Sound Wave Symposium, San Diego, 2018

Developmental Plasticity and Progressive Hearing Loss

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Developmental Plasticity and Progressive Hearing Loss

[1] Developmental plasticity in the auditory system:

Knowledge from basic science (animal) models.

General principles e.g.: age related plasticity, critical or sensitive developmental periods.

Clinical perspectives from cochlear implantation in children.

[2] Some perspectives on progressive hearing loss:

The peripheral "cascade" effect.

Timing of progressive hearing loss in relation to age related plasticity.

[3] Novel perspectives on progressive hearing loss in children after CI.

Speech and language improvement can be like a progressive hearing loss.

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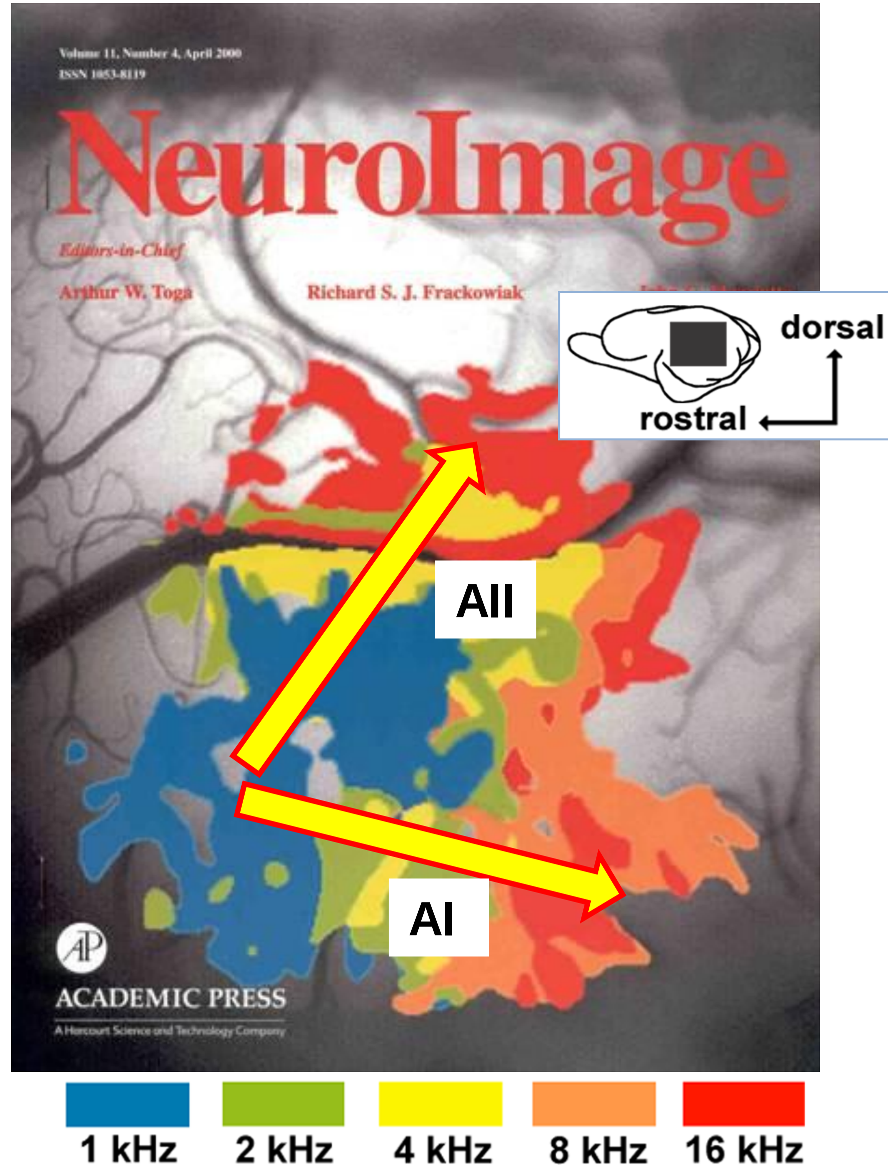
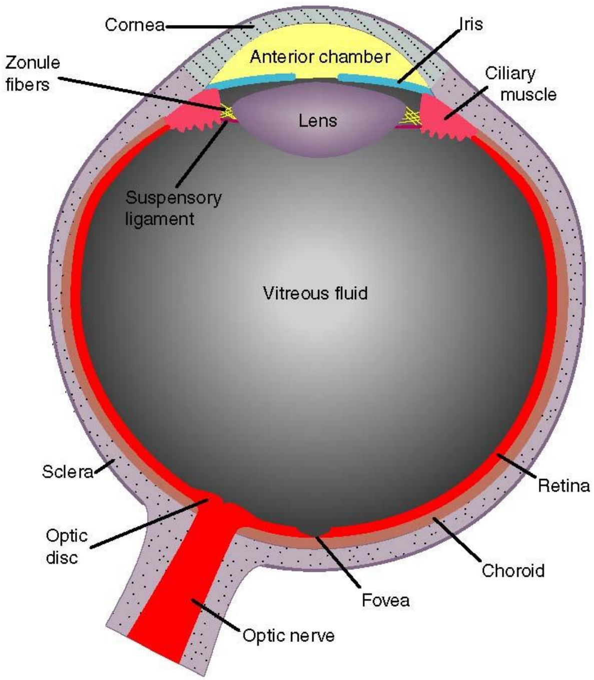
Speech and language improvement can be like a progressive hearing loss.

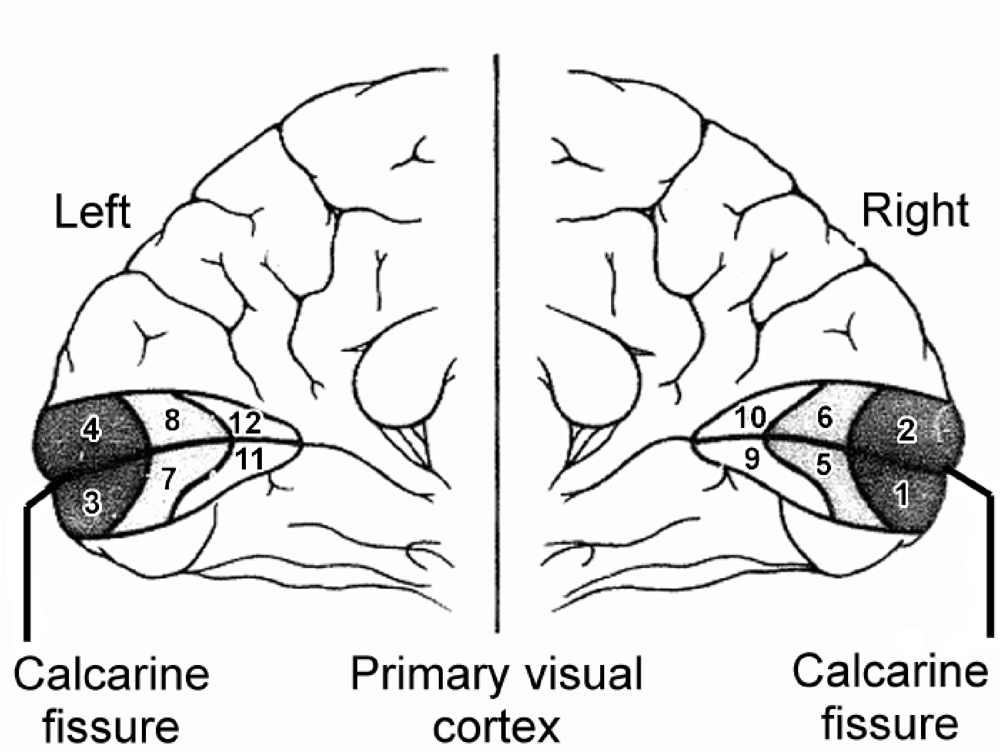
The sensory epithelium of the cochlea projects in organized way to auditory cortex.
(tonotopic /cochleotopic organization)

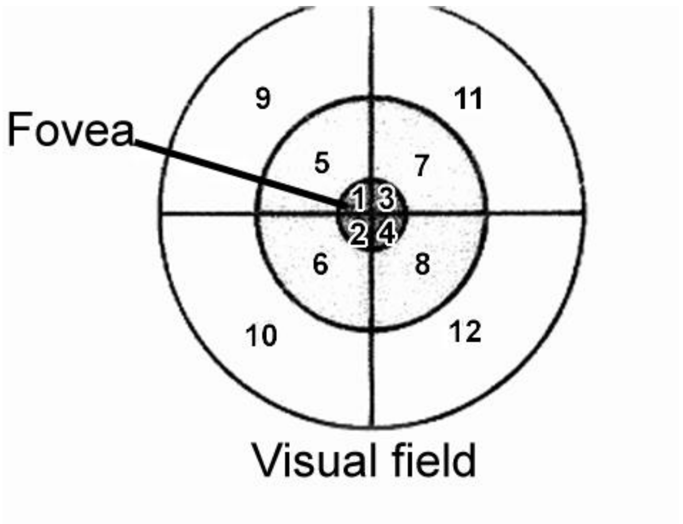


HAREL N, MORI N, SAWADA S, MOUNT RJ, **HARRISON, R.V.** (2000): Three distinct auditory areas of cortex (AI, AII, AAF) defined by optical imaging of intrinsic signals. NeuroImage 11:302-312

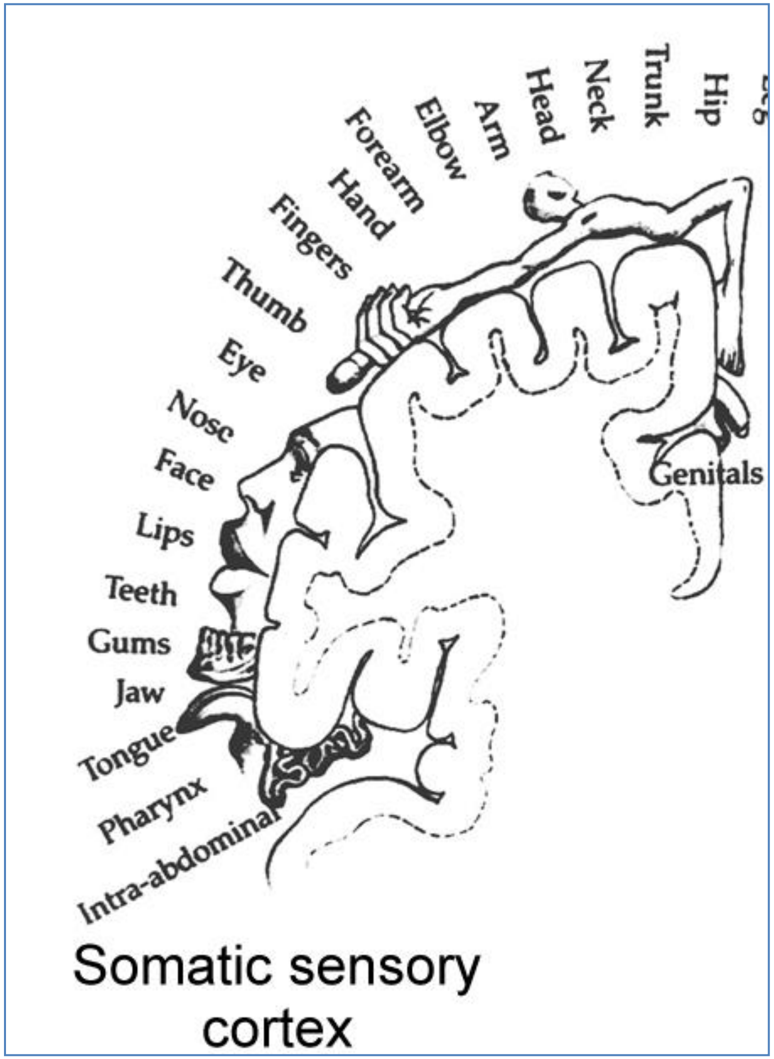
The RETINOTOPIC organization of the visual system



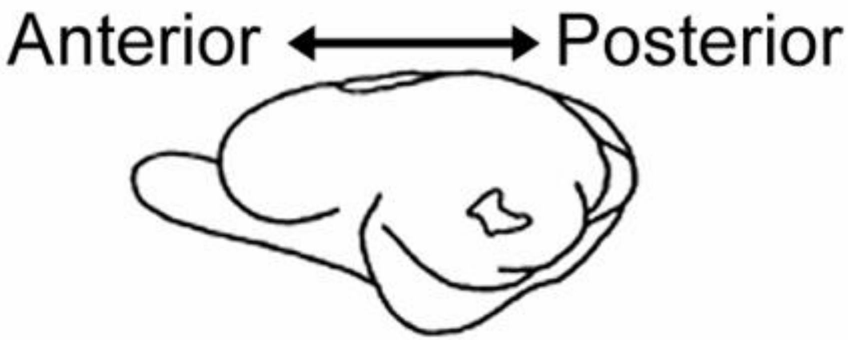


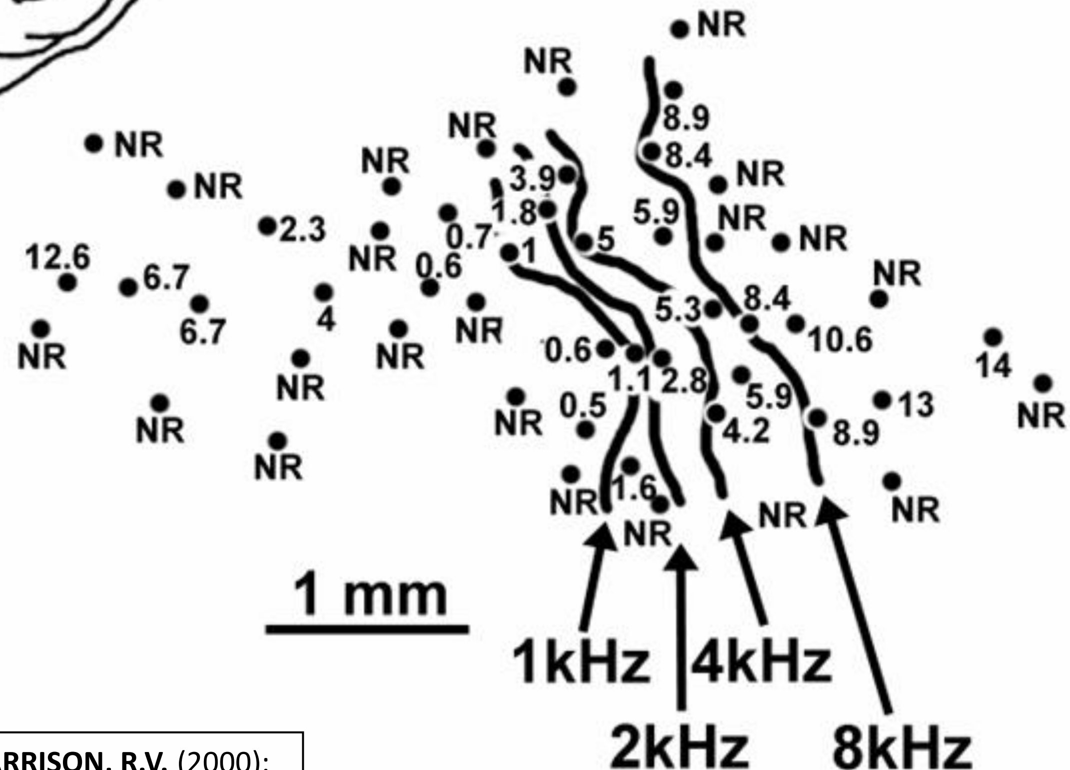


Somatotopic representation of the sensory surface of the skin



Mapping the tonotopic organization of auditory cortex using single unit electrophysiology



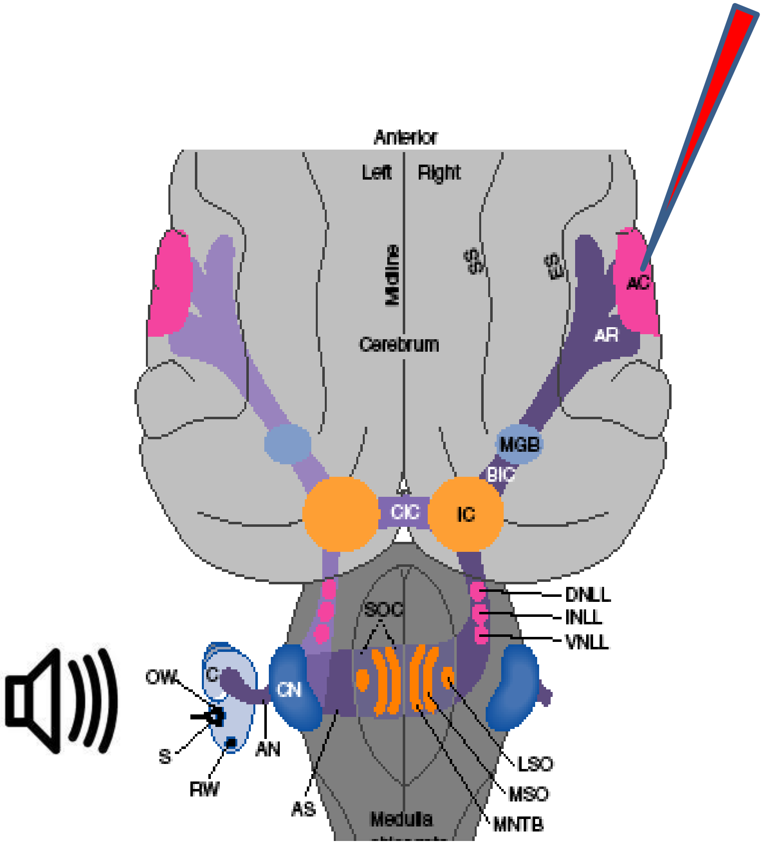


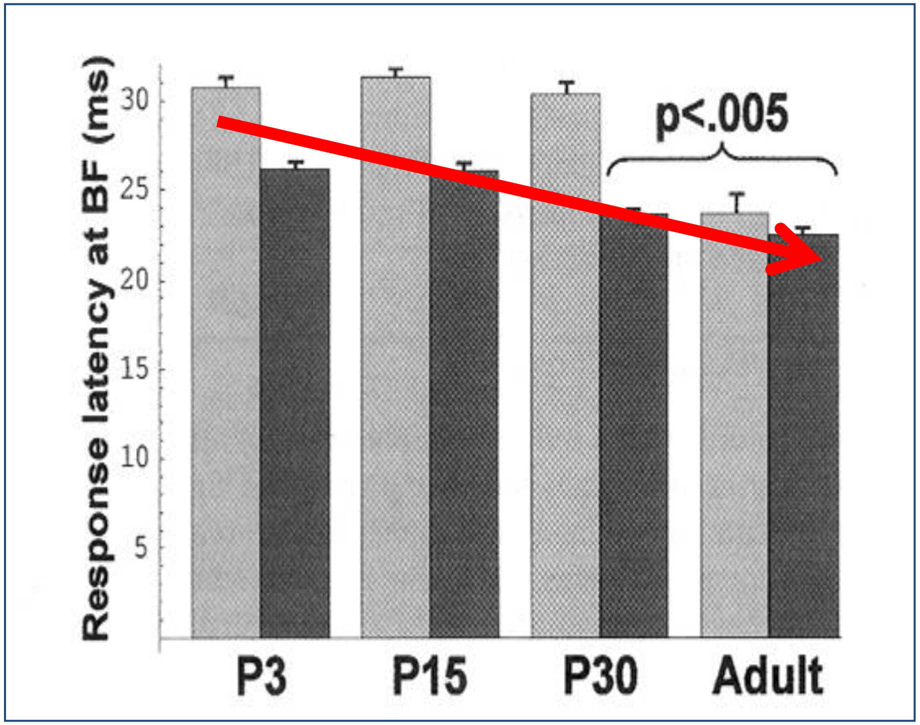
(chinchilla)

KAKIGI A, HIRAKAWA H, HAREL N, MOUNT RJ, **HARRISON, R.V.** (2000): Tonotopic mapping in auditory cortex of the adult chinchilla with amikacin induced cochlear lesions. Audiology 39:153-160

Neural "connectivity" improves with age

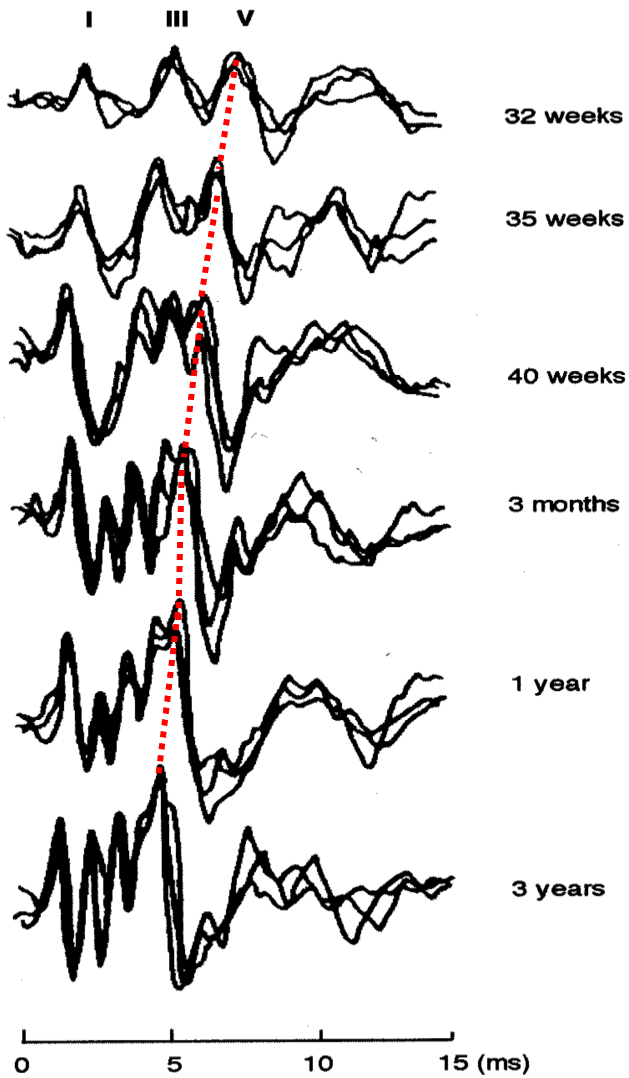
cortical neuron onset response latencies (chinchilla) at different ages



