PLASTICITY AND RE-ORGANIZATION IN THE DEVELOPING AUDITORY BRAIN: EVIDENCE FROM CHILDREN WITH HEARING IMPAIRMENT AND AUDITORY NEUROPATHY

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CHILDREN WITH COCHLEAR IMPLANTS

6

AUDITORY NEUROPATHY SPECTRUM DISORDER (ANSD)

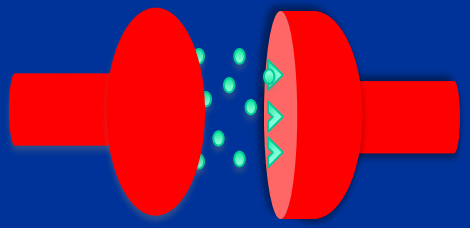
AIM

To examine plasticity in the developing central auditory nervous system.

To explore implications for clinical intervention.

Plasticity

The brain's ability to change in structure and function in response to input from the environment.

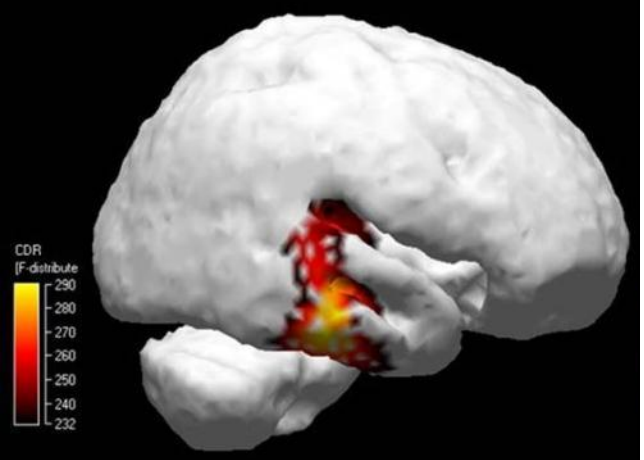


Early in life, neurons begin to form connections or synapses. Proper connections are essential for learning.

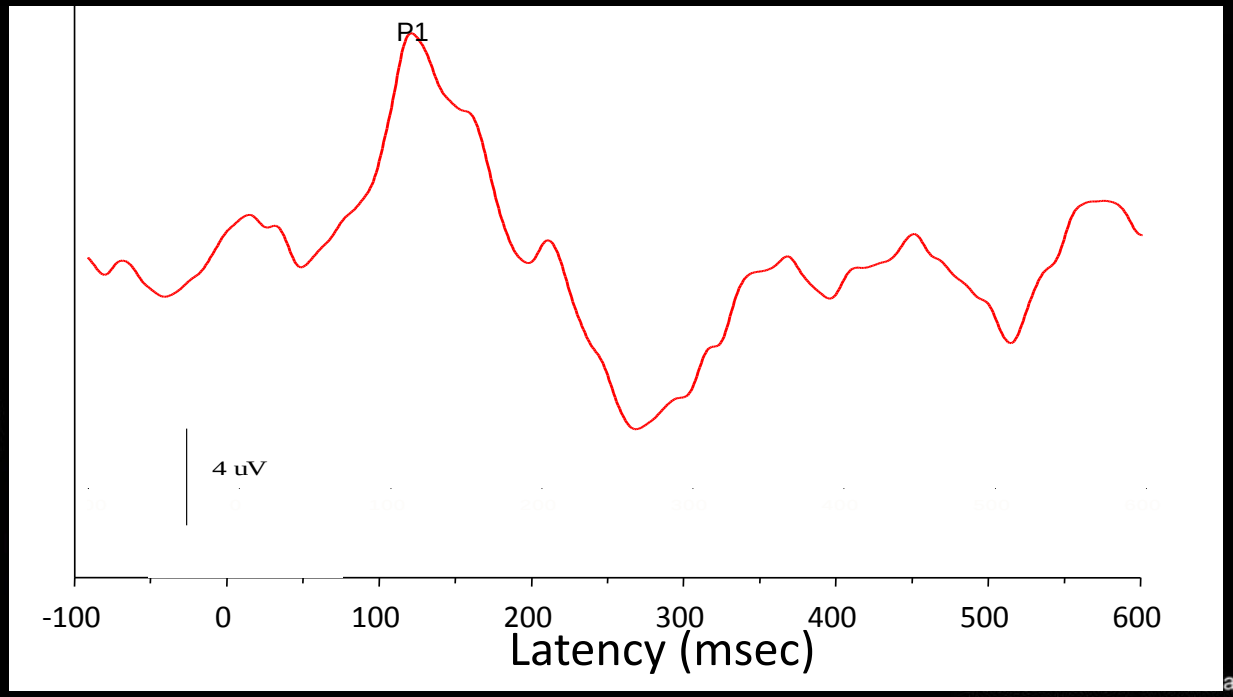
Plasticity begins before birth and continues into adulthood

EEG, FMRI, MEG, PET scans

High density EEG

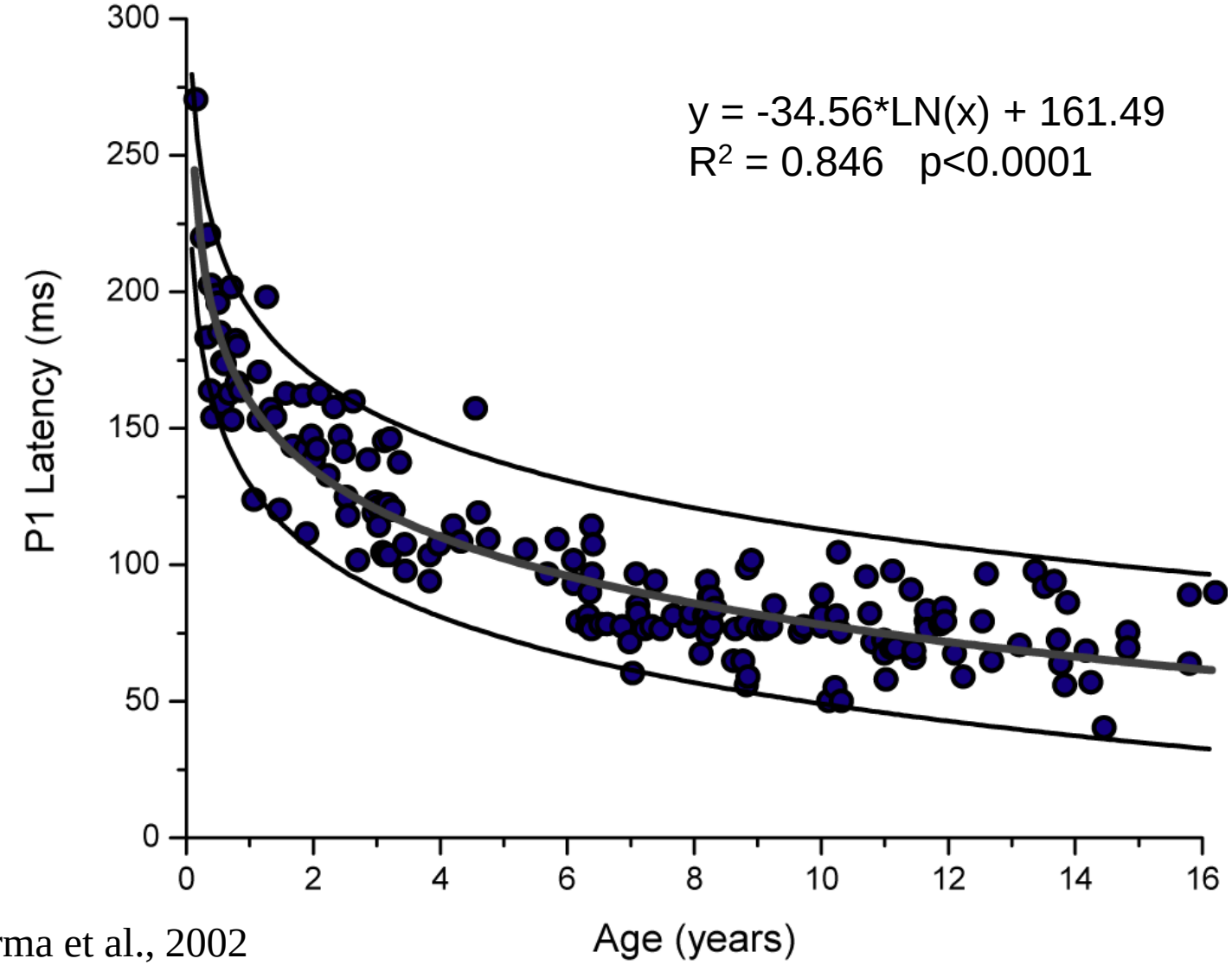


Cortical Auditory Evoked Potentials

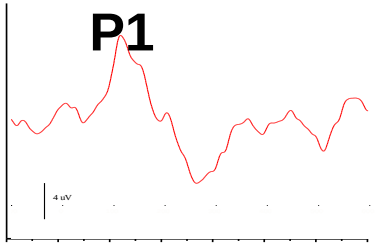


P1 generated in primary and secondary auditory cortex

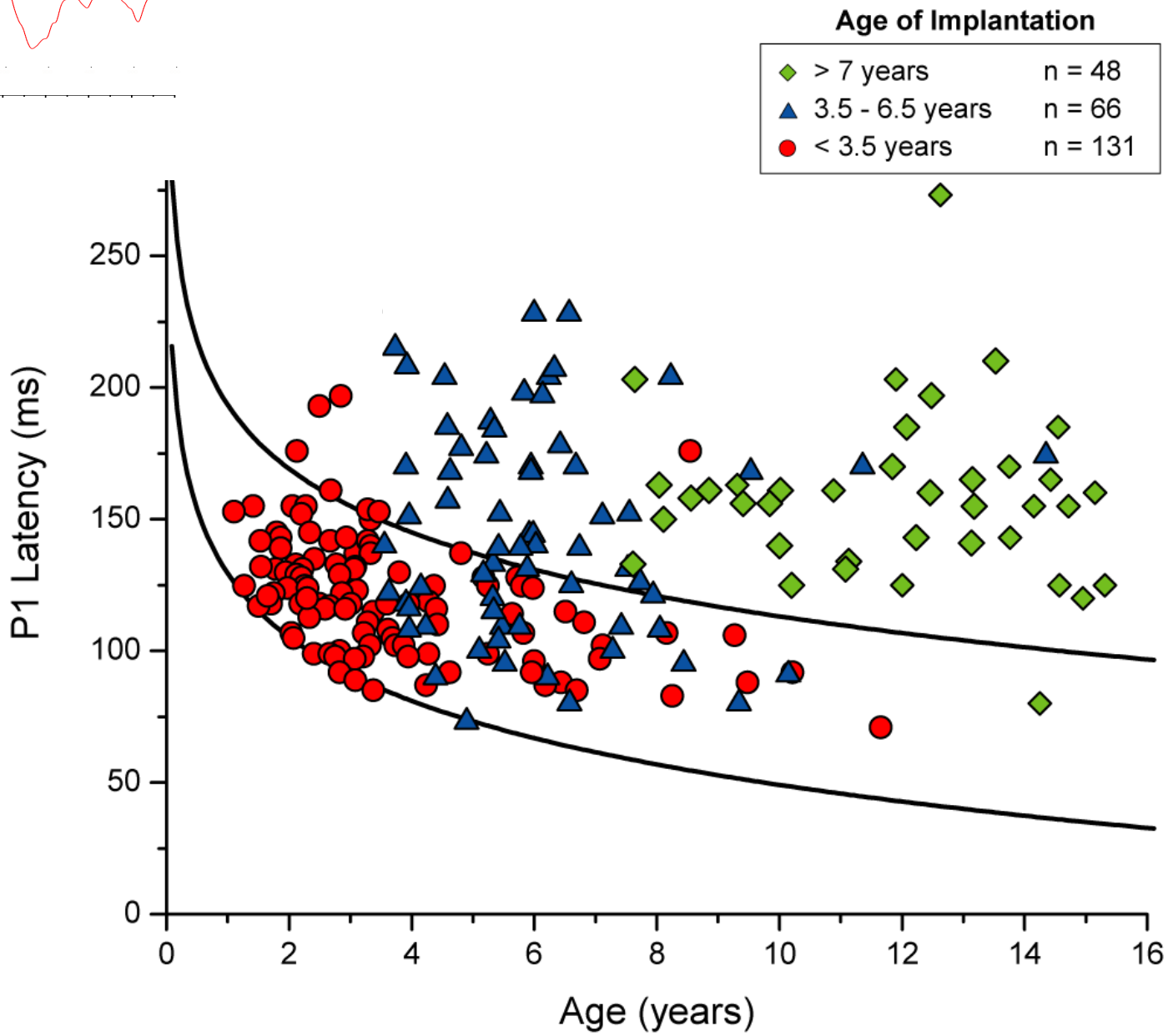
Normal Hearing Children (N=190)



Sharma et al., 2002



Cochlear Implanted Children (N = 245)

