Electrophysiology and Pediatric Hearing Disorders: Implications for Care Strategies and Language Development in Infants and Children

Celine Richard, MD, PhD
Thierry Morlet, PhD

Introduction and Overview

Setting the Stage: Hearing, Brain Development, and Early Language Acquisition

Cochlear Maturation

The maturation of the auditory cortex is complete

Sensory cell differentiation

Onset of function

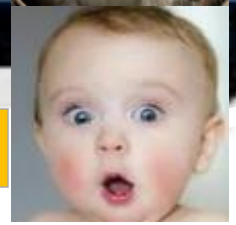
Maturation completion

BIRTH

10 DAYS

20 DAYS

2 MONTHS



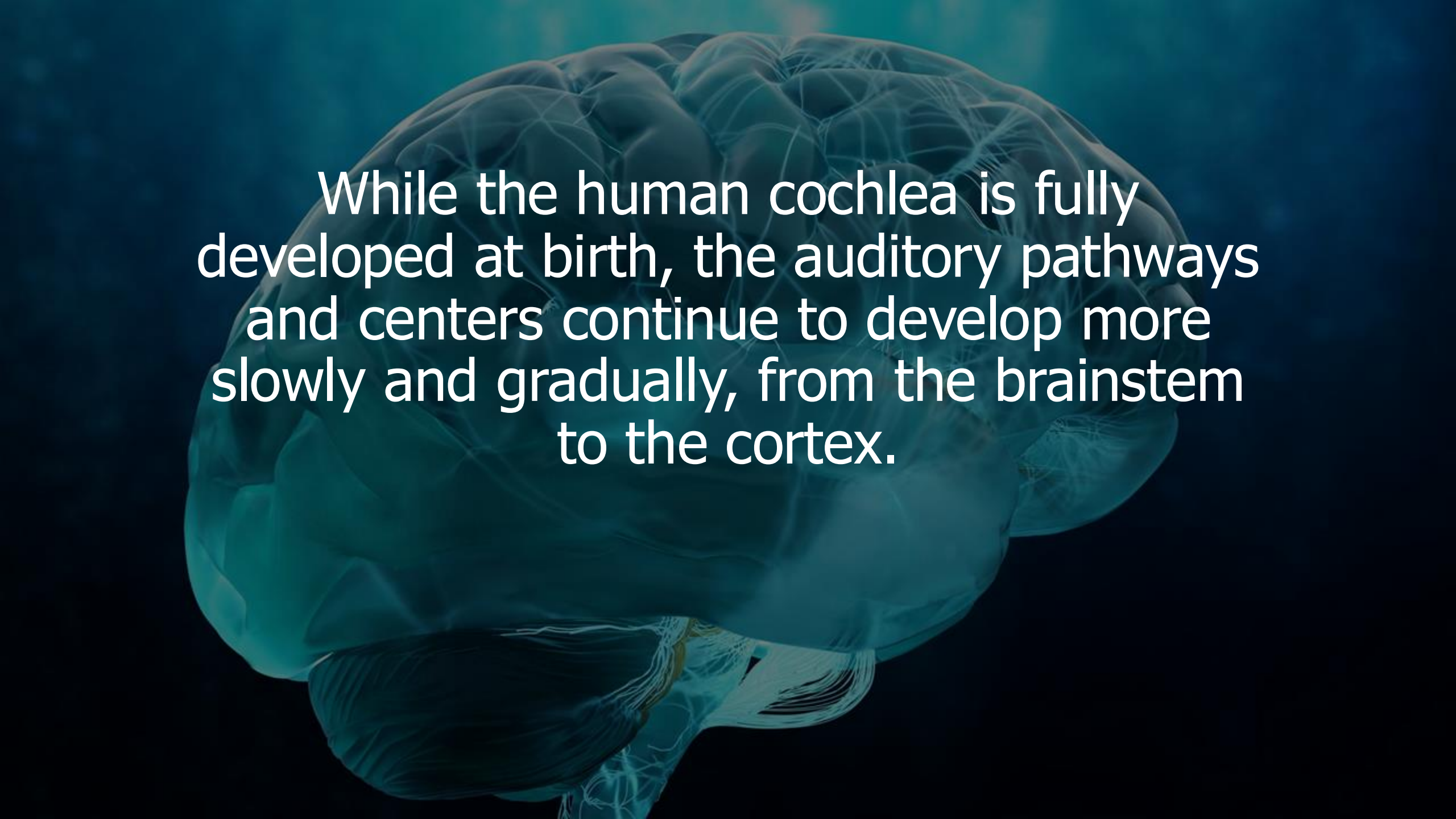
3 MONTHS (IN UTERO)

4 1/2 MONTHS (IN UTERO)

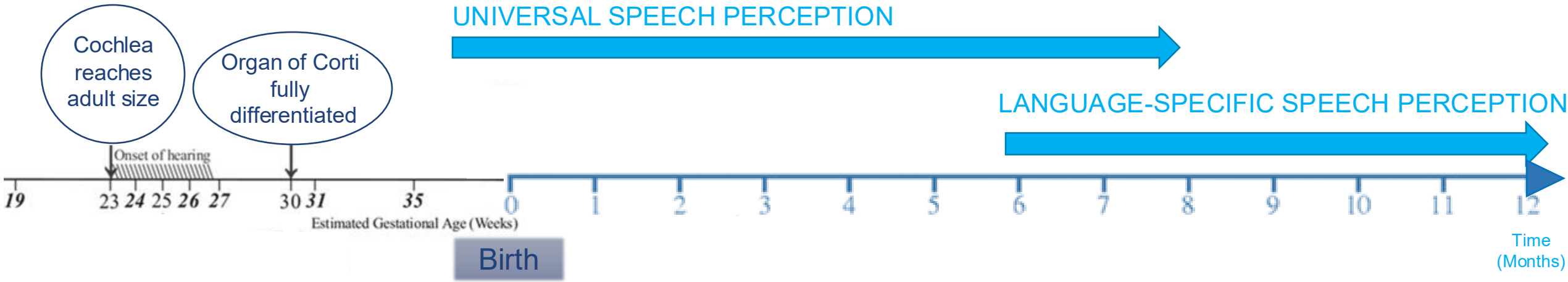
BIRTH

6 YEARS

- For the auditory brain to mature properly, it requires a fully developed and functional cochlea.
- Early detection and treatment of any hearing deficits matters!!


While the human cochlea is fully developed at birth, the auditory pathways and centers continue to develop more slowly and gradually, from the brainstem to the cortex.

Auditory-Speech Developmental Timeline



SYNAPTOGENESIS

NEUROGENESIS

MYELINATION

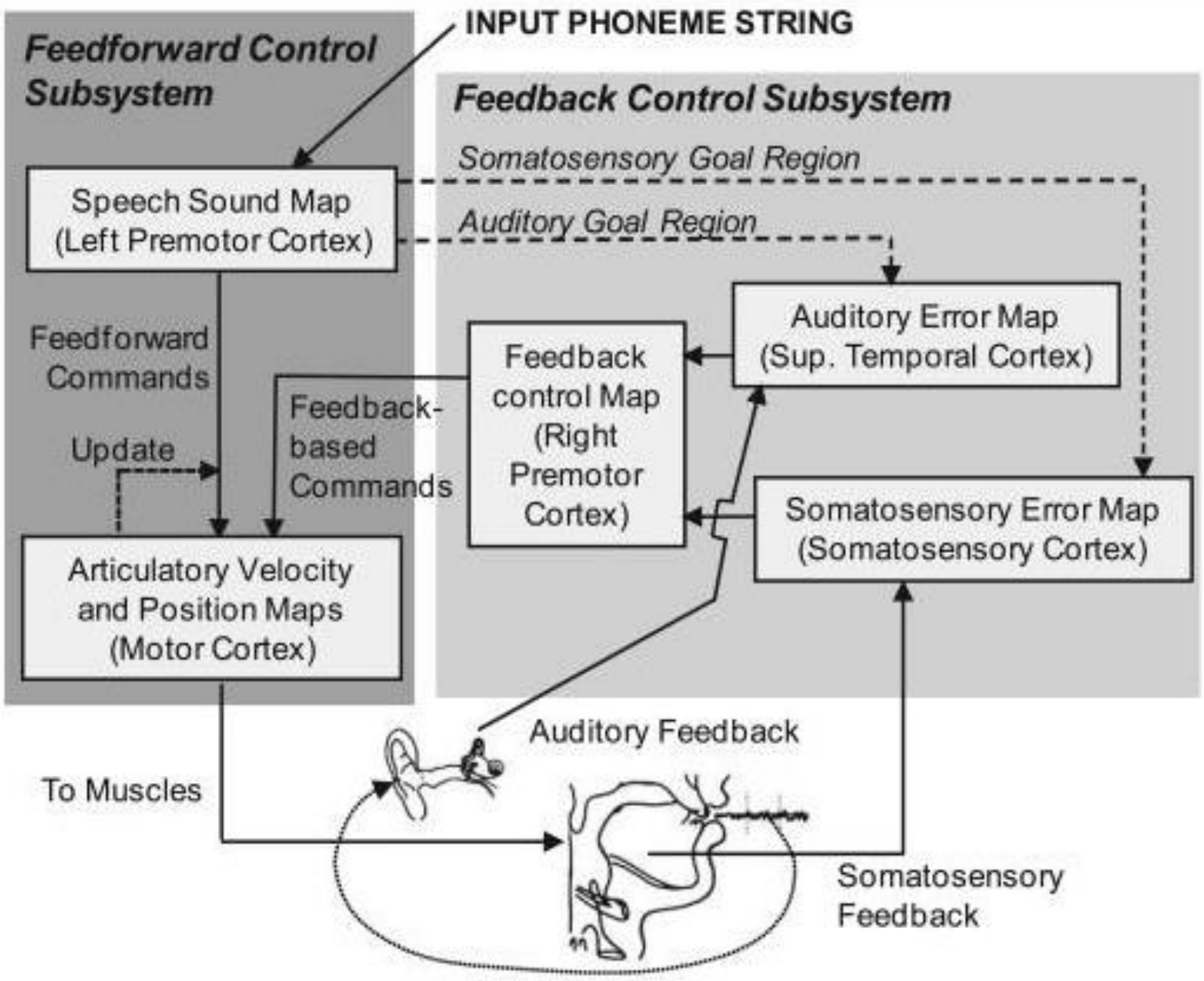
Adapted from:
Kuhl et al. 2008
Richard et al. 2017

Epidemiology & Impact

- Permanent childhood hearing loss (PCHL) affects roughly 1–3 per 1,000 live births; even mild–moderate losses are linked to measurable delays in vocabulary, syntax, and pragmatics.
- Children with mild-to-severe bilateral loss historically show deficits in vocabulary, morphology, advanced syntax, and social communication compared with hearing peers.
- Congenital infections (e.g., CMV, syphilis) are key etiologies; in one TORCH cohort, 31% had SNHL and these children showed significantly greater delays in expressive and receptive language and global development.

Critical Periods & Neuroplasticity

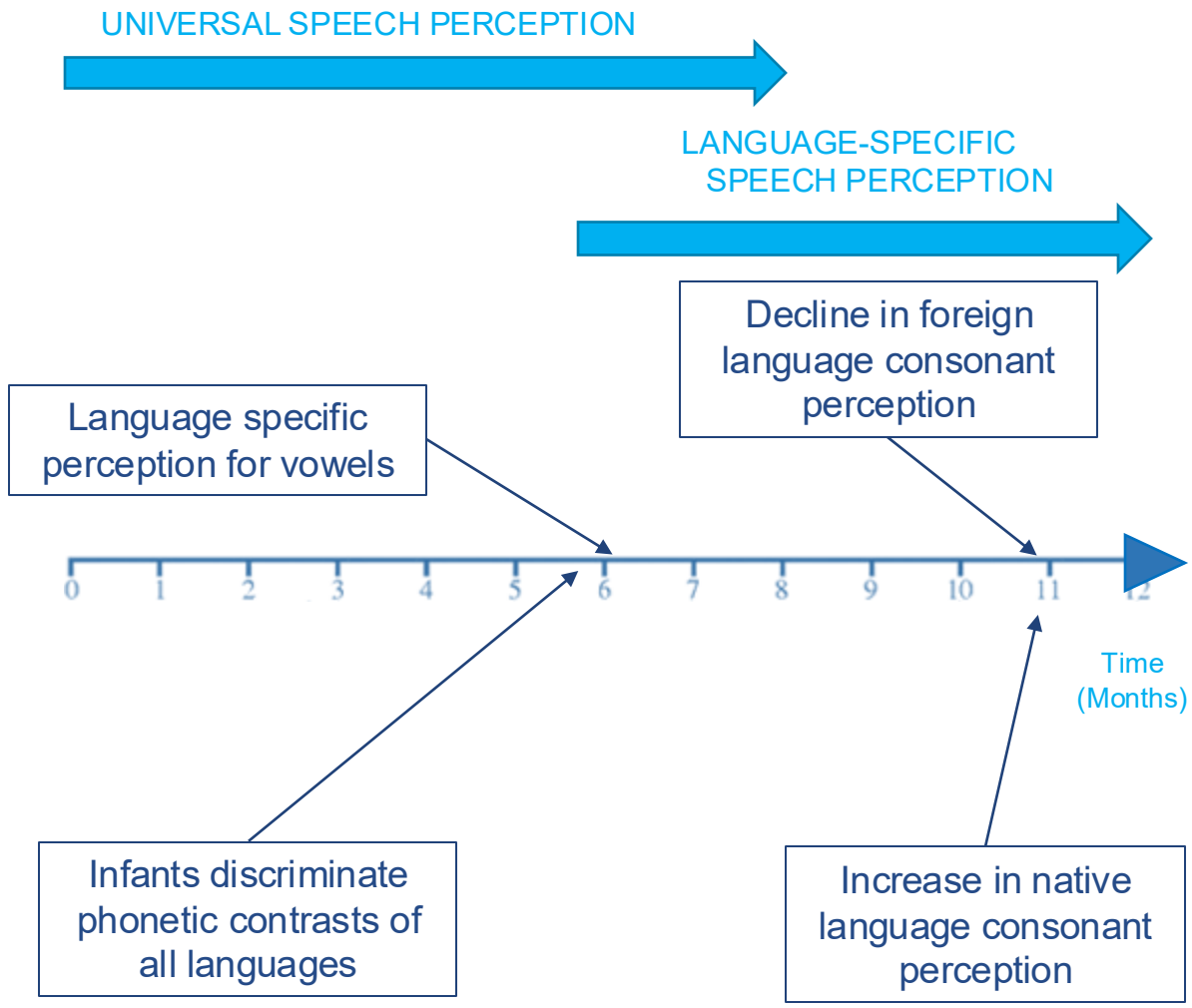
- The first 2–3 years represent a high-plasticity window in which auditory input sculpts cortical language networks.
- Earlier amplification/implantation yields better 5-year language: starting hearing aids at 3 vs 24 months leads to markedly higher language scores, with larger benefits at greater degrees of loss; cochlear implantation at 6 vs 24 months yields a ~21-point language advantage.
- Across multiple cohorts, entry to intervention by 6 months (EHDI 1-3-6) predicts higher vocabulary and global language outcomes into preschool and early school years



- Speech sound production relies on perceptual processes Neurocomputational models propose dynamic interplay between **feed forward** and **feedback** mechanisms.
- **Feedforward mechanisms** involve cortico-cortical projections and cerebellar contributions to speech planning and execution.
- **Feedback mechanisms** regulate speech output through auditory and somatosensory systems.
- The auditory feedback subsystem detects and corrects mismatches between intended targets and actual auditory output.
- In typically developing infants, auditory–articulatory cortical connections supporting speech perception and production are present early in life

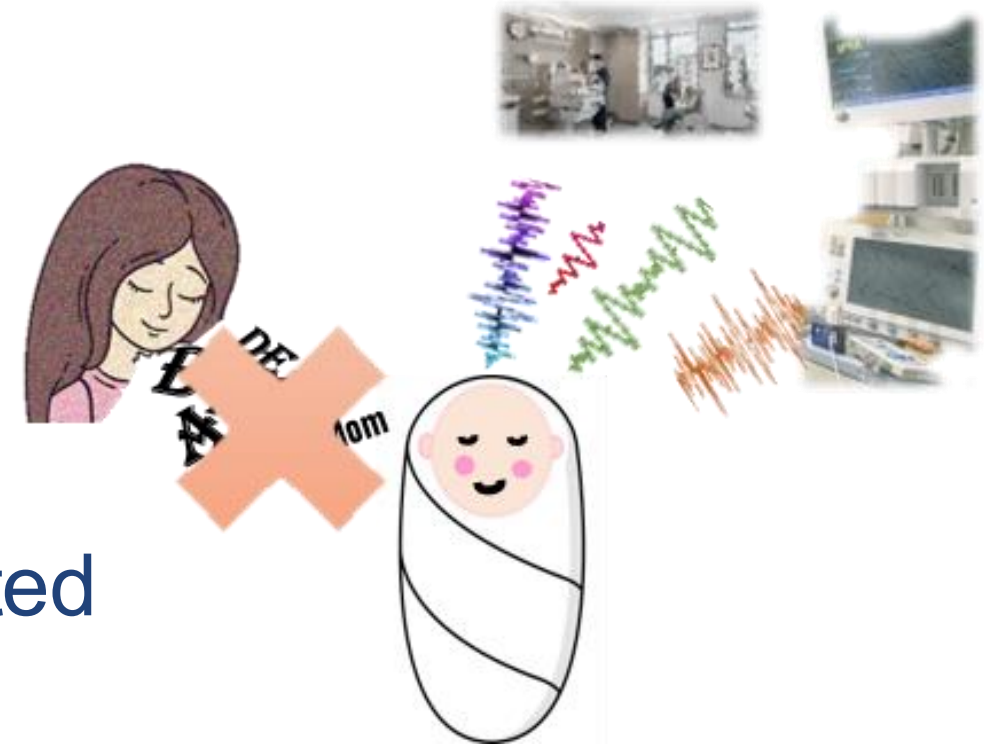
Tuning of the Auditory System in the First Year

- Tuning optimizes perception of Native language
- Perceptual narrowing and specialization occur
- **Plasticity starts as early as sound exposure**



Short and Long-Term Influences on Neurodevelopment in the NICU

Altered sensory experiences



- Environmental sounds
- Infant medical background
- Decreased exposure to infant directed speech

Speech Sound Differentiation, Outcomes and Contingent Language Exposure

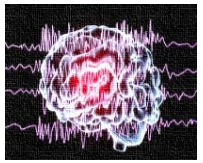
1. Speech sound differentiation near term equivalent age depends on length of time spent in the NICU (Key 2012)
2. Speech sound differentiation near term equivalent age predicts receptive language outcomes at 24 months CA (Maitre, 2013)
3. Contingent language exposure increases speech sound differentiation in preterm infants more than passive exposure. (Chorna, 2018)

ERP

Study Design

20 sessions, 30 infants

EEG recording



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/ma/ /mi/ /pa/ /pi/ /ta/ /ti/

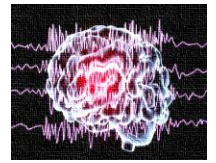
Infant-directed speech

= Control group = **Passive** Listening

+ = **Suck-contingent** Listening

INTENSITY=55dB(A)

EEG recording



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/ma/ /mi/ /pa/ /pi/ /ta/ /ti/

- Stable infants from monolingual English families
- Aged 36-75 weeks PMA at study start
- Maternal Educational level (Hollingshead index)

2 to 3 WEEKS

Intervention Content

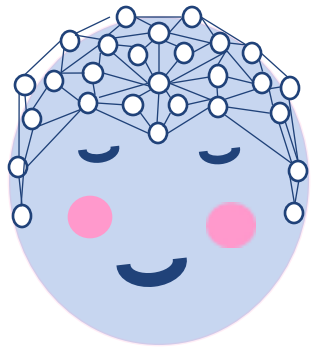
For both group: Infant directed speech

- Recorded female voice
- Infant-directed speech
- Singing and reading

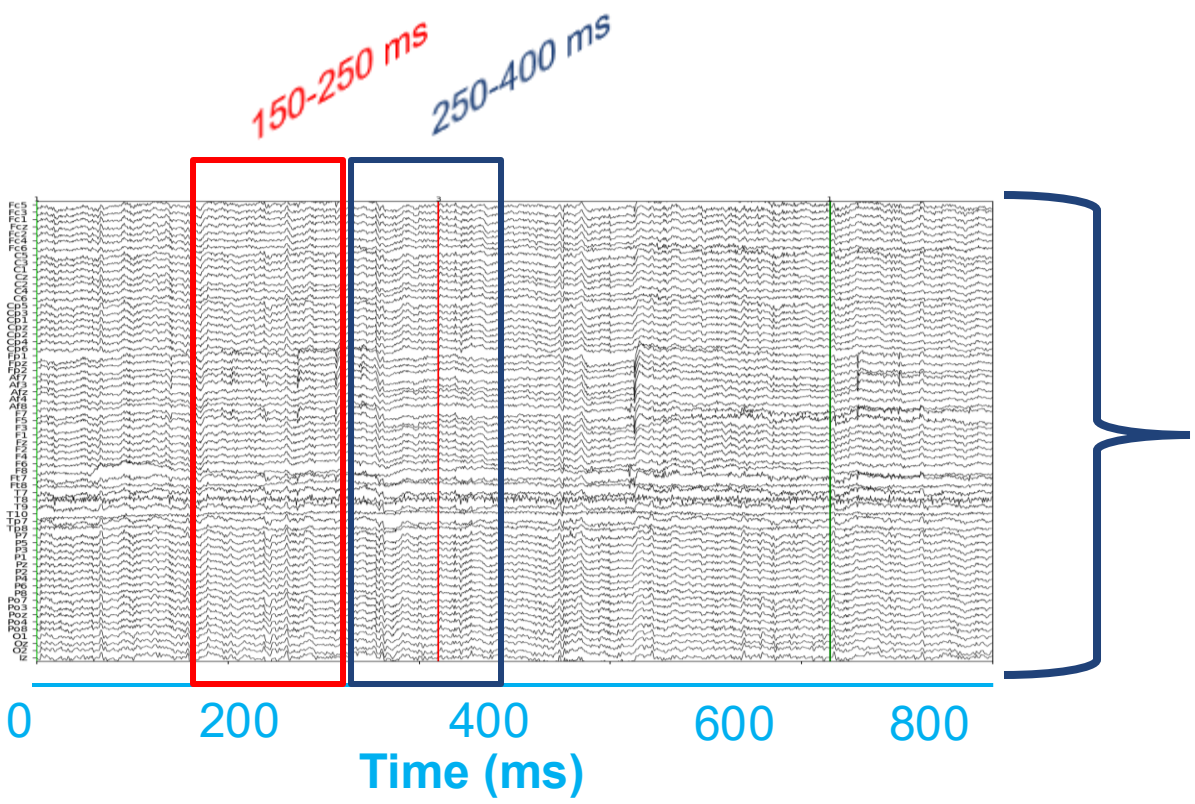
- **Articulation:** exaggerated articulatory movements
- **Voice:** high-pitched and a broader range of inflections and stress
- **Speech rate:** slow
- **Semantics:** small vocabulary set; more repetitions
- **Syntax/grammar:** short utterances with simple syntax, frequent pauses

Analyses

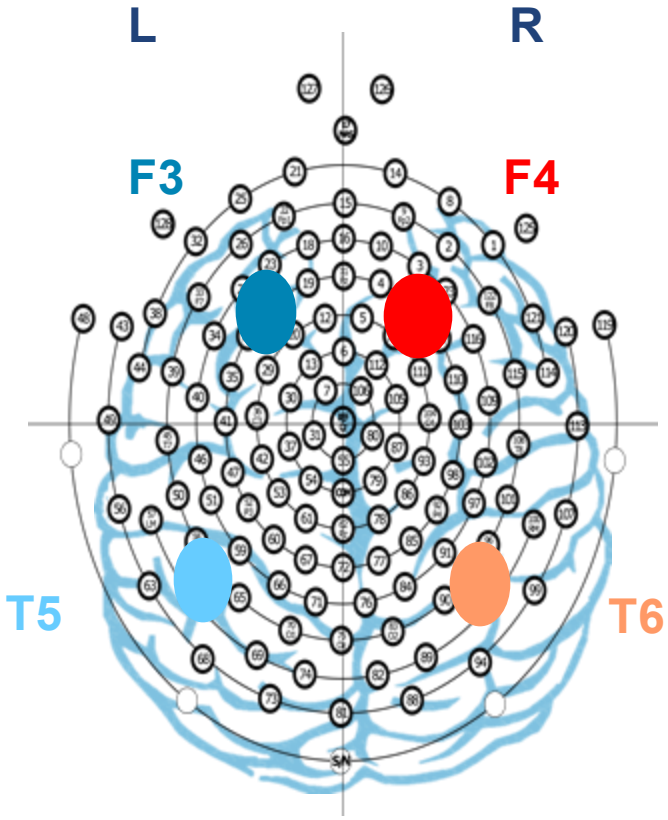
128 electrodes EEG cap



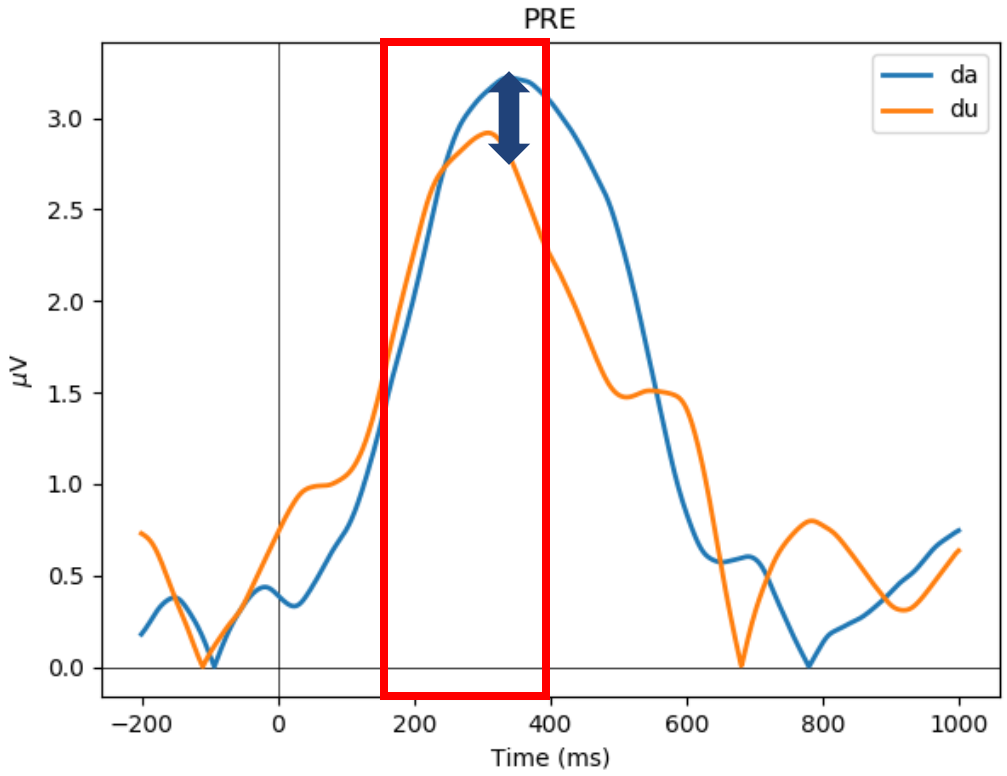
2 TIME-WINDOWS

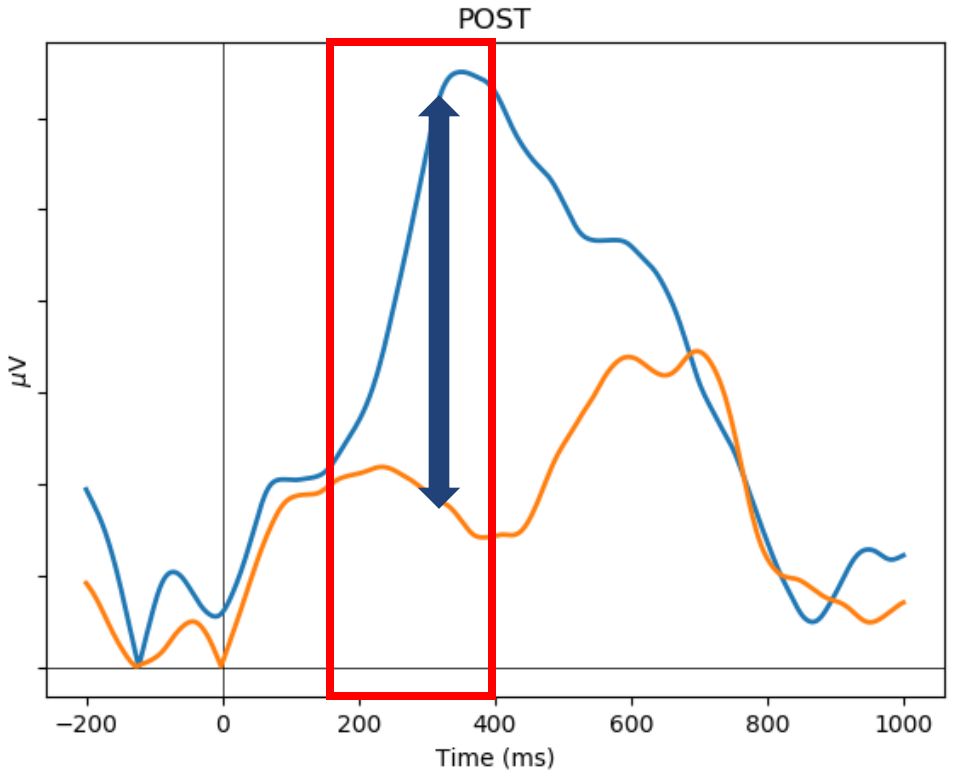


4 LOCATIONS



Mean Absolute Differences in Amplitude





Stimuli

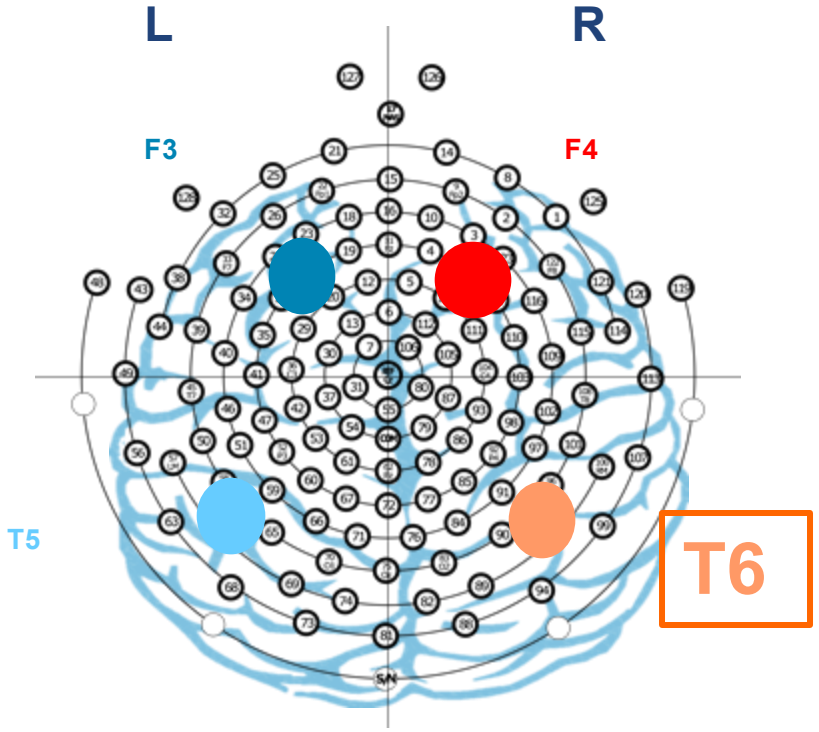
Contrasts:

		Vowels	Consonants
/ba/ /bu/ /da/ /du/ /ga/ /gu/		/a/–/u/	/b/–/g/, /d/–/g/, /b/–/d/
/ba/ /bi/ /pa/ /pi/ /ta/ /ti/	→	/a/–/i/	/b/–/p/, /t/–/p/, /b/–/t/
/ma/ /mi/ /pa/ /pi/ /ta/ /ti/		/a/–/i/	/m/–/p/, /t/–/p/, /m/–/t/

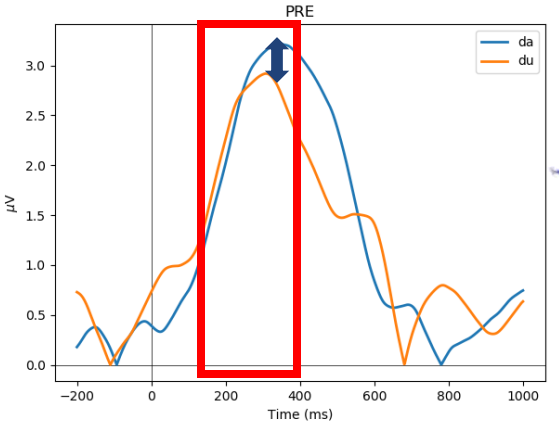
Effect of French Active Learning on French Contrasts

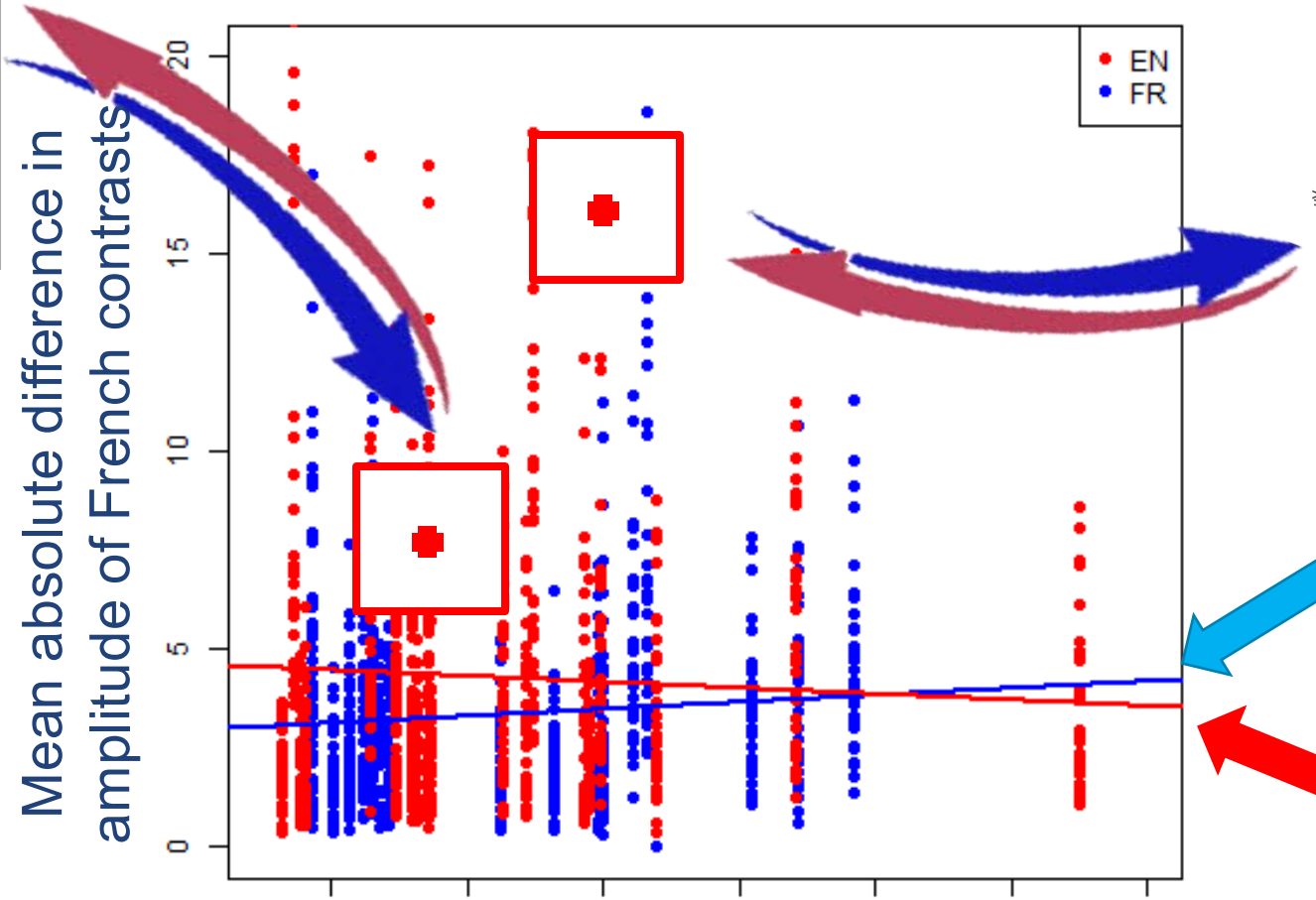
- Better perception of French contrasts in comparison with the English enrichment group