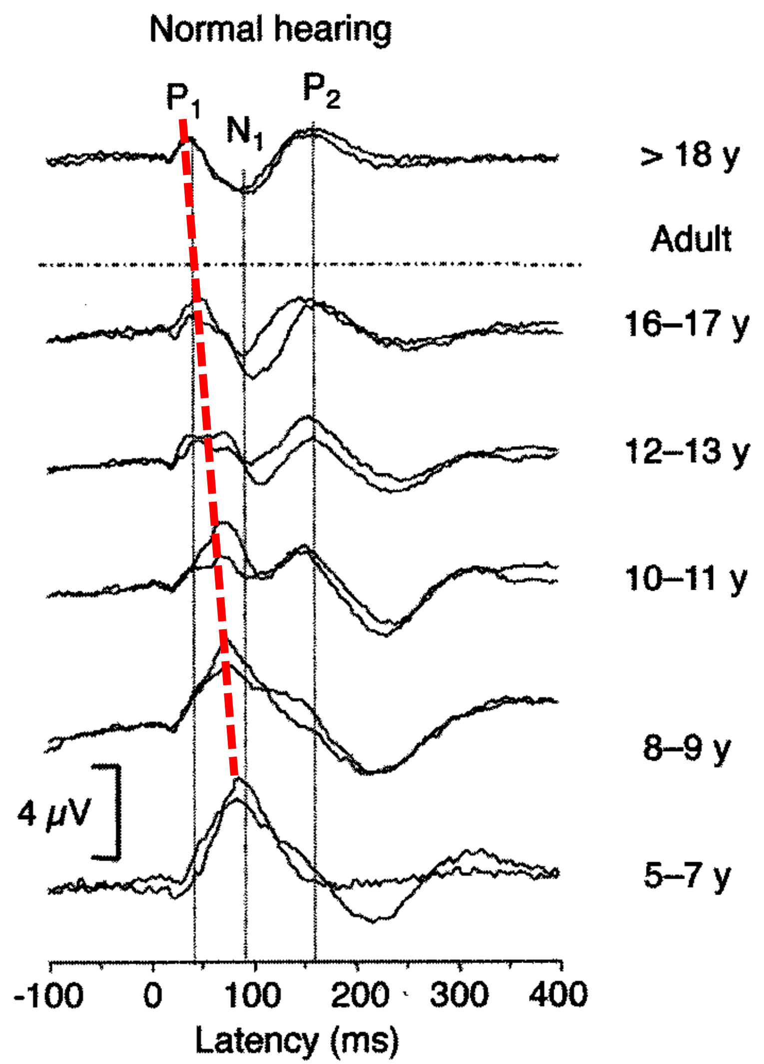


PIENKOWSKI M, **HARRISON RV**. (2005). Tone frequency maps and receptive fields in developing chinchilla auditory cortex.
J Neurophysiol. 93: 454-466

Evoked potential studies of human auditory system development



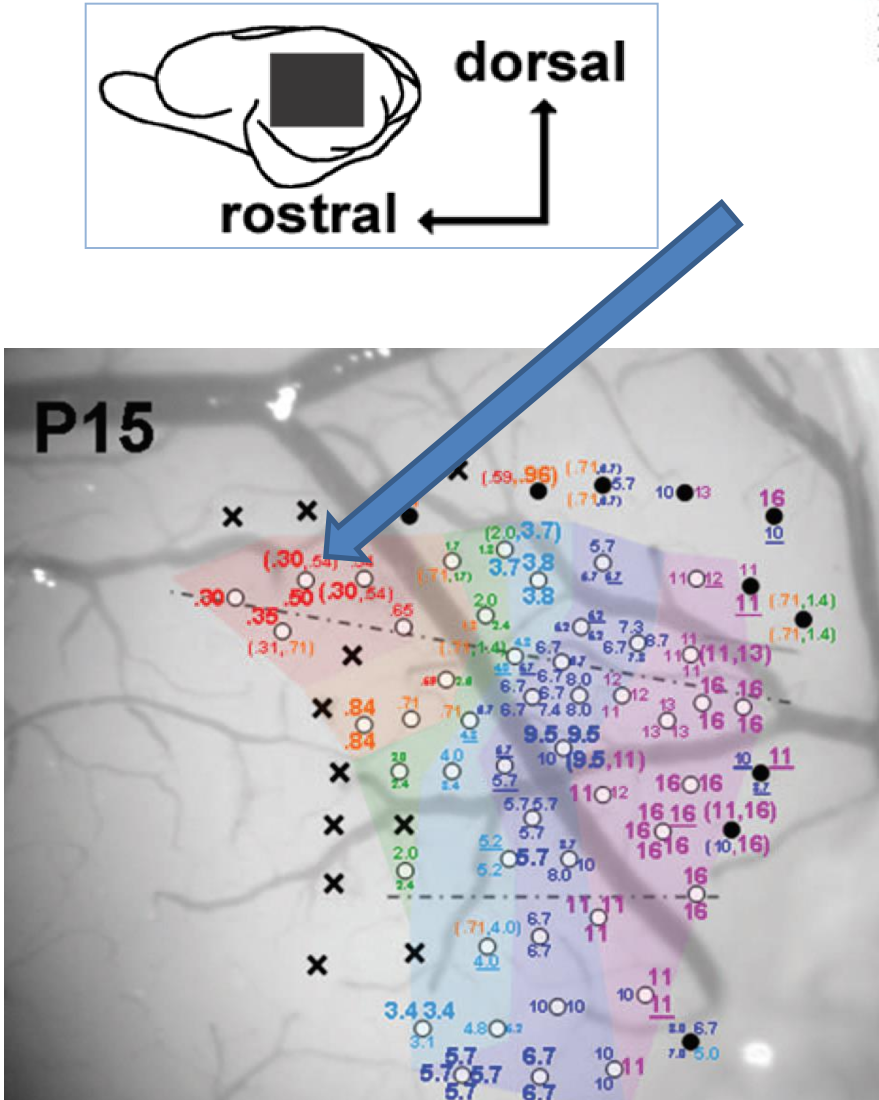
Auditory Brainstem evoked Responses ABR

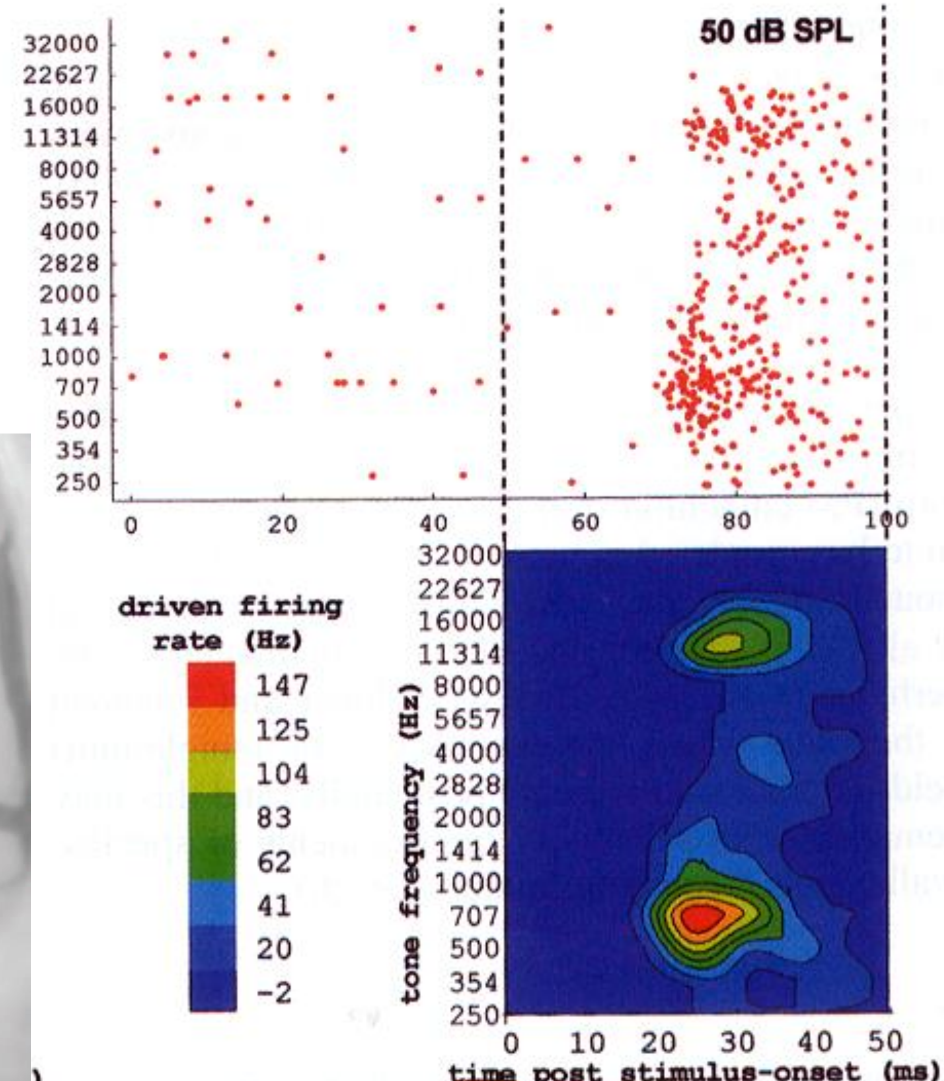


Auditory Cortex, Evoked Potentials

Data from various works by Jos Eggermont

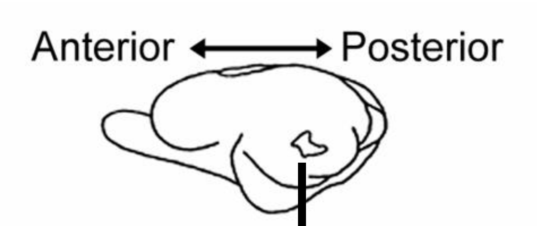
Recording the response properties of cortical neurons to tone stimuli





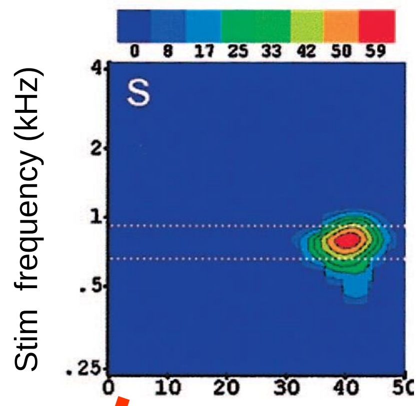
PIENKOWSKI M, **HARRISON RV**. (2005). Tone frequency maps and receptive fields in developing chinchilla auditory cortex. J Neurophysiol. 93: 454-466

Increase in complexity of neuron responses in auditory cortex with age



"simple response"

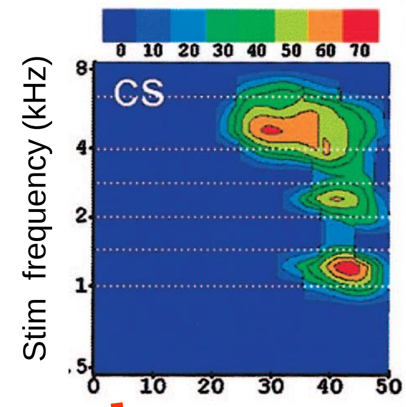
Neuron firing rate



Time (ms)

"complex response"

Neuron firing rate



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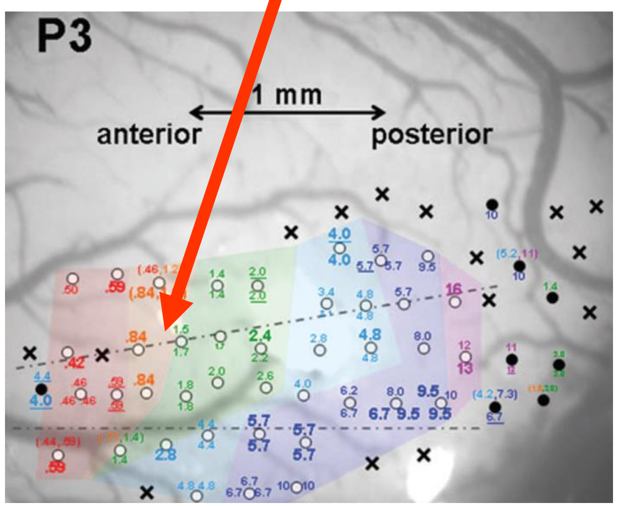
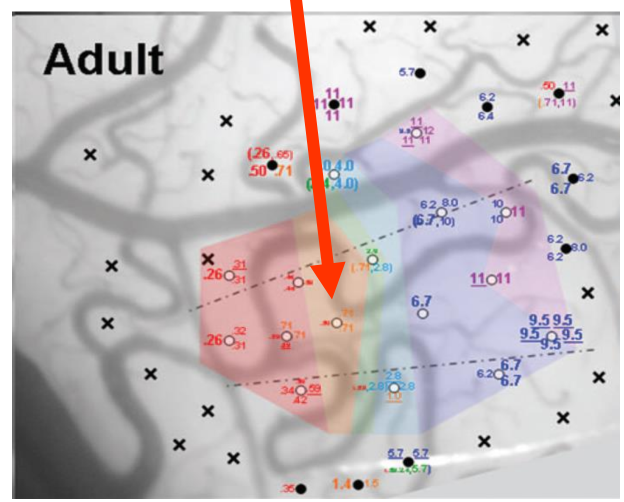


neonate

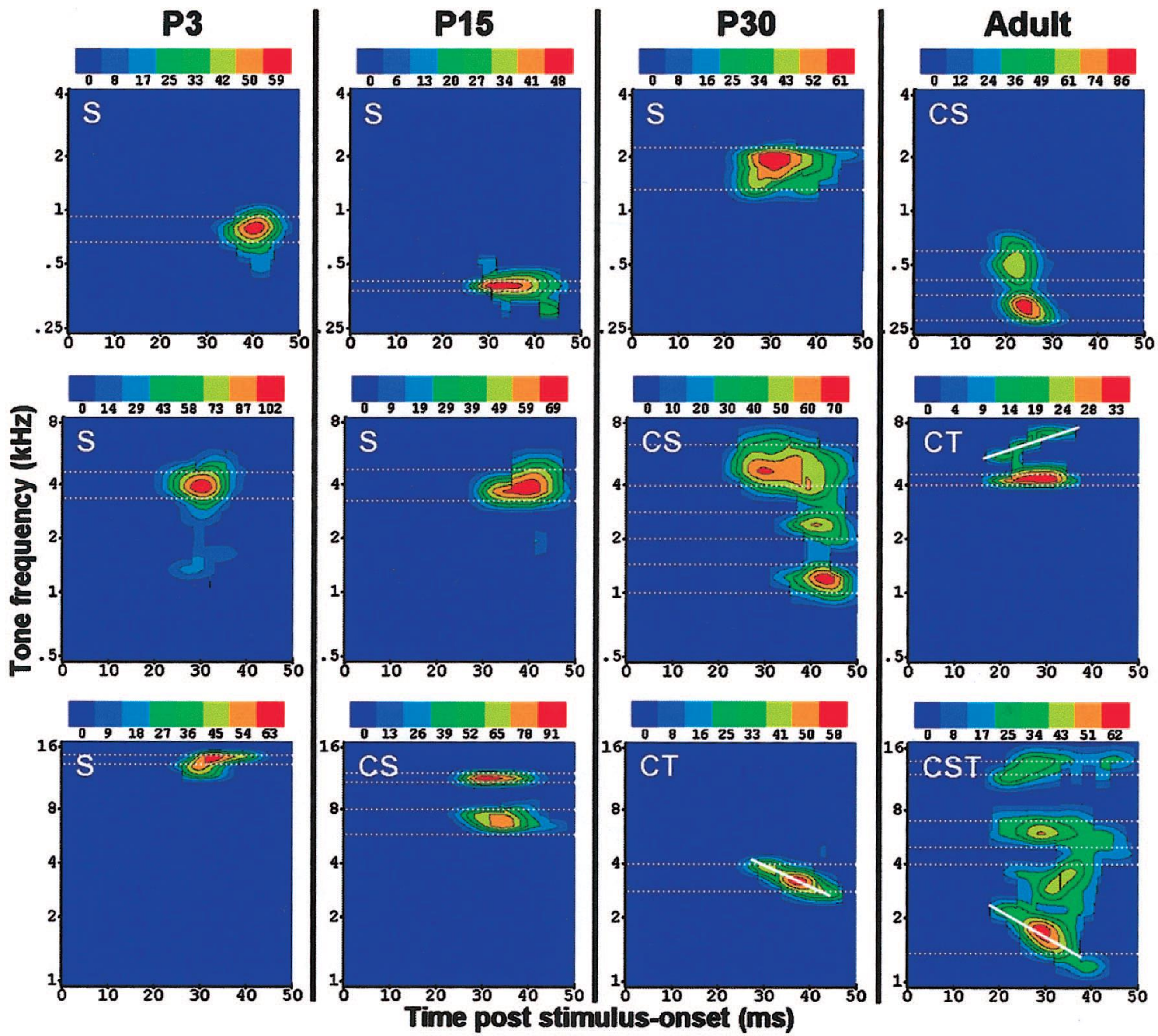


adult

PIENKOWSKI M, **HARRISON RV**. (2005). Tone frequency maps and receptive fields in developing chinchilla auditory cortex. J Neurophysiol. 93: 454-466

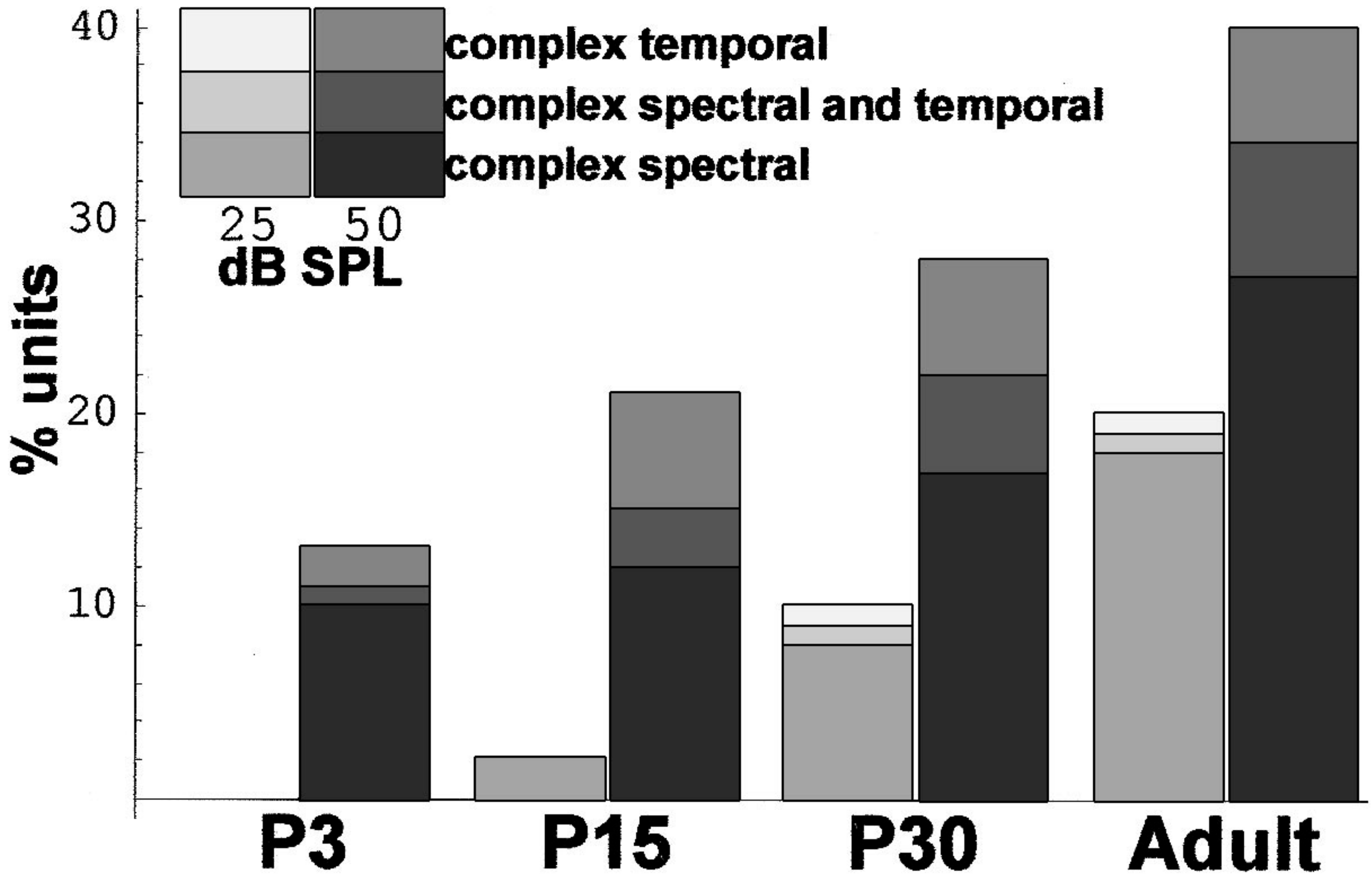
(nature vs. nurture)

Increase in complexity of neuron responses in auditory cortex with age



PIENKOWSKI M, **HARRISON RV**. (2005). Tone frequency maps and receptive fields in developing chinchilla auditory cortex. J Neurophysiol. 93: 454-466

Proportion of "complex cells" in auditory cortex with age



PIENKOWSKI M, **HARRISON RV**. (2005). Tone frequency maps and receptive fields in developing chinchilla auditory cortex. J Neurophysiol. 93: 454-466

Increased complexity of auditory neuron responses reflects development of inter-neuronal connections

