An Update on Auditory Neuropathy Spectrum Disorder in Children

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Sound Foundations Through Early Amplification Meeting, Chicago, Dec 2013

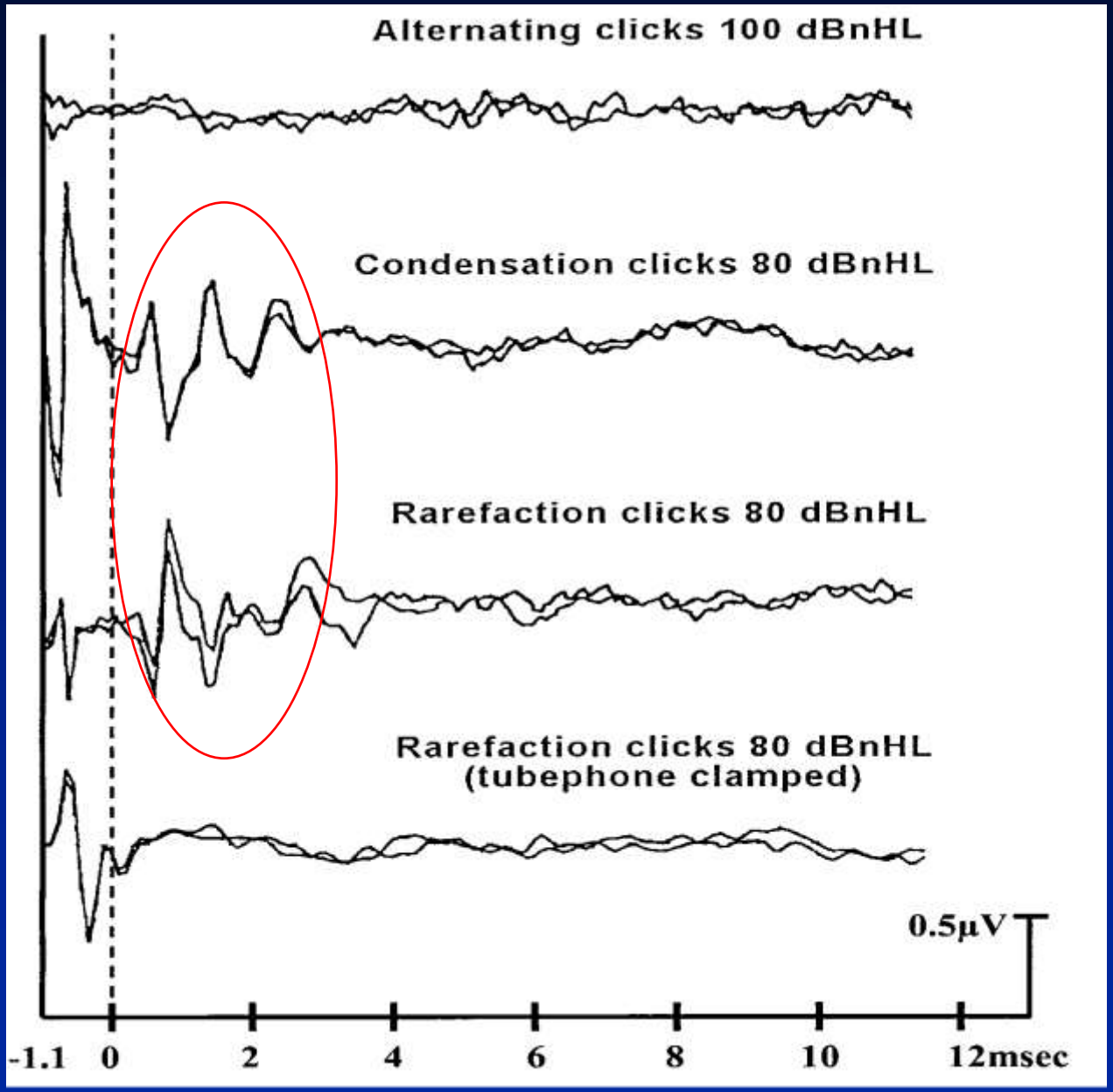
Overview

- Auditory neuropathy spectrum disorder (ANSD) often described as "a newly identified form of hg loss"
- 1984: Kraus et al. presented children with inconsistency between auditory evoked potential and audiometric results
- 1991: Starr et al. described ANSD in an adolescent subject
- 1999: Rance et al. presented a group of infants with ANSD pattern
- 1671 scientific papers
- Today's presentation
  - Provide an overview of what we have learnt
  - Consider some of the current clinical challenges
  - Research questions for the future

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) with absent or severely disrupted auditory neural responses (ABR)

CM /ABR assessment for a 3 mo old with ANSD



Paediatric ANSD

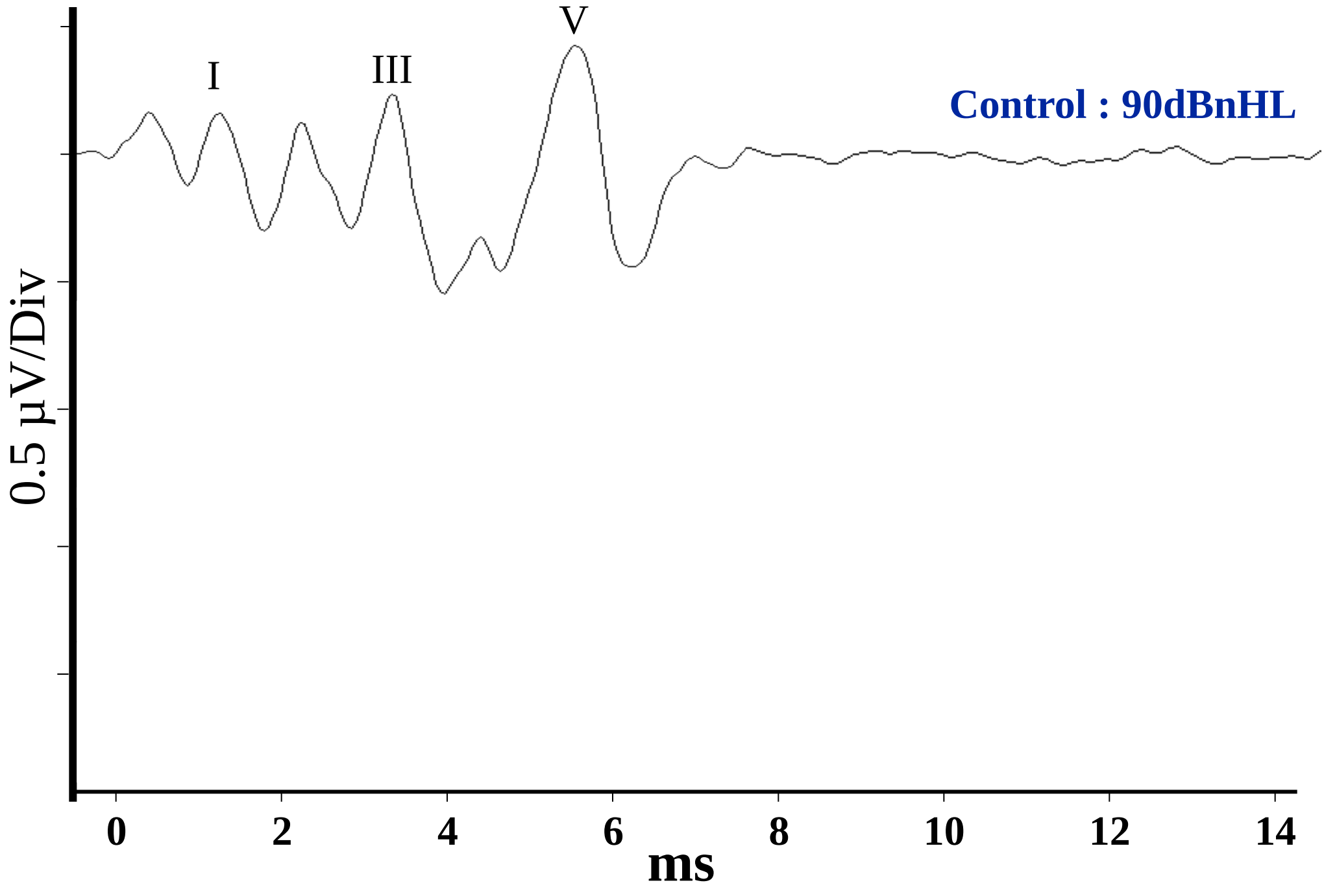
- Congenital/Perinatal
  - » anoxia
  - » hyperbilirubinaemia
- Progressive
  - – Neurodegenerative disease
    - » Onset physical symptoms usually in adolescence
    - » Identified earlier (routinely see 1-4 yr olds in clinic)
    - » Hearing difficulties often the first presenting symptom

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
  - tumour

Axonal & Demyelinating ANSD

- Charcot-Marie-Tooth Syndrome
- Progressive genetic disorder characterized by loss of muscle tissue and touch sensation (motor & sensory neuropathies)
- CMT1: demyelinating process
- CMT2: axonal loss
- Later stages see absent ABR but early in the disease course responses still present