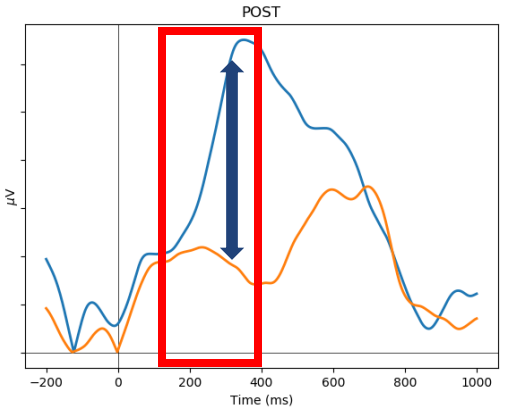
Area	Time-window (ms)	F	*p*
T6	150-250	2.75	*0.007*
T6	250-400	2.8	*0.006*



Effect of French Active Learning on French Contrasts







F= 5.424
p=0.02

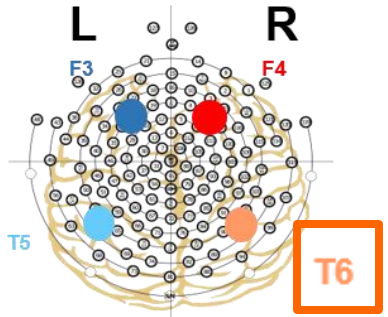
Specific Effect of French active learning on French Contrasts Differentiation

➢ **Vowels: /a/-/i/**

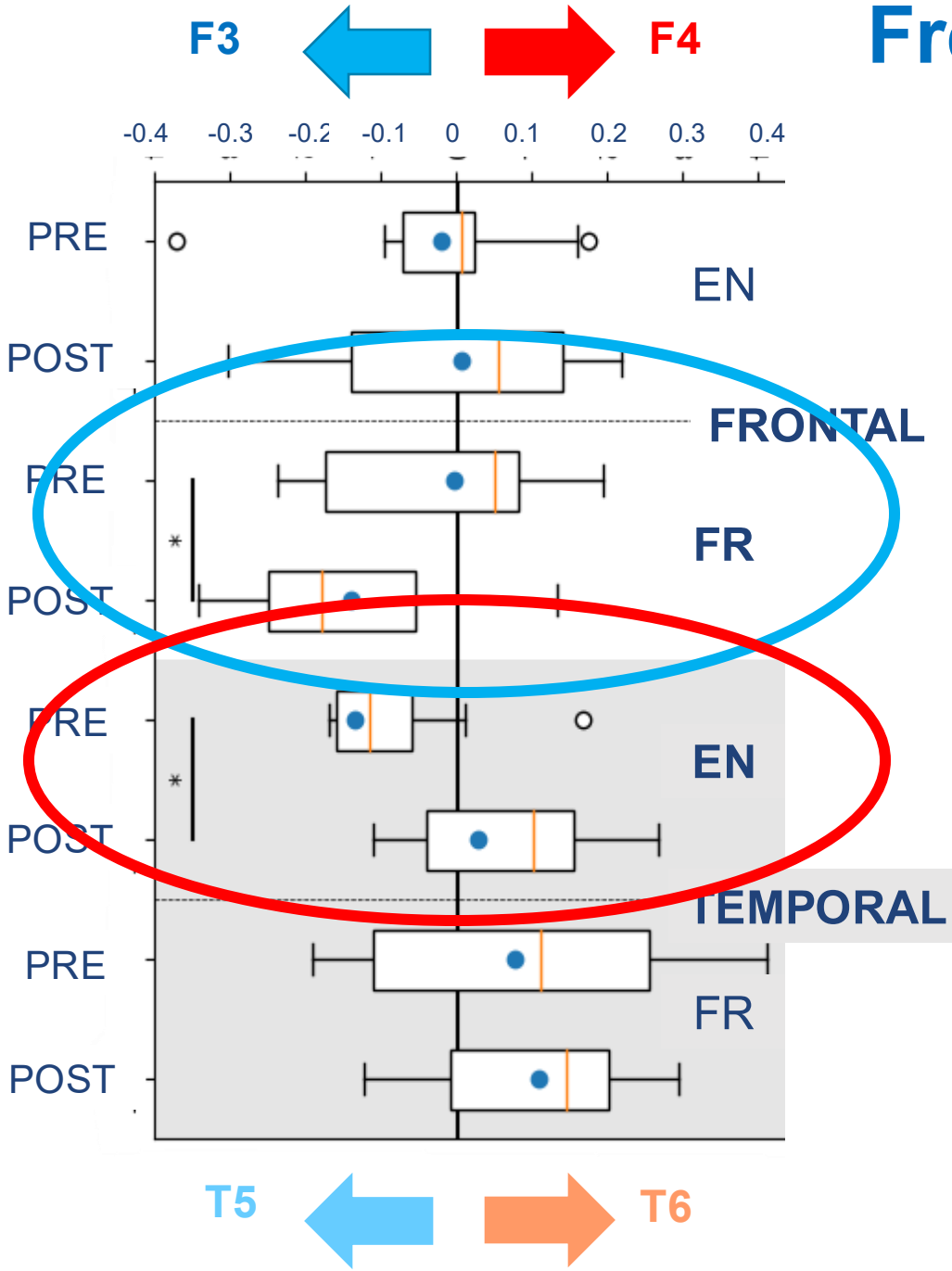
Area	Contrast	Time-window (ms)	F	*p*
T6	**/pa/-/pi/**	150-250	2.81	*0.005*
T6	**/pa/-/pi/**	250-400	2.8	*0.006*

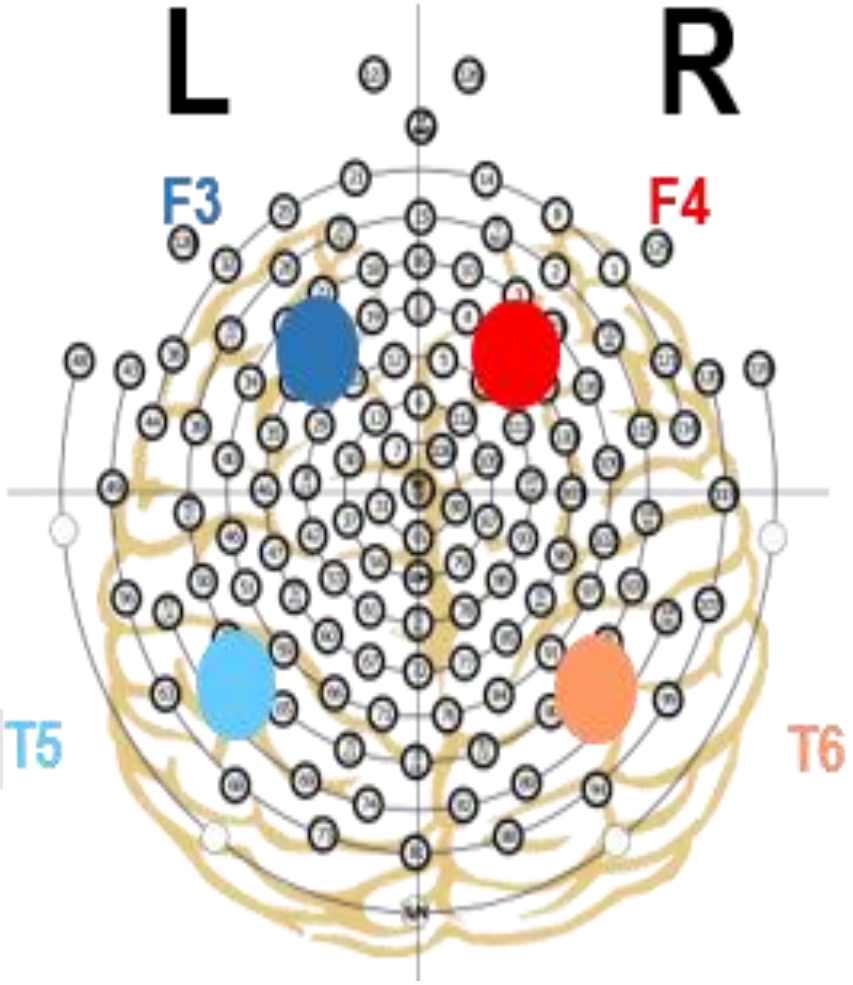
➢ **Consonants: /t/-/p/**

Area	Contrast	Time-window (ms)	F	*p*
T6	**/ta/-/pa/**	250-400	2.1	*0.037*
T6	**/ti/-/pi/**	250-400	2.2	*0.032*



French Speech Sounds Differentiation



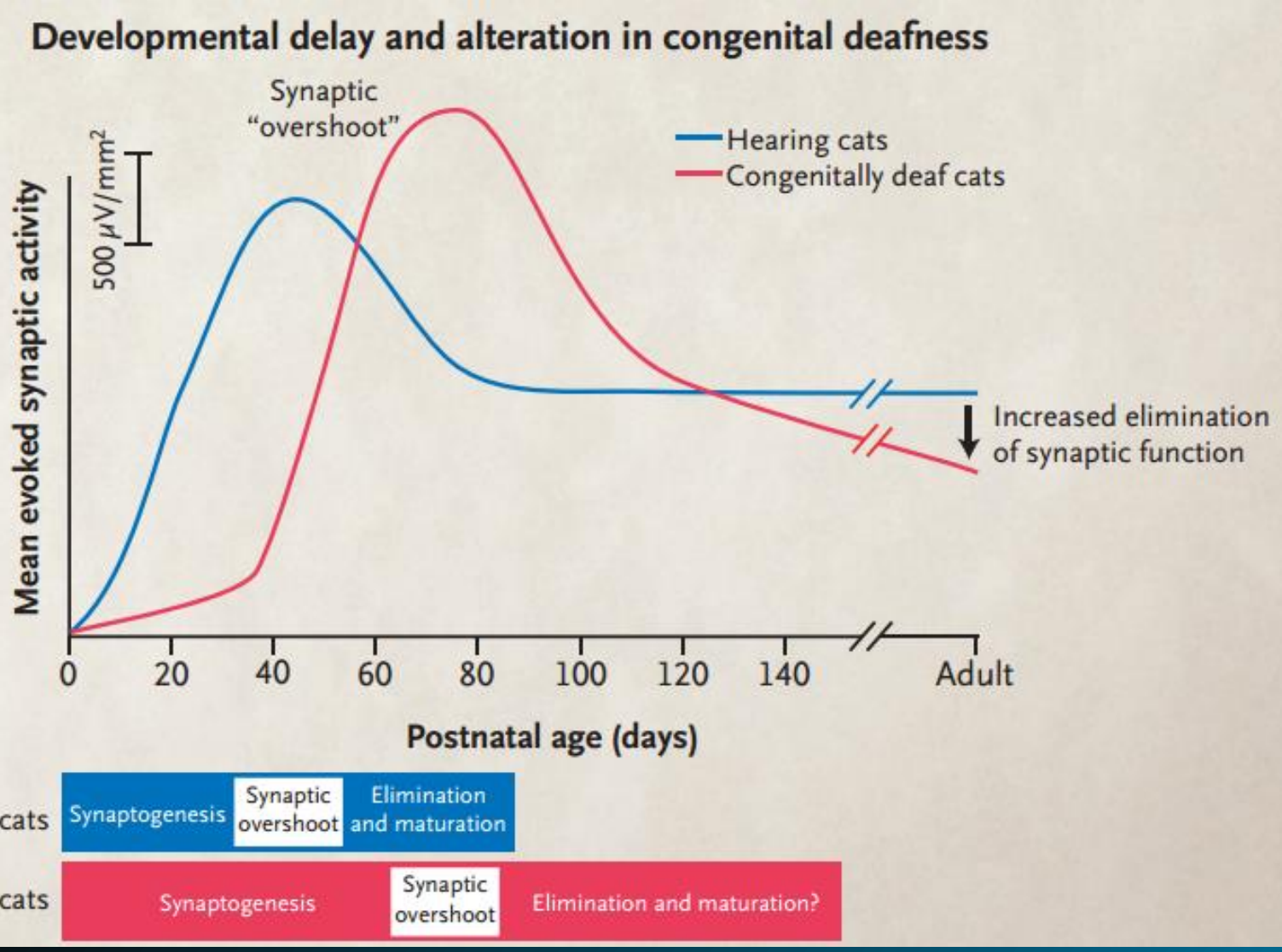


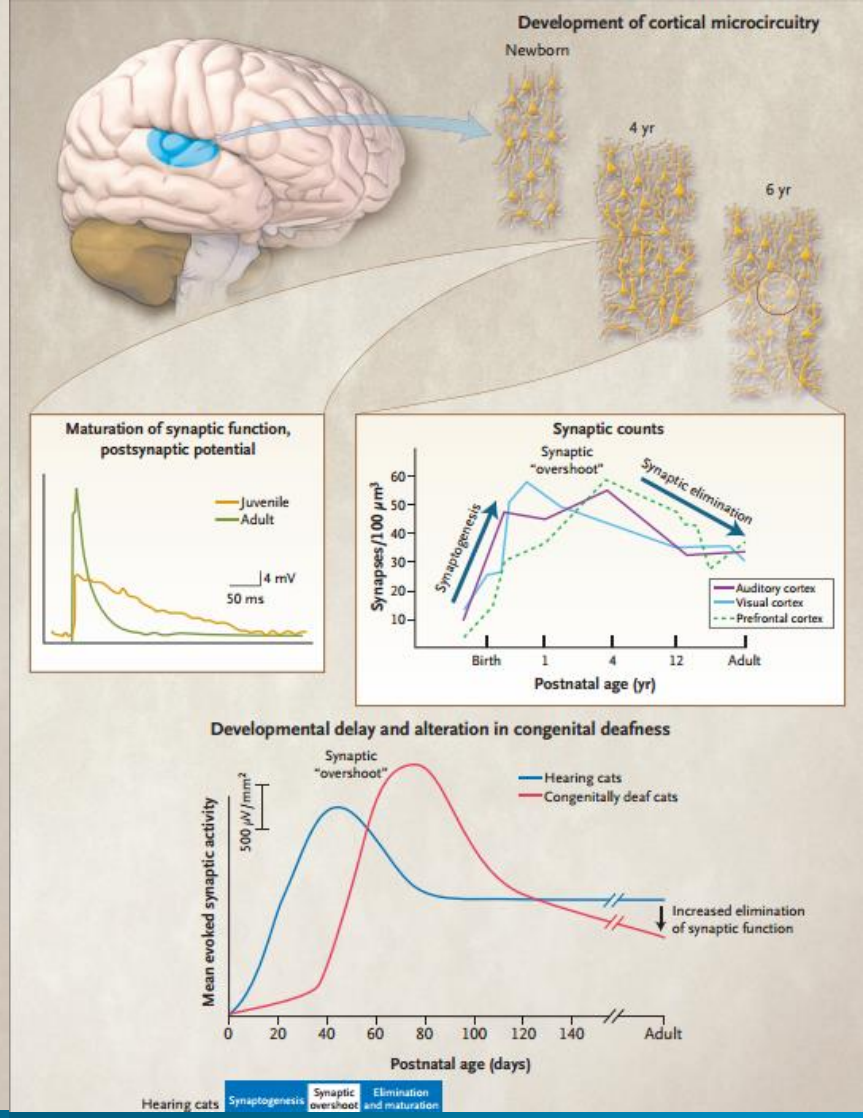
French active learning: *effect seen in frontal area: left lateralization*

Non-exposure to French: *effect seen in temporal area: right lateralization*

	Pre-linguistic phase				Early linguistic phase		
	0–2 months	2–4 months	4–6 months	6–9 months	1 yr	1.5 years	2 yr
Perception and comprehension	Phonetic discrimination across all linguistic contexts			Initiate specialization in native language consonant perception	Vocabulary ±70 words	Vocabulary ± 300 words	
Speech development	Phonation stage	Goo stage=primitive articulation stage	Expansion stage	Canonical or reduplicated babbling stage	Holophrase	Telegraphese	
Typically developping infants	Infants can imitate caregivers' vocalizations	Production of rudimentary syllable-like sequences featuring velar consonant-like and vowel-like elements	Infant introduce various sound types	Infants establish links between auditory and somatosensory representations of vocalizations and corresponding articulator movements	Adjustment of somatosensory maps to tactile and proprioceptive feedback during sound production in the native language		
Infants with CP	Often limited infant-directed speech, oromotor movements are frequently restricted	Progression through distinct phases varies depending on the extent of impairment in the motor, somatosensory, and auditory systems, as well as the impact of early interventions.					

F of life. Findlen &Richard. Pediatr Research.2024 Jul 13.





A critical period

Kral A, O'Donoghue GM.
Profound deafness in childhood. *Engl J Med. 2010 Oct 7;363(15):1438-50.*

Why Integrate Electrophysiology Early?

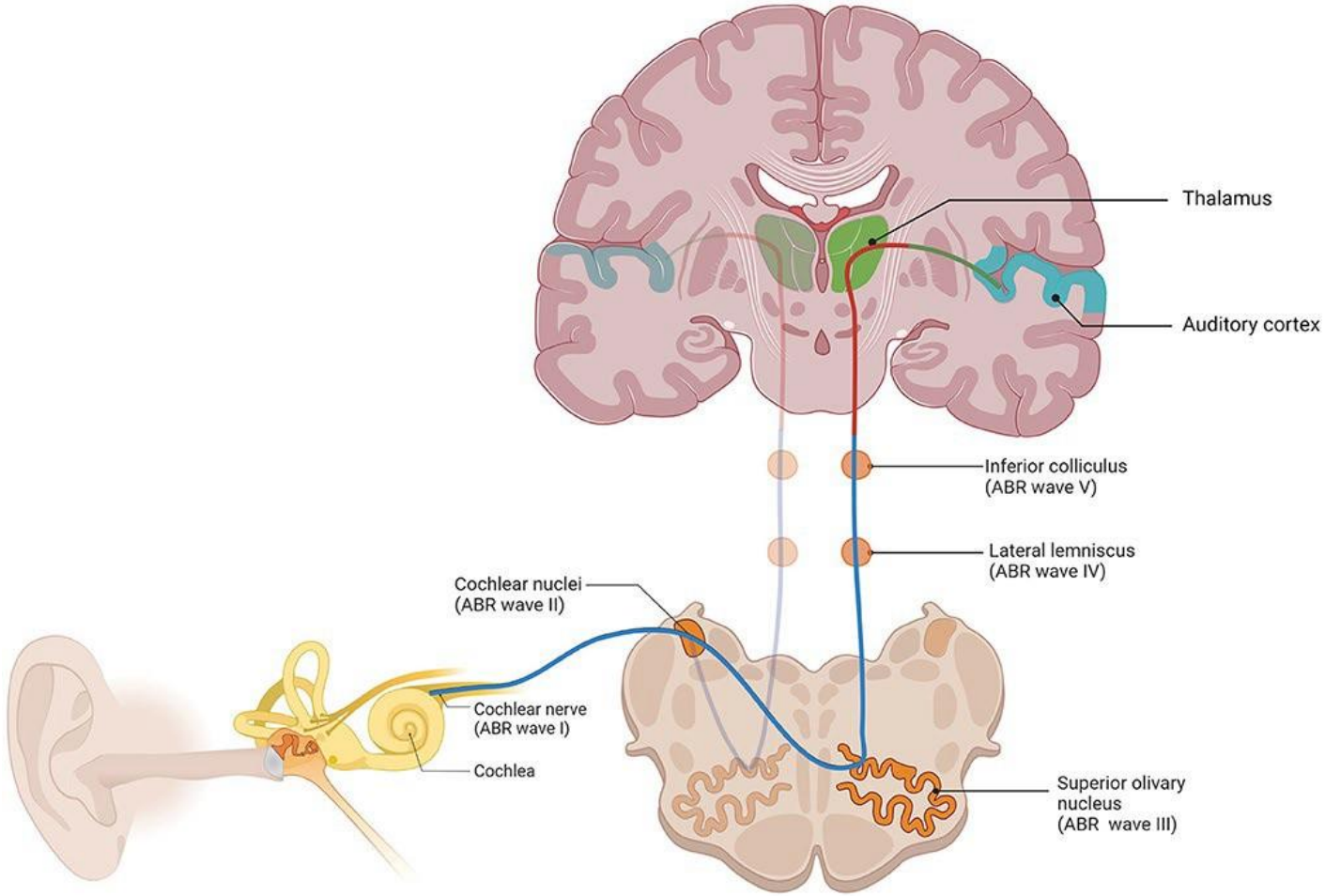
- Objective measures (OAE, ABR, cortical AEPs) enable diagnosis in non-behavioral infants, opening the door to treatment within the critical window.
- Early Hearing Detection and Intervention (EHDI) frameworks and treatment-focused medical workups are explicitly designed around neural plasticity in the first 2 years of life.
- Electrophysiology supports risk-stratified care (e.g., NICU graduates, congenital infections, suspected central disorders) and feeds into timing and candidacy decisions for hearing aids, cochlear implants, and more complex cases such as cochlear nerve deficiency

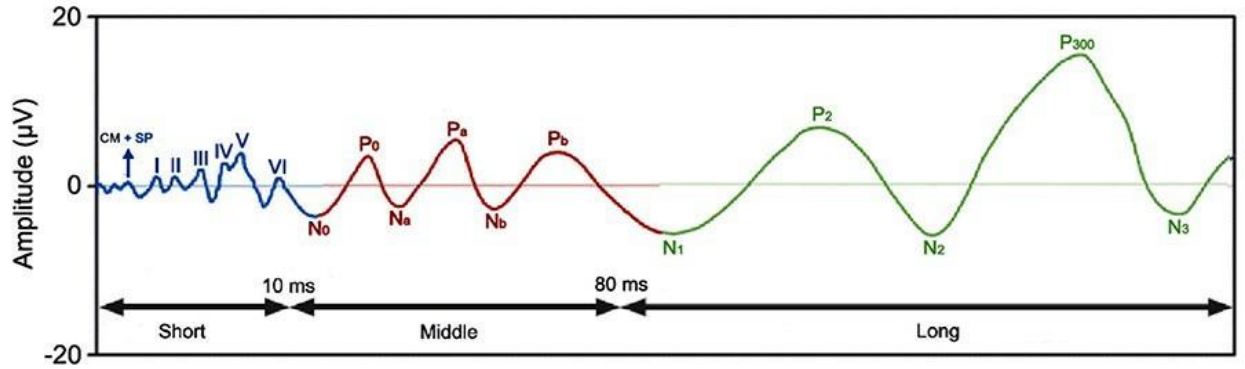
Fundamentals of Pediatric Electrophysiology

Measuring the Developing Brain: Electrophysiological Markers in Infancy and Childhood

- Overview of auditory evoked potentials (ABR, MLR, CAEP, MMN)
- Age-related changes in electrophysiological responses
- Normative data and interpretation challenges in young populations

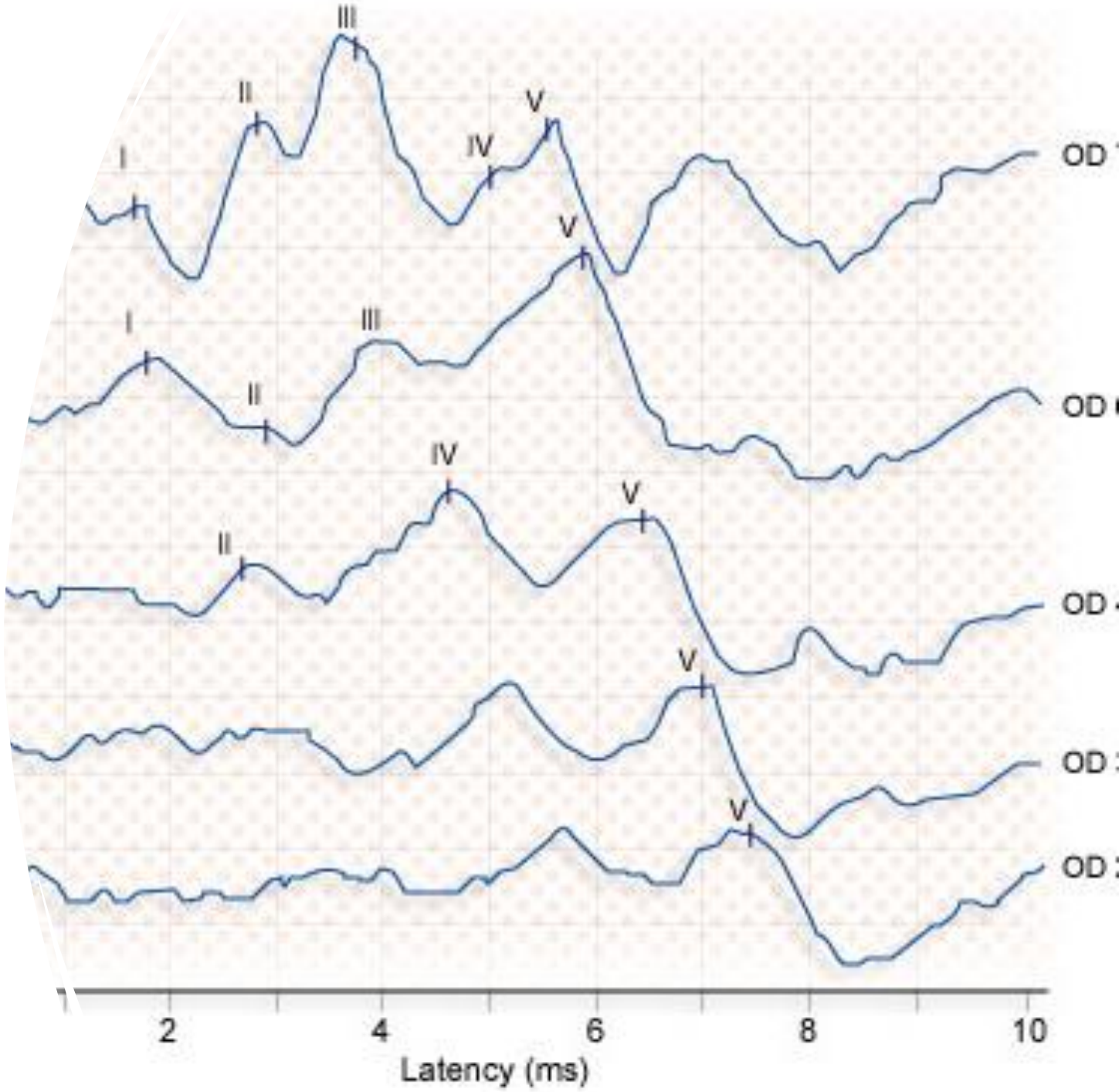
Overview of Auditory Evoked Potentials (ABR, MLR, CAEP, MMN)



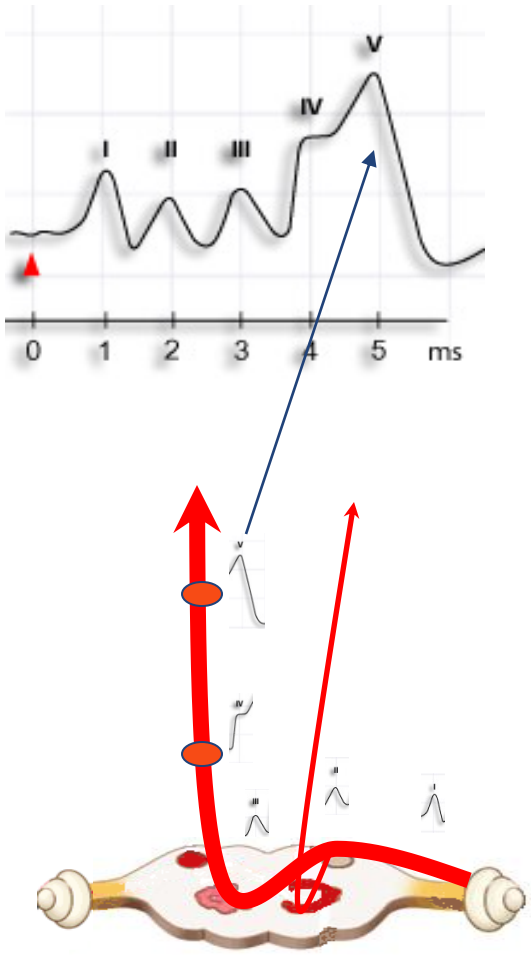


Early Components: ABR

- Auditory Brainstem Response (ABR)
  - Click stimuli/TB/Chirp
  - Occurs within 12.5 – 15 msec post stimulus time
  - Very stable, reliable, and repeatable



Auditory Brainstem Responses: Development



ABR wave latencies are not mature at birth.

Increase of nervous fiber synchronization, myelinization and synaptic efficiency will induce a decrease in latency of ABR waves with age. Degree of brainstem myelination at 1 year approximates that of the adult state.

An adult latency is obtained at 5 weeks after birth for wave I.

The II-III interval does not reach an adult level until between 1 and 2 years of age.

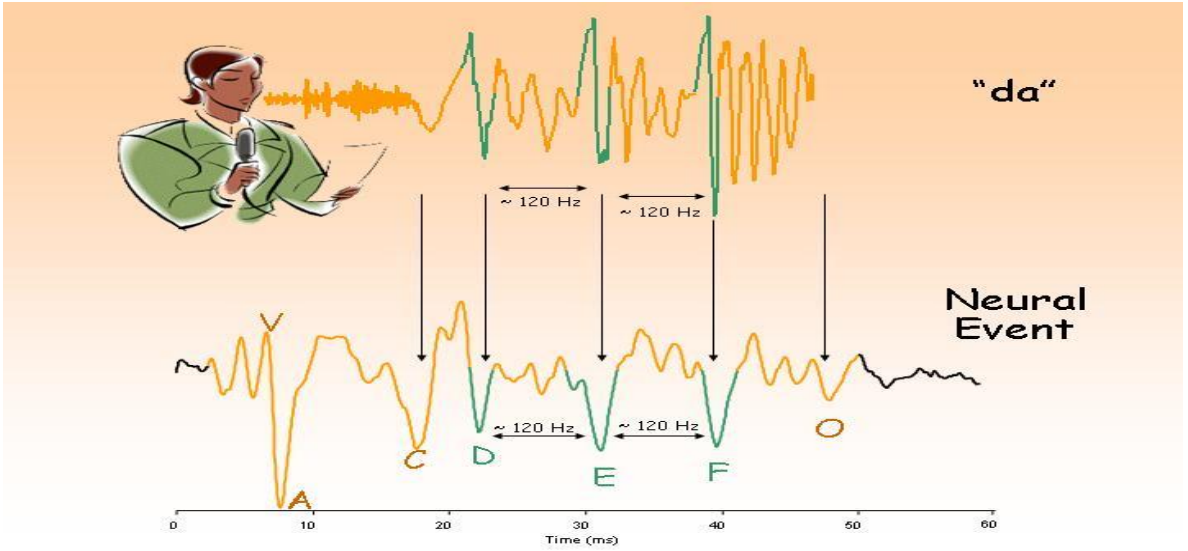
An adult latency for wave V is observed around 3 to 5 years of age.

ABR thresholds at birth are elevated by to 10-25 dB relative to adult thresholds.

They become adult-like around 12 months of age.

Speech ABR

- Speech elicited auditory brainstem responses have been shown to be an objective measurement of speech processing in the brainstem.



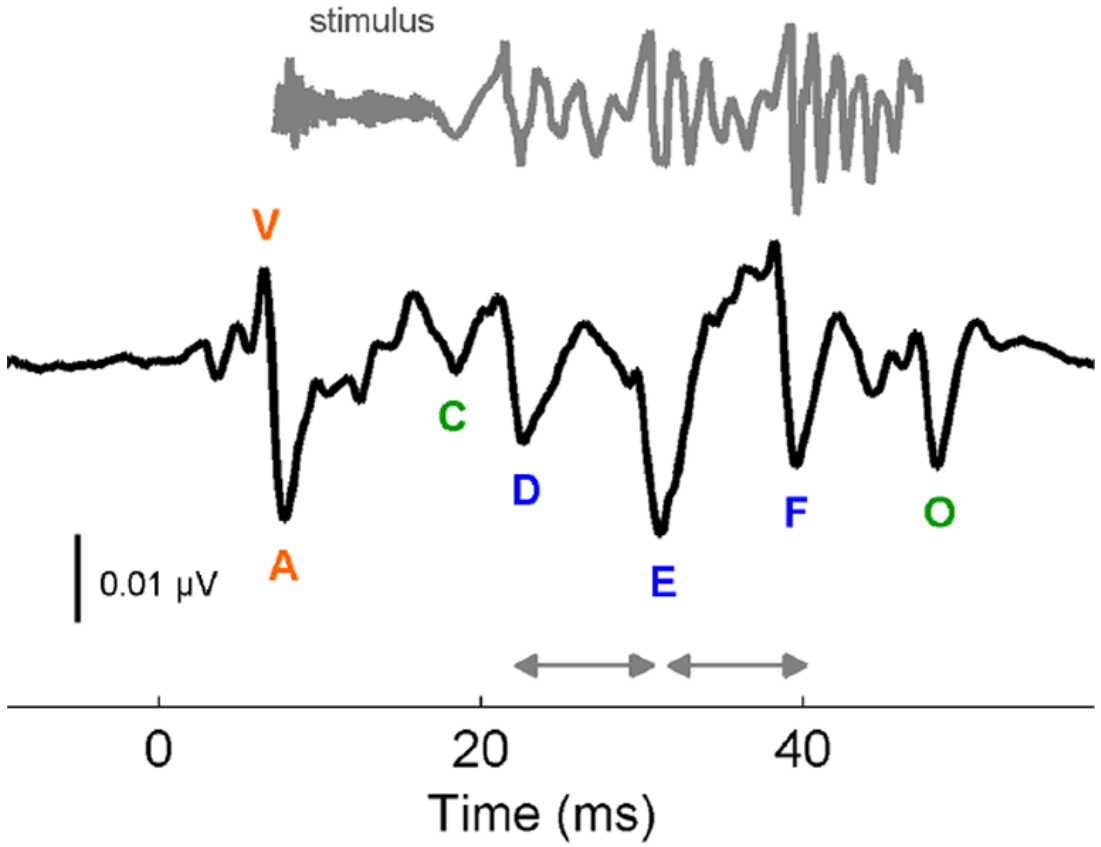
Biomark. Kraus et al.