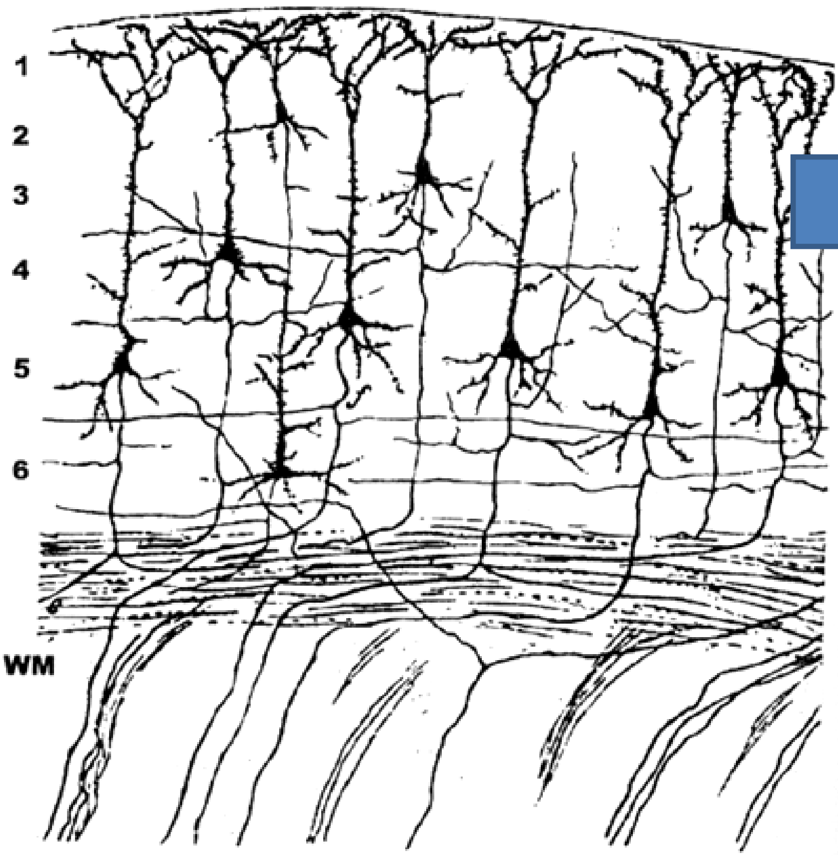
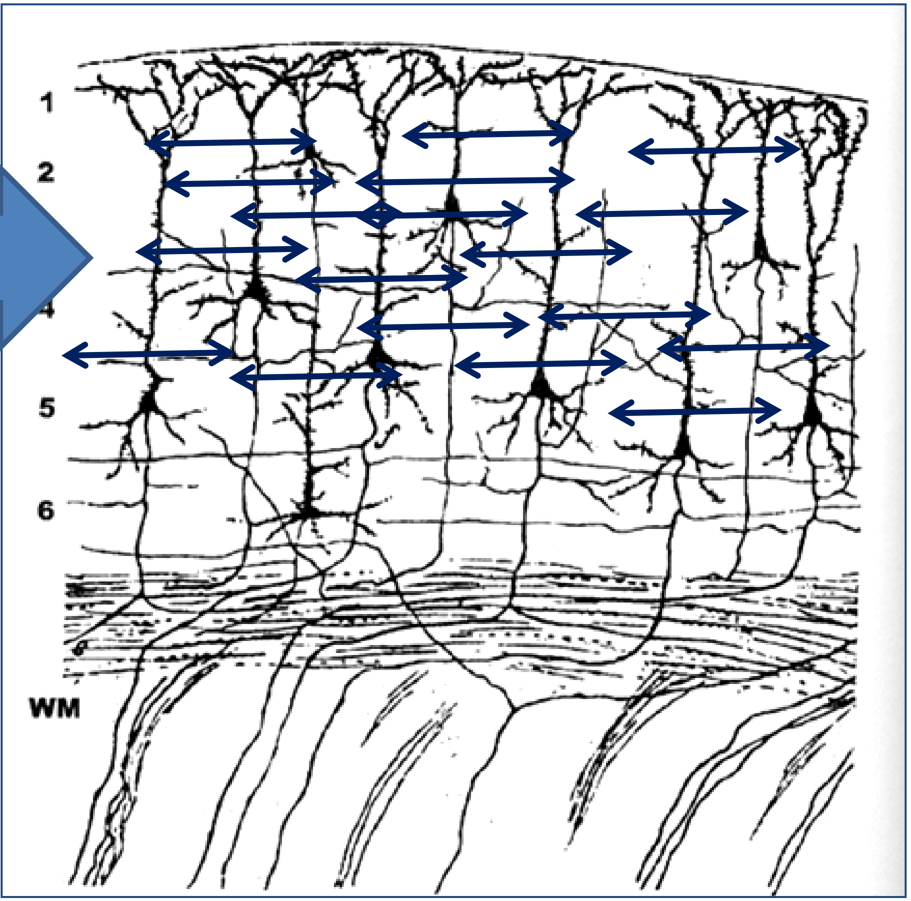


Fig 2. Illustration of laminar organization of cortex. Numerals 1 to 6 indicate cortical layers. WM — deep white matter. Adapted from Ramon y Cajal.[6]

Cortex in early development



Mature cortex

(highly schematic)

Increased complexity of auditory neuron responses reflects development of inter-neuronal connections

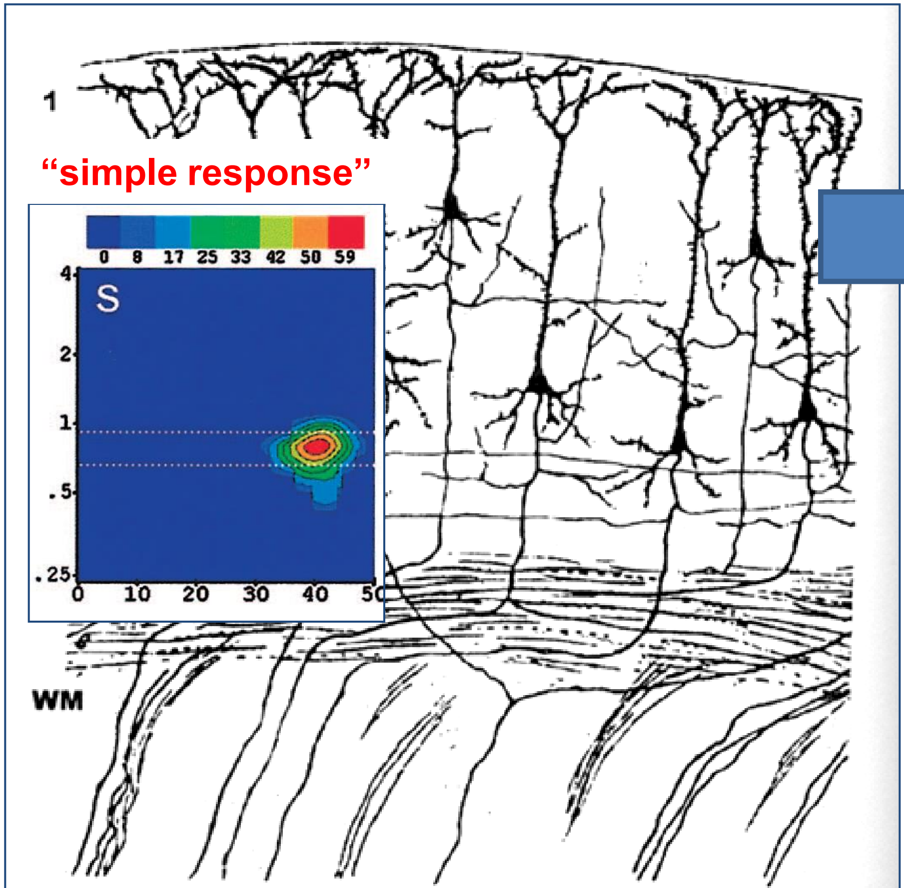


Fig 2. Illustration of laminar organization of cortex. Numerals 1 to 6 indicate cortical layers. WM — deep white matter. Adapted from Ramon y Cajal.[6]

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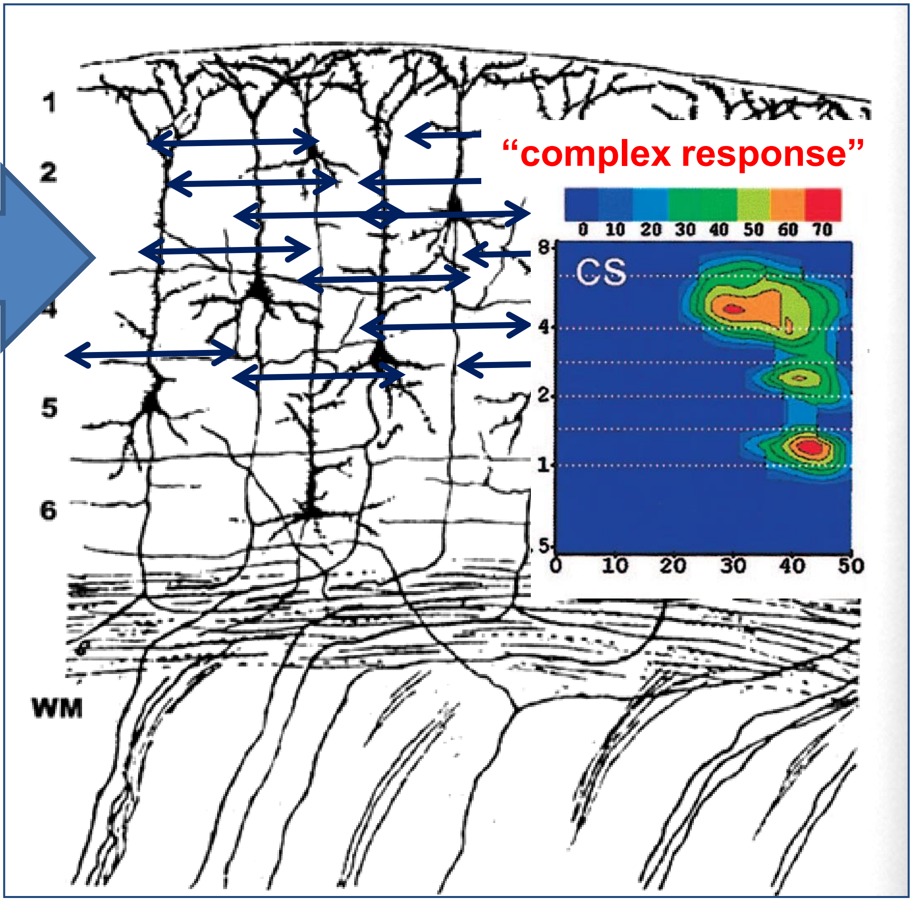
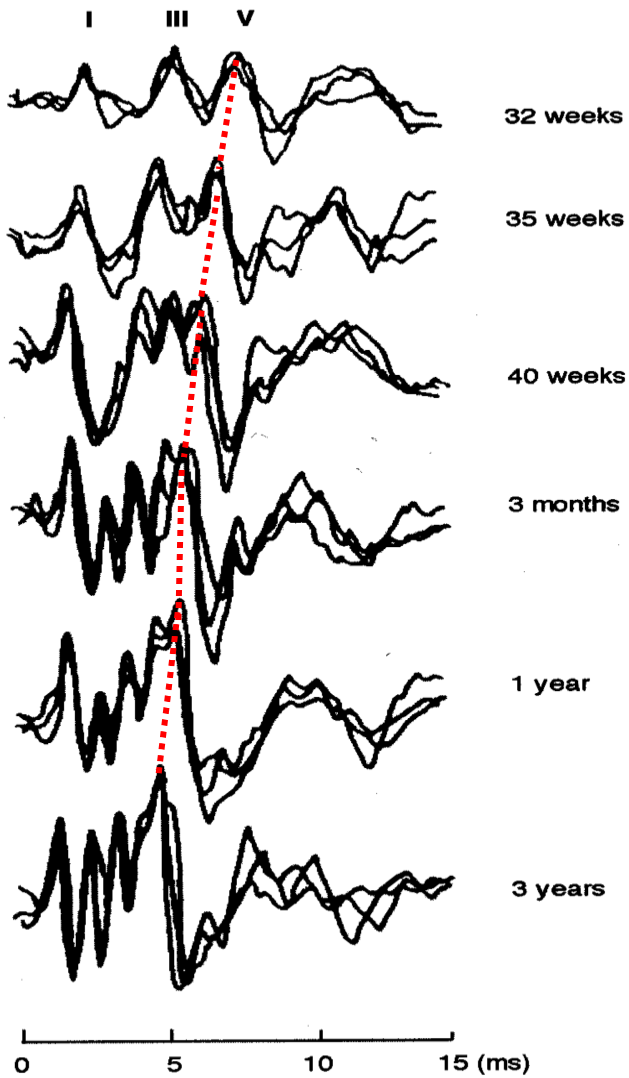


Mature cortex

(highly schematic)

Evoked potential studies of human auditory system development



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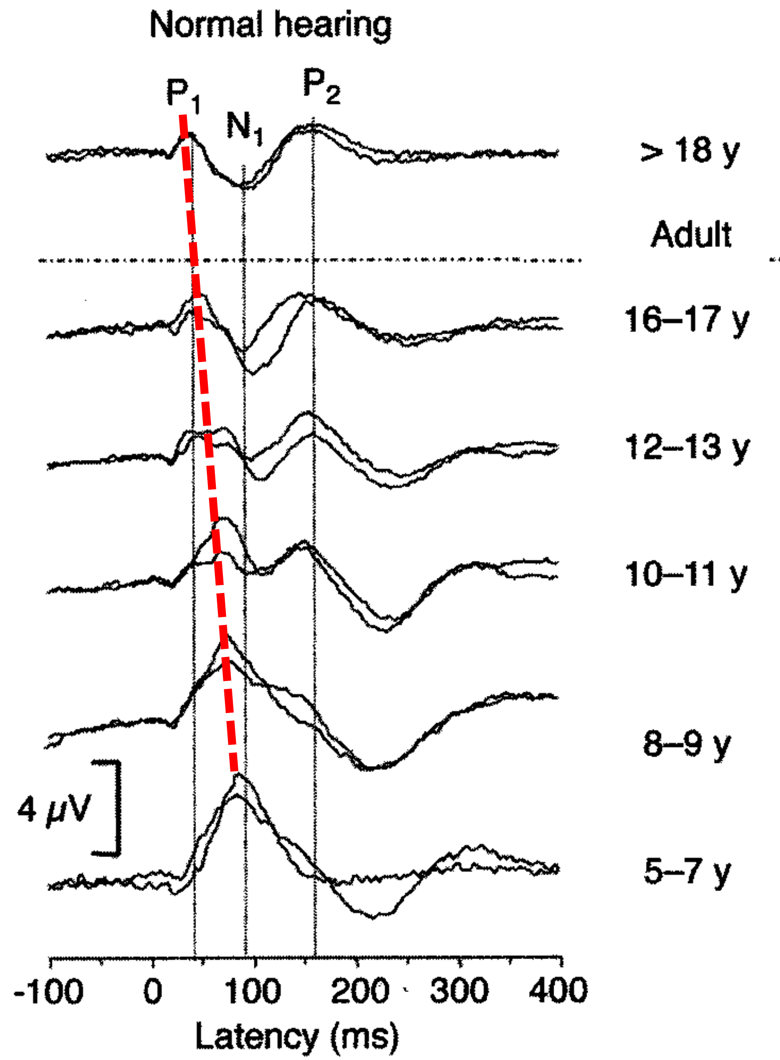

Auditory Cortex, Evoked Potentials

Data from various works by Jos Eggermont

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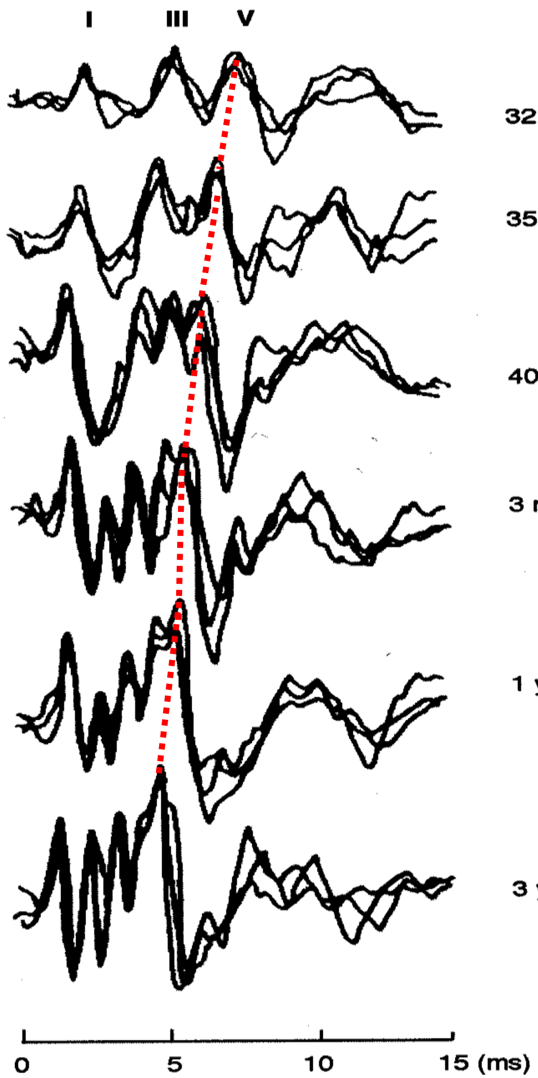

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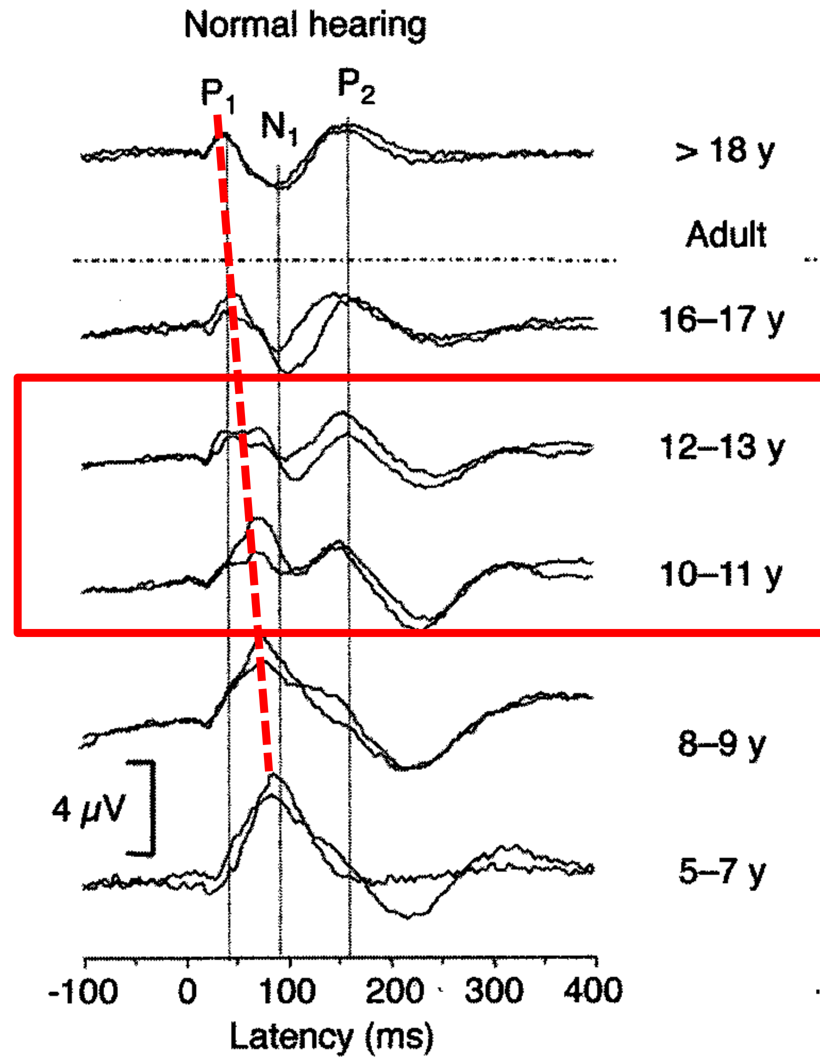

Auditory Cortex, Evoked Potentials

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Post natal development of auditory cortex takes many years

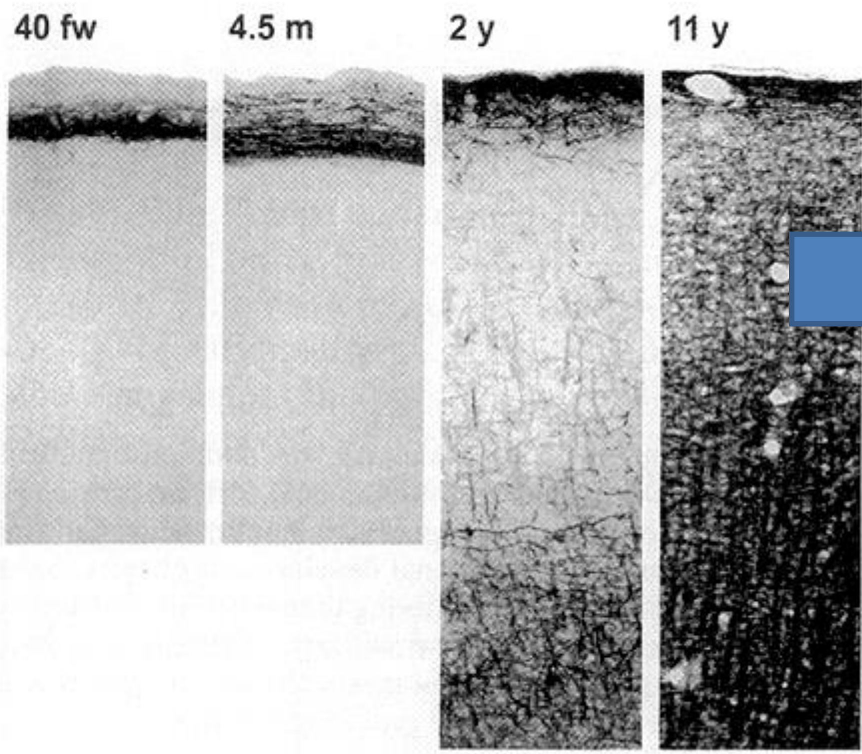
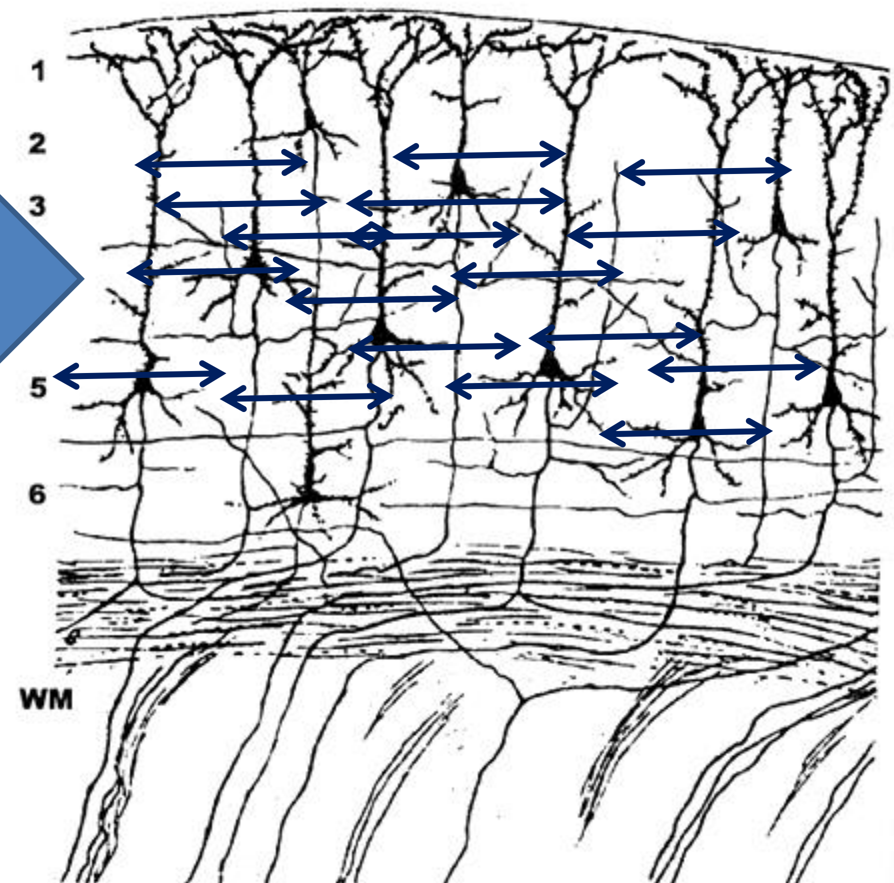


Fig 1. Neurofilament-immunostained sections of cortical tissue. At 40th fetal week (fw) and at 4.5 months' postnatal age, mature axons are present only in marginal layer. By 2 years of age, mature neurofilament-expressing axons are entering deeper cortical layers. By 11 years, mature axons are present with adult-like density in all cortical layers.