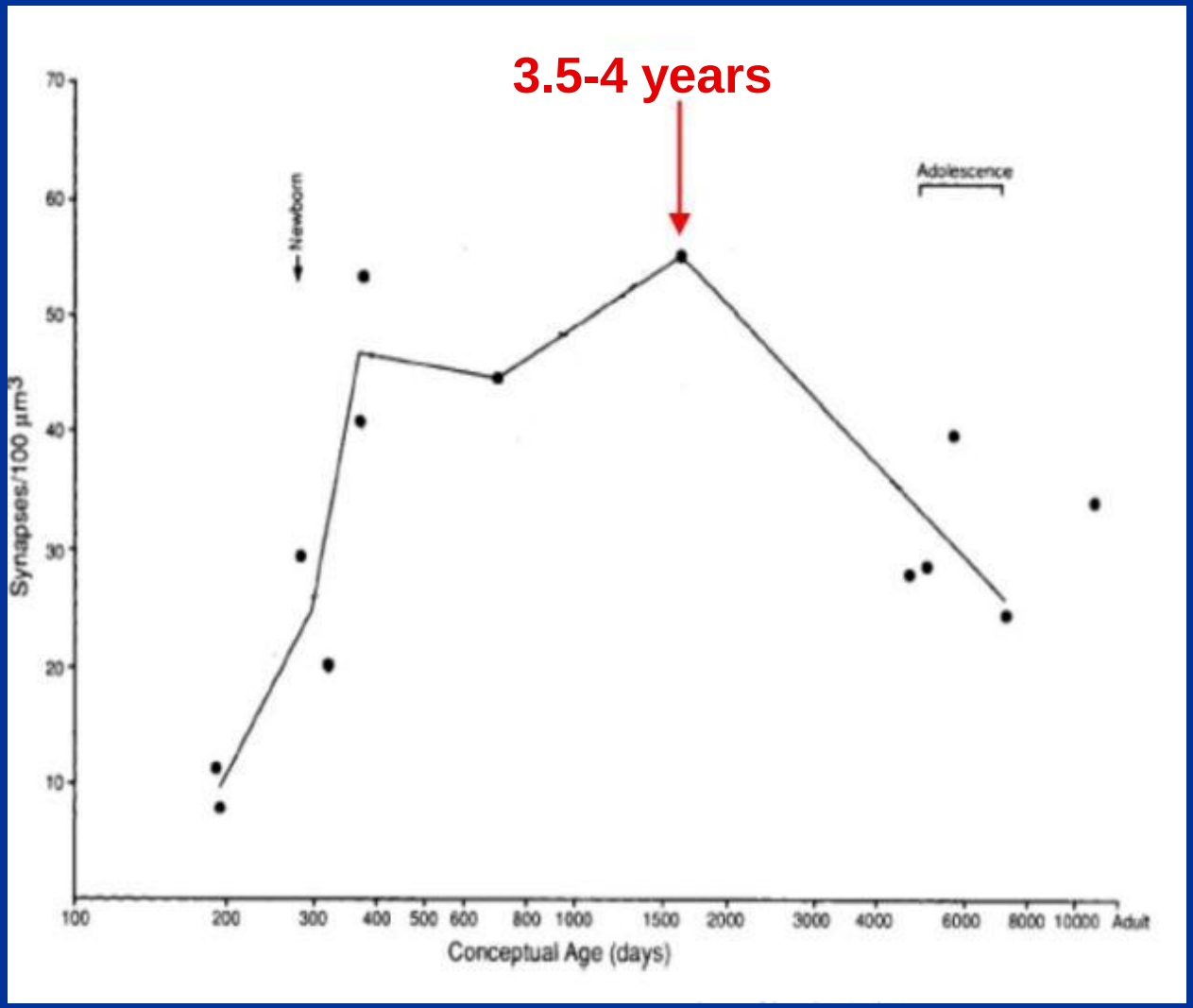


Sharma et al., (2002; 2006)

Lee et al. (2003)

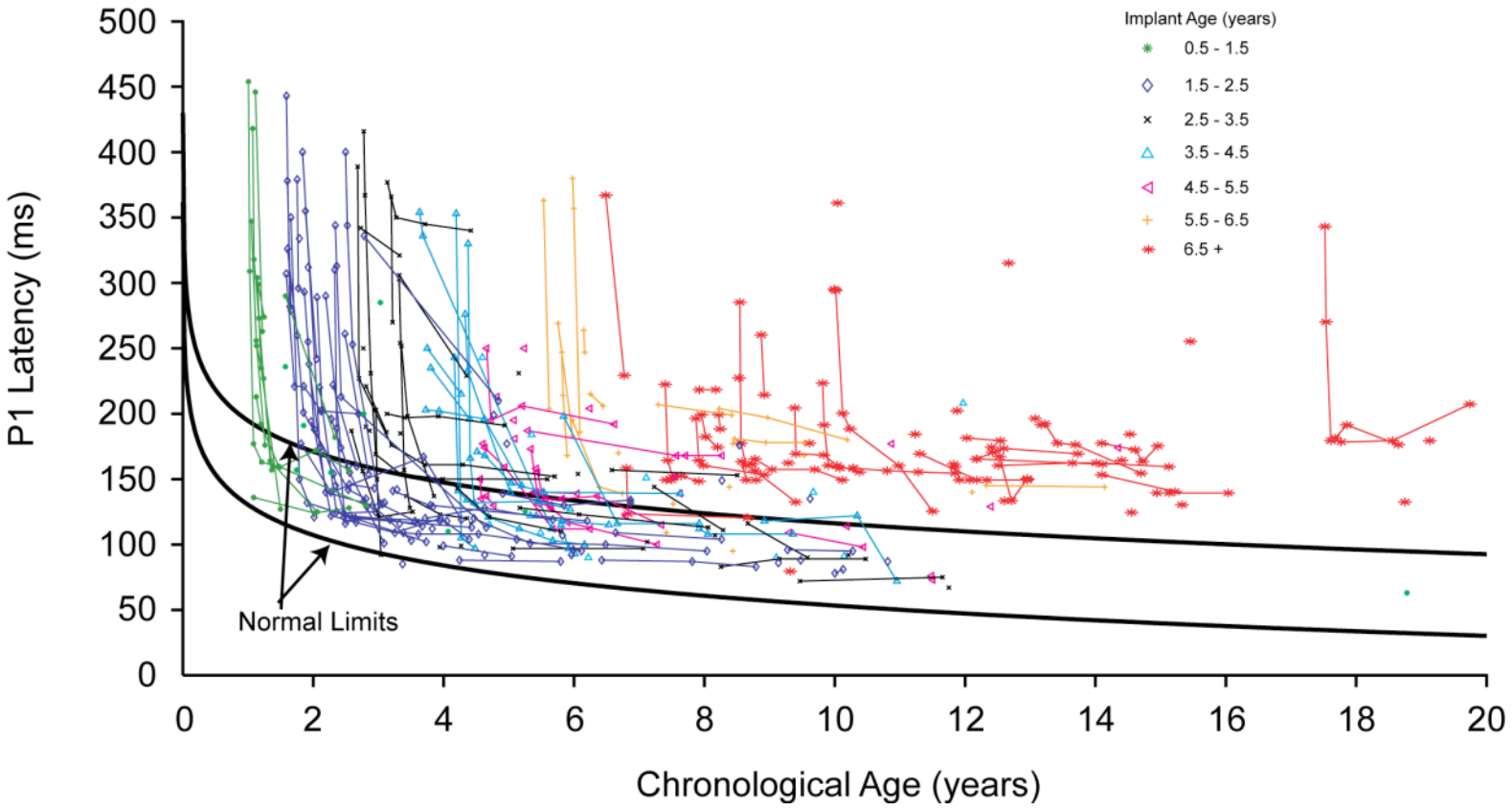
There is a sensitive period of 3.5 years during which implantation takes place into a highly plastic auditory cortex.

Synaptic Density in Auditory Cortex

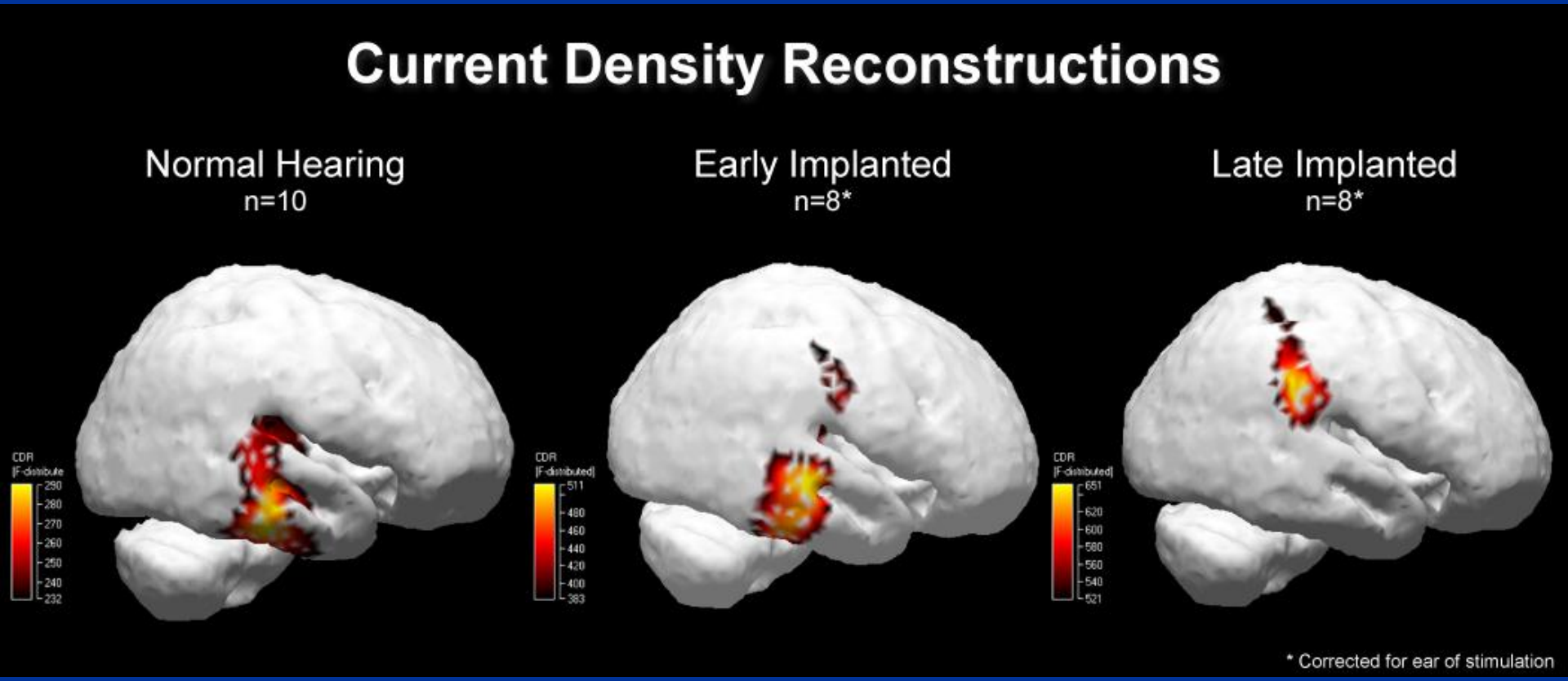


Huttenlocher and Dhabolkar (1997)

Cochlear Implanted Children: Individual Developmental Trajectories n=(231)



