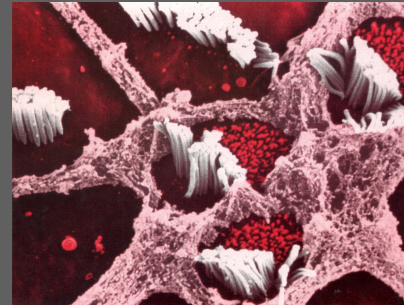


IPOACUSIA CORRELATA ALL'ETÀ (PRESBIACUSIA)

Francesco Fiorino



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Ospedale “Mater Salutis” Legnago (VR
AULSS9 - Scaligera*

PRESBIACUSIA

Progressiva perdita della funzione uditiva, bilaterale e simmetrica, causata dai cambiamenti degenerativi legati all'età



PRESBIACUSIA

È difficile distinguere il risultato
dell'invecchiamento vero e proprio
dall'accumulo di eventi avversi
intrinseci ed estrinseci



CAUSE “INTRINSECHE”

- Degenerazione “fisiologica”
- Fattori genetici
- Patologie (malattie cardiovascolari, diabete, etc.)

CAUSE “ESTRINSECHE”

- Fattori esogeni e ambientali ad effetto cumulativo (traumi acustici e fisici, agenti ototossici, fumo, etc.)

Interazioni difficili da quantificare
(organo bersaglio comune)



- Il 25-37% dei soggetti tra 60 e 70 anni presenta una significativa perdita uditiva in grado di influenzare negativamente le capacità di comunicazione verbale
- Tale percentuale aumenta al 40% nelle persone >75 anni e al 50% negli over80

Davis 1989; Ives et al 1995

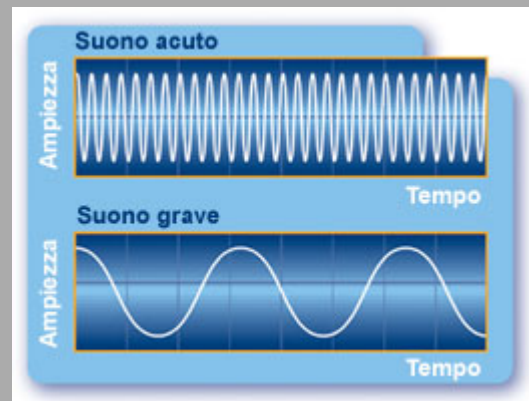
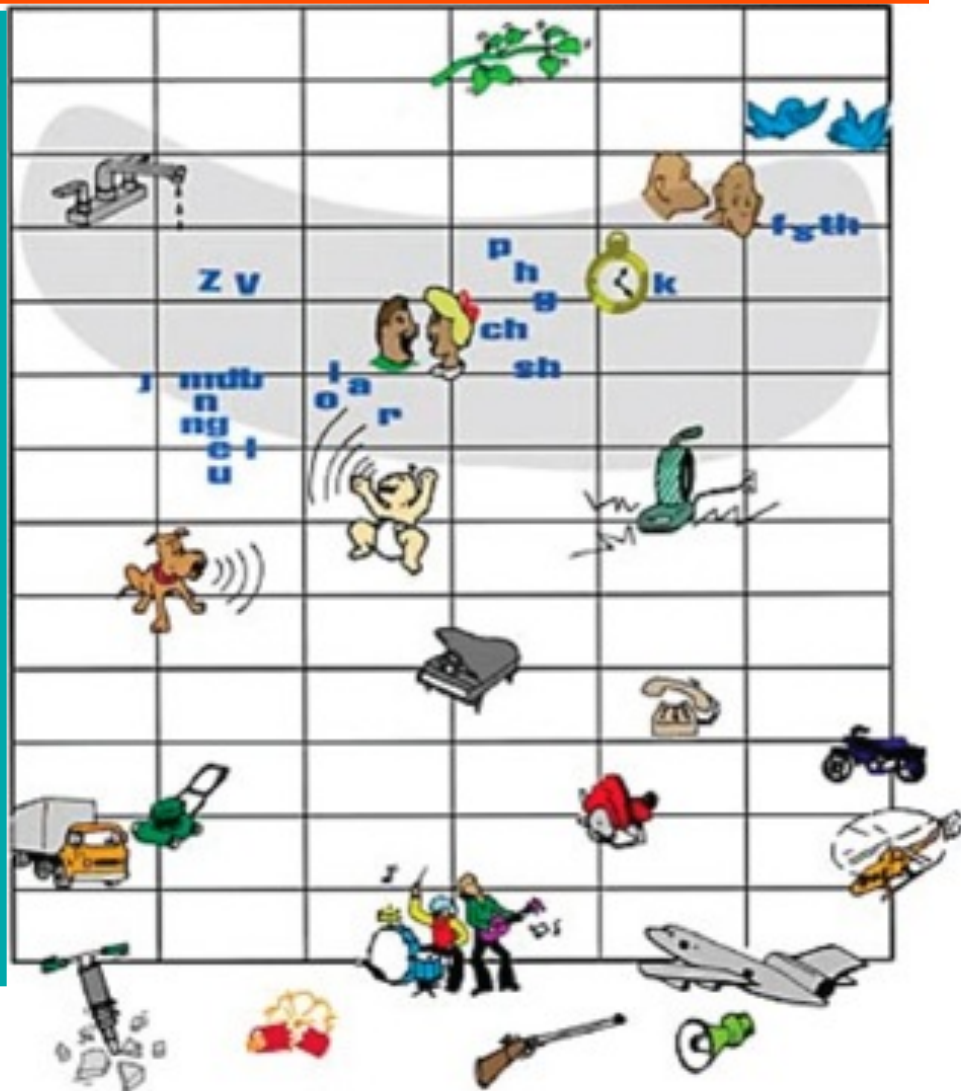
AUDIOGRAM OF FAMILIAR SOUNDS

FREQUENCY IN CYCLES PER SECOND (HZ)

125 250 500 1000 2000 4000 8000

HEARING LEVEL IN DECIBELS (dB)