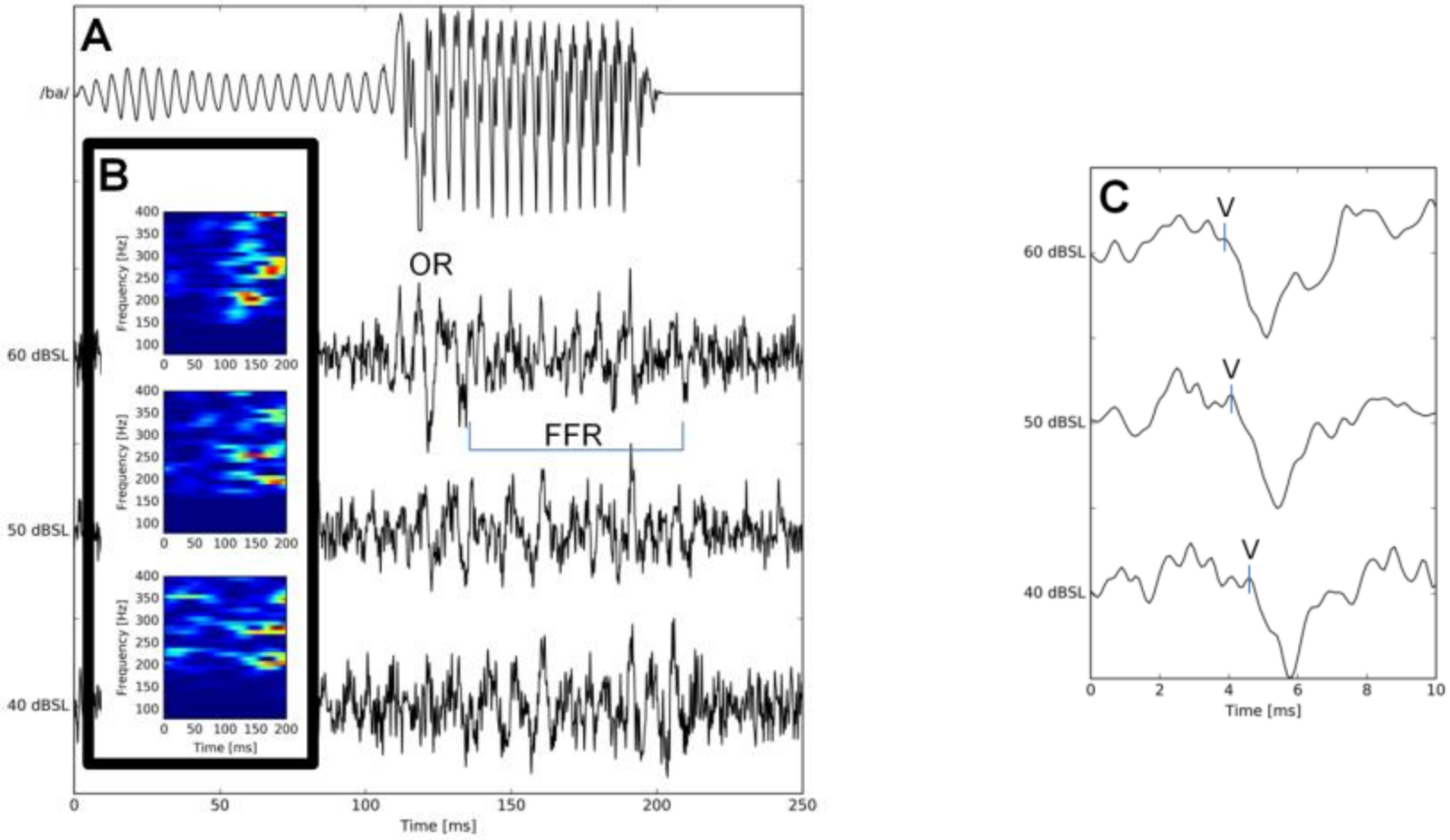
Click ABR	Speech ABR
Uses brief clicks or tone bursts	Uses **speech sounds** (most often */da/*)
Assesses neural synchrony & threshold estimation	Assesses **speech encoding fidelity**
Widely used clinically	Primarily **diagnostic + research**
Short stimulus	Longer, acoustically complex stimulus

Speech ABR

Speech-ABR reflects how well the brainstem:

- Encodes timing (temporal precision)
- Represents fundamental frequency (F_0)
- Tracks harmonics and formants
- Preserves phase locking to speech
- A key component is the Frequency Following Response (FFR), where neural activity mirrors the periodic structure of the speech stimulus.
- Speech-ABR bridges hearing and language, showing not just whether sound reaches the brainstem, but how faithfully speech is encoded at this early neural level.

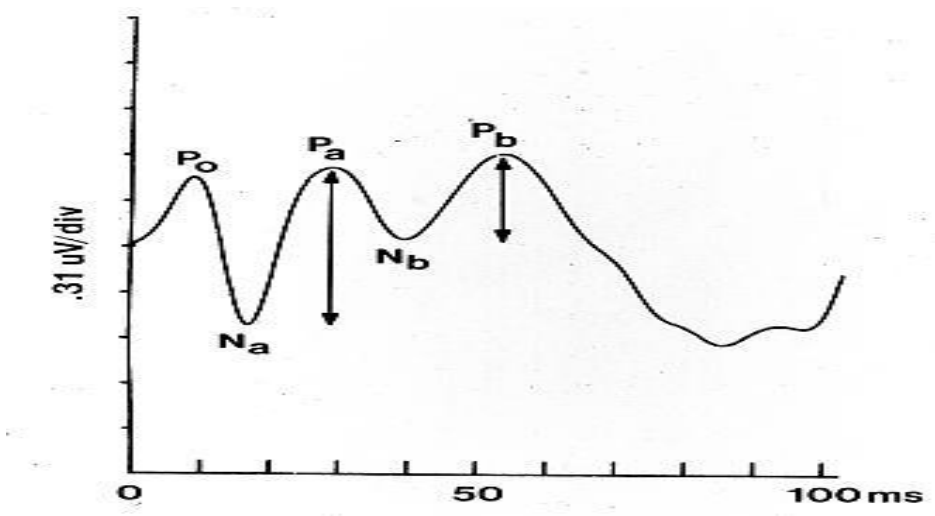




Single subject onset response (OR) and Frequency Following Response (FFR) components, in response to the /ba/ stimulus (upper row), were clearly identified on temporal representation from 40 to 60 dBSL (A). Corresponding spectrograms (B) show elicited activity in the F0 bandwidth. Click responses of the same subject at the 3 corresponding intensities are shown in C. Knebel at al. 2018

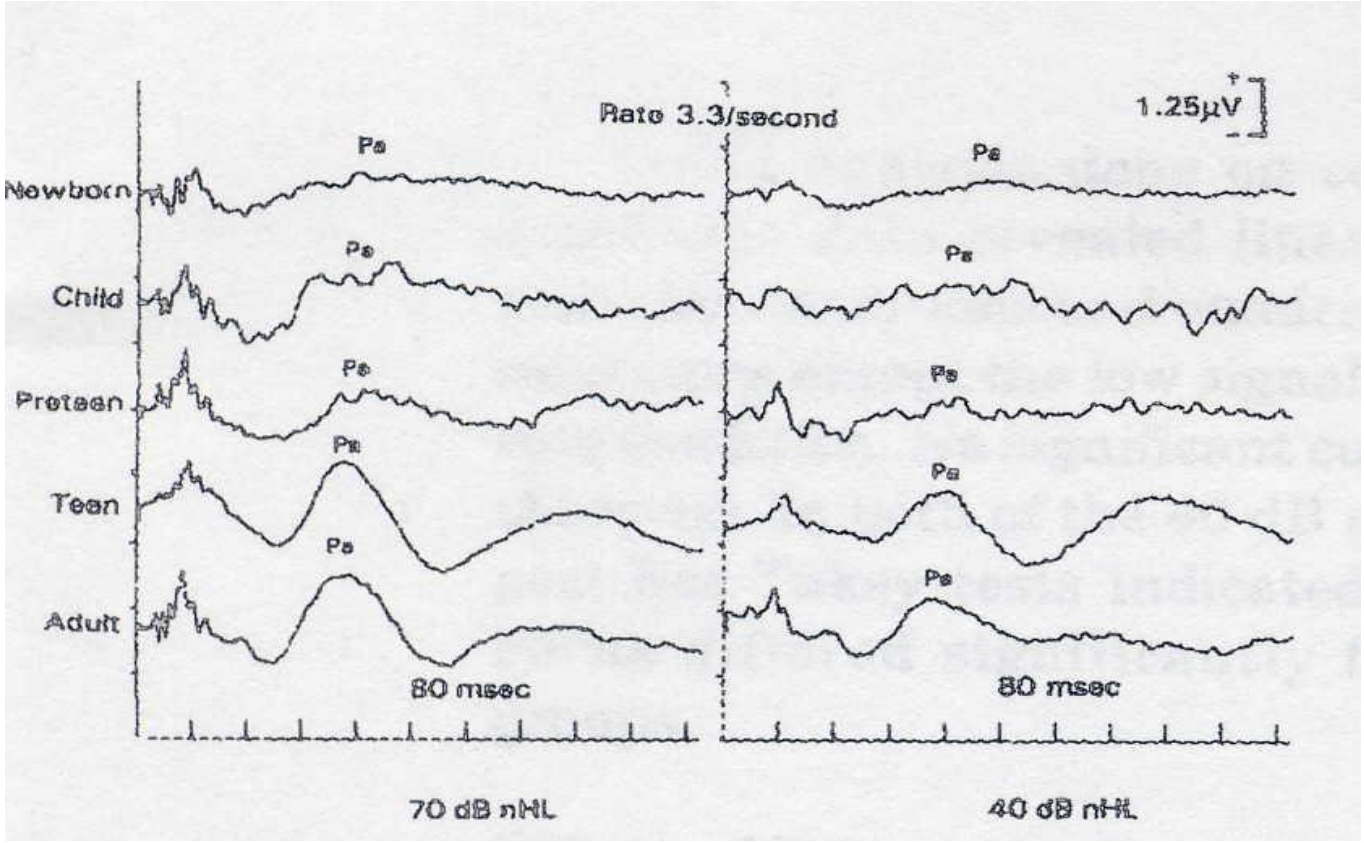
Auditory Middle Latency Response (MLR)

- Activity occurring between 8 and 80 msec post-stimulus onset.
- Mainly generated by the auditory cortex, with some possible contribution of the upper brainstem and thalamus (still some disagreement as to specific sites exists which limits somehow the clinical interpretation).
- These MLR generators are rostral to the ABR generator sites; this allows the MLR to provide insight as to function in an additional region of the higher auditory system.
- A consistently absent MLR combined with a normal or near normal ABR, good hearing sensitivity, and a suggestive history can be a strong indicator of central auditory involvement
- Potential value of the MLR from the diagnostic perspective across lesion types, especially for lesions affecting the cortical and subcortical areas rostral to the brain stem.
- In the MLR, the amplitude measures seem to be more sensitive than latency measures.
- The AMLR components are estimated to reflect different aspects of auditory processing such as activities involved in the primary (recognition, discrimination, and figure-ground) and non-primary (selective attention, auditory sequence, auditory novelty and audio-visual integration) listening skills.



Middle Latency Responses

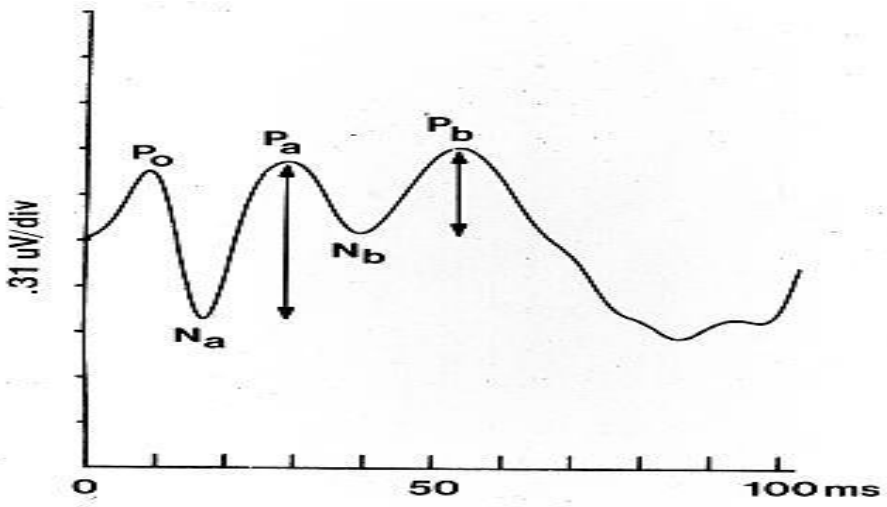
- As with ABRs, the MLR latencies decrease with age. Changes can be seen well into childhood, and adult characteristics are not reached until 10-12 years of age.



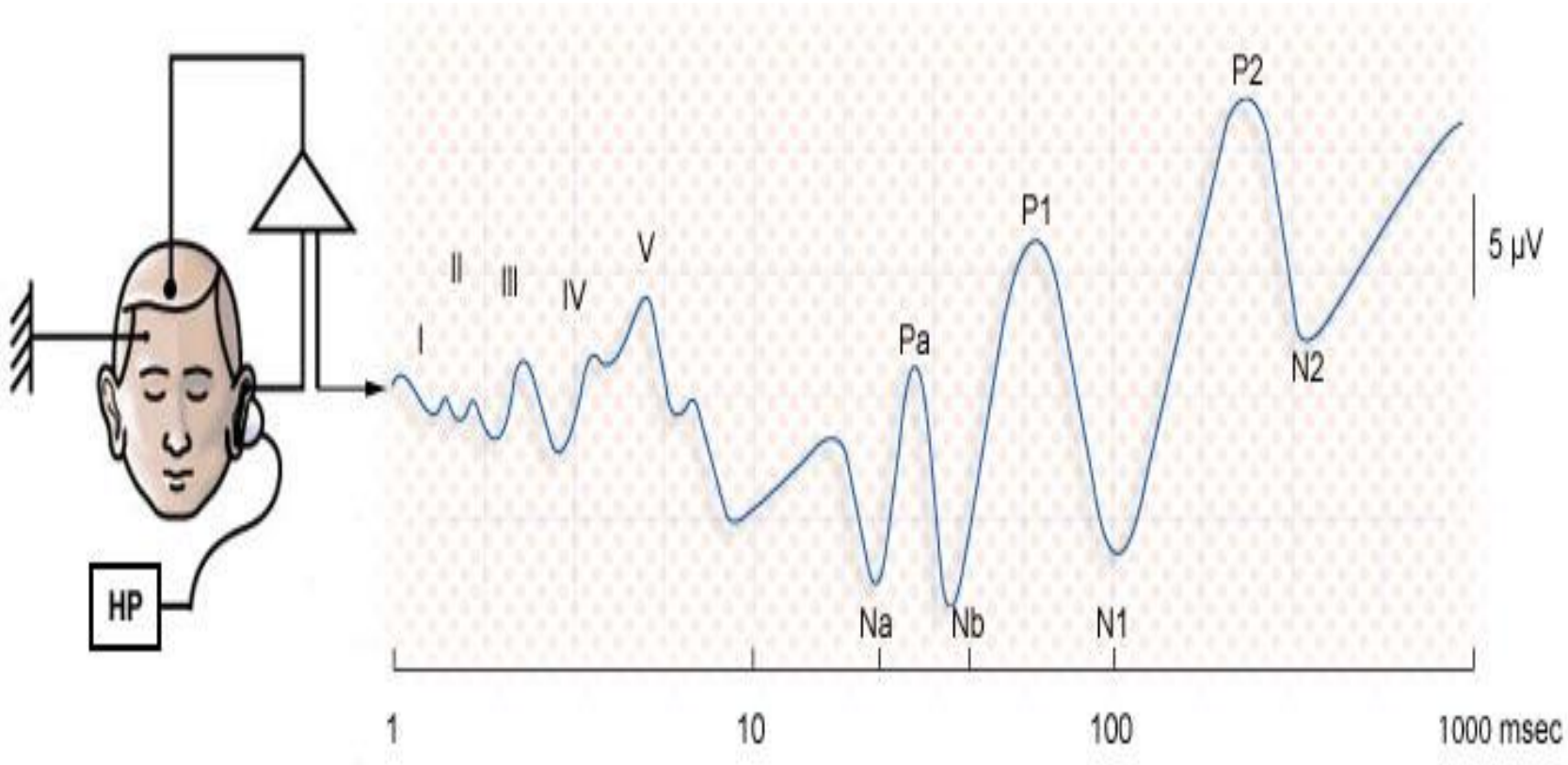
From Tucker and Ruth, 1996

Auditory Middle Latency Response (MLR)

- The AMLR is used to identify (central) auditory processing disorders and used to measure post-therapy improvements in central auditory function.
- Tinnitus
- Multiple sclerosis
- Strokes
- Traumatic brain injury
- The AMLR should be considered as part of a differential diagnosis test battery in specific patient populations as long as the test limitations are understood.



Late Auditory Evoked Potentials

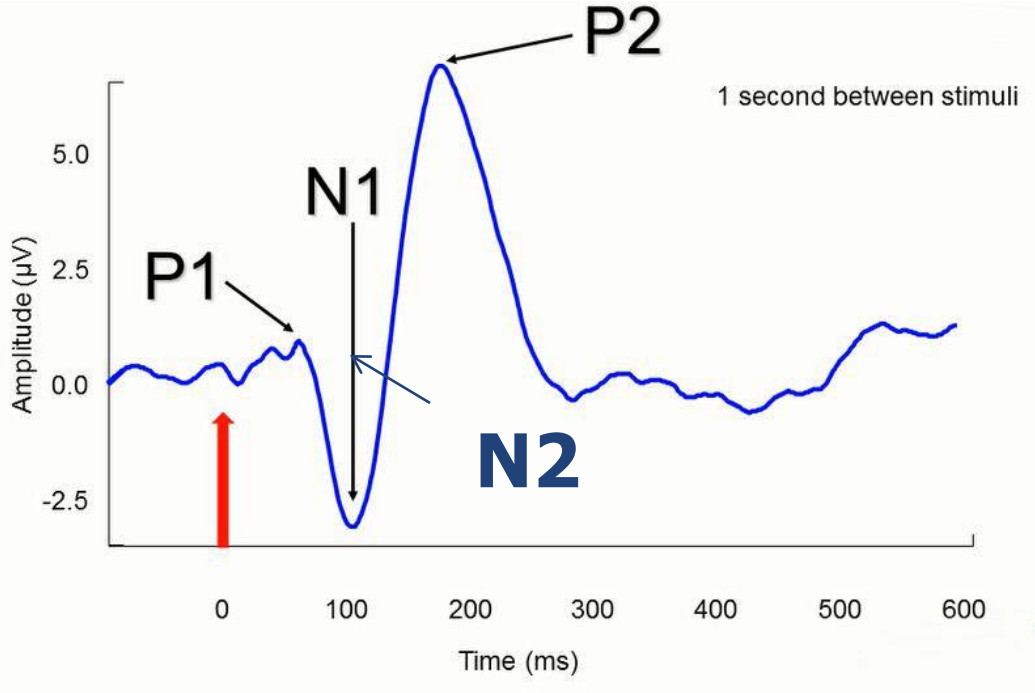


AEPs provide an objective means of evaluating how the auditory cortex codes acoustico-phonetic cues crucial to speech and language processing with high temporal precision, including in presence of background noise. AEPs also inform about hemispheric lateralization.

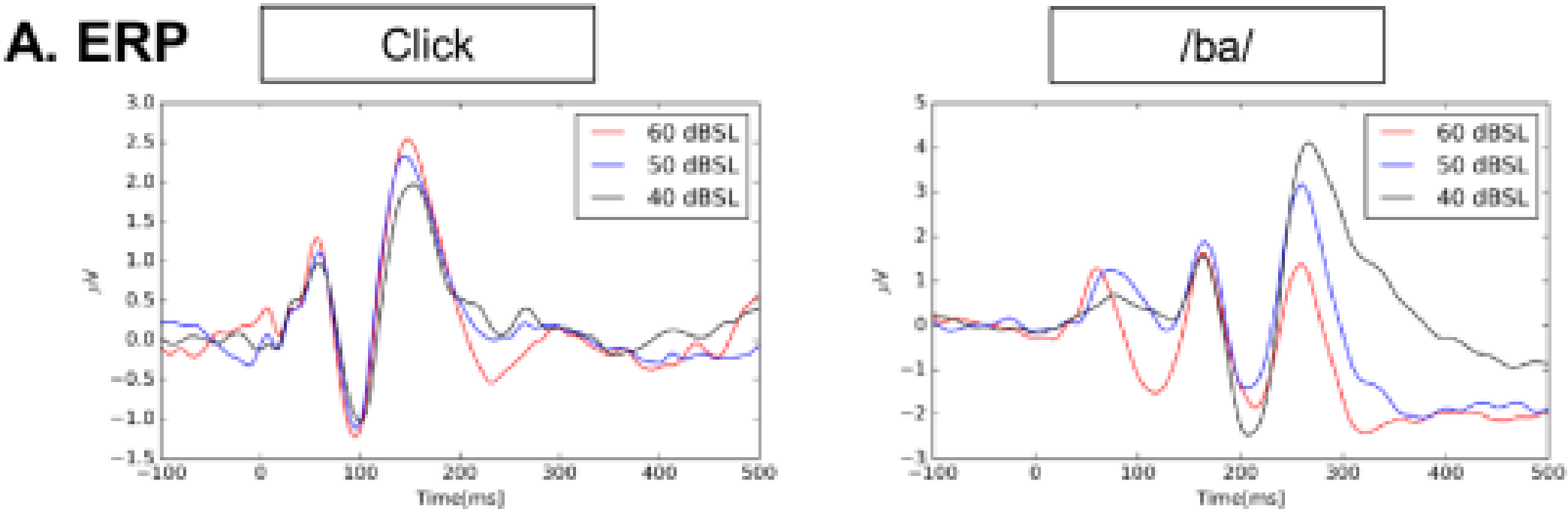
P1-N1-P2-N2 Complex

- The P1-N1-P2 complex provides information regarding the arrival of sound information to the auditory cortex.
- Obligatory response: no need to attend to the stimuli and no task to complete.
- Sensitive measure of hearing sensitivity with physiological thresholds falling within approximately 10 dB of behavioral thresholds in most cases.

- **Amplitudes are usually quite large: there is a signal to noise advantage with greater response detectability, particularly in noisy subjects (need less averages than ABRs).**



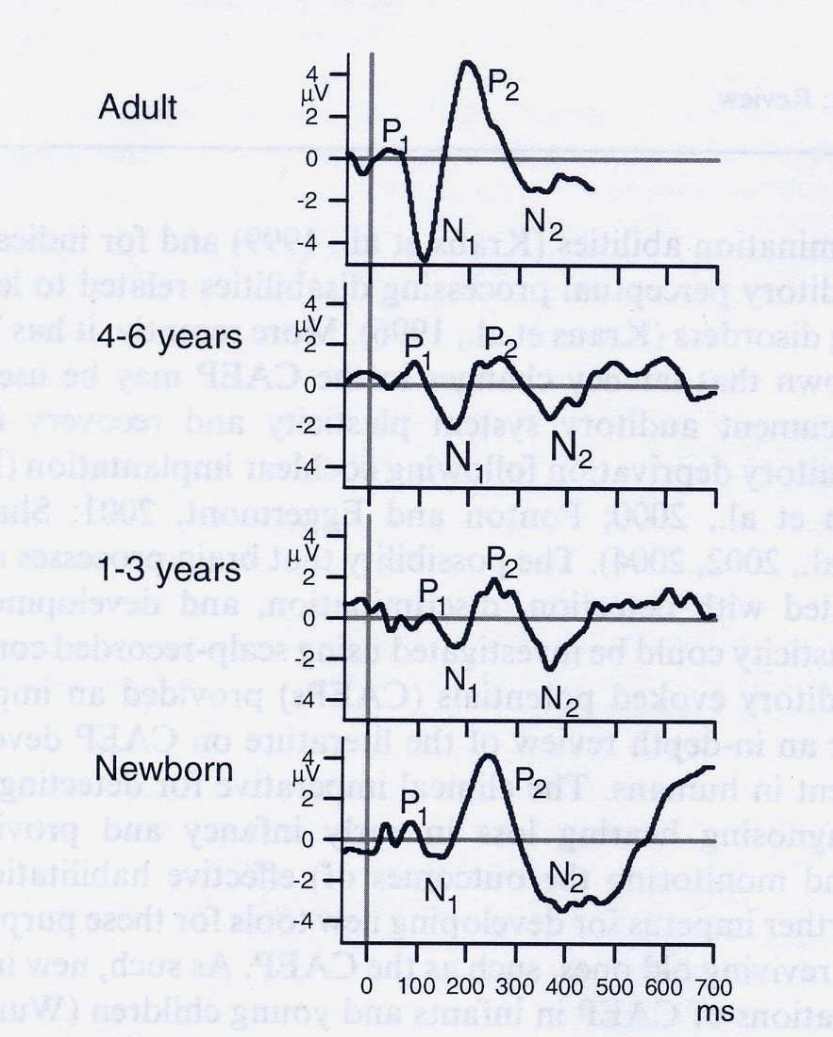
Adult cERPs



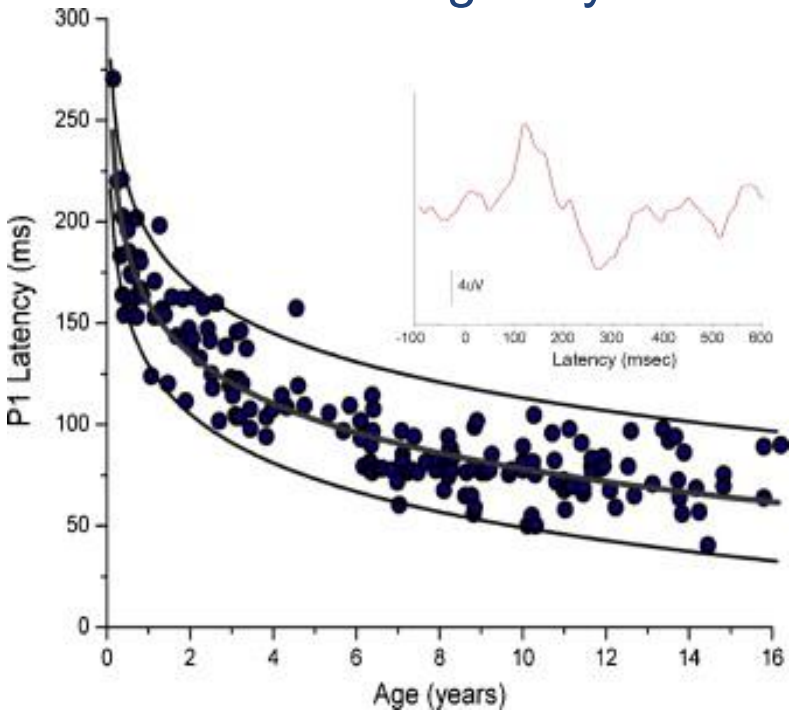
Knebel et al. 2018

Age and CAEP

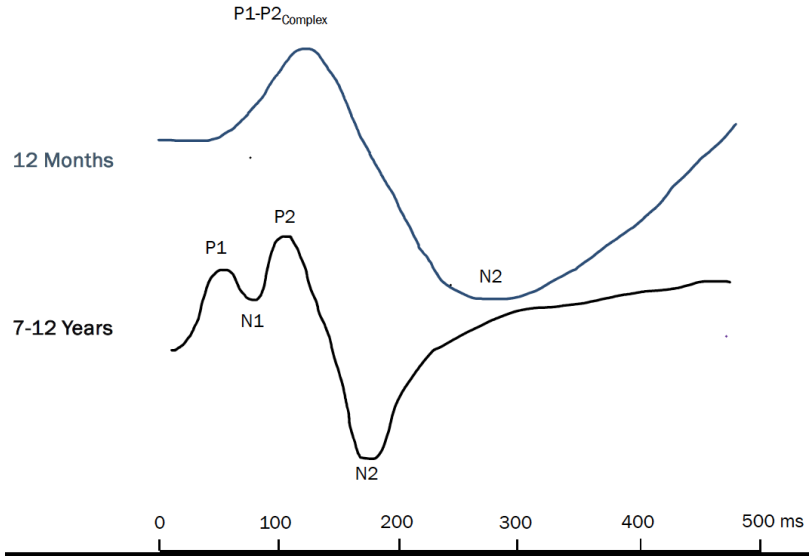
- Cortical potentials are present in premature babies.
- Components P1 and N2 decreased in amplitude, while component N1 and P2 increase in amplitude from birth to adulthood.
- The general waveform morphology reaches maturity around 12 years of age, although latencies and amplitudes of the various components continue to change beyond this age.



Wunderlich and Cone-Wesson,2006

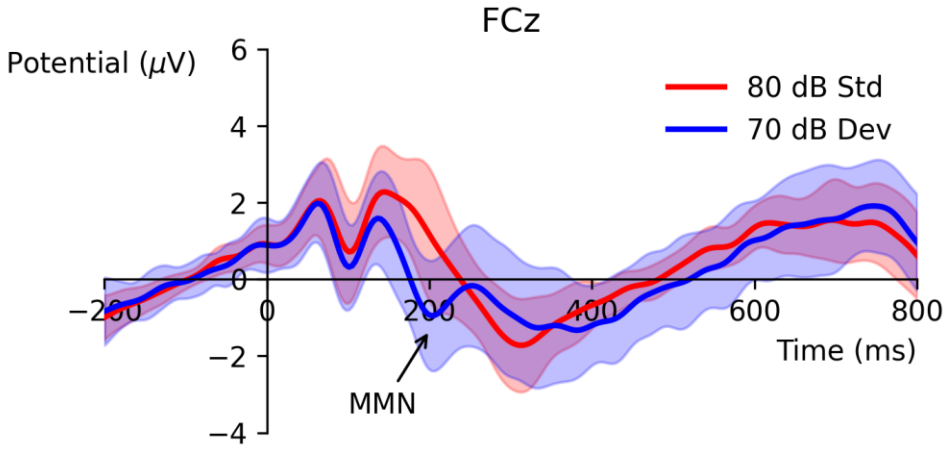


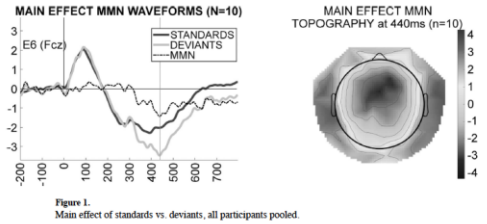
Dorman et al., 2007

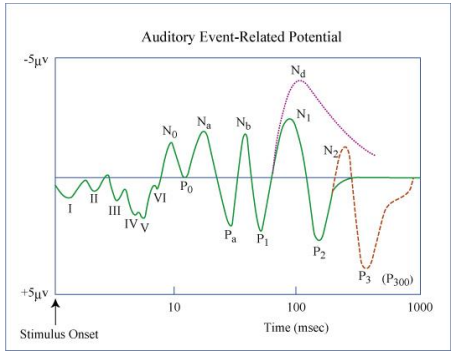


Event-Related Potentials

- Mismatch negativity and P300: occur when the brain makes a decision about whether one stimulus differs from another. Limited pediatric application.