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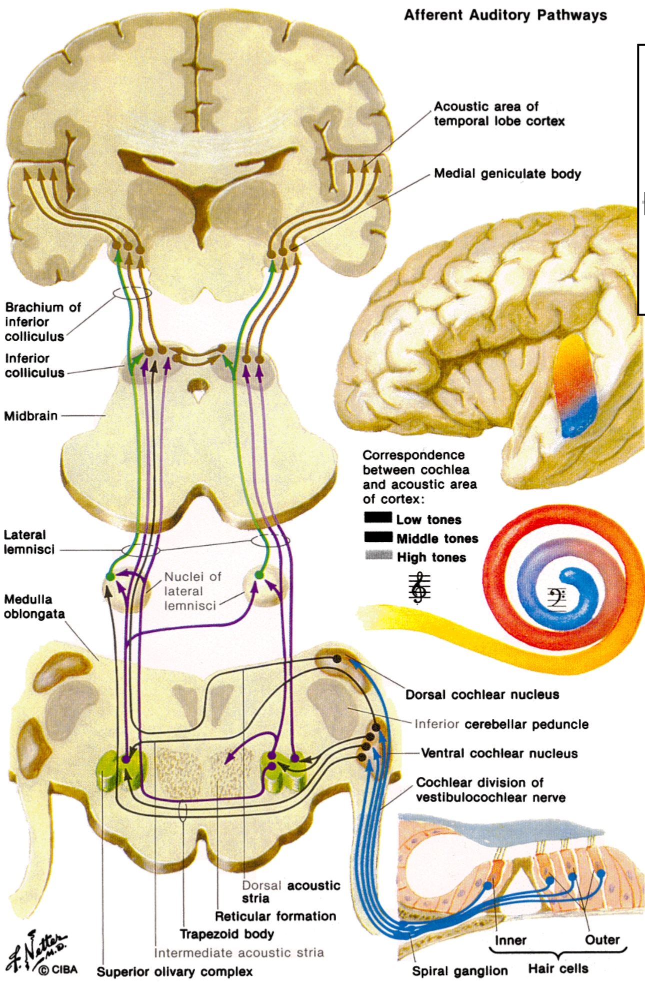
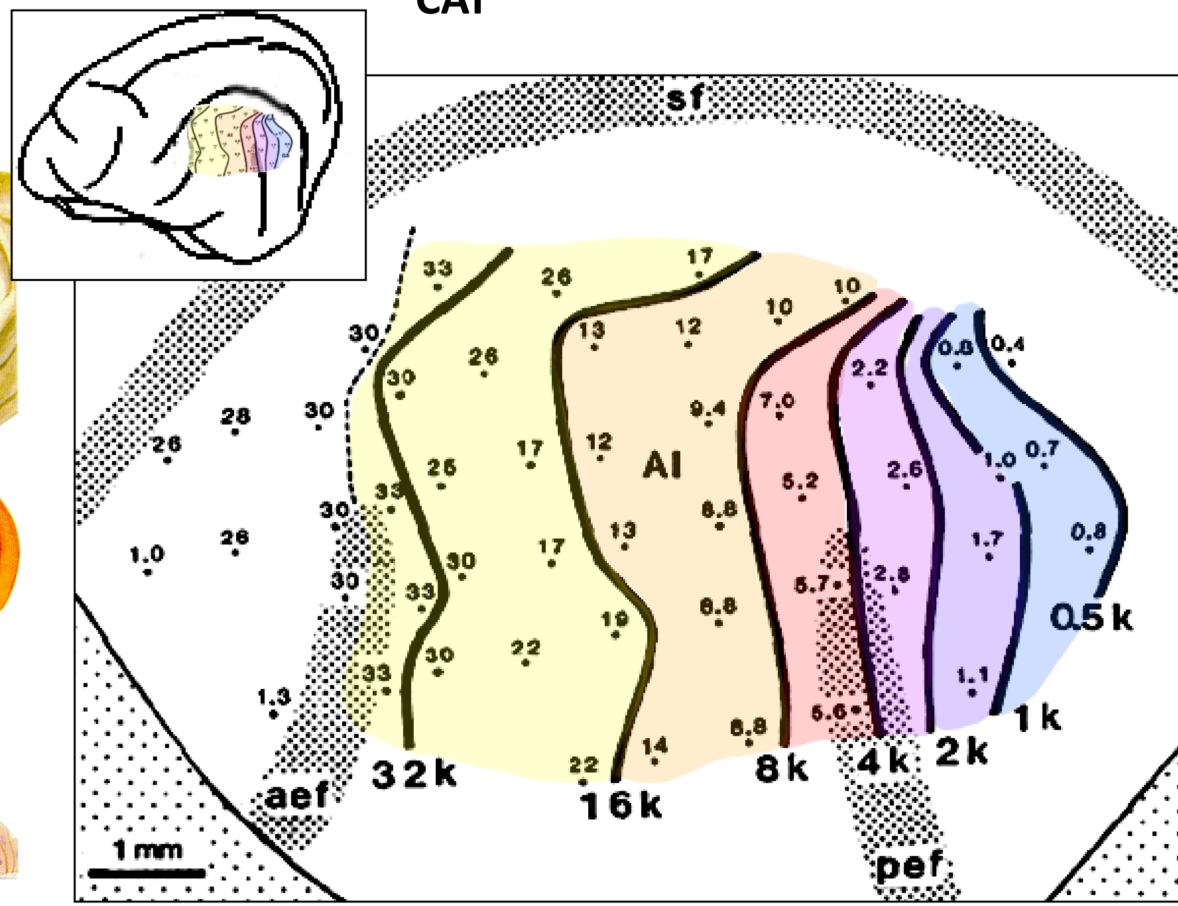
Reference: Moore J.K 2002 ann otol rhinol laryngol 111, 7-10

Cochleotopic (tonotopic) organization of primary auditory cortex

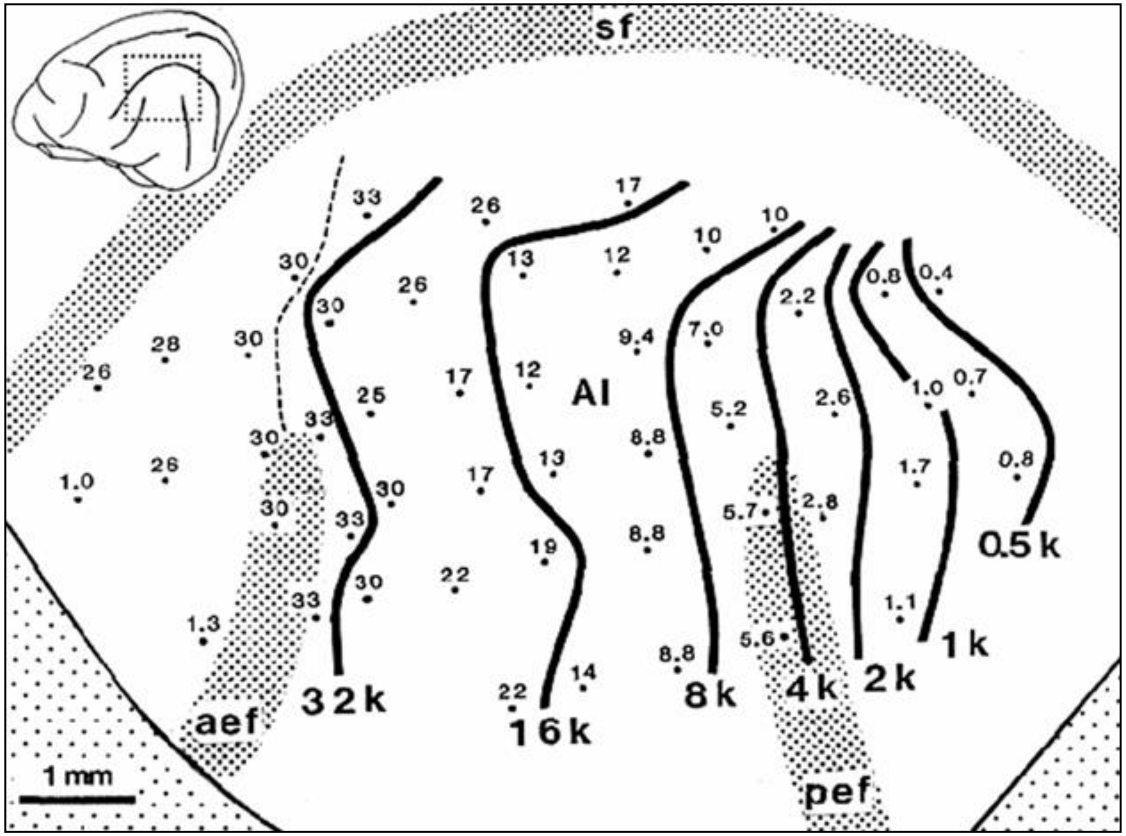
HUMAN



CAT

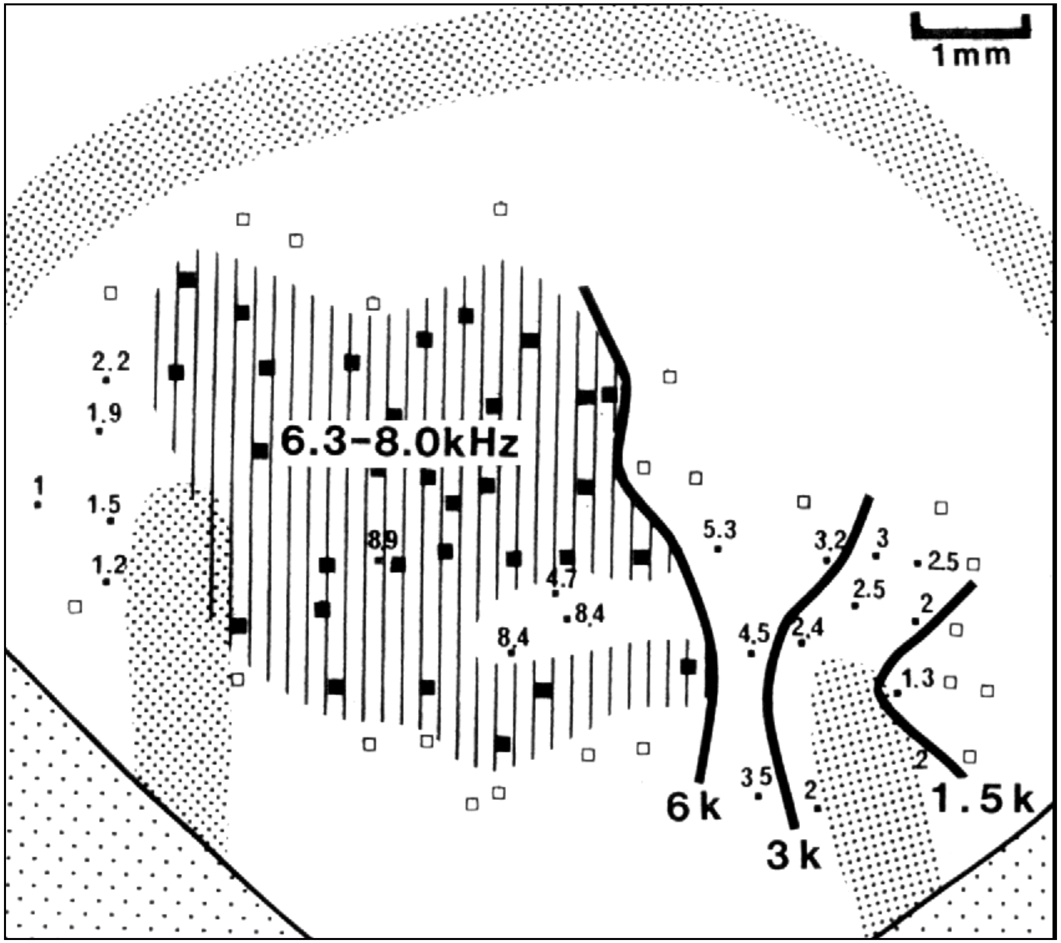


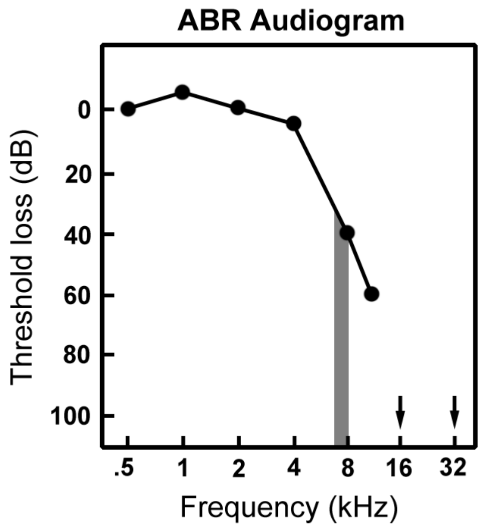
Tonotopic map in auditory cortex of subject with normal activity patterns at the cochlear level



HARRISON, R.V., NAGASAWA A., SMITH D.W, STANTON S. and MOUNT R.J. (1991): Reorganization of auditory cortex after neonatal high frequency cochlear hearing loss. Hearing Research, 54, 11 -19

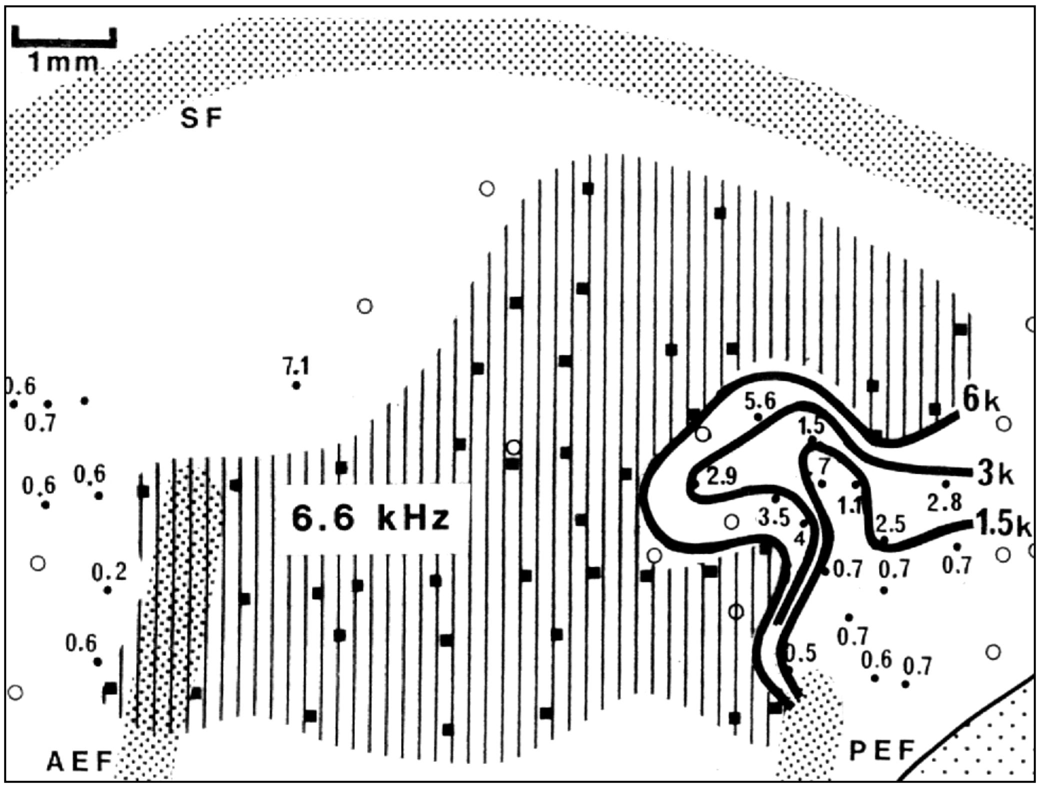
Cortical tonotopic map in subject with basal cochlear lesion from birth (high frequency sensorineural hearing loss)

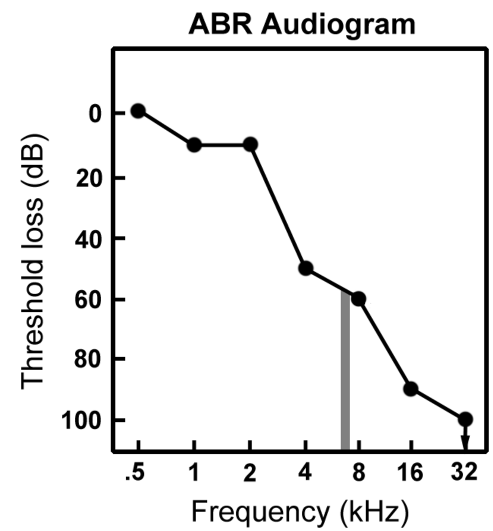




HARRISON, R.V., NAGASAWA A., SMITH D.W, STANTON S. and MOUNT R.J. (1991): Reorganization of auditory cortex after neonatal high frequency cochlear hearing loss. Hearing Research, 54, 11 -19

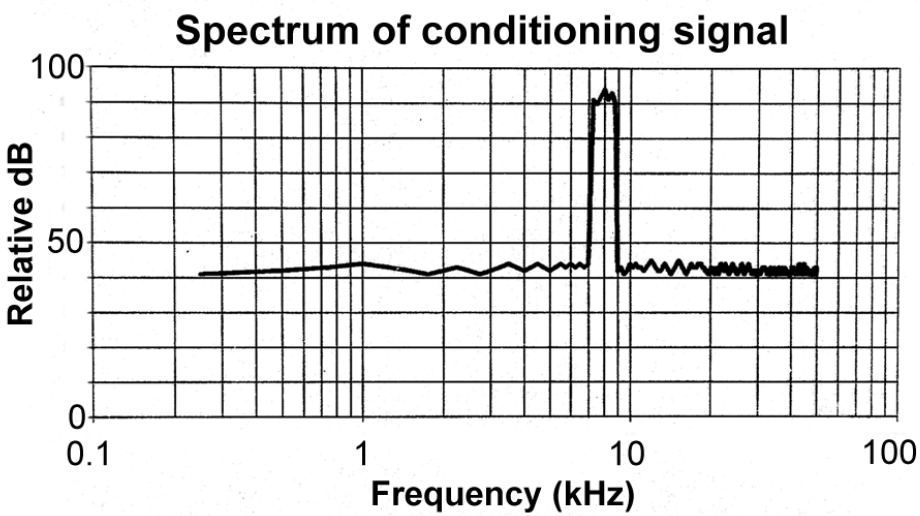
Cortical tonotopic map in subject with extensive cochlear lesion from birth (neonatal sensorineural hearing loss)



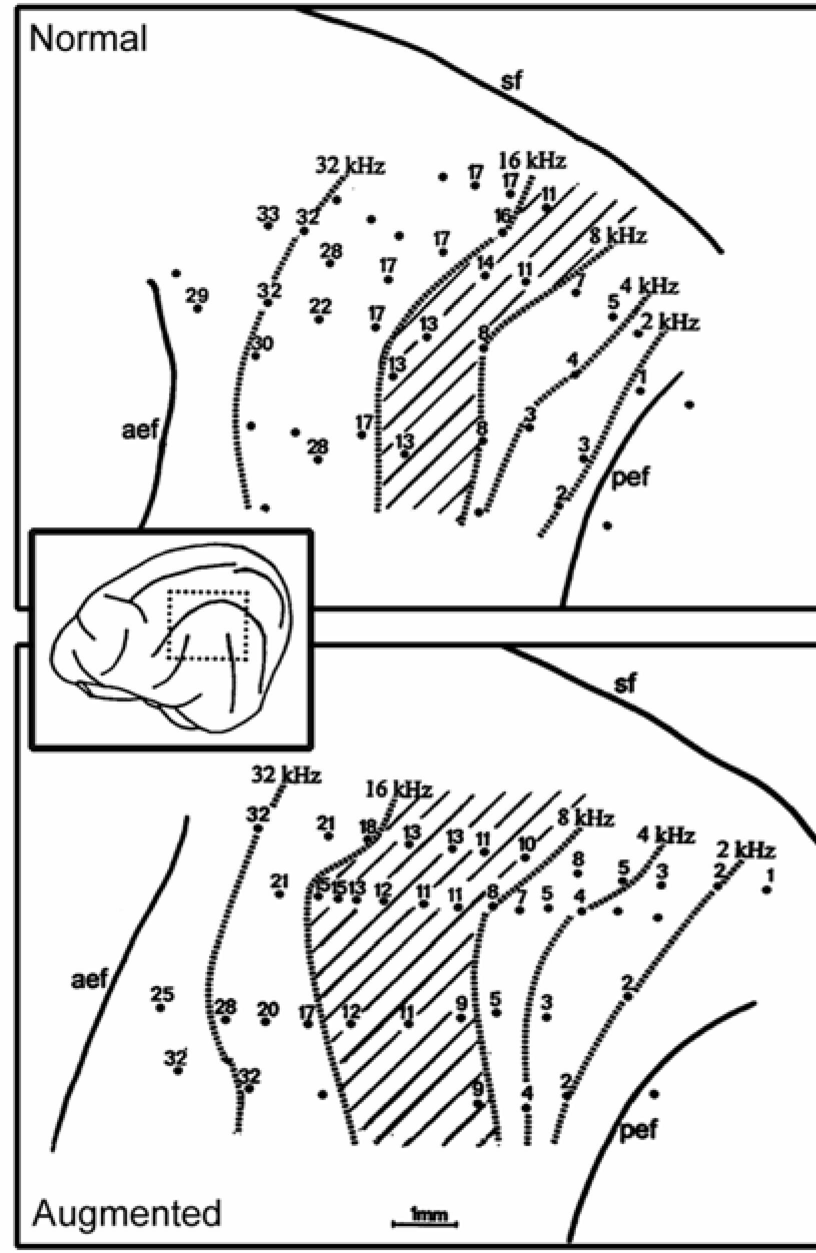


HARRISON, R.V., NAGASAWA A., SMITH D.W, STANTON S. and MOUNT R.J. (1991): Reorganization of auditory cortex after neonatal high frequency cochlear hearing loss. Hearing Research, 54, 11 -19