Sharma et al., 2007



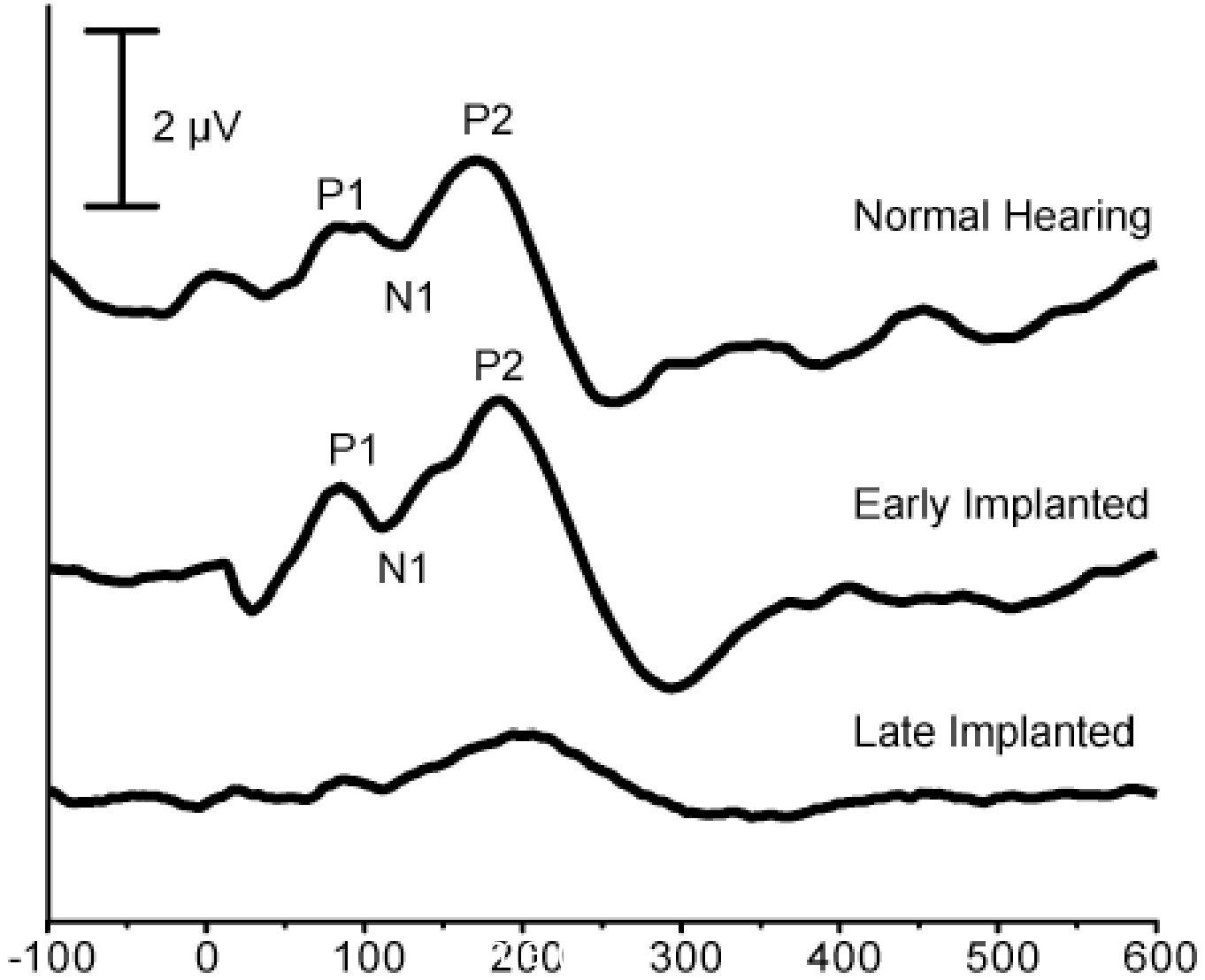
Right ITG
Bilateral STS

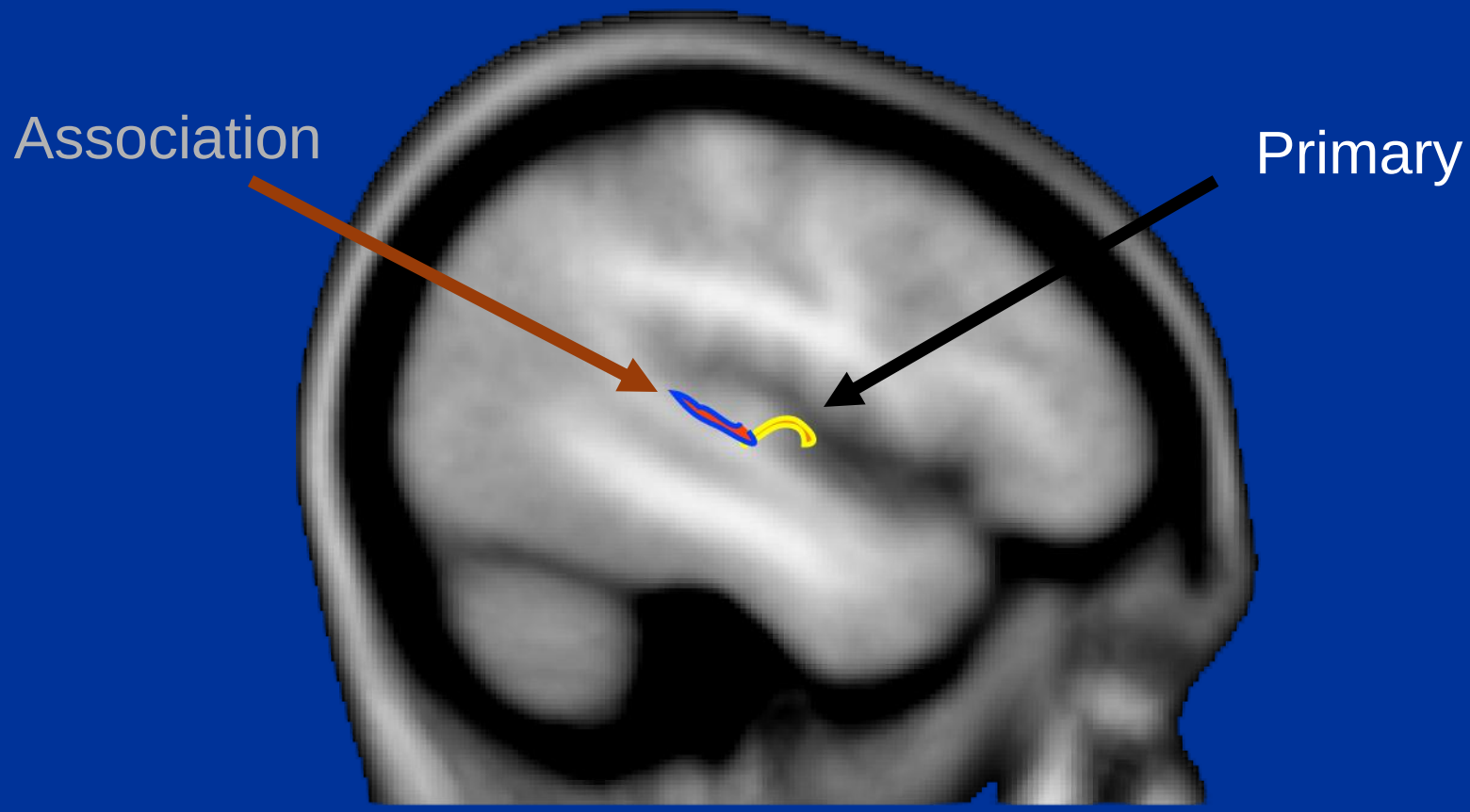
Right ITG
Contralateral STS

Contralateral Parieto
Temporal

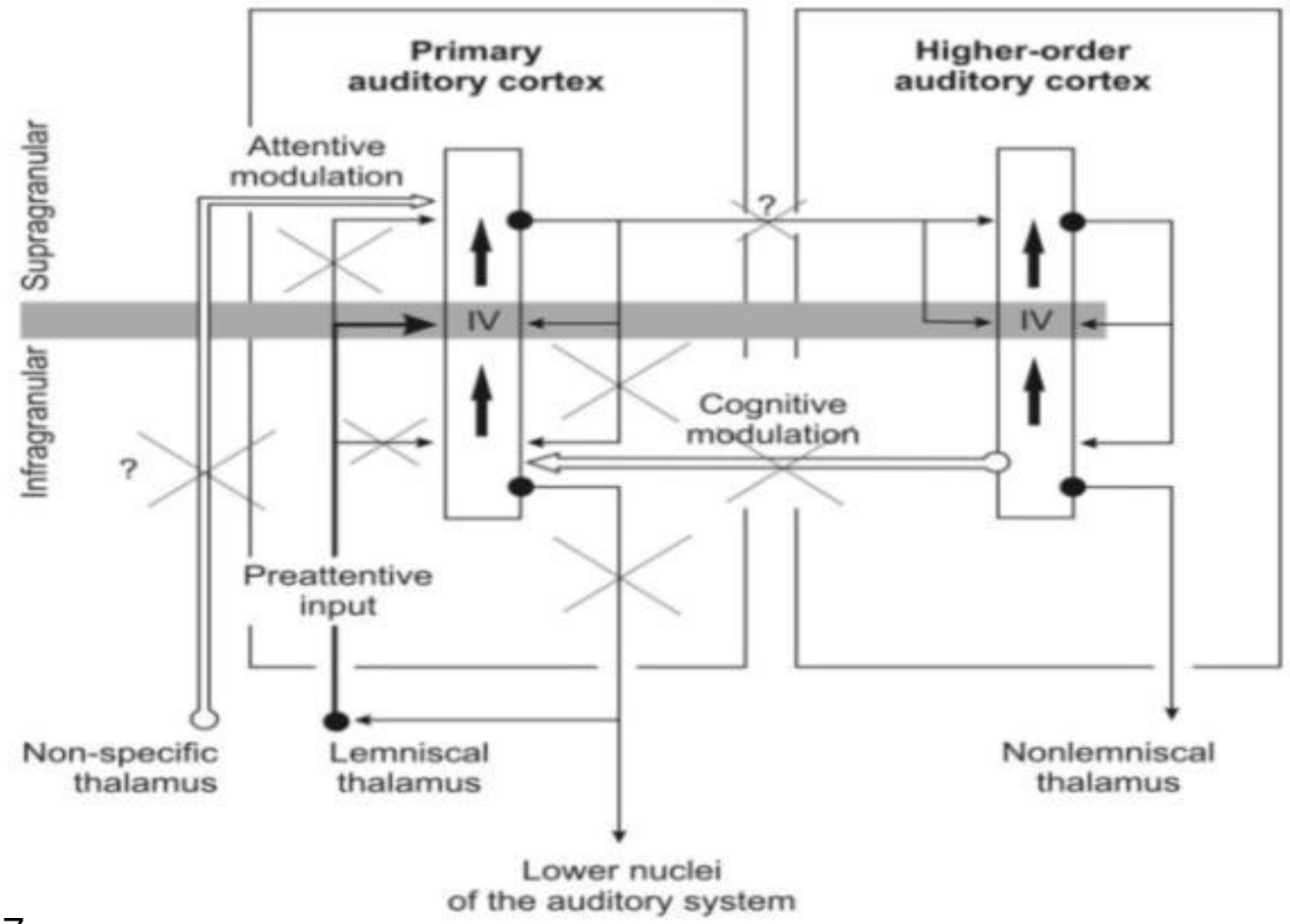
Gilley, Sharma, Dorman, 2008

Age-matched groups of children (n=26)




Association
Primary

Partial or Complete Decoupling between Primary & Higher Order Cortex



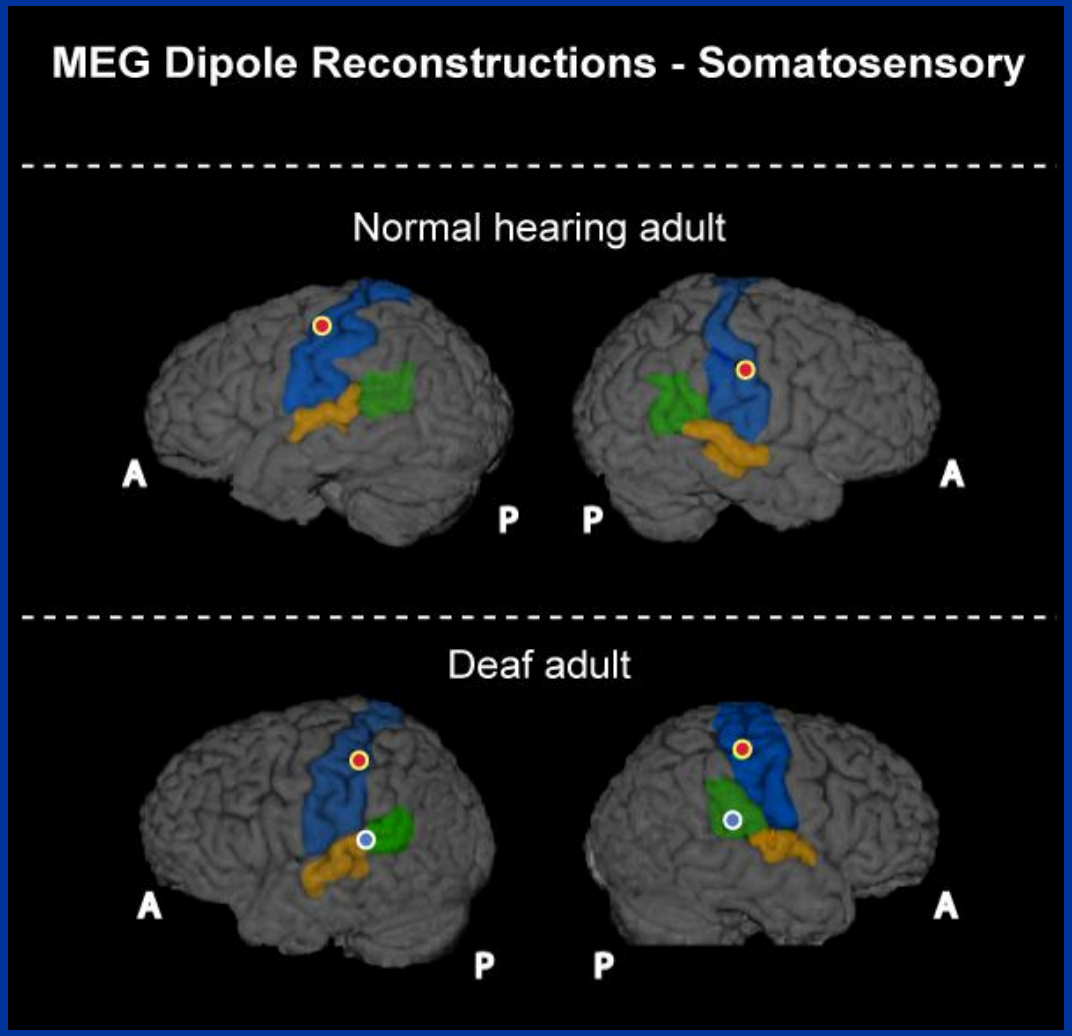
Kral, 2007

If proper auditory stimulation is not provided then there may be a disconnection between areas of the brain which connect sound with meaning.

These children will have difficulty learning oral language.

Compensatory or Maladaptive plasticity: Cross Modal Re-organization

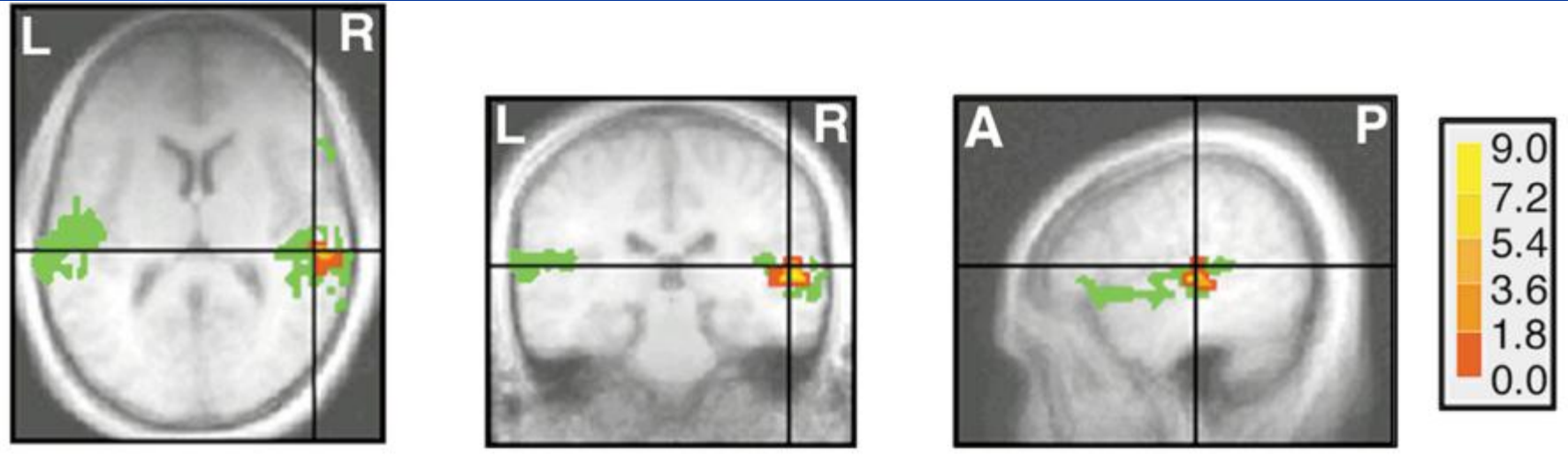
CROSS-MODAL PLASTICITY: SOMATOSENSORY-AUDITORY



Sharma et al., 2007

CROSS-MODAL PLASTICITY: VISUAL-AUDITORY

fMRI activity in deaf adults in response to visual stimuli



Visual activity in temporal cortex at STS

Finney et al., 2001

If auditory stimulation is not delivered in a timely fashion, then areas of the auditory cortex will re-organize to process stimuli from other sensory modalities.

Does cross-modal plasticity affect outcome?