0
10
20
30
40
50
60
70
80
90
100
110
120



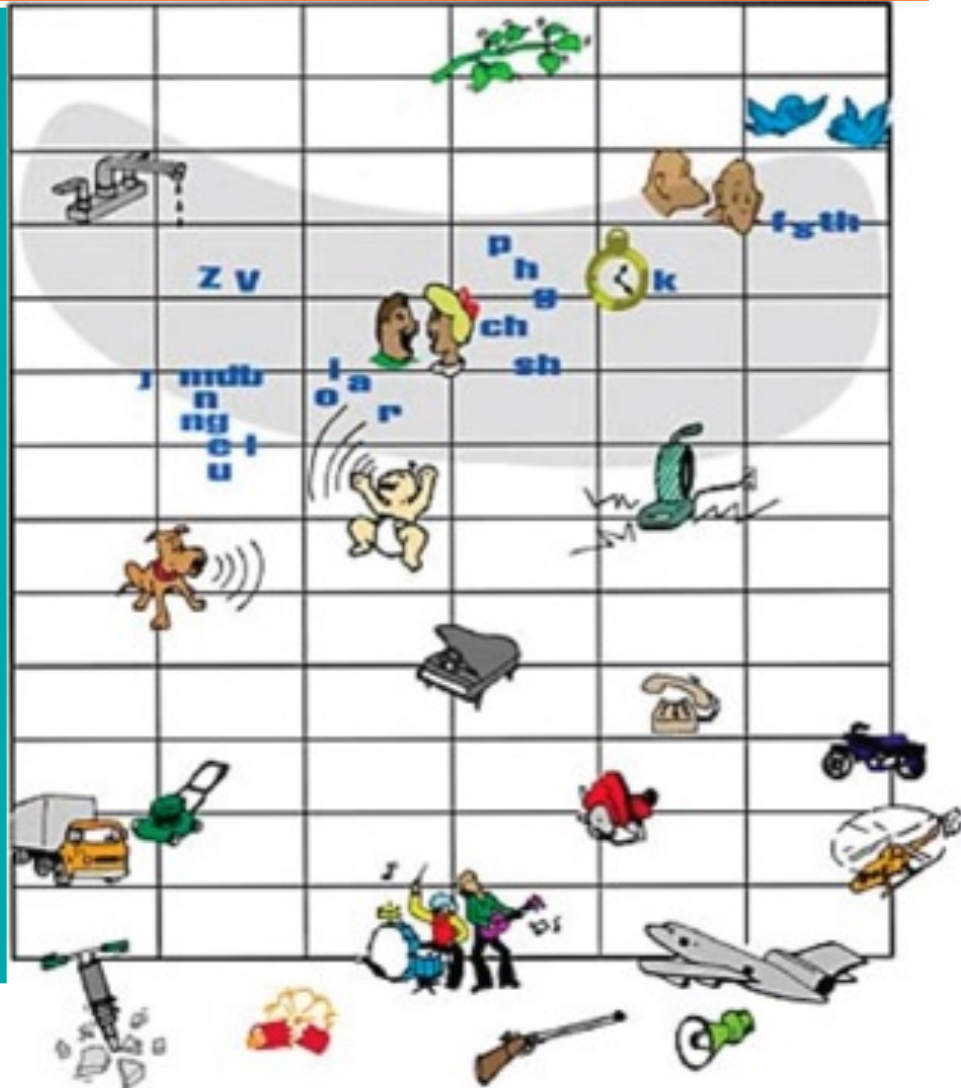
AUDIOGRAM OF FAMILIAR SOUNDS

FREQUENCY IN CYCLES PER SECOND (HZ)

125 250 500 1000 2000 4000 8000

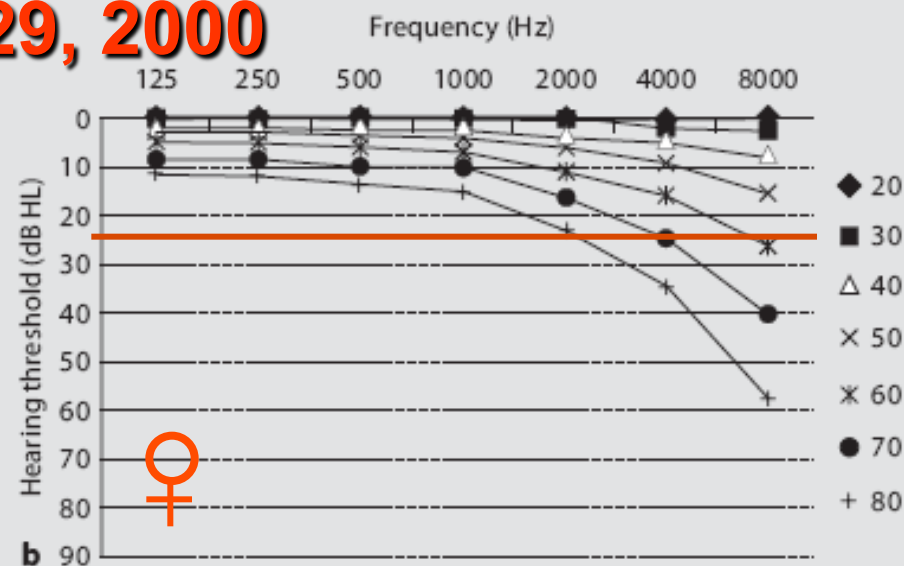
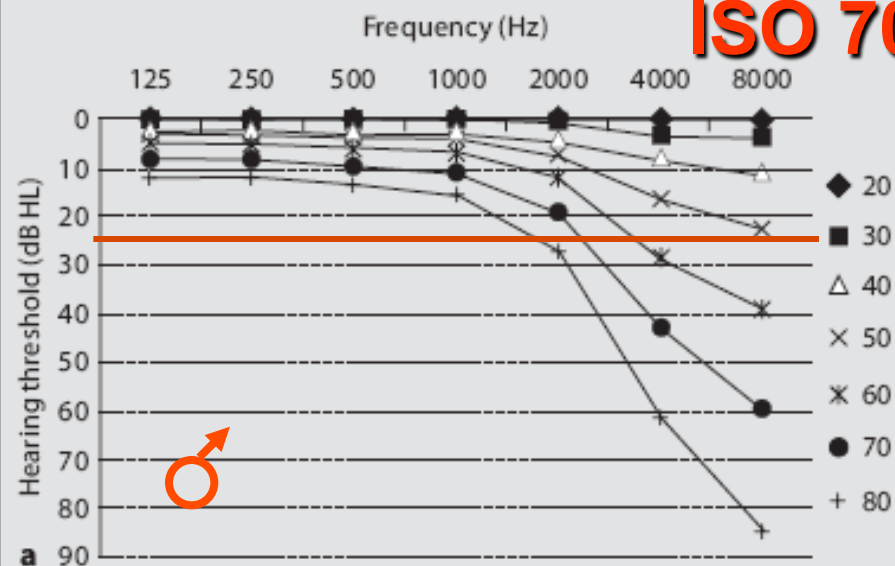
HEARING LEVEL IN DECIBELS (dB)

0
10
20
30
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120

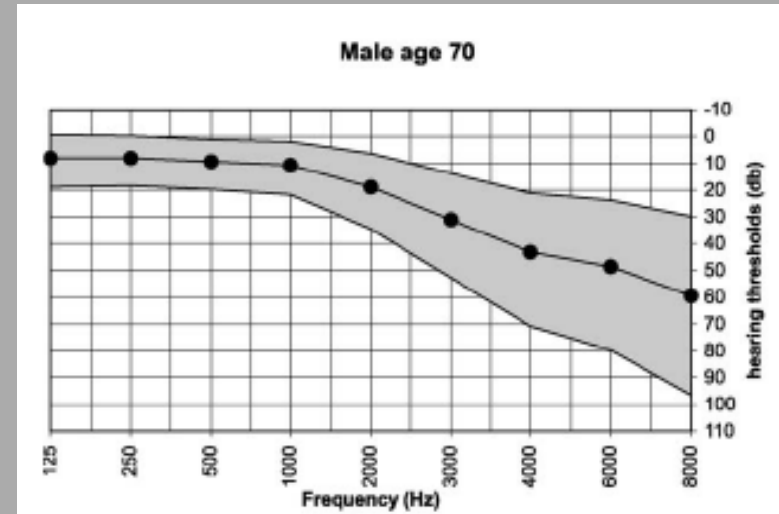
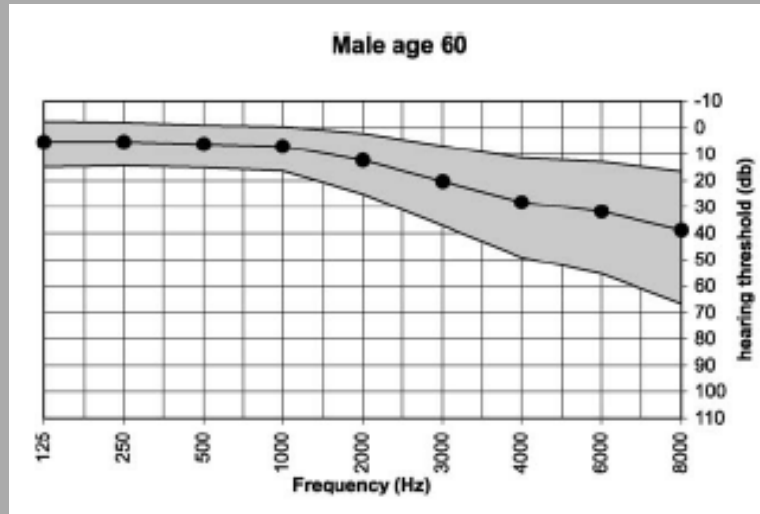


Quando inizia ?