I
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Control : 90dBnHL
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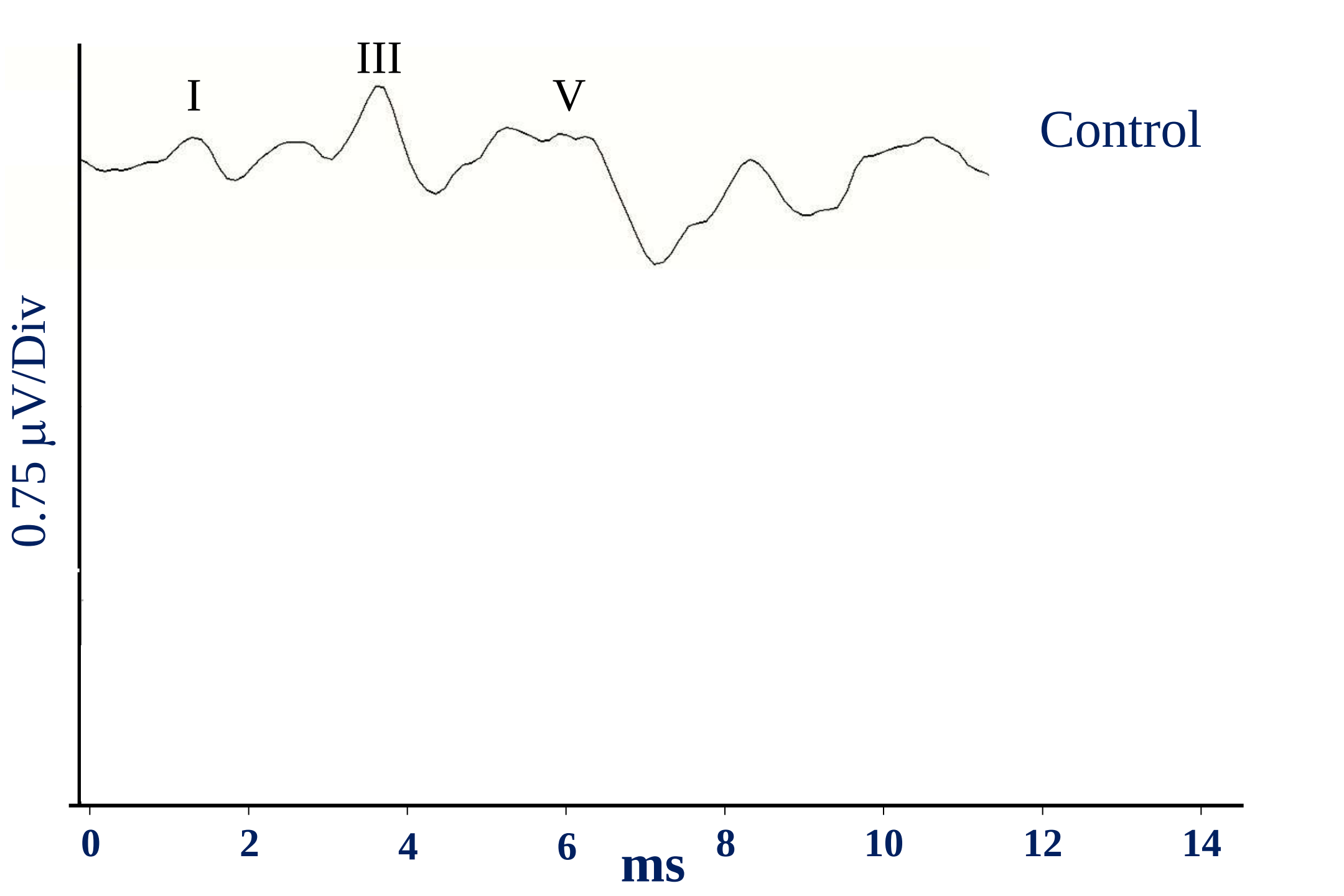
ms

ANSD Clinical Profile

- Prevalence
  - Congenital/Perinatal ANSD
    - » 1 in 800-1000 children show permanent hearing loss
    - » 5-15% of those present with the ANSD result pattern
  - Neurodegenerative disease
    - » List of diseases associated with ANSD growing
      - FRDA/CMT/LHON/ADOA...
    - » relatively rare
    - » Friedreich ataxia most common: ≈ 1 in 20,000
      - All show ANSD at some point in the disease course


I
III
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Control
0.75 µV/Div
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ms

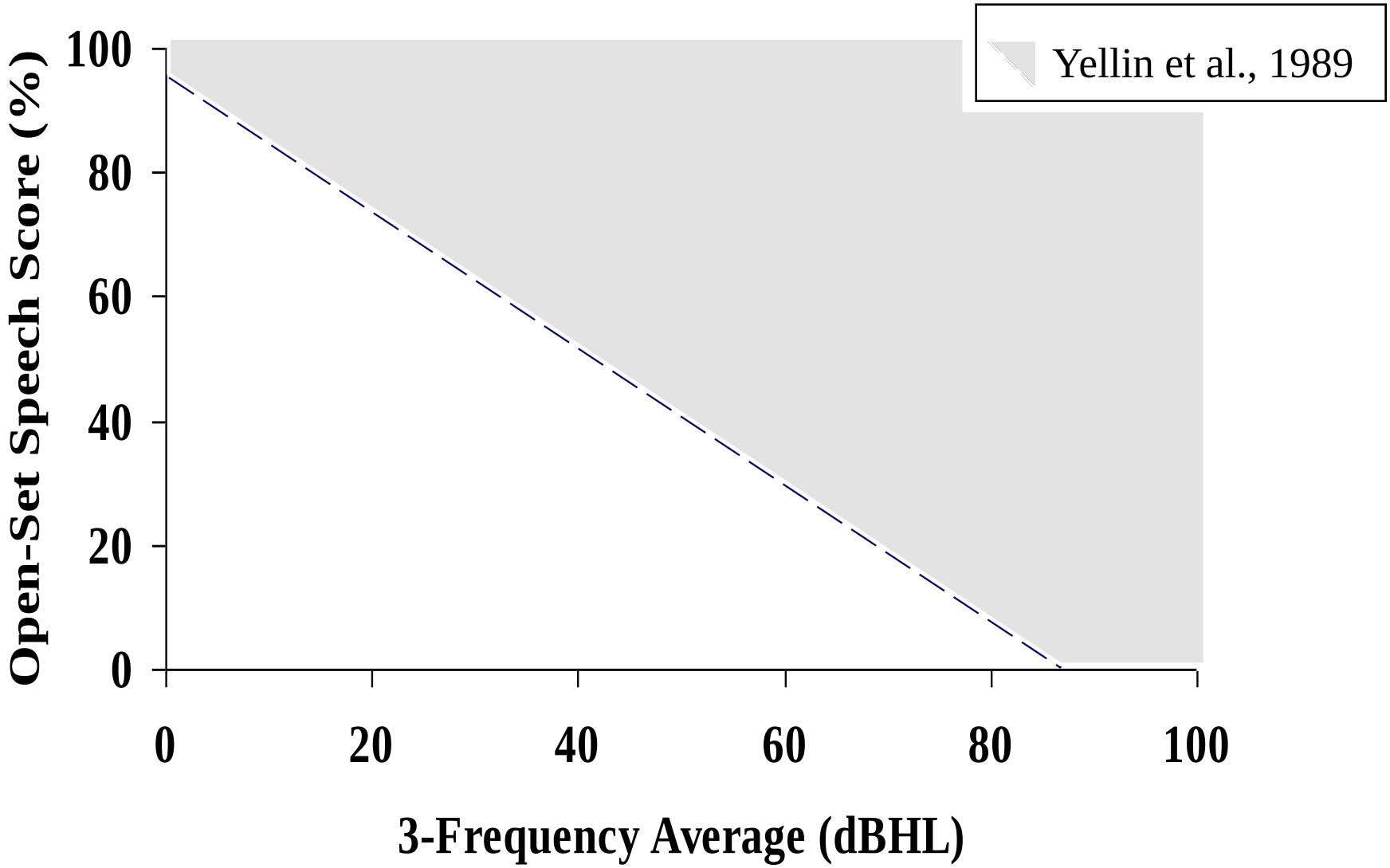
ANSD Clinical Profile

- Behavioural audiogram
  - Level: normal hearing to profound loss
  - All configurations: ≈30% low frequency
  - Fluctuating hearing
- Acoustic reflexes
  - Typically absent (regardless of hearing level)
- Functional hearing
  - Impaired speech perception

Speech Perception

- 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 elevated hearing thresholds show speech perception poorer than for SN loss of equivalent degree

