ Inspiro FM devices coupled to bilateral iSense micro receivers (Phonak)

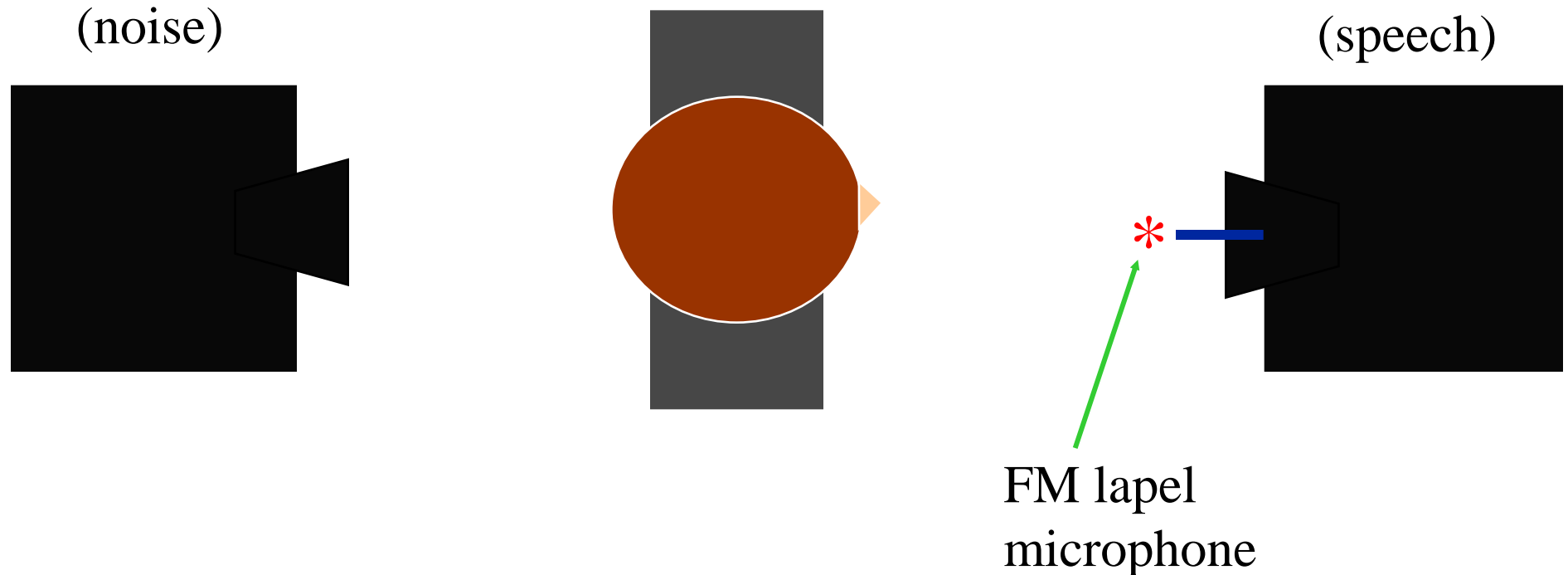


Study Design

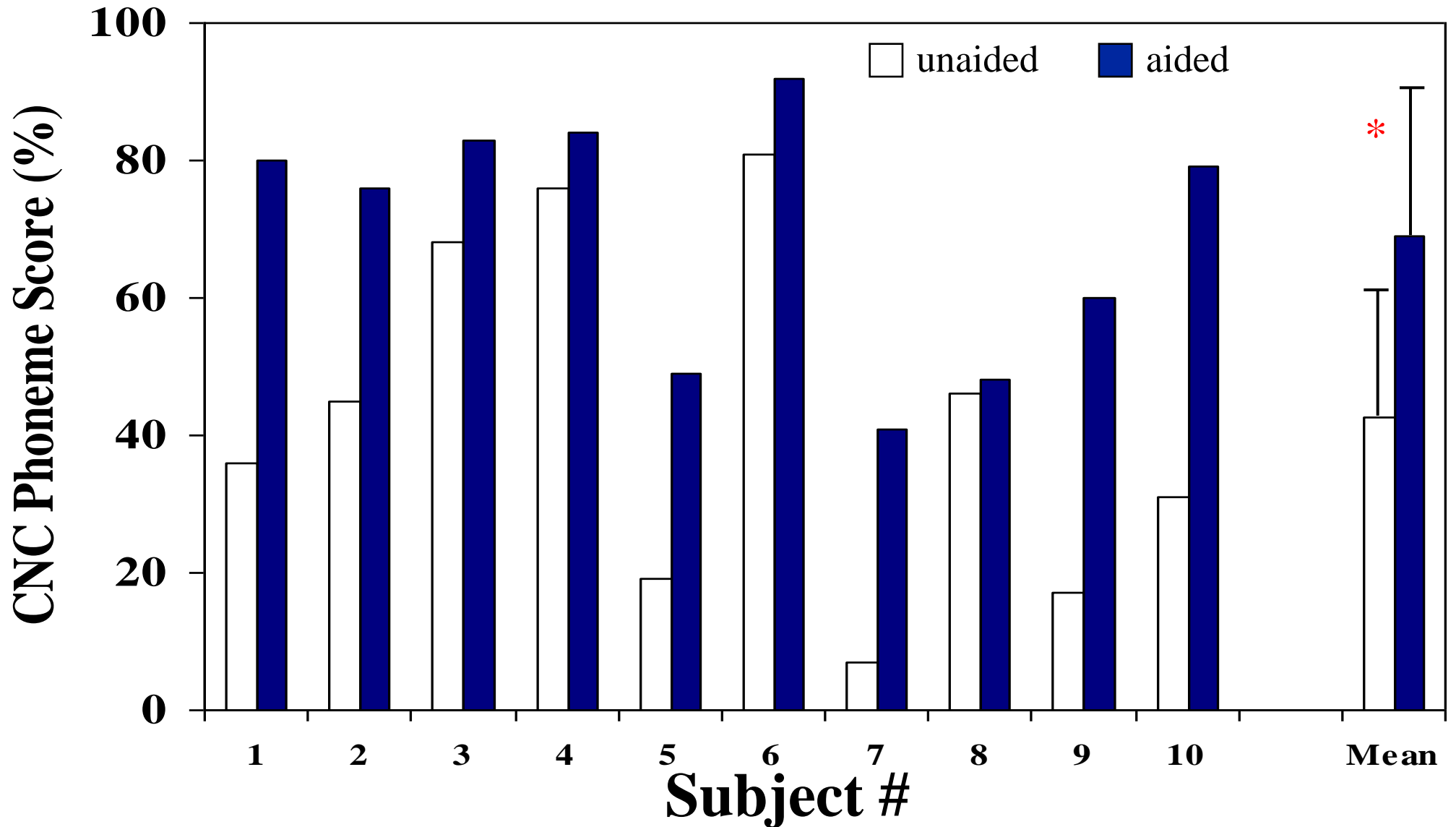
- ◆ Formal speech perception testing
 - Comparison of aided (FM) and unaided scores
- ◆ 6 week FM trial (balanced design)
 - » 1. Period of non-use (prior to fitting)
 - » 2. Two week period wearing the device
 - » 3. Another two week period wearing the device
 - » 4. Two week period of non-use
- Subjects completed a hearing disability questionnaire at the end of each period
 - » Abbreviated Profile of Hearing Aid Benefit (APHAB)

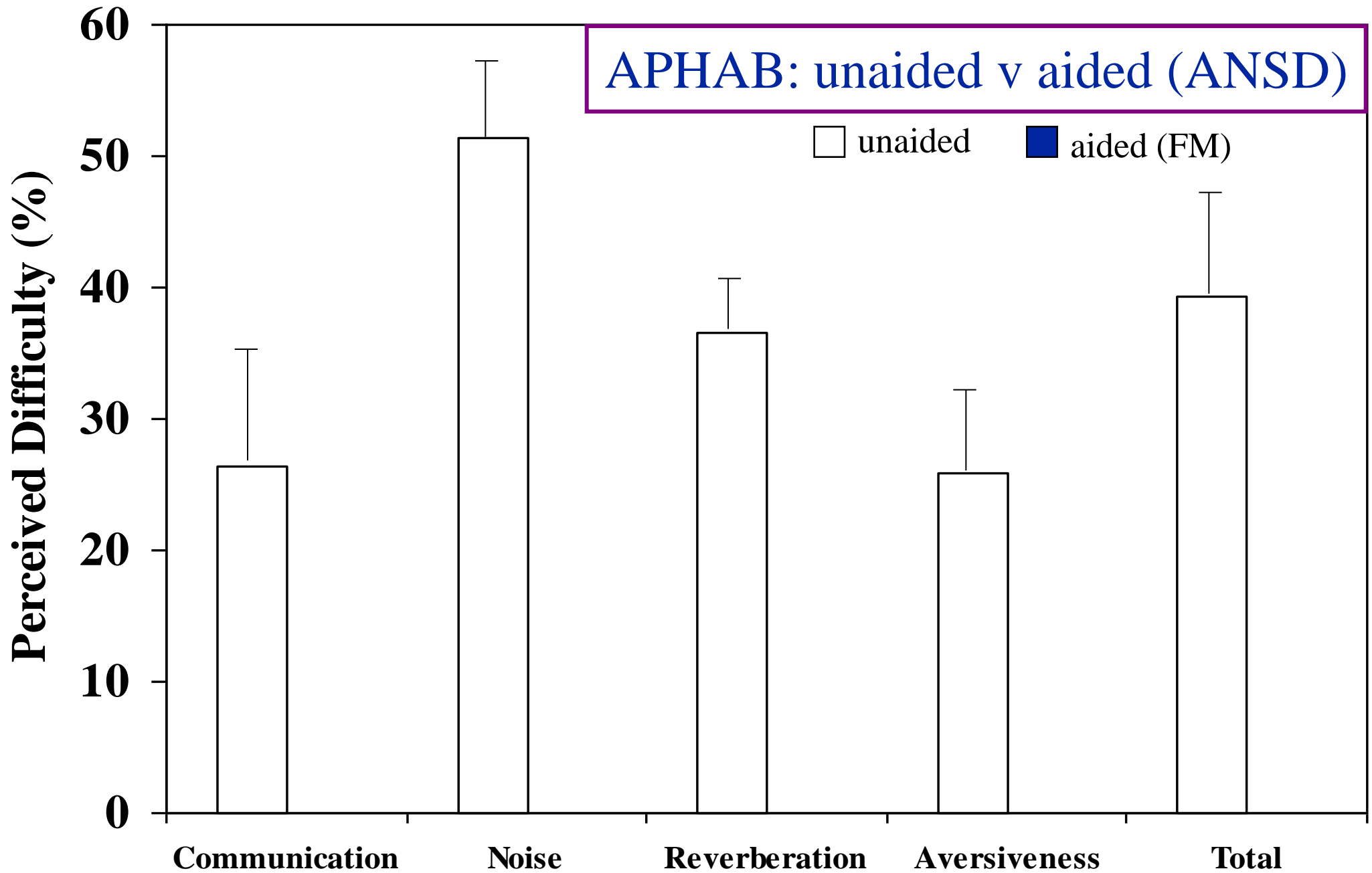
FM Test Setup: Free Field Speech in Noise

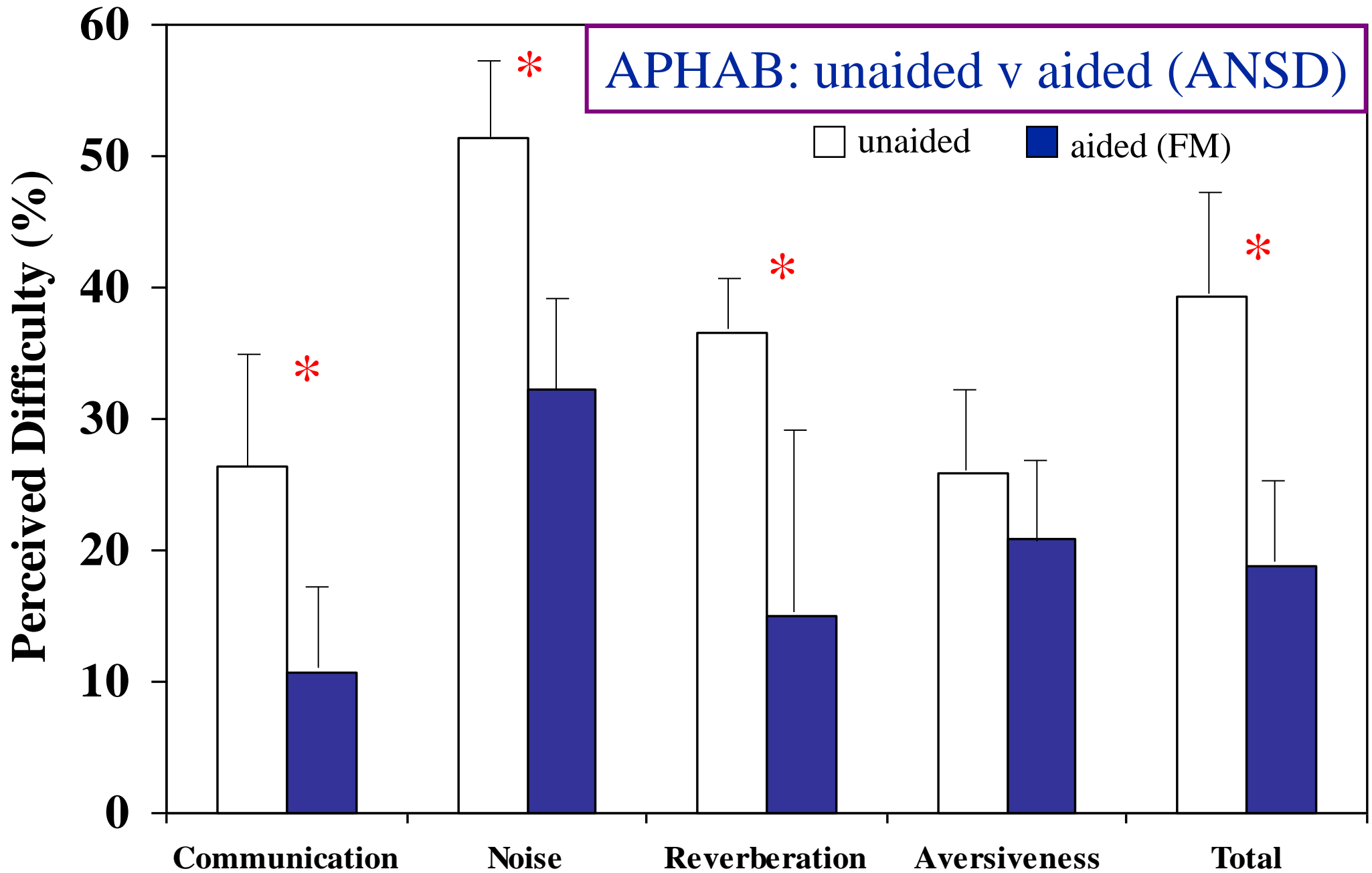
- ◆ Speech: CNC words - 65 dBSPL
- ◆ +0 dB S/N ratio (at the subject's head)