ISO 7029, 2000



Variabilità

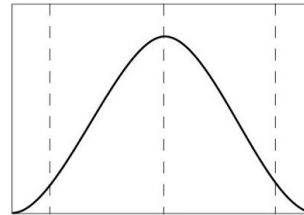


ISO 7029, 2000

A 60 anni

✓ 10% soglia < 10 dB

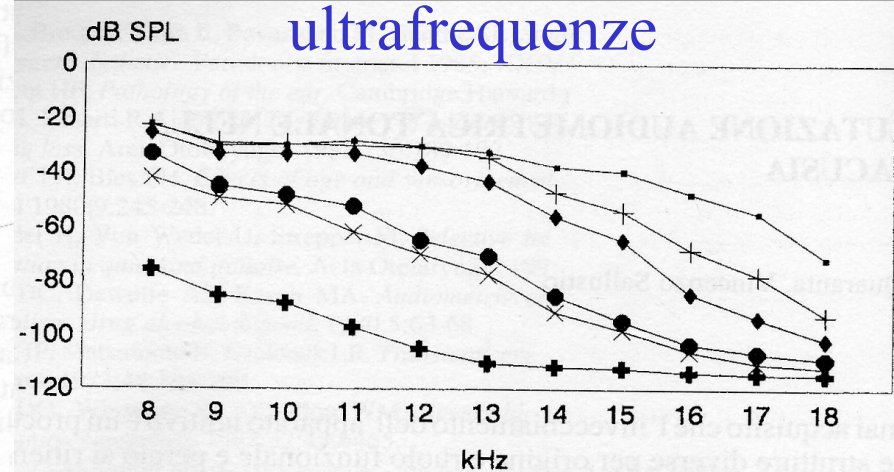
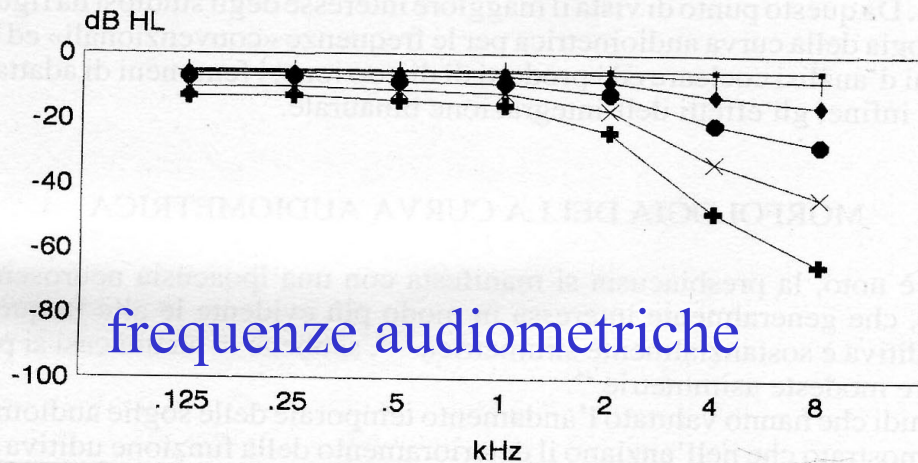
✓ 10% soglia a 55-75 dB



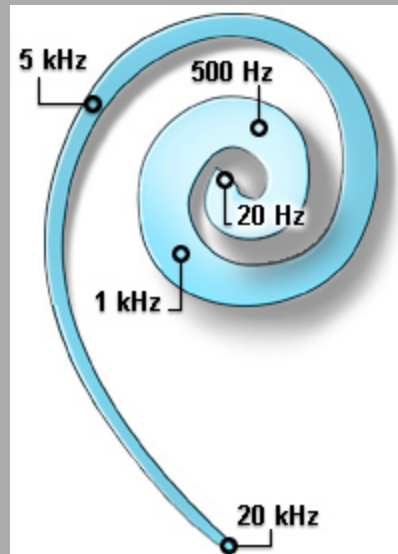
La variabilità è direttamente proporzionale alla frequenza (Hz) e all'età

Quando inizia ?

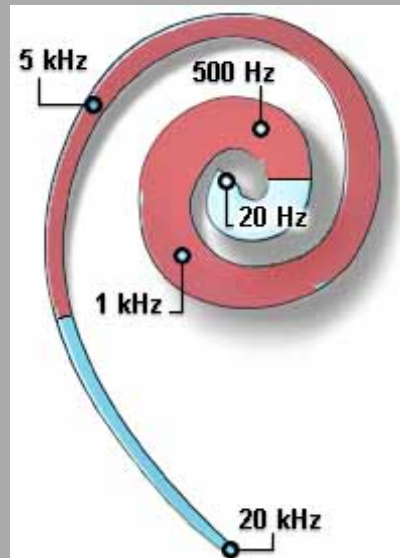
Il deterioramento della funzione uditiva inizia a partire dalla III decade con l'innalzamento di soglia per le frequenze >15-17 kHz



Sensibilità in frequenza: 20 – 20.000 Hz



Sensibilità in frequenza: 20 – 20.000 Hz

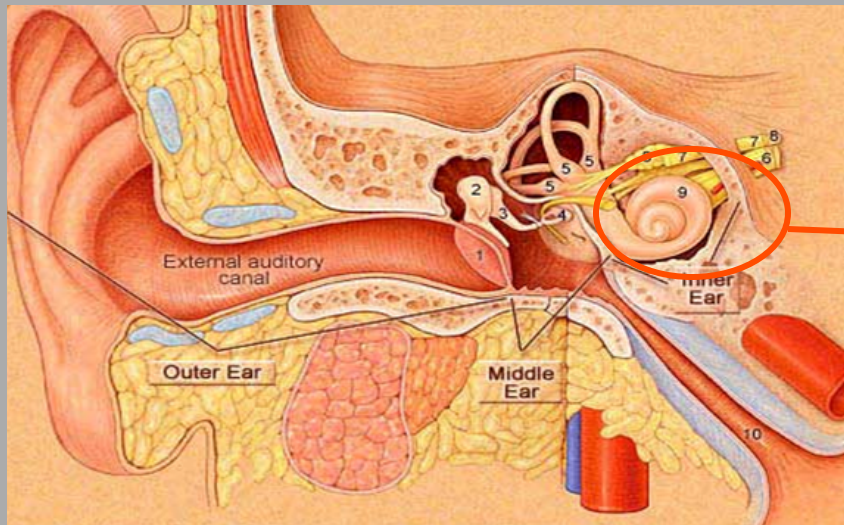


Frequenze audiometriche: 250 – 8.000 Hz

Dov'è localizzato il danno ?



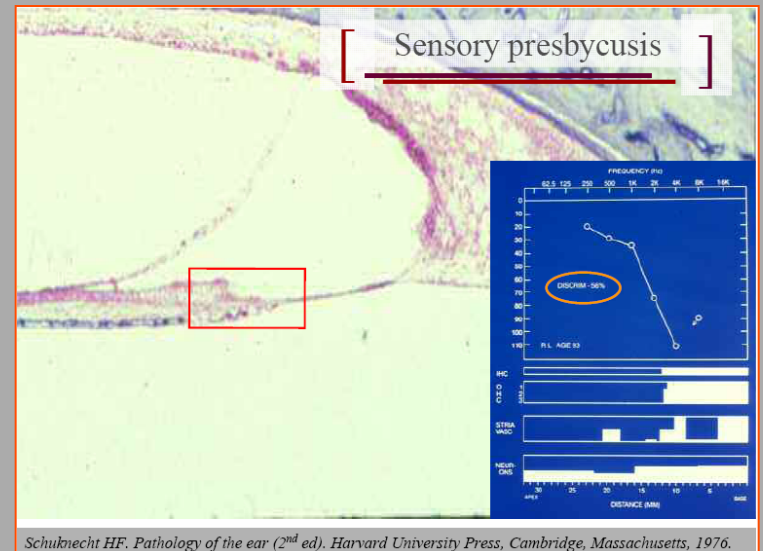
Nella coclea



Dov'è localizzato il danno ?