Reorganization of auditory cortex by neonatal environmental sound stimulation

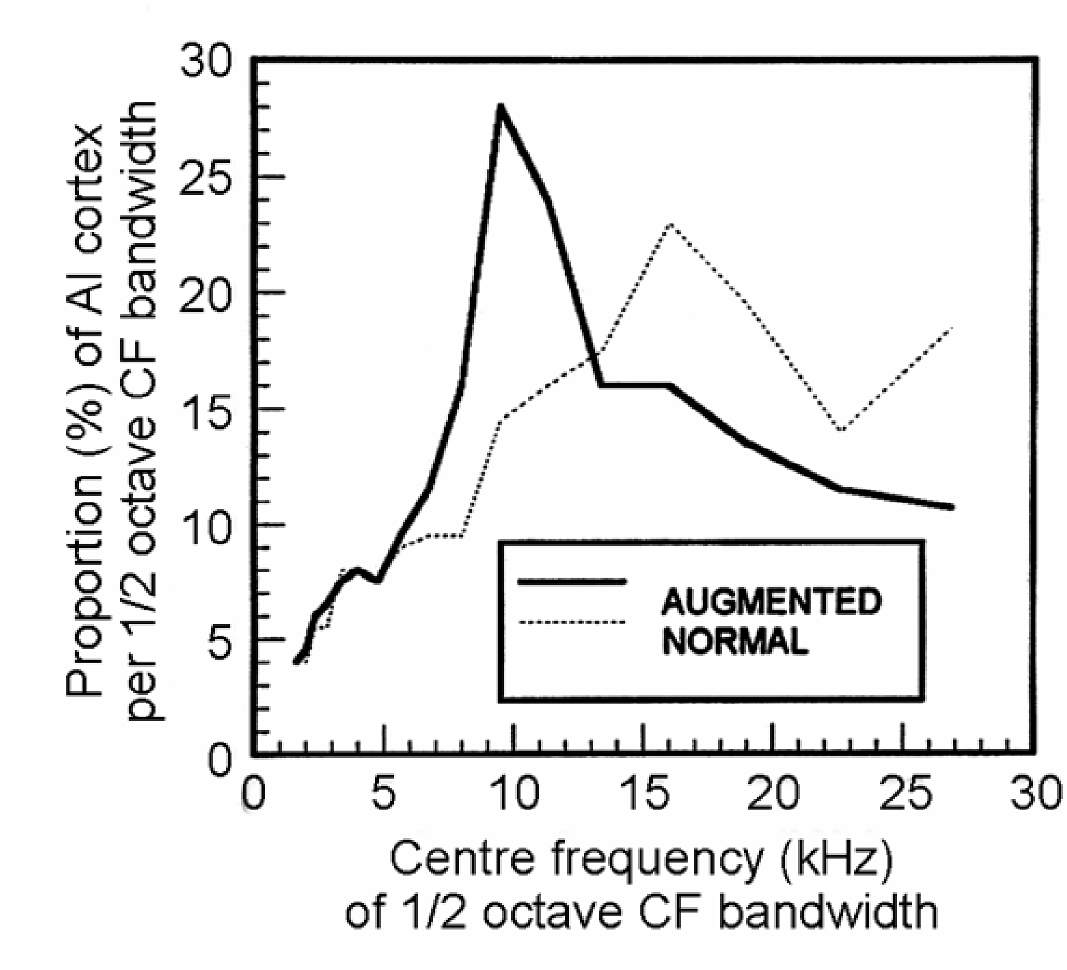


Subject reared with constant 8kHz signal developed cortical over-representation of 8-16kHz



STANTON, S.G. and **HARRISON, R.V.** (1996):
Abnormal cochleotopic organization in the auditory cortex of cats reared in a frequency augmented environment.
Auditory Neuroscience 2, 97-107

Pooled data (N=3), subjects reared in environment with 8kHz acoustic signal



STANTON, S.G. and **HARRISON, R.V.** (1996):
Abnormal cochleotopic organization in the auditory cortex
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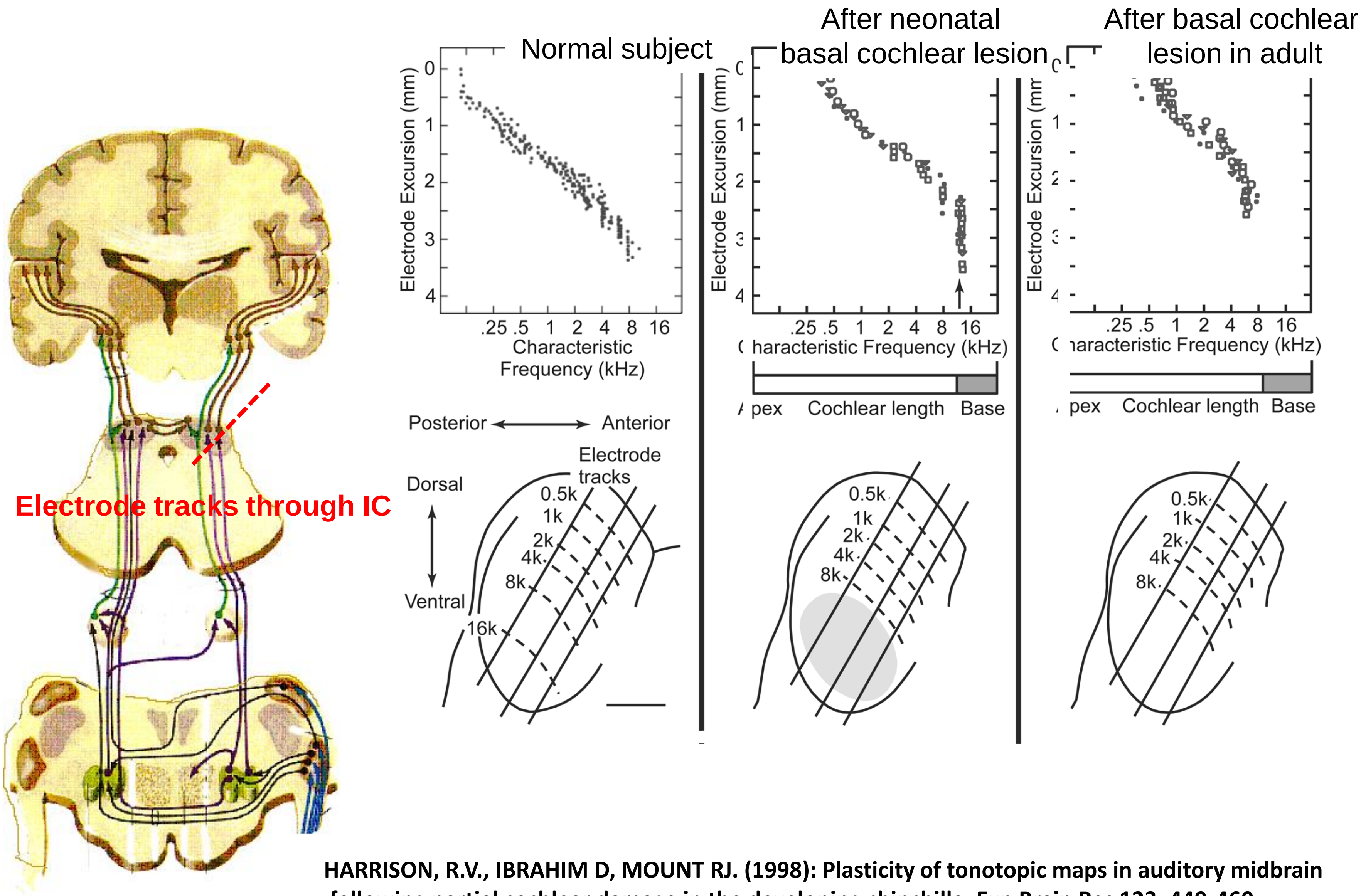
Frequency map reorganization in auditory midbrain after neonatal versus adult cochlear lesions



HARRISON, R.V., IBRAHIM D, MOUNT RJ. (1998): Plasticity of tonotopic maps in auditory midbrain following partial cochlear damage in the developing chinchilla. Exp Brain Res 123; 449-460.

Sound Wave Symposium, San Diego, 2018

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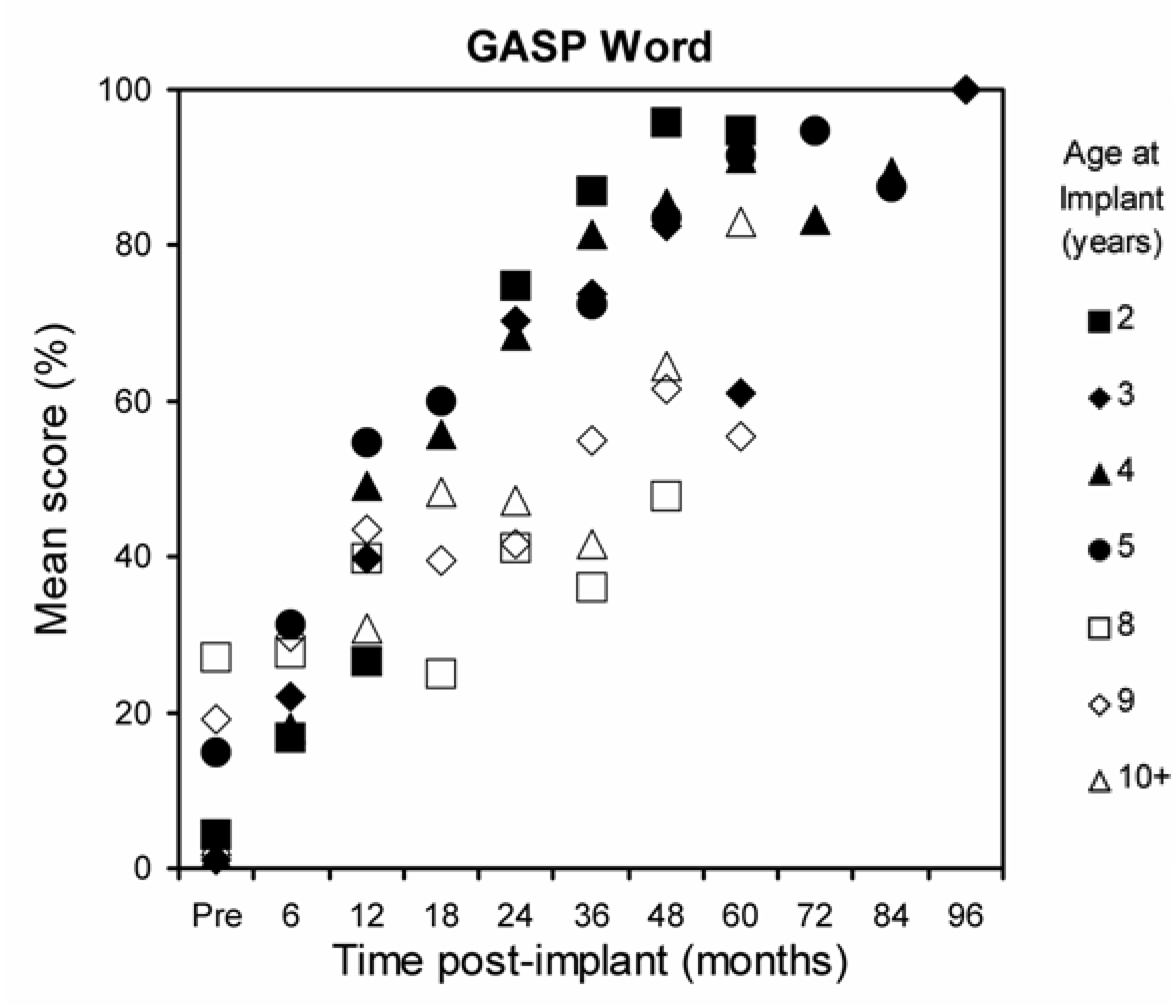
Speech and language improvement can be like a progressive hearing loss.

A "sensitive period" of developmental plasticity in children. Speech understanding in children after cochlear implantation

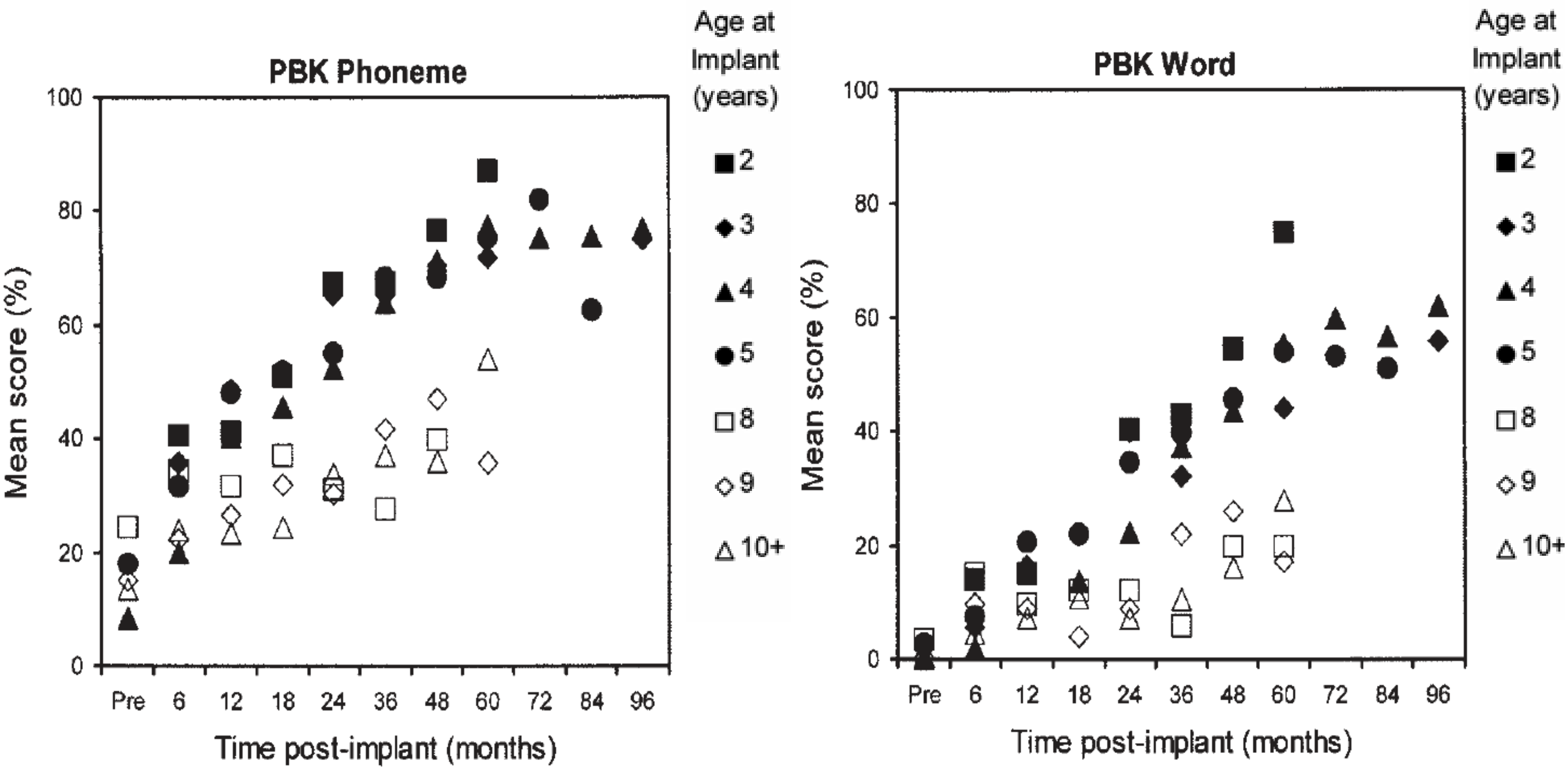


duration of auditory deprivation

Mean scores in the GASP word test, pre and post-implantation for each age at implant group

PAPSIN BC, GYSIN C, PICTON N, NEDZELSKI J. and HARRISON, R.V. (2000): Speech perception outcome measures in prelingually deaf children up to four years after cochlear implantation. Ann Otol Rhinol Laryngol Suppl 185 38-42.

Congenital deafness, cochlear implantation in children under six versus over six



HARRISON, R.V., PANESAR J, EL-HAKIM H, ABDOLELL M, MOUNT RJ, PAPSIN B. (2001). The effects of cochlear implantation on speech perception outcomes in prelingually deaf children. Scand. Audiol 30: suppl 53: 73-78

EL-HAKIM H, HARRISON, R.V.HARRISON RV (2002) Influence of age at implantation and of residual hearing on speech outcome measures after cochlear implantation: binary partitioning analysis. Ann Otol Rhinol Laryngol 189, 102-108

Vocabulary tests

(individually administered using only oral stimulus)

- ***PPVT***

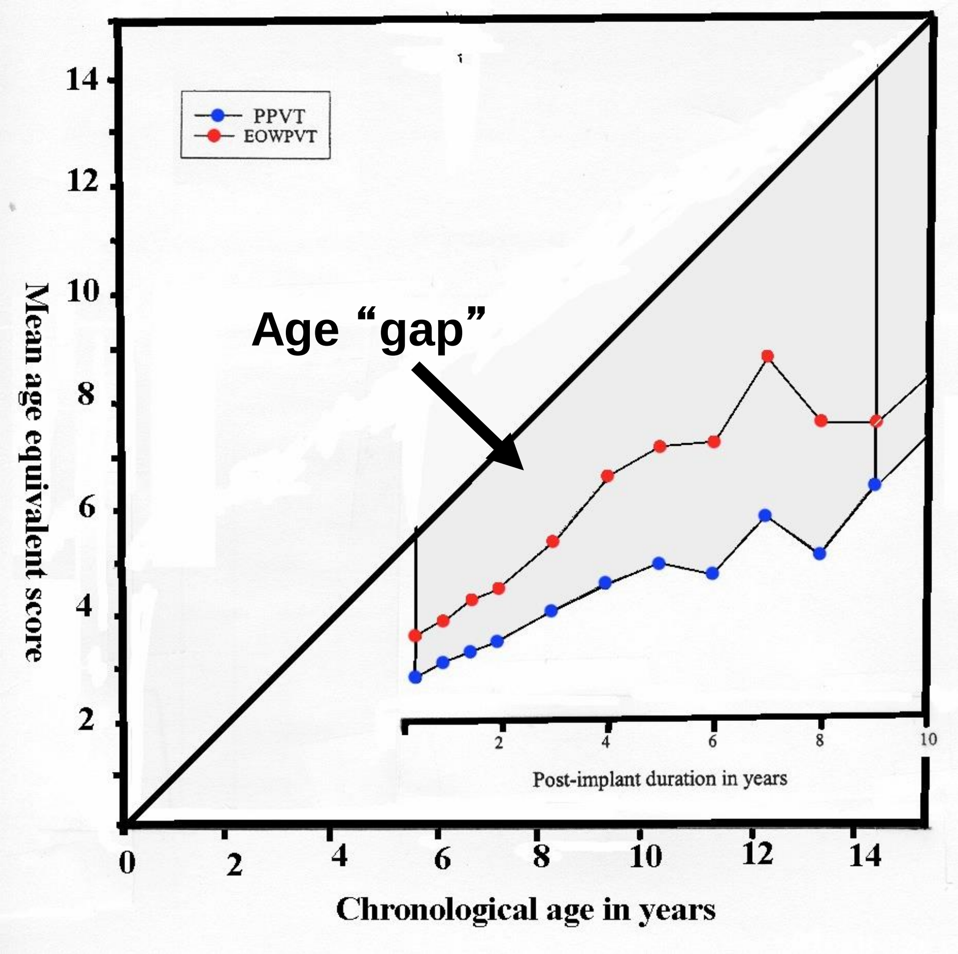
Estimates the *receptive* vocabulary. The subject selects the picture considered to illustrate the meaning of a stimulus word.

- ***EOWPVT***

Estimates the *expressive* vocabulary. The subject selects the word considered to best illustrate a stimulus picture.

Followed children (N=38) after cochlear implantation for 8-10 years

Vocabulary development post cochlear implantation [Receptive vocabulary and expressive vocabulary]

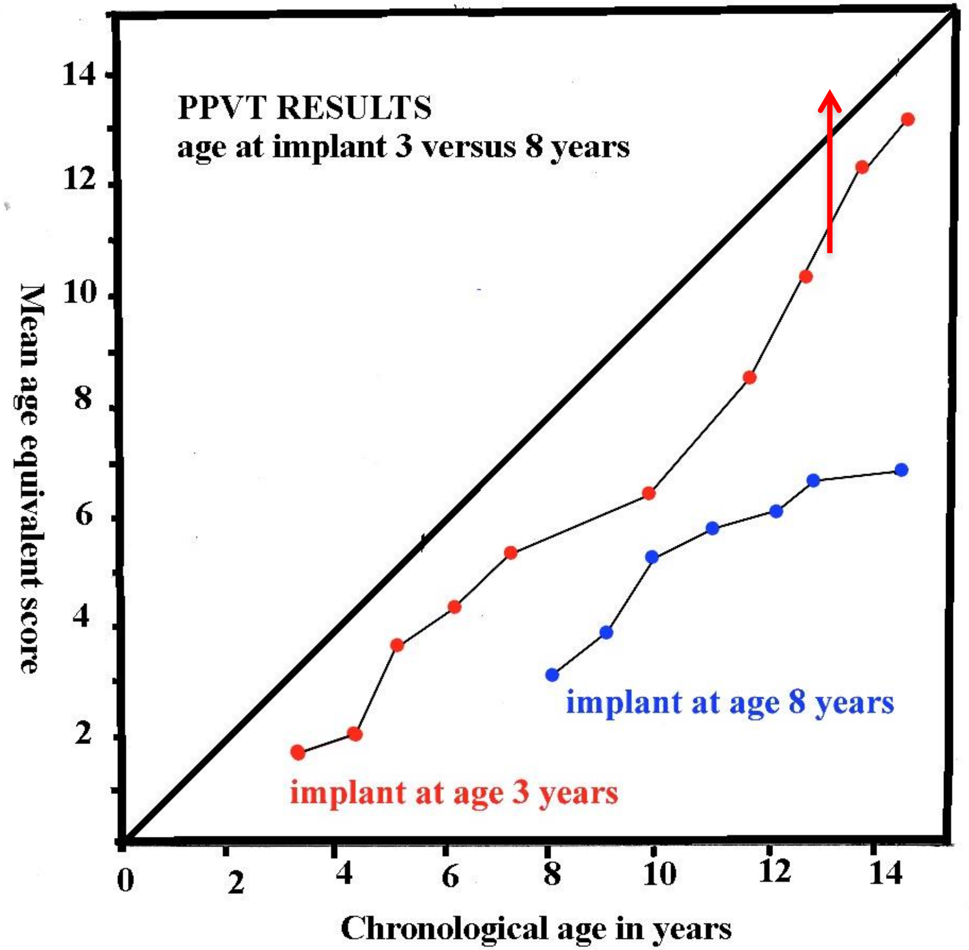


On average, vocabulary acquisition rates decline in the early post implantation period

Pooled data N=38 average age at implantation 5.7 years

EL-HAKIM H, LEVASSEUR J, PAPSIN B, PANESAR J, MOUNT RJ, STEVENS D, **HARRISON, R.V.** (2001) Assessment of vocabulary development in children after cochlear implantation. Arch Otolaryngol Head Neck Surg 127: 1053-1059

Vocabulary development (PPVT)
Effect of early versus late cochlear implantation



In early implantation age “gap” starts out reduced.