Table 1 Clinical profile of CI patients

Subject	Sex	Age	Age at onset of deafness (years)	Cause of deafness	Degree of loss (dB threshold)	Deaf. duration (years)	CI duration (years)	Side of CI	Speech recognition with the CI (%)	Communication
S1	M	21	3	Unknown	Left = 118 Right = 105	16	2	L	73	Oral + lip-reading
S2	F	52	47	G.-Sjogren syndrome	Left = 110 Right = 105	2	3	R	98	Oral + lip-reading
S3	M	37	12–25 (progressive)	Hereditary	Left = 113 Right = 113	11–24	1	L	80	Oral + lip-reading
S4	F	42	27	Unknown	Left = 110 Right = 87	13.5	1.5	L	92	Oral + lip-reading
S5	F	18	0–15 (progressive)	Hereditary	Left = 93 Right = 105	1–16	2	R	85	Oral + lip-reading
S6	M	54	30–50 (progressive)	Hereditary	Left = 108 Right = 107	2–22	2	R	82	Oral + lip-reading
S7	F	25	0	Hereditary	Left = 107 Right = 107	23	2	R	92	Oral + lip-reading
S8	F	23	2	Meningitis	Left = 100 Right = 100	18	3	R	0	Sign language + lip-reading
S9	F	50	5	Chronic otitis media	Left = 118 Right = 115	44	1	R	0	Sign language + lip-reading
S10	F	41	2–12 (progressive)	Meningitis	Left = 117 Right = 117	28–38	1	R	0	Sign language + lip-reading
S11	M	18	0	Hereditary	Left = 97 Right = 93	16	2	L	0	Sign language + lip-reading
S12	M	62	10	Meningitis	Left = 113 Right= 115	52	1	L	0	Sign language + lip-reading
S13	M	49	0	Hereditary	Left = 105 Right= 110	47	2	L	0	Sign language + lip-reading

Visual Stimuli

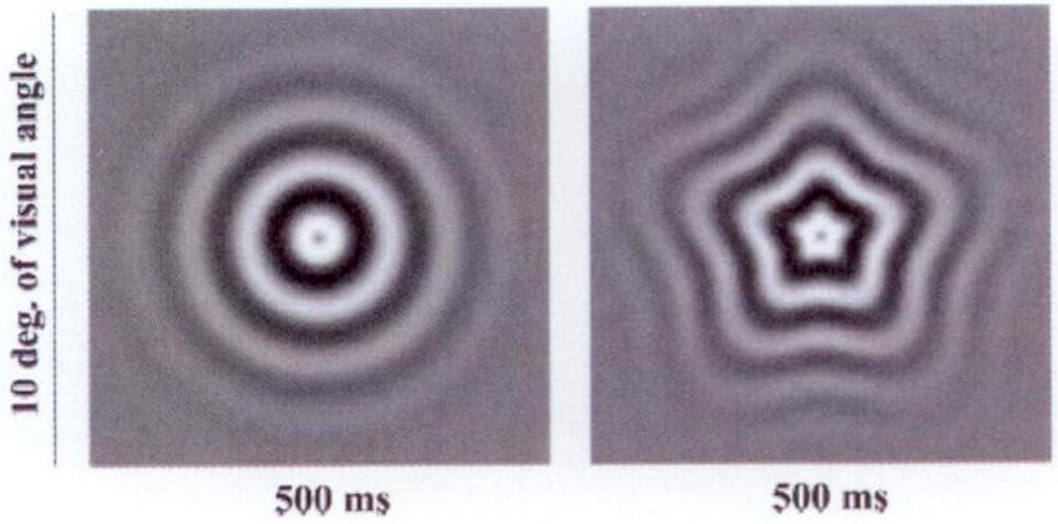


Fig. 1 High contrast sinusoidal concentric grating (0.8 c/deg), subtending 10 deg^2, followed, 500 ms after onset, by a similar grating radially modulated in frequency.

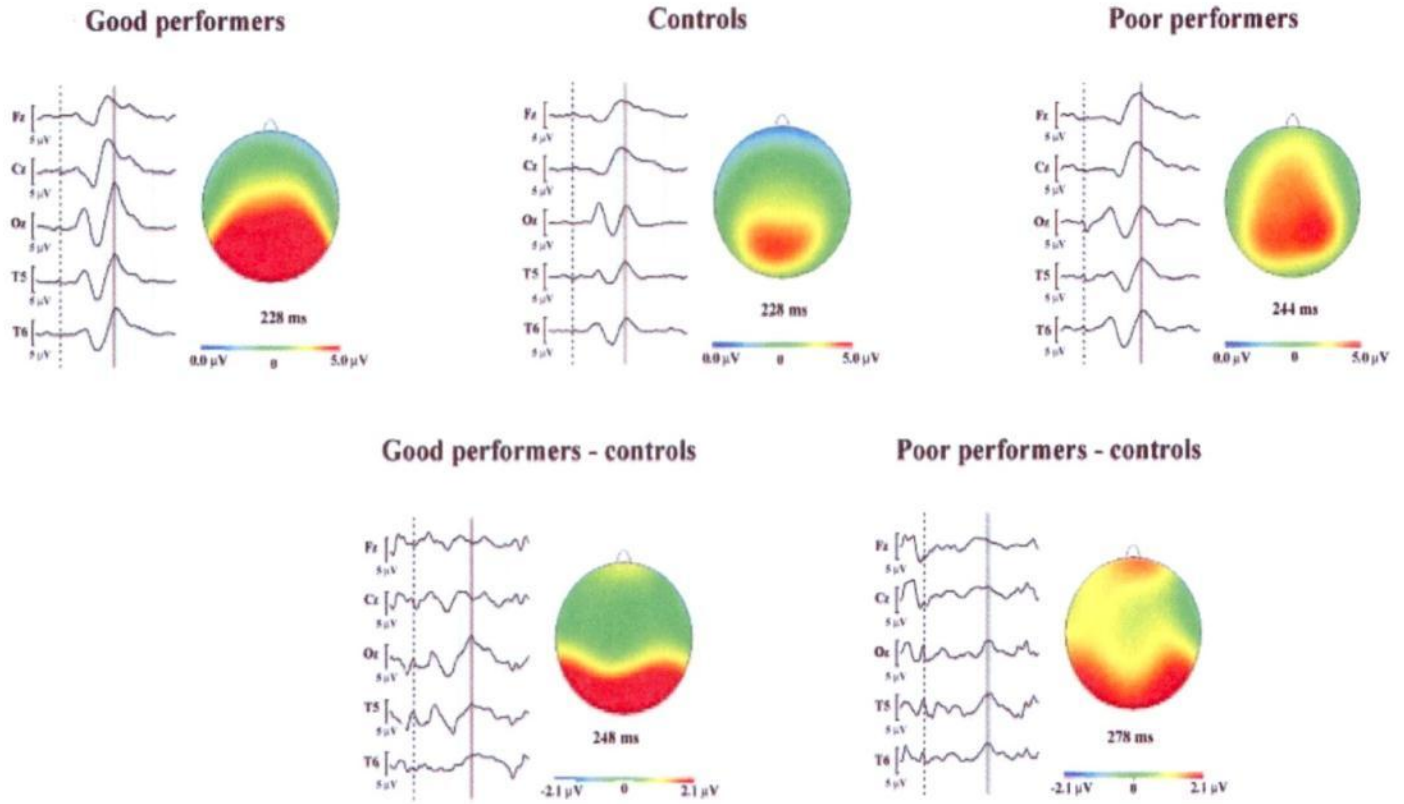


Fig. 3 *Top*: Waveforms for five electrodes (Fz, Cz, Oz, T5, T6) next to topographical maps of the mean voltage amplitudes (μV—see middle colour bar) in good performers (*left*), controls (*middle*) and poor performers (*right*) groups, at the maximum amplitude of the Oz P2 component (see blue vertical line on the curves at left side of each map). *Bottom*: Subtraction waves next to topographical maps representing *t*-statistics of the differences between the good performers and controls (*left*) as well as the poor performers and controls (*right*).

Cross-modal plasticity appears to be correlated to outcome.

128 channel high density EEG net
Clinically feasible high-density EEG testing

Photo courtesy EGI

Due to proprietary information contained on this slide, you will not be able to view it.

Thank you for your understanding.

How does cross modal re-organization affect integration across auditory and visual modalities?

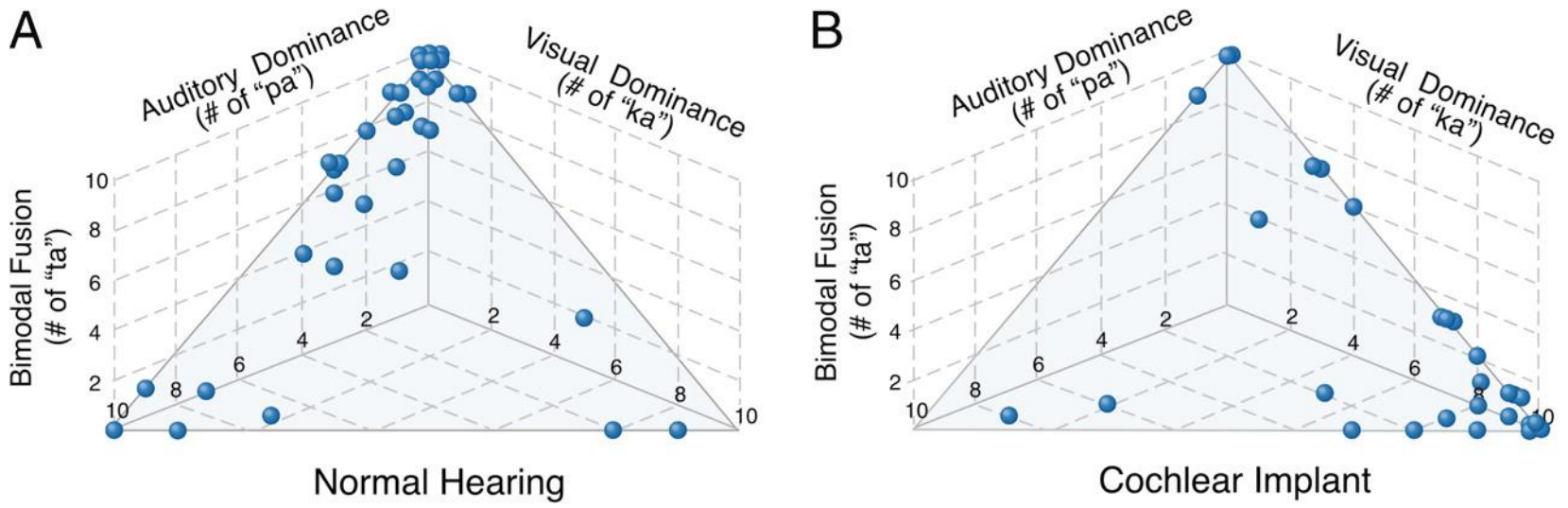
McGurk Effect

Auditory-Visual Fusion

e.g., hear /pa/, see /ka/

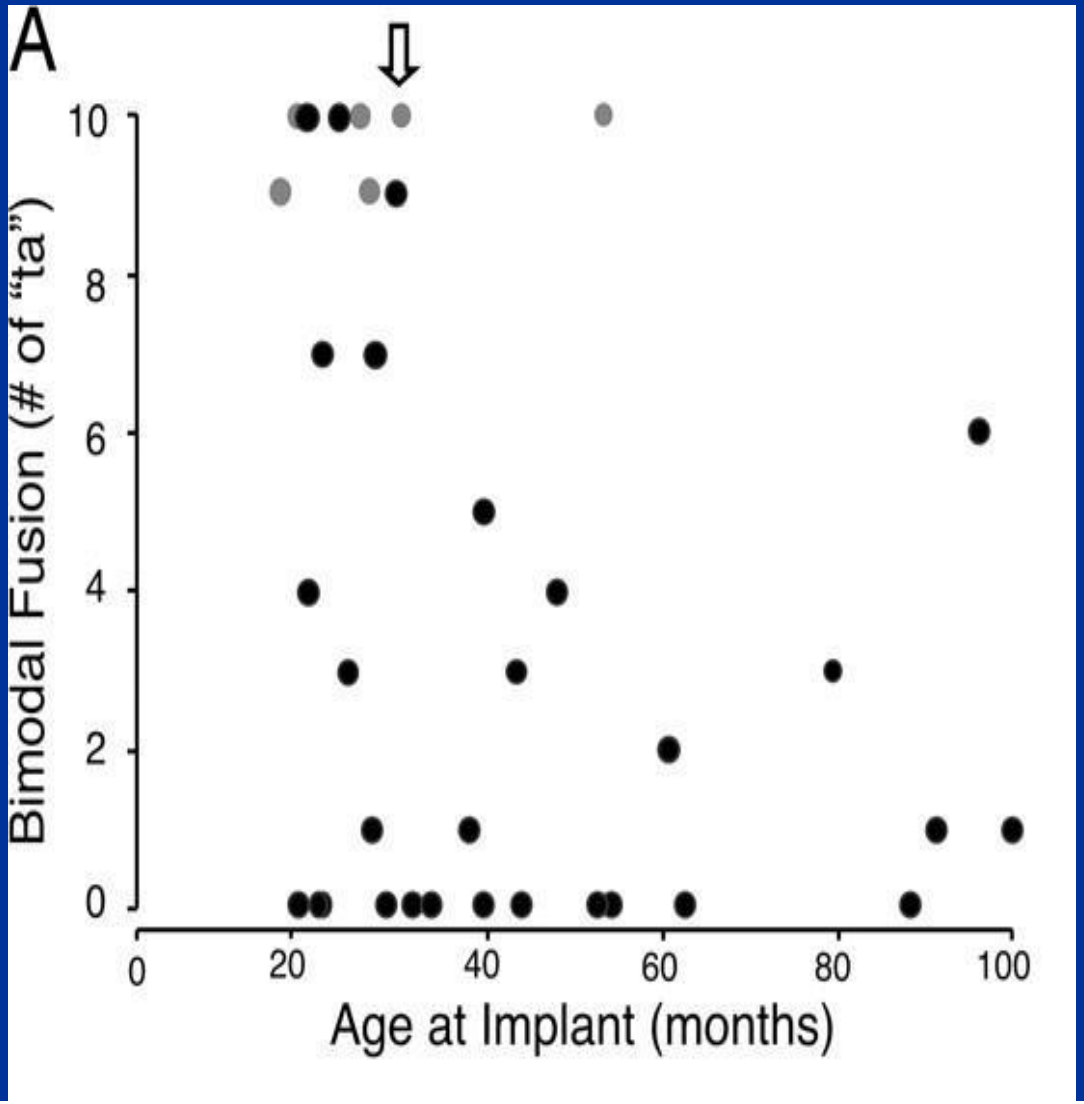
perceive /ta/

Responses of individual subjects to the incongruent auditory-visual/pa/ka/stimulus (McGurk test). “ta” responses indicate audiovisual fusion, “pa” responses indicate auditory dominance, and “ka” responses indicate visual dominance.