Unaided/Aided (FM) Speech Scores (ANSD subjects)







Rance et al. 2010

◆ Conclusions

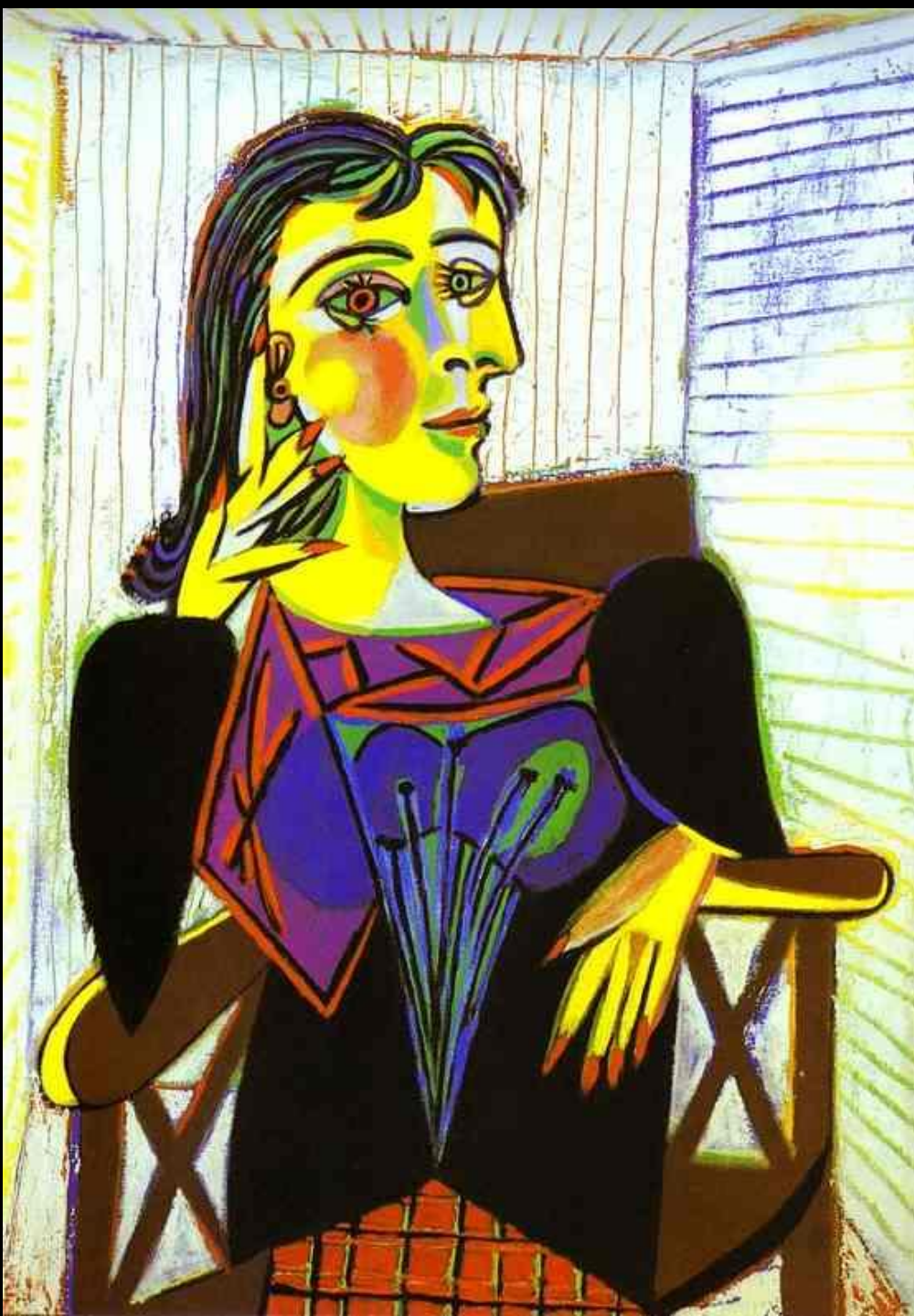
- ◆ FM-systems did not restore normal perception
(inherent auditory pathway limitations)
- ◆ Did significantly improve speech perception and everyday communication

Signal Distortion in ANSD

- ◆ Speech perception ability not related to sound detection
- ◆ Suggests **signal distortion**
- ◆ Distortion also occurs with significant sensorineural loss
 - **SN**: cochlear damage
 - affects processing of frequency cues
 - **ANSD**: disruption of neural transmission
 - timing of the electrical signal
- ◆ Functional effects quite different
 - eg. Different aspects of speech perception disrupted
(Rance et al., 2010)

Implications for Management

- ◆ ANSD listeners functionally different from their SN counterparts
- ◆ Our experience with managing peripheral hearing loss may not apply



Management of ANSD

Hearing Aids

Management of ANSD

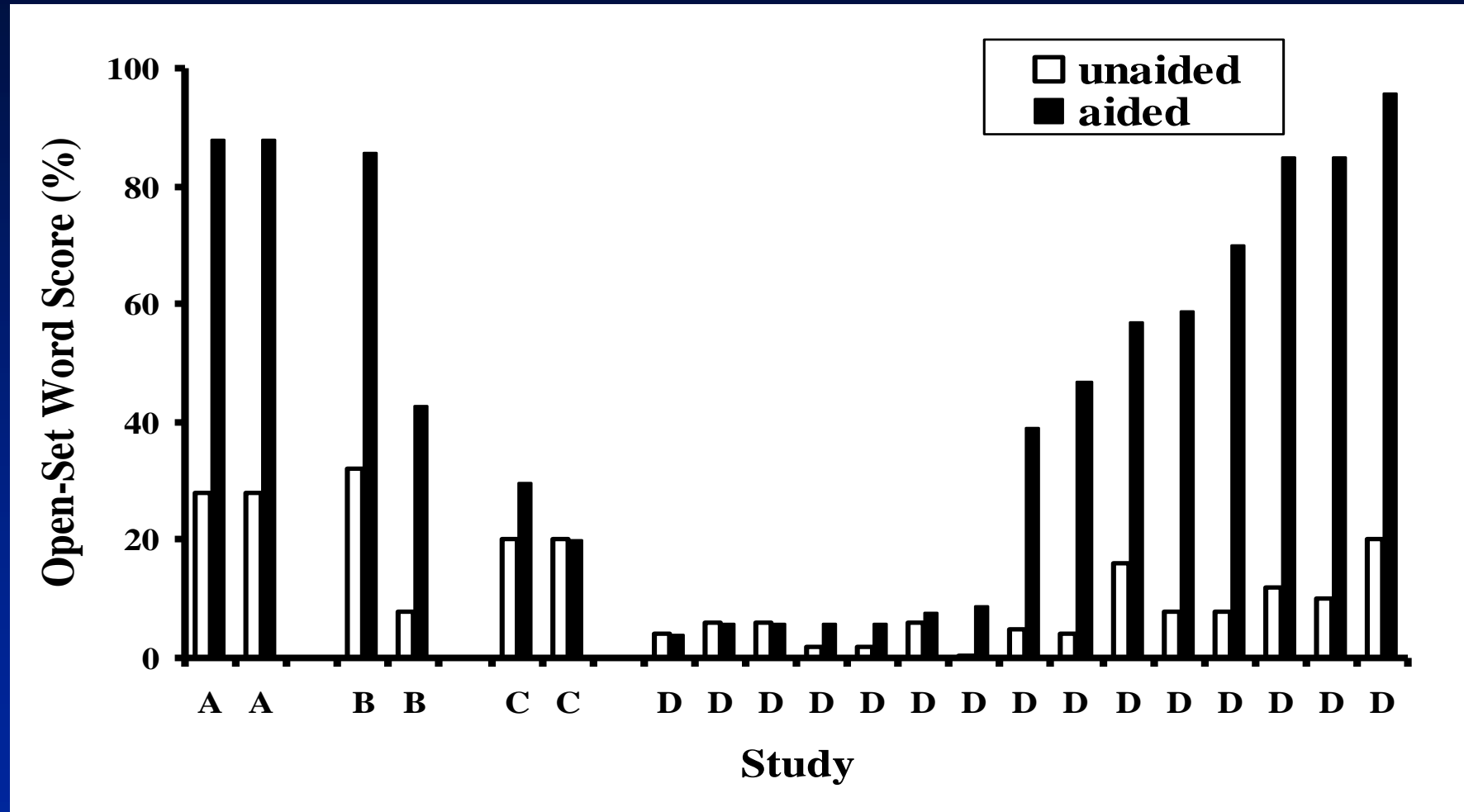
◆ Conventional Amplification

- Fitting of hearing aids to ANSD patients has been a controversial issue
- Arguments against amplification
 - » Inherent auditory pathway limitations
 - » Potential for cochlear damage
- Argument for amplification
 - » Increased access to the speech signal
(if sufficient gain is provided)

Aiding Outcomes in ANSD Patients

- ◆ **Adults:** almost universally poor
- ◆ **Children:** reports more varied
 - Many show little or no perceptual ability despite improved access to speech sounds
 - Some children ($\approx 40\%$) do show significant benefit

Open-set speech perception (unaided/aided) for children with ANSD



A: Deltenre et al. (1999) B: Rance et al. (1999)

C: Lee et al. (2001) D: Rance et al. (2002)



Management of ANSD

Cochlear Implants

Management of ANSD

◆ Cochlear Implantation

- Currently the remediation option of choice for most ANSD patients
- Most reported cases have performed at levels similar to their implanted peers with SN-type loss

How might a Cochlear Implant help?

- ◆ Broad access to the speech spectrum
- ◆ Direct stimulation of the spiral ganglion (perhaps bypassing peripheral sites of lesion)
- ◆ Electrical signal may stimulate the auditory pathway more efficiently

Speech Perception in Children with ANSD Managed with Either Hearing Aids or Cochlear Implants

Gary Rance & Elizabeth Barker

Otology & Neurotology (2008)

Subjects

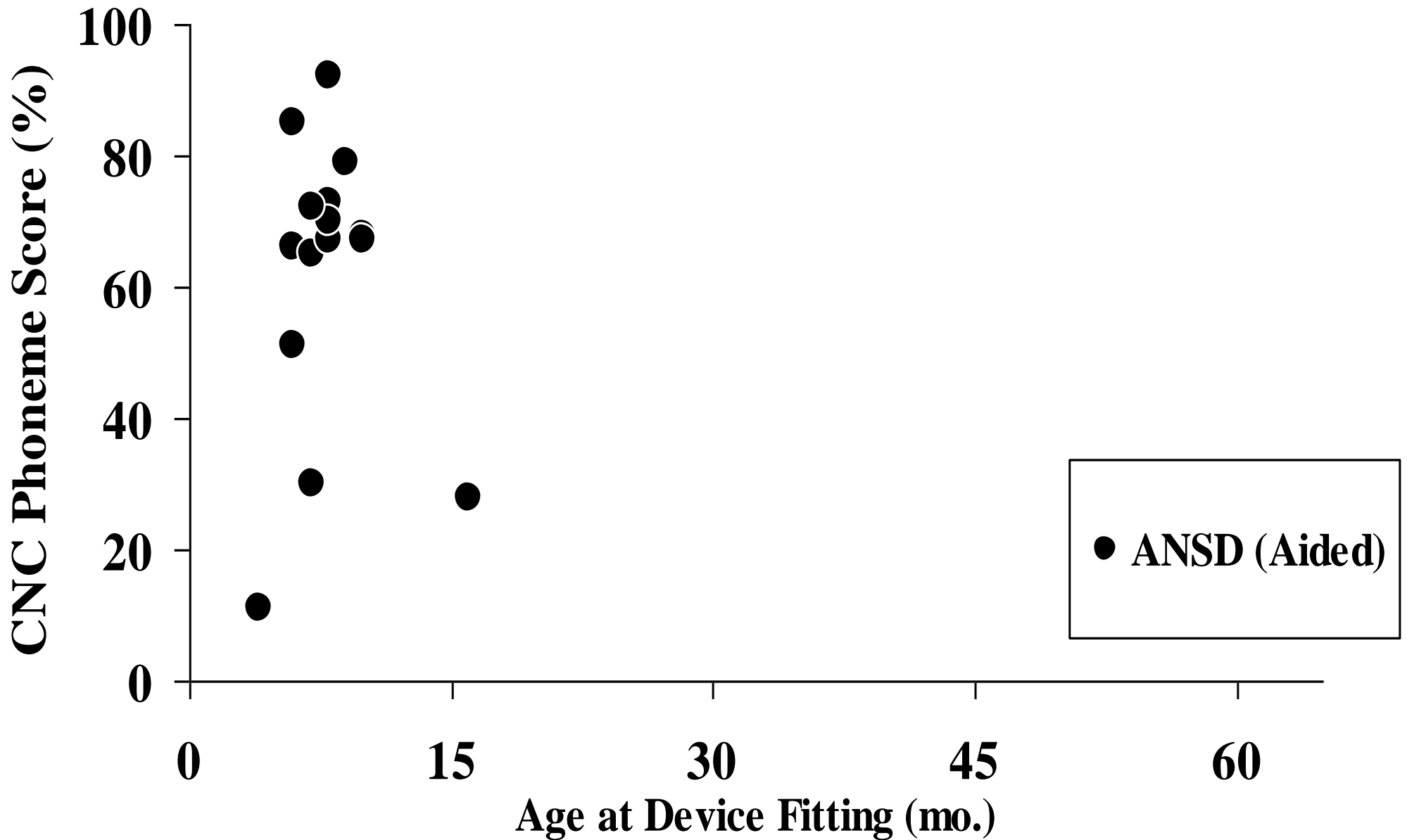
- ◆ Aided ANSD children (n=15)
- ◆ Implanted ANSD children (n=15)
- ◆ Implanted SN children (n=15)

- ◆ Matched for age at assessment
- ◆ Implantees matched for age at device fitting
- ◆ Long-term device users (>2 yrs)