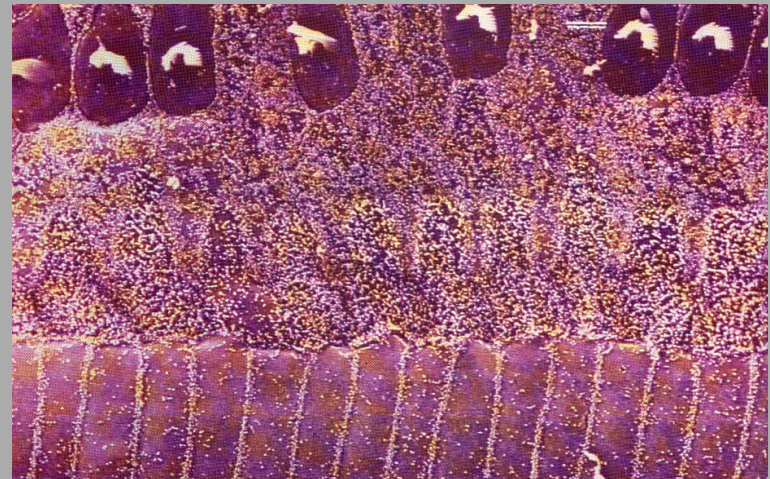
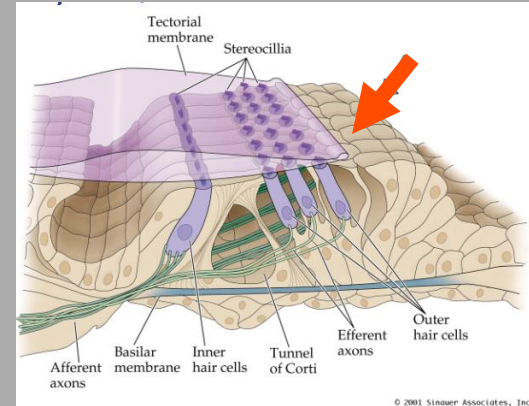
Presbiacusia

- Sensoriale
- Neurale
- Metabolica



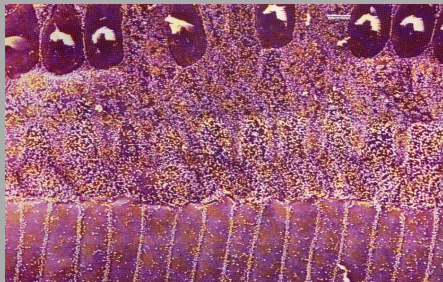
Presbiacusia Sensoriale

- Le alterazioni morfologiche sono a carico delle cellule sensoriali ciliate (perenni)



Presbiacusia Sensoriale

- Degenerazione della porzione basale dell'organo del Corti (specie le cellule ciliate esterne)



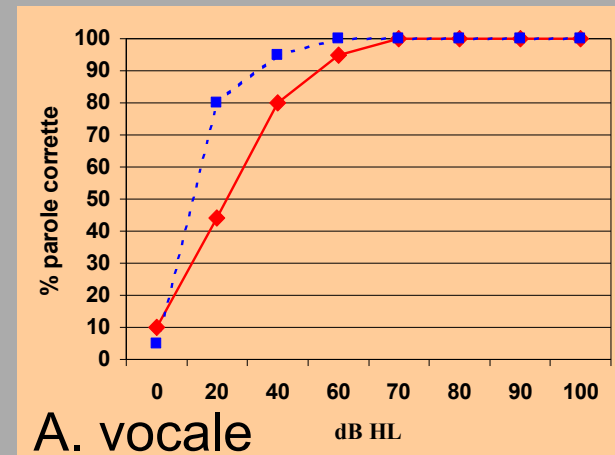
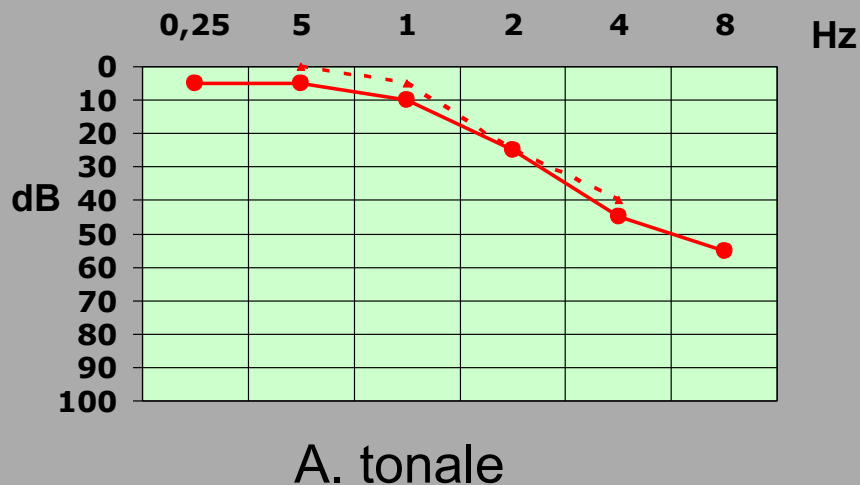
exaggerated basilar membrane width



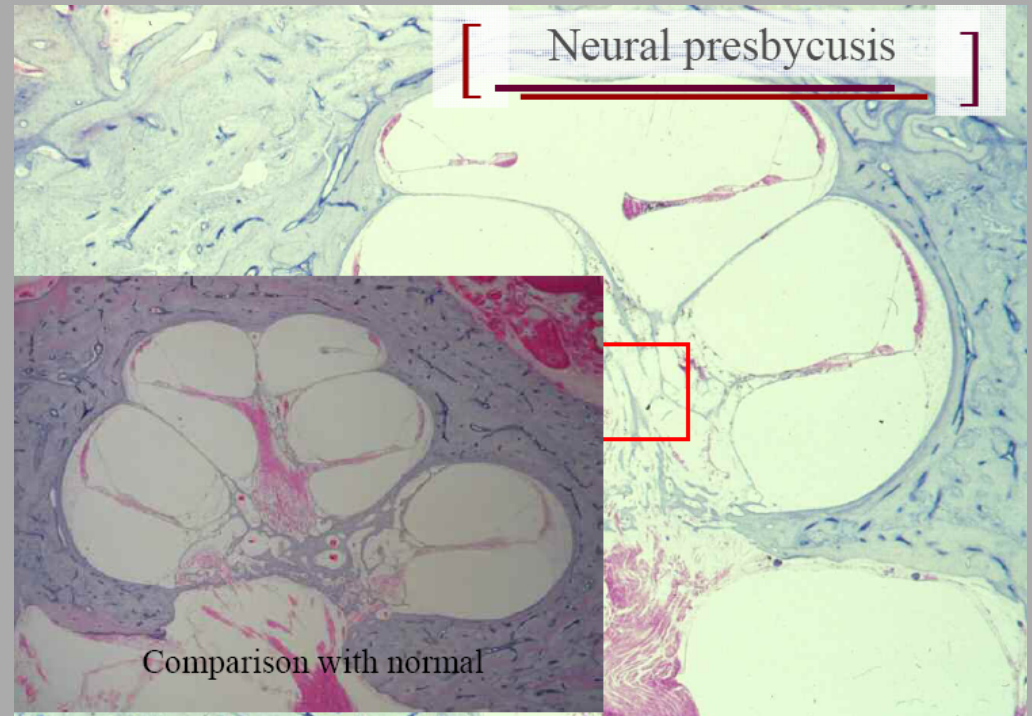
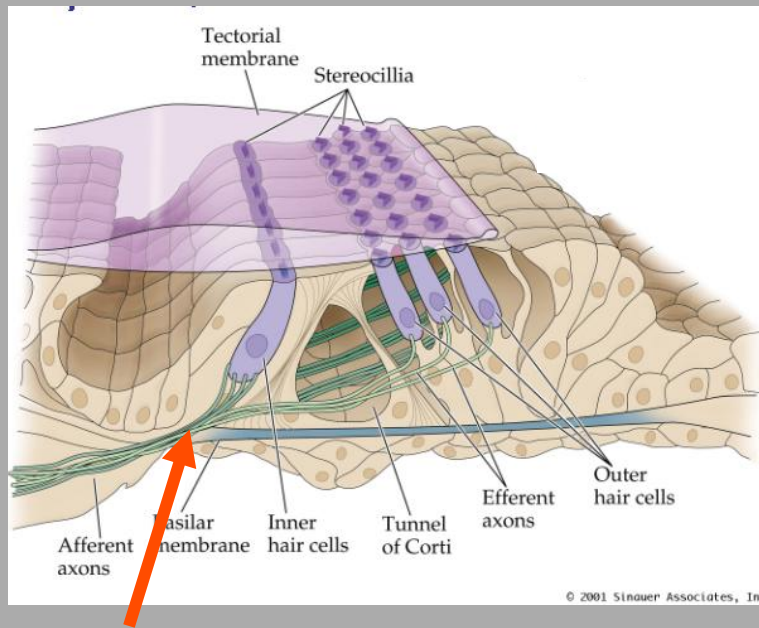
exaggerated basilar membrane width