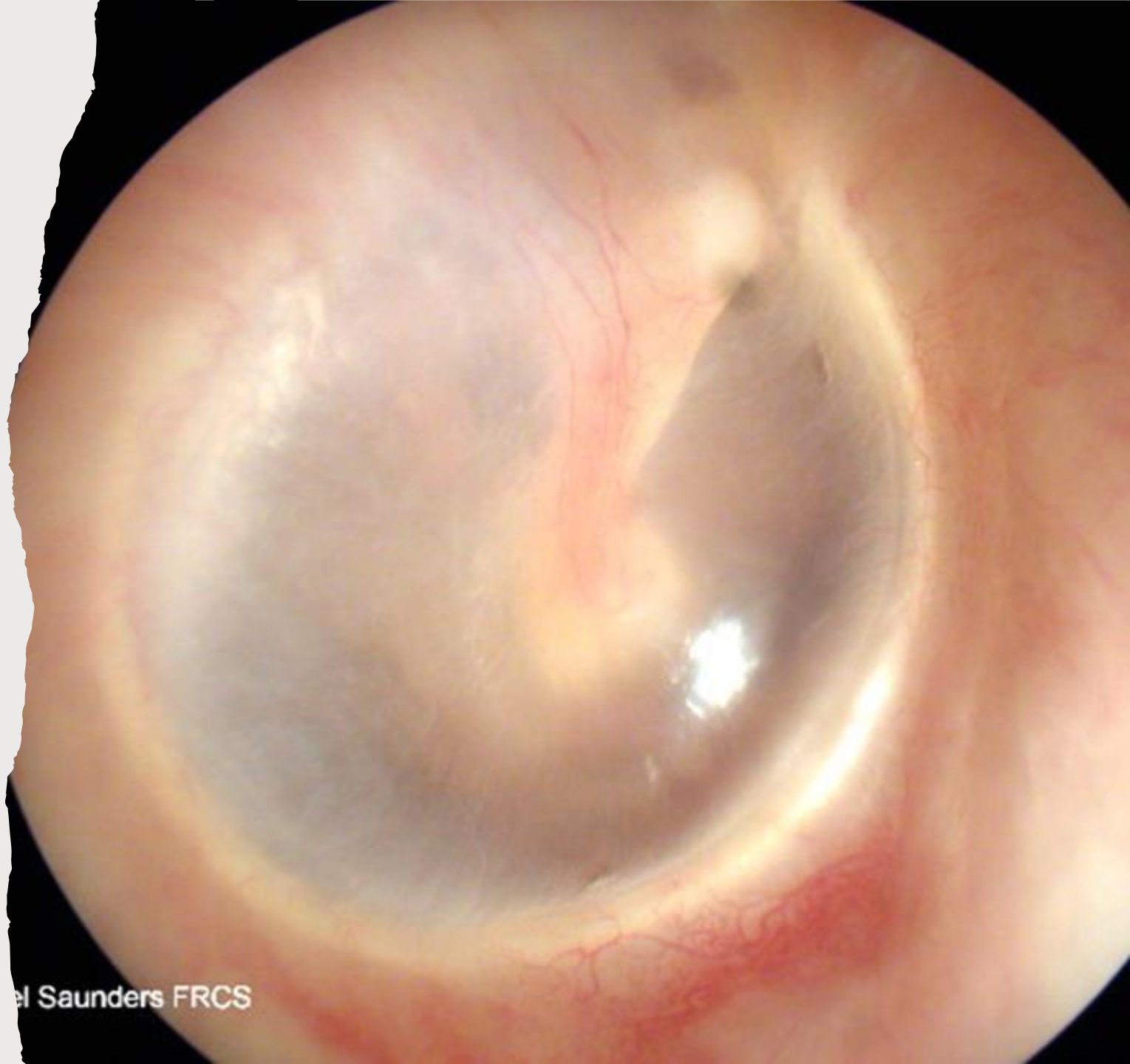


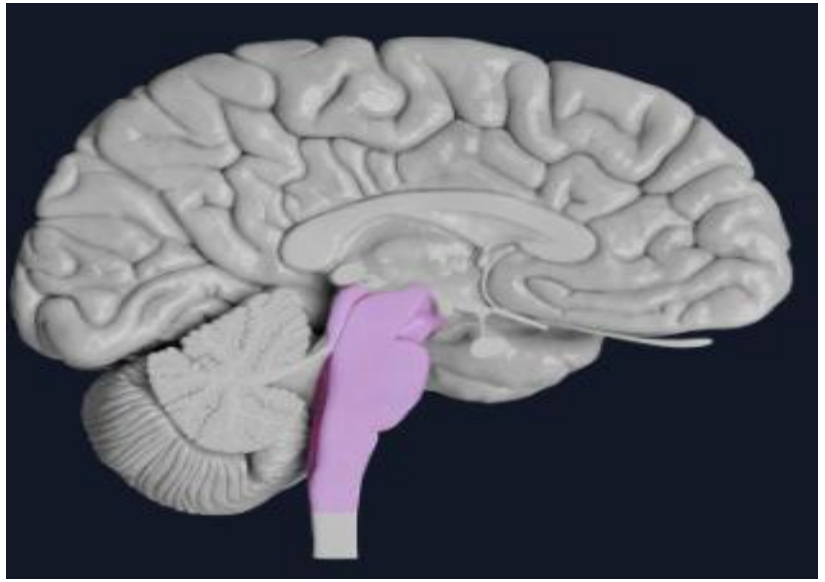




Clinical Spectrum of Hearing Disorders in Pediatrics

- From Peripheral to Central: Characterizing the Pediatric Hearing Profile
  - Conductive vs. sensorineural vs. central auditory processing disorders
  - Syndromic vs. non-syndromic etiologies
  - The intersection of hearing loss with neurodevelopmental disorders (e.g., ASD)


el Saunders FRCS



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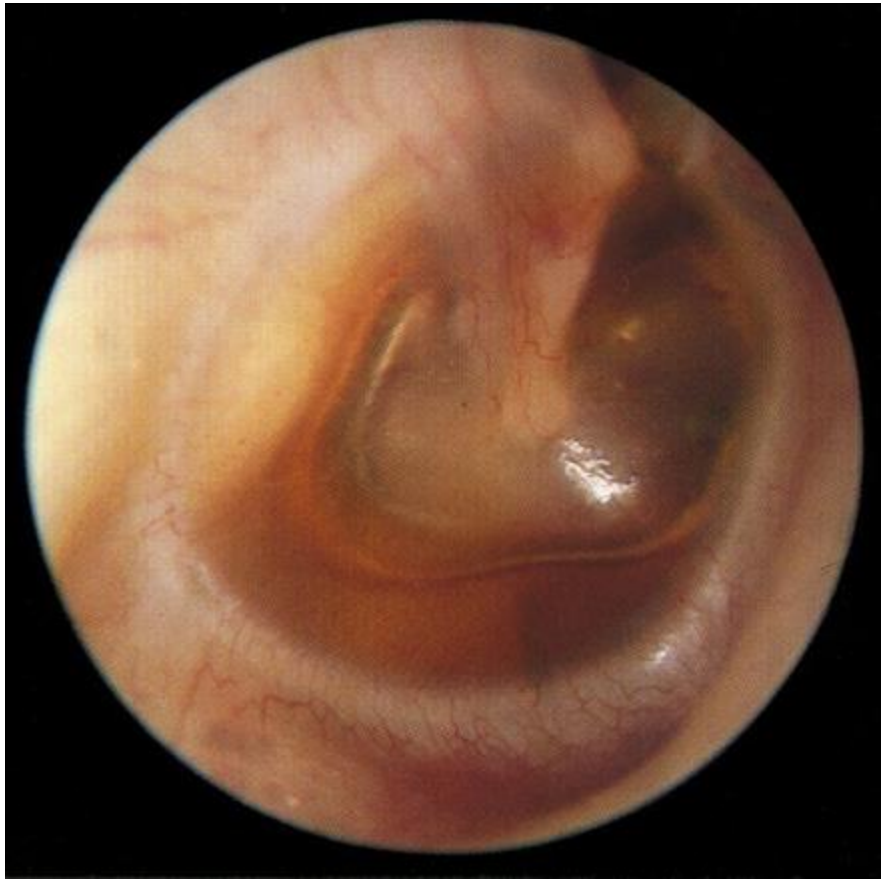
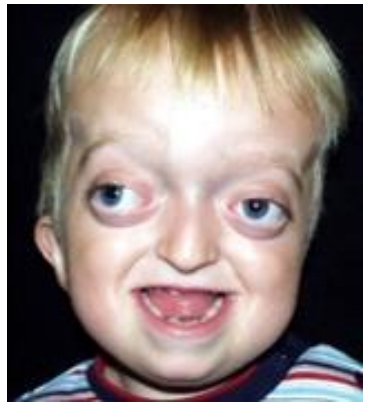
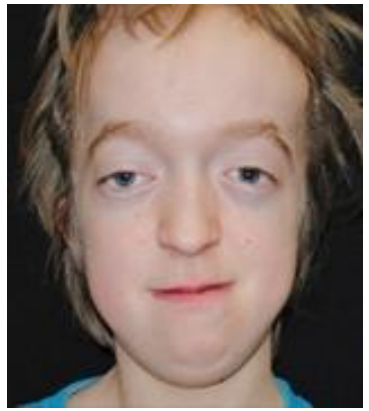
Conductive HL

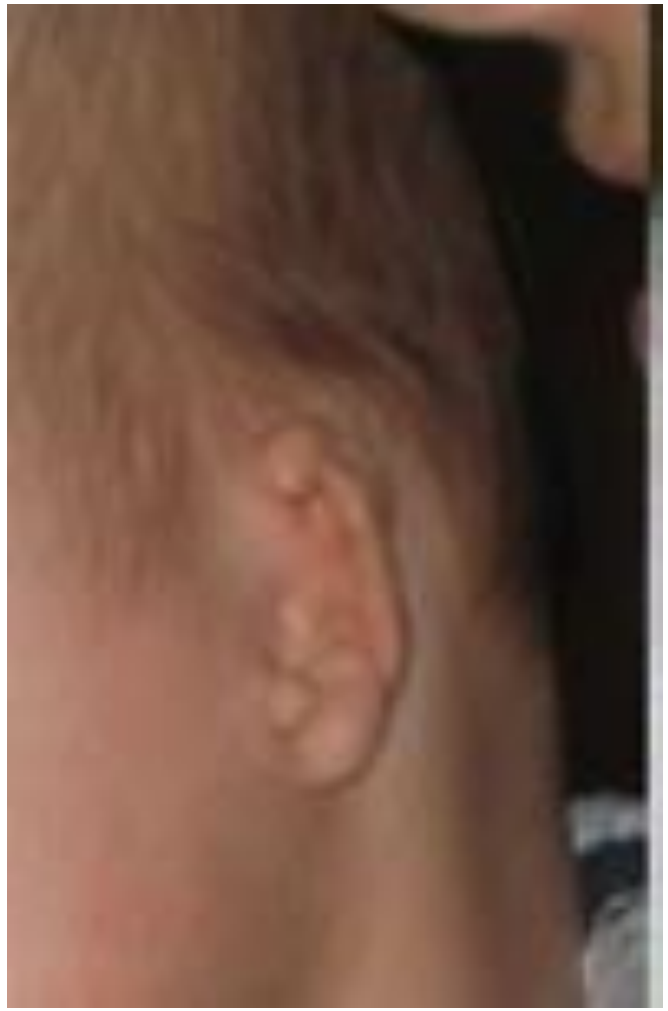


Crouzon



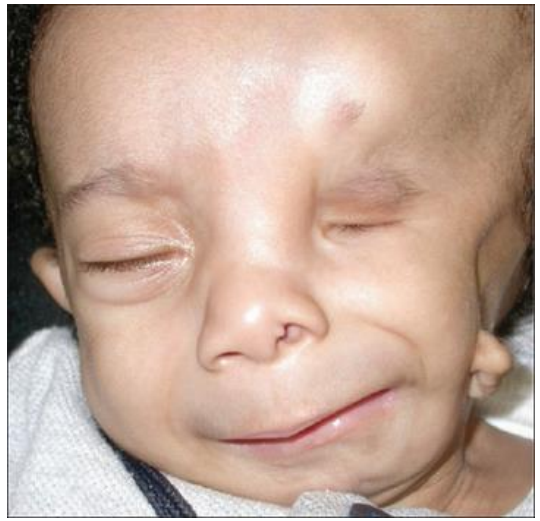


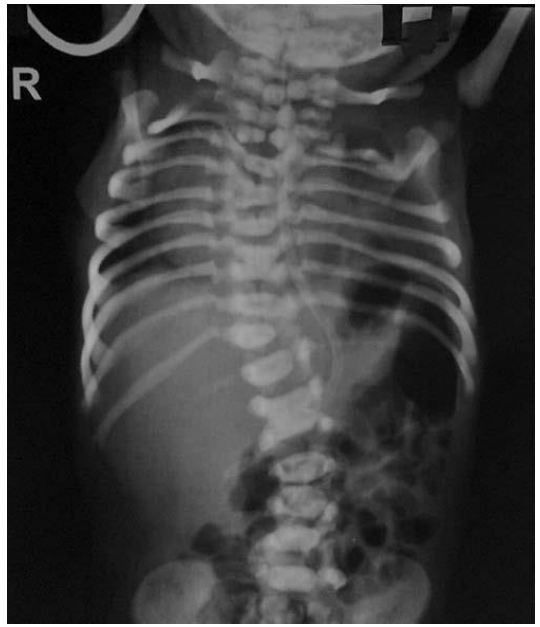
- aka “craniofacial dysostosis”
- **Etiology: AD**
  - FGFR2 – like apert, pfeiffer
- **Hearing loss**
  - Typically CHL- atresia/microtia, TM thickening, stapes fixation
  - Can have SNHL
- **Other Clinical Features**
  - may have normal IQ
  - Craniosynostosis, cervical fusion
  - “wide/short face”, hypertelorism, proptosis
  - low nasal bridge, parrot-beaked nose, choanal atresia
  - midface hypoplasia, class III malocclusion, high arched palate, short upper lip, cleft palate possible



Goldenhaar

- aka oculo-auriculo-vertebral syndrome
- Etiology: AD & AR, multifactorial
  - anomalous development of 1st & 2nd branchial arches
- Clinical features: Hemifacial microsomia + ...
  - Hearing loss: often mixed
  - Eye: colobomas (upper lid), Epibulbar dermoids
  - Vertebral abnormalities
    - Typically scoliosis





Stickler syndrome

- Etiology
  - Type 1: Mutation in collagen-producing genes (*COL2A1)* = type 2 collagen
    - Several collagen genes/types of collagen can be affected
    - These include type 1-4
- Clinical features
  - Hearing loss: Progressive, SNHL or MHL
  - Ocular abnormalities (myopia, retinal detachment, cataracts)
  - Marfanoid habitus, Mitral valve prolapse
  - cleft palate
  - Most common syndrome associated with PRS

Branchio-Oto-Renal (BOR)

- AKA Melnick-Fraser syndrome
- Etiology
  - Mutation most commonly *EYA1*
  - Thought to be a transcription factor for development of neural crest structures
- Clinical features
  - Hearing loss: CHL, SNHL or mixed (ossicular & cochlear malformations possible)
  - Branchial abnormalities/preauricular pit
  - Varied renal abn – agenesis, dysplasia.

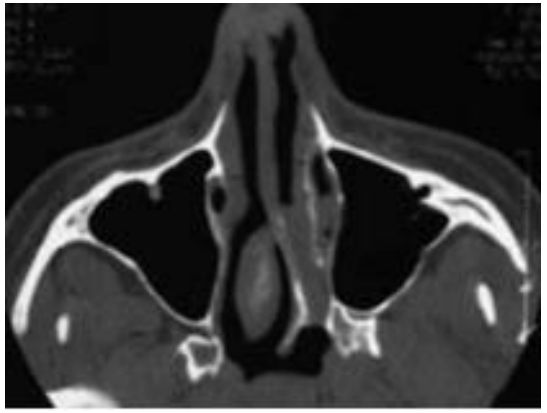
Figure 1 – A neck sinus and malformed ear (arrows) can be seen in this newborn.

Treacher Collins (aka mandibulofacial dystosis)

- Etiology
  - Gene: TCOF1 (treacle protein) mutation most common (involved in rRNA in craniofacial development)
  - Inheritance: AD
- Hearing loss:
  - Hearing loss – ossicular malformations common, incomplete partition
  - Other otologic associations: Microtia, atresia
- Clinical Features:
  - Hypoplastic midface, mandible hypoplasia, PRS
  - coloboma lower eyelids (77%); downslanting palpebral fissures
  - normal intelligence
  - cleft palate

CHARGE

- Etiology: ↓ circulating T cells (CHD7 mutation)
- Clinical features = CHARGE
  - C (***C***oloboma of the eye) – often bilateral; can have retinal detachment
  - H (***H***eart disease) – MC are septal defects & conotruncal malformations
  - A (***A***tresia of the choanae): can't pass ___ Fr catheter; R>L, bony >cartilaginous, ♀
  - R (***R***etarded development & growth)
  - G (***G***enital anomalies)
  - E (***E***ar anomalies &/or deafness) ~100%
    - High incidence of middle ear malformation/ossicle dysplasia
    - High incidence of SCC dysplasia/aplasia

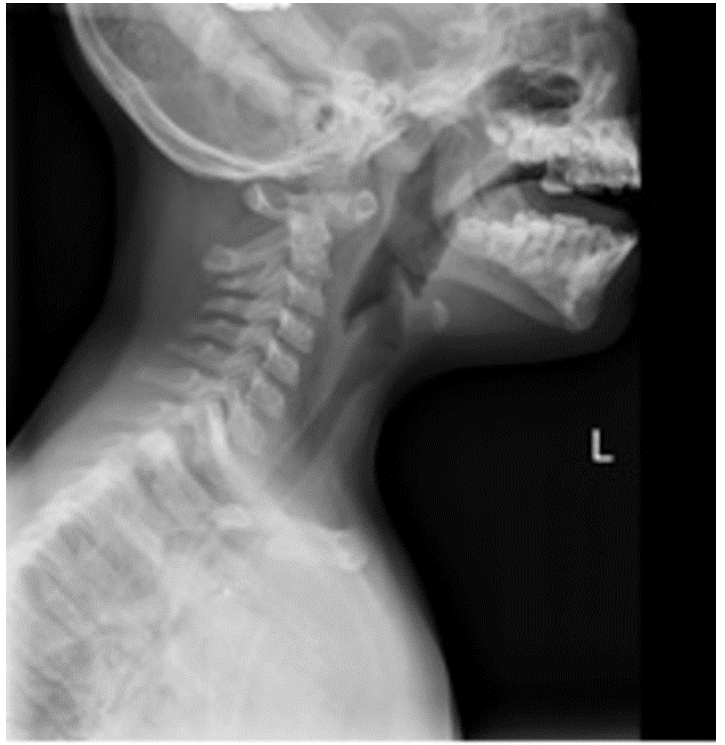


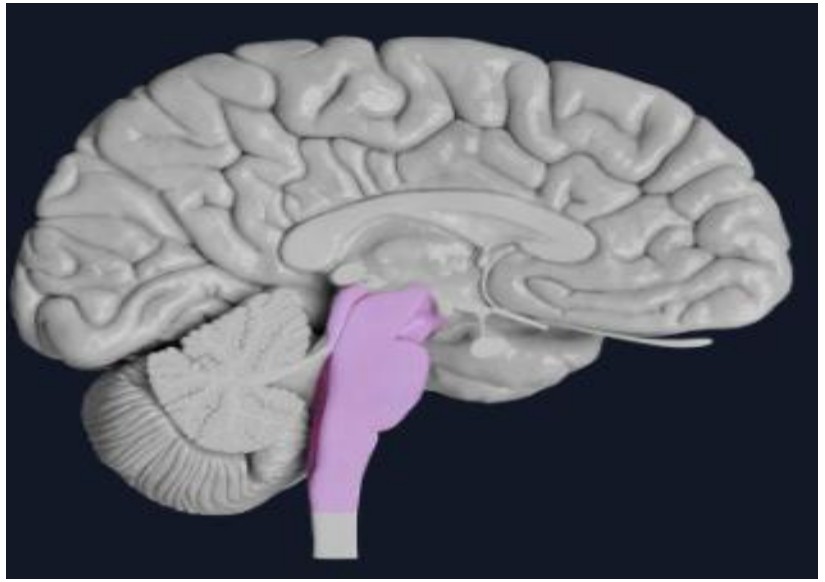
Trisomy 21

- Subglottic stenosis (25%), macroglossia, OSA
- Atlanto-axial instability (careful during DL!)
- Otologic: hearing loss, EAC stenosis, otitis media

TABLE 107.1 TEN CARDINAL FEATURES OF DOWN SYNDROME IN THE NEWBORN

Features	Percentage
Flat facial profile	90
Poor moro reflex	85
Hypotonia	80
Hyperflexibility of joints	80
Excess skin on back of neck	80
Slanted palpebral fissures	80
Dysplastic pelvis	70
Anomalous auricles	60
Dysplasia of midphalanx of 5th finger	60
Simian crease	45





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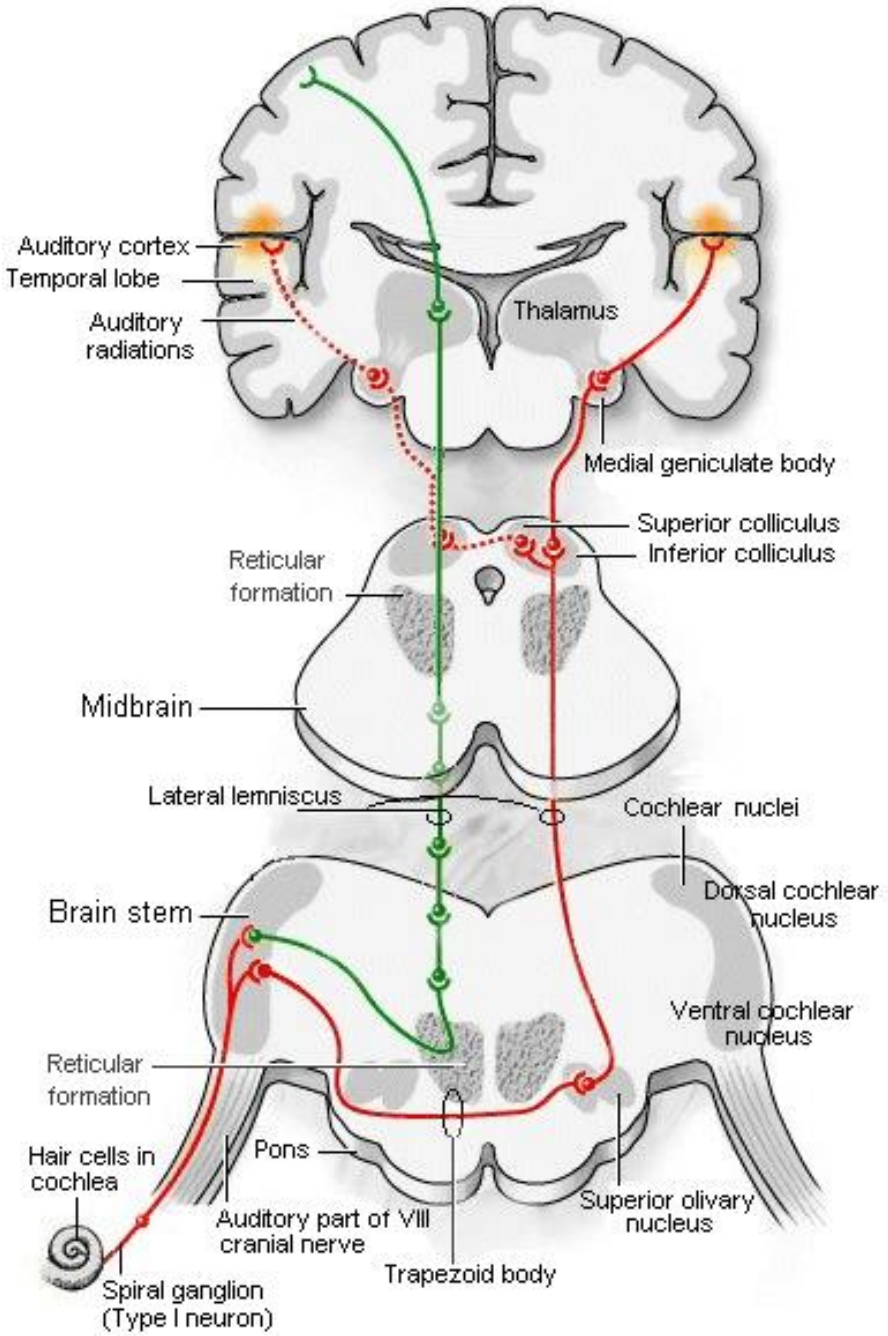
Physiology

- ECOLI

1. Eighth Nerve
2. Cochlear Nucleus
3. Olivary Nucleus
4. Lateral Lemniscus
5. Inferior Colliculus

Auditory Cortex



Infectious

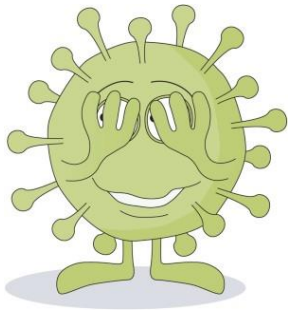
- TORCHES:
  - Toxoplasmosis-

Chorioretinitis
Hydrocephalus
Intracranial calcifications

Rubell

Cataract
Heart defect
SNHL

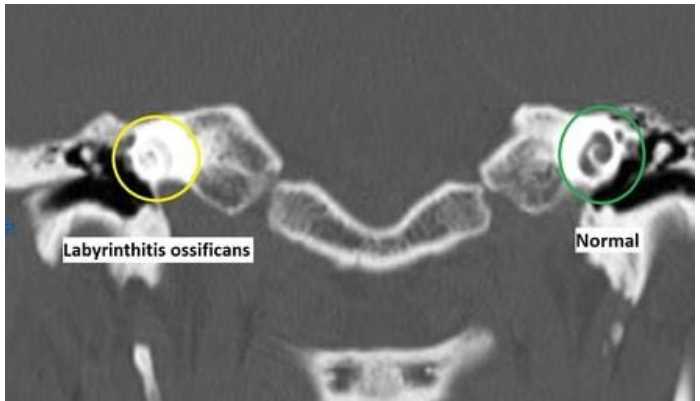
CMV



Delayed onset SNHL
Dev Delay
Visual issues
Microcephaly

Others:
- Herpes
- Syphilis
- HIV
- Lyme disease
- Mumps

Bacterial meningitis:
- 33% incidence sequela
- MC after s. pneumo
- Poss benefit with steroids
- Strong recommendation for screening



Trauma/Toxicity

- Noise induced
  - Rising incidence of noise induced hearing loss in adolescents
  - Estimated that 20% of adolescents may have HL by the time they reach adulthood
- Traumatic head injury
  - Temporal bone fracture: Higher incidence of hearing loss in pediatrics (15-20% SNHL) although lower risk of FN injury compared to adults
  - TBI/concussion: possible risk of HL as well
- Ototoxicity
  - Aminoglycoside, systemic chemotherapy, macrolides, loop diuretics

Malformations of the Membranous & Osseous Labyrinth

- Cochlear Anomalies
  - Cochlear Aplasia
    - arrest of the cochlear bud at the 5th week of gestation, rare; only a vestibule and SCCs (usually malformed) are present, absence of otic capsule, no auditory function
  - Cochlear Hypoplasia
    - arrest in the 6th week; single turn or less; 15% of all cochlear anomalies, small bud, usually enlarged vestibule and often SCC malformations (50%); variable hearing

TABLE 13-1. **Relative Incidence of Cochlear Malformations**

Malformation	Incidence (%)
Incomplete partition (Mondini dysplasia)	55
Common cavity	26
Cochlear hypoplasia	15
Cochlear aplasia	3
Complete labyrinthine aplasia (Michel aplasia)	1

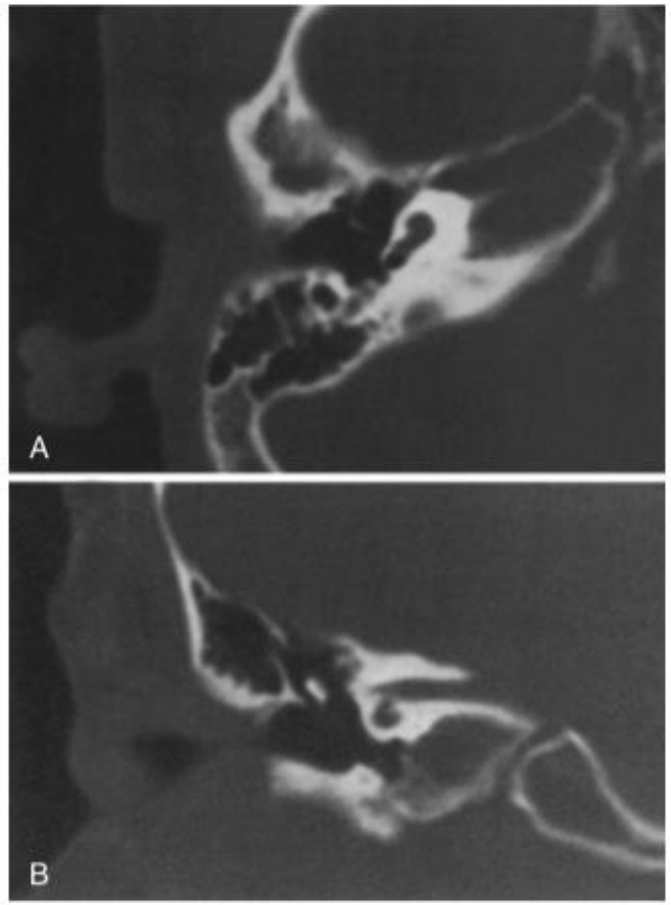
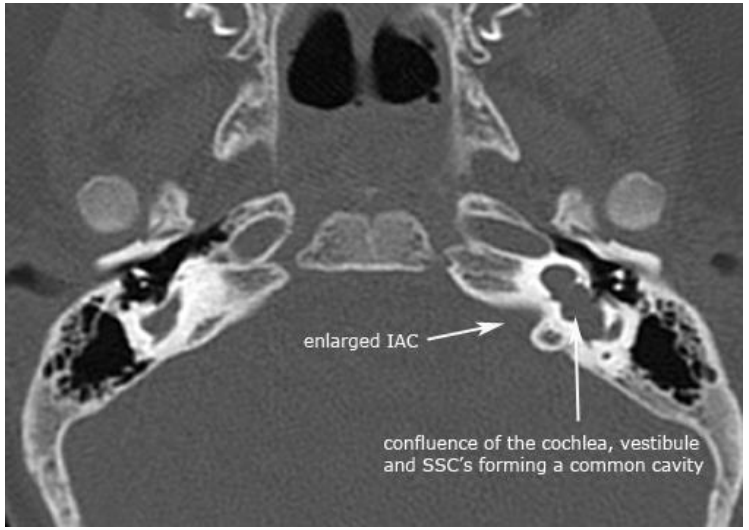
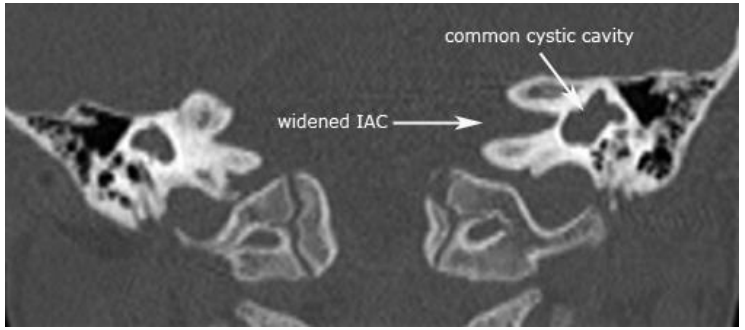


FIGURE 13-6. Cochlear hypoplasia as seen on axial (**A**) and coronal (**B**) computed tomography scans. The cochlea consists only of a small bud off the vestibule.

Malformations of the Membranous & Osseous Labyrinth

- Common Cavity
  - Cochlea and vestibule are confluent
  - Ovoid space without architecture
  - Arrest at week 4 otocyst stage (common cavity lies anterior to the EAC)
  - Neural population usually is sparse or absent. Hearing typically poor.

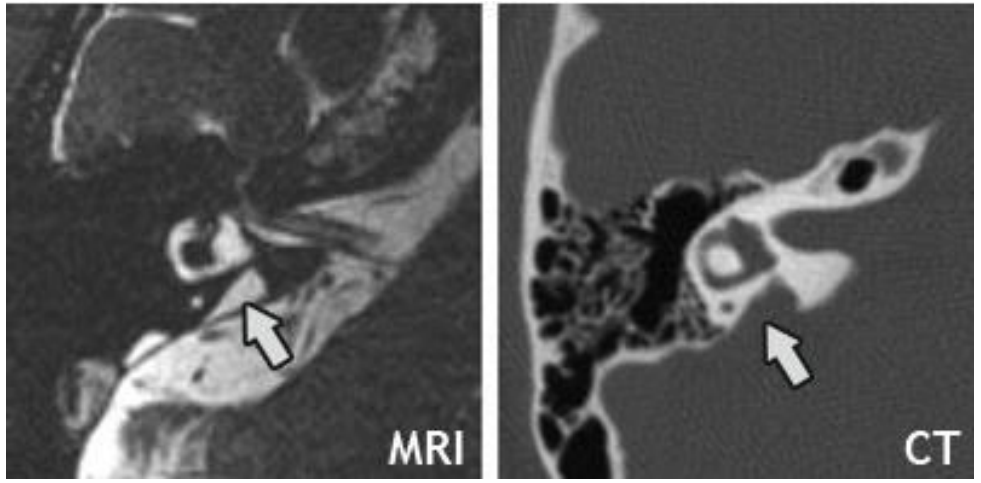




Malformations of the Membranous & Osseous Labyrinth

Enlarged Vestibular Aqueduct

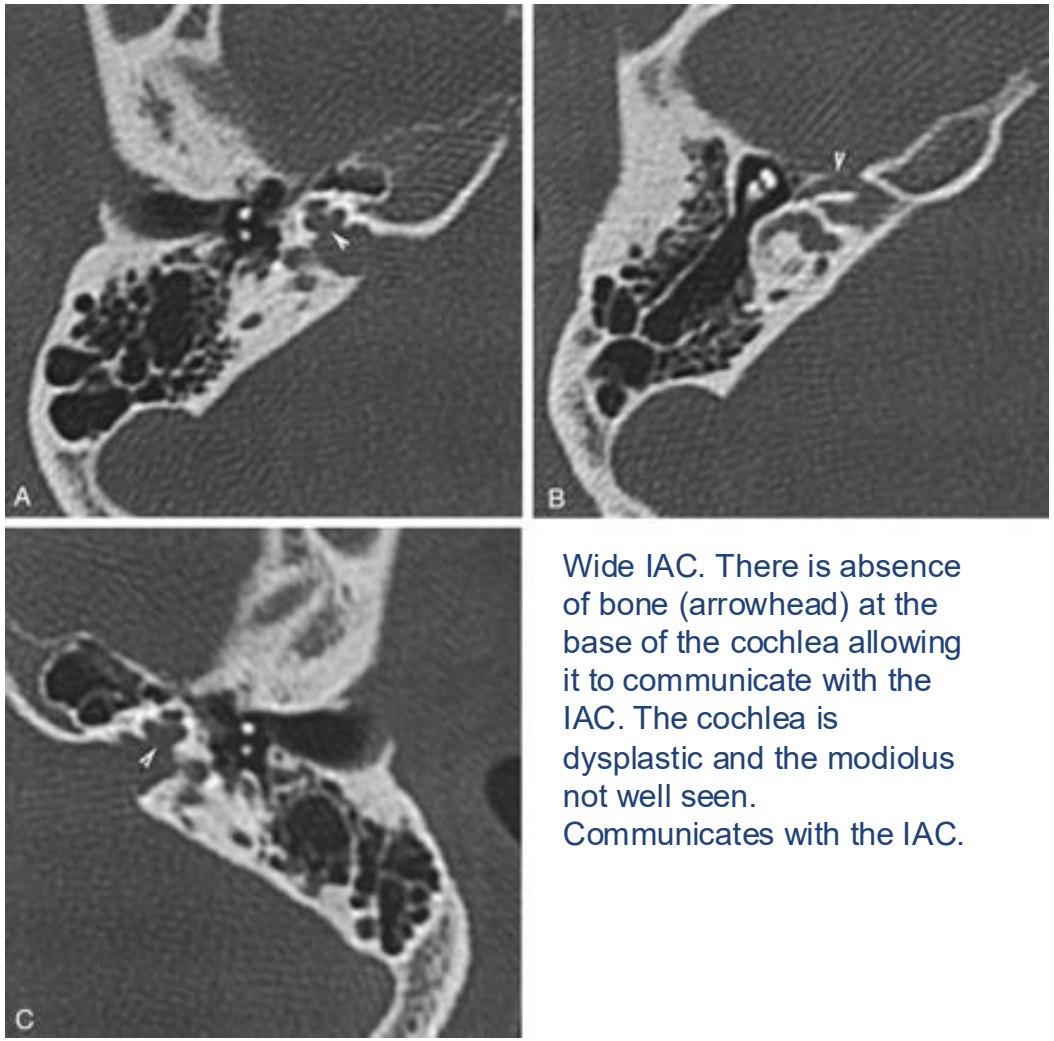
- Typically bilateral
- Fluctuating, progressive SNHL
- SNHL associated with trauma
- High risk for CSF otorrhea
- Frequent vestibular symptoms
- Associated with Pendred, BOR, and Waardenburg
- Steroids may slow hearing loss or assist in recovery
- Cochlear Implants are effective



- Most common radiographically detectable malformation of the inner ear
- Normal VA measures 0.4 and 1 mm
- EVA diagnosed when >2 mm