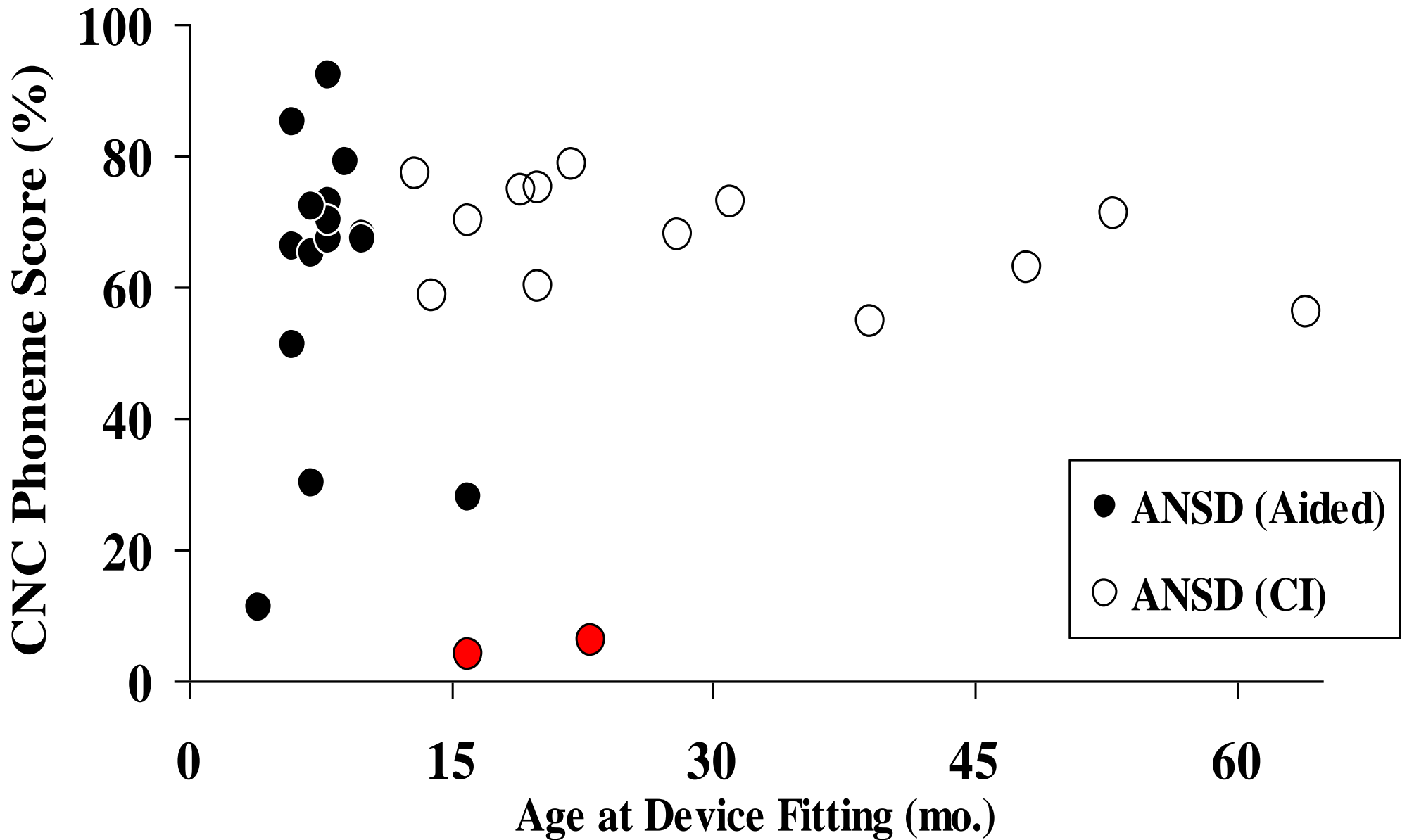
Speech Perception

- ◆ Free field presentation (70 dBSPL)
- ◆ Subject in “normal” listening condition
 - Hearing aids
 - CI alone
 - CI & hearing aid
 - Bilateral CI
- ◆ CNC words (quiet)

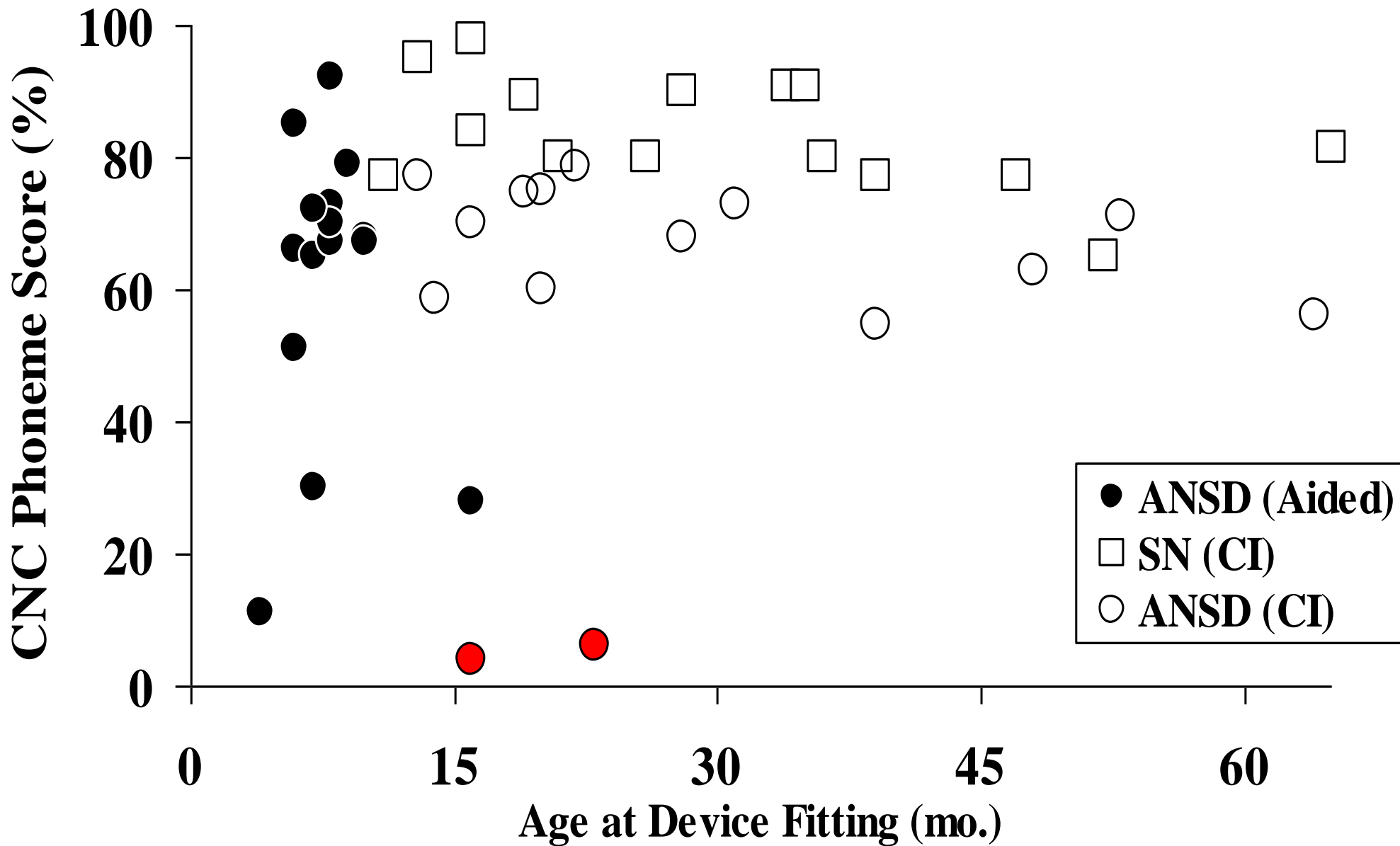
Open Set Speech Perception



Open Set Speech Perception



Open Set Speech Perception



Speech & Language Outcomes in
Children with ANSD Managed with
Either Hearing Aids or Cochlear Implants

Gary Rance & Elizabeth Barker

International Journal of Audiology (2009)

Subjects

- ◆ Aided ANSD children (n=10)
- ◆ Implanted ANSD children (n=10)
- ◆ Implanted SN children (n=10)

- ◆ Matched for age at assessment
- ◆ Implantees matched for age at device fitting
- ◆ Long-term device users (>2 yrs)

Assessments

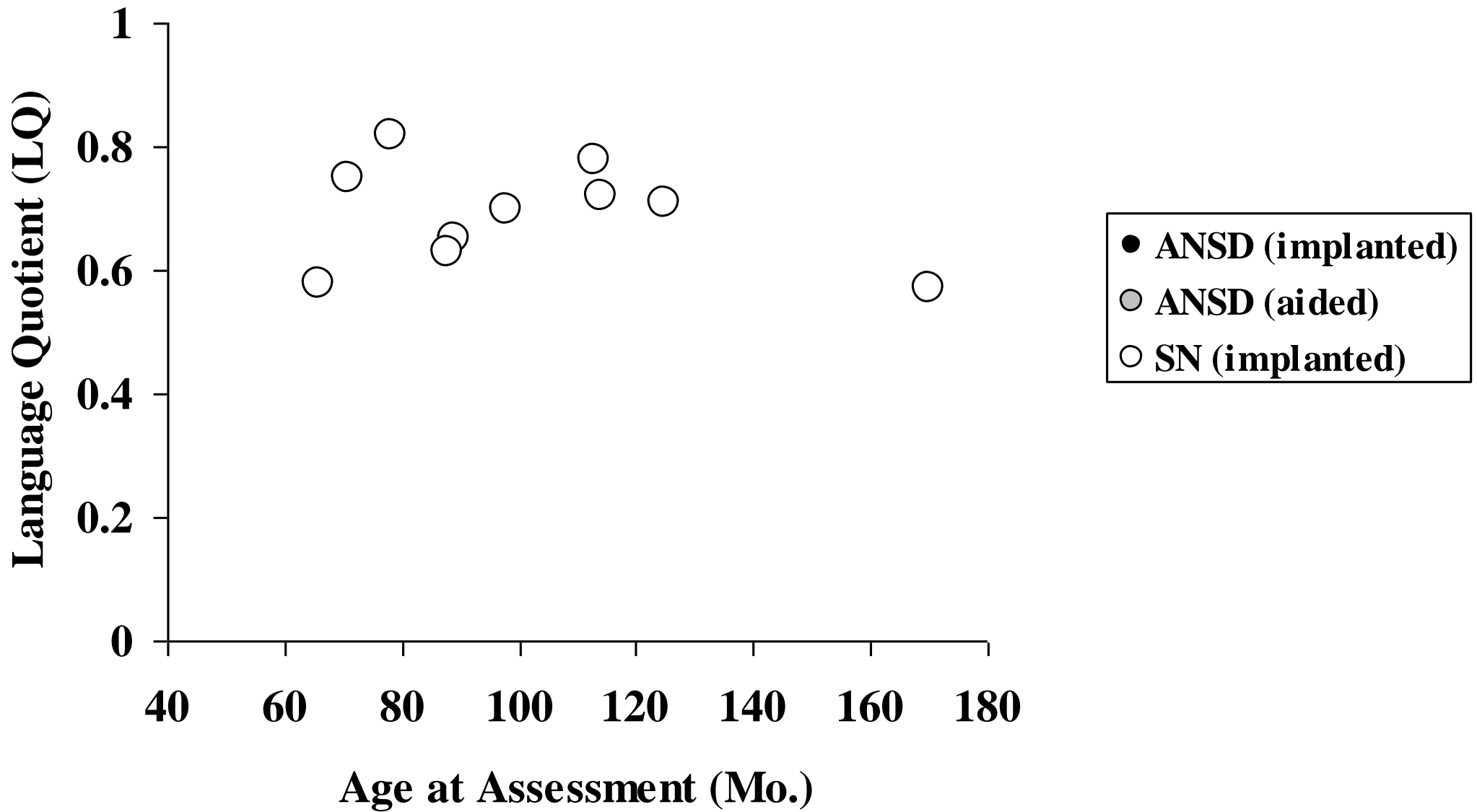
◆ Receptive Language

- **Peabody Picture Vocabulary Test (PPVT)**
- determines an “equivalent language age” based on norms for normally hearing/developing children

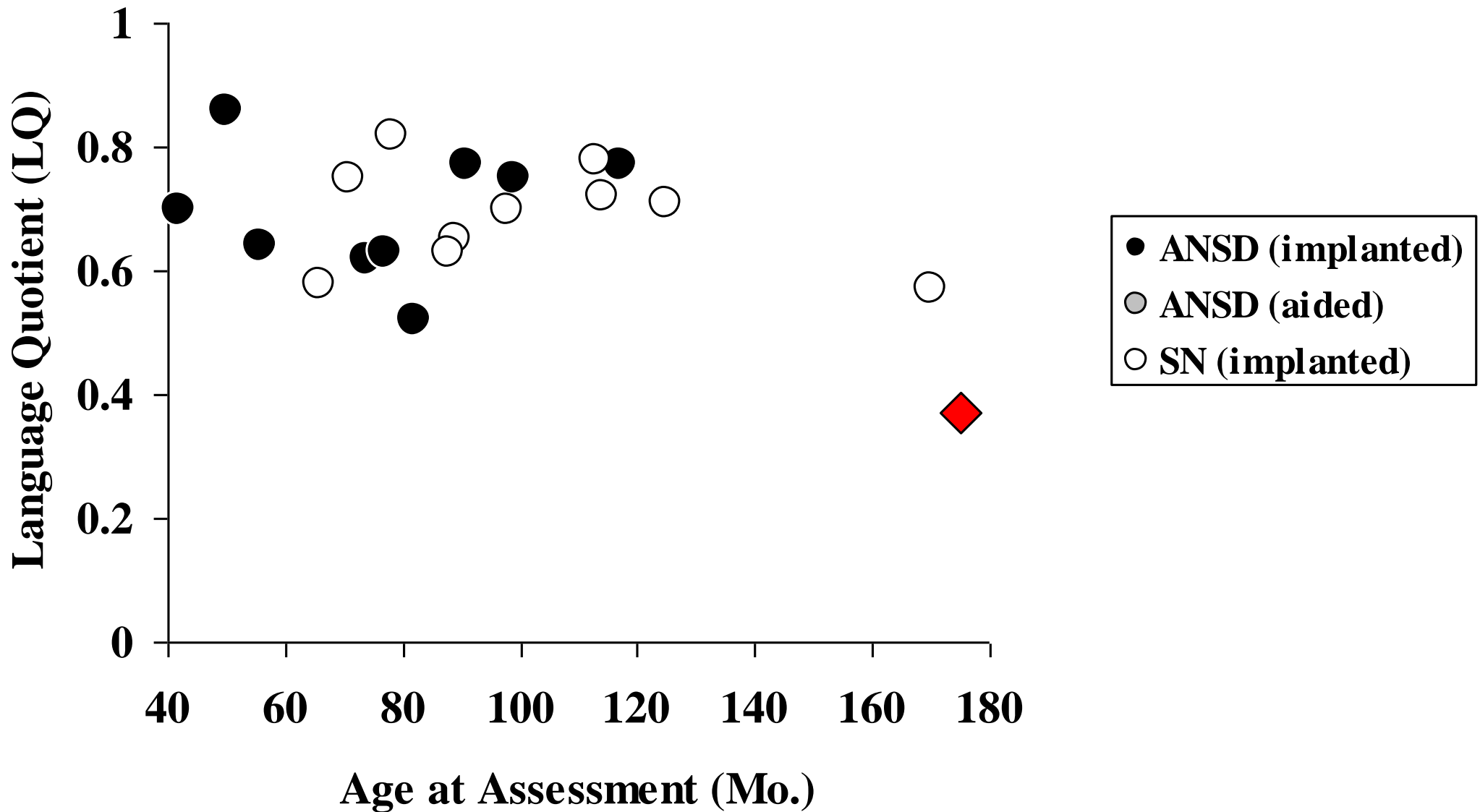
◆ Speech Production

- **Diagnostic Evaluation of Articulation and Phonology (DEAP)**
- Measures phoneme production as the child orally labels 50 pictures