Some trend towards gap closure in longer term

EL-HAKIM H, PAPSIN B, MOUNT RJ, LEVASSEUR J, PANESAR J, STEVENS D, **HARRISON, R.V.** (2001)
Vocabulary acquisition after pediatric cochlear implantation and the impact of age at implantation
Int J Ped Otorhinolaryngol 59: 187-194

International Journal of Pediatric Otorhinolaryngology
journal homepage: www.elsevier.com/locate/ijporl

Review Article

Auditory neuropathy spectrum disorder (ANSD) and cochlear implantation

Robert V. Harrison [a,b,*], Karen A. Gordon [a,b], Blake C. Papsin [a,b], Jaina Negandhi [a], Adrian L. James [a,b]

Int J Pediatr Otorhinolaryngol. 2015 79(12):1980-7.

Sometimes hearing ability in ANSD can improve over time.

Need to wait a longer than normal before implantation

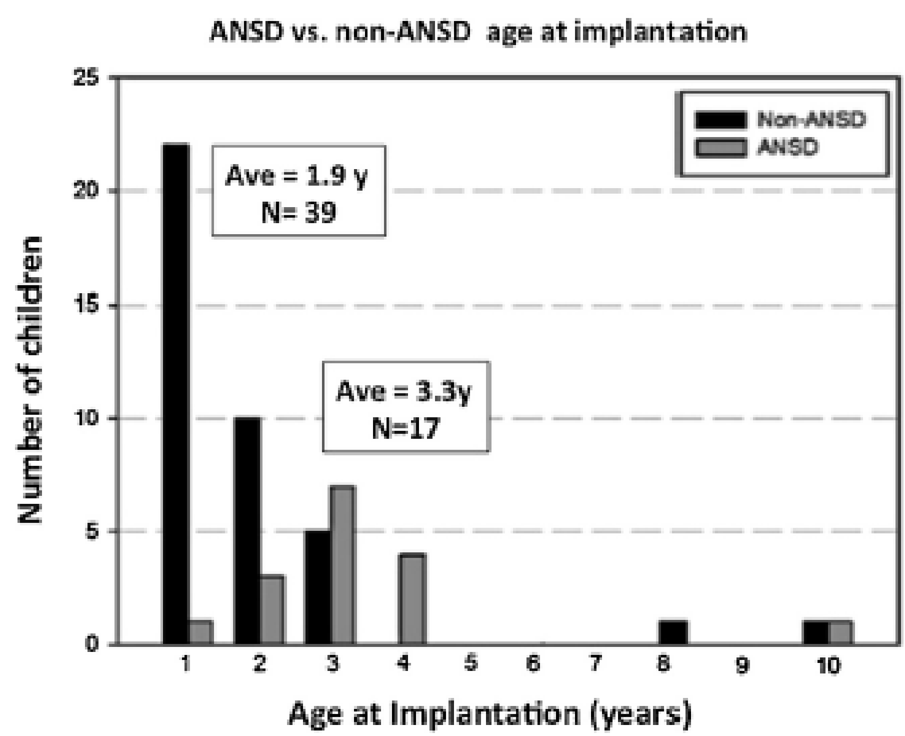


Fig. 4. Age at implantation of 17 ANSD patients compared to 39 non-ANSD implanted children.

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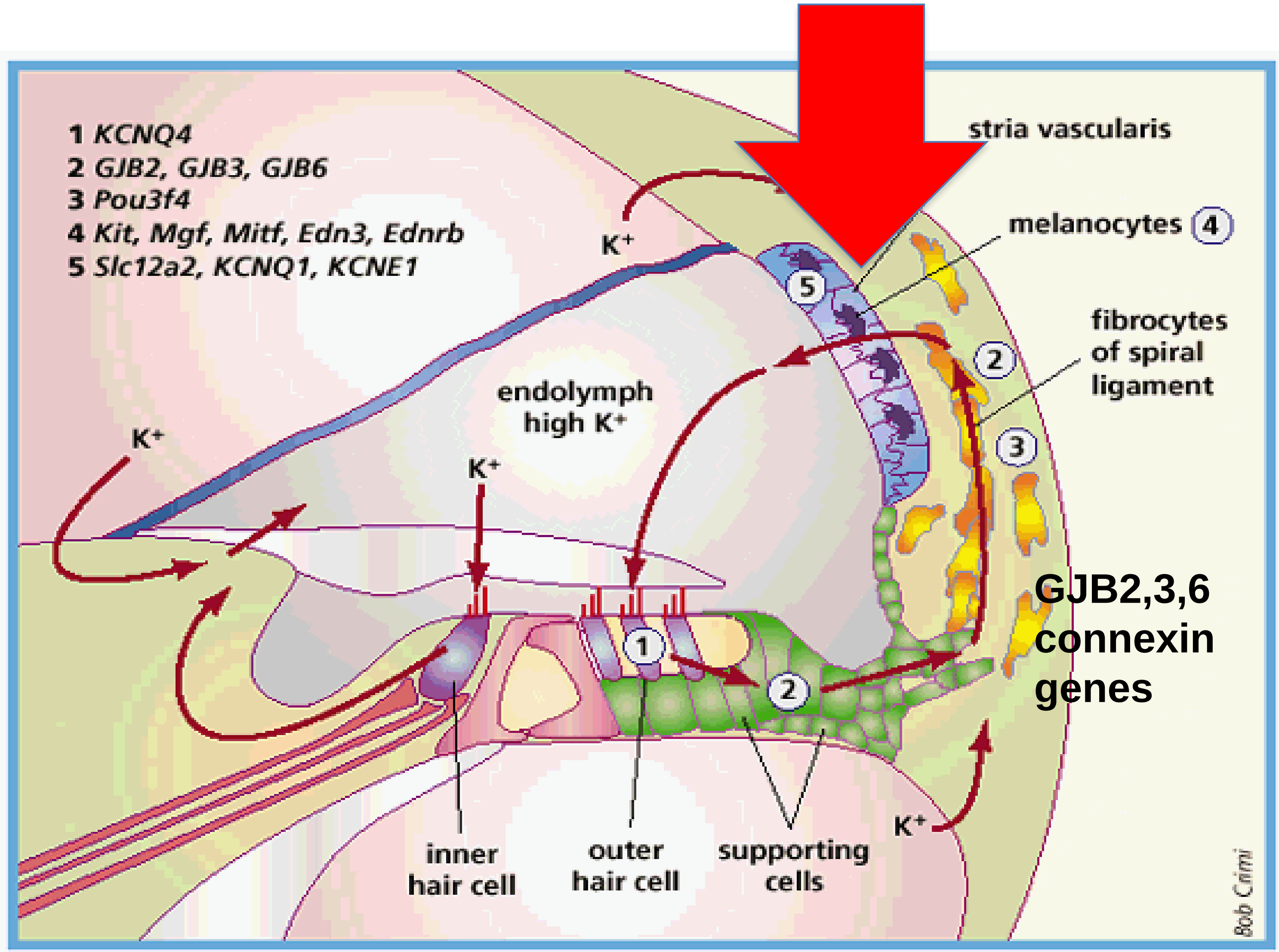
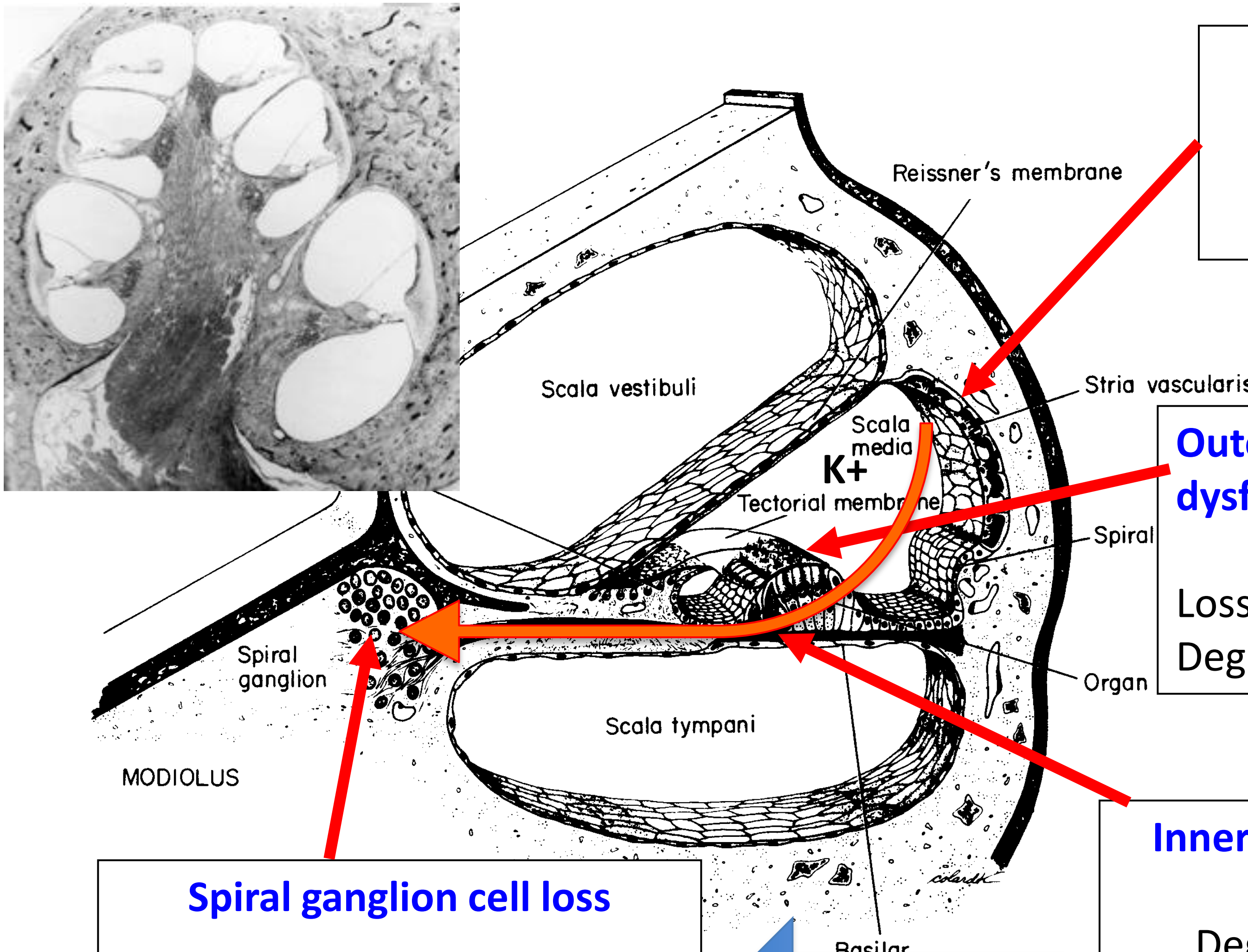
Speech and language improvement can be like a progressive hearing loss.

Progressive loss has many causes, some of which start at the level scala media and stria vascularis, e.g. connexin (and many other) gene mutations, enlarged vestibular aqueduct, CMV infection, strial presbycusis (strial?)



Cochlear damage CASCADE effect



Strial dysfunction

Loss of endocochlear potential

Outer haircell dysfunction

Loss of cochlear amplifier
Degeneration inner haircells

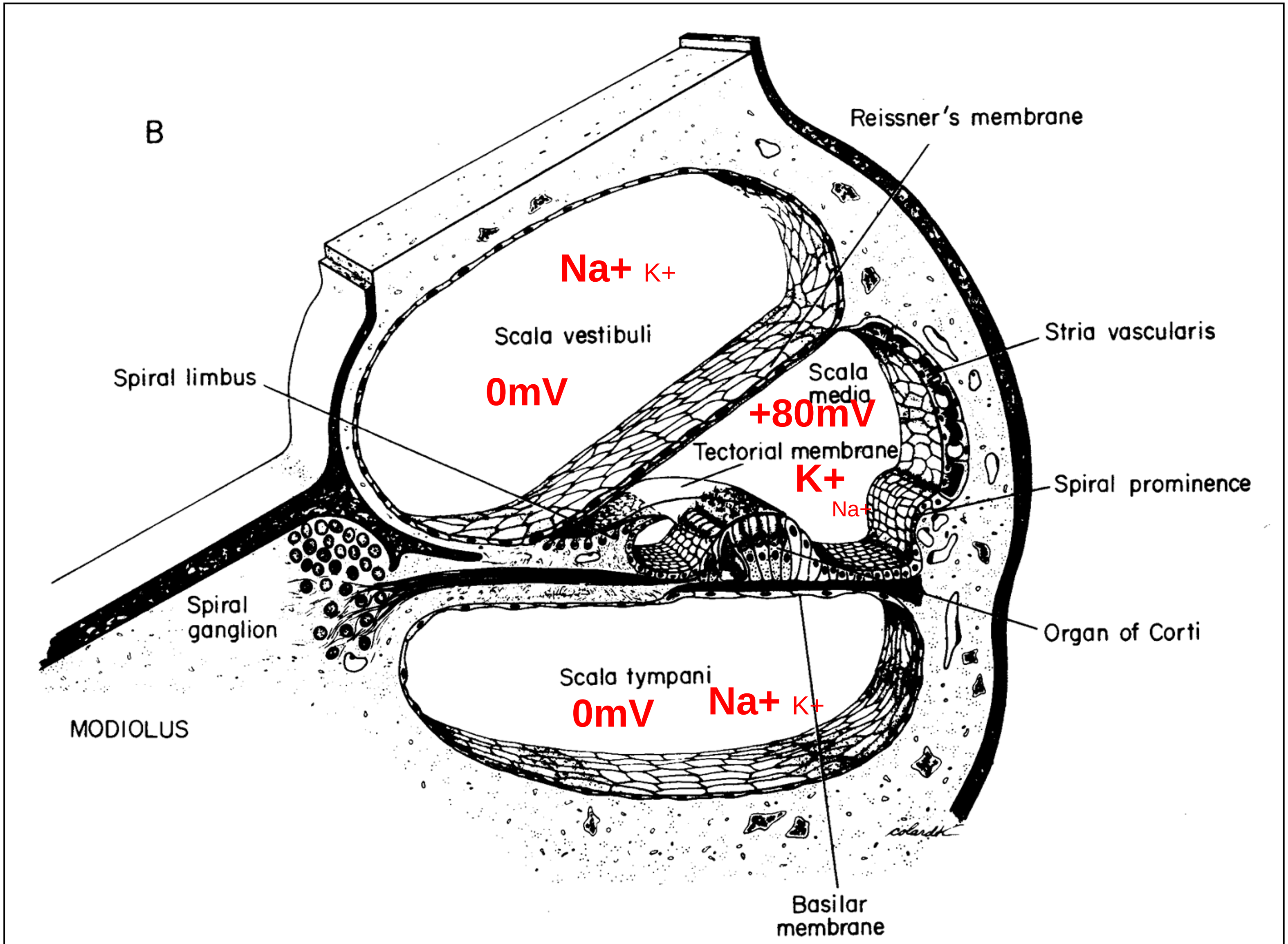
Inner haircell synaptopathy

Degeneration of neural connections with spiral ganglion cells

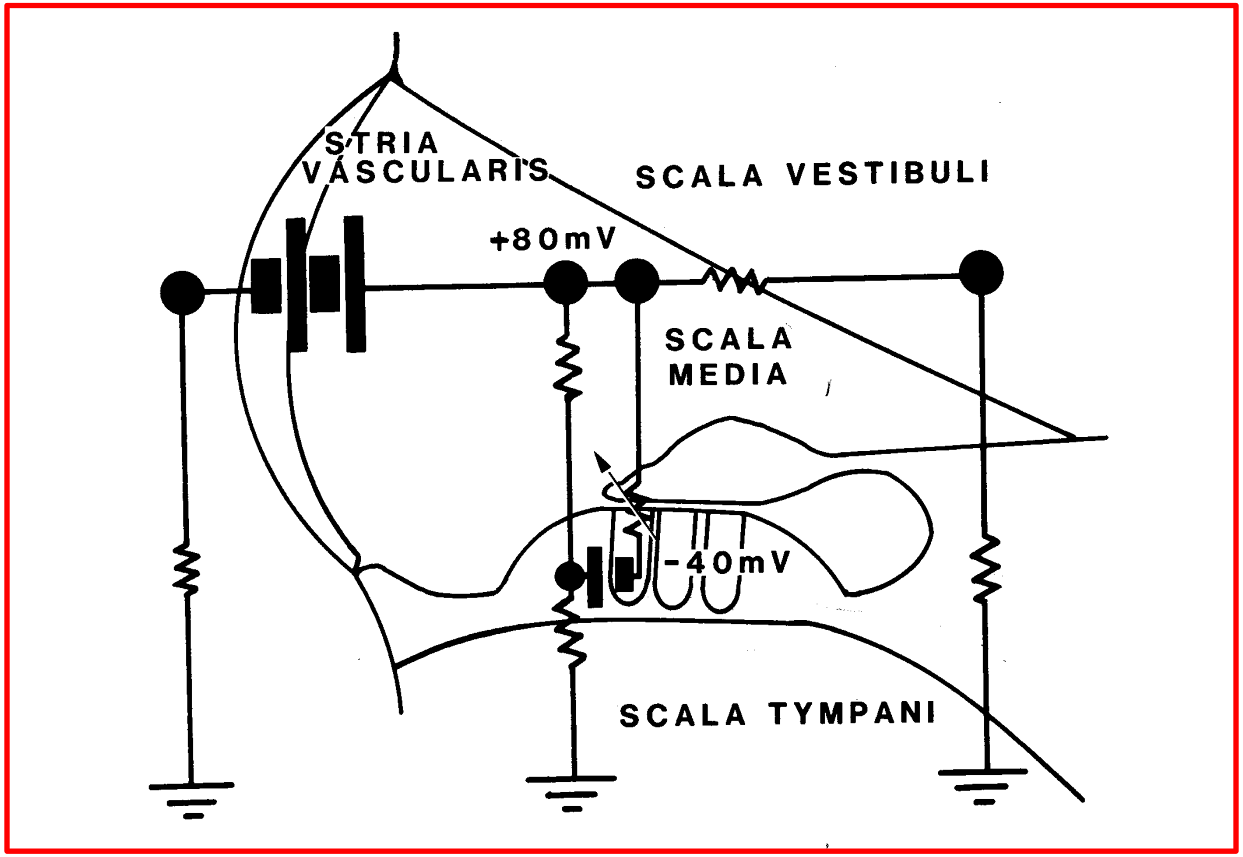
Spiral ganglion cell loss

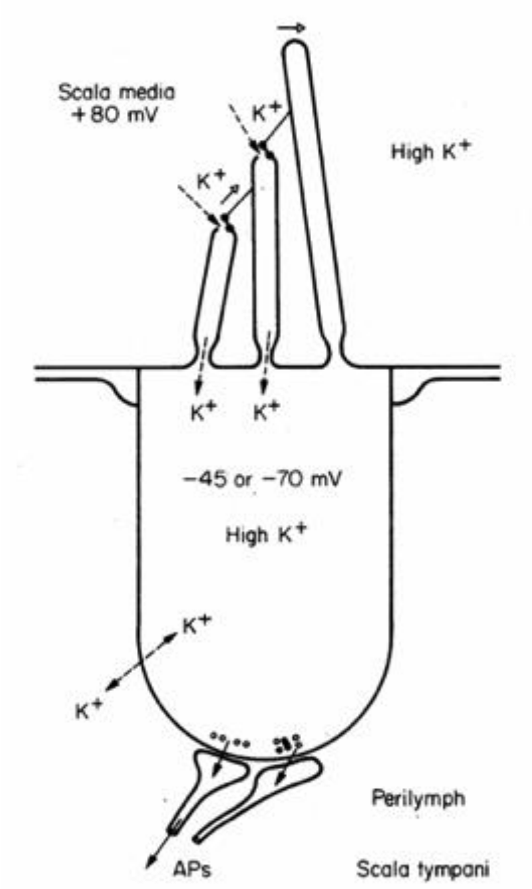
progressive neuropathy in second and third order neurons

The stria vascularis is the power-house of the cochlea



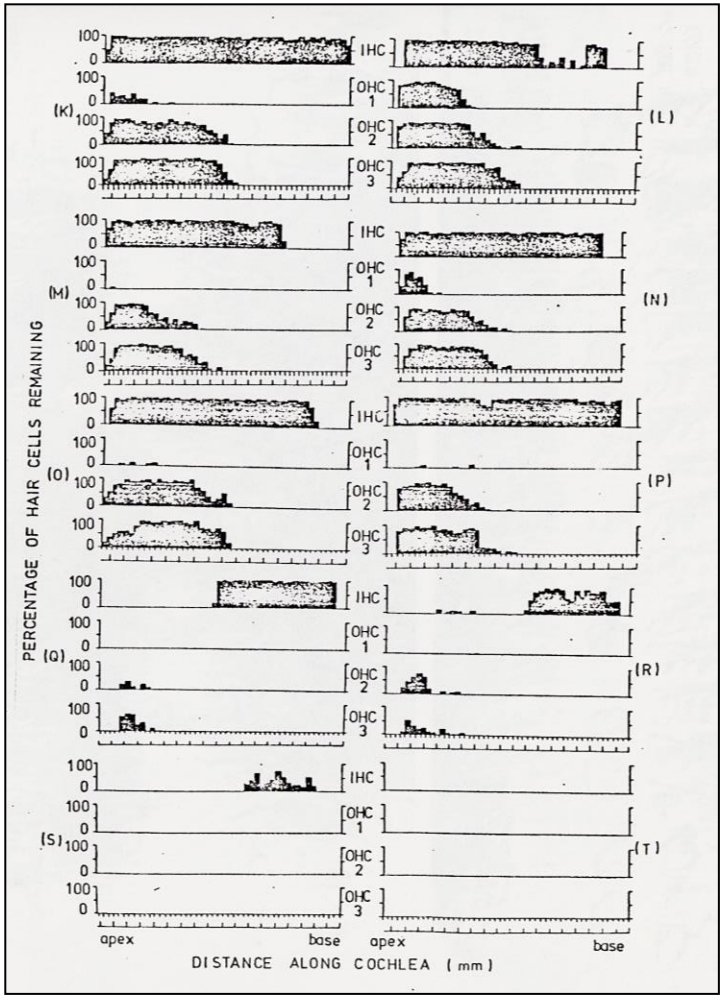
Impairment of strial function reduces electrical driving force for haircell activation