Other Inner Ear Causes for Hearing Loss

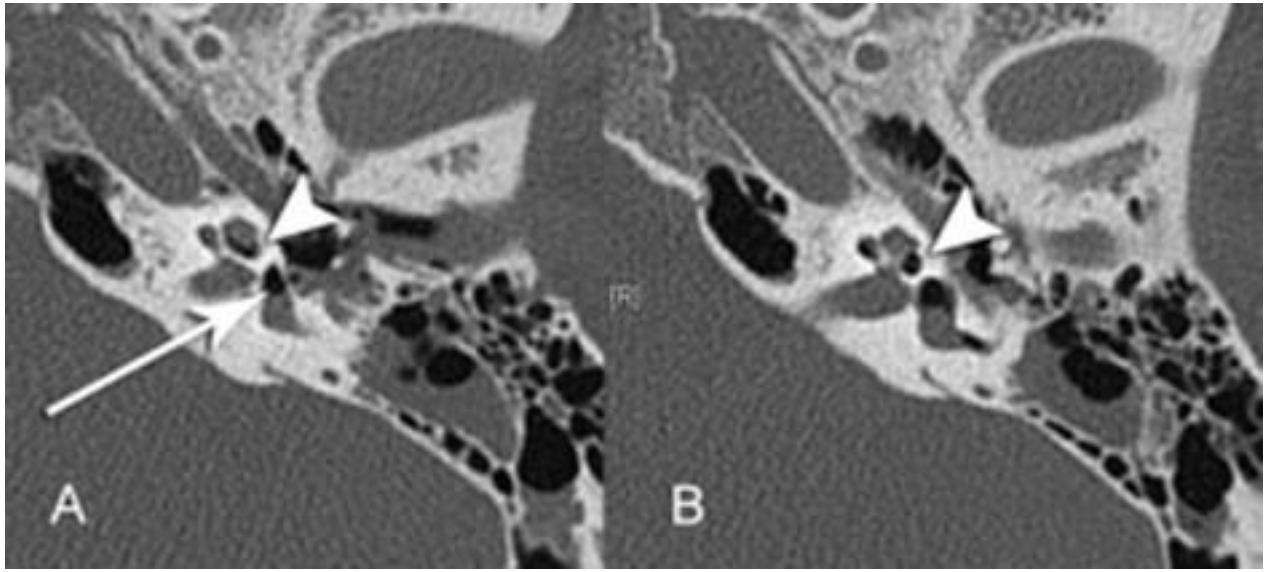
- X-linked Stapes gusher syndrome
  - May be seen radiographically with deficient cholera modiolus and bulbous lateral IAC
  - Often a congenital mixed hearing loss
  - Stapes surgery high risk for perilymph gusher
  - if undergone, often results in anacusis
  - Consider CT scan if there is congenital conductive hearing loss to screen for inner malformation
  - Mutation of POU3F4 gene

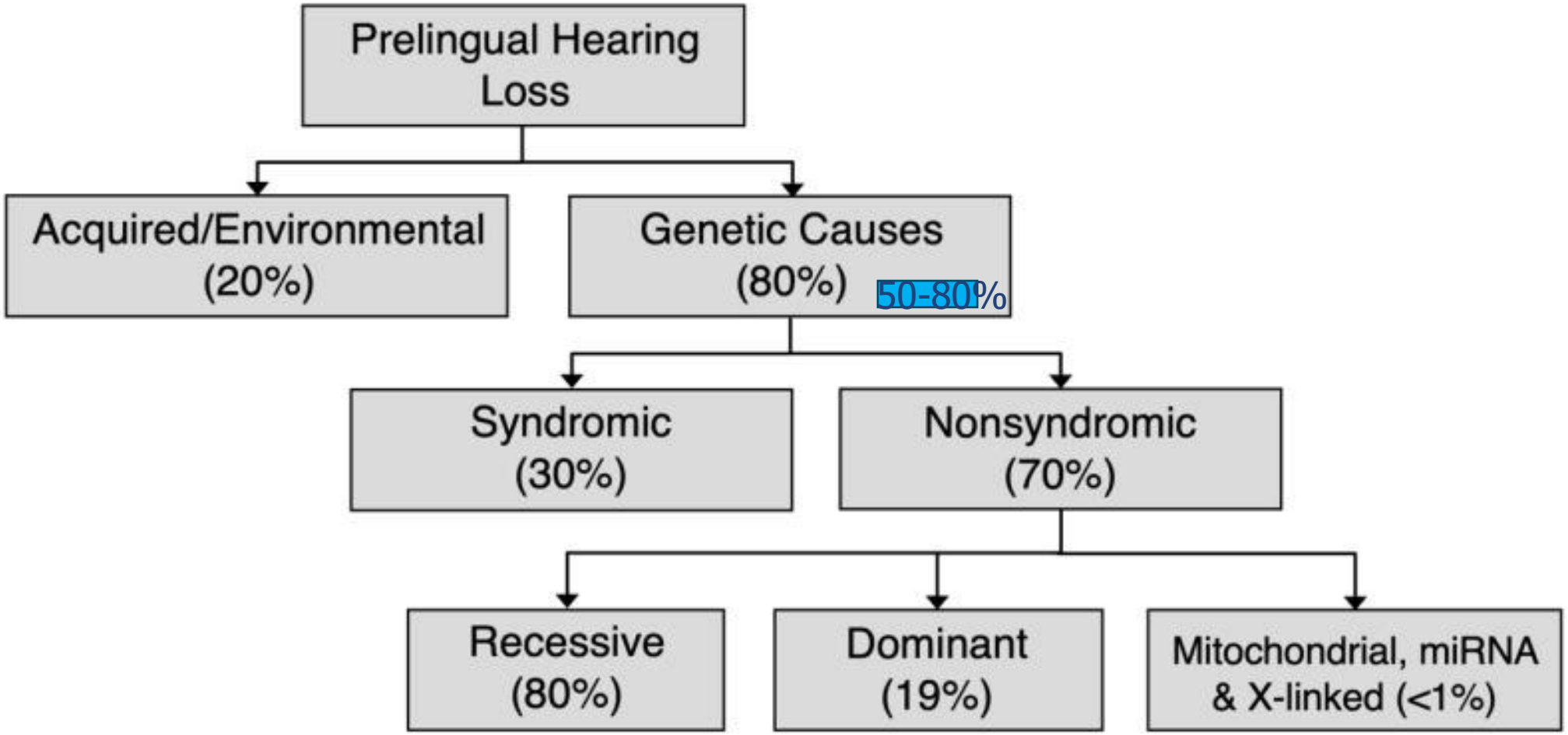


Wide IAC. There is absence of bone (arrowhead) at the base of the cochlea allowing it to communicate with the IAC. The cochlea is dysplastic and the modiolus not well seen. Communicates with the IAC.

Other Inner Ear Causes for Hearing Loss

- Perilymphatic fistula
  - Inner connection of inner ear and tympanic cavity
  - Can have sudden progressive hearing loss and vestibular symptoms (vertigo)
  - CT may show pneumolabyrinth
  - Often head or barotrauma related





https://www.ncbi.nlm.nih.gov/books/NBK1434/

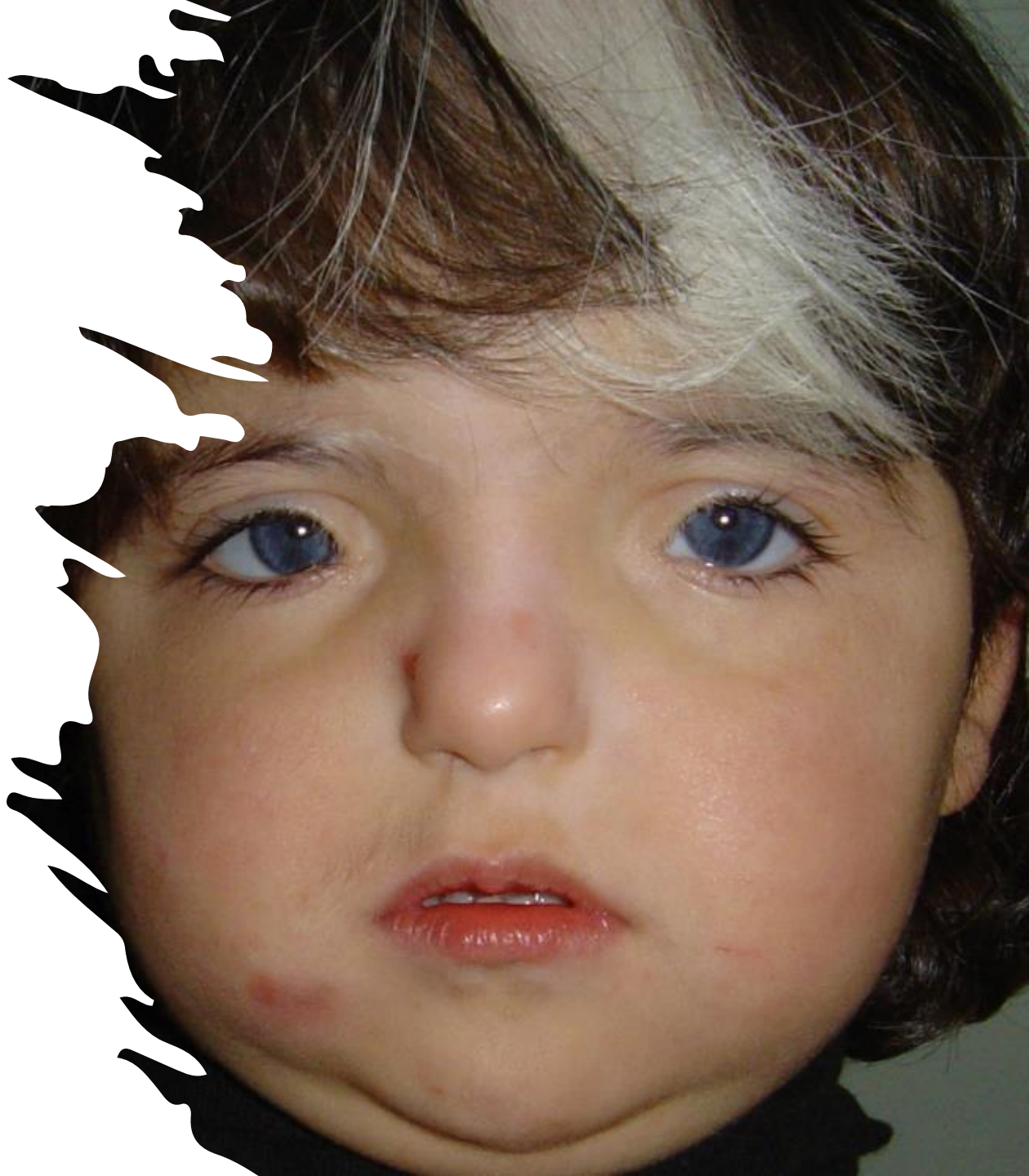
https://www.ncbi.nlm.nih.gov/books/NBK580517/

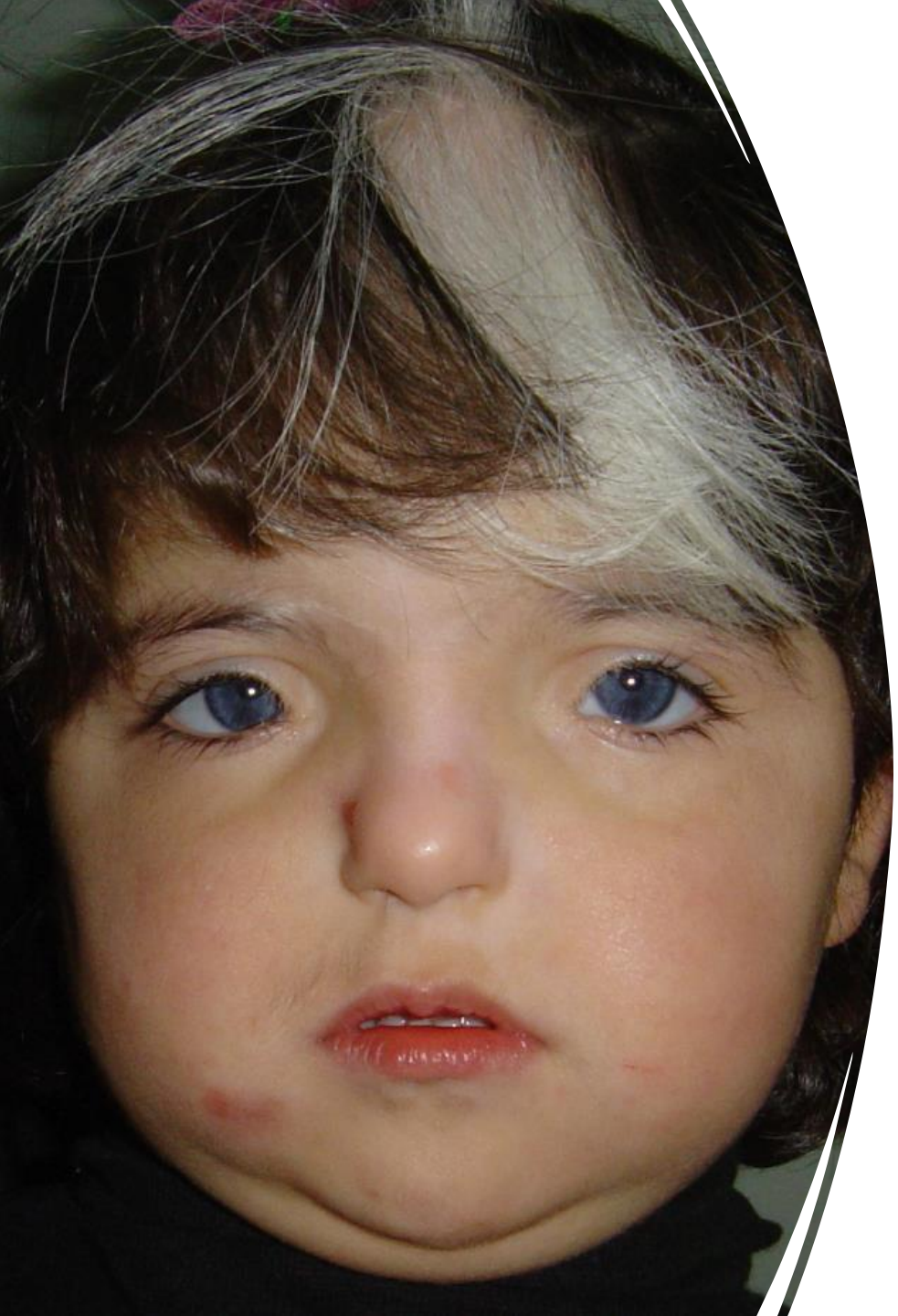
Non-syndromic HL

- Etiology:
  - DFNB/A genes (DF = Deaf, N = non-syndromic, B = AR and A = AD)
  - Accounts for about 50% of non-syndromic HL
  - DFNB1 locus = GJB2 gene (Gap junction B2 gene)
  - Organ of corti expresses several GJB proteins
- Specific genes:
  - GJB2
    - Produces Connexin 26 = potassium ion channel
    - Most common, specifically in white and Ashkenazi Jews
    - Prognosis is related to genotype (how severe the mutation is)
  - Otoferlin
    - DFNB9 gene = calcium sensor
    - Potentially implicated in auditory neuropathy

Case 1

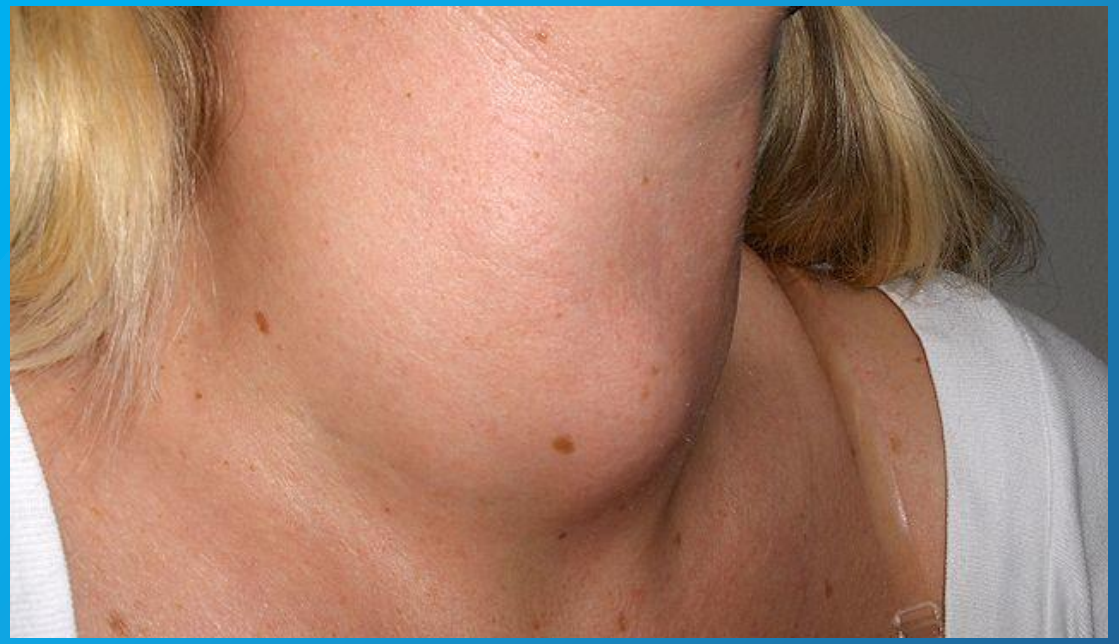
what abnormalities do you note?

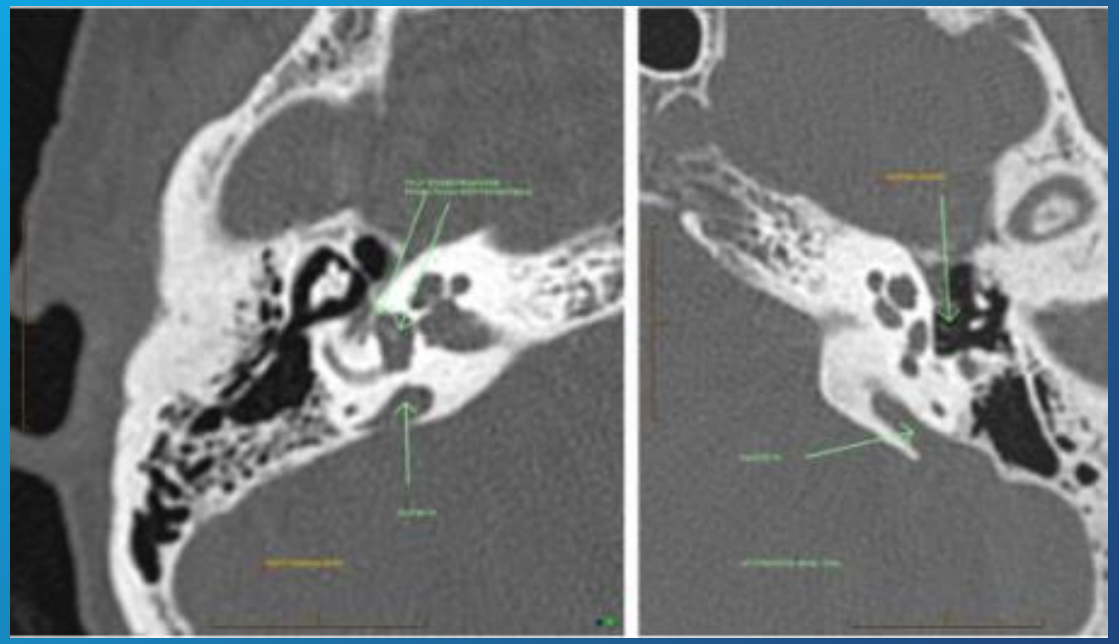




Waardenburg

- Gene: PAX 3 (tyrosine metabolism)
- Most common cause of AD syndromic hearing loss
- Clinical features:
  - piebaldism (melanocyte disorder)
    - **White forelock**
    - vitiligo
  - heterochromia iridis
  - SNHL
  - **Dystopia canthorum**
  - heterchromia iridis
  - unibrow (synophrys)
  - Cleft lip/palate
- Types:
  - Type 1: Dystopia canthorum
  - Type 2: worse hearing loss
  - Type 3: + skeletal malformation
  - Type 4: Hirschsprung





Case 2

- 13 year old F presents to clinic with new R hearing loss after getting hit in the head with a soccer ball at her soccer game. No loss of consciousness

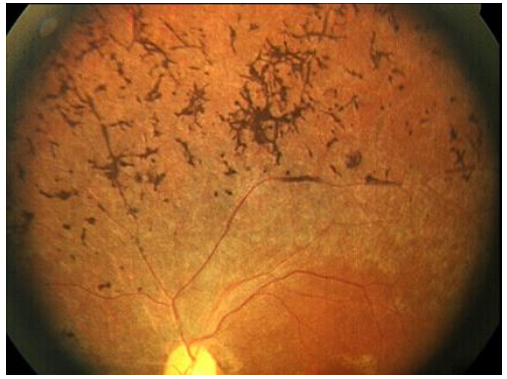
Pendred syndrome

- Etiology:
  - SLC26A4 gene affecting Pendrin protein → defective iodine/chloride metabolism + organification
  - Inheritance: AR
- Dx :
  - genetic test (old perchlorate)
- Clinical Features:
  - Incomplete partition or EVA (susceptible to SNHL following head trauma)
  - Goiter – often euthyroid
  - variable vestibular dysfunction

Case 3

- 13 yo F referred for dizziness.
- She’s worn hearing aids for most of her life & parents are also worried that her glasses are no longer helping despite increasing her prescription over the last several years

Usher syndrome

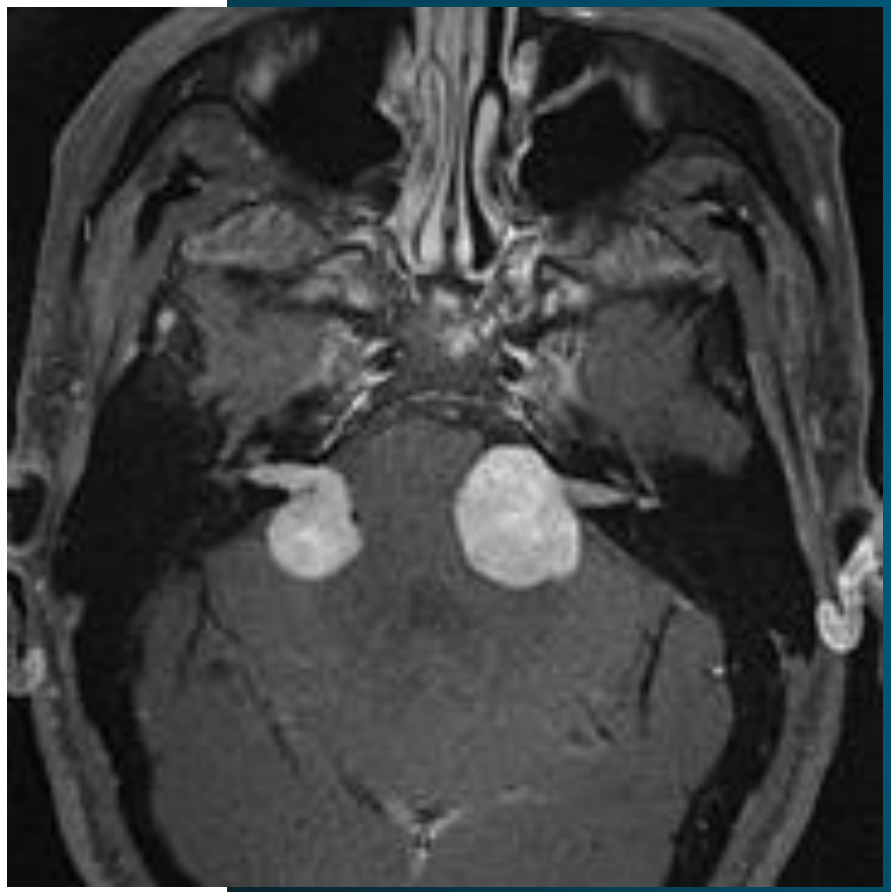


- Etiology: 5 different genes
  - AR inheritance
- MCC syndromic profound HL

  (**U**sher = **U**biquitous)
- Clinical Features: SNHL + Retinitis pigmentosa
  - Type 1 – congenital bilateral profound SNHL + absent vestibular function, blind by early adulthood
    - USH1 gene = Myosin gene in hair stereocilia
  - Type 2 – moderate HL, normal vestib function, blind by mid adulthood
  - Type 3 – progressive HL, variable vestib function, varied blindness

Case 4

- 17 yo F with progressive difficulty hearing teachers at school.
- & your MRI looks like this



Neurofibromatosis

Etiology: AD

- NF1: chromosome 11 neurofibromin
- NF2 gene on chromosome 22 = Protein encoded is **MERLIN**

Both syndromes

- Café au lait spots
- Multiple fibromas

How to differentiate NF1 and NF2:

- NF1: Lisch nodules, optic glioma, less likely to have HL
- Bilateral Acoustics with NF2 in 95%
- Unilateral Acoustic in NF1 in 5%

Peripheral vs Central Disorders

Peripheral: conductive, sensorineural, mixed; severity and bilaterality strongly predict language level, type of loss is the strongest predictor of total linguistic performance, followed by age at diagnosis and age of device fitting.

Central: listening difficulties/APD often reflect broader neurodevelopmental vulnerabilities. Systematic review shows children labeled with APD differ from peers not only in auditory but also visual, cognitive, language, and reading domains.

Recent models recommend reframing as “listening difficulty” with contributions from auditory, speech, language, attention, and memory systems that can be disentangled using structured test batteries and electrophysiology.

Syndromic and High-Risk Etiologies

Syndromic/non-syndromic genetic HL, congenital infections (esp. CMV), and oncology-related ototoxicity are major contributors.

In congenital infection cohorts, CMV is highly associated with SNHL (80% of CMV cases), and SNHL in this group is tightly linked to more severe language delay.

Cochlear nerve deficiency, once considered a contraindication to CI, now shows group-level improvement in speech perception after implantation, though outcomes are heterogeneous, highlighting the need for integrated imaging, electrophysiology, and counseling

Comorbidities and Complex Populations

Many hearing-impaired children have additional disabilities (≈50% in some cohorts) which strongly affect cognitive and language outcomes but do not preclude auditory cortex maturation; P1 still normalizes with intervention.

Oncology/ototoxicity (cisplatin, cranial RT), NICU histories, and congenital infections (e.g., CMV) create high-risk groups where electrophysiology helps separate peripheral, neural, and central contributions.

Overlap with Neurodevelopmental Disorders

Children with listening difficulties frequently carry additional diagnoses: attention disorders (32%), language disorders (28%), anxiety (16%), ASD (6%) in one tertiary cohort.

Integration of psychology into pediatric ENT/audiology clinics is recommended to address co-occurring psychopathology, caregiver distress, and broader neurodevelopmental needs beyond speech and hearing alone.

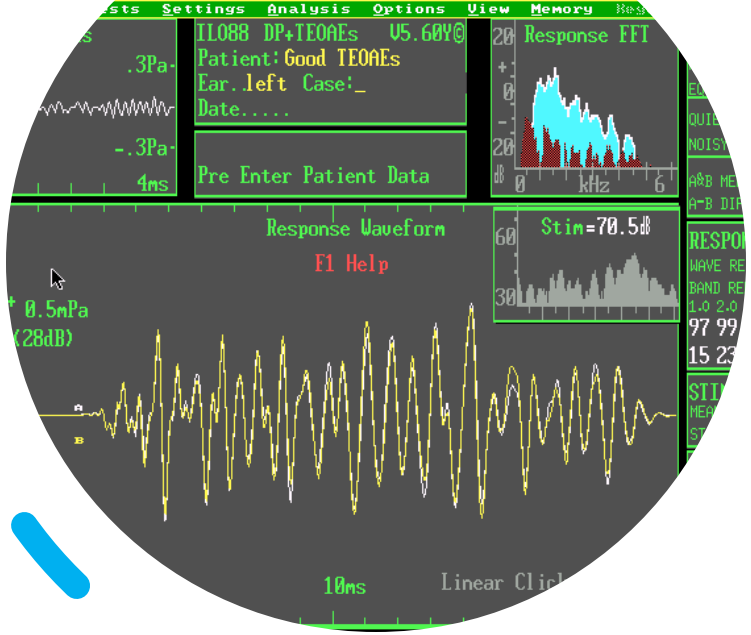
Electrophysiology in Early Detection and Diagnosis

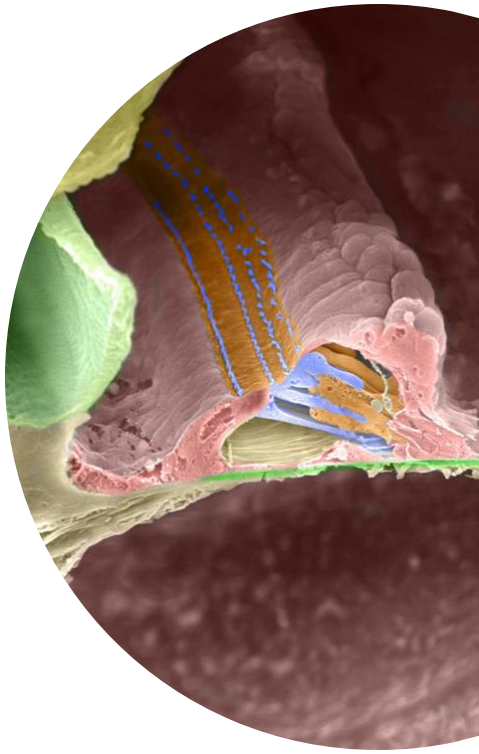
Early Detection through Neural Metrics: Diagnostic Value of Electrophysiology

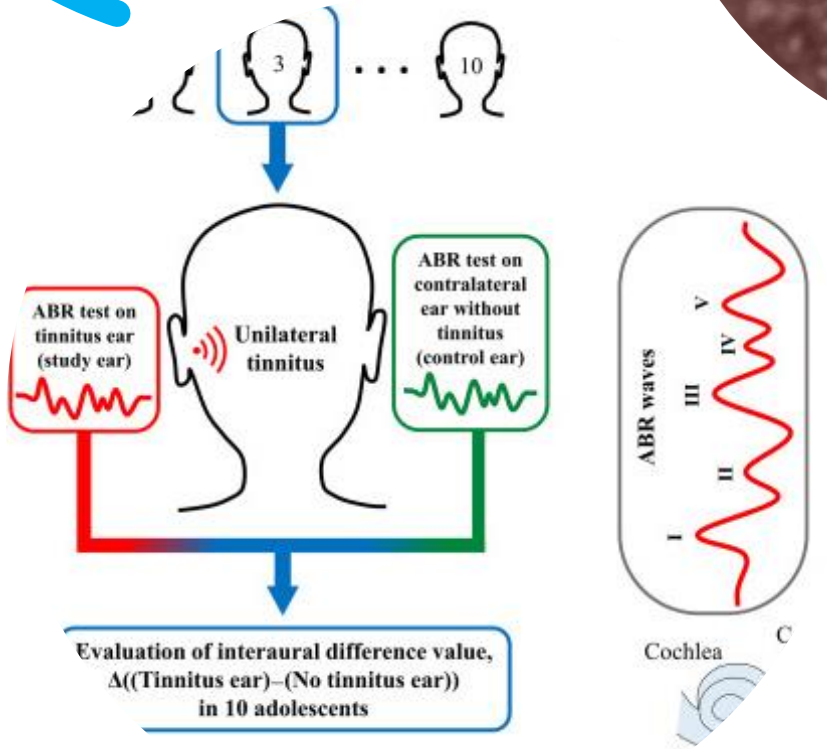
- Role of newborn hearing screening (OAE, ABR)
- Central auditory assessments in at-risk infants (e.g., NICU, preterm)
- Case examples of electrophysiology altering clinical trajectory

Role of newborn hearing screening (OAE, ABR)

- The Otoacoustic Emissions (transient-evoked otoacoustic emissions and distortion product otoacoustic emissions) and Auditory Brainstem Responses (ABRs) dominate the field of screening tests for newborns and infants under about six months developmental age.
- These technologies are objective in nature: they can be applied to a variety of pediatric populations, including those too young for behavioral screening or those with developmental delays that preclude behavioral screening.
- There are important differences between the two technologies, and it is important to consider the advantages and limitations of each.
- OAEs are cochlear responses generated by the outer hair cells in response to acoustic stimuli. As such, they provide useful information regarding the **preneural** status of the auditory system.
- ABRs reflect neural activity in the auditory nerve and brainstem.
- OAEs provide an assessment of cochlear (outer hair cell) function, while ABRs provide a measure of neural integrity and synchrony beyond the level of the cochlea in the auditory nerve and brainstem.
- ABRs are usually complex waveforms that are the net result of superposition of thousands of synchronized action potentials and post-synaptic potentials elicited from the auditory nerve and brainstem pathways.
- Automated ABR (AABR) are usually used for screening purposes.
- Keep in mind that neither the ABR nor the OAE are direct tests of hearing in the perceptual sense.
- Auditory brainstem response (ABR) has proven successful as a means of assessing the integrity of the auditory system from the cochlea to the lateral lemniscus and has demonstrated a 95% success rate in the identification of pathology of the lower and upper brainstem.

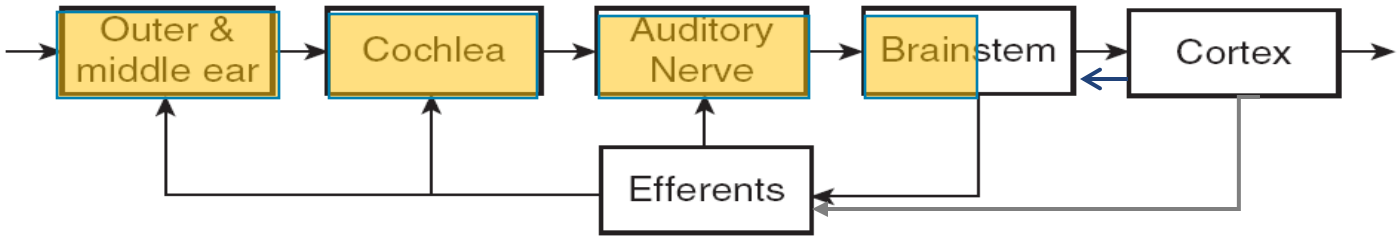






Central auditory assessments in at-risk infants (e.g., NICU, preterm)

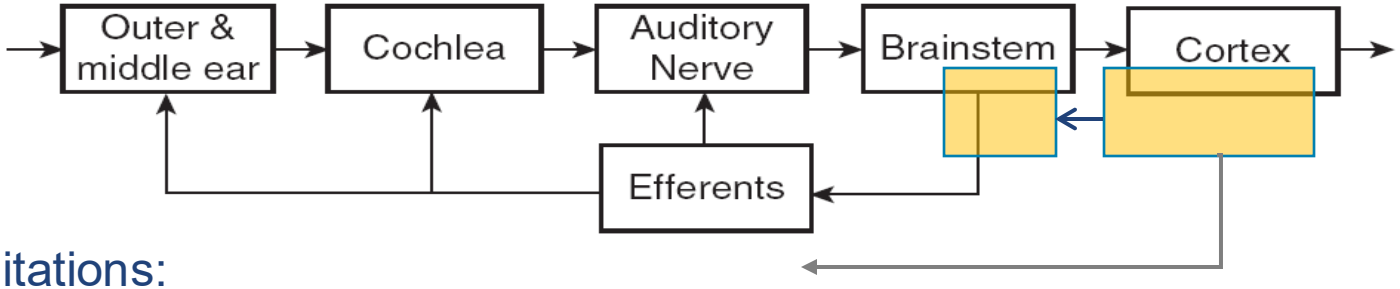
- Although a necessary step in assessing the auditory system, the ABRs have significant limitations.
- An absent ABR does not necessarily indicate deafness (auditory neuropathy spectrum disorder and neurological disorders):
  - Some patients who have normal thresholds on pure tone audiometry will have no recordable ABRs.
  - In many neurological disorders , the response may be sufficiently desynchronized to render the ABR undetectable but still permit hearing.