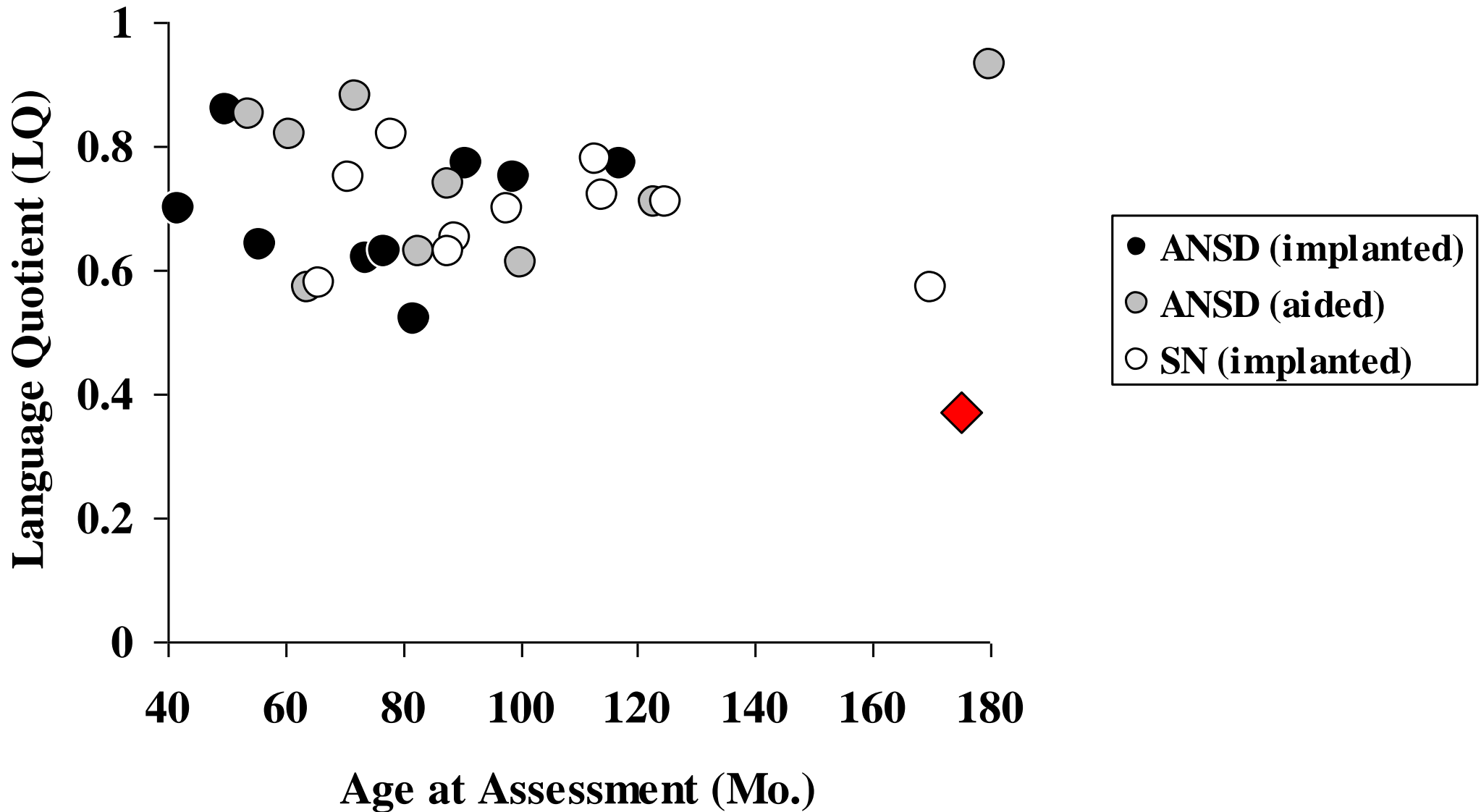
Peabody Picture Vocabulary Test



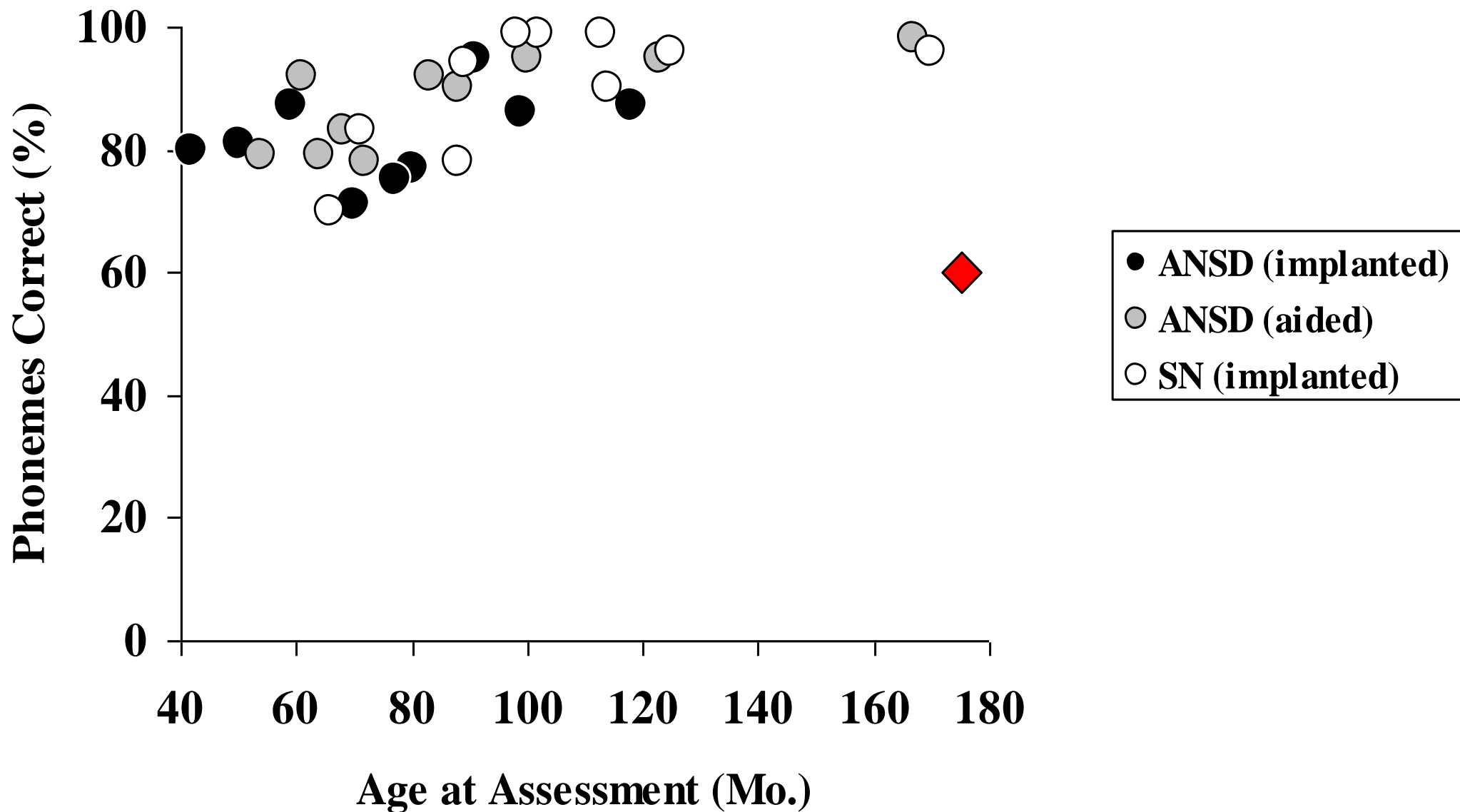
Peabody Picture Vocabulary Test



Peabody Picture Vocabulary Test



Diagnostic Evaluation of Articulation and Phonology



Long-Term Outcome Summary: CI / Amplification

◆ Speech Perception & Oral Language

- ◆ Most (but not all) implanted ANSD children showed significant post-operative improvement
- ◆ the auditory pathway disorder may not be overcome by cochlear implantation in all cases
- ◆ Some aided ANSD children performed at levels comparable to their implanted peers
- ◆ Children with ANSD should not automatically be considered CI candidates

Cochlear Implant Candidature

- ◆ Which children with ANSD should be considered for CI?
- ◆ Those who have an auditory nerve
- ◆ Those with sound detection in the severe/prof. range
 - ie. the same audiometric criteria as for children with SN-loss
- ◆ **In addition:** those children with lesser degrees of “hearing loss” but poor functional hearing

Cochlear Implant Candidature

- ◆ Assessment of Functional Hearing (adults and older children)
 - Aided speech perception testing (quiet/noise)
 - Compare performance with CI norms
- ◆ How can we predict auditory capacity in infants with ANSD?

Measuring Auditory Capacity in Infancy

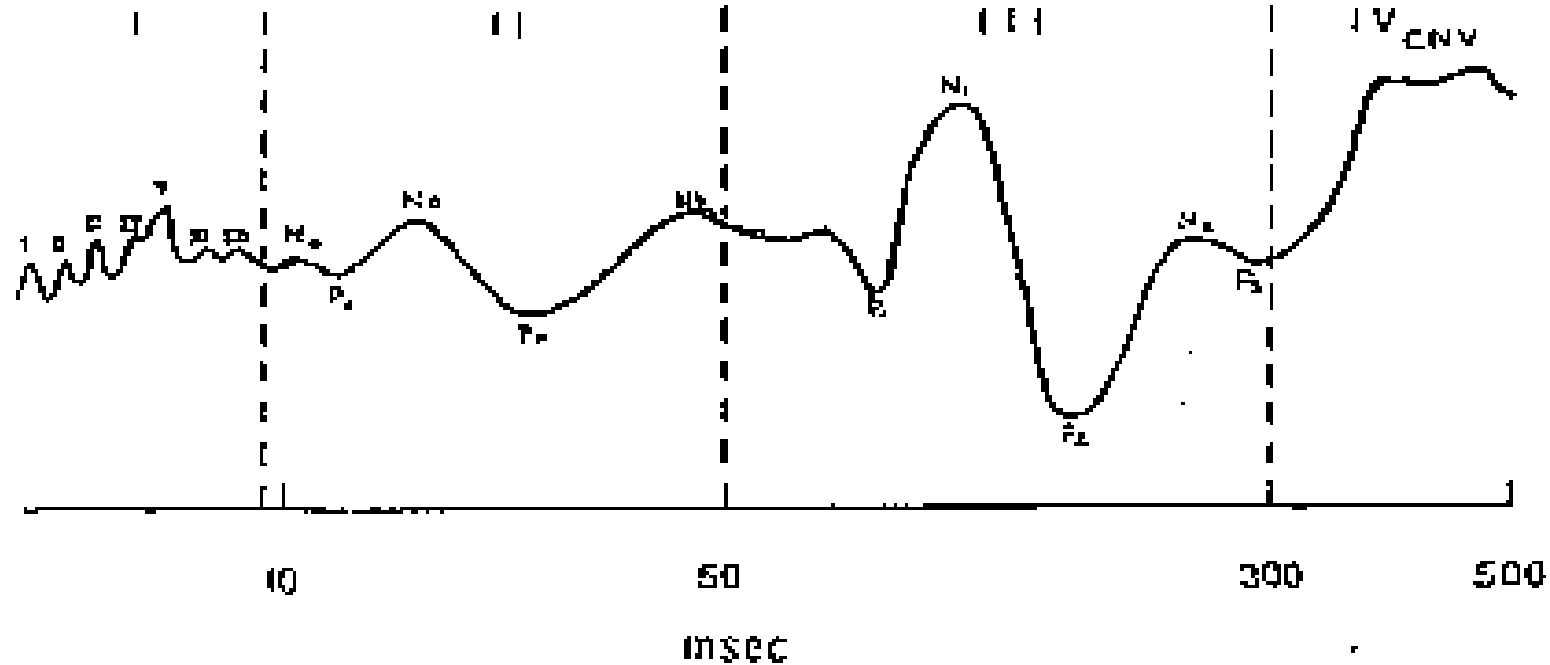
- ◆ Cortical auditory evoked potentials (CAEP)
- ◆ Auditory steady-state responses (ASSR)
- ◆ Infant psychophysics

CAEP and Speech Perception Findings in Children with Auditory Neuropathy

Gary Rance, Barbara Cone-Wesson, Julia Wunderlich
and Richard Dowell

Published: Ear & Hearing, 2002

Auditory Evoked Potentials



- ◆ Approximate sites of origin
 - 0-10 msec - brainstem
 - 10-50 msec - midbrain
 - 50-300+ msec - cortex