Presbiacusia Sensoriale

- Degenerazione della porzione basale dell'organo del Corti (specie le cellule ciliate esterne)
- Ipoacusia neurosensoriale in discesa sulle alte frequenze
- Buona discriminazione vocale



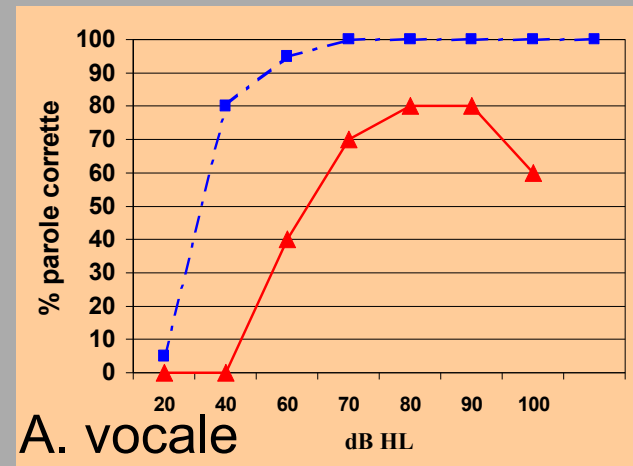
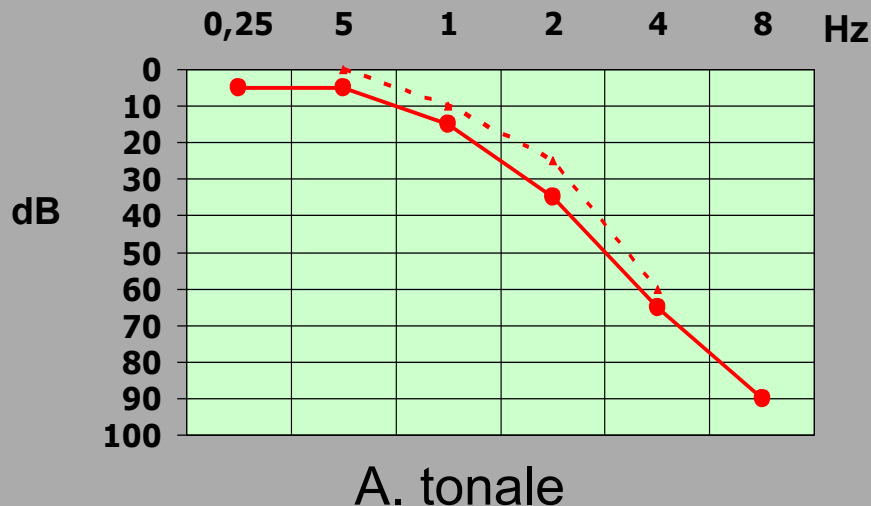
Presbiacusia Neurale



Schuknecht HF. Pathology of the ear (2nd ed). Harvard University Press, Cambridge, Massachusetts, 1976.

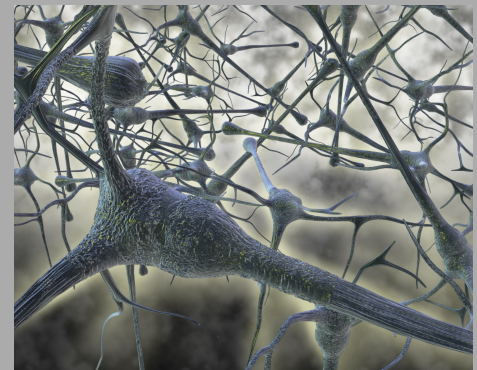
Presbiacusia Neurale

- Ipoacusia di differenti tipologie; frequente la “caduta” sui toni acuti
- Rapida progressione
- Alterata discriminazione vocale



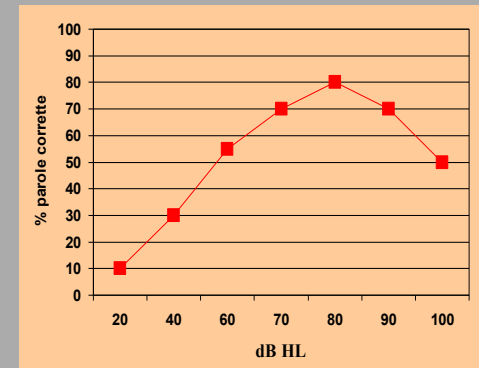
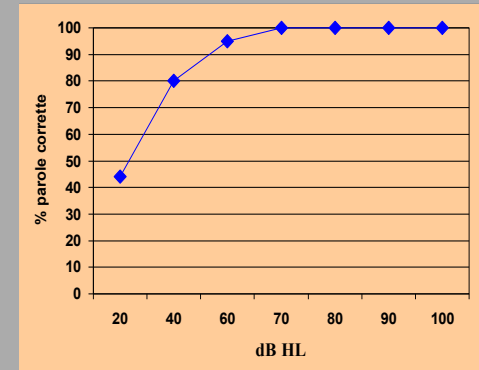
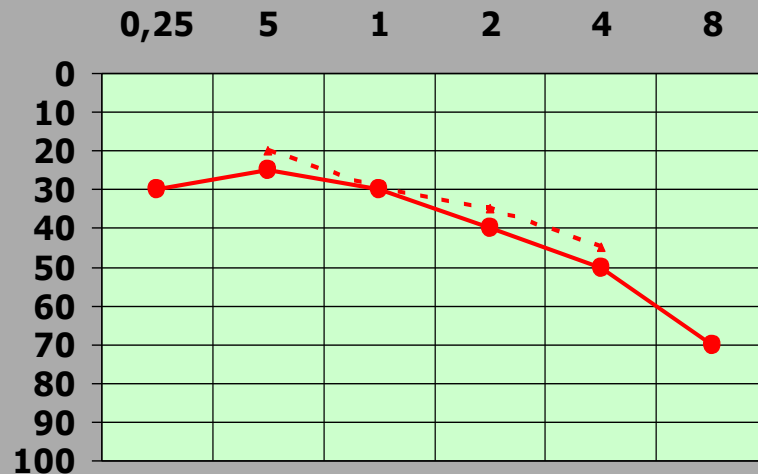
Presbiacusia Neurale

- Degenerazione gangliare (da ~40.000 nella I decade di vita a ~ 20.000 nella IX decade, *Otte et al, 1978*)
- Una perdita dei neuroni afferenti fino al 90% può avere effetti limitati sulla soglia tonale
- La discriminazione vocale è invece influenzata da perdite più contenute (~50%)