- A normal ABR does not rule out deficits that may interfere with central auditory processing and normal development of speech and language (Auditory Processing Disorder).

Cortical Auditory Evoked Potentials (CAEPs)

- CAEPs provide a direct, instantaneous, millisecond-resolution measure of neurotransmission-mediated neural activity (appropriate for answering questions that require high temporal resolution).
- When evoked by speech sounds, CAEPs provide information about the biological processes underlying speech processing.
- Online measure of auditory processing when a behavioral response is impossible or problematic.



- Limitations:
  - Ability to track the time course of processing but not to measure the operation of specific neural systems.
  - It is difficult to determine the neural generator locations of the underlying components.
  - Spatial information is limited, notably in the clinic as multichannel recordings are difficult to use.

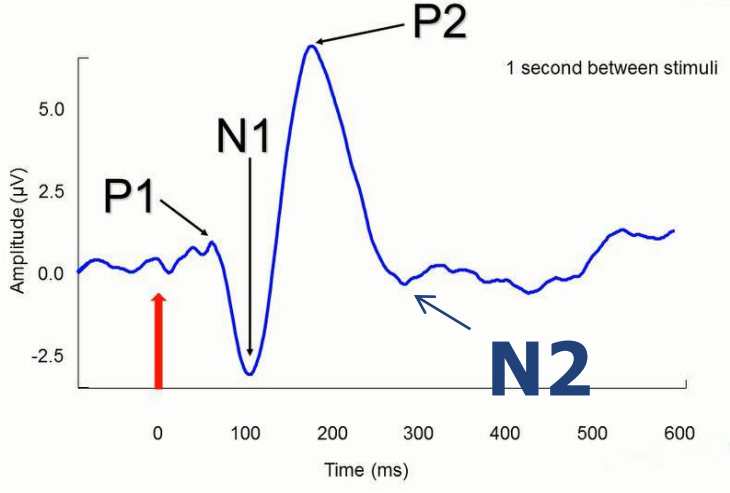
Clinical Use of CAEPs

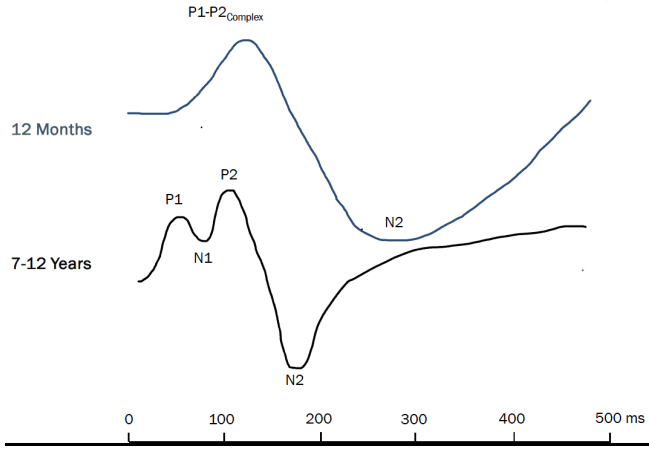
- Cortical potentials are useful in assessing maturation and function of the auditory cortical areas.
- Because normal maturation and functioning of these areas is a precondition for normal development of speech and oral language skills, recording CAEPs can prove useful in many infants and children (with hearing loss, risk factors, etc.).
- CAEPs provide an objective means of evaluating how the auditory cortex codes cues crucial to speech and language processing with high temporal precision.
- Predicts future language abilities.
- May also provide useful information for individuals showing difficulties with speech perception even with appropriately fit amplification/CIs.
- Useful with patients:
  - too young to evaluate behaviorally.
  - Unable to be evaluated behaviorally

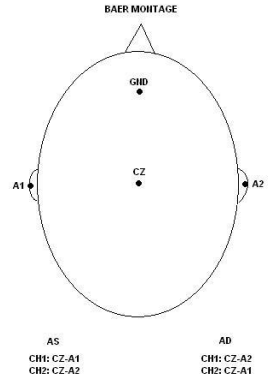
  (cognitive impairment, autism, severe ADHD…).
  - With any kind of neurological disorders

Cortical Auditory Evoked Potentials

- Recorded passively (obligatory response): no need to attend to the stimuli and no task to complete (unlike P300).
- CAEP can be recorded with same montage as for the ABR.
- Ear specific.
- Sound field can be used (HA, CI).
- Amplitudes are usually quite large: there is a signal to noise advantage with greater response detectability, particularly in noisy subjects (need less averages than ABRs).
- Response thresholds agree very well with audiometric thresholds determined behaviorally.
- CAEPs inform about speech processing and can also predicts future language abilities.







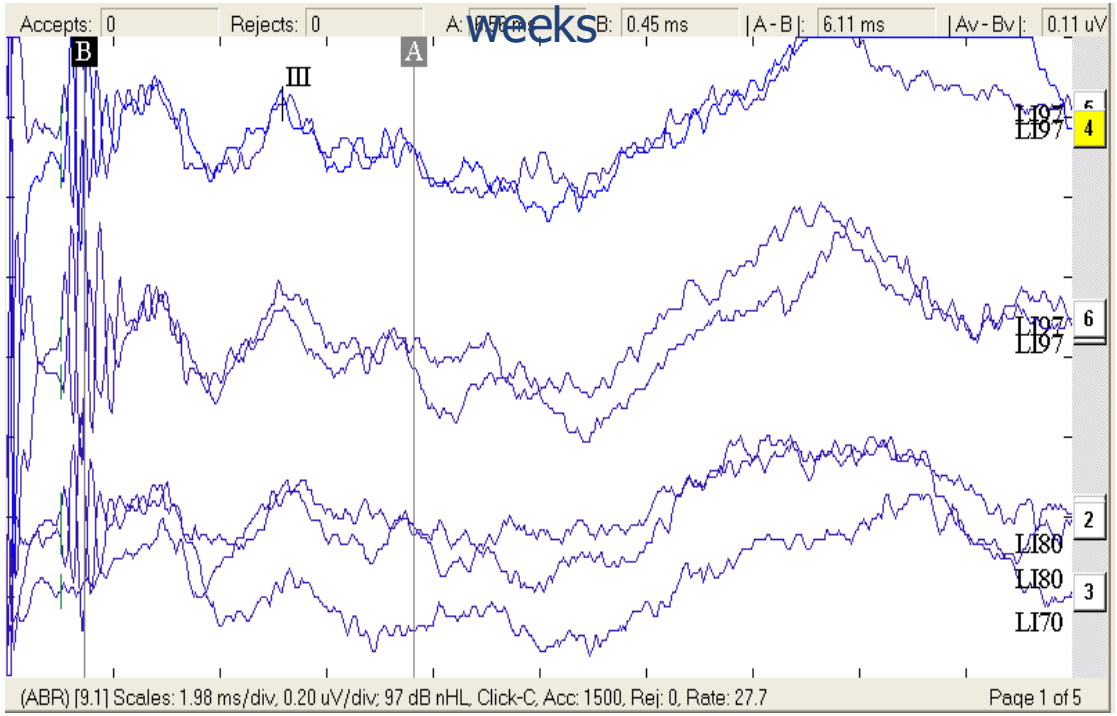
CAEPs in Patients with abnormal or absent ABRs

- Pre-verbal infants, ANSD, Neurological Disorders, etc.
- First step: knowing that the auditory cortex can be stimulated by sounds is an important piece of information in infants with absent or abnormal ABRs.
- If CAEPs are absent: auditory deprivation. Monitor for maturation. Implement mode of visual communication asap. CI candidacy.
- Second step: if CAEPs are present:
  - Assess morphology and latency
  - Estimate the hearing thresholds
- The response, however, does not indicate if the child can correctly process different speech sounds, or hear well in noisy environments unless we use a discrimination task and/or add background noise.

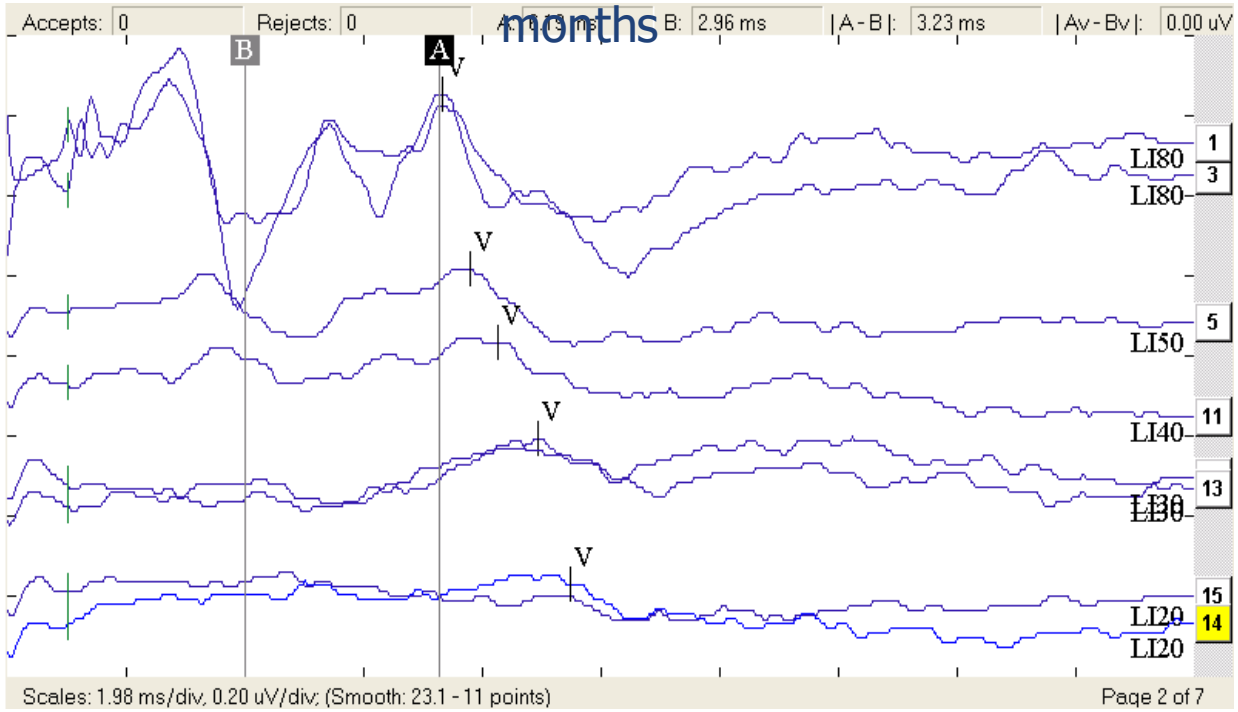
Case examples of electrophysiology altering clinical trajectory: Neuromaturation

- Neonates with hypoxia or bilirubinemia can show improvement over time of both ABRs and behavioral measures of hearing.

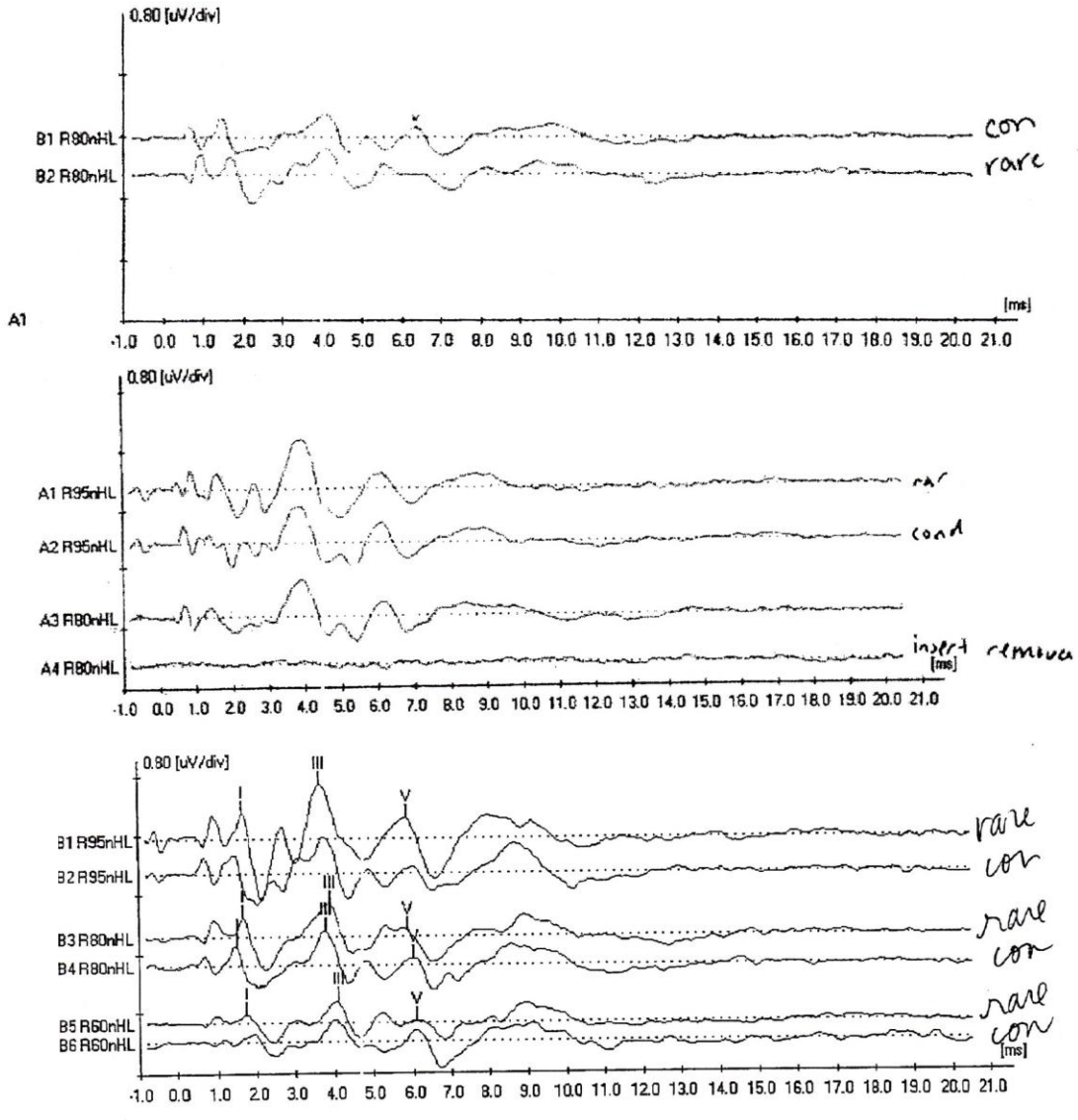
6 weeks



10 months



Neuromaturation



4 ½ months

7 ½ months

13 months

Cochlear Nerve Deficiency

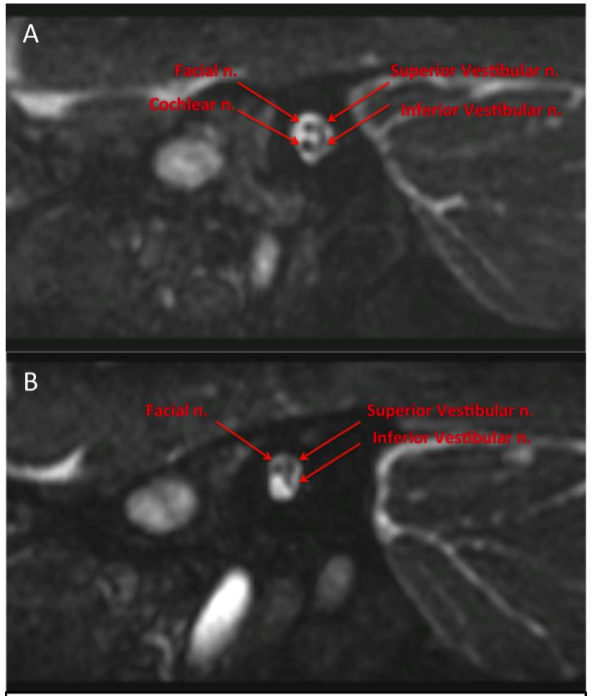
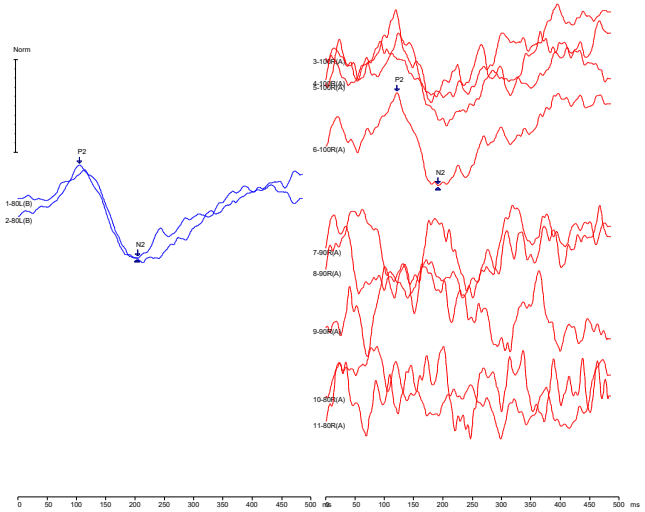


Figure 1. T-2 weighted MRI of a patient with unilateral cochlear nerve dysplasia. A. Right IAC with evidence of facial, cochlear, superior and inferior vestibular nerves. B. Left IAC with absent cochlear nerve



Unilateral CND

Absent Cochlear Nerve

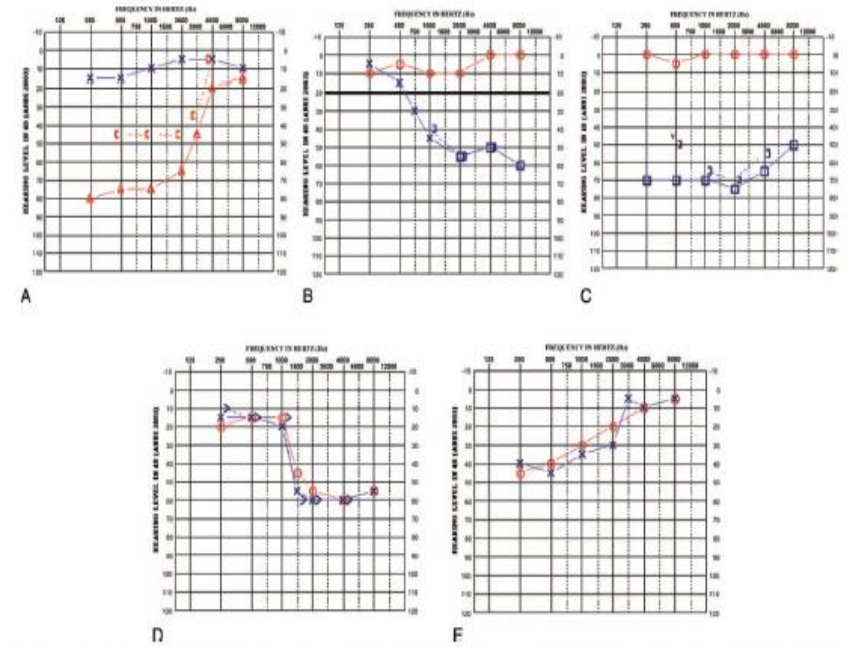
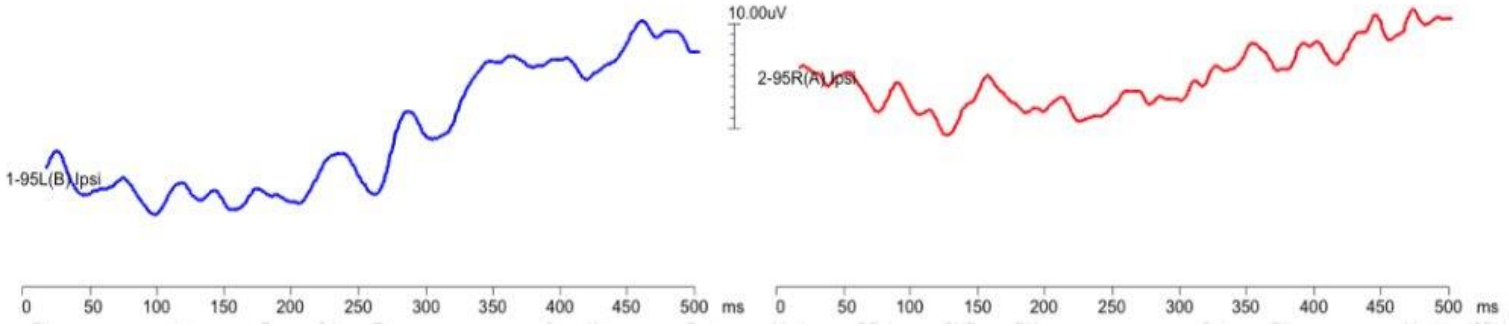


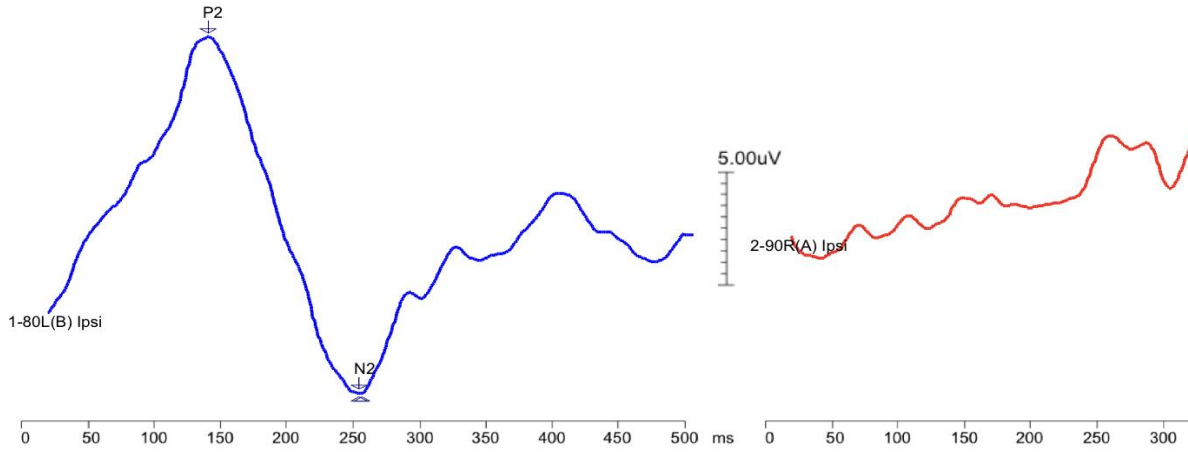
FIG. 3. Pure tone audiometry in three different children with an imperceptible nerve (*top*) and two children with bilateral hypoplastic cochlear nerve (*bottom*). *A*, Subject #28 with "absent" right cochlear nerve; *B*, Subject #24 with "absent" left cochlear nerve; *C*, subject #3 with "absent" left cochlear nerve; *D*, subject #32; *E*, subject #41.

CND



Bilateral CND

Absent responses bilaterally. Aplastic CND.

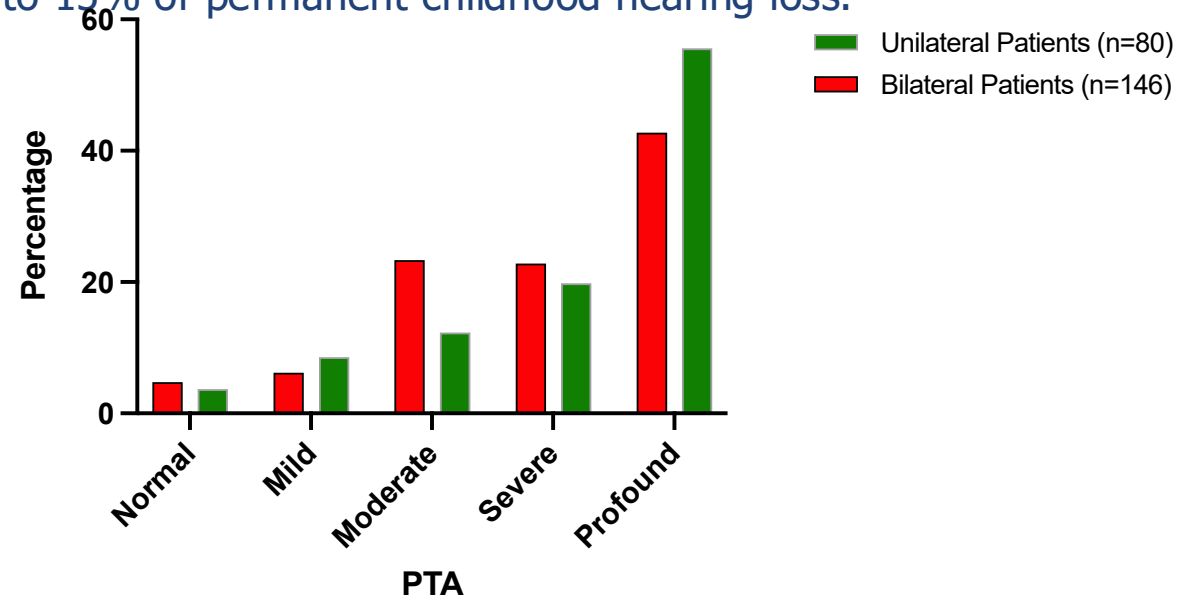


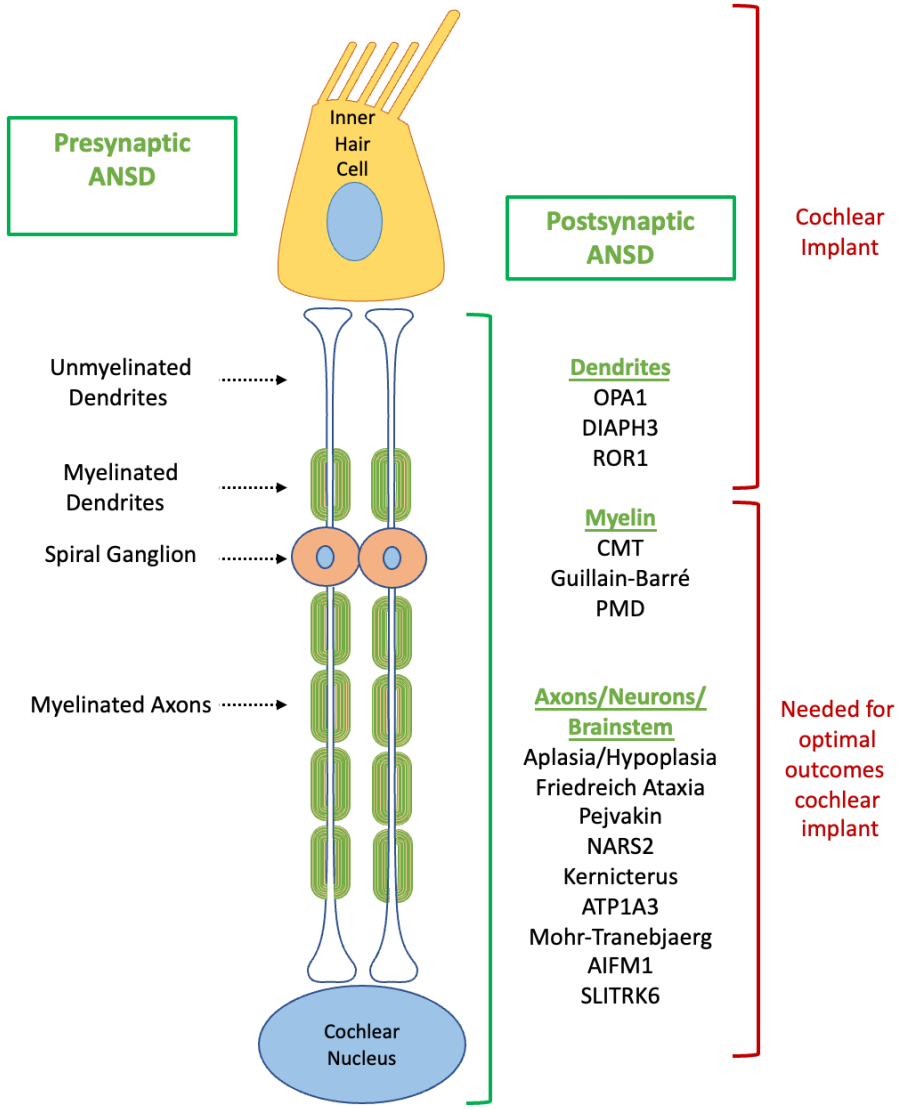
Unilateral CND

Absent response on right ear CND. Present response on left ear with no abnormal peripheral findings.

Auditory Neuropathy Spectrum Disorder (ANSD)

- Presynaptic ANSD: inner hair cells or synapses are affected, resulting in a receptor or synaptic disorder respectively
- Postsynaptic ANSD: significant loss of auditory nerve fibers and spiral ganglion cells while the number of outer hair cells remained unchanged.
- Common cause of hearing impairment, accounting for 10 to 15% of permanent childhood hearing loss.



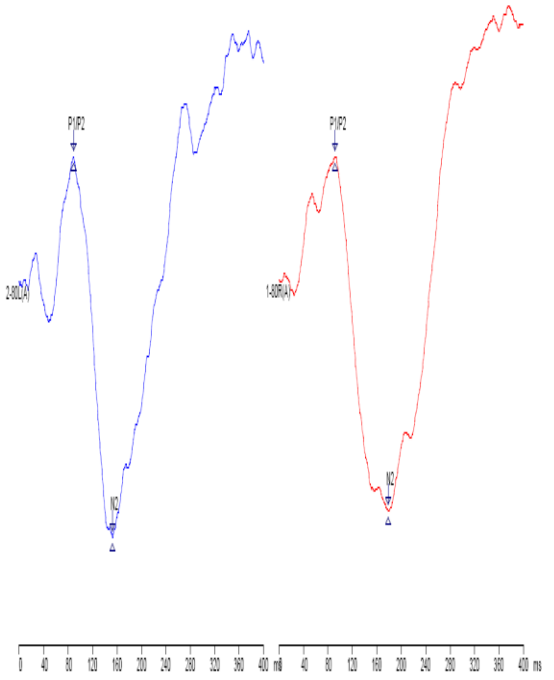


Absent ABR does not mean Deafness

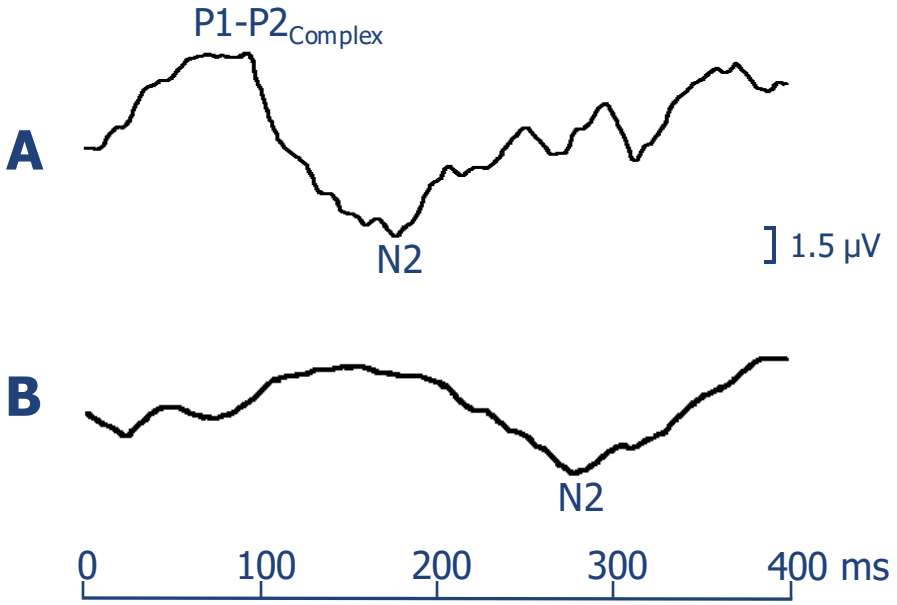
- ABR can be absent in patients who show preserved hearing by behavioral measures.
- Failure of auditory nerve to discharge at the same latency to each stimulus so that the averaged neural response can not be distinguished from the background potentials.
- In some instances, neural synchrony is still sufficiently preserved to allow an averaged cortical response to be detected.

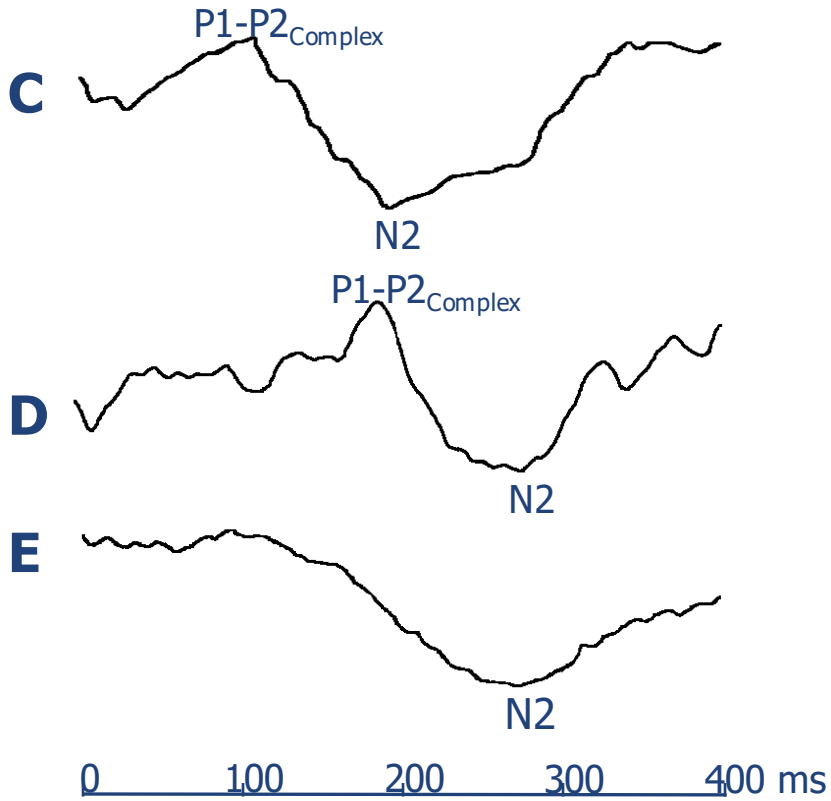
CAEPs in ANSD

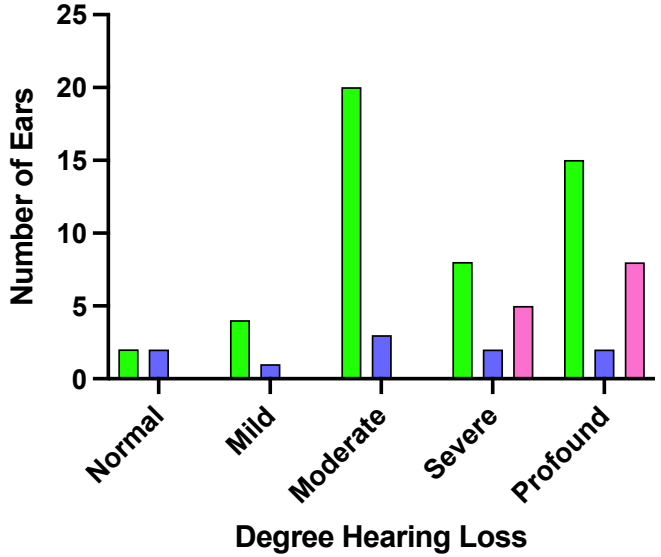
- Despite absence of ABR, CAEPs are often present in ANSD patients.
- CAEPs can be recorded before behavioral responses can be obtained.
- Support behavioral measures (auditory and speech language development) and parental observations.
- Can help evaluate hearing aid benefit.
- Monitor changes overtime.
- Should be part of the test battery.