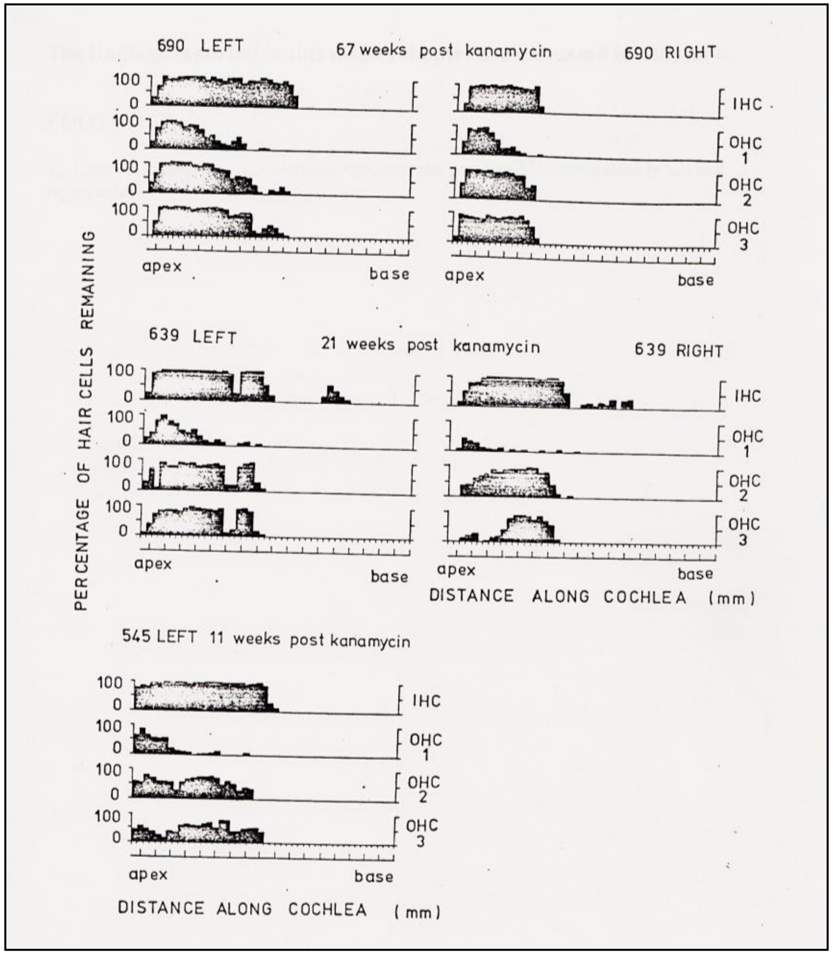


Standing cochlear potentials Davis' battery theory

When outer haircells are lost, inner haircell degeneration may follow later



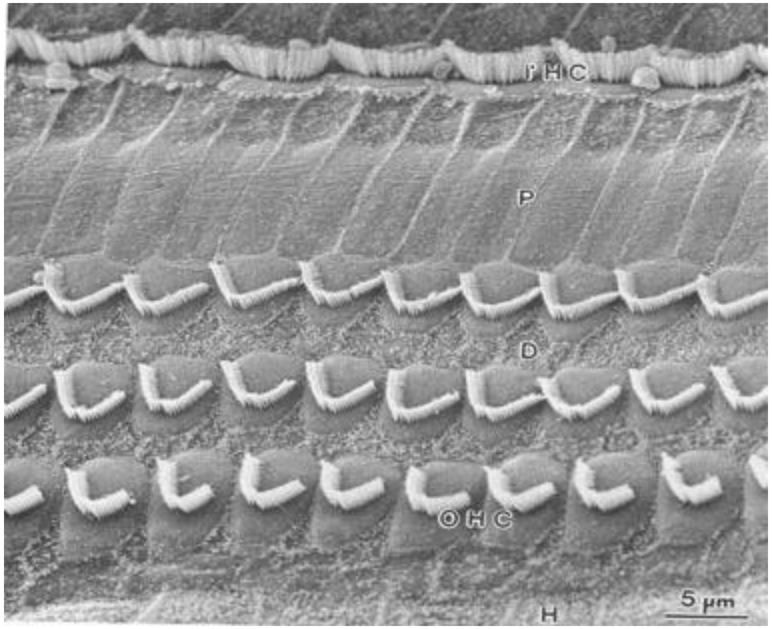
Cochleograms showing pattern of haircell degeneration cause by kanamycin poisoning (400mg/kg/day; 8-10 days). Animals sacrificed 2- 6 weeks after treatment.

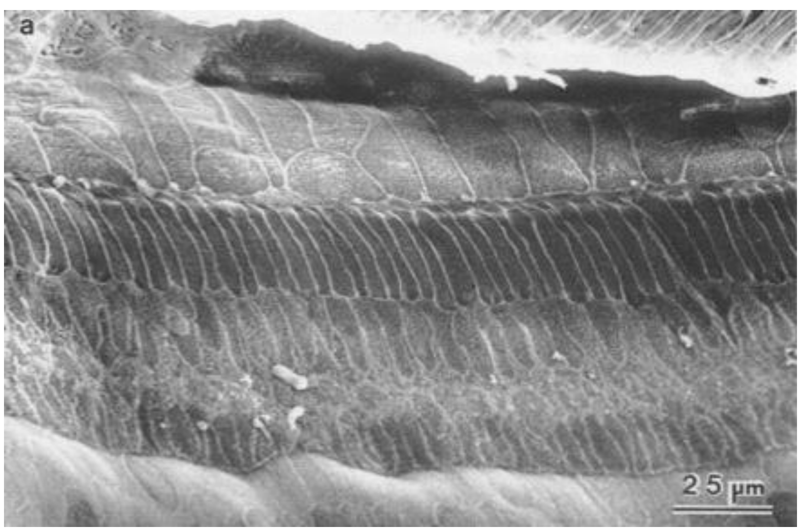


Long term inner and outer haircell degeneration
In GPs treated with kanamycin (400mg/kg/day; 8 days).
Animals sacrificed after 11, 21 & 67 weeks

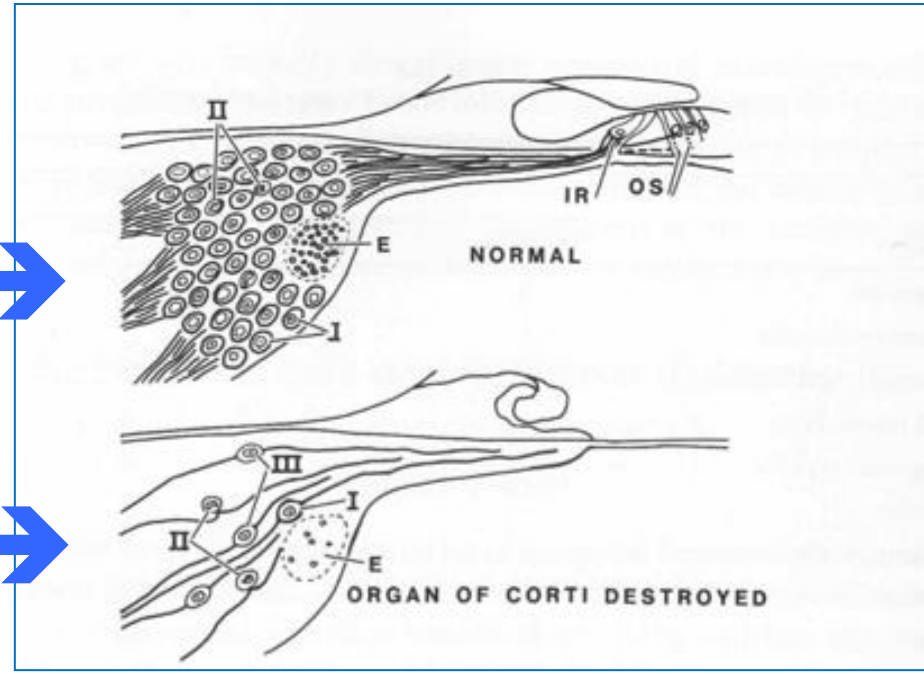
HARRISON RV, PhD thesis 1978, un-published data

When inner hair cells are damaged, spiral ganglion cells degenerate





From studies by Dr. H. Spoendlin



Inner haircell loss causes
spiral ganglion cell degeneration
AND degenerative change
in second and third order
central auditory neurons

THIS IS, OF COURSE, A MAJOR ISSUE IN COCHLEAR IMPLANTATION

ALMOST ALL HEARING LOSS (of peripheral origin) INVOLVES (more central) AUDITORY NEUROPATHY

- **Many cochlear insults can cause inner haircell degeneration and /or IHC synaptic damage (synaptopathy). e.g. ototoxic drugs, hypoxia, noise exposure, etc.**
- **When outer haircell damage is extensive, inner haircell degeneration often follows.**
- **When inner haircells are lost, there is spiral ganglion cell degeneration (These effects can also extend to second-order auditory neurons).**
- **After neonatal SNHL, central auditory pathways develop abnormally. Neural pathways reorganize, with both neuronal and synaptic growth and degeneration (pruning).**

So, what cochlear insults don't involve some degree of auditory neuropathy?

Sound Wave Symposium, San Diego, 2018

Developmental Plasticity and Progressive Hearing Loss

[1] Developmental plasticity in the auditory system:
Knowledge from basic science (animal) models.
General principles e.g.: age related plasticity, critical or sensitive developmental periods.
Clinical perspectives from cochlear implantation in children.

[2] Some perspectives on progressive hearing loss:
The peripheral "cascade" effect.
Timing of progressive hearing loss in relation to age related plasticity.

[3] Novel perspectives on progressive hearing loss in children after CI.
Speech and language improvement can be like a progressive hearing loss.

Timing of progressive hearing loss in relation to age related plasticity.

If the integrity of the auditory periphery is intact during an early developmental period (pre and post natal) then robust auditory pathways and brain networks will be established.

There is a sensitive or critical period for this early development.

If a progressive hearing loss starts late, or is very slowly progressing then this important early development can be relatively unimpaired.

In this case, an intervention (e.g. CI) can have a good prognosis.
(Similar to an patient with an acquired, short duration hearing loss)

If the progressive loss starts early on pre-natally or even prelingually, then it will impact the important early developmental process.

In this case the after CI or HA intervention, the prognosis for speech and language development will be poor.

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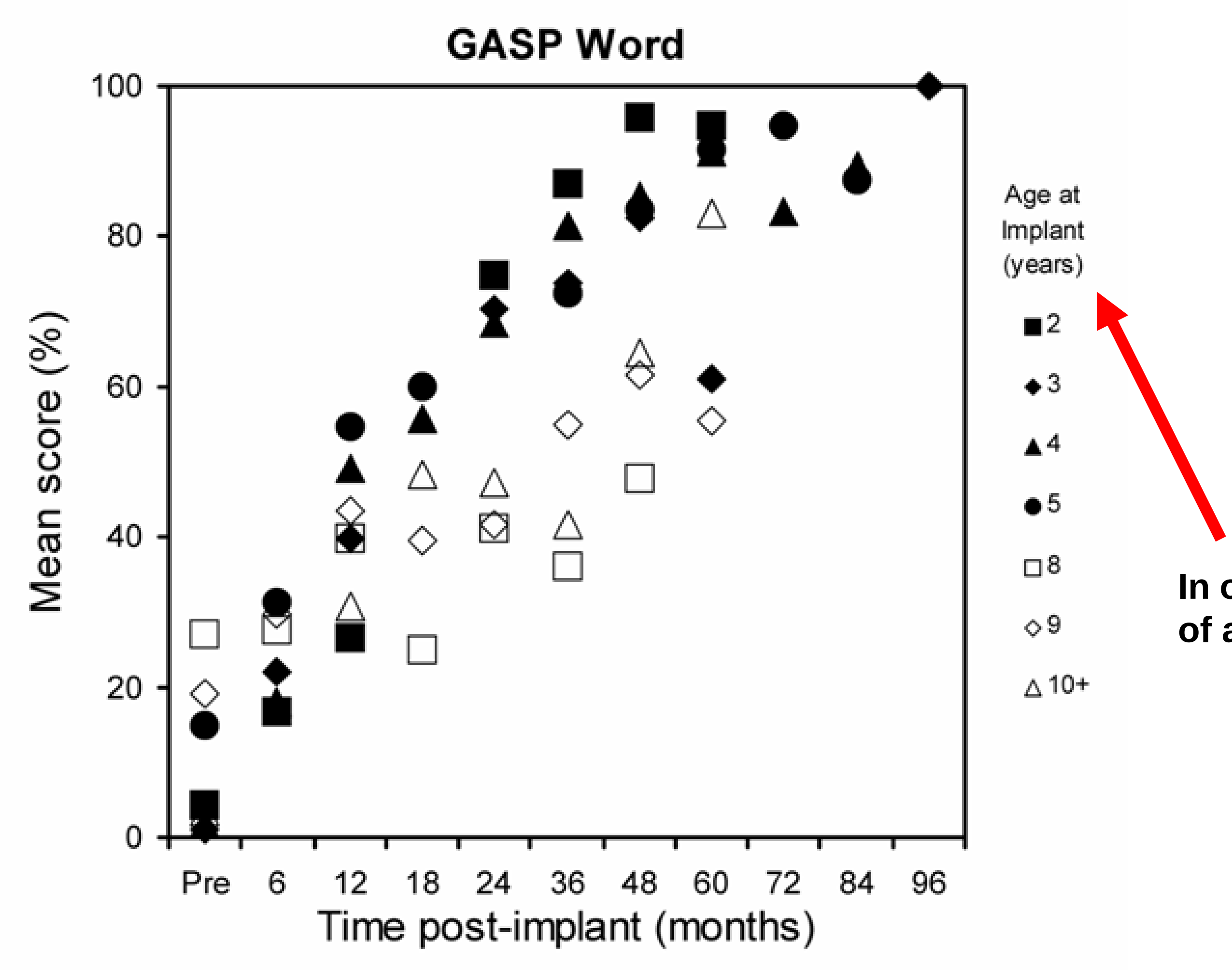
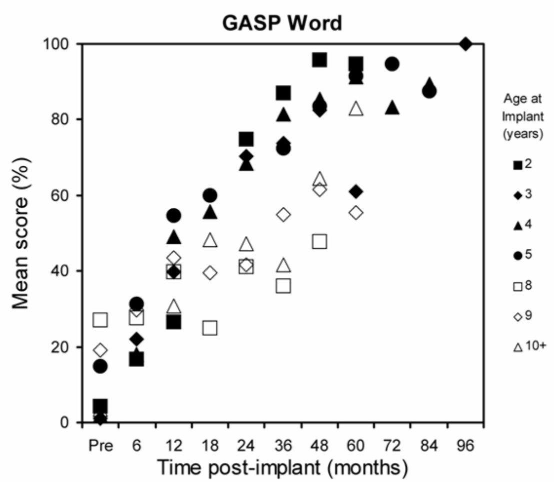
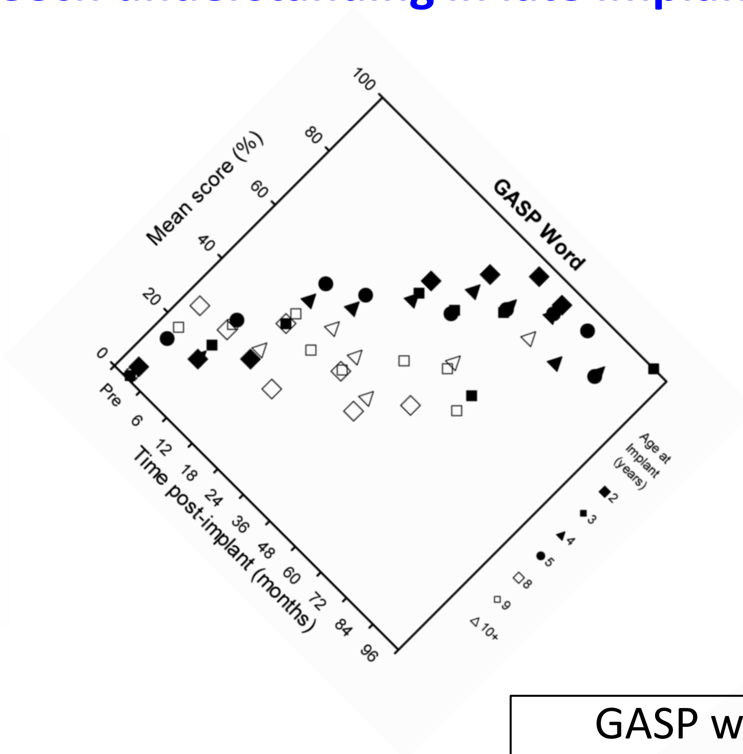


In other words, duration of auditory deprivation

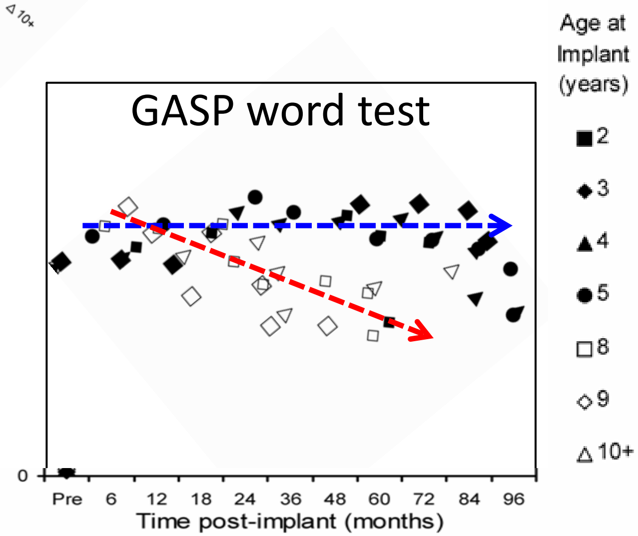
Mean scores in the GASP word test, pre and post-implantation for each age at implant group as indicated by the symbols key (right).

“Progressive loss” of speech understanding in late implanted children [1]

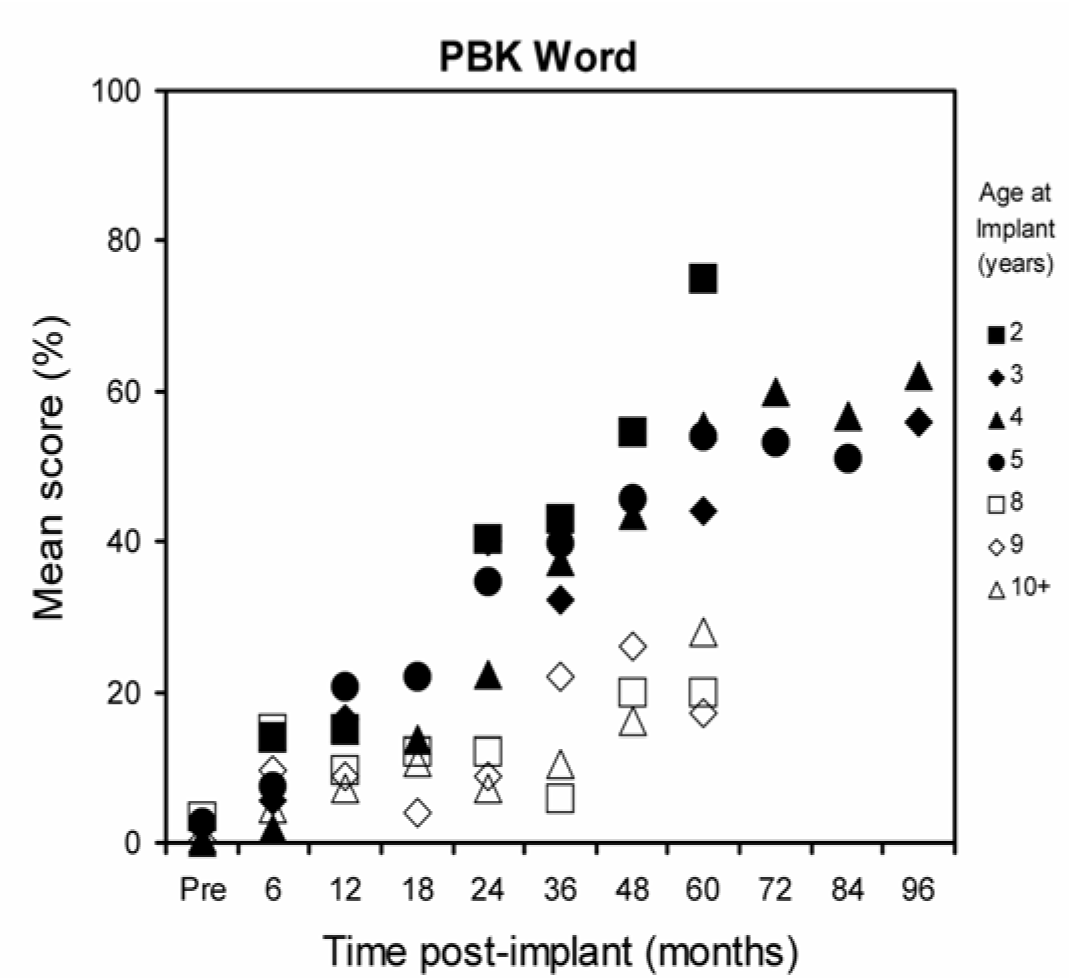




Trajectory of speech understanding (GASP word)
in children after early implantation



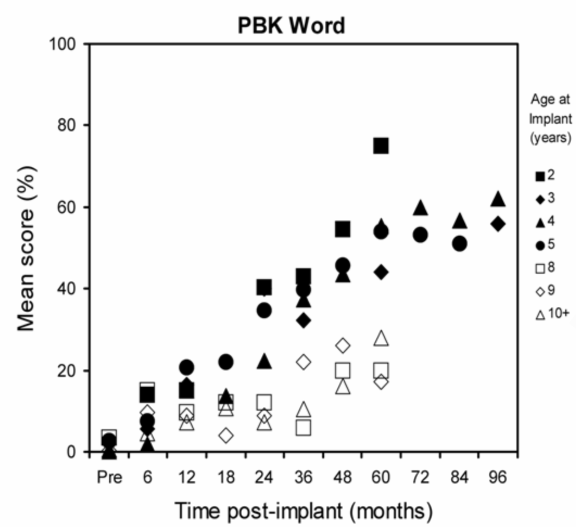
“progressive loss” of
speech understanding
In late implanted children

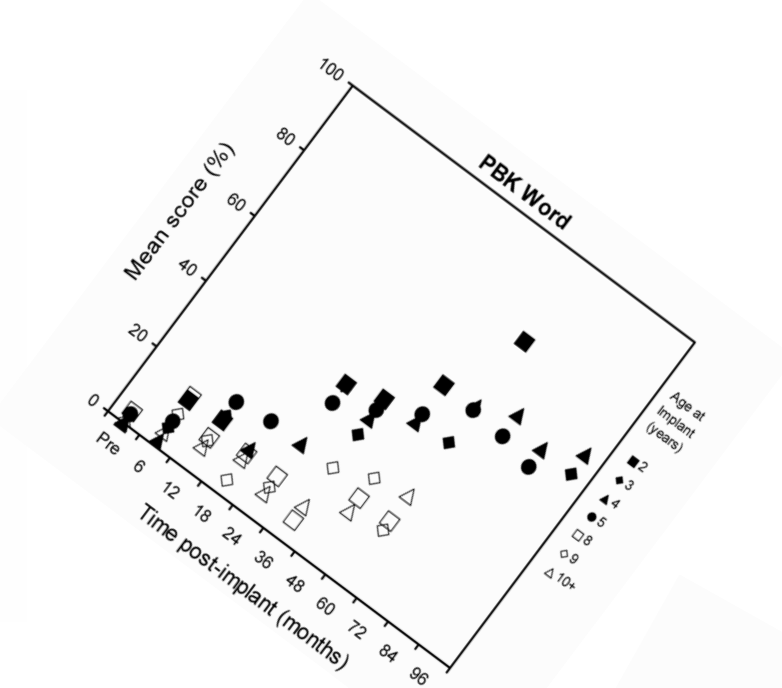


In other words, duration of auditory deprivation

Scores in the PBK word test for deaf children before a cochlear implant (far left) and at intervals post-implantation. Mean values are shown for each age at implant group, as indicated by the symbols key (right).