Open-set Speech Perception v Hg Level for Children & Adults with ANSD



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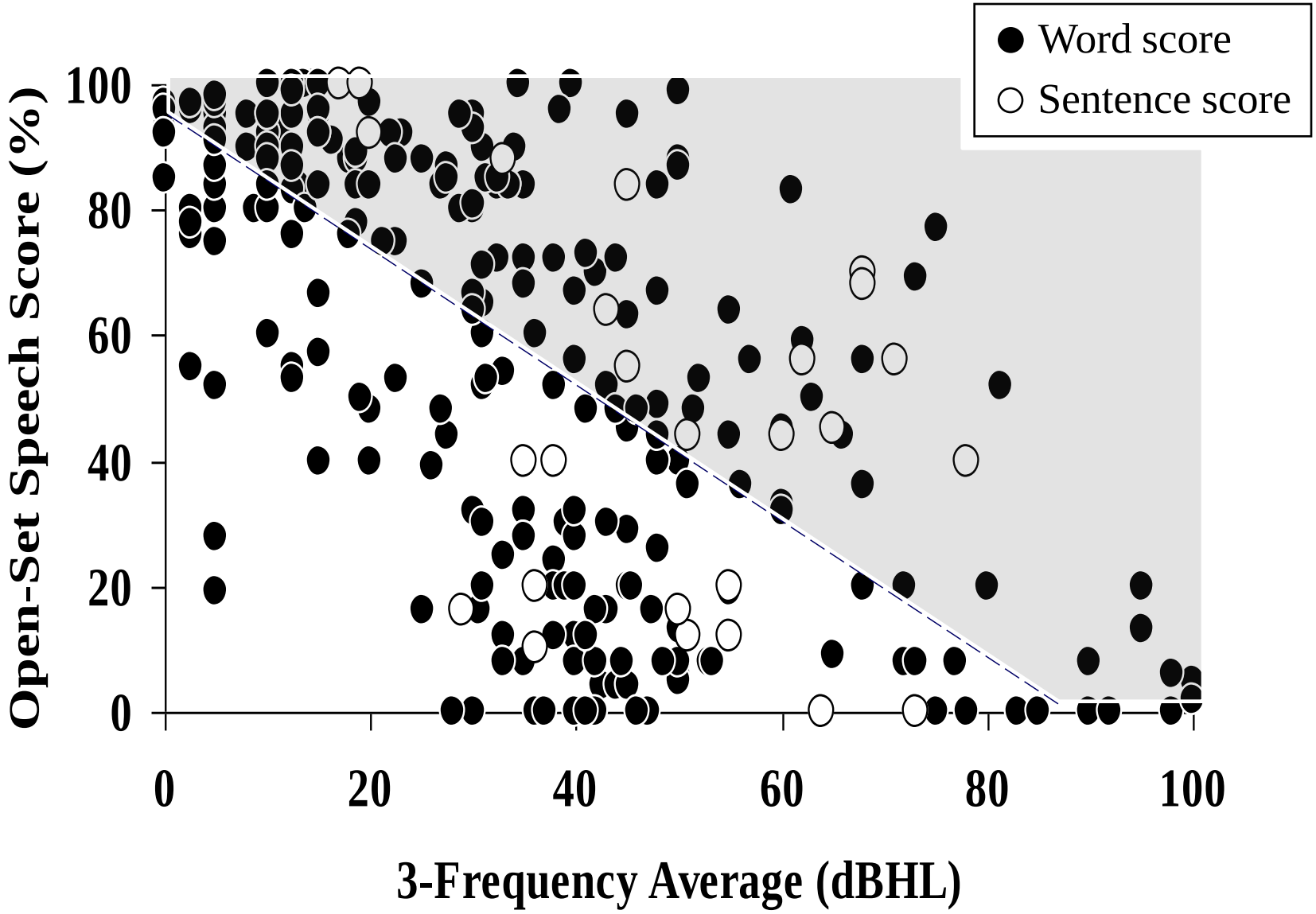


Why is speech perception often poorer than expected?

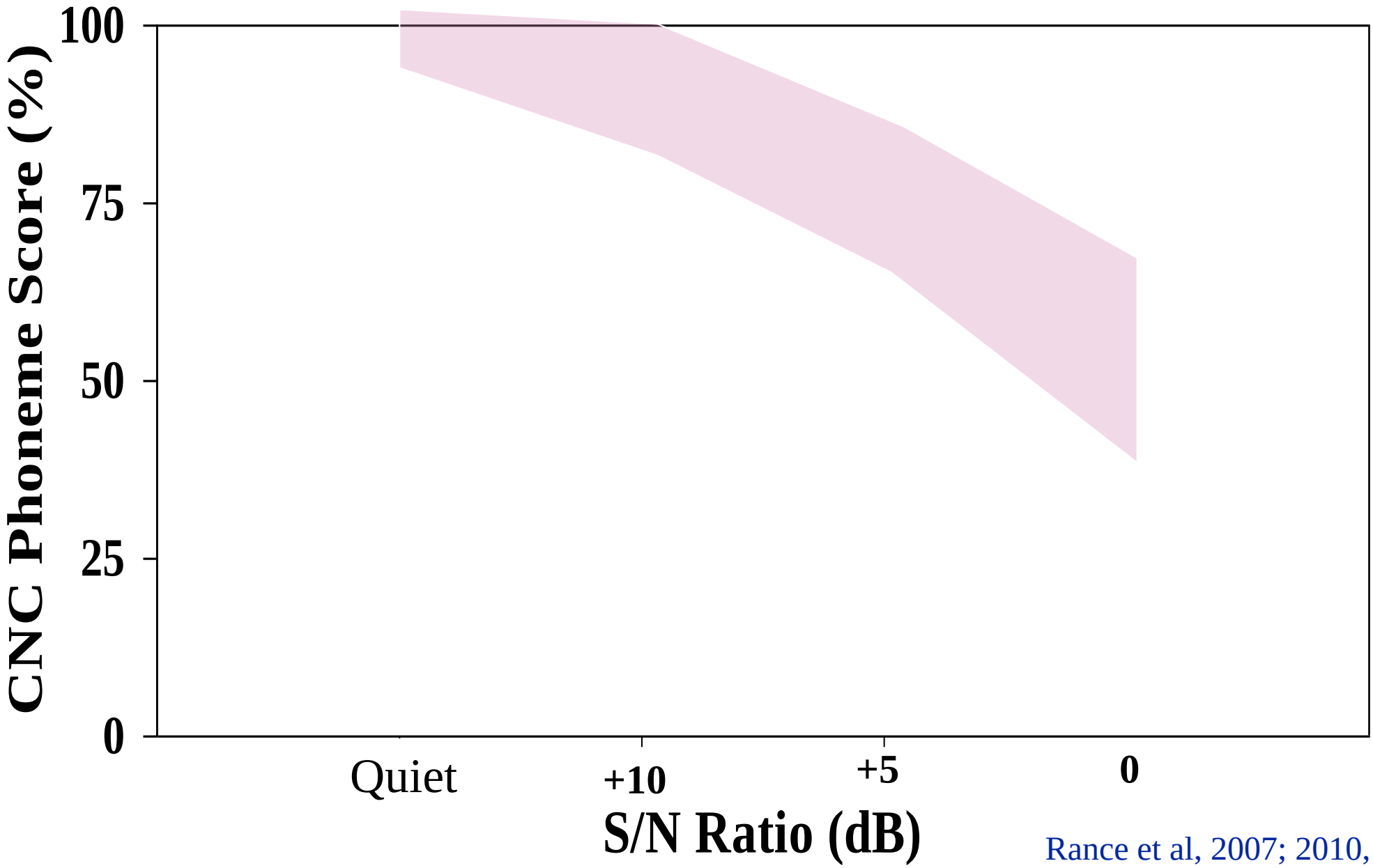
- Signal distortion
  - Timing of neural conduction disrupted
  - Impaired perception of temporal cues in speech
    - Inability to judge vowel duration
      - » eg. h**i**d vs h**ee**d
    - Inability to discriminate consonants based on timing cues
      - » eg. **p**in vs **b**in
        tin vs **d**in
  - Degree of distortion not consistent across children

Speech Perception in Noise

- Extreme difficulty reported in adults and children with ANSD (Kraus et al., 2000; Rance et al., 2007; 2010; 2012; Starr et al., 1998)
- Some cases show normal understanding in quiet and negligible perception in "everyday" listening conditions

Speech Perception in Noise for Children with ANSD

(essentially normal sound detection)



Rance et al, 2007; 2010, 2012

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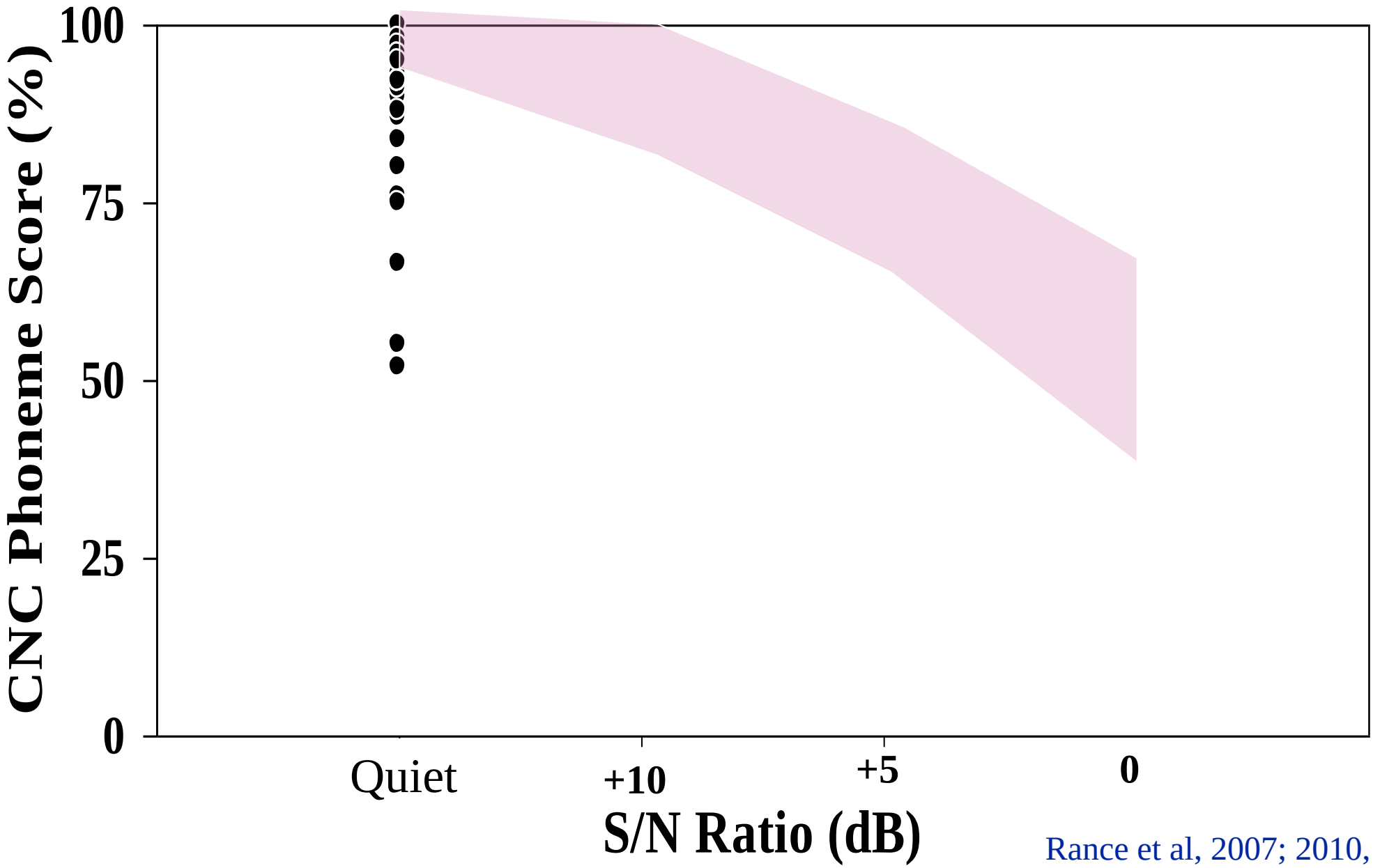

