Auditory Development and Brain Plasticity

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AGENDA

Cochlear development
Connecting the cochlea to the brain
When do we first “hear”?
Early formation of the central auditory pathways.
Basic science studies of central auditory system development.
Evoked potential studies of human auditory system development.
Tracking auditory brain development in children after cochlear implantation.
Age related plasticity in auditory system development.
How does basic science inform us about clinical issues?
Some “bench to bedside” discussion; take home messages.

Key developmental stages at the cochlear level (time lines for human)

- **Onset of “hearing”?**
- **Indications of cochlear function**
  - Hair cells connect to brainstem 20-30wk
  - Onset of cochlear potentials
  - End of CM development
  - CAP and cochlear frequency selectivity complete
  - AP latency normal

- **HUMAN**
  - 12 wk
  - 20 wk
  - 36 wk
  - 4 wk

- **Structural growth**
  - Hair cell differentiation
  - Start of tectorial membrane growth
  - Final maturation of basilar membrane, tectorial membrane, and OHC synapses
  - Full myelination of auditory nerve
Key developmental stages at the cochlear level
(time lines for human and rat species)

Indications of cochlear function

Onset of cochlear potentials
End of CM development
CAP and cochlear frequency selectivity complete
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Structural growth

Hair cell Differentiation. Start of tectorial membrane growth. Final maturation of basilar membrane, tectorial membrane, and OHC synapses

HUMAN
RAT

Hair cells connect to brainstem 20-30wks

Development of the tectorial membrane

Haircells well developed before tectorial membrane growth
Development of the tectorial membrane

Haircells well developed before tectorial membrane growth

The cochlea at birth
precocious vs. altricious species

Chinchilla, Human (precocious species)

An altricious species (immature at birth).
Connecting the cochlea to the brain

- Immature neurons in the otocyst grow centrally towards brainstem.
- They split (twice) to connect with target cells in AVCN, PVCN and DCN.
- Mid regions of the cochlea connect up first, apical and basal areas later.
- Initial projections/connection are cochleotopic.
- Initial wiring occurs before any sound driven auditory input.
- May be a role for intrinsic (spontaneous) activity.

- Connections in humans complete at 20-30 weeks (i.e. 10 -20 weeks before birth)

When do we first “hear”?

- Cochlea connects up at 10 - 20 weeks before birth
- First “function” is some weeks later
- ABR can be recorded in babies born 15 weeks premature
- Blink startle reflex to acoustic stimulation observed (by ultrasound) at 24-25 weeks gestational age

Discussion
Does this mean the baby really can “hear”? What do we mean by “hear”? What acoustic signals can be detected?
Step 1: Early formation of the auditory pathways
Step 2: Both ascending and descending pathways develop at the same time.
Step 3: Auditory nuclei at all levels connect up at the same time.
Step 4: Initial MAINLINE connections are made BEFORE acoustically driven activity from the periphery.
Step 5: Both ascending and descending pathways develop at the same time.
Developmental refinements of the auditory pathways

[1] Sound frequency representation (tonotopic maps) in auditory cortex

[2] Increased complexity of auditory processing in cortex

[3] Improved information transmission from cochlea to cortex

The sensory epithelium of the cochlea projects in organized way to auditory cortex. (tonotopic /cochleotopic organization)
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Cochleotopic (tonotopic) organization of primary auditory cortex
(in Human and Cat)
Cortical frequency map development after a neonatal cochlear lesion


Reorganization of auditory cortex by neonatal environmental sound stimulation

Organization and programming of central auditory system shows age related plasticity

• All sensory systems have an early period of plasticity; visual, somatosensory, auditory.
• Early changes to cochlear activity patterns (e.g. caused by hearing loss) results in a reorganization and reprogramming of auditory cortex.
• Early changes to cochlear activity patterns also causes sub cortical reorganization (e.g. thalamus, midbrain).
• In more mature subjects the degree of plasticity is significantly reduced. Cortex can only be remodelled if sounds are “behaviourally significant”.
• Age related plasticity has very important impact on how we approach hearing loss in children. Early detection, early intervention.