Schorr E A et al. PNAS 2005;102:18748-18750

Late-implanted children show deficits in auditory-visual integration



Schorr, Efrat A. et al. (2005) Proc. Natl. Acad. Sci. USA 102, 18748-18750

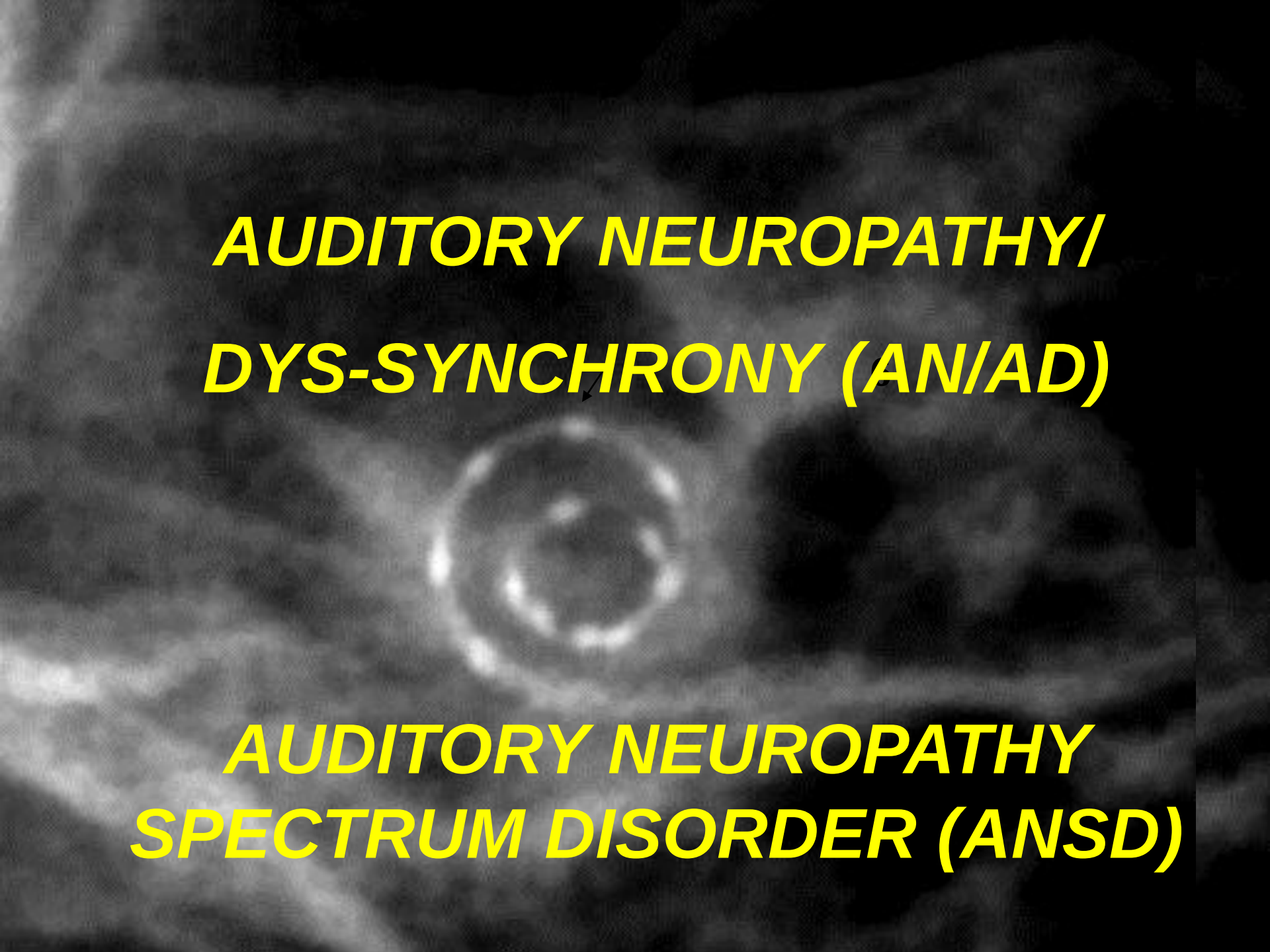
PNAS

Conclusions

There is a sensitive period for optimal performance with the cochlear implant in congenitally deaf children.

Deafness that continues beyond these sensitive periods results in cortical re-organization.

Cortical re-organization typically results in poor outcomes for oral language learning.


AUDITORY NEUROPATHY/
DYS-SYNCHRONY (AN/AD)
AUDITORY NEUROPATHY
SPECTRUM DISORDER (ANSD)

DEMOGRAPHICS

INCIDENCE- 10% -15% of children with sensorineural hearing loss.

Sininger, Hood, Berlin, Uus. (Talaat et al., 2009, Kirkhim et al., 2008)

Characteristics of ANSD: Summary

Evidence of outer hair cell function in the cochlea

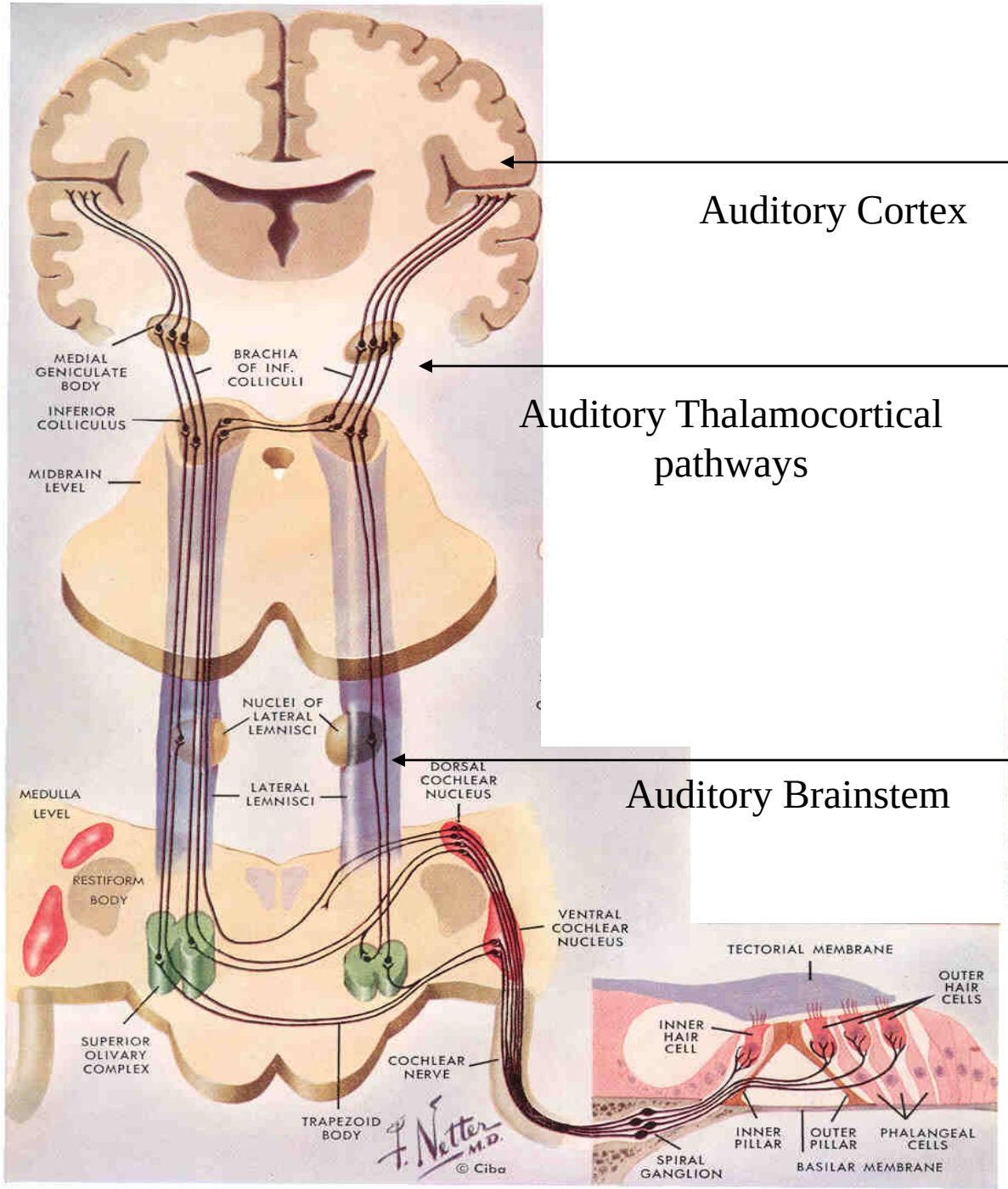
- Present OAE's
- Cochlear microphonic present in ABR

Evidence of neural impairment

- ABR is absent/abnormal
- Acoustic Stapedial reflexes are absent/abnormal
- Audiogram ranges from normal to profound, can fluctuate
- No correlation between speech perception skills and audiogram

- High inter and intrasubject variability

Lack of neural synchrony is a hallmark of children with ANSD



Auditory Cortex

?

Auditory Thalamocortical pathways

?

Auditory Brainstem

ABR

No Response/Abnormal resulting in degraded acoustic signal

Cochlea

CAEP in ANSD

CAEP can be measured in many patients with ANSD

- Starr et al., (1991), Kraus et al., (2000), Rance et al., (2002, 2004, 2005, 2008, 2009), Michalewski et al., (2005, 2009), Pearce et al. (2007)

Aim

To explore development and plasticity of the central auditory pathway in with ANSD.

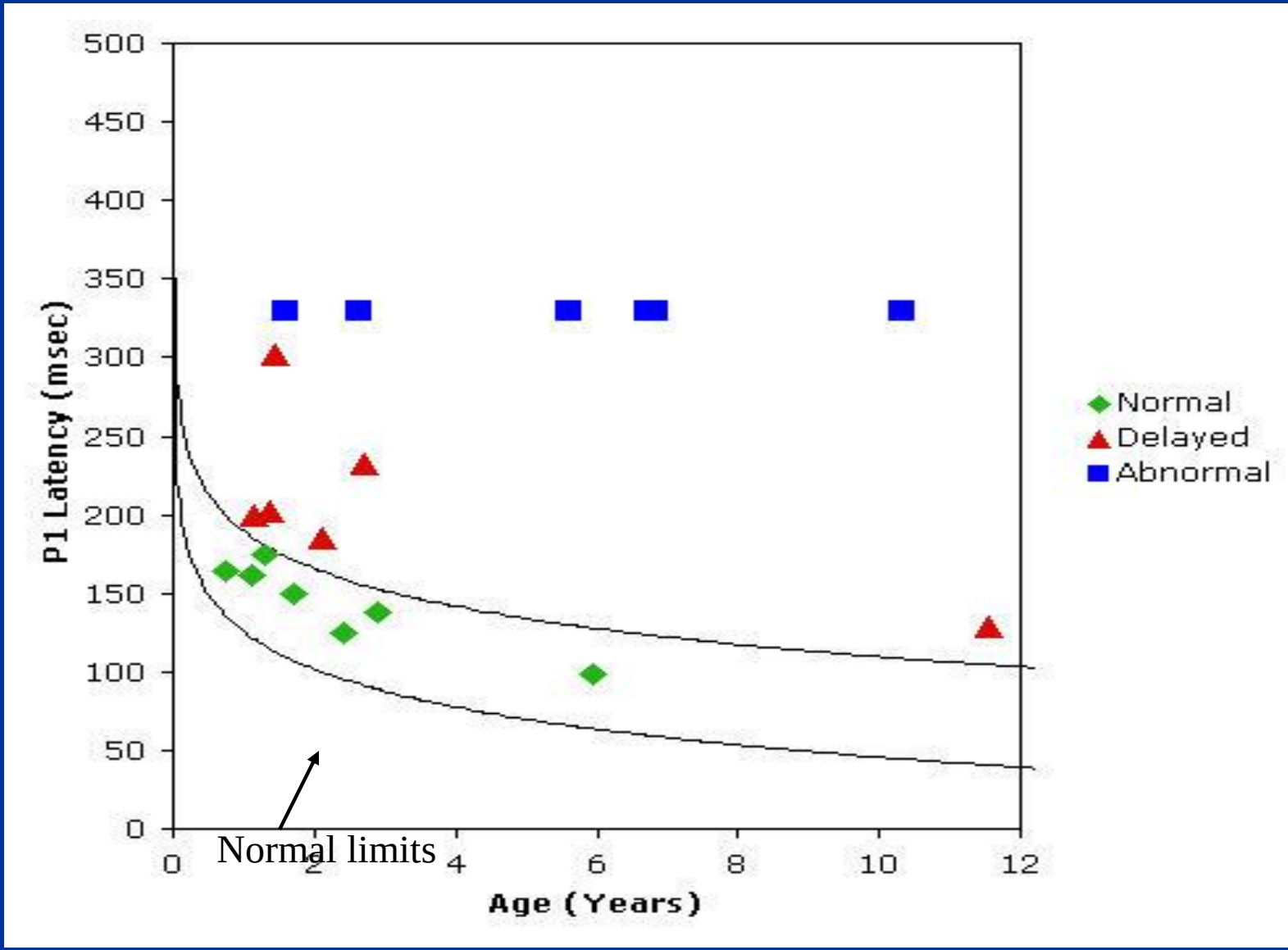
Cortical Maturation in Children with ANSD

- Existing data base of 115 children with ANSD on whom we have cortical maturation data.
- Majority have congenital disorder
- Initial analysis on subset of children

Sharma et al., (2011) *Int J Audiol* 50(2):98-106.

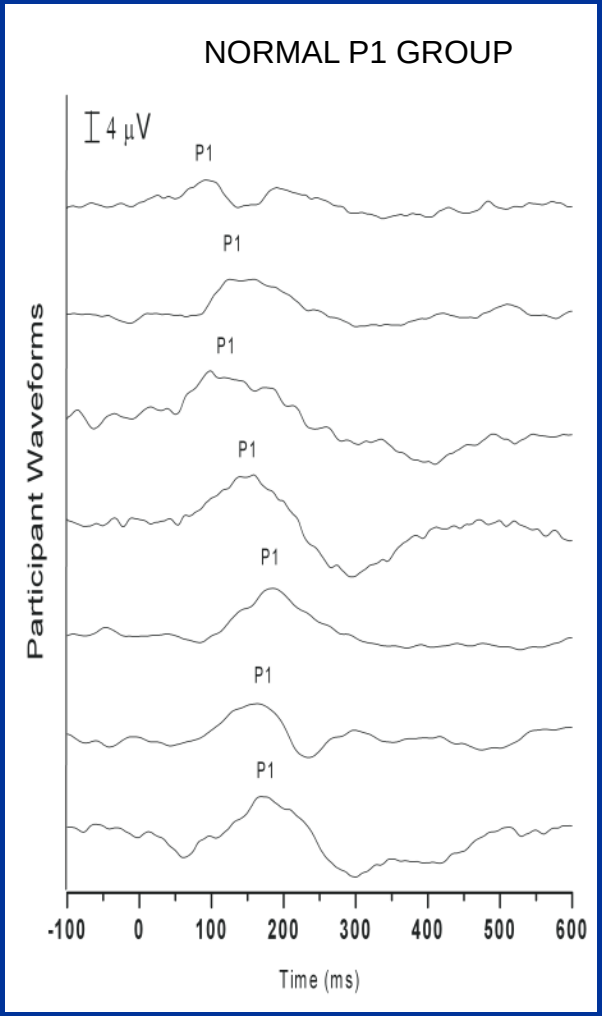
Participant	Etiology	ABR	OAE - R	OAE - L	PTA unaided R	PTA unaided L	HA Fit Age
NORMAL							
1	Jaundiced - no trtmt	CM present Au - 92 dBnHL	DPs absent	DPs absent	118	108	1.08
2	no risk factors	CM present Au; Wave V component developed over time down to 50 dBnHL(prolonged interpeak latencies)	TEOAEs present	TEOAEs/DPOAEs present	63	31	1.19
3	oxygen deprivation @ birth	CM present Au (100) Wave V @ 100	DPOAEs absent	DPOAEs absent		95	1.68
4	prematurity (27 week), low birth weight, hyperbilirubinemia, chronic lung disease, ototoxic meds	CM present Au (80dBnHL)	TEOAEs absent	TEOAEs absent	62	70	0.77
5	prematurity (36 weeks), mech vent, diaphragmatic hernia, ototoxic meds	CM present Au - initially no Wave V. Wave V emerged with CM Au(60 RE/70LE) at age 2 mo	TE and DPOAEs partially present -reduced amp over time	TE and DPOAEs partially present -reduced amp over time	72	75	0.27
6	prematurity (31 week), NICU stay, jaundice (blood transfusion), mech. Vent	CM present Au (90)	TE and DPOAEs present	TE and DPOAEs present	38	70	0.36
7	premature	CM Present (down to 65) Au	absent	absent	82	78	0.33
DELAYED							
8	prematurity, failure to thrive, kidney problems, blood transfusion	CM clear for RE (85), no distinguishable wave V LE	tracings unavailable	tracings unavailable	95		0.63
9		CM noted - clearer for LE	DPOAEs absent	DPOAEs absent	90	80	0.16
10	prematurity (24 week), low birth weight, hyperbilirubinemia, 3 blood transfusions	CM present Au (90)	TE and DPOAEs absent	TE and DPOAEs absent	60		1.29
11	prematurity (36 week), acute hepatitis and kidney failure, ototoxic meds, NICU stay, mech ventilation	CM present Au (90, 80) - larger left ear	TEOAEs absent	TEOAEs absent	70	67	2.62
12	family history - no known risk factors	CM present, (90, 21.1) Au, reversal down to 11.1	TE absent, DPOAE present	TE absent, DPOAE present	82	85	2.38
13	prematurity (28 week), jaundiced, mech vent, chronic lung disease, hypothyroidism	unilateral AN - CM RE only	TEOAEs absent	TEOAEs absent	80	82	0.59
ABNORMAL							
14	maternal tuberculosis + medication, radiation exposure (X-Ray in utero), hernia on umbilical cord	CM Present Au (90)	DP/TEOAEs partially present	reported absent	93	68	6.72
15	jaundiced	CM present Au (90dBnHL)	TE and DPOAEs present	TE and DPOAEs present	98	93	2.4
16	prematurity (gest. Age 6 mo), transfusions, extended NICU stay, ototoxic meds	CM present Au (90/95 R)	DPOAEs absent	DPOAEs absent	83	85	2
17	seizures, family history of hearing loss	CM present, (90, 21.1) Au, reversal down to 11.1	TEOAEs absent/DPOAEs present	TEOAEs absent/DPOAEs present	93	98	6.12
18	epilepsy, other developmental delays	CM Present (92) Au, more clear for left ear	TEOAEs absent	TEOAEs absent	111	80	1.82
19	prematurity (32 week), NICU stay, mech vent, blood transfusions, ototoxic meds	CM present Au (80)	TE and DPOAEs absent	TE and DPOAEs absent	62	93	0.72