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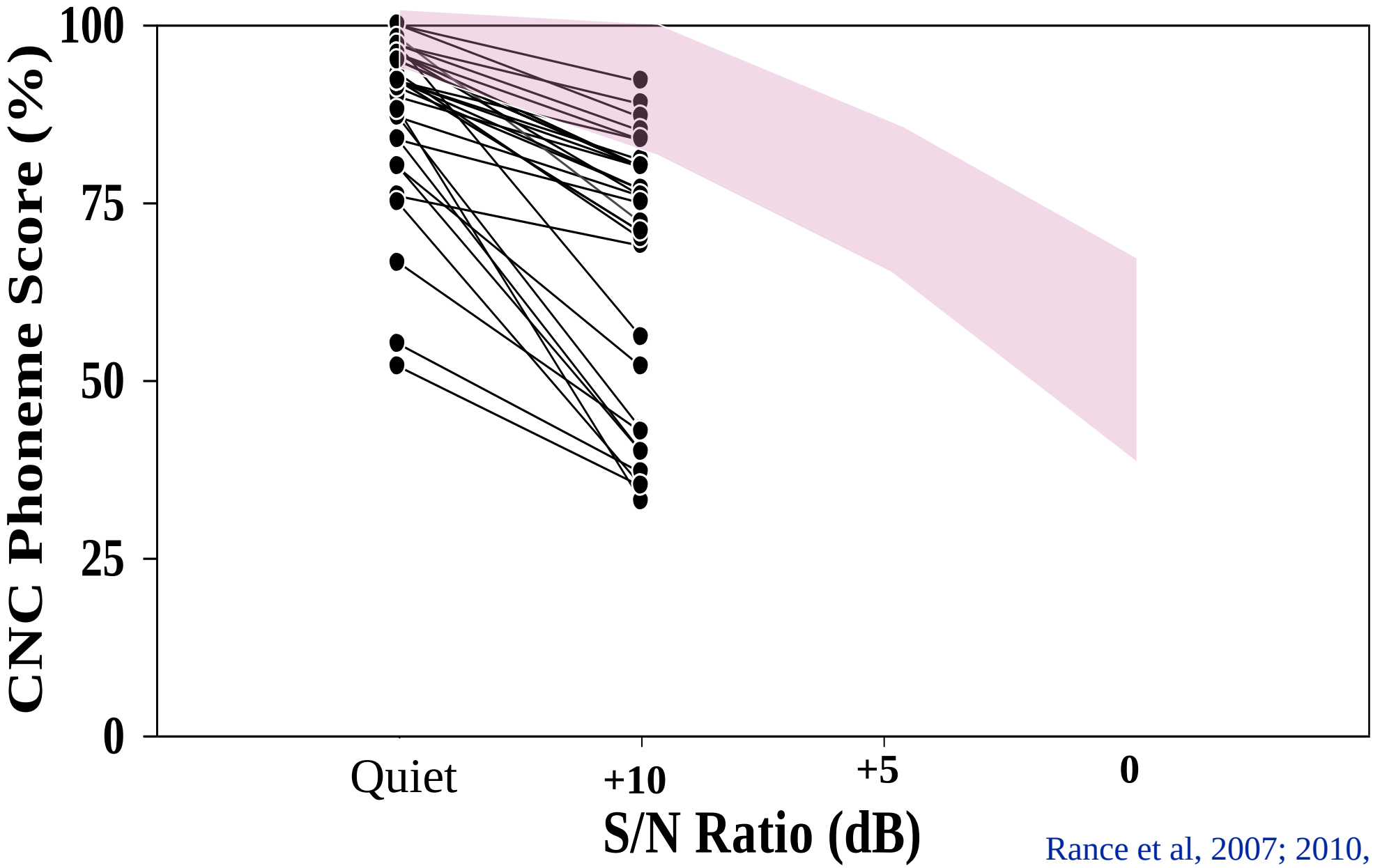

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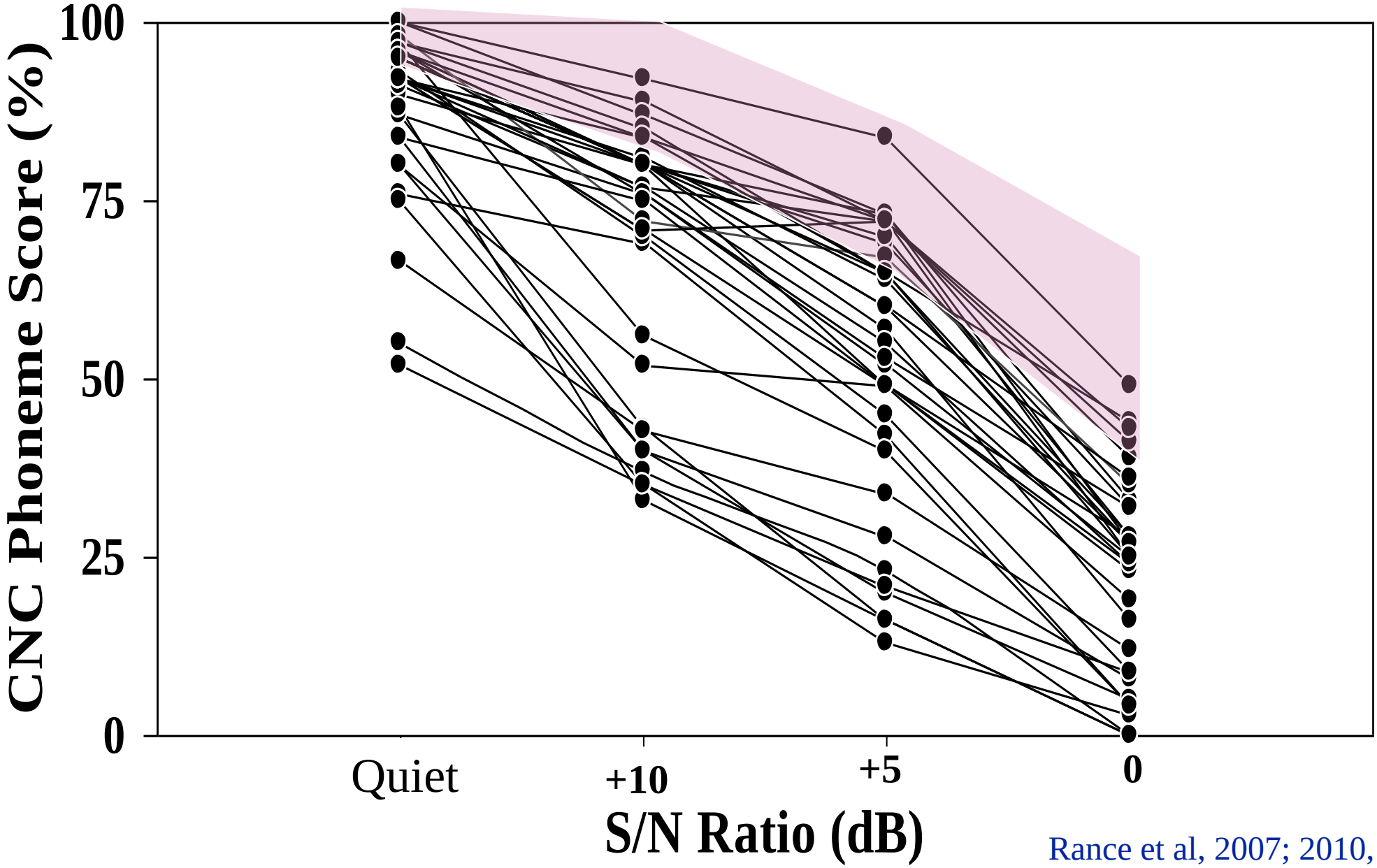


Rance et al, 2007; 2010, 2012

Why is speech perception in noise a particular problem in ANSD?