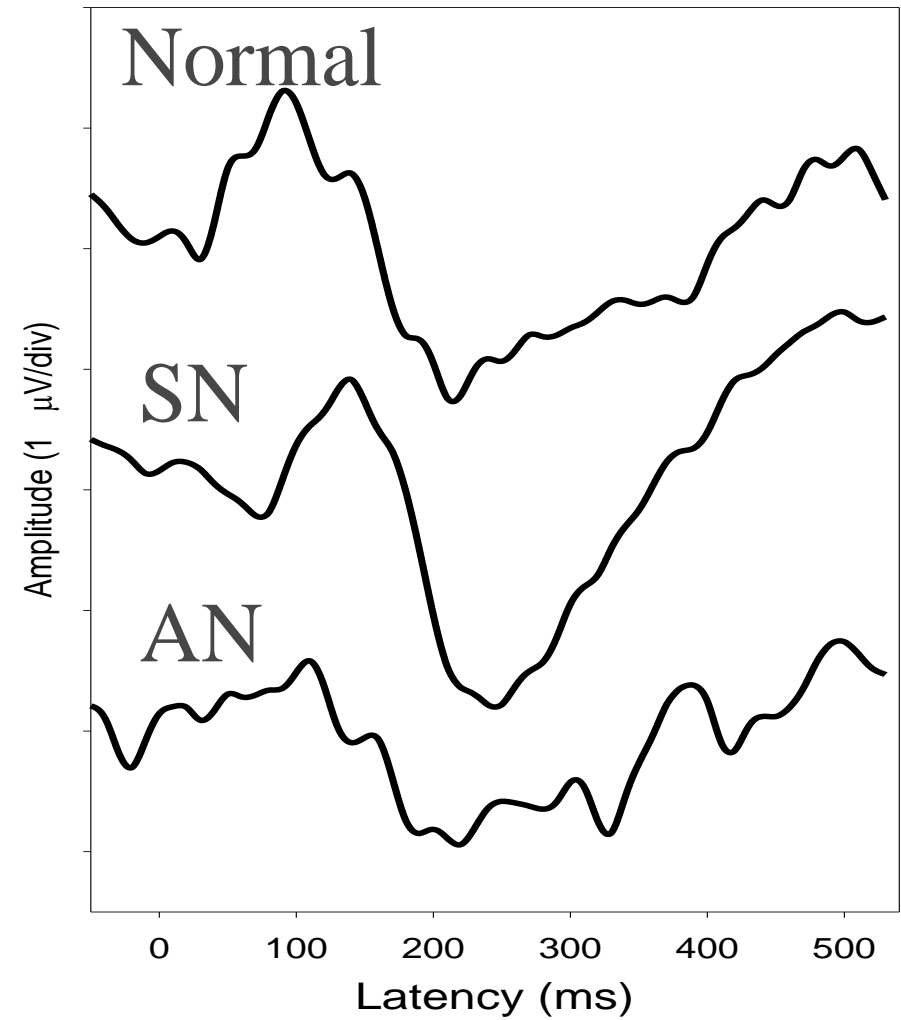
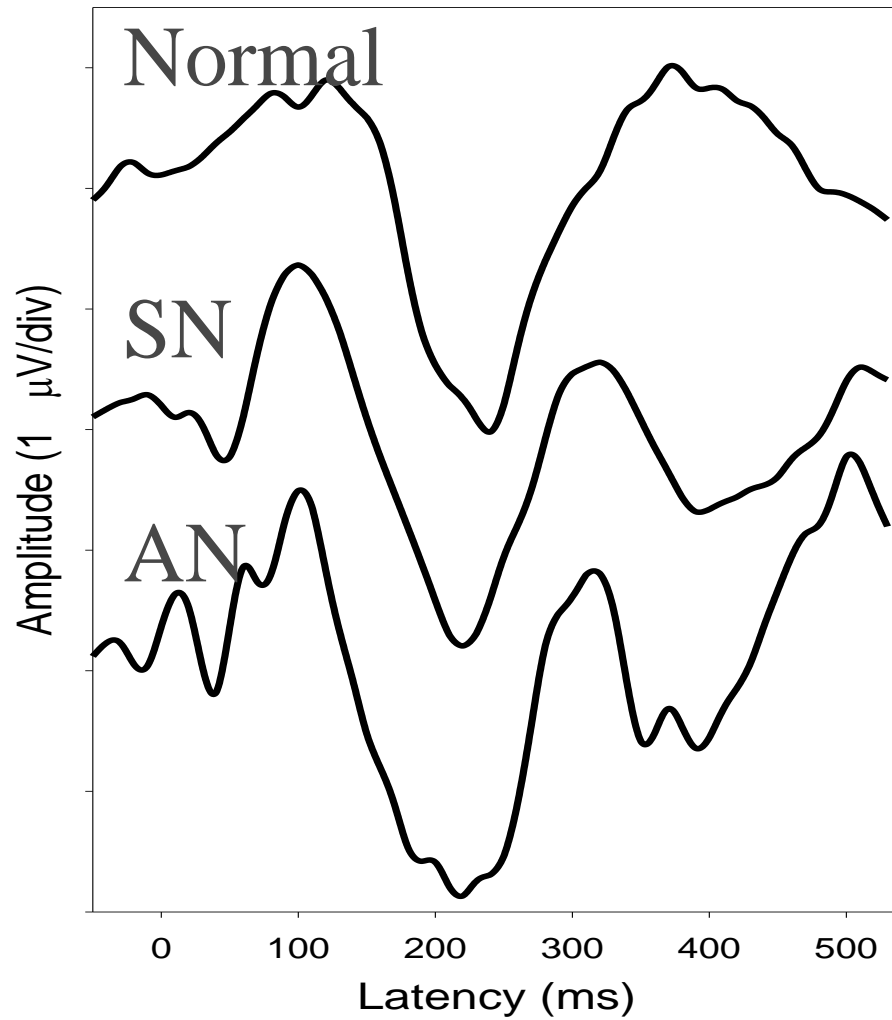
Subjects

| Category | n | Mean Age | 3 Freq. Average (dBHL) |
|----------|----|------------|------------------------|
| ANSD | 18 | 4 yrs 8 mo | 70.2 |
| SN | 18 | 5 yrs 6 mo | 76.1 |
| Normal | 6 | 4 yrs 9 mo | 10.0 |

Cortical auditory evoked potentials (group averages)

440 Hz

dad



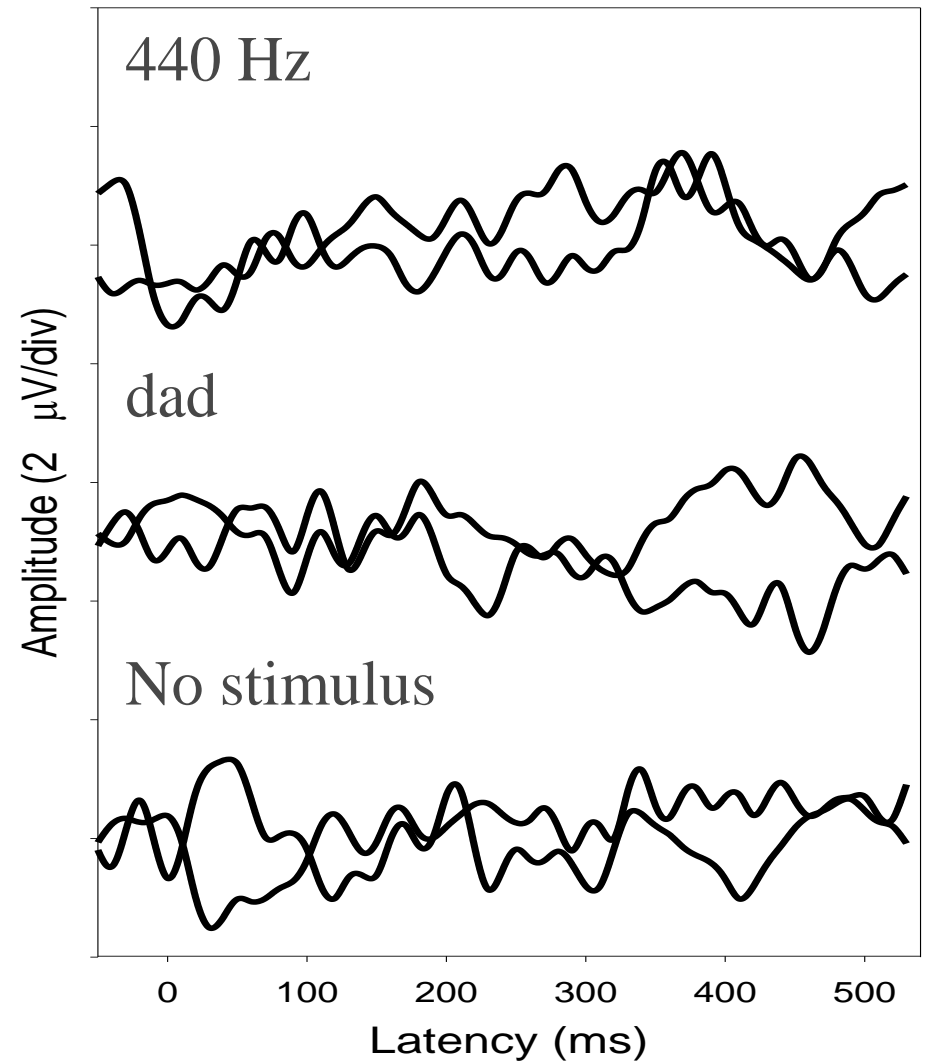
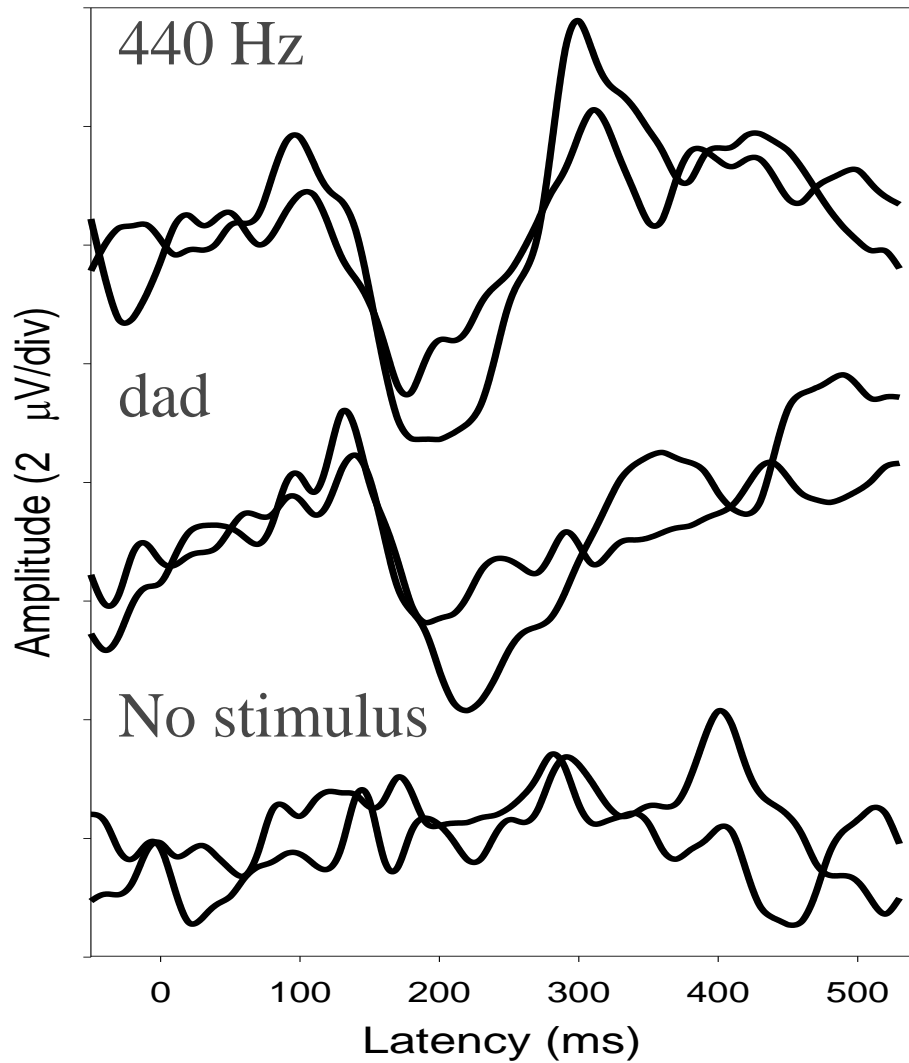
How is it possible to record CAEPs in children with ANSD?

- ◆ i.e. absent ABR but recordable cortical potentials
- ◆ Evoked potentials requiring different degrees of neural synchrony
 - ABR: disrupted by timing variations of ≥ 0.5 msec
 - CAEP: slower response/broader peaks
 - can still record with timing variations up to 20 msec

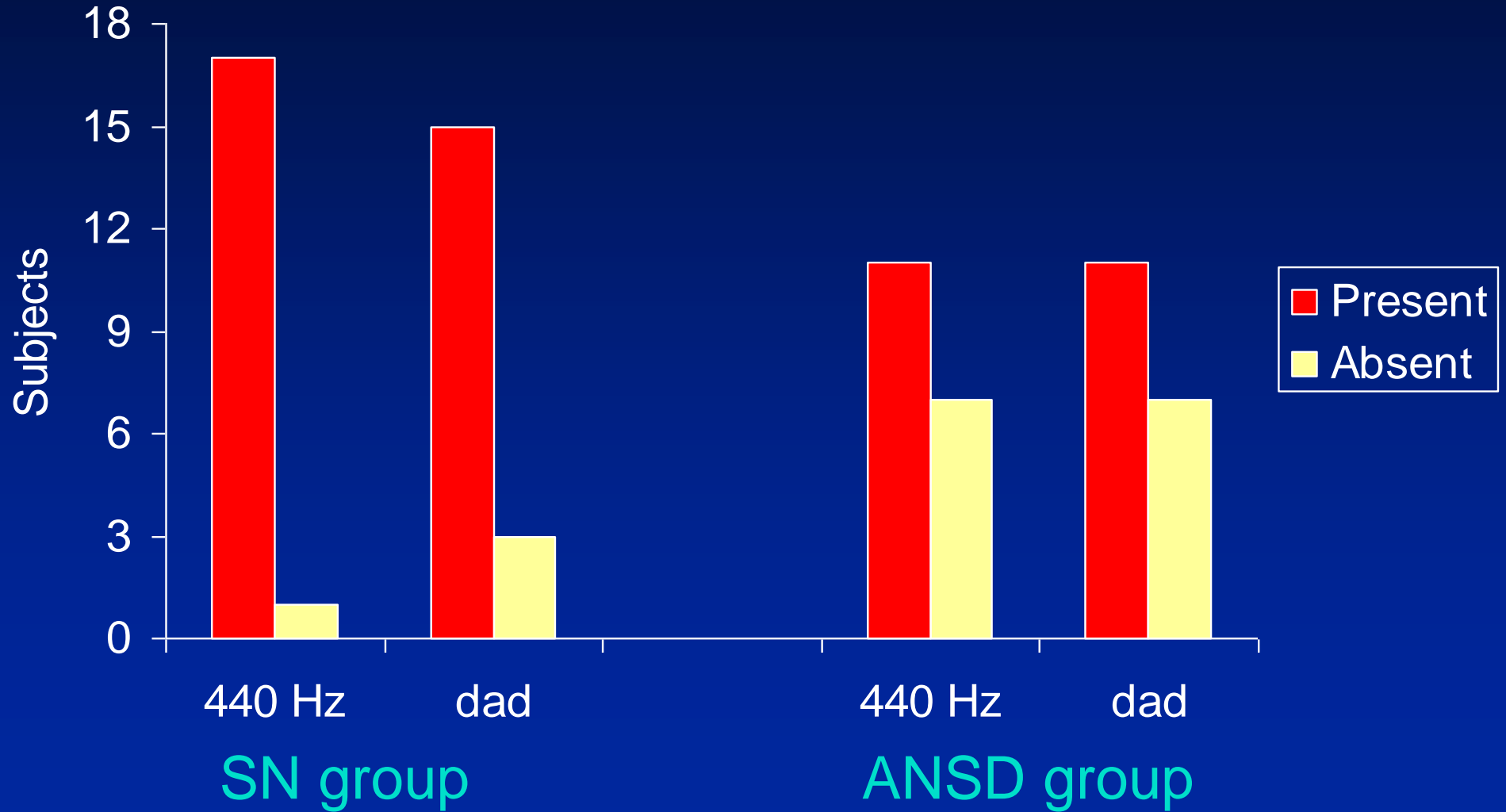
Cortical auditory evoked potentials (ANSD examples)