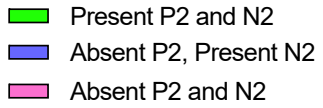


CAEPs in ANSD

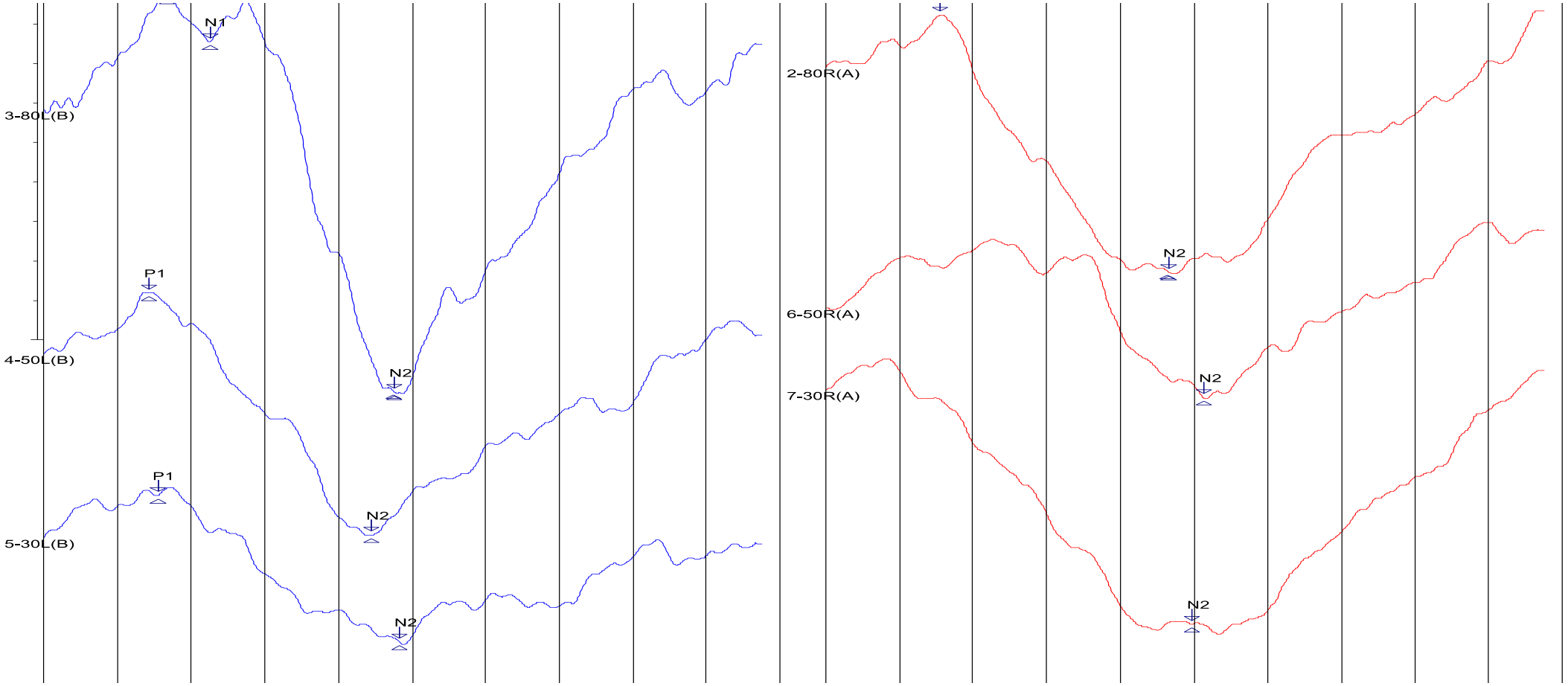








Threshold Search

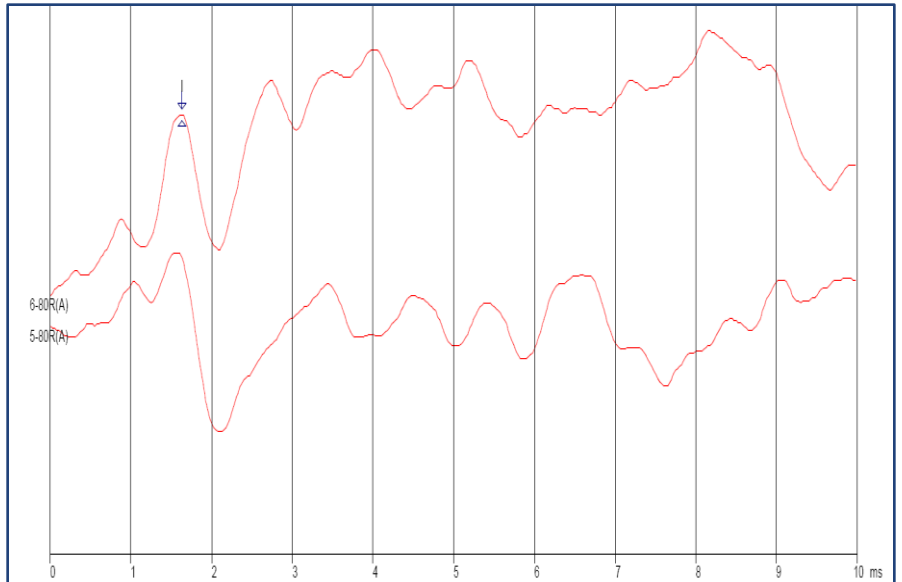


Neurological Disorders

- Abnormal/absent ABRs
- Cognitive Impairment
- Behavioral testing impossible or unreliable

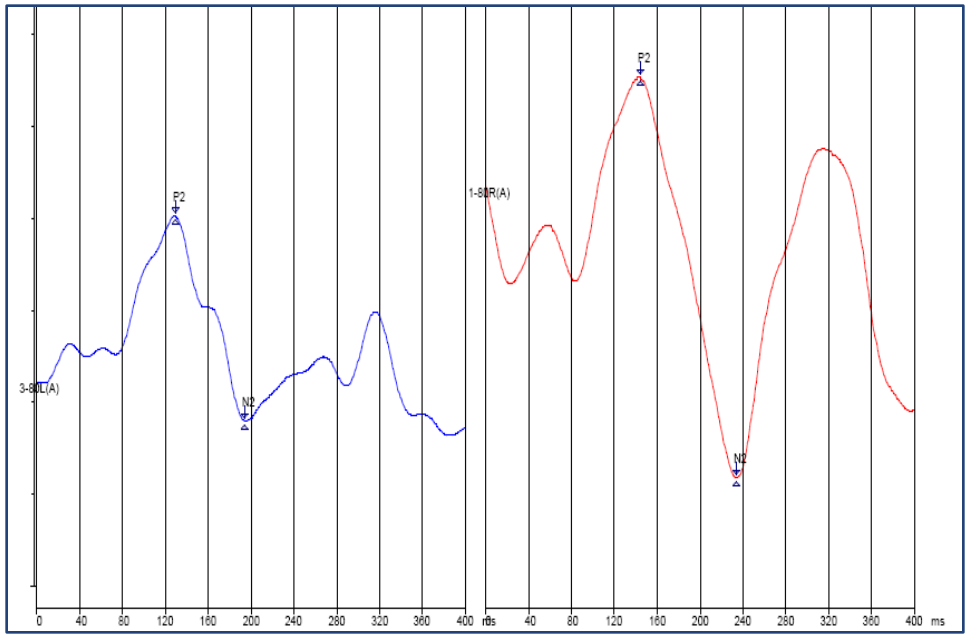
Neurological Disorders: Pelizaeus-Merzbacher Disease

- Characterized by defective central nervous system myelination: muscular hypotonia, nystagmus and delayed motor development. Speech and language development are also affected.
- Wave I is usually present in these patients, but its latency can be mildly delayed. Wave II can be present in some instances although it is usually poorly defined. Waves III and V are absent.
- ABR abnormalities increase with progression of the disease.



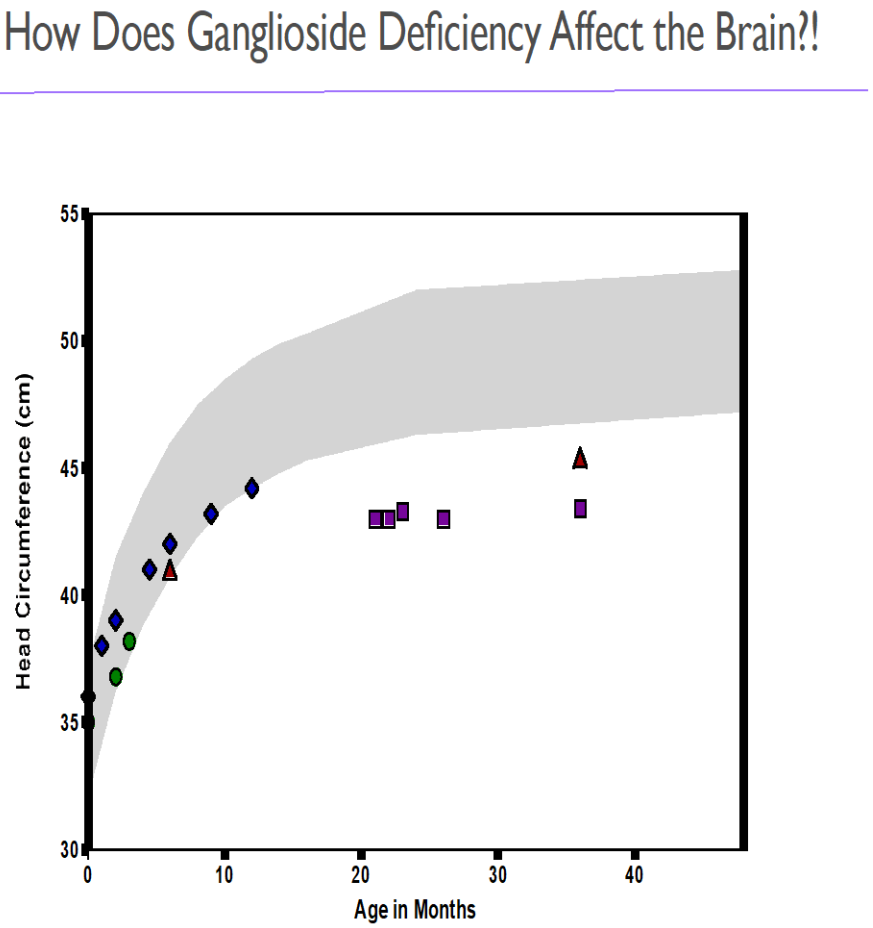
PMD

- PMD patients present with a central type of auditory neuropathy and their hearing behavior resembles those of patients with auditory neuropathy who are on the bright side of the spectrum.
- Because CAEP are present in many patients with PMD, they seem to be a better clinical tool than ABRs to assess the hearing function and manage these patients.

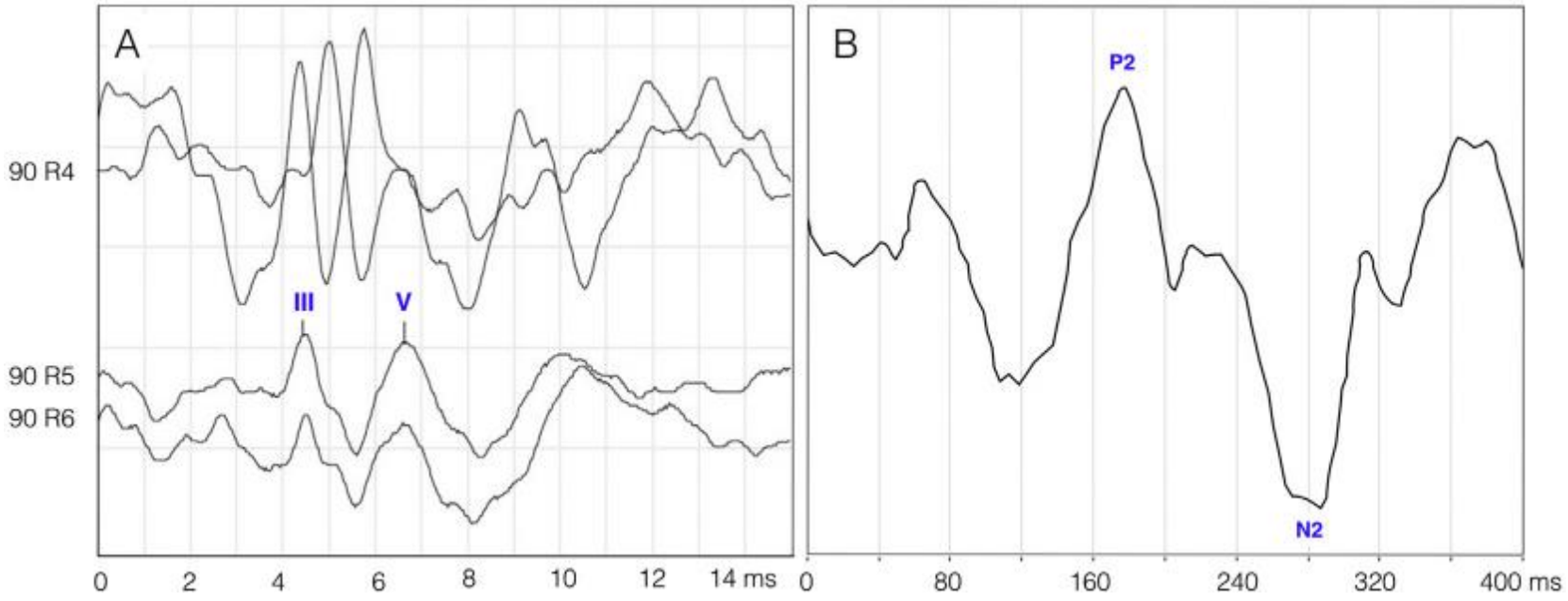


GM3

- Cerebral gangliosides influence neuron proliferation, dendrite elaboration, synapse formation, axon growth and myelination, protein localization, etc., and are therefore vital to normal brain development and function.
- Loss-of- function mutations of GM3 synthase cause systemic ganglioside deficiency and are associated with infantile-onset epileptic encephalopathy, slow brain growth, stagnant psycho- motor development, growth failure, blindness, dyspigmentation and deafness.



GM3


A
B
90 R4
90 R5
90 R6
III
V
P2
N2
0
2
4
6
8
10
12
14 ms
0
80
160
240
320
400 ms

Implications for Language Development

Sound, Brain, and Speech: Linking Auditory Input to Language Outcomes

- Longitudinal data on hearing loss and language acquisition

Neuroplasticity and critical intervention windows

- Impact of auditory deprivation on cortical language networks

Intervention Strategies and Tailored Care

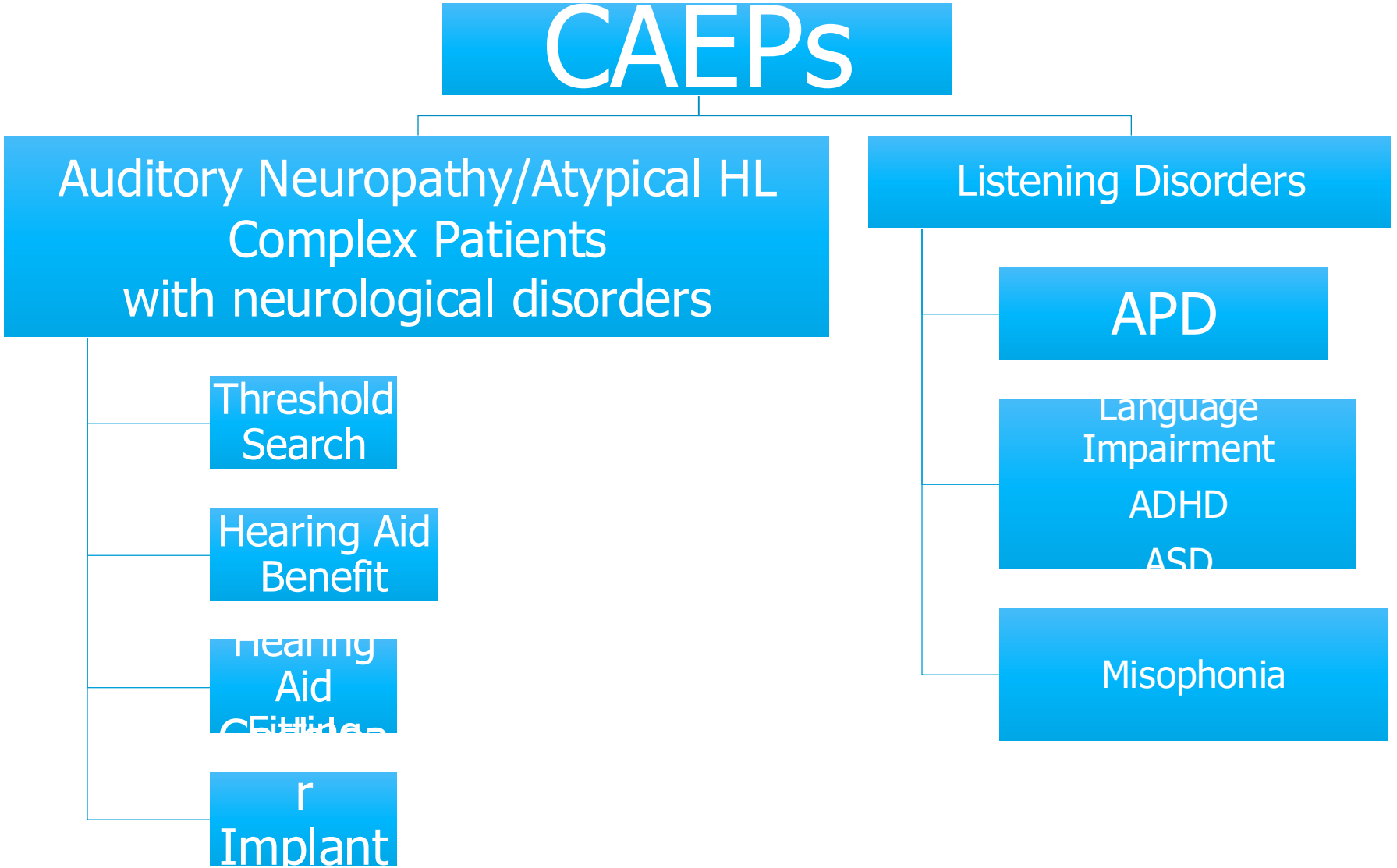
Precision Audiology: Informing Intervention Through Neurophysiological Insight

- Evaluating hearing aid benefit with cortical responses
- Cochlear implants and electrophysiological monitoring
- Auditory training and language therapy post-intervention
- Family-centered care models and interdisciplinary coordination

Limitations of Current Clinical Tests in Infants

- Main focus is on access to sounds (not how these are processed)
- An absent ABR does not necessarily indicate deafness (Auditory Neuropathy Spectrum Disorder):
  - Some patients who have normal thresholds on pure tone audiometry will have no recordable ABRs.
  - Some neurological disorders affect the pathways responsible for the ABRs but spare other auditory pathways that can mediate hearing.
  - In other patients, the response may be sufficiently desynchronized to render the ABR undetectable but still permit pure tone hearing.
- No information about central auditory processing.
- A normal ABR does not rule out deficits that may interfere with normal development of speech and language (Auditory Processing Disorder).
- Behavioral testing is extremely limited in infants and young children and difficult or even impossible to achieve in children with complex conditions.

Use of Cortical Auditory Evoked Potentials to Improve Diagnosis and Management of Pediatric Hearing Loss

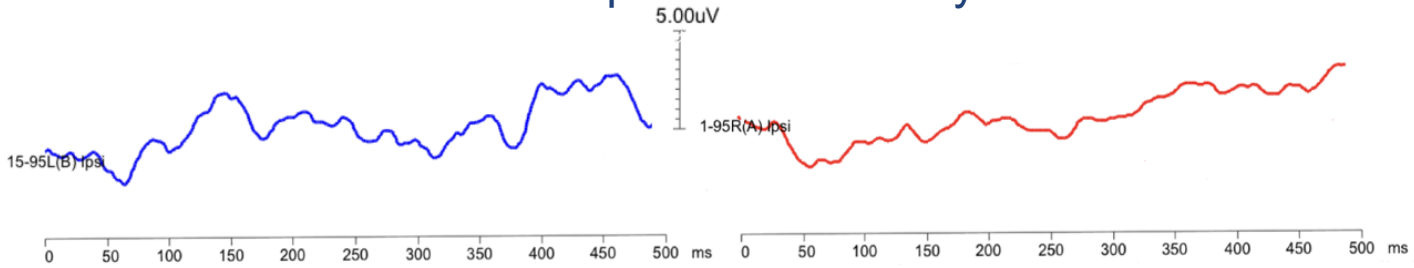


Evaluation of HA Benefit

Bilateral ANSD

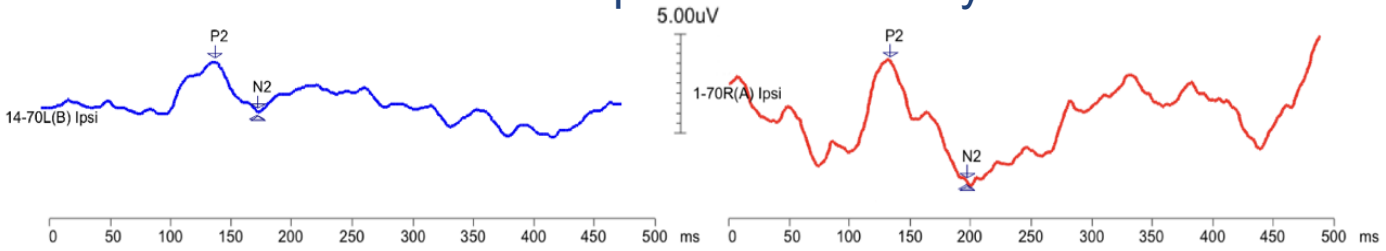
Unaided

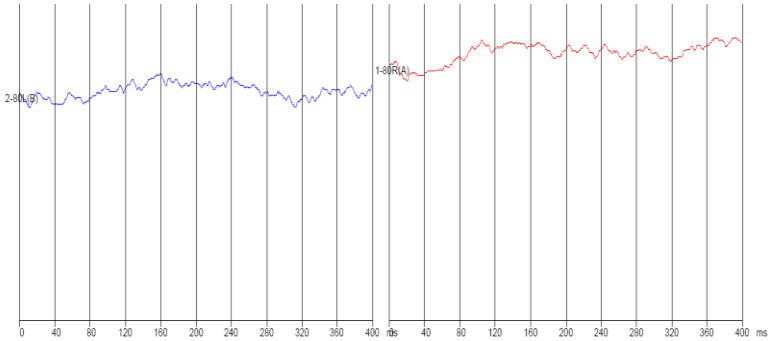
Absent responses bilaterally.



HA Aided

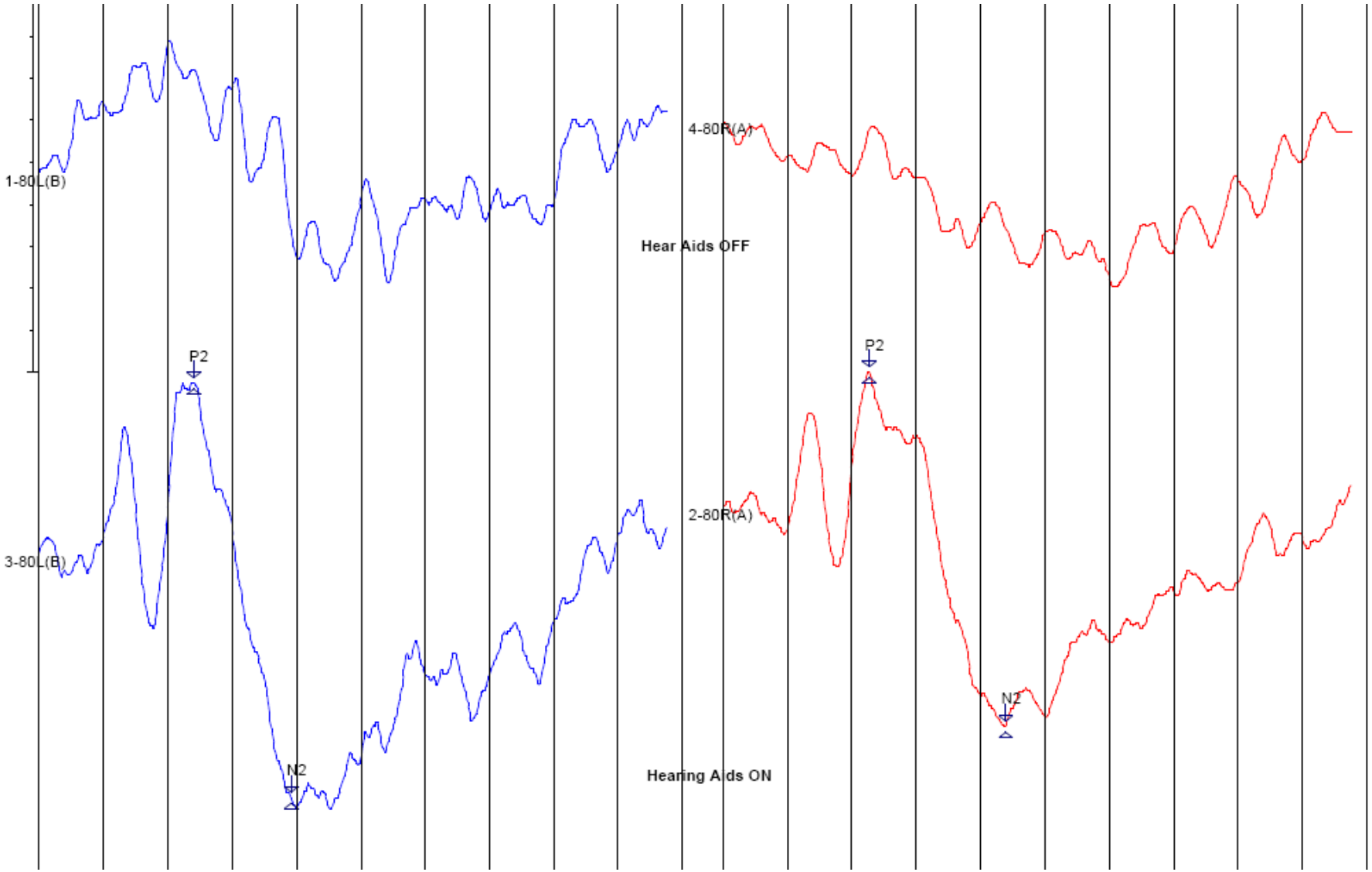
Present responses bilaterally.



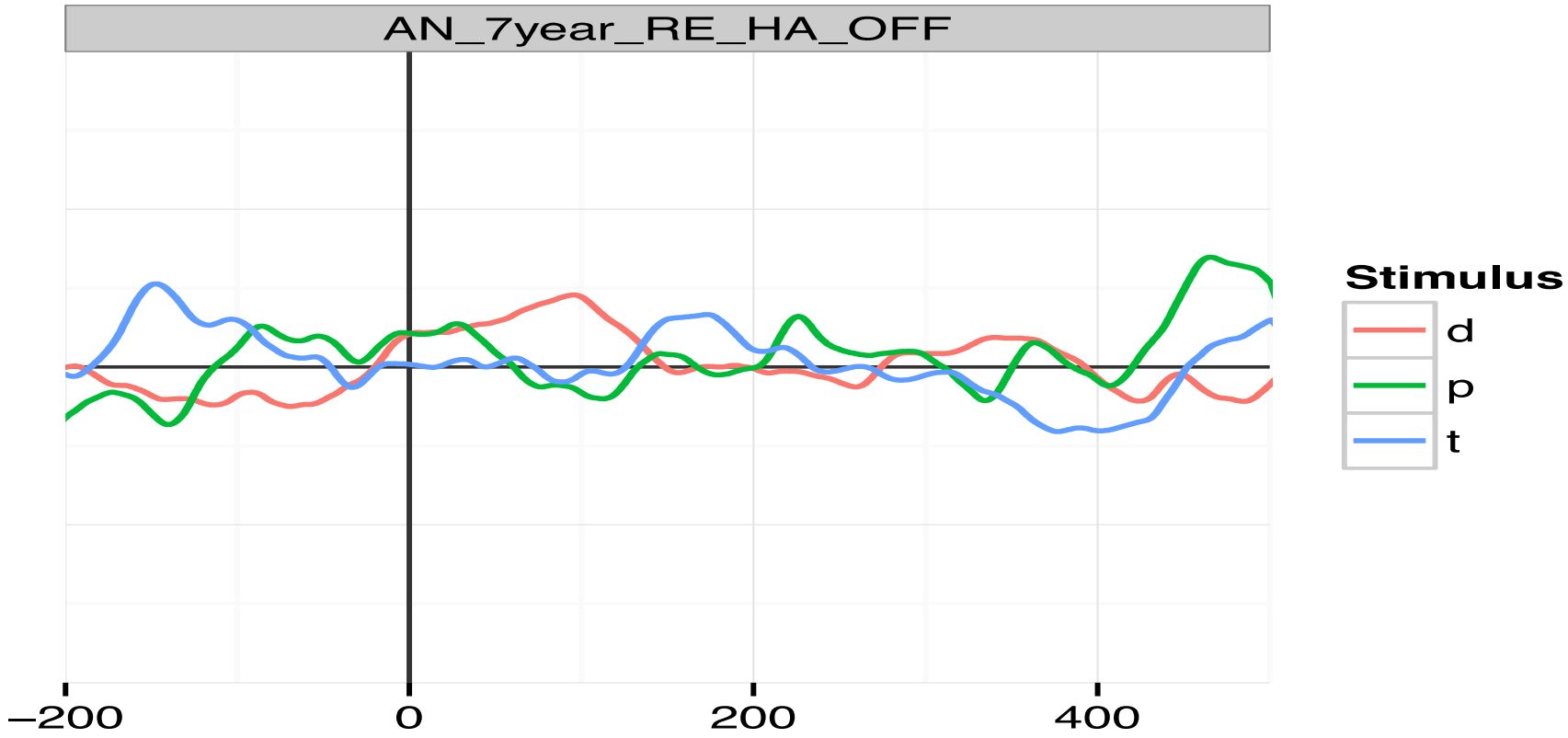


No HA benefit. Successful CI User

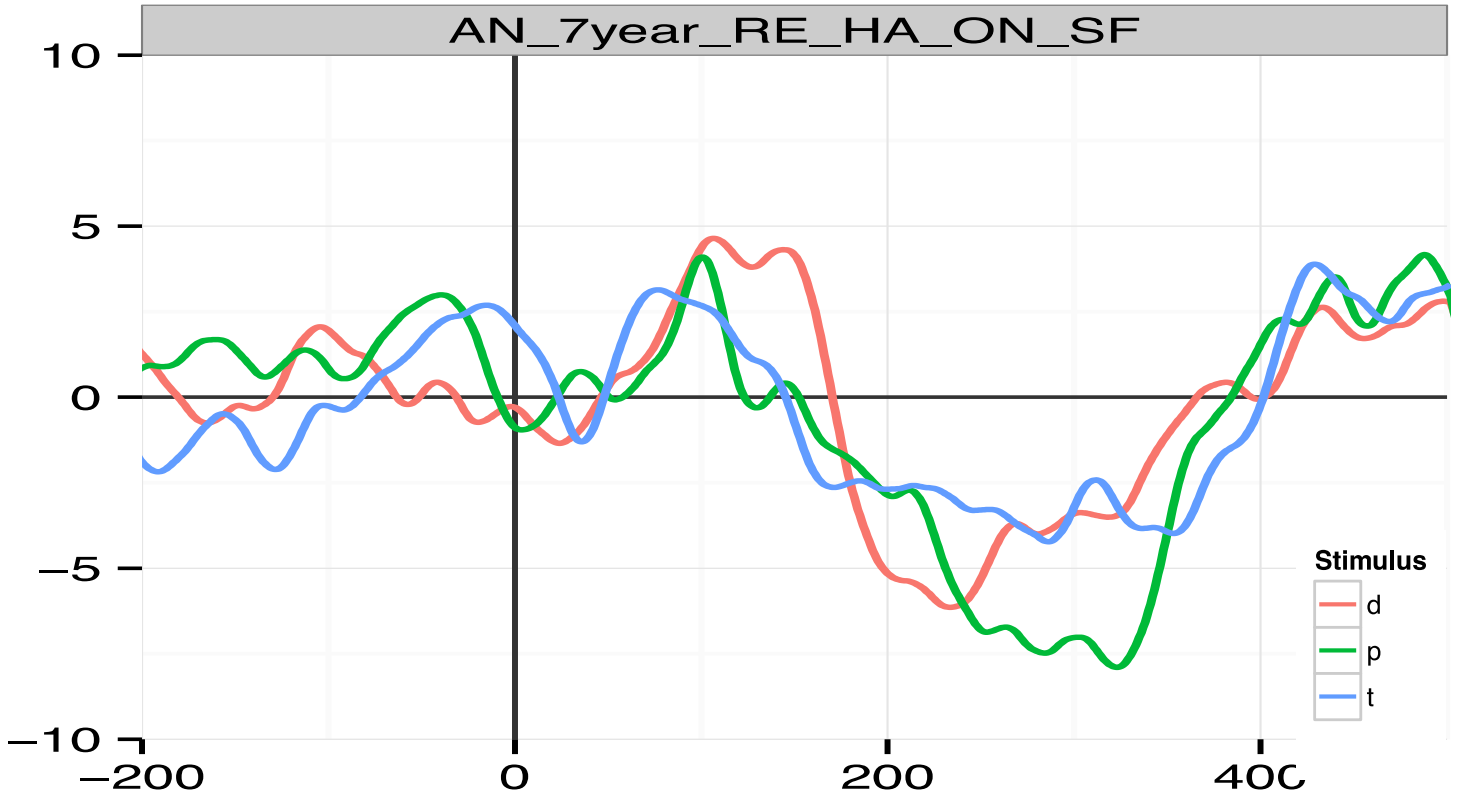
Measure of Hearing Aid Benefit



No speech discrimination in a child with Auditory Neuropathy



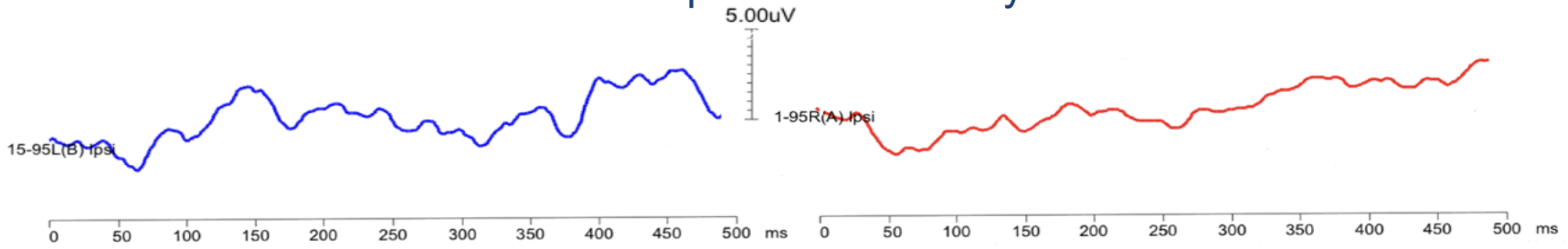
Benefit of HA in the same child



Bilateral ANSD

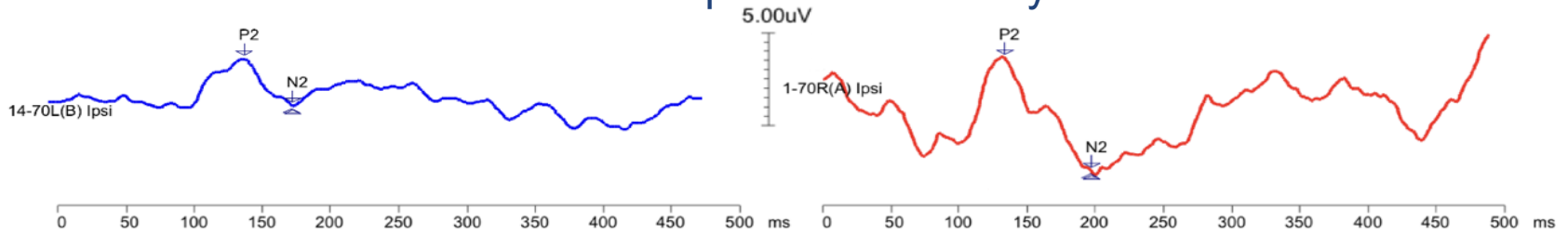
Unaided

Absent responses bilaterally.