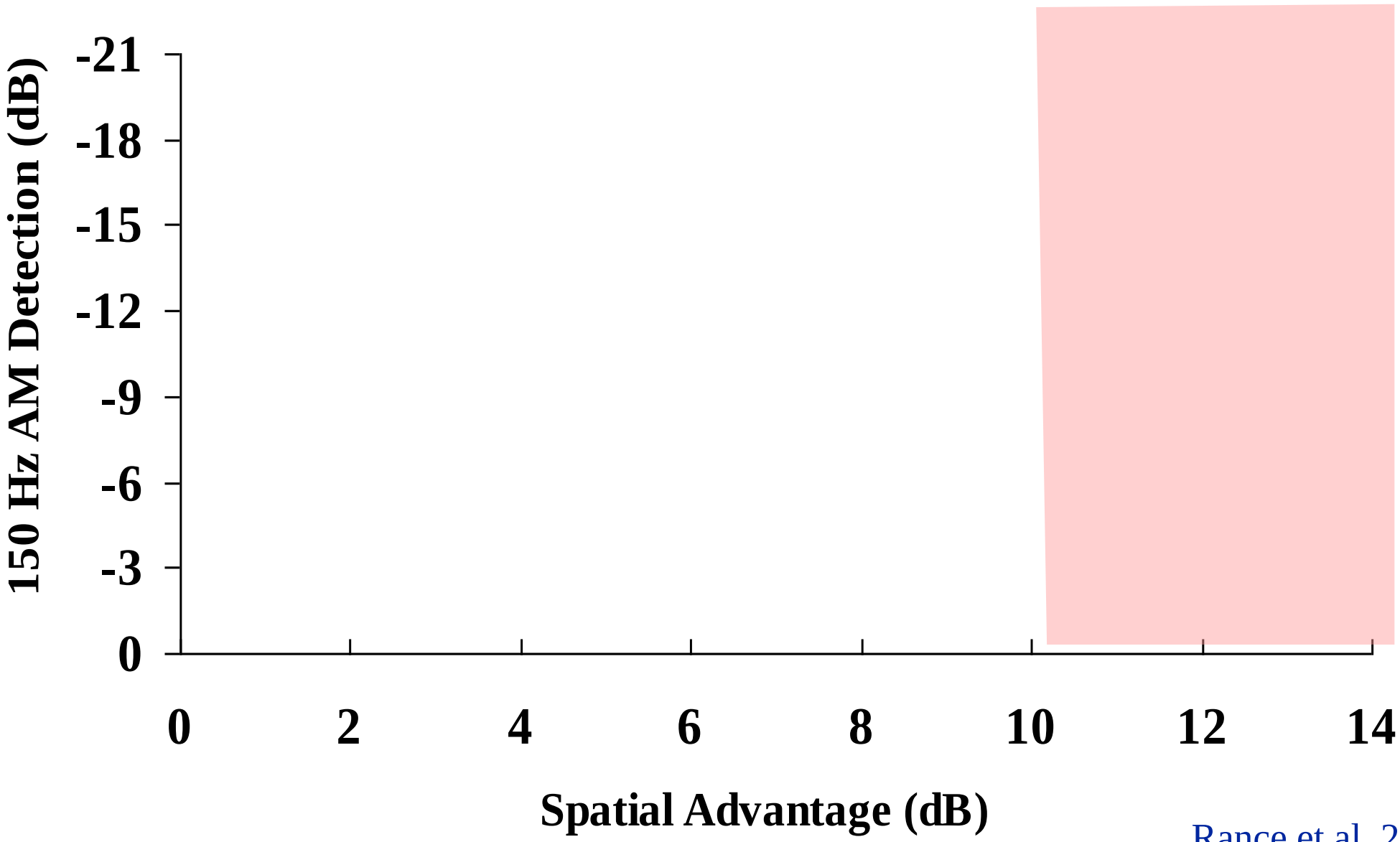
- Gap listening
  - Impaired ability to use brief quiet periods in the noise to access the signal
- Spatial processing
  - Impaired ability to use inter-aural timing cues to localize sound sources

Spatial Processing

- Affected in ANSD as the neural representation of timing cues in left/right auditory nerves is degraded
- inter-aural difference cues [<1 msec] can't be effectively combined in the brainstem

- Listening in Spatialized Noise Test (LiSN-S)
  - sentences in noise
  - spatial advantage: the improvement in speech perception when the signal and background noise are presented from different directions

Spatial Advantage (LiSN-S) for Children with ANSD



Rance et al. 2012

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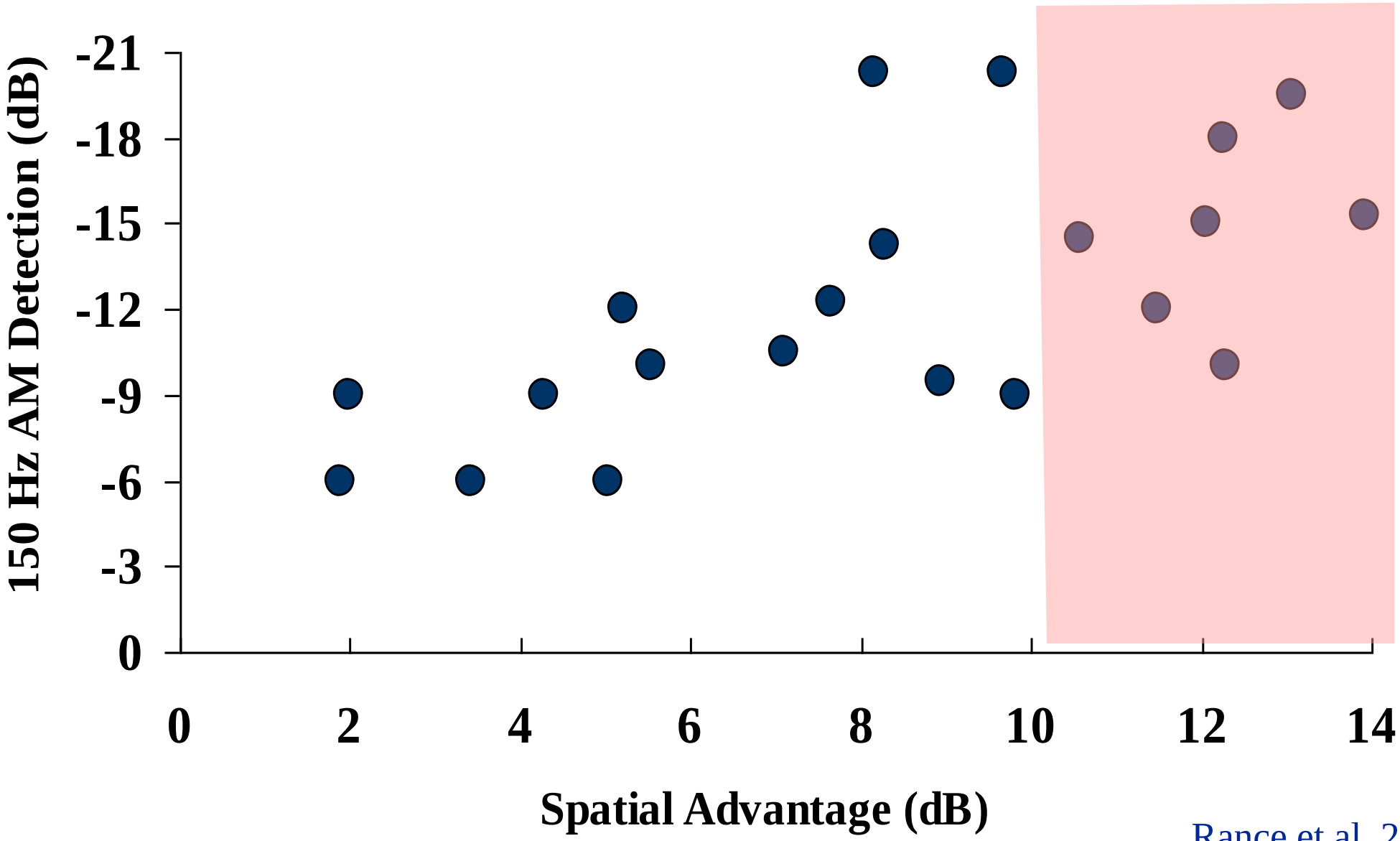

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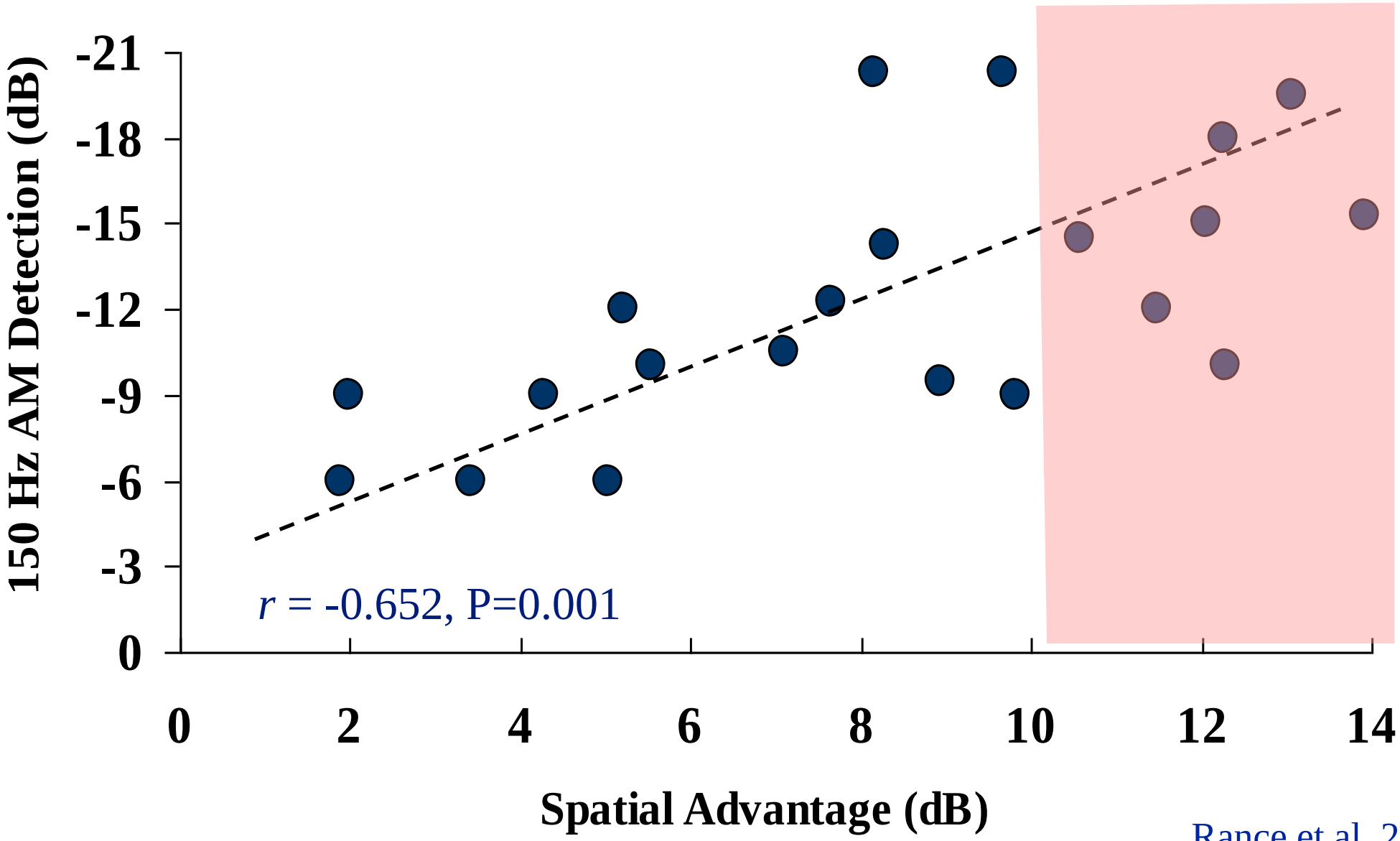