CR

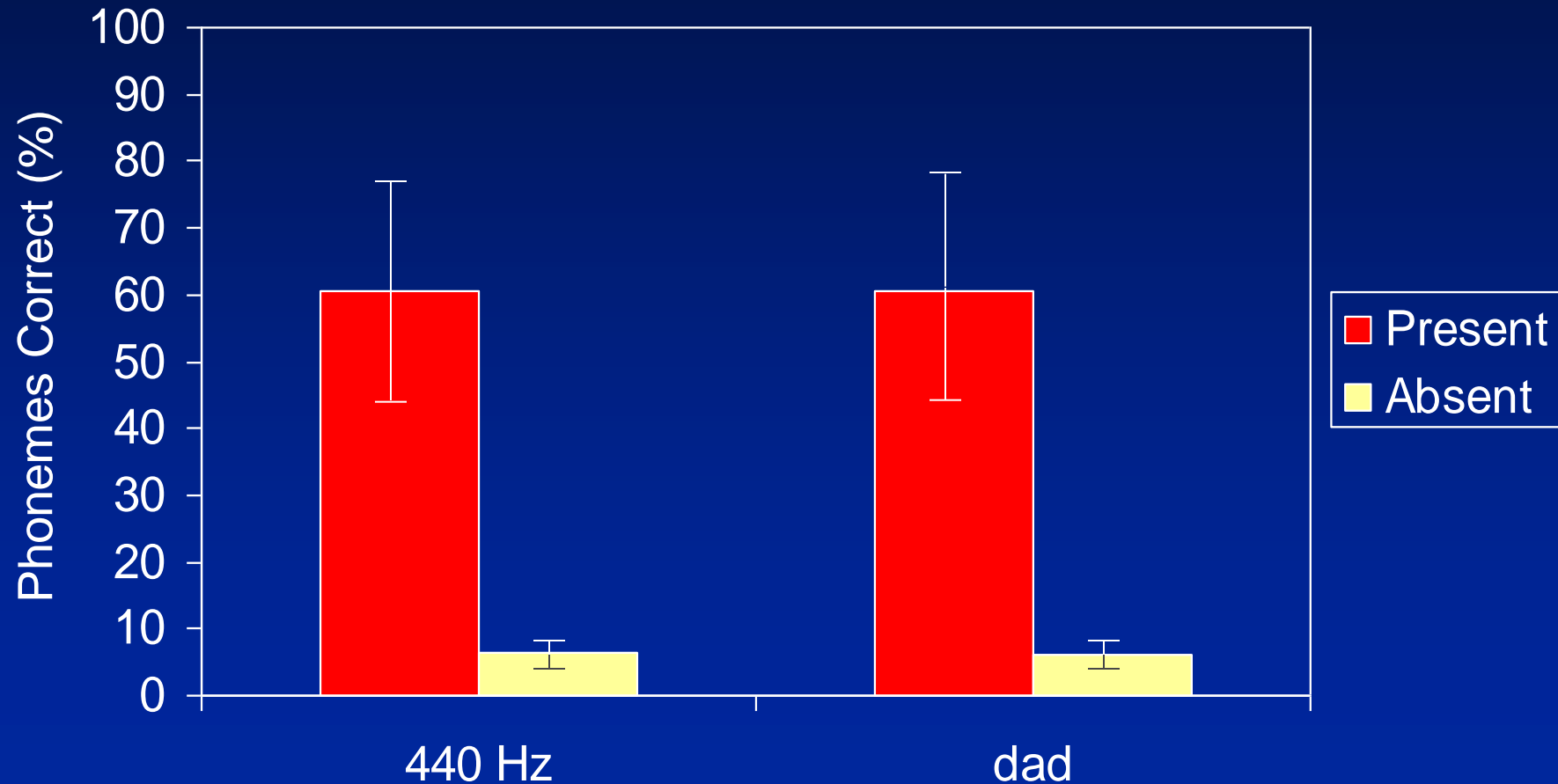
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CAEP Presence/Absence



Aided Speech Score vs CAEP result (ANSD subjects)

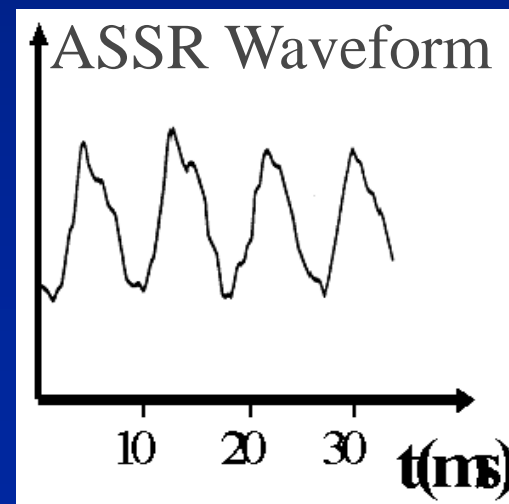
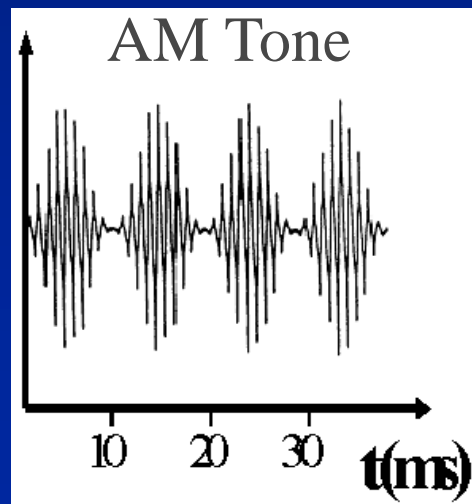


Clinical Implications

- ◆ Auditory cortex is where “hearing” actually occurs
- ◆ CAEPs offer insights into the integrity of the neural signal at this level
- ◆ Current Limitations
 - 2002 study involved school-aged children
 - yet to be established if CAEPs in babies can predict subsequent perceptual ability

ASSR as a Measure of Temporal Processing

- ◆ Well established relationship between the processing of timing cues and speech understanding
- ◆ One psychophysical measure of temporal resolution is based upon perception of rapid amplitude modulations
- ◆ The stimulus typically used to elicit the ASSR is also an amplitude modulated tone



Study currently underway...

◆ Adults/older children:

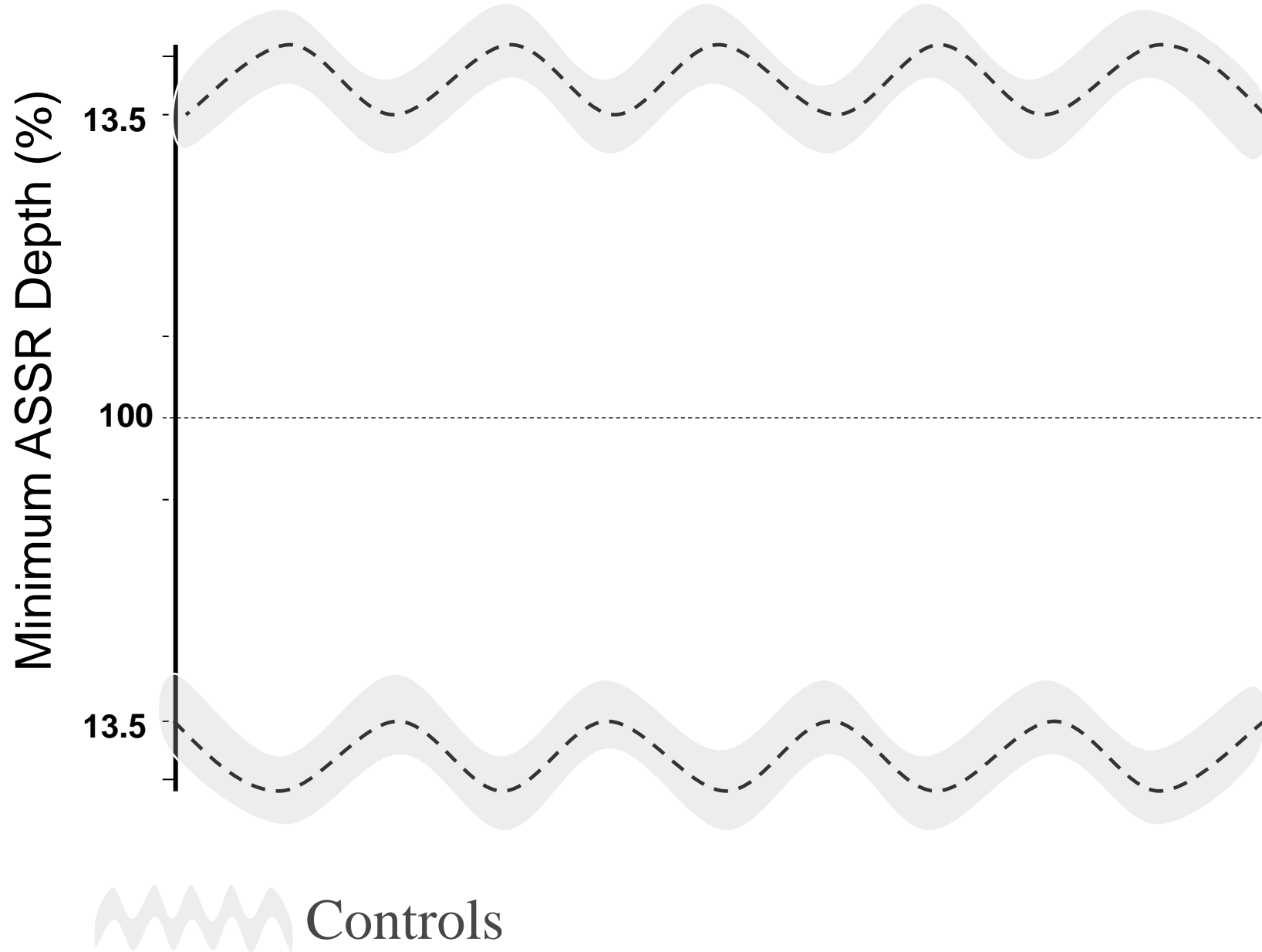
- Measuring the smallest perceptible modulation depth (psychophysics)
- Smallest modulation depth that can elicit a recordable ASSR

◆ Normal babies:

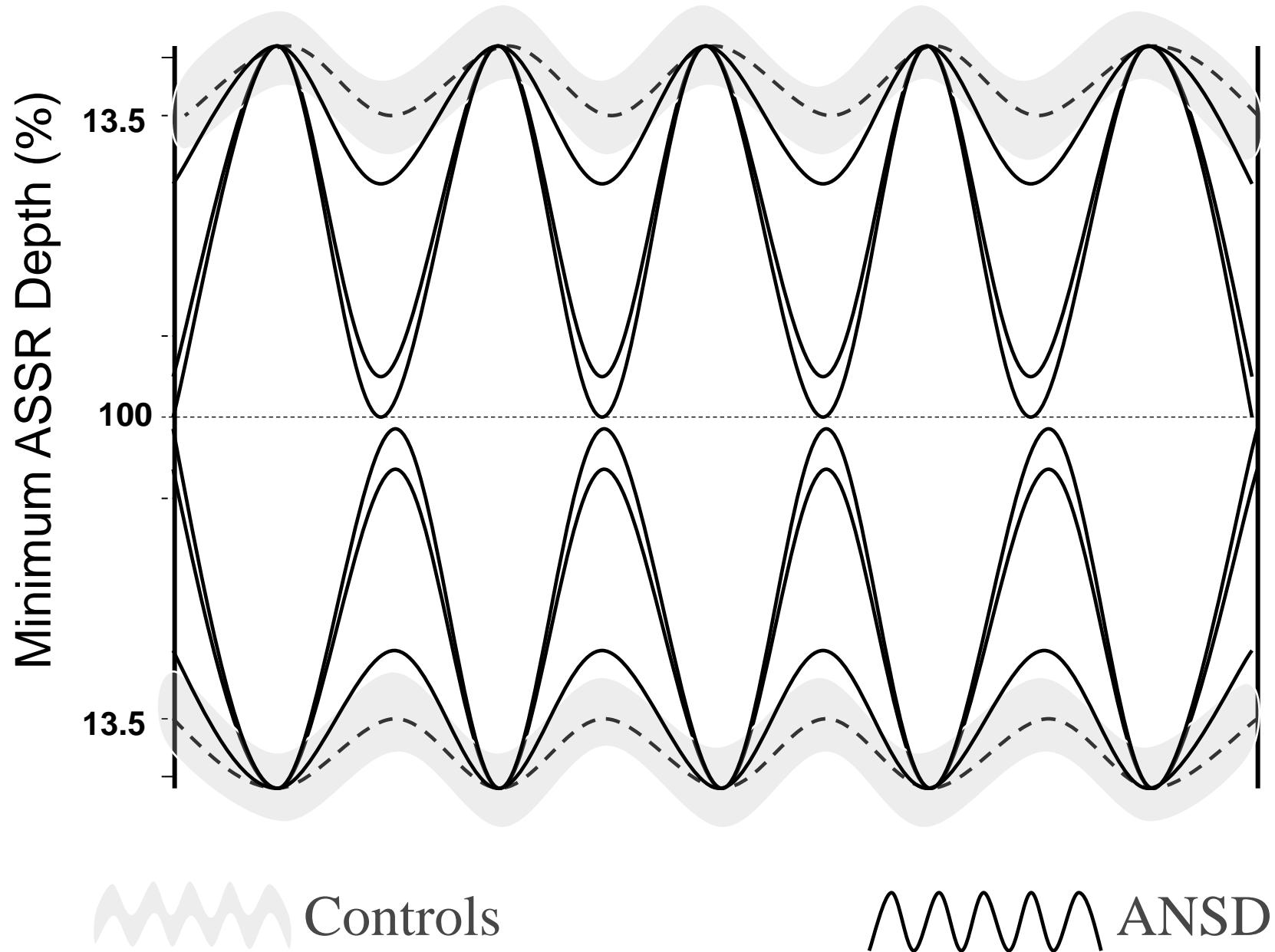
- Smallest modulation depth that can elicit a recordable ASSR

◆ ANSD babies: (N=3)

Infant Data (June 2011)



Infant Data (June 2011)



Possible Clinical Implication

- ◆ ASSR may offer an objective measure of temporal processing ability
- ◆ Temporal processing correlated with long-term speech perception ability and hearing aid outcomes

Infant Psychophysics

- ◆ Adults: “3 alternative forced choice”