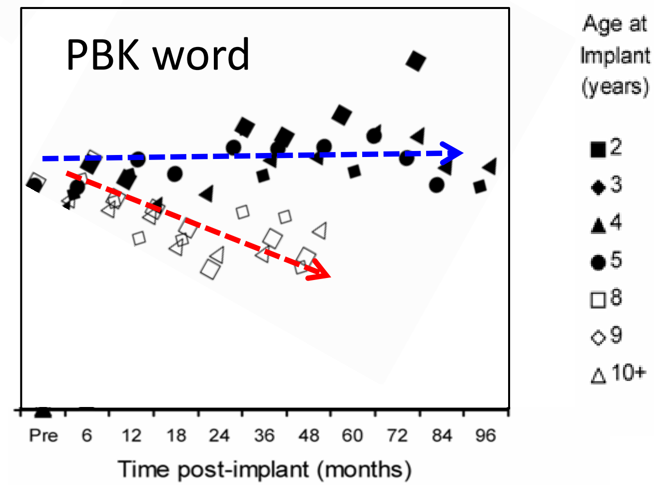
“Progressive loss” of speech understanding in late implanted children [2]



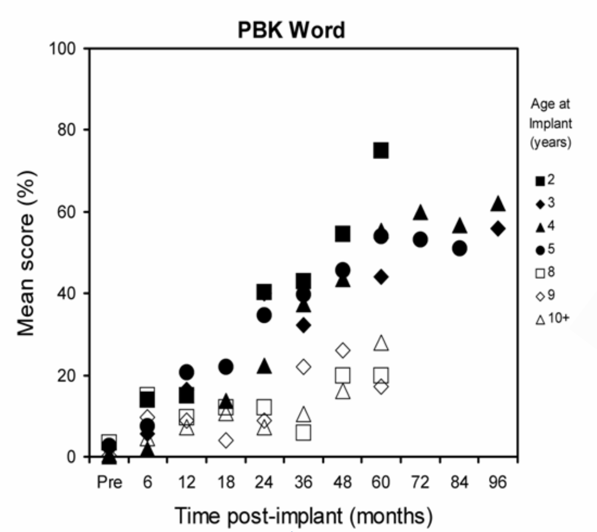


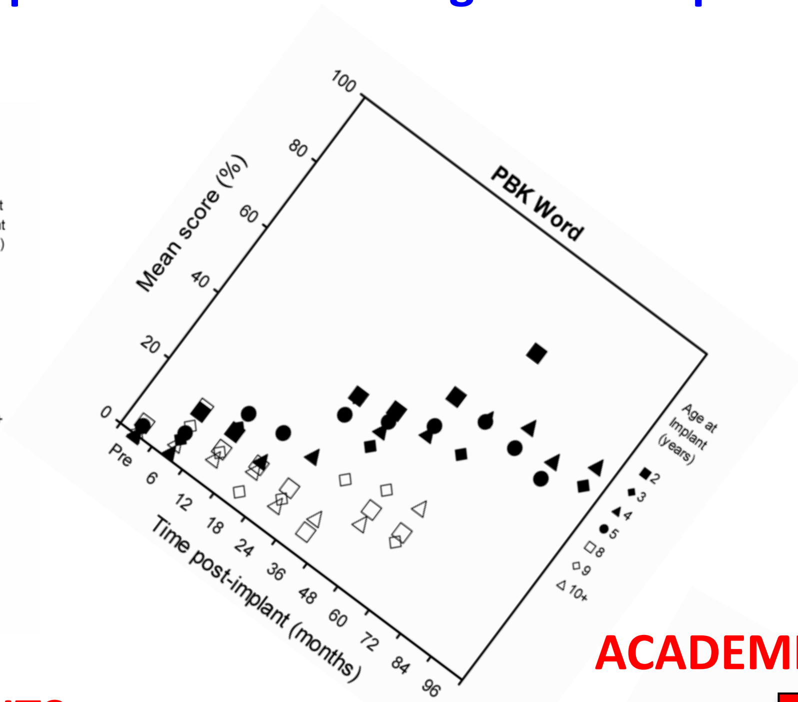
Trajectory of speech understanding
(PBK word) in children
after early implantation

“progressive loss” of
speech understanding
In late implanted children



“Progressive loss” of speech understanding in late implanted children [2]



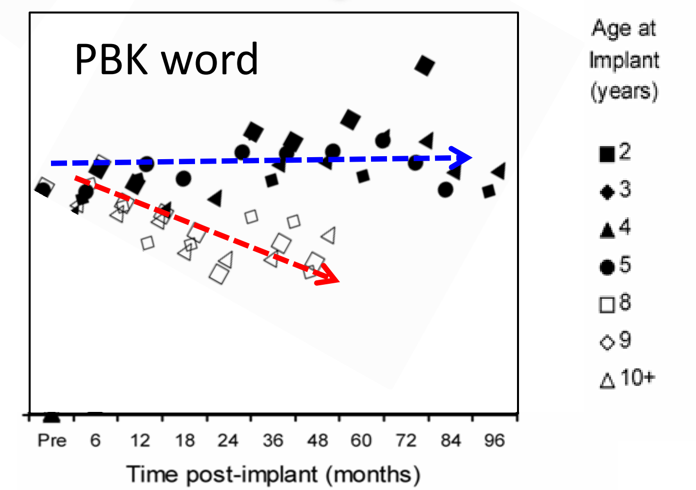


FOR PARENTS and PATIENTS

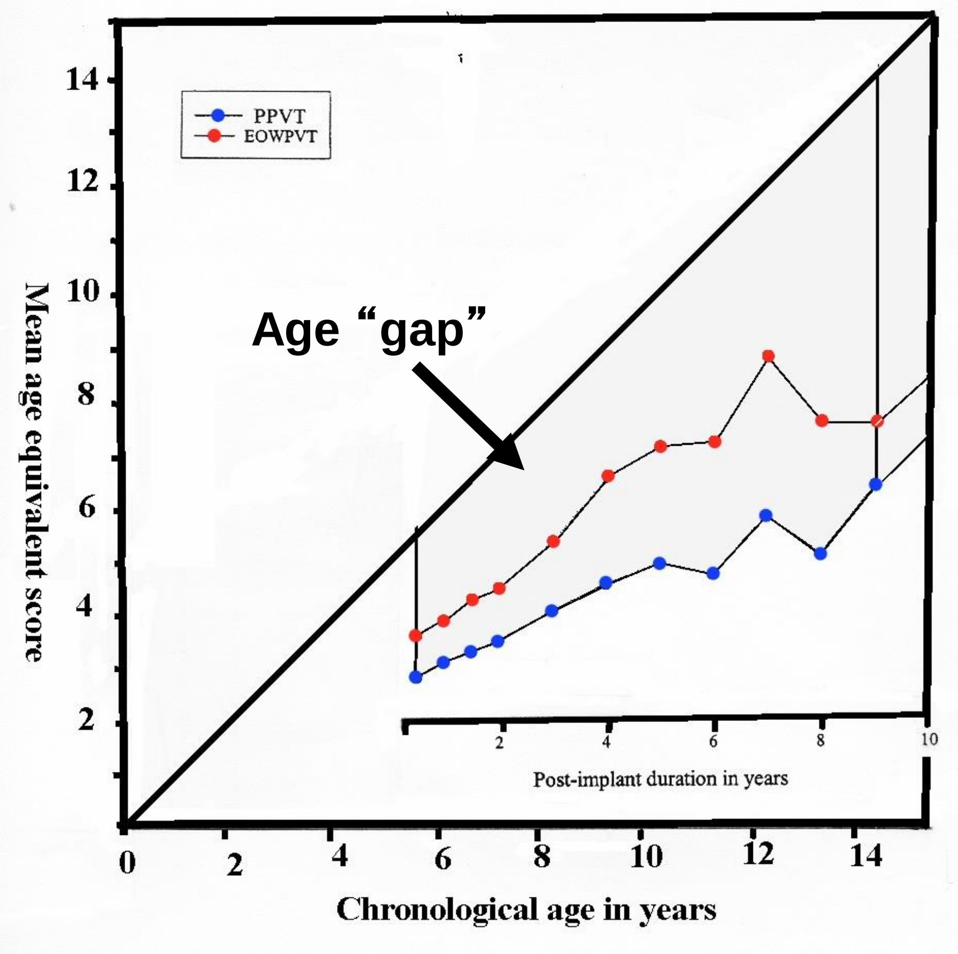
ACADEMIC PERSPECTIVE

Trajectory of speech understanding
(PBK word) in children
after early implantation

“progressive loss” of
speech understanding
In late implanted children



Vocabulary development post cochlear implantation [Receptive vocabulary and expressive vocabulary]

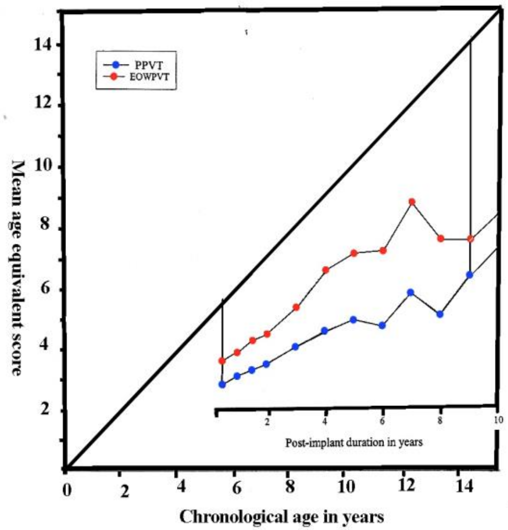


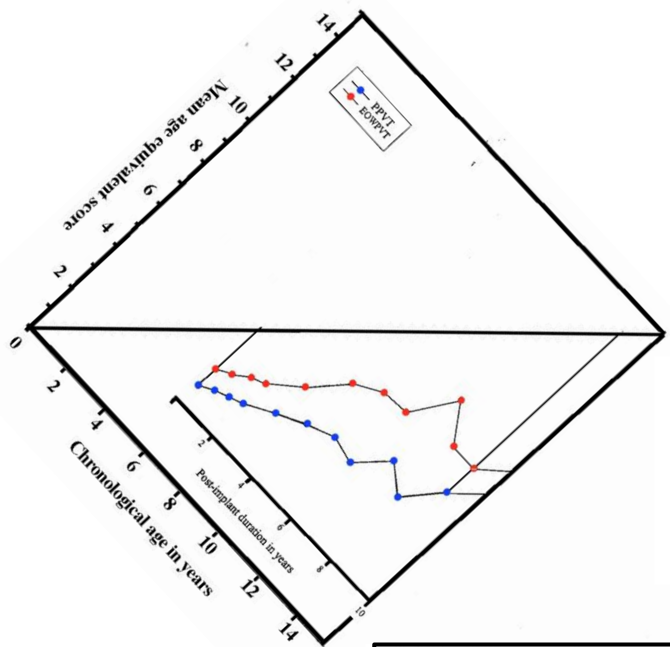
On average, vocabulary acquisition rates decline in the early post implantation period

Pooled data N=38 average age at implantation 5.7 years

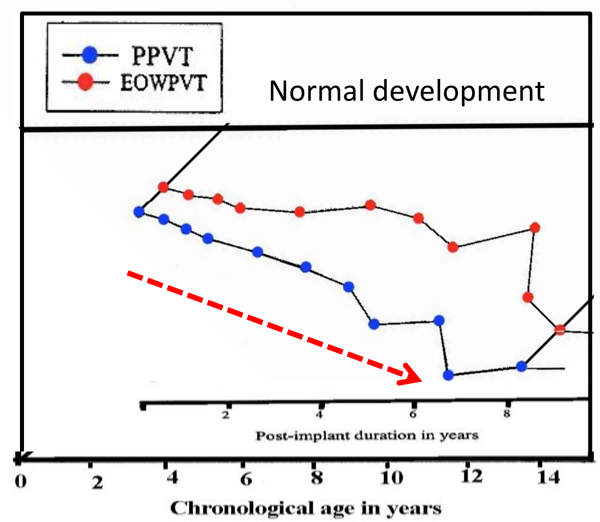
EL-HAKIM H, LEVASSEUR J, PAPSIN B, PANESAR J, MOUNT RJ, STEVENS D, **HARRISON, R.V.** (2001) Assessment of vocabulary development in children after cochlear implantation. Arch Otolaryngol Head Neck Surg 127: 1053-1059

Progressive loss in vocabulary development post cochlear implantation [Receptive vocabulary and expressive vocabulary]



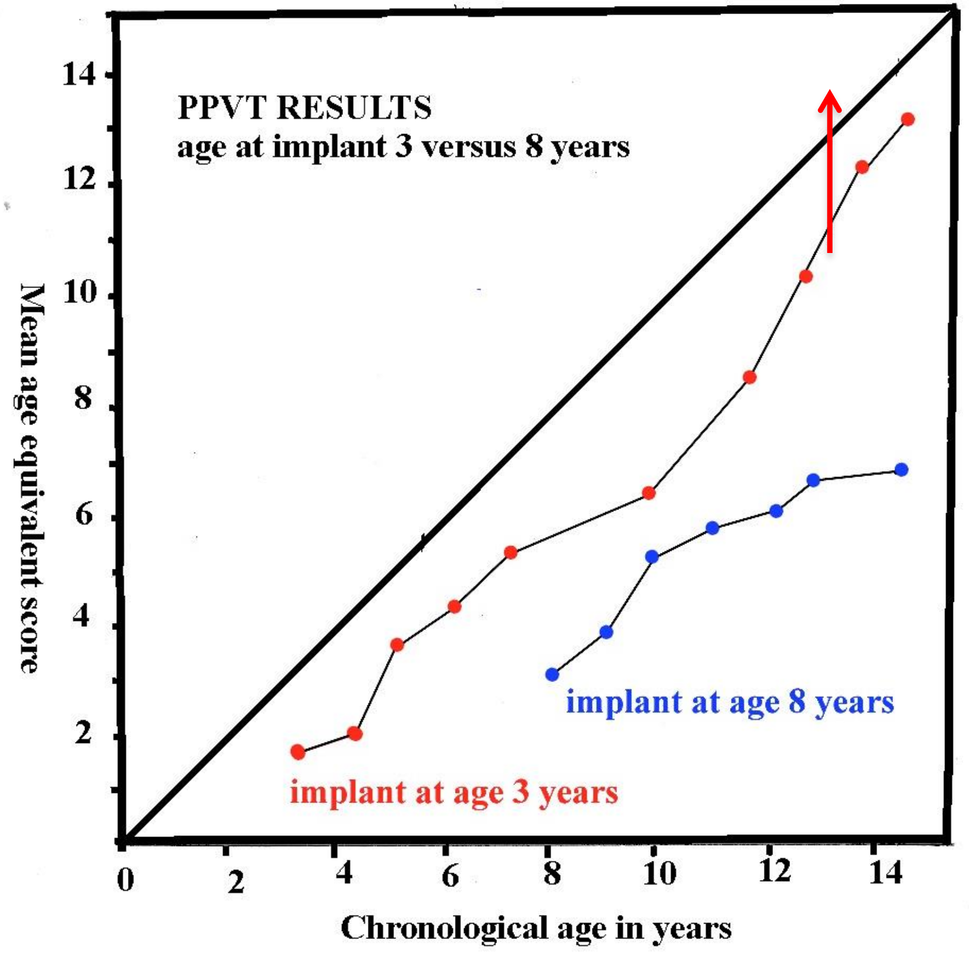


Trajectory of normal language development



Progressive loss in language development in children post cochlear implantation

Vocabulary development (PPVT)
Effect of early versus late cochlear implantation

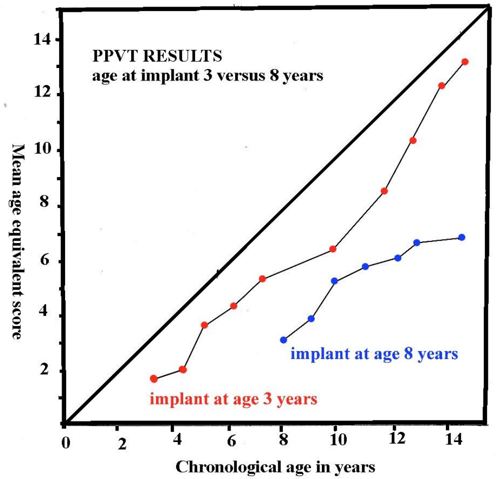


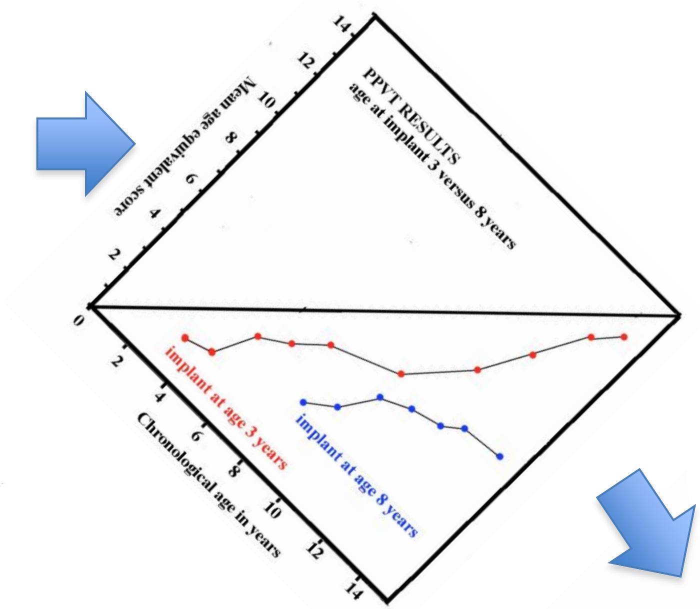
In early implantation age "gap" starts out reduced.

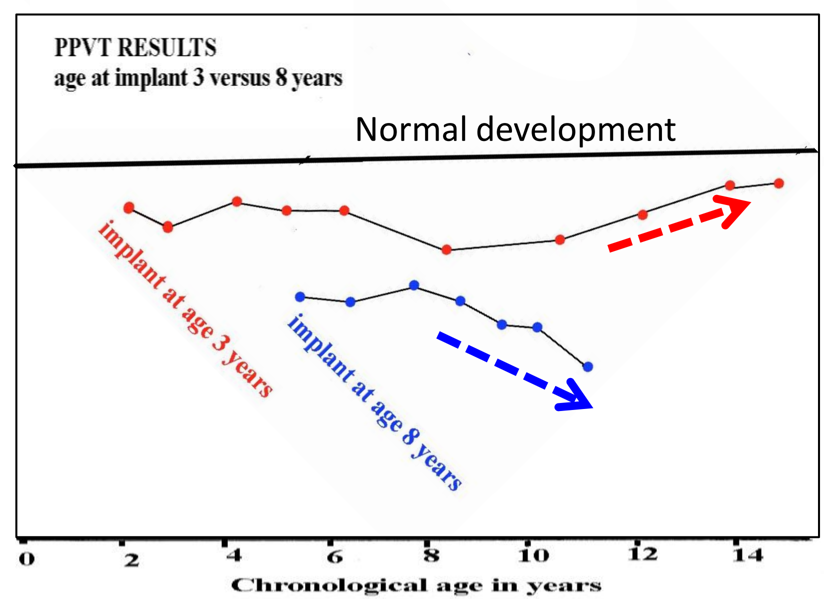
Some trend towards gap closure in longer term

EL-HAKIM H, PAPSIN B, MOUNT RJ, LEVASSEUR J, PANESAR J, STEVENS D, **HARRISON, R.V.** (2001)
Vocabulary acquisition after pediatric cochlear implantation and the impact of age at implantation
Int J Ped Otorhinolaryngol 59: 187-194

Development of language in children after cochlear implantation







Children implanted early keep up with normal language development

Children implanted late have
a PROGRESSIVE loss
in language development
Relative to normal

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Developmental Plasticity and Progressive Hearing Loss

SOME TAKE HOME MESSAGES

There are many causes of progressive hearing loss. Many etiologies suggest that a peripheral "cascade" effect may underlie some of the progressive loss.

Neural plasticity involves growing neurons, making or strengthening synaptic connections, pruning of connections etc.) Through such mechanisms the auditory brain is "programmed" from birth by environmental experience.

In an early post-natal period there is a very high level of plasticity. Important neural wiring occurs during this critical or sensitive period.

In a congenitally deaf infant, intervention has to be as early as possible and within this sensitive period. A sensitive period in regard to CI outcomes is at 5-6 years of age.

In the case of a progressive hearing loss, prognosis may relate to the timing of the hearing loss in relation to sensitive periods in age-related plasticity.

After pediatric cochlear implantation, speech and language improvement (glass half full) can considered to be a progressive hearing loss (glass half empty).

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Developmental Plasticity and Progressive Hearing Loss

FIN