Rance et al. 2012

Clinical Management of ANSD

- Children with ANSD form a heterogeneous group
  - Range of different aetiologies
  - Different clinical presentations
- Range of different management challenges
- Some questions explored in the recent literature include:
  - How should ANSD children with normal sound detection be managed?
  - Should hearing aids and CI be used in concert?
  - Should the contra-lateral ear be occluded in children with unilateral CI?
  - Can we predict cochlear implant outcomes for ANSD children in the pre-operative phase?

Management of Children with ANSD

Hearing Aids vs Cochlear Implants

- Conventional Amplification
  - Arguments against amplification
    - » Inherent pathway limitations
    - » Potential for cochlear damage
  - Argument for amplification
    - » Increased access to the speech signal (if sufficient gain is provided)
  - Speech perception outcomes
    - » 40-50% show significant benefit
- Digital Speech Processing Aids
  - Manipulate speech signal to make temporal cues more salient
    - » Limited results/success (so far)

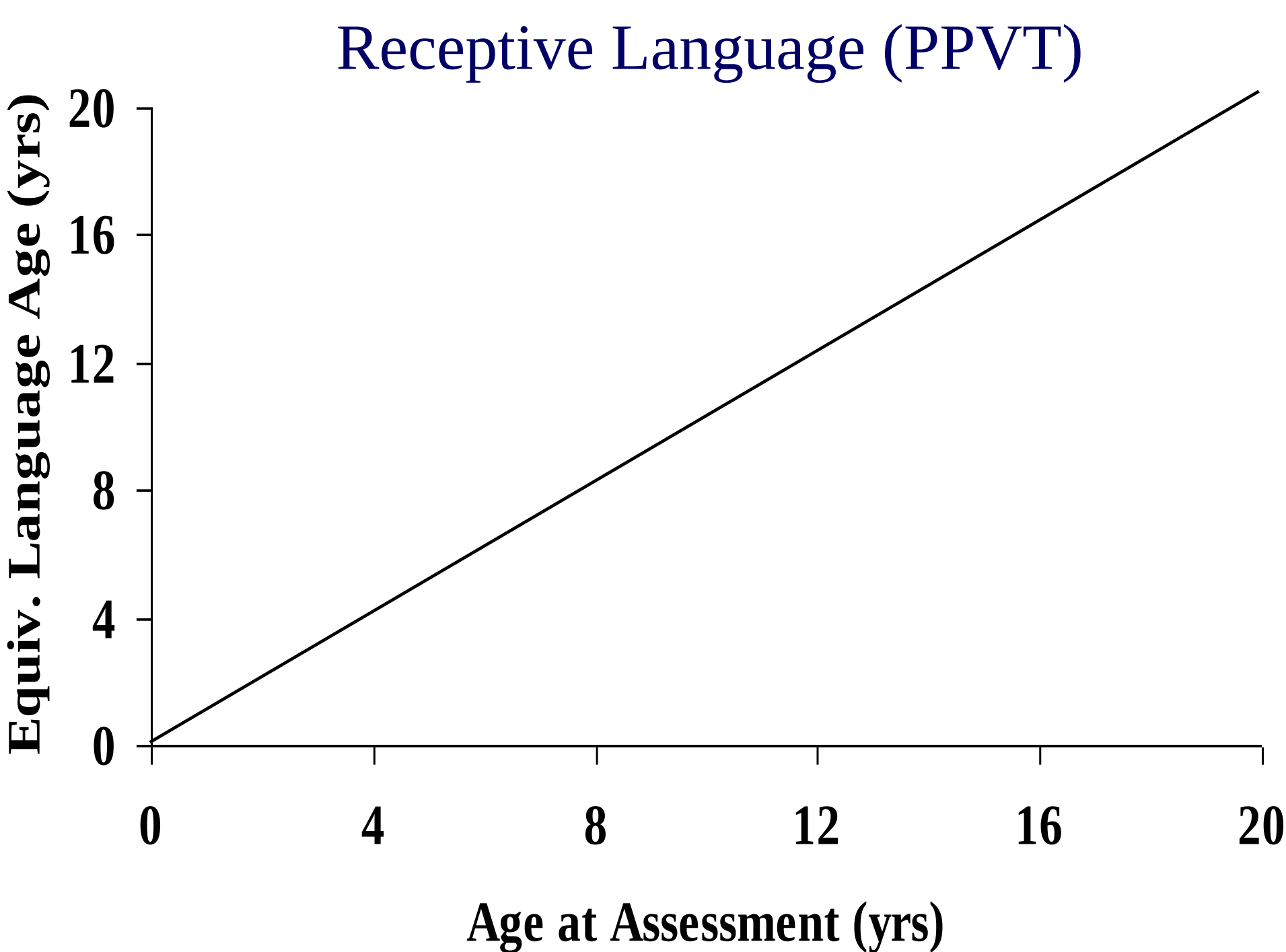
- Cochlear Implantation
  - Currently the option of choice for most individuals with ANSD
  - Speech Perception Outcomes
    - » Most reported cases have performed at levels similar to peers with SN-loss
    - » Some poor results
    - » Teagle et al. (2010)
    - » 52 children with open-set scores
    - » 27% of cases showed speech perception scores <30%

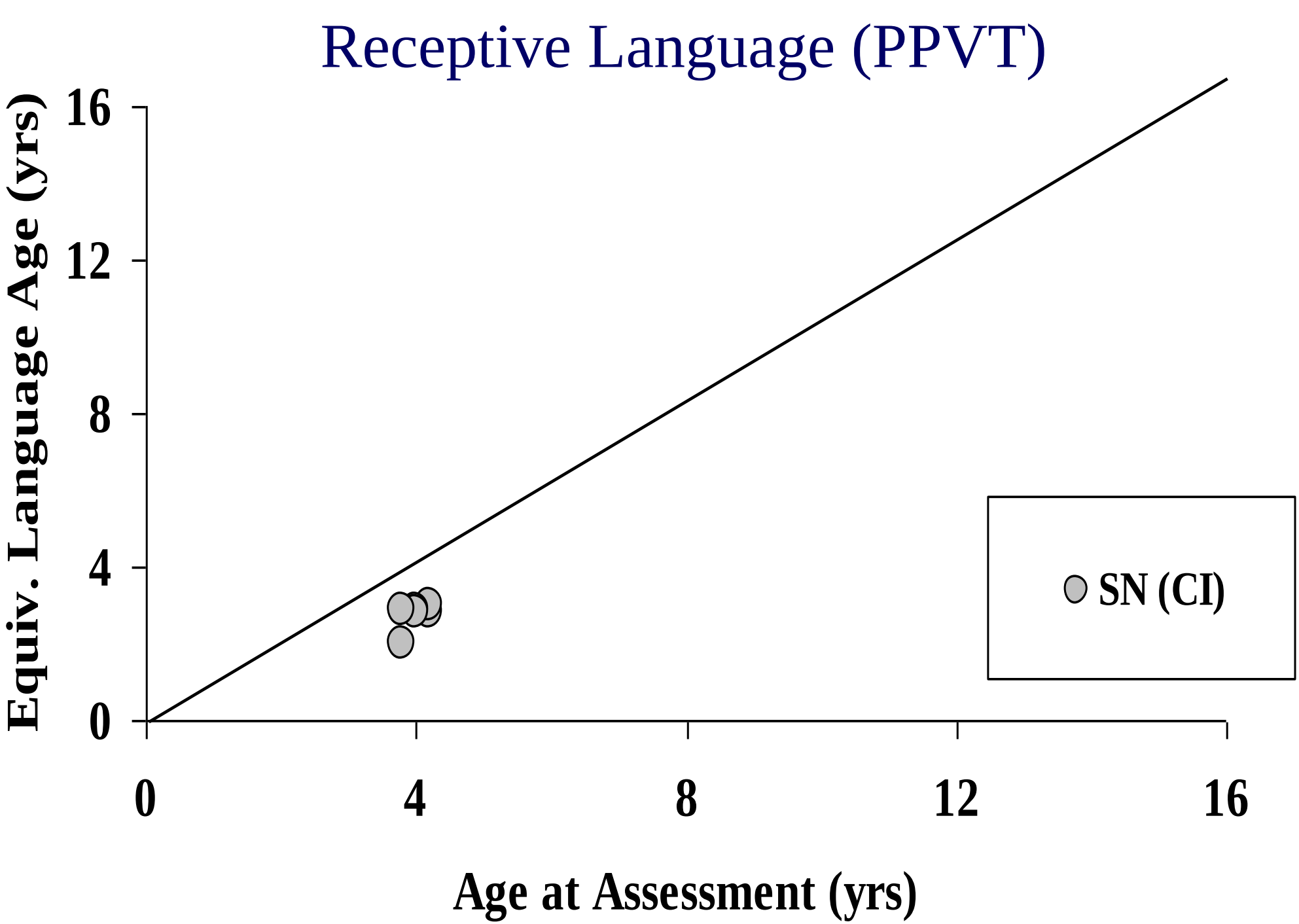
ANSD Management: Hearing Aids / Cochlear Implants