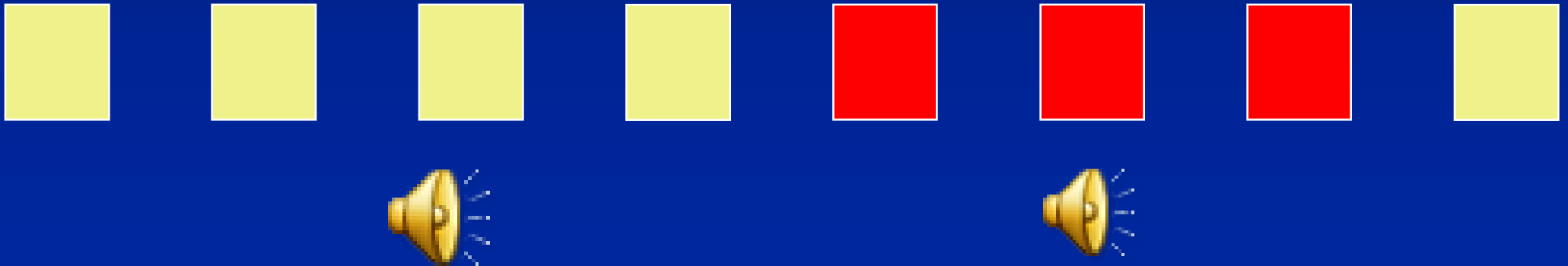


- ◆ “Which of these sounds is different?”
- ◆ Inappropriate for infants
- ◆ Can use a modified stimulus/response task (for children old enough to be conditioned ≥ 6 months)

Rance et al (2004)

◆ Psychophysical procedure

- Target stimuli (3) inserted into a sequence of background noise bursts
- Child conditioned to respond to the “difference”



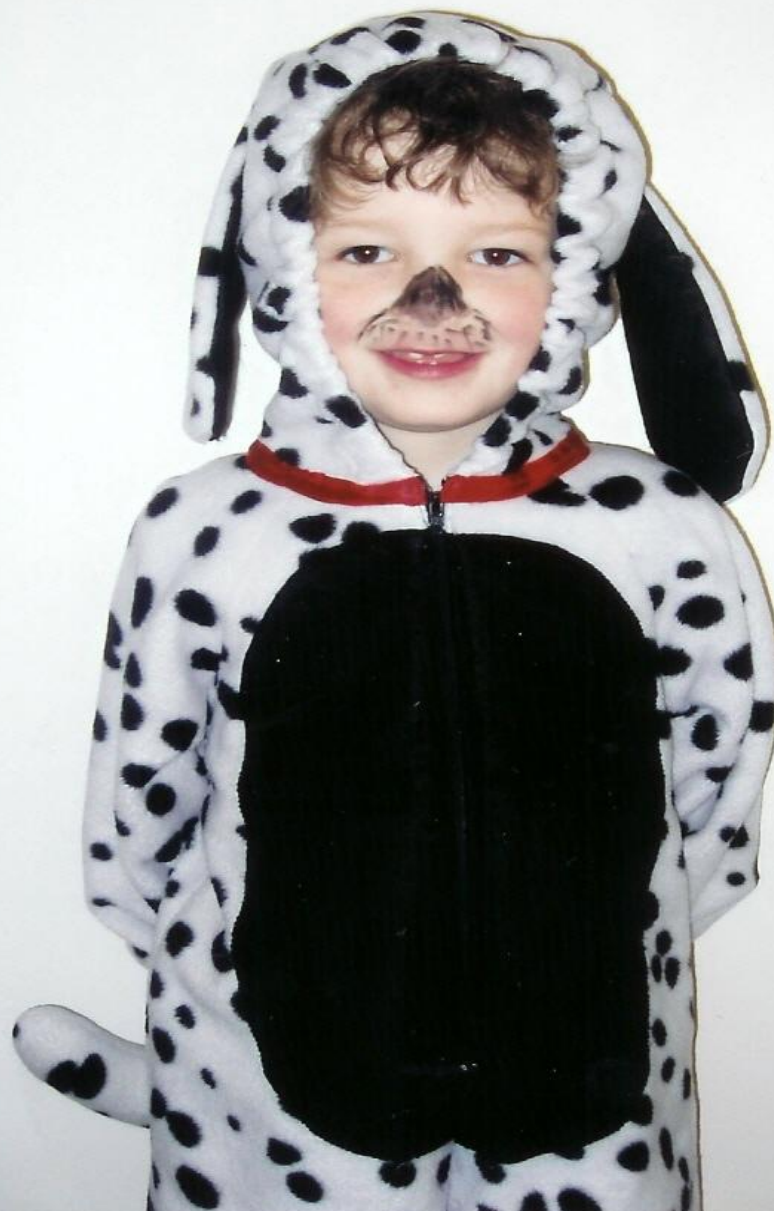




Possible Clinical Implication

- ◆ Infant psychophysics has the potential to measure temporal processing in babies old enough to be conditioned
(Developmental Age: ≥ 6 months)
- ◆ Possible early predictor of long-term outcomes

ANSD Case Study



History

Referral: Diagnostic assessment
(44 weeks post-conceptual age)

Pregnancy/birth:

- *born at 29 weeks

- * intraventricular haemorrhage

- *NICU – 2 weeks SCU – 6 weeks

- *hyperbilirubinaemia

- *still on O₂ at assessment

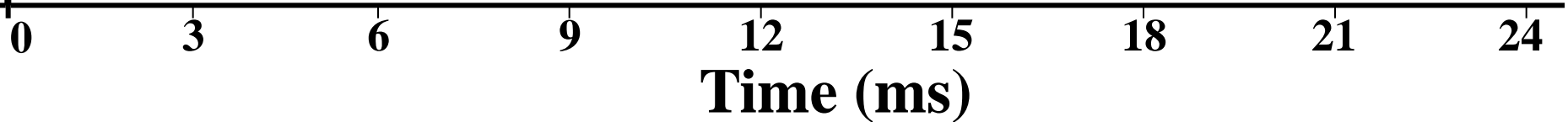
44 Weeks PCA: Air Conduction ABR

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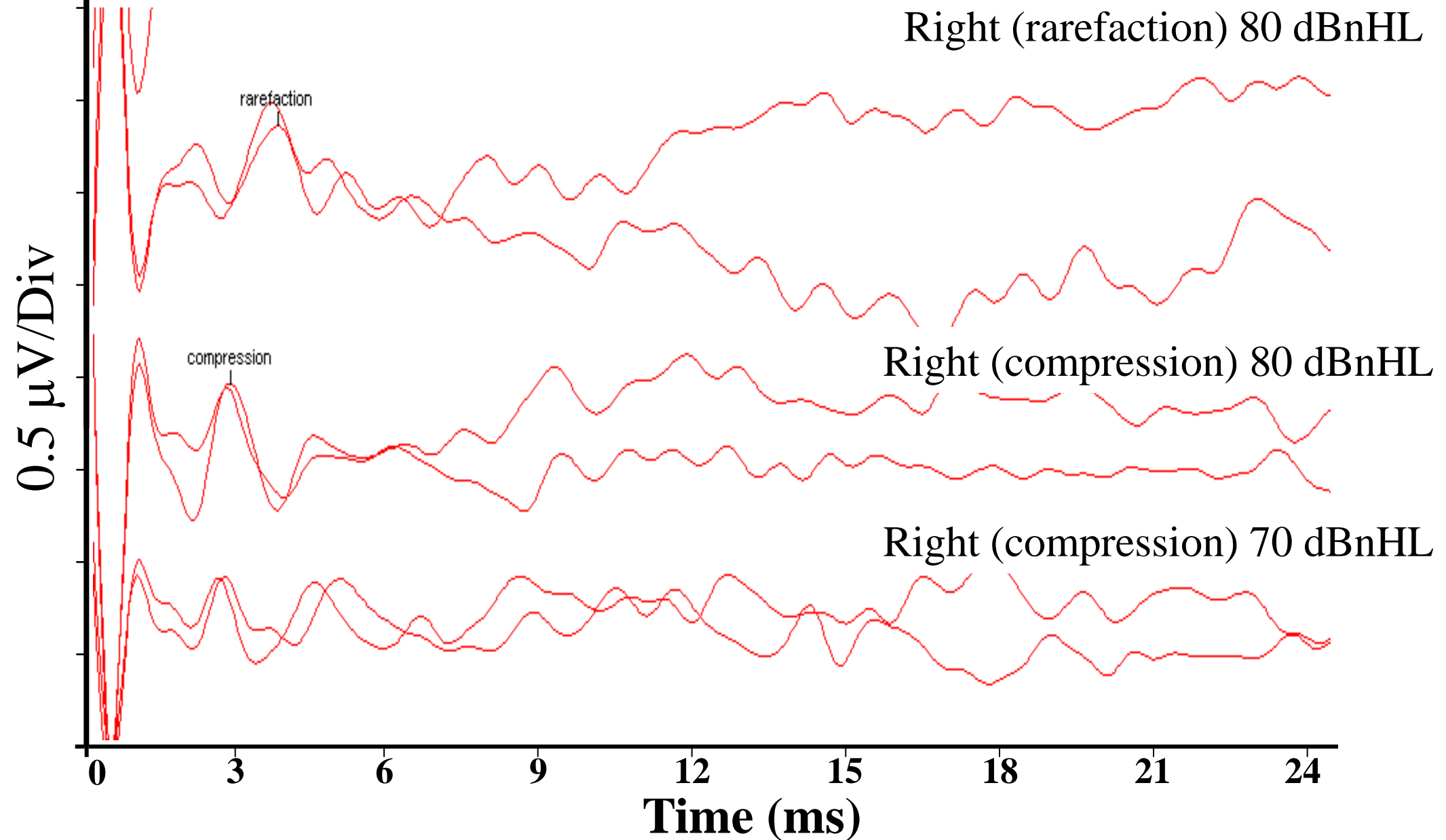
Left: Alt. Clicks 60 dBnHL