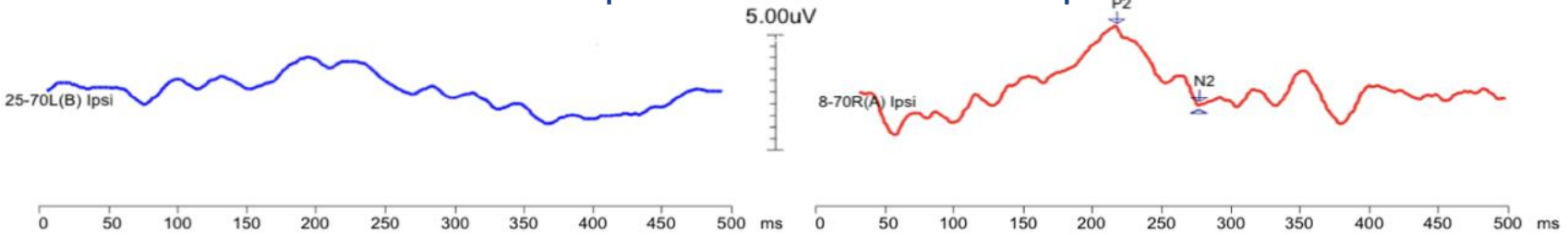
HA Aided

Present responses bilaterally.



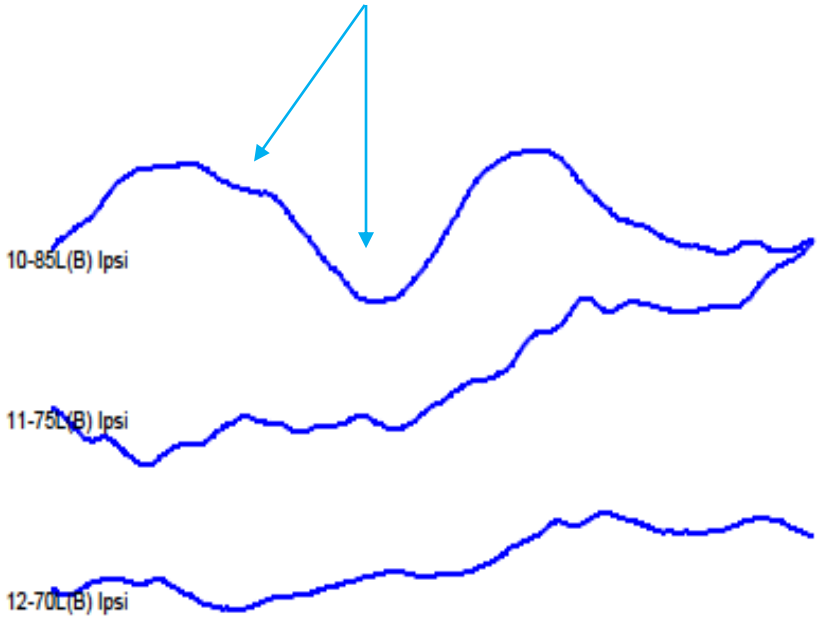
HA Aided with +10 dB SNR

LE: No response. RE: Present response.

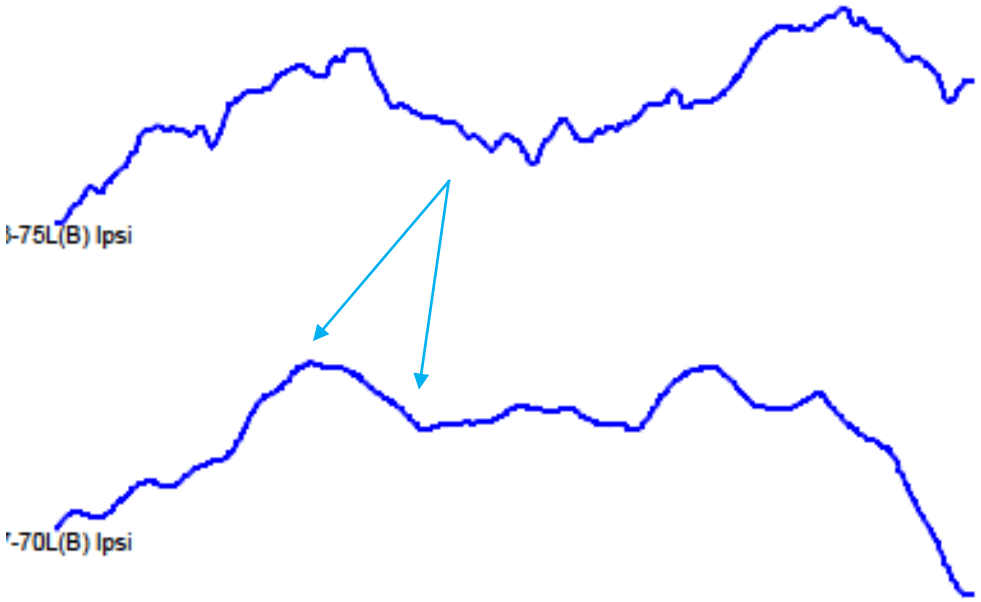


HA fitting with CAEP in absence of ABR

1st setting



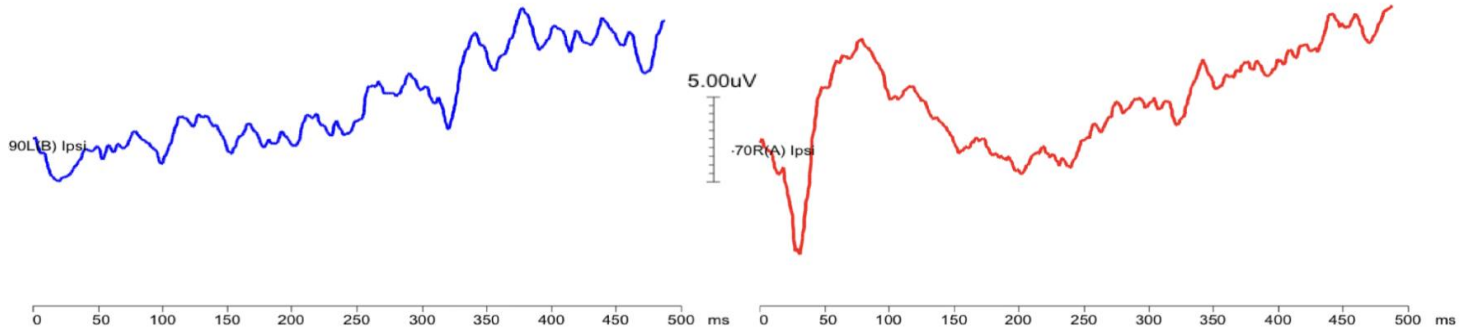
2nd setting



Bilateral ANSD

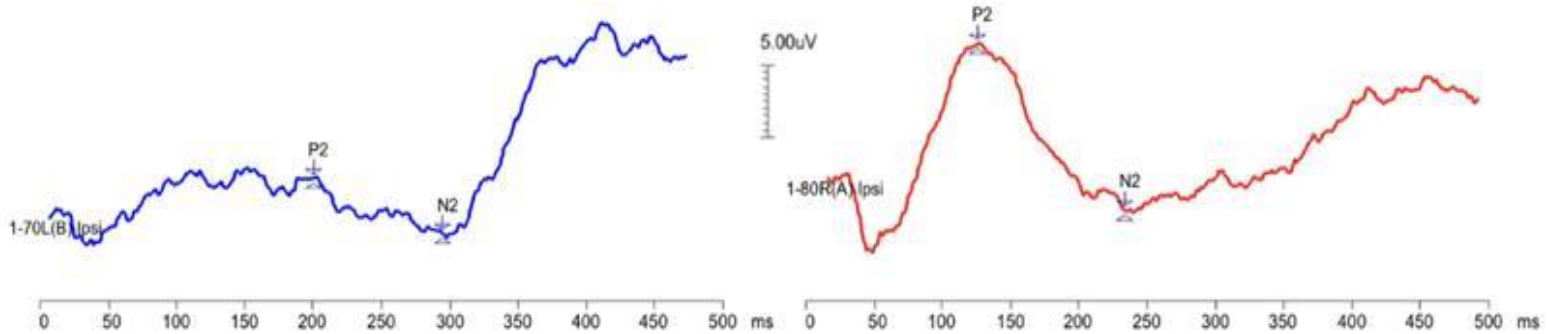
2a. LE: Unaided, RE: CI Aided

LE: Absent response. RE: Present response.

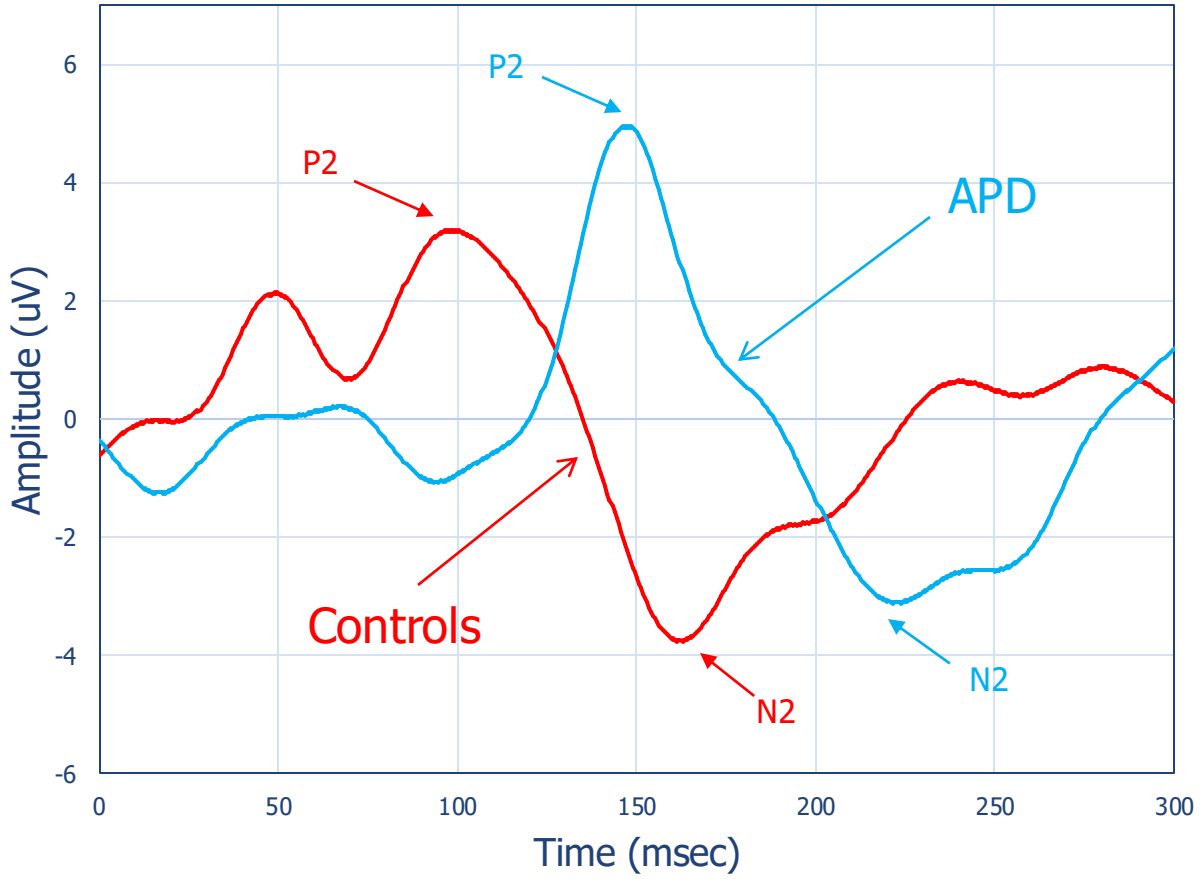


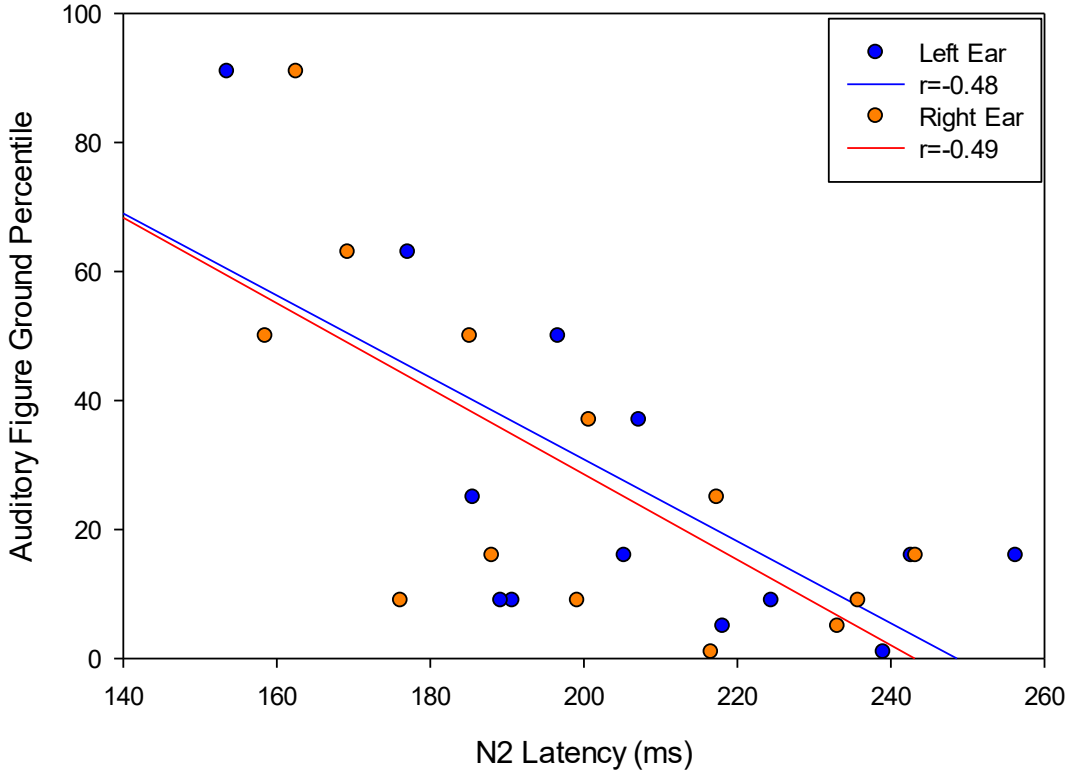
2b. CI Aided

Present responses bilaterally.



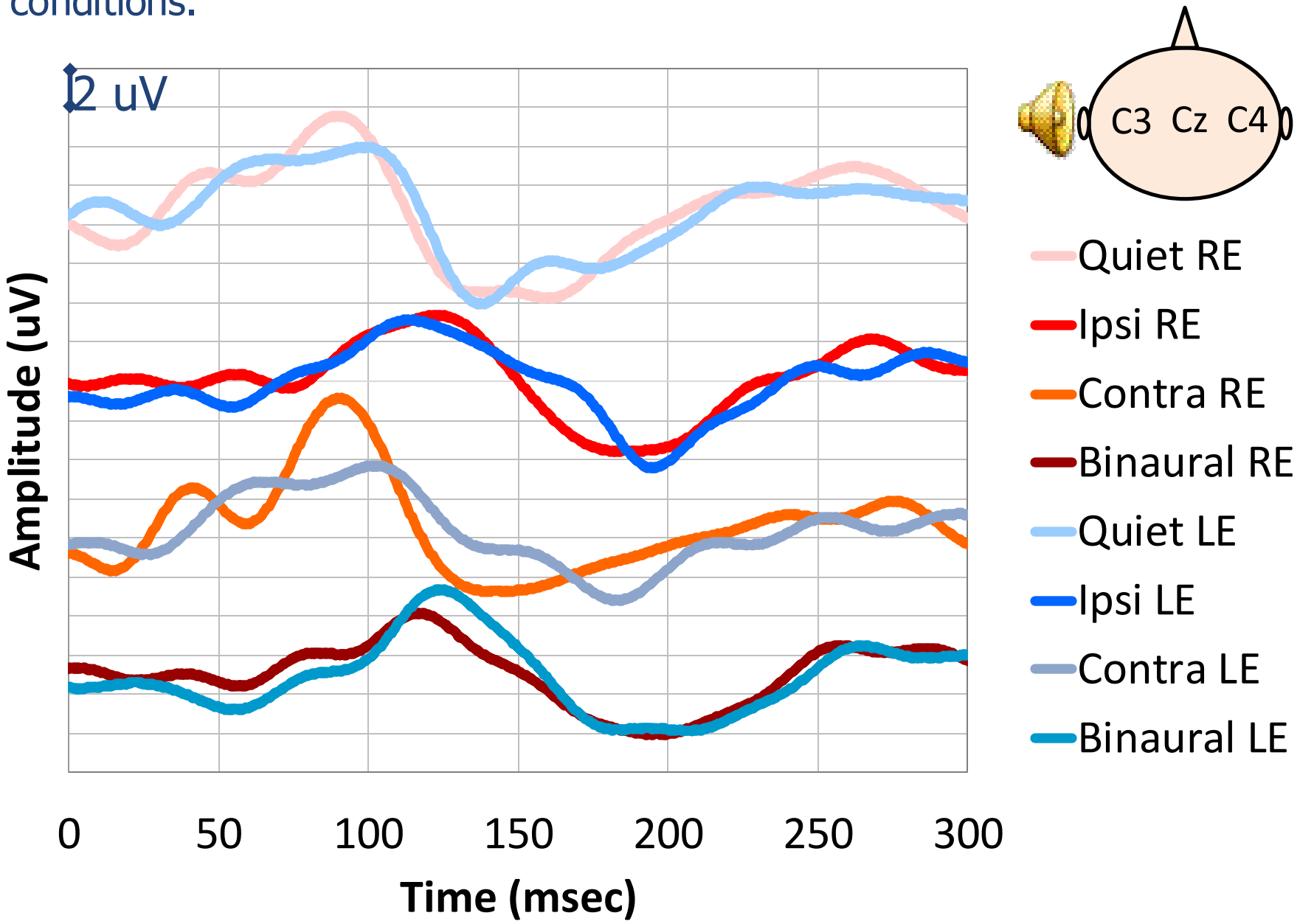
CAEPs in Children with Auditory Processing Disorder



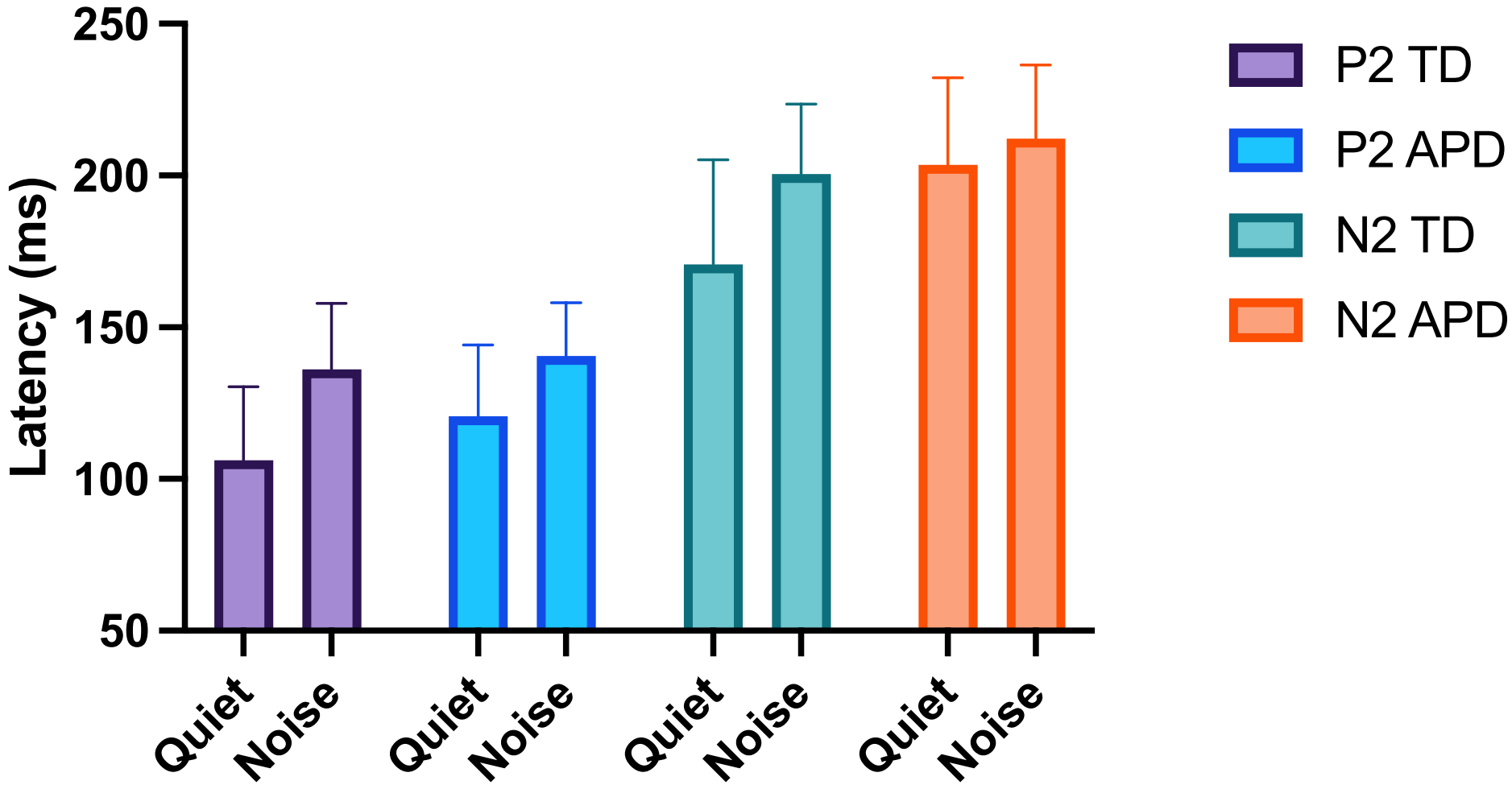


- Normal PTA, Present OAEs and ABR

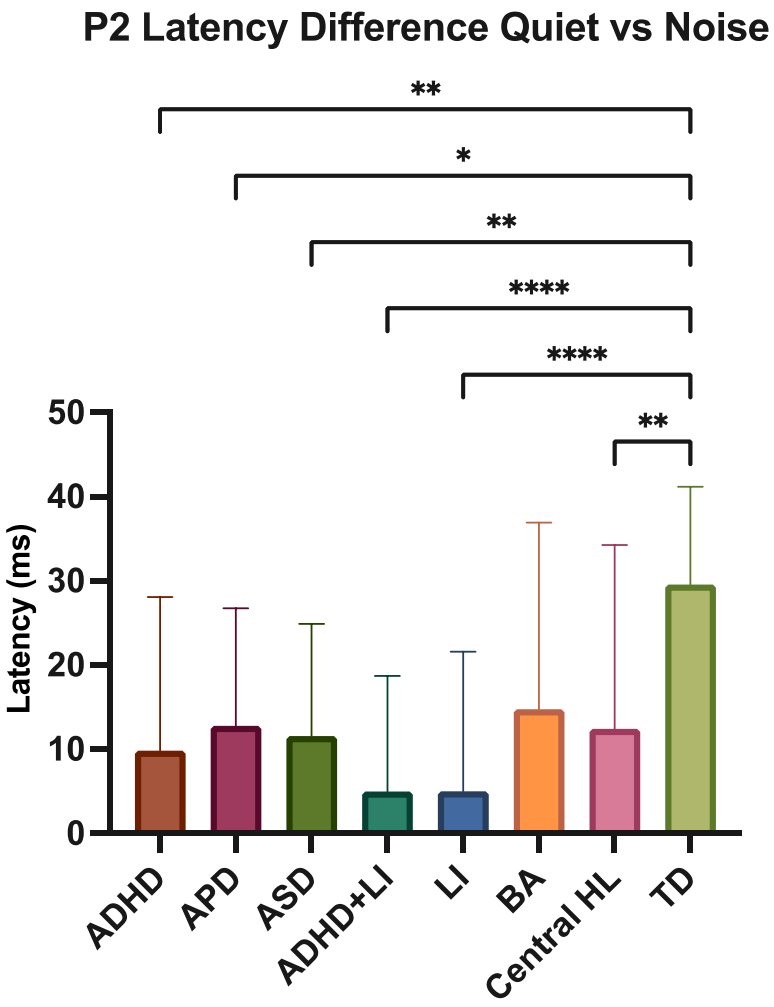
Examples of AEP waveforms recorded with /da/ in Quiet and Noise conditions.

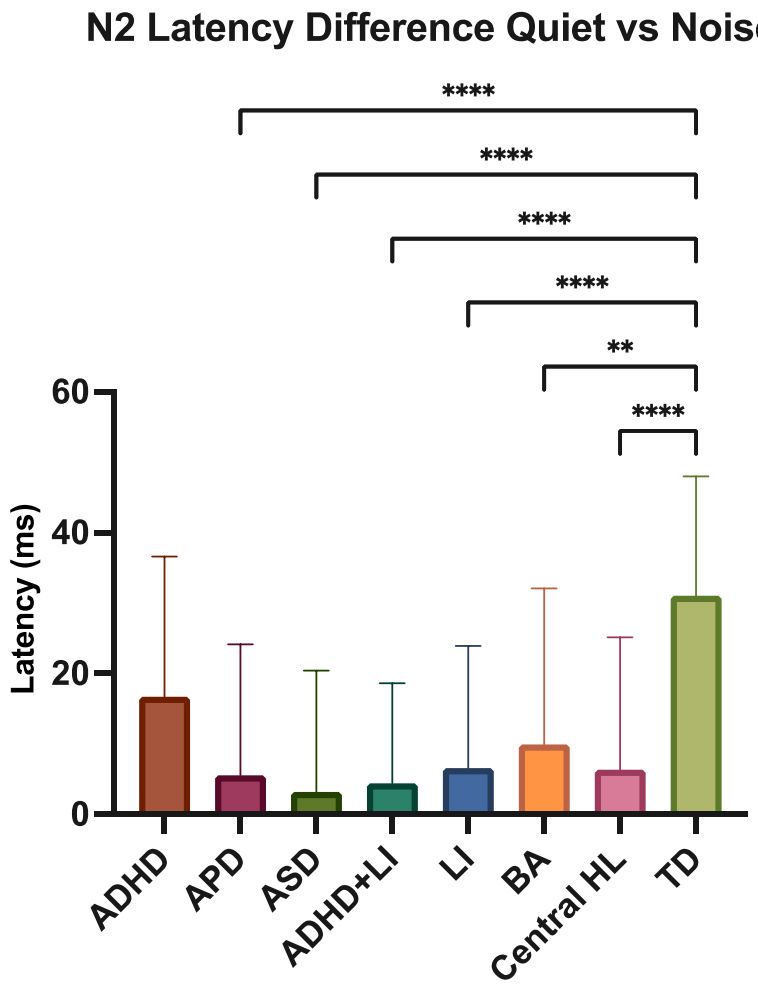


Noise effects on CAEPs in APD Children



CAEPs in Children with Listening Difficulties





Future Directions and Research Horizons

From Diagnosis to Precision Care

Objective electrophysiology is not just diagnostic

It guides:

- intervention timing,
- device selection,
- and language outcomes.

Beyond the Audiogram

- The audiogram tells us:

  “How loud must sound be?”

- Electrophysiology tells us:

  “How well is sound encoded by the brain?”

- Speech and language development depend on:
  - Temporal precision
  - Envelope tracking
  - Phoneme discrimination
  - Subcortical–cortical coupling

- Objective markers can help:

  Cochlear Implant candidates
- Assess neural survival
- Predict speech outcomes
- Monitor cortical maturation post-implant

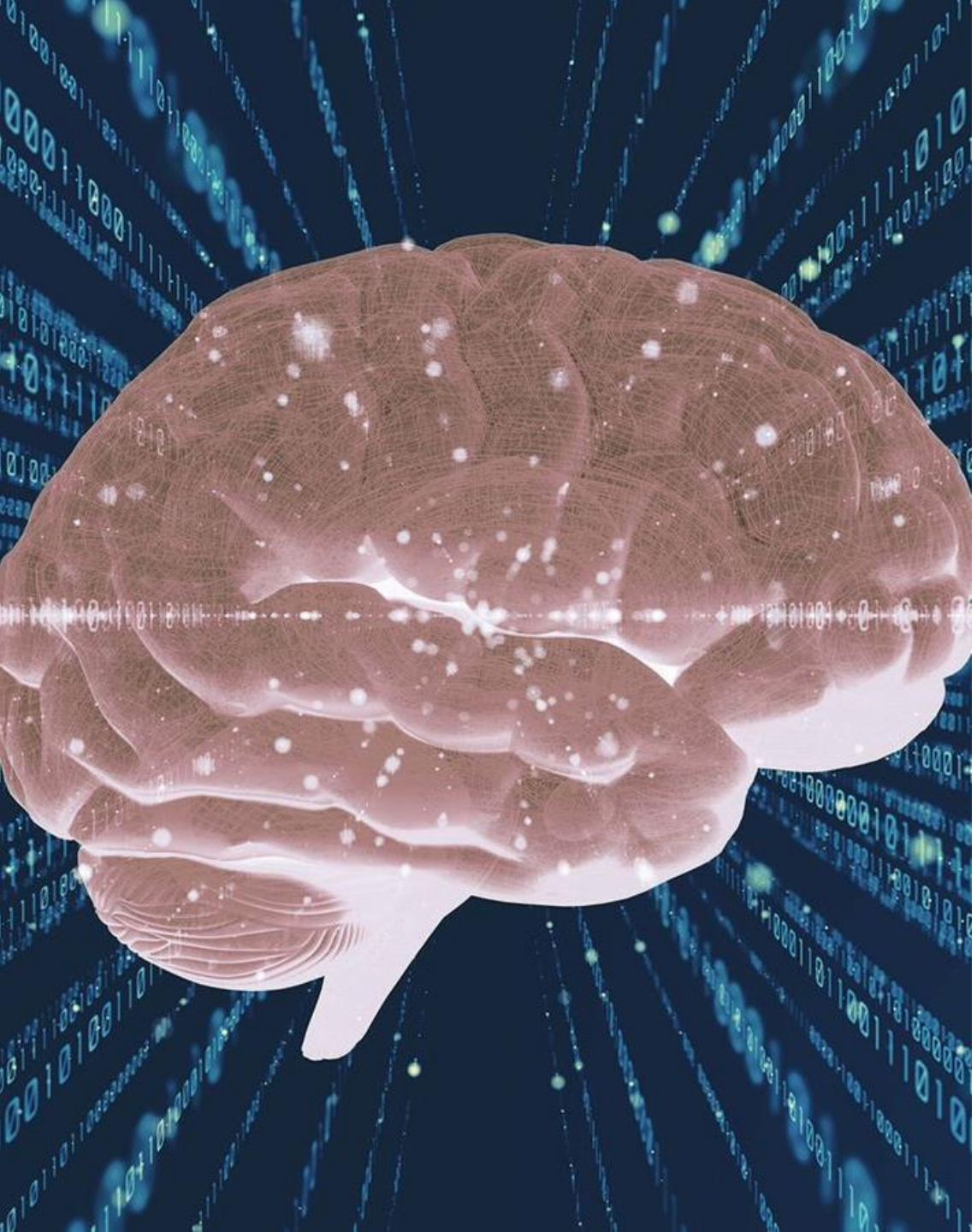
  BAHA / Bone Conduction Devices
- Track restoration of binaural timing
- Assess cortical rebalancing in unilateral loss

  Hearing Aids
- Evaluate speech-in-noise encoding
- Identify central processing vulnerabilities

Guiding Rehabilitation Strategies

The Next Frontier: Mapping Subcortical and Cortical Speech Encoding

- https://moshmem
  m/mosh-
  showtimes/space-t
  new-frontier-2d/



Toward Brain-Based Personalization of Pediatric Hearing Rehabilitation


MEMPHIS