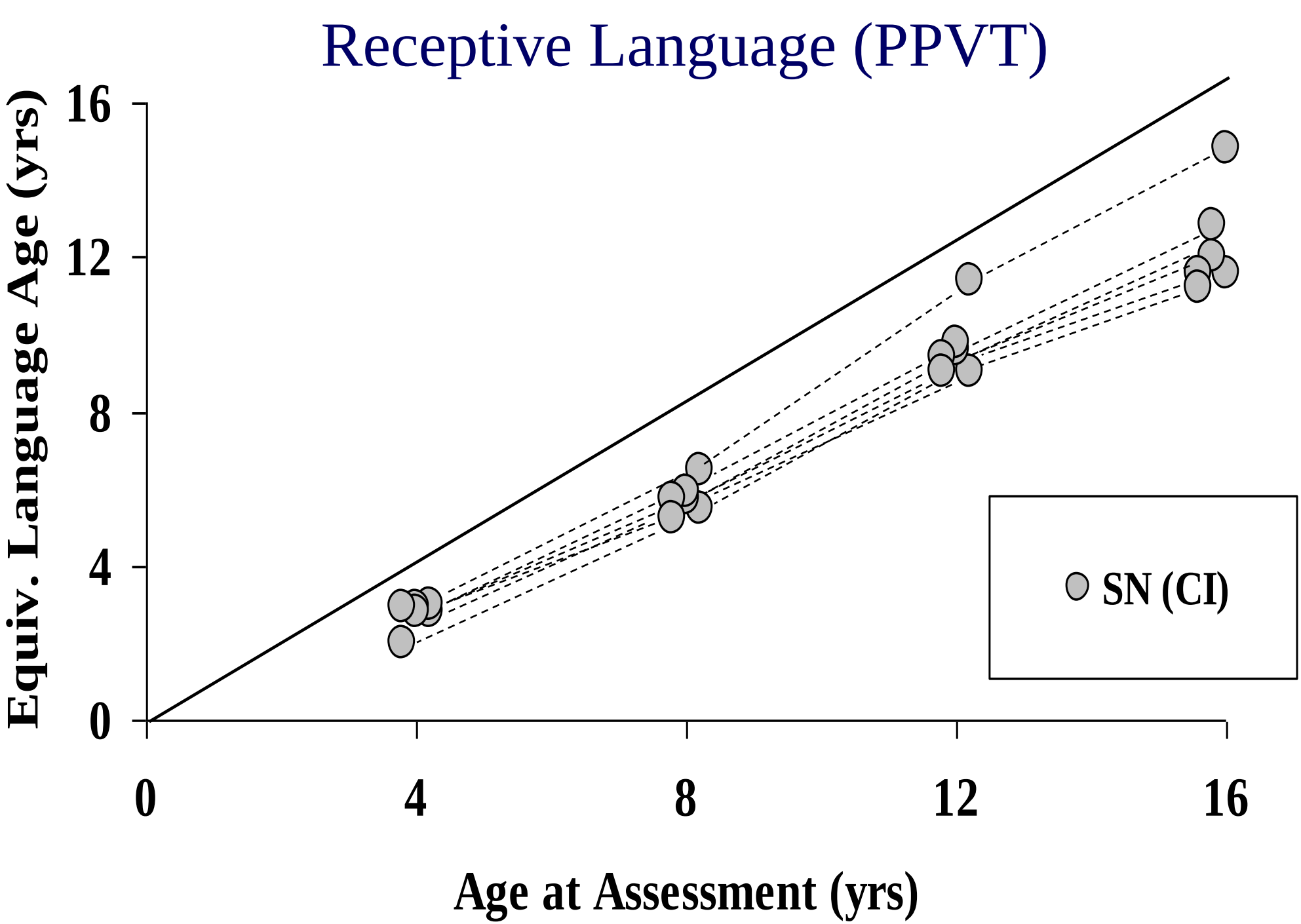
- Melbourne Long-Term Outcome Study
  - Infant ANSD first identified in Melb (1989)
  - Tracking these individuals from infancy to adulthood
- Longitudinal data
  - Audiometry
  - Basic auditory perception (temporal/frequency processing)
  - Speech perception (quiet/noise)
  - Hearing disability ratings
  - Expressive/receptive language development

Long-term Language Development in ANSD

- Receptive Language
  - Peabody Picture Vocabulary Test (PPVT)
  - determines an "equivalent language age" based on norms for normally hearing/developing children
- Longitudinal data: (4 yrs – 20 yrs)
- Subjects (November 2013)
  - Aided ANSD children (n=8)
  - Implanted ANSD children (n=6)
  - Implanted SNHL children (n=6)


Receptive Language (PPVT)
Equiv. Language Age (yrs)
0
4
8
12
16
20
0
4
8
12
16
20
Age at Assessment (yrs)


