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
devontmental 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.

   Speech and language improvement can be like a progressive hearing loss.
Developmental Plasticity and Progressive Hearing Loss

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

The RETINOTOPIC organization of the visual system

Calcarine fissure  
Primary visual cortex  
Calcarine fissure

Left  
Right

Fovea

Visual field
Somatotopic representation of the sensory surface of the skin
Mapping the tonotopic organization of auditory cortex using single unit electrophysiology

Neural “connectivity” improves with age
cortical neuron onset response latencies (chinchilla) at different ages

Evoked potential studies of human auditory system development

**Auditory Brainstem evoked Responses ABR**

Data from various works by Jos Eggermont
Recording the response properties of cortical neurons to tone stimuli

Increase in complexity of neuron responses in auditory cortex with age

**“simple response”**

Neuron firing rate

Stim frequency (kHz)

Time (ms)

**“complex response”**

Neuron firing rate

Stim frequency (kHz)

Time (ms)


(nature vs. nurture)
Increase in complexity of neuron responses in auditory cortex with age

Proportion of “complex cells” in auditory cortex with age

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

Cortex in early development

Mature cortex

(highly schematic)
Evoked potential studies of human auditory system development

Auditory Brainstem evoked Responses ABR

Normal hearing

Auditory Cortex, Evoked Potentials

Data from various works by Jos Eggermont
Evoked potential studies of human auditory system development

Auditory Brainstem evoked Responses (ABR)

Data from various works by Jos Eggermont
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.

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

Reference: Moore J.K 2002 ann otol rhinol laryngol 111, 7-10
Cochleotopic (tonotopic) organization of primary auditory cortex
Tonotopic map in auditory cortex of subject with normal activity patterns at the cochlear level

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

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

Reorganization of auditory cortex by neonatal environmental sound stimulation

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

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

Frequency map reorganization in auditory midbrain after neonatal versus adult cochlear lesions

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


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.

Assessment of vocabulary development in children after 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

Vocabulary acquisition after pediatric cochlear implantation and the impact of age at implantation
Int J Ped Otorhinolaryngol 59: 187-194
Sometimes hearing ability in ANSD can improve over time.

Need to wait a longer than normal before implantation
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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. Inner hair cell 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?
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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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   Speech and language improvement can be like a progressive hearing loss.
Mean scores in the GASP word test, pre and post-implantation for each age at implant group as indicated by the symbols key (right). In other words, duration of auditory deprivation.
“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
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).

In other words, duration of auditory deprivation
“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

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

Assessment of vocabulary development in children after cochlear implantation.
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

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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.
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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