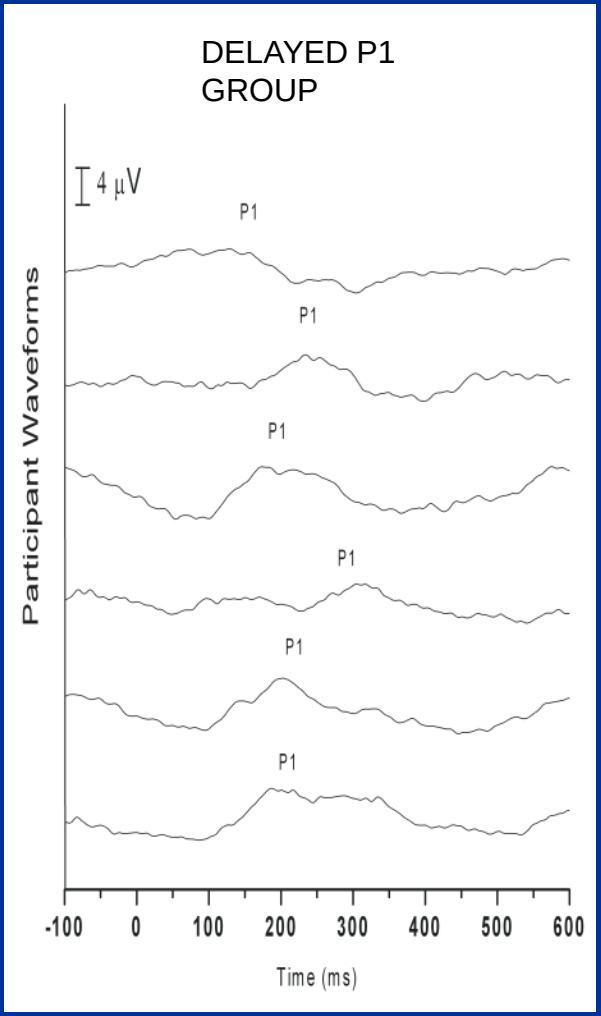
Cortical response (P1) latencies

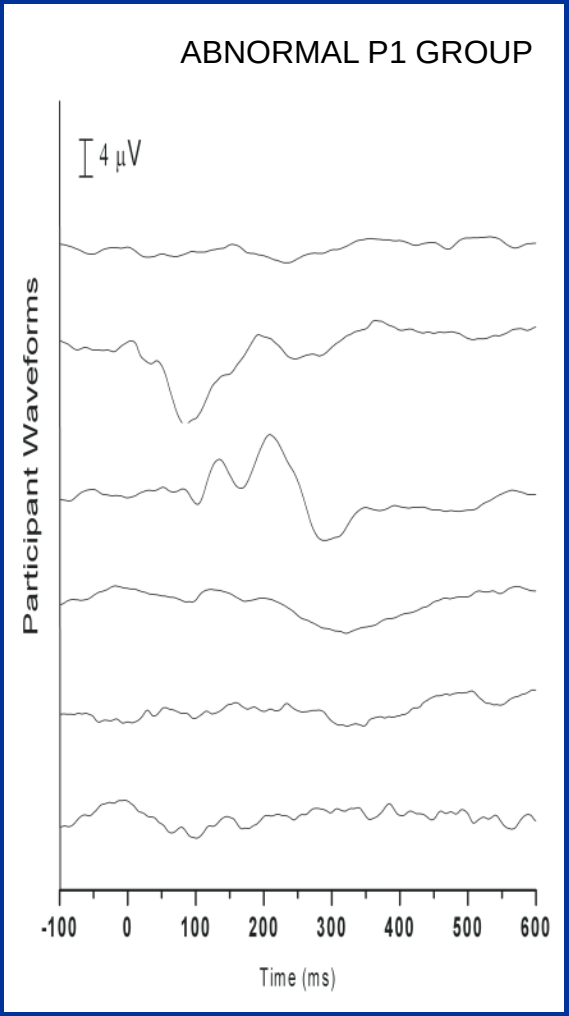


Sharma et al., (2011) *Int J Audiol* 50(2):98-106

ANSD CHILDREN FELL INTO 3 DISTINCT GROUPS REFLECTING THE EXTENT OF DISRUPTION IN NEURAL DYS-SYNCHRONY AND ITS EFFECT IN CORTICAL DEVELOPMENT.







Sharma et al., (2011) *Int J Audiol* 50(2):98-106.

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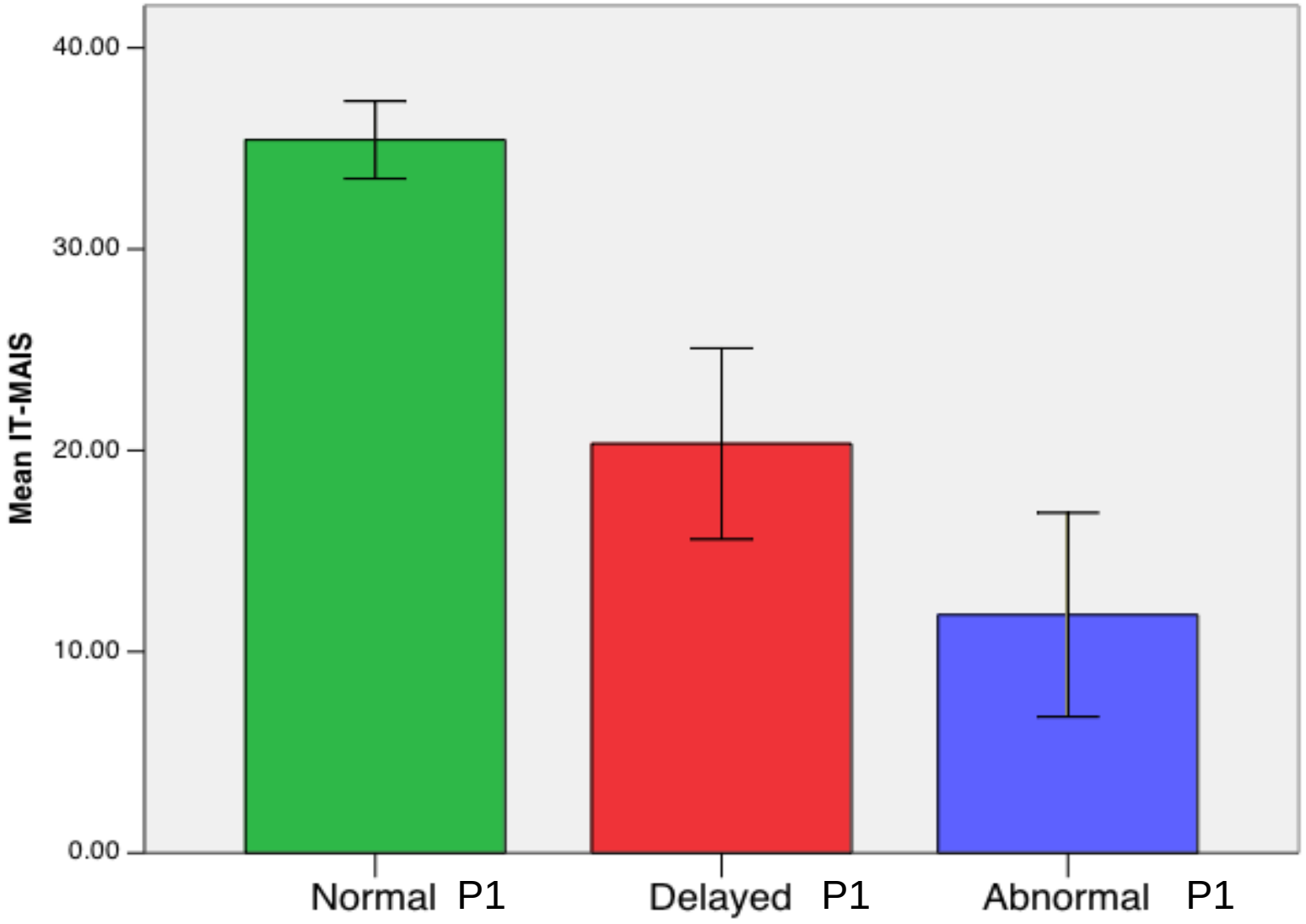
Thank you for your understanding.

We correlated the P1 against the IT-MAIS test of auditory skill development.

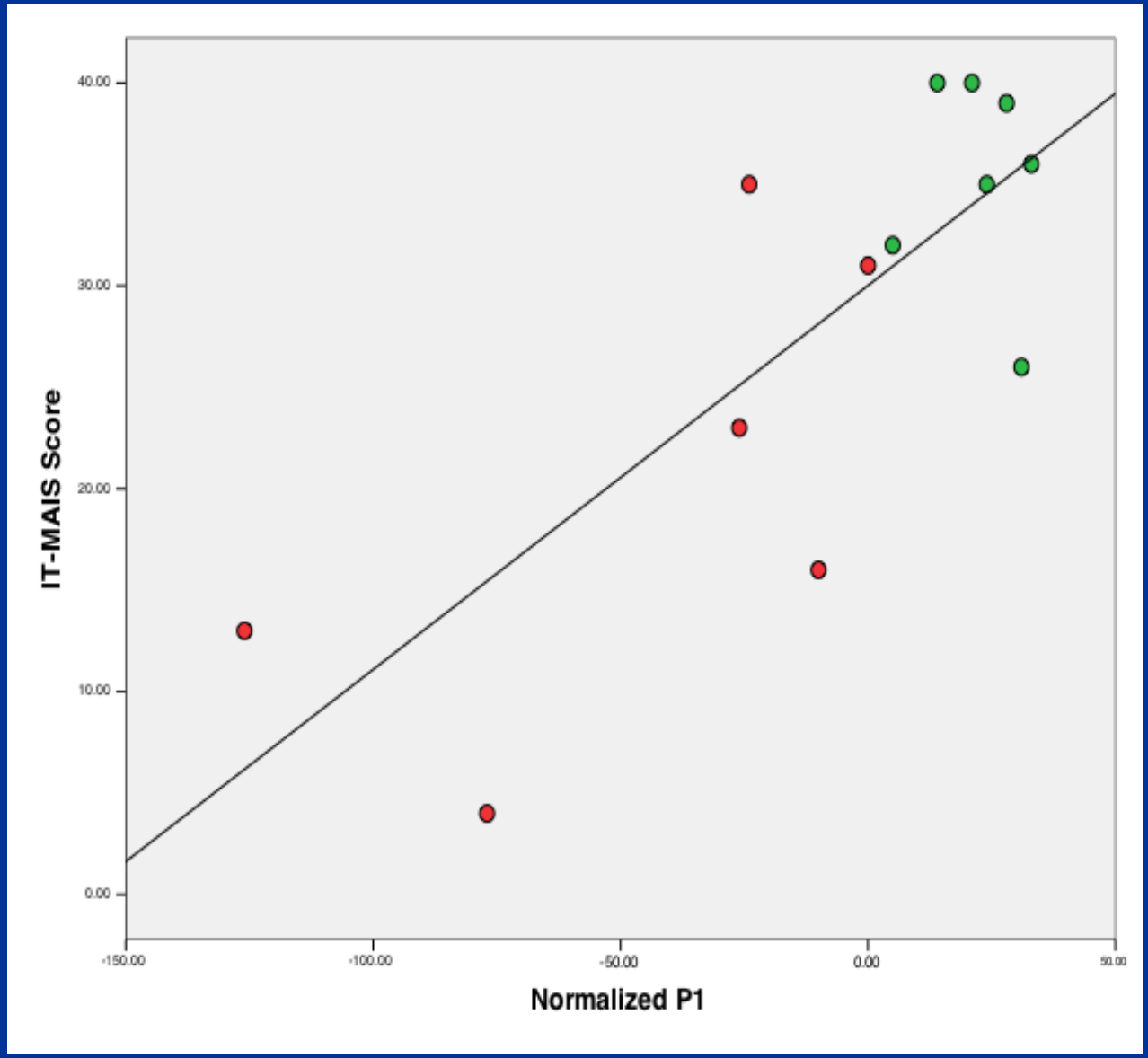
P1 vs auditory development



Sharma et al., (2011) *Int J Audiol* 50(2):98-106

$p<0.05$

Relationship between cortical maturation and behavioral auditory skill development.