Left: Alt Clicks 100 dBnHL

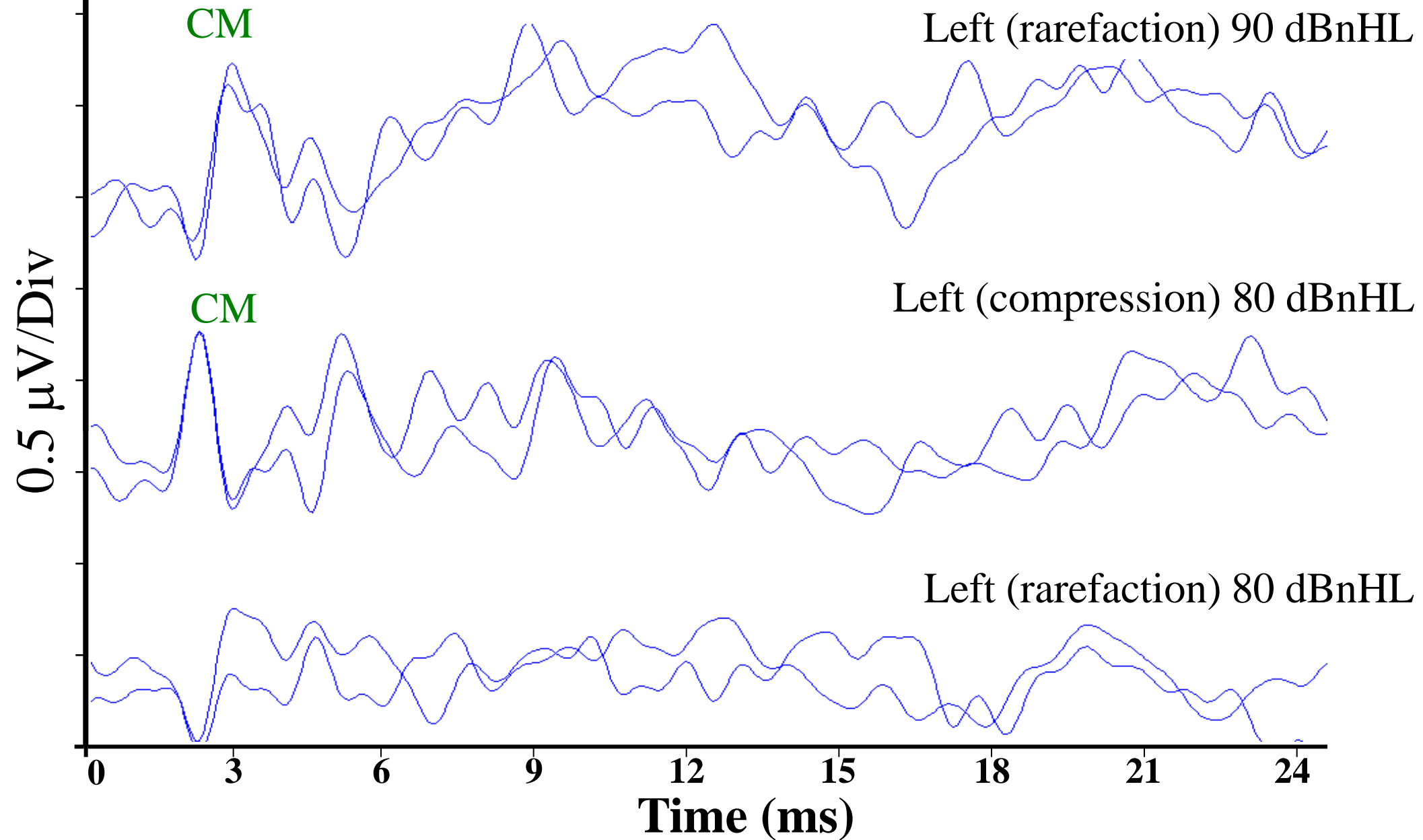
Right: Alt. Clicks 100 dBnHL



44 Weeks PCA: Air Conduction ABR

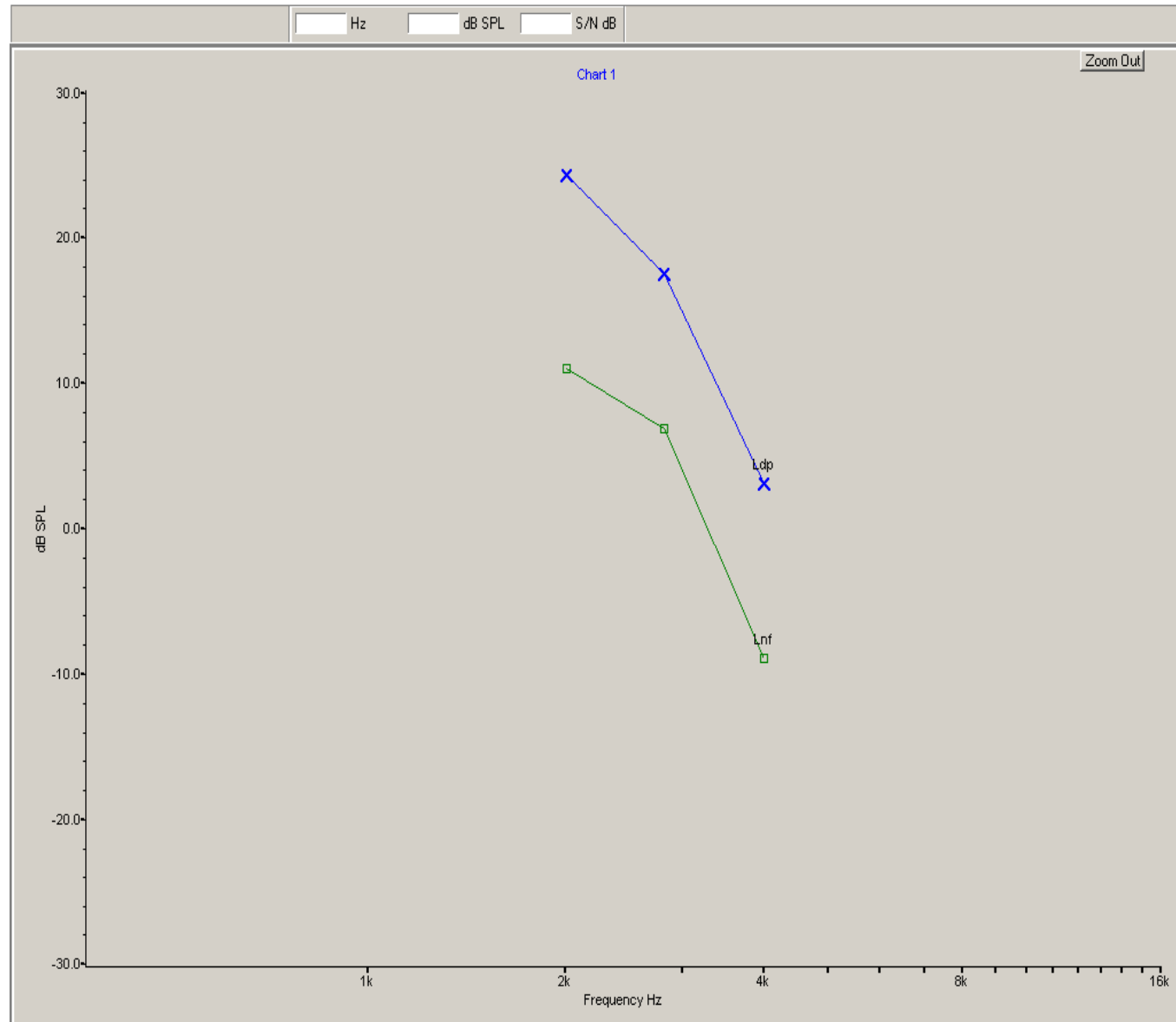


44 Weeks PCA: Air Conduction ABR



Distortion Product Otoacoustic Emissions

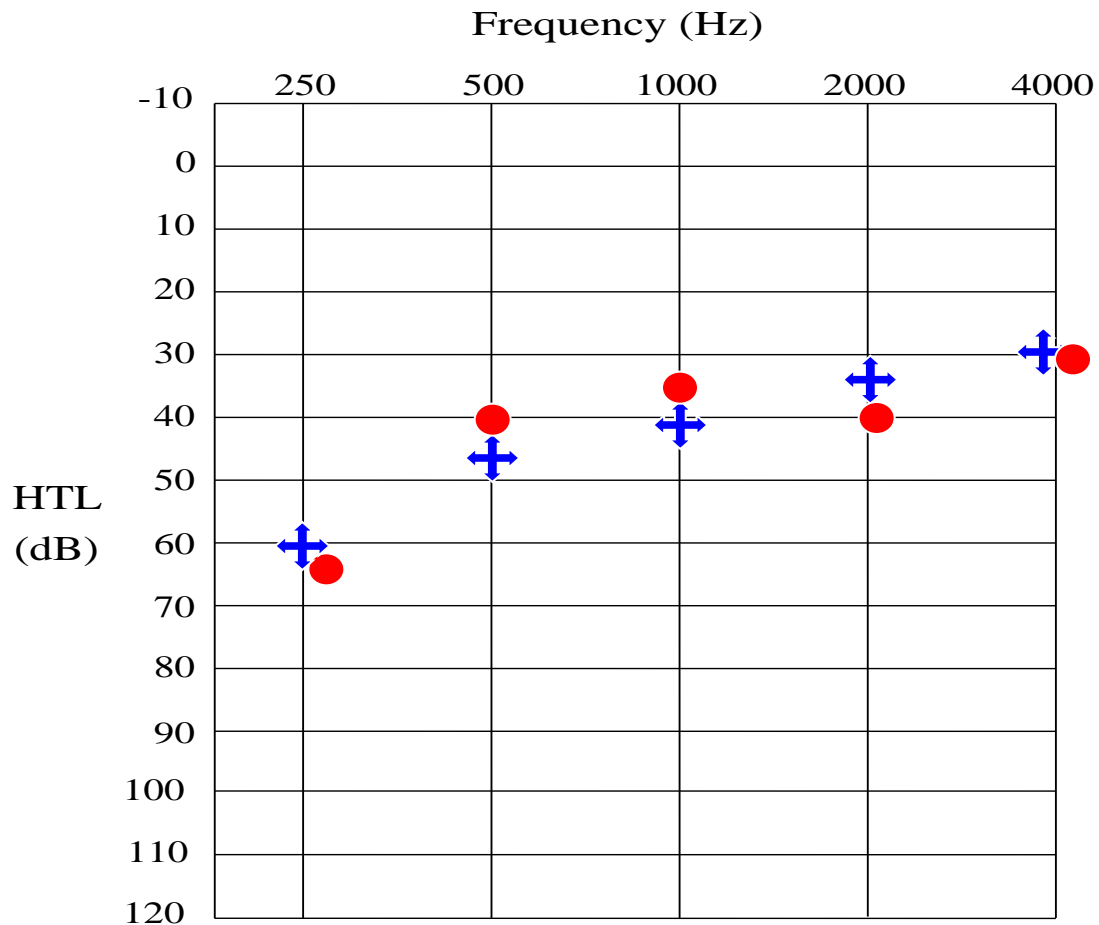
◆ Present bilaterally



Management

- ◆ Otologist referral
- ◆ Paediatric Neurologist
- ◆ Early Intervention Centre
- ◆ Australian Hearing
 - No immediate aid fitting
 - Low gain aids fit bilaterally at 5 months
 - *based upon mildly elevated *Behavioral Observation Audiometry (BOA)* responses

Hearing Thresholds at 8 months

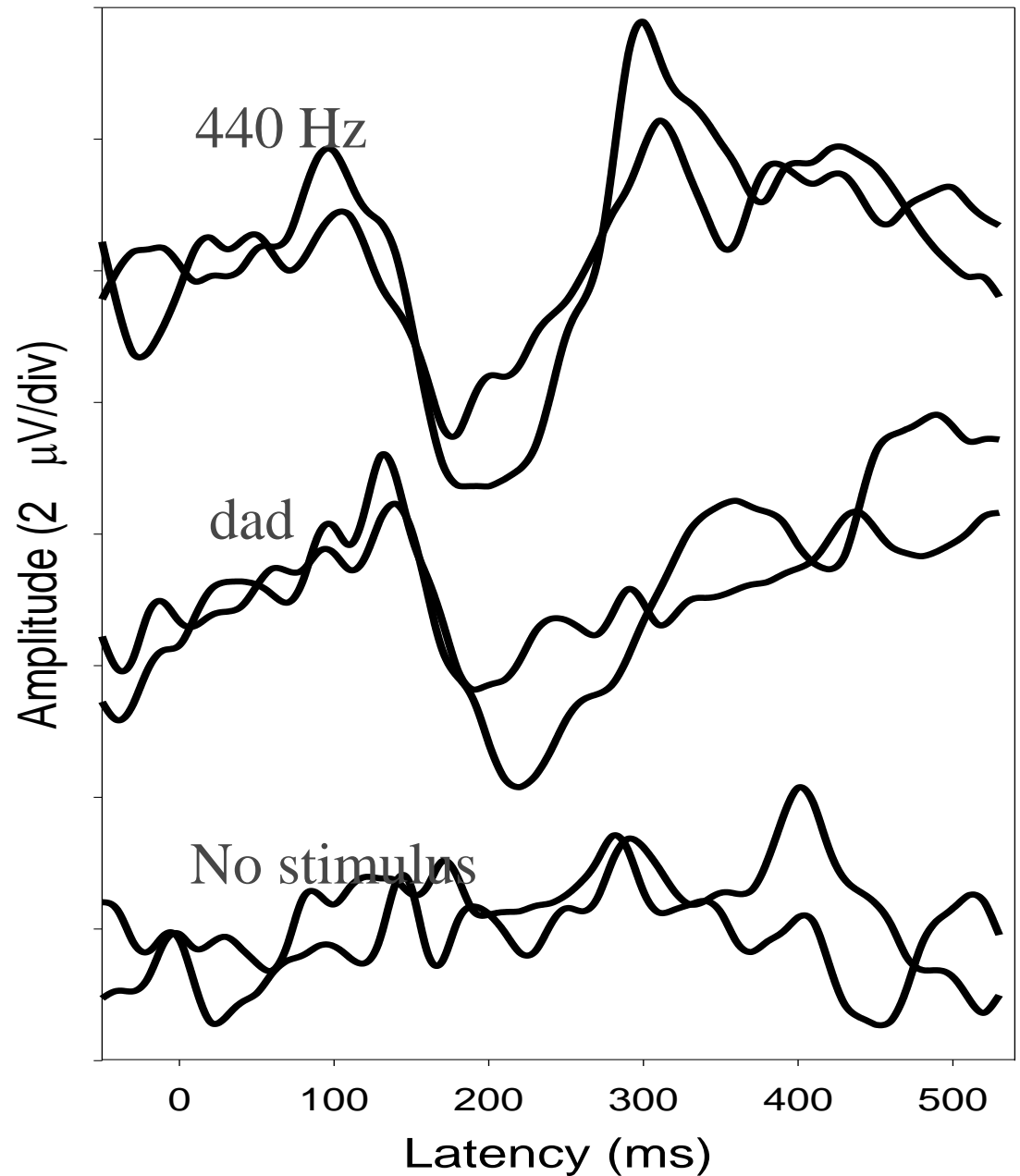


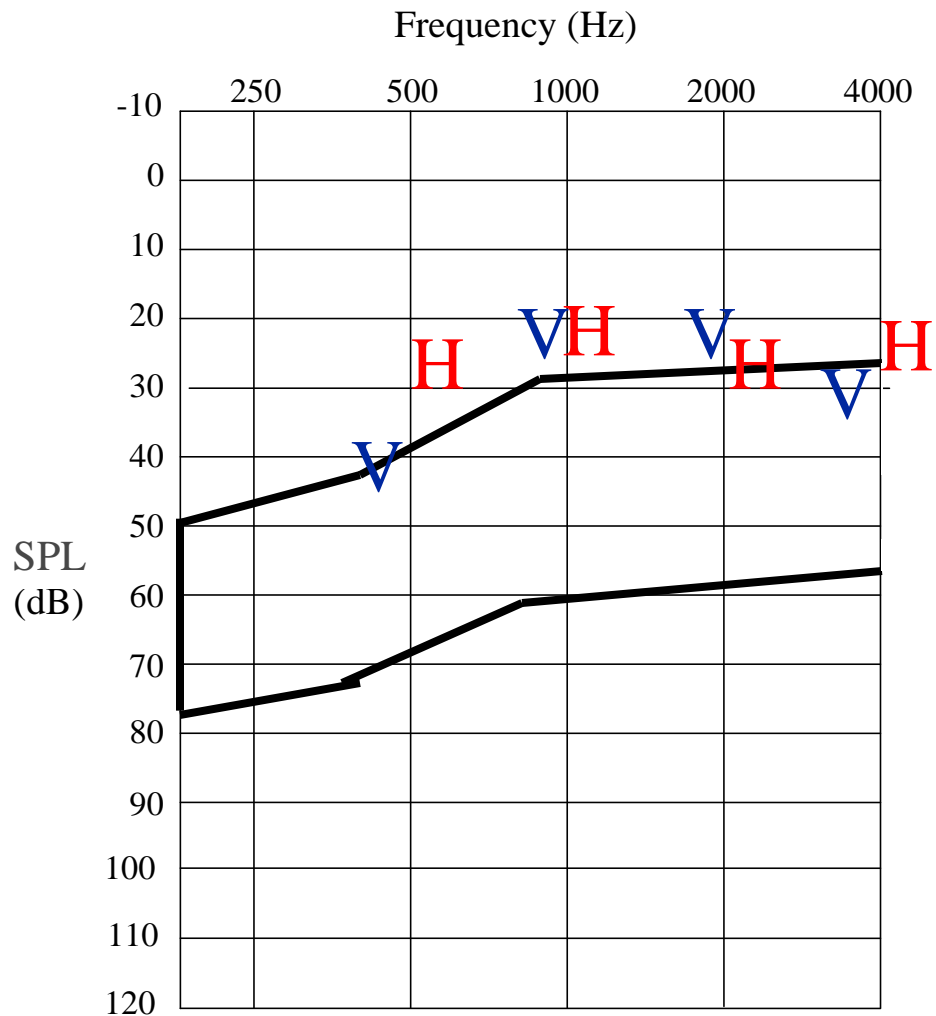
*mild/moderate
hearing loss

⊕ Behave. (left)

● Behave. (right)

CAEP assessment
at 8 months
(corrected age)





Aided thresholds at 11 months

- Threshold improvements consistent with amplification
- Good access to 70 dB SPL speech spectrum

Educational Management

- ◆ Taralye Early Intervention Centre
- ◆ Oral/aural education program
- ◆ Progress (to 3yrs of age):
 - Consistent hearing aid user
 - Good listening skills (generally)
[occasional episodes of reduced responsiveness]
 - Good speech and language development



Speech Perception: 5 years

◆ CNC words (phoneme score)

| | | |
|-------------|-----|----------------|
| Quiet: | 63% | (Mean CI: 73%) |
| +10 dB S/N: | 52% | (Mean CI: 58%) |
| +5 dB S/N: | 47% | (Mean CI: 41%) |
| 0 dB S/N: | 9% | |



Progress at 6 years

- ◆ Pretending to be the teacher
- ◆ Carrying out the
Peabody Picture Vocabulary Test (PPVT)



ANSD Case Study

- ◆ Why might this child have progressed with amplification when others with ANSD have not?
 - Lesser degree of temporal disruption
 - Good aided access to speech sounds
 - Consistent aid user
 - Amplified signal from young age

Summary

- ◆ Long-term outcomes for children with ANSD are highly variable
- ◆ CI beneficial in **most** cases
- ◆ Some children with ANSD can do well with conventional hearing aids
- ◆ Diagnosing this form of hearing loss is straightforward
- ◆ Developing techniques that can measure auditory capacity (in infancy) is the next challenge...

Thankyou.