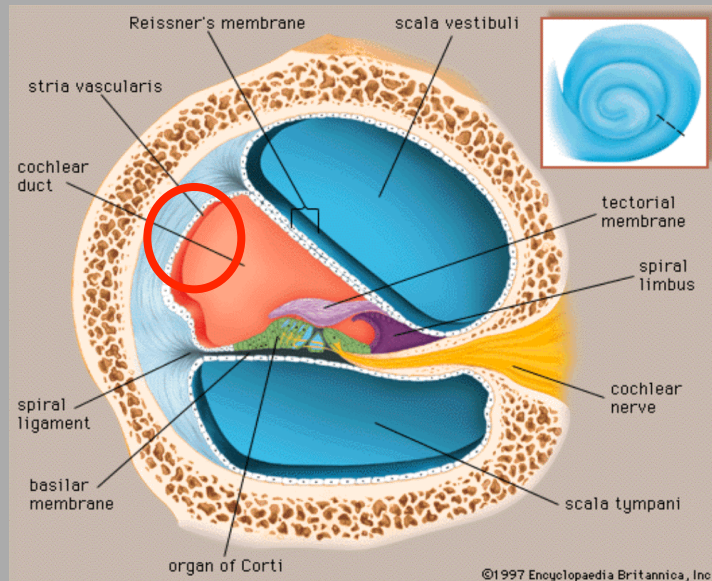
Presbiacusia Neurale

- L'audiogramma tonale non è quindi sufficiente a definire la capacità uditiva



Presbiacusia Metabolica

Alterazione della **stria vascolare**

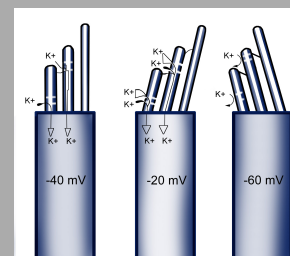
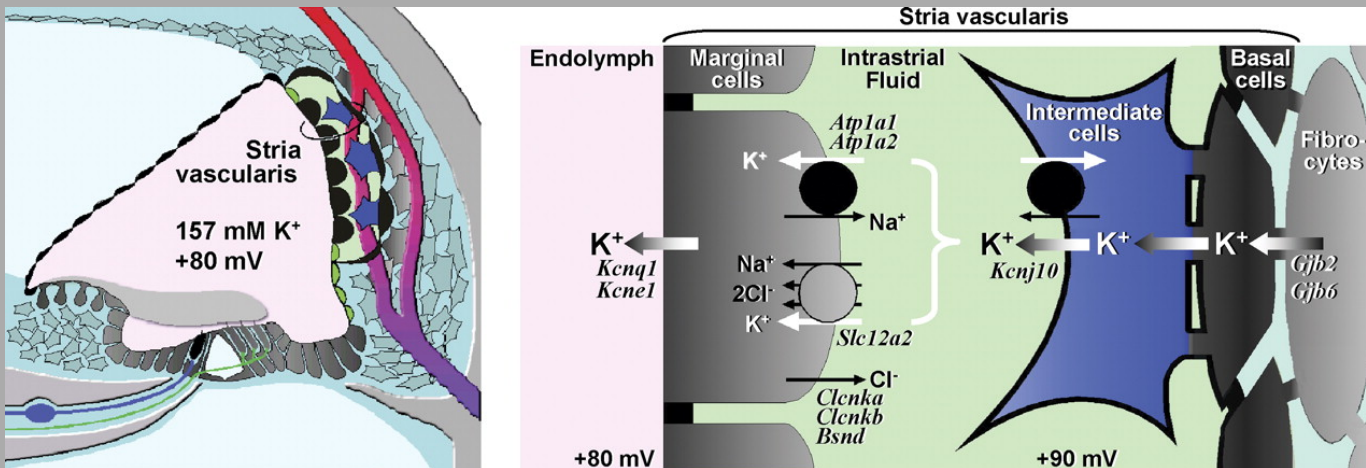


Schuknecht, 1976

Presbiacusia Metabolica

Stria vascolare

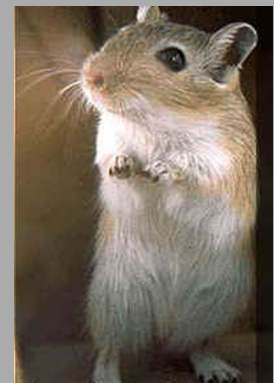
- Regola l'omeostasi e la concentrazione ionica cocleare
- Genera i potenziali elettrici endococleari (“*batteria cocleare*”)



Presbiacusia Metabolica

- Teoria dell' "esaurimento della batteria"
- Riduzione Na^+ / K^+ ATPasi
- Studi su animali (gerbilli) tenuti in quiete dimostrano che la degenerazione della stria vascolare è il meccanismo principale dell' invecchiamento cocleare

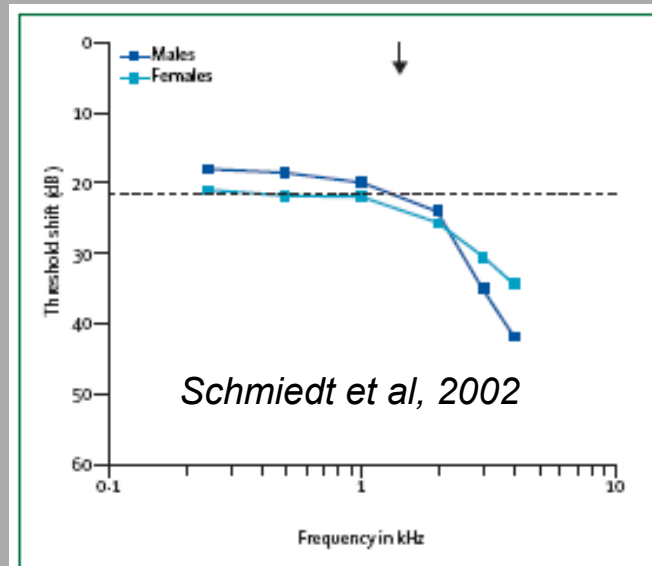
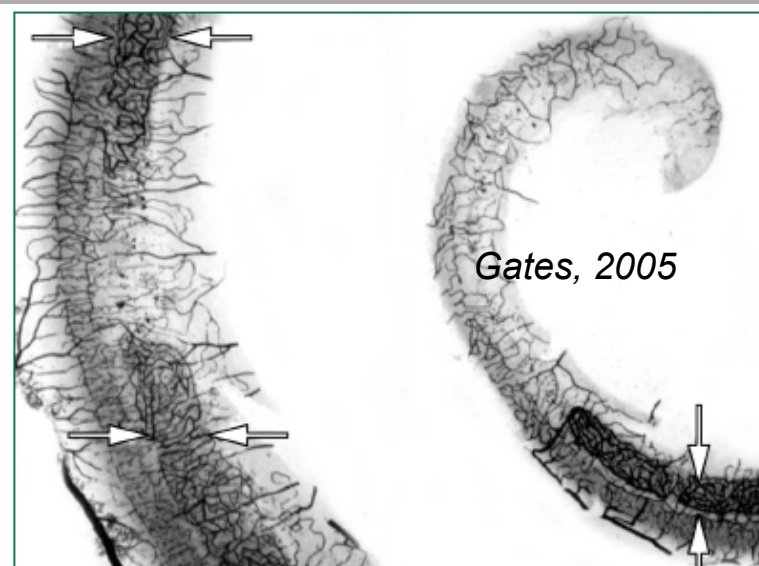
(Gratton & Schulte, 1995)