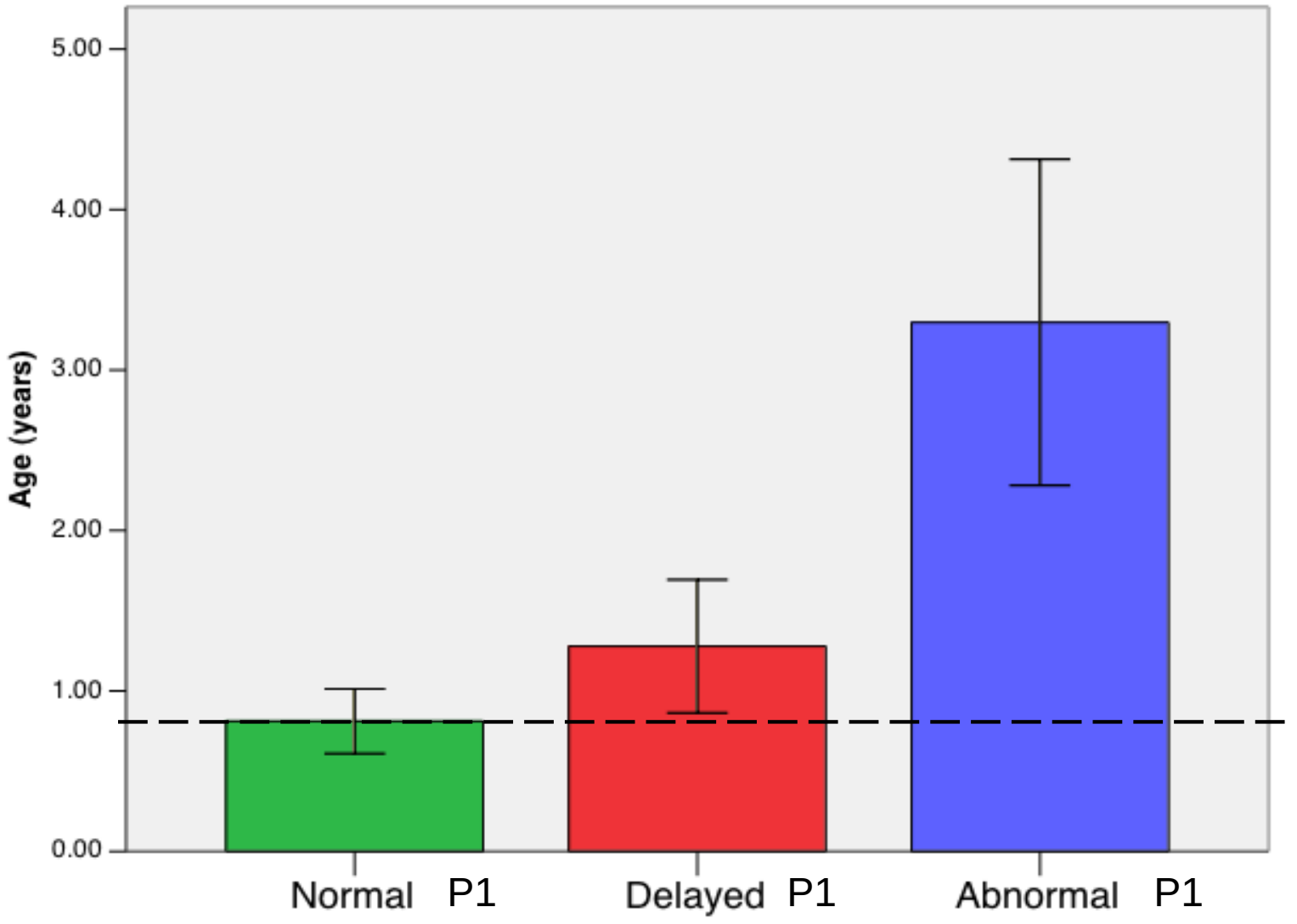
$r=0.8$ $p<0.05$

$R^{2=}0.6$

Sharma et al., (2011) *Int J Audiol* 50(2):98-106

Cortical maturation may be an important predictor of speech/language outcomes in children with ANSD.

Hearing aid fit age



Sharma et al., (2011) *Int J Audiol* 50(2):98-106

P<0.05

- There are likely sensitive periods for cortical maturation in children with congenital ANSD.

- Appropriate treatment options provided within these time frames may increase likelihood of successful outcomes for children with ANSD.

Summary

- 38% of children showed normal cortical development and good behavioral outcomes.
- *Normal cortical development is suggestive of mild synchrony problem which may benefit from hearing aids consistent with Rance et al., (2002).*

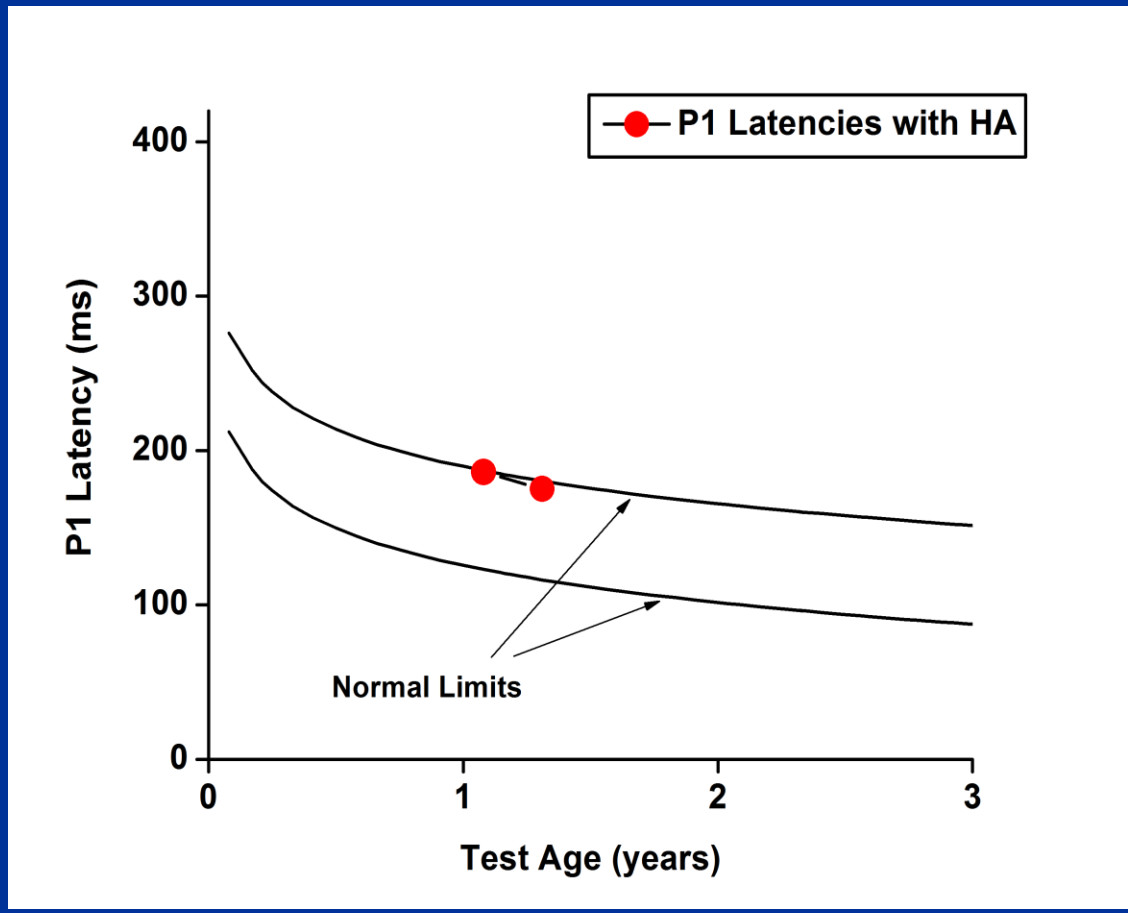
- 33% showed delayed and 29 % showed abnormal cortical development and poor behavioral outcomes.
- *Delayed and abnormal cortical development likely reflect more severe synchrony problems.*

Sharma, Cardon et al., International Journal of Audiology 2011; 50: 98–106

We are exploring the use of cortical potentials to assist in management of children with ANSD.

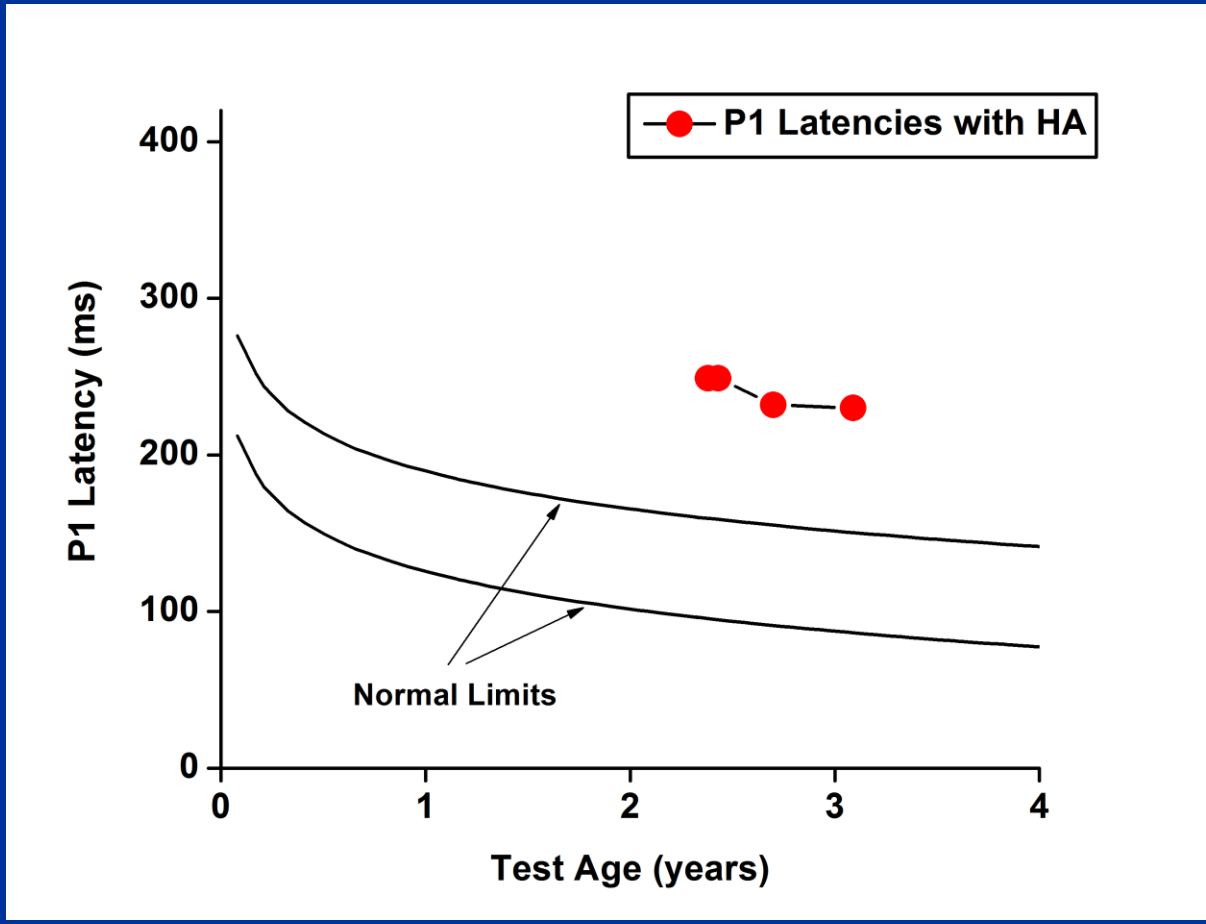
Benefit From Hearing Aid Use

- IT-MAIS Score: 32
- IT-MAIS Age: 1.08
- PTA Unaided: 62
- PTA Aided: 40
- HA Fit Age: .77
- Etiology: prematurity (27 week), low birth weight, hyperbilirubinemia, chronic lung disease, ototoxic meds



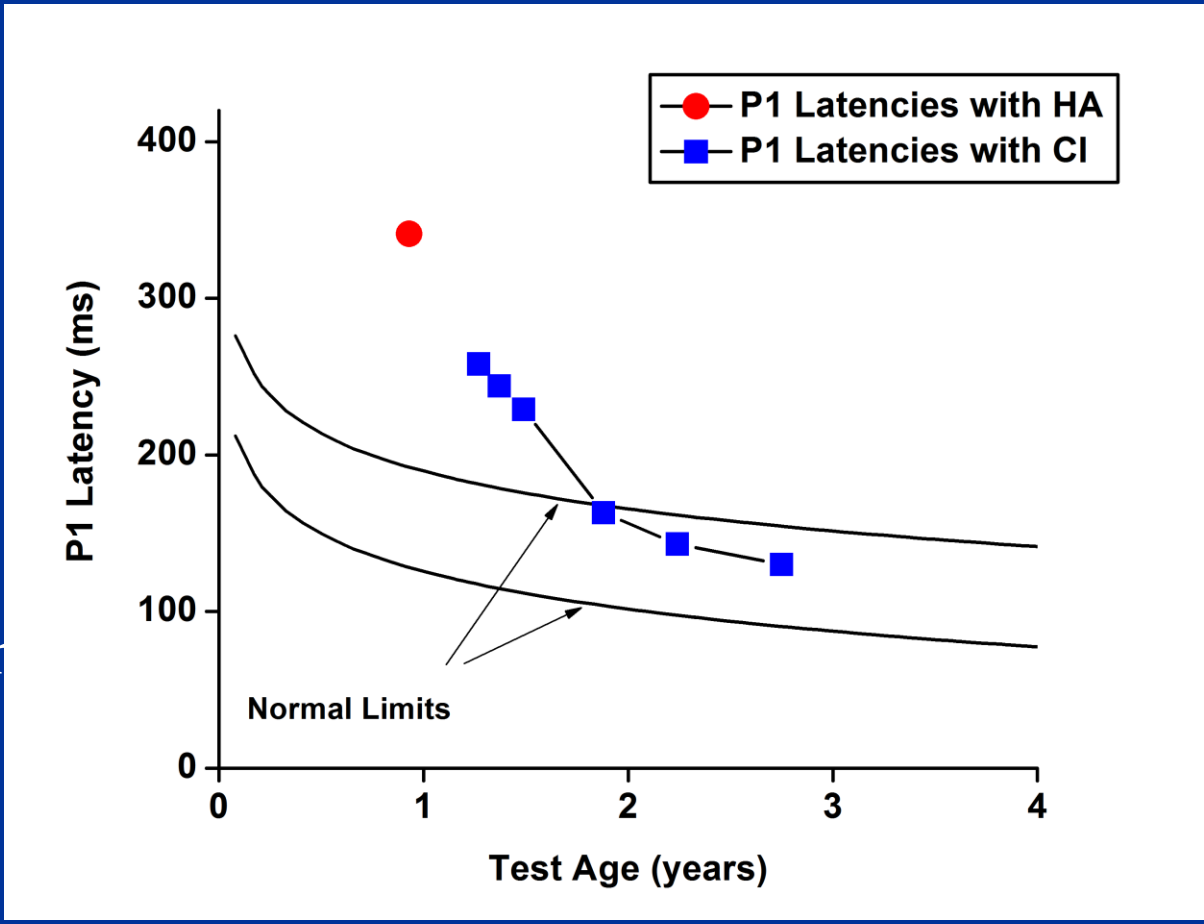
No Benefit From Hearing Aid Use

- IT-MAIS Score: 4
- IT-MAIS Age: 1.08
- PTA Unaided: 83
- PTA Aided: 57
- HA Fit Age: 2.38
- Etiology: family history no known risk factors