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

Speech perception outcome results at age 6 years. Results from four tests: TAC, PBK word; PBK phoneme; GASP word. The mean score (%) for congenitally deaf children, at six years of age, who have not yet received an implant is shown (black bar), and who had a cochlear implant device implantation at ages 2, 3, 4 or 5 years of age (see key).


Recording the response properties of cortical neurons to tone stimuli

Increase in complexity of neuron responses in auditory cortex with age

Pienkowski and Harrison (2005)
J. Neurophysiol. 93: 454-466

Increase in complexity of neuron responses in auditory cortex with age

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Proportion of “complex cells” in auditory cortex with age

Pienkowski and Harrison (2005)
J. Neurophysiol. 93: 454-466

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

Cortex in early development

Mature cortex

(howly schematic)
Increased complexity of auditory neuron responses reflects development of inter-neuronal connections

Cortex in early development

Mature cortex

Developmental refinements of the auditory pathways

[1] Sound frequency representation (tonotopic maps) in auditory cortex

[2] Increased complexity of auditory processing in cortex

[3] Improved information transmission from cochlea to cortex
Neural "connectivity" improves with age
cortical neuron onset response latencies (chinchilla) at different ages

Pienkowski and Harrison (2005)
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Acoustically evoked auditory potentials

Cortical AEP
MLR
ABR
CAP

Acoustic stimulation.
Evoked potential studies of human auditory system development

Auditory Brainstem evoked Responses ABR

Auditory Cortex, Evoked Potentials

Data from various works by Jos Eggermont
Electrically evoked auditory potentials in children with cochlear implants

Auditory development through cochlear implant use

Evoked potential studies of human auditory system development

Auditory Brainstem evoked Responses ABR

Auditory Cortex, Evoked Potentials

Data from various works by José 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. Numbers 1 to 6 indicate cortical layers. WM — deep white matter. Adapted from Ramón y Cajal.5

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Reference: Moore J.K 2002 annotolrhinolaryngol 111, 7-10

Developmental issues related to bi-lateral cochlear implantation in children

What are the effects on auditory system development of having input from only one side (single CI)?

Does a second, later implanted, contralateral cochlear implant work?

Simultaneous versus sequential bilateral cochlear implantation.

Normal neural substrate for binaural processing

Auditory brainstem

Superior olivary complex
Developmental plasticity of the binaural system
Effects of early input from only one ear (one cochlea ablated)

Question: - how is this different from a congenitally deaf child with one cochlear implant?

Effects on neonatal cochlear damage on the development of auditory pathways (in gerbil). (Kitzes L.M 1986)

Aberrant axonal branching in brainstem after unilateral otocyst removal (Parks and Jackson, 1986)

Using objective measures (ABRs) to assess binaural processing in kids with bilateral cochlear implants

- Binaural processes are first established at the level of the brainstem
- Timing and level differences between the ears are compared for sound localization
Testing auditory connections on both sides in kids with bilateral cochlear implants

Mismatched timing of input to auditory brainstem (ABR) in children with sequential bilateral cochlear implantation.

Child A: Simultaneous

Gordon, et al., 2007
Mismatched timing of input to auditory brainstem (ABR) in children with sequential bilateral cochlear implantation.

Child A: Simultaneous

No latency difference

Latency difference(ms)

Time (years)

Right to left side difference in eABR (V) latency

First activation  3 months bilateral use  9 months bilateral use

Wave eV, Electrode 20

Latency relative to Right (ms)

Speech perception in children using bilateral cochlear implants

% improvement in speech perception using both implants versus only one

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Some clinically relevant “take home messages”:

The pattern of cochlear nerve activity in the neonatal subject influences central auditory system organization.

Sensorineural hearing loss from an early age will result in cortical frequency map reorganization as well as many other aspects of auditory brain “programming”.

Stimulation of the cochlear nerve by electrical stimulation with a cochlear implant drives the formation of auditory pathways in a rather “unusual” way.

The timing of binaural cochlear implantation is important.

A cochlear implant in a congenitally deaf infant serves two functions hearing AND development.

The auditory system has age related plasticity (especially in sub-cortical areas) and this has important implications for early hearing loss detection and intervention (next talk).
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