Receptive Language (PPVT)
Equiv. Language Age (yrs)
16
12
8
4
0
0
4
8
12
16
Age at Assessment (yrs)
SN (CI)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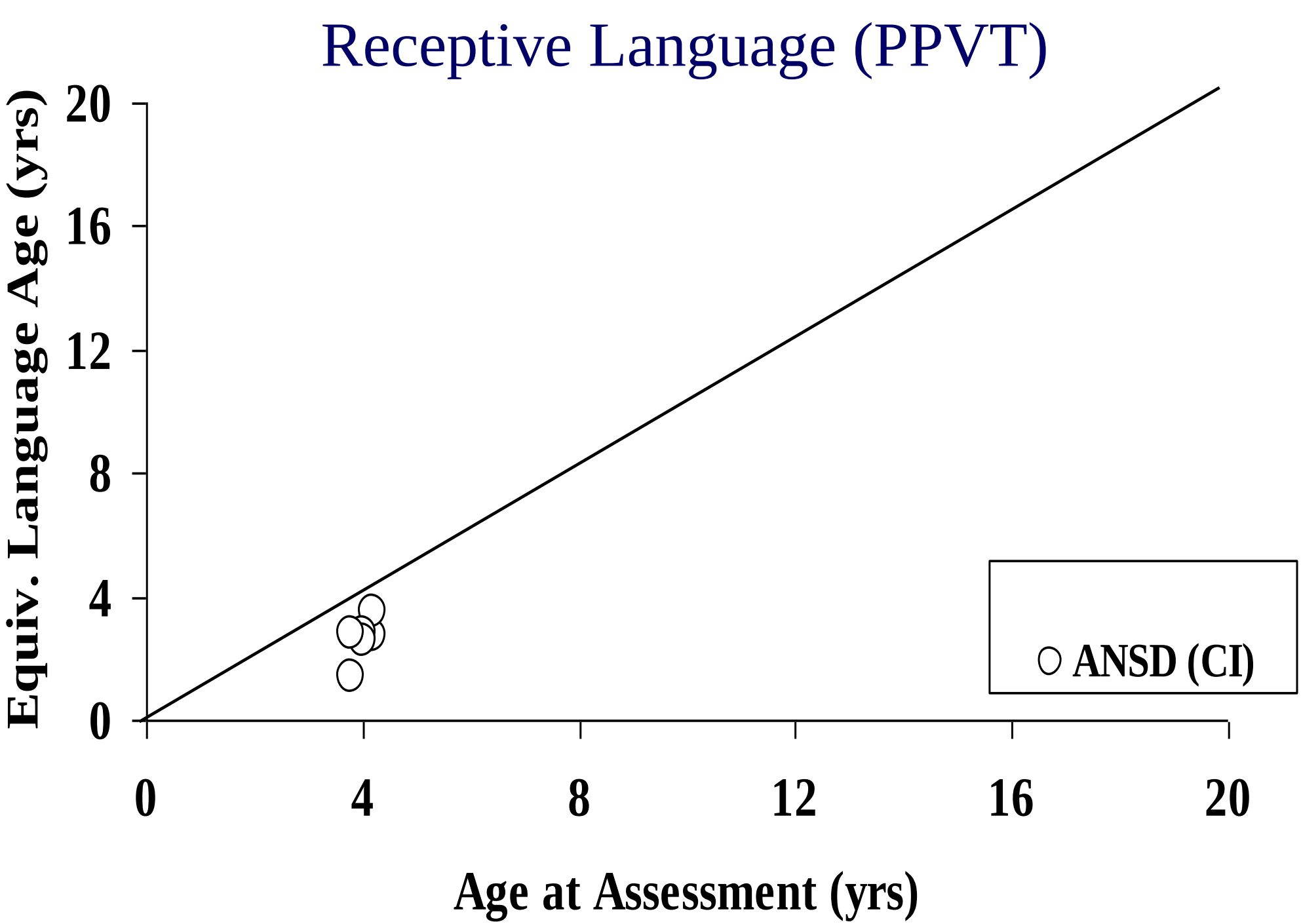
16
12
8
4
0
0
4
8
12
16
Age at Assessment (yrs)
SN (CI)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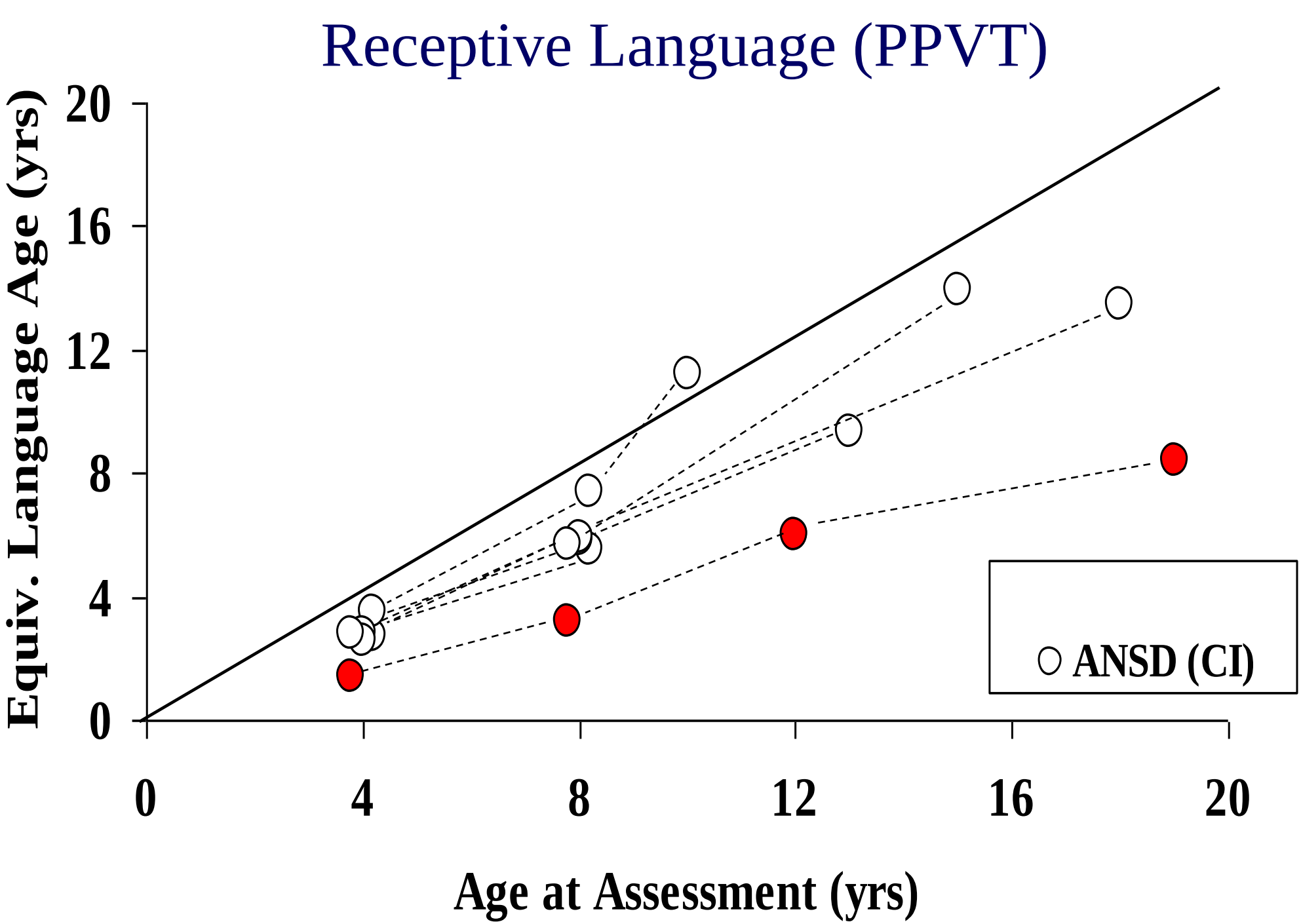
ANSD (CI)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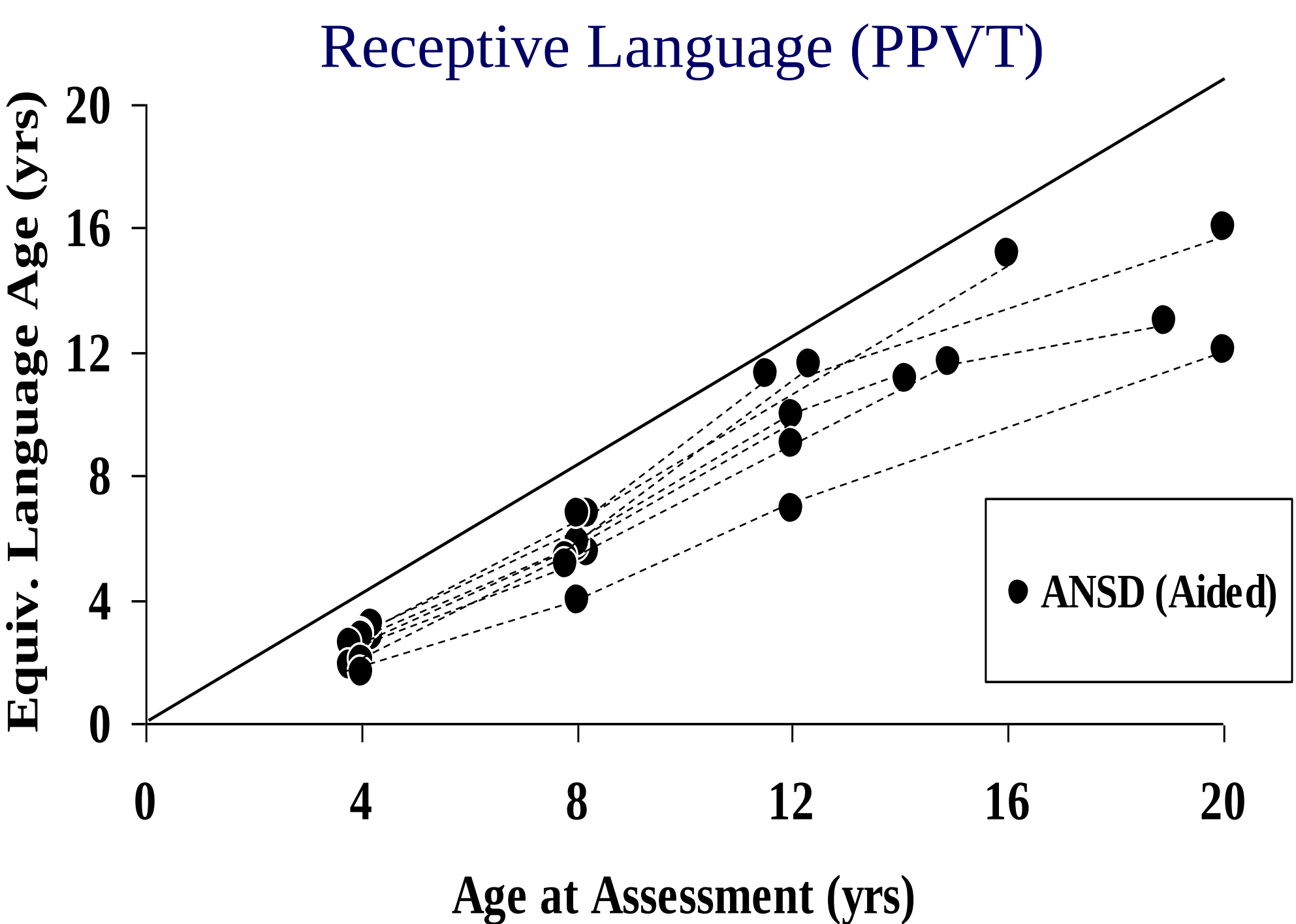
20
Age at Assessment (yrs)
ANSD (CI)


Receptive Language (PPVT)
Equiv. Language Age (yrs)
0
4
8
12
16
20
Age at Assessment (yrs)
ANSD (Aided)

Longitudinal Study Conclusions (Preliminary)

- Most implanted children with ANSD show long-term language outcomes equivalent to those of young implantees with SN-loss

- Some children with ANSD managed with conventional hearing aids can perform as well as the average implantee

Clinical Challenge

- How to predict whether a newly diagnosed baby will perform better with conventional hearing aids or CI?
- Considerations
  - Anatomy: if a child has no nerve then a CI will not be beneficial
  - Sound detection thresholds: if hg levels are in the severe/profound range the child is unlikely to benefit from amplification (same audiologic selection criteria as for SN-loss)
  - Auditory capacity: perceptual ability in cases with hg. levels in the mild/severe loss range determined by the degree of temporal distortion

Measuring Auditory Capacity in Infancy

- Measuring the degree of temporal processing deficit ⇨ predicting long-term outcomes remains a major challenge

- Current research directions
  - Behavioural techniques
    - » Conditioned psychophysics (VRA)
    - » Unconditioned psychophysics
      - Eg. eye tracking technologies

Measuring Auditory Capacity in Infancy

- Measuring the degree of temporal processing deficit ⇨ predicting long-term outcomes remains a major challenge
- Current research directions
  - Evoked potential techniques
    - » Cortical Auditory Evoked Potentials
      - Acoustic Change Complex (where the response is elicited by temporal variations in the stimulus)
    - » Auditory Steady State Responses
      - where the potential is elicited by fluctuations in a continuous stimulus

Summary & Conclusions

- 20+ years of experience with paediatric ANSD has led to significant advances
  - Understanding of mechanisms
  - General pattern of functional outcomes
- Results in individual children are highly variable and so the management of affected youngsters remains a challenge…

Thankyou