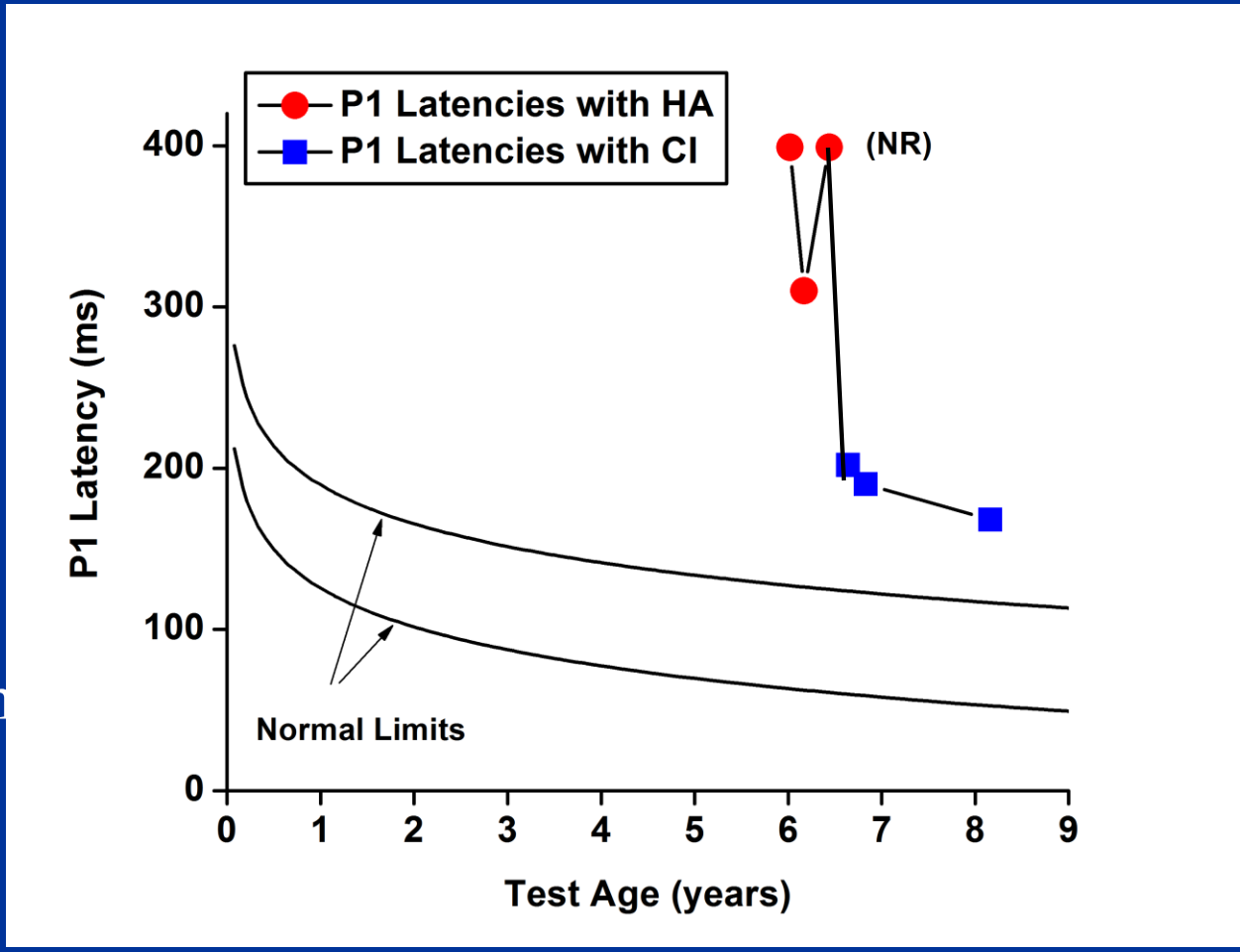
Benefit From CI Use

- IT-MAIS Score:
- IT-MAIS Age:
- PTA Unaided: 105
- PTA Aided: 85
- HA Fit Age: .90
- CI Fit Age: 1.27
- Etiology: twin - no other known risk factors

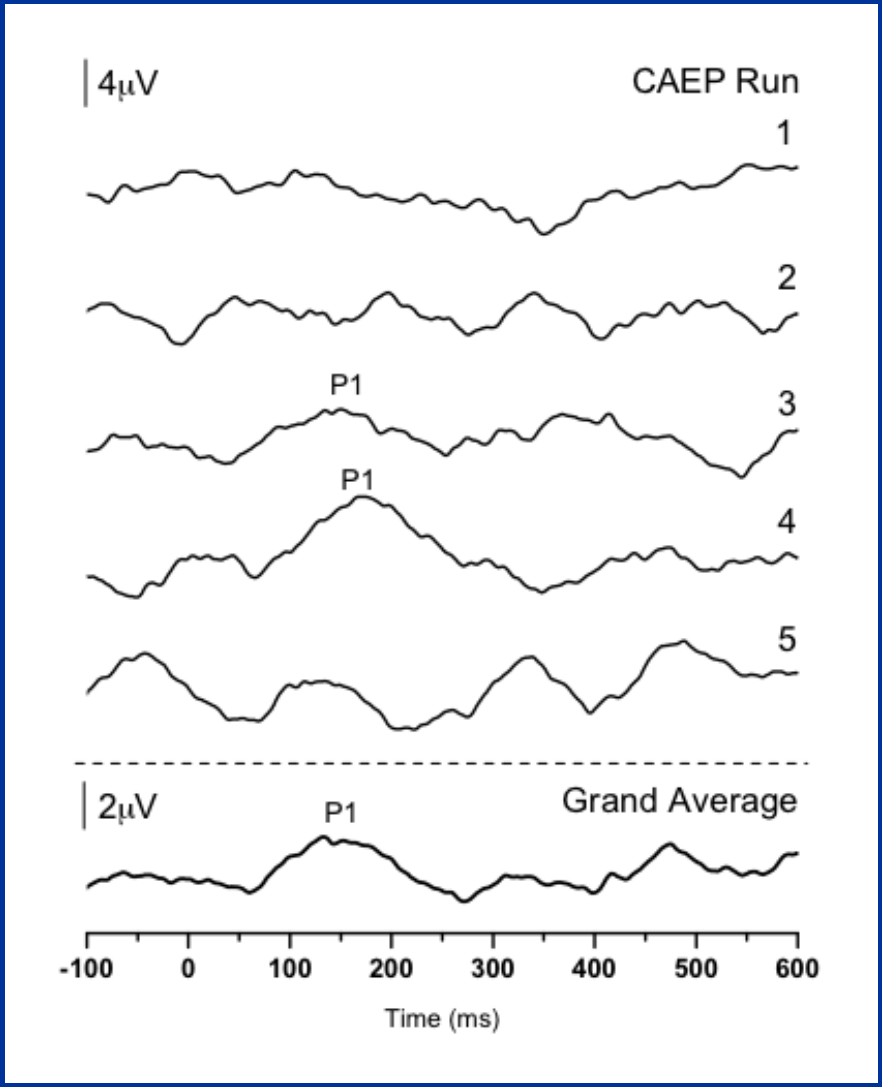


Persistently Delayed Post-implant

- IT-MAIS Score: 9
- IT-MAIS Age: 6.83
- PTA Unaided: 95
- PTA Aided: 65
- HA Fit Age: 6.12
- CI Fit Age: 6.62
- Etiology: seizures, fam
  history of hearing loss



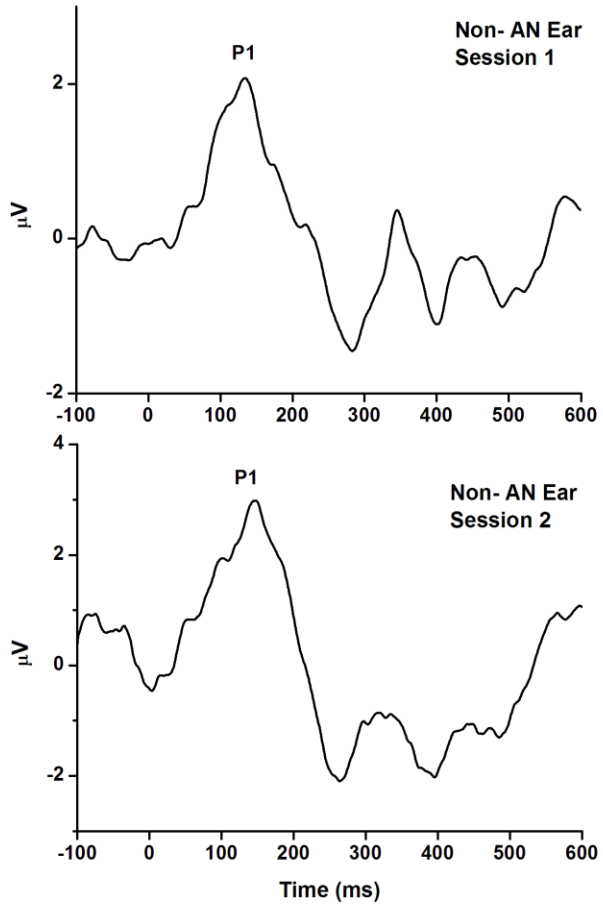
High Intra-individual variability in some patients with ANSD



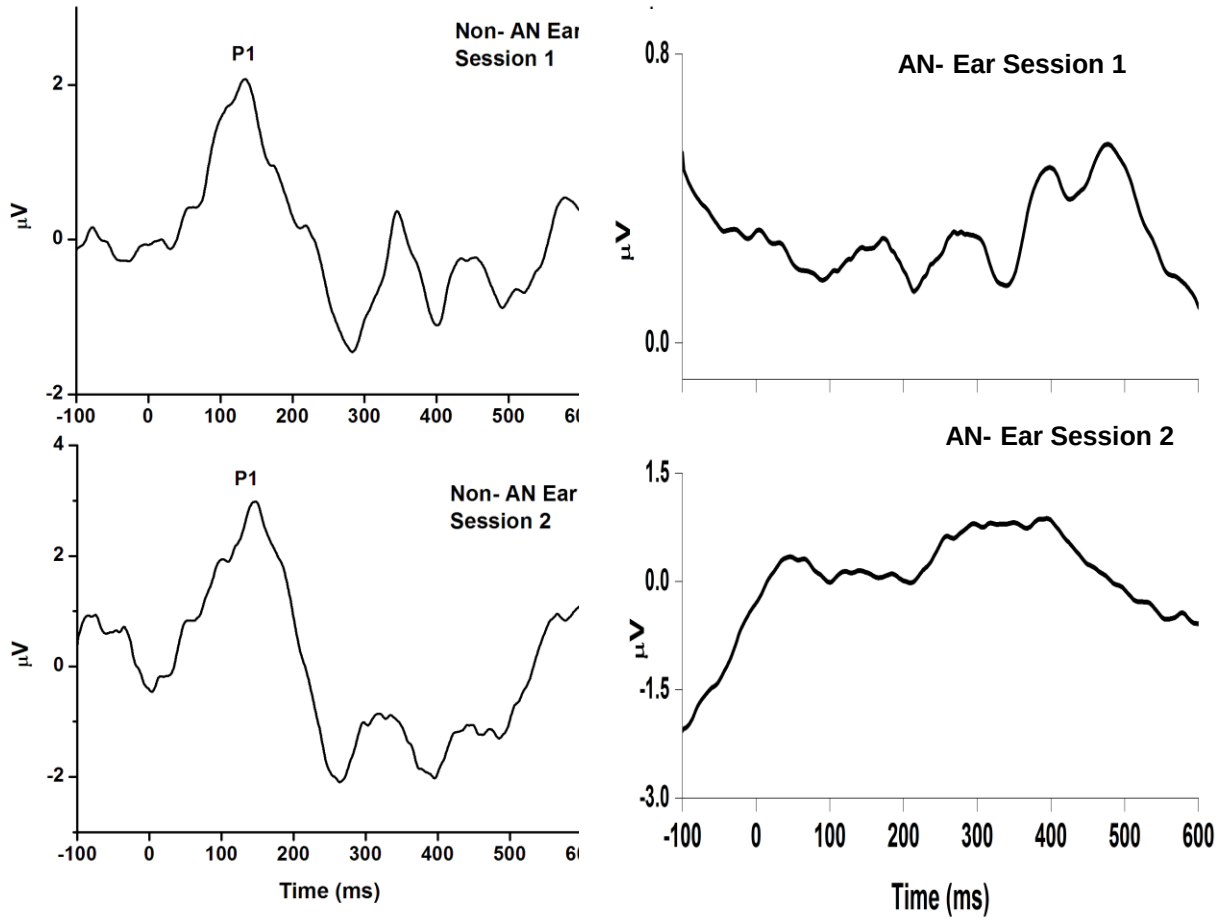
Case Study

- 9 year old child with congenital unilateral AN in left ear.
- AN ear: Normal OAE, Abnormal ABR; mild hearing loss, speech discrimination 20%, poor speech perception in noise.
- Non AN ear: Normal OAE, ABR, normal pure tone thresholds, speech discrimination 92%, good speech perception in noise.

9 yr. old with unilateral ANSD



9 yr. old with unilateral ANSD



High Density EEG study

Cortical Auditory Evoked Potentials

from 64 scalp electrodes

Due to proprietary information contained on this slide, you will not be able to view it.
Thank you for your understanding.

CONCLUSIONS

Children with ANSD show different patterns of cortical maturation.

Normal cortical maturation appears to reflect better synchrony and is a good predictor of acquisition of oral speech and language.

On the other hand, delayed, abnormal and variable cortical potentials reflect poor dys-synchrony and correlates with poor speech outcomes.

Overall Conclusions

Cortical potentials are powerful objective bio-markers of central auditory system plasticity and maturation.

Biomarkers of plasticity are useful to guide clinical intervention via hearing aids and/or cochlear implants for children with hearing loss and ANSD.

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