Presbiacusia Metabolica

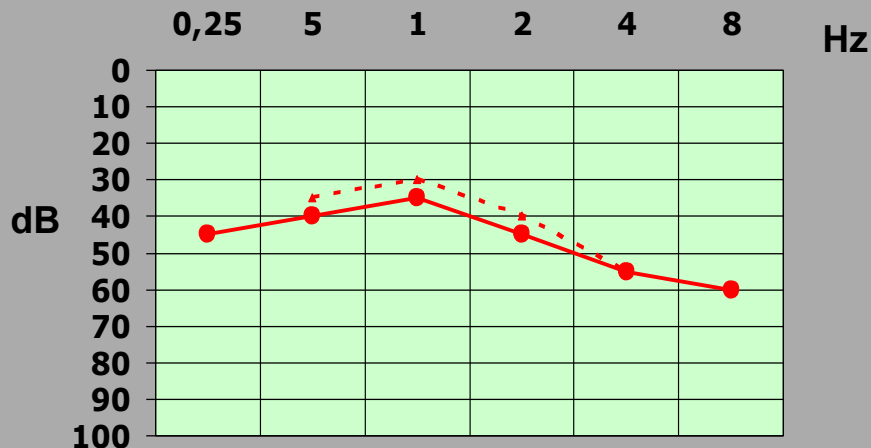
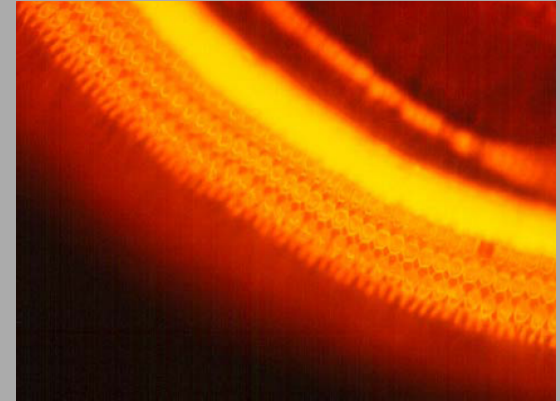
Atrofia della stria vascolare > 50%:

- riduzione drastica dei potenziali cocleari endolinfatici (da 90 mV a <20mV)
- deterioramento uditivo simile a quanto riscontrato nella presbiacusia
- reversibile con la somministrazione di corrente continua

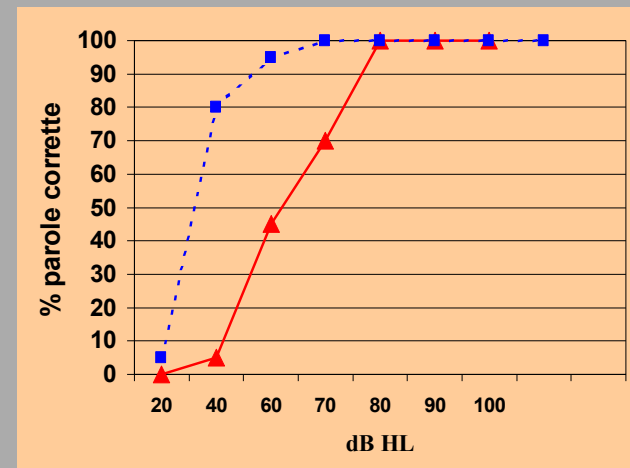


Presbiacusia Metabolica

- Ipoacusia pantonale piatta
- Graduale progressione
- Buona discriminazione vocale



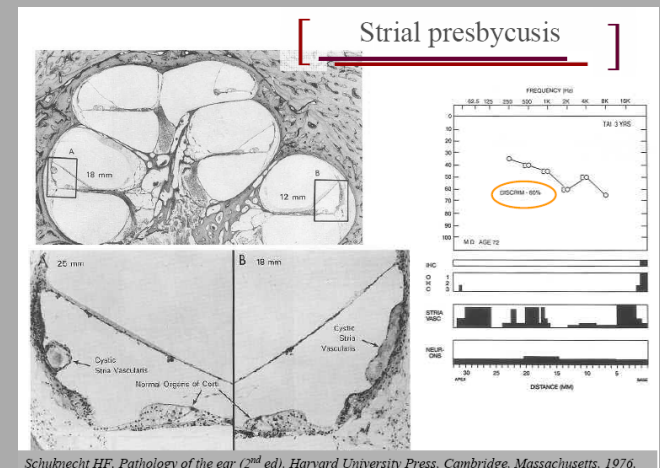
A. tonale



A. vocale

Presbiacusia Metabolica

- Significativa componente ereditaria
- Più frequente nelle donne
(*Deemester et al 2009*)
- ✓ Possibile componente ormonale (deficit di estrogeni)
- ✓ Effetto protettivo (modesto) della terapia sostitutiva
(*Hederstierna et al, 2007*)



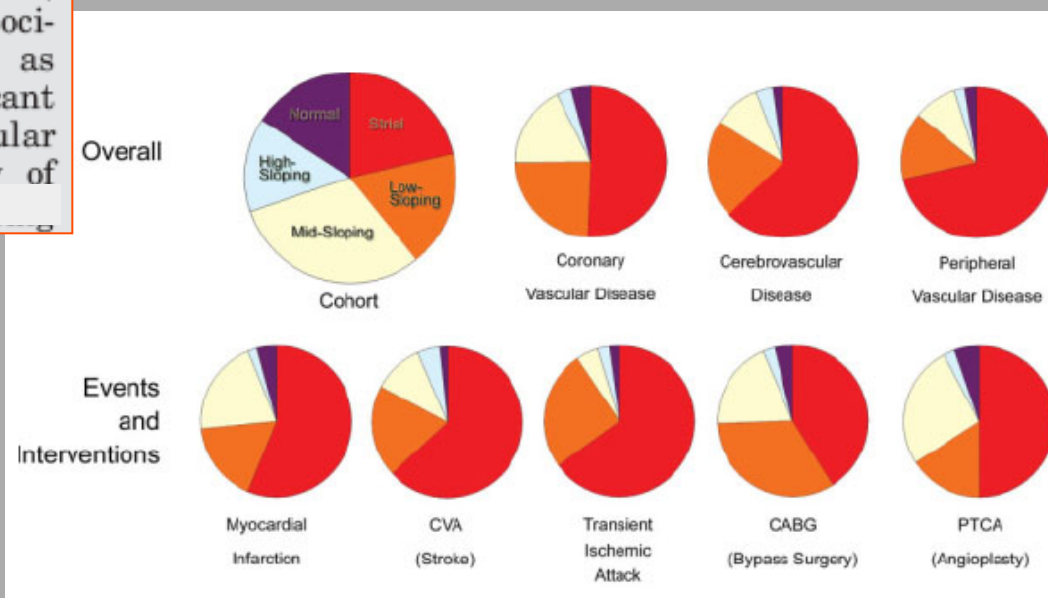
Audiometric Pattern as a Predictor of Cardiovascular Status: Development of a Model for Assessment of Risk

Laryngoscope, 119:473–486, 2009

David R. Friedland, MD, PhD; Christopher Cederberg, MD; Sergey Tarima, PhD

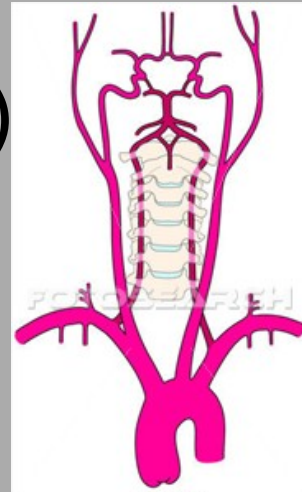
Results: A significant association was found between low-frequency hearing loss and cardiovascular disease and risk factors. When controlling for age, hypertension, diabetes, smoking, and hyperlipidemia, low-frequency presbycusis was significantly associated with intracranial vascular pathology such as stroke and transient ischemic attacks. Significant associations were also seen with peripheral vascular disease, coronary artery disease, and a history of myocardial infarction.

First, there was also a strong association between peripheral vascular disease and low-frequency hearing loss, suggesting a systemic, rather than local, vasculopathy. Second, the high metabolic demand of the inner ear and brain may render these regions more sensitive to systemic vascular disease rather than represent local circulatory issues.



Presbiacusia e fattori di rischio cardio-vascolare

- Correlazione tra ipertensione sistolica e ipoacusia sulle frequenze gravi e medie nell'uomo (*Rosenhall, 2006*)
- Ratti con ipertensione spontanea: degenerazione stria vascolare e ipoacusia (organo del Corti indenne) (*McKorick et al, 1982; Kappelmann et al, 1987; Tachinaba et al, 1984*)



- Ipoperfusione cocleare: incremento intracellulare di radicali liberi dell'O₂
- Concomitante riduzione delle difese anti-ossidanti



- STRESS OSSIDATIVO, alla base di molte affezioni dell'orecchio interno, inclusa la presbiacusia



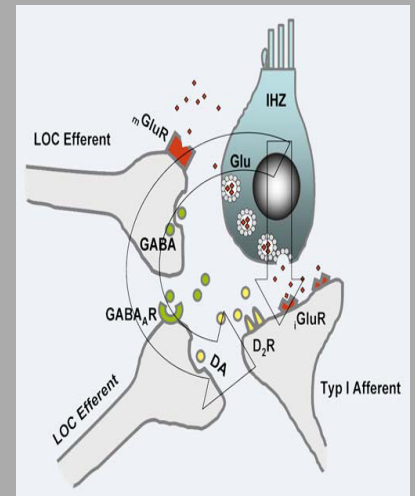
Stress ossidativo

- La ridotta funzione antiossidante può avere base genetica
- Circa il 50% dei caucasici ha un genotipo nullo per il gene GSTM1 (glutathione-S-transferasi), con ridotta risposta allo stress ossidativo

(Pemble et al, '94)

Stress ossidativo

- Sbilanciamento tra la neurotrasmissione eccitatoria e inibitoria
- Principali neurotrasmettitori coinvolti: GLUTAMMATO (ecc.), GABA (inib.), ACETILCOLINA (ecc./inib.)
- **Eccitotossicità** da glutammato



The Contribution of Family History to Hearing Loss in an Older Population

Catherine M. McMahon,¹ Annette Kifley,² Elena Rochtchina,² Philip Newall,¹
and Paul Mitchell²

(Ear & Hearing 2008;29;578–584)

Results: Our findings indicate that family history was most strongly associated with moderate to severe age-related hearing loss. We found a strong association between maternal family history of hearing loss and moderate to severe hearing loss in women (adjusted OR 3.0; 95% CI 1.6–5.6 in women with without a maternal history). Paternal family history of hearing loss was also significantly, though less strongly, associated with moderate-severe hearing loss in men (adjusted OR 2.0; CI 1.01–3.9 in men with than without a paternal history).

TABLE 2. Age-standardized proportion of subjects with family history of hearing loss, by the magnitude of bilateral measured hearing loss

	Magnitude of bilateral hearing loss			<i>p</i> across groups
	None % (<i>n</i> = 1799)	Mild % (<i>n</i> = 587)	Moderate to severe % (<i>n</i> = 283)	
Any family history	44.5	52.6	63.8	<0.0001
Parent	36.9	44.3	56.3	<0.0001
Father	20.0	27.6	24.7	<0.0001
Mother	21.8	22.0	40.3	<0.0001
Sibling	13.5	15.3	32.0	<0.0001
Parent only	30.6	36.2	33.4	0.006
Sibling only	7.4	8.3	7.6	0.6
Parent and sibling	6.5	8.0	22.8	<0.0001
Mother only	20.4	12.9	16.8	0.2
Father only	12.4	17.2	8.8	0.3

Fattori genetici



- Studi su gemelli mono ed eterozigoti e su gruppi familiari evidenziano che il peso dell'ereditarietà nella presbiacusia è del 33-55%
- Il fattore genetico sembra più importante nella presbiacusia “metabolica”
- I fattori ambientali aumentano d'importanza con l'aumento di età

(Karlsson et al, '97; Gates et al, '99; Christenses et al, '01)

Fattori genetici



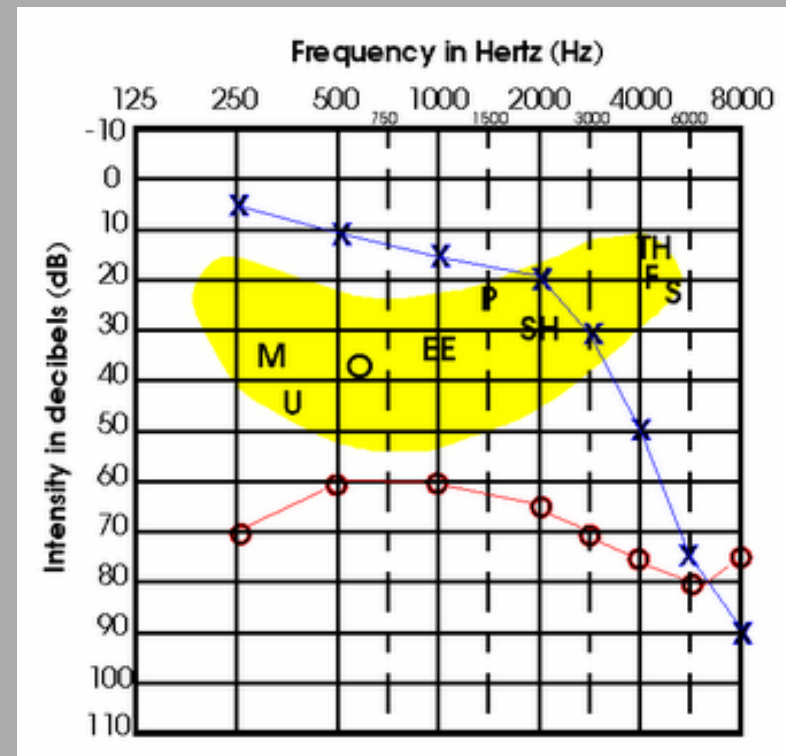
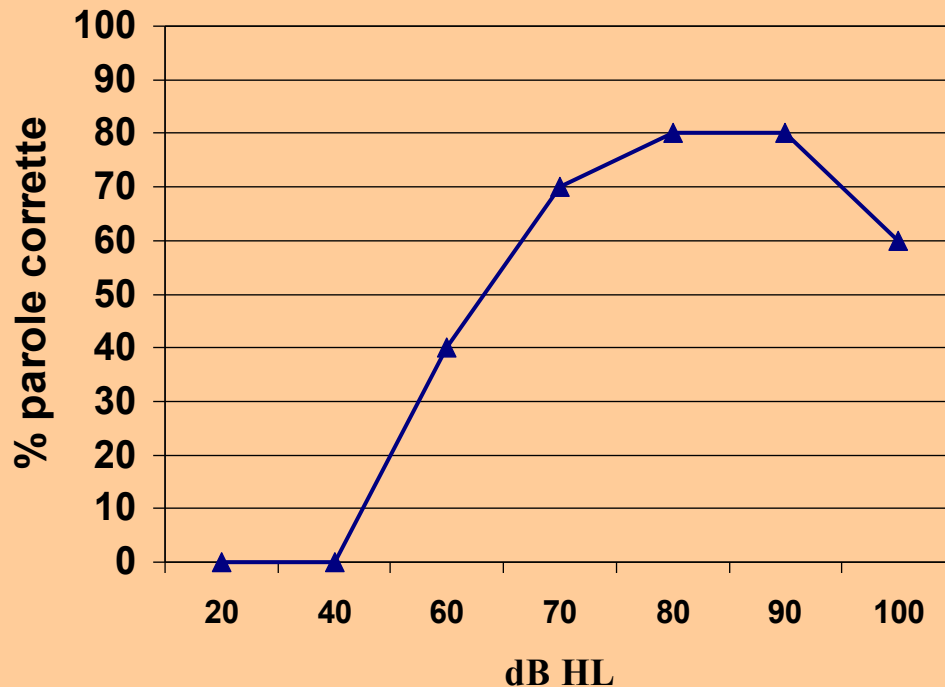
- Studi di linkage nell'uomo hanno identificato regioni cromosomiche (11p; 11q; 14q) sovrapposte a geni riconosciuti come causa di ipoacusia congenita
- Variazioni genetiche nel locus DFNA18 sul cromosoma 3q: maggiore suscettibilità verso la presbiacusia
(*De Stefano et al 2003; Garringer et al 2006*)
- Associazione positiva con gene GRHL2 (fattore di trascrizione espresso nell'organo del Corti) (*Van Laer et al 2008*)

*I can hear you, but I
can't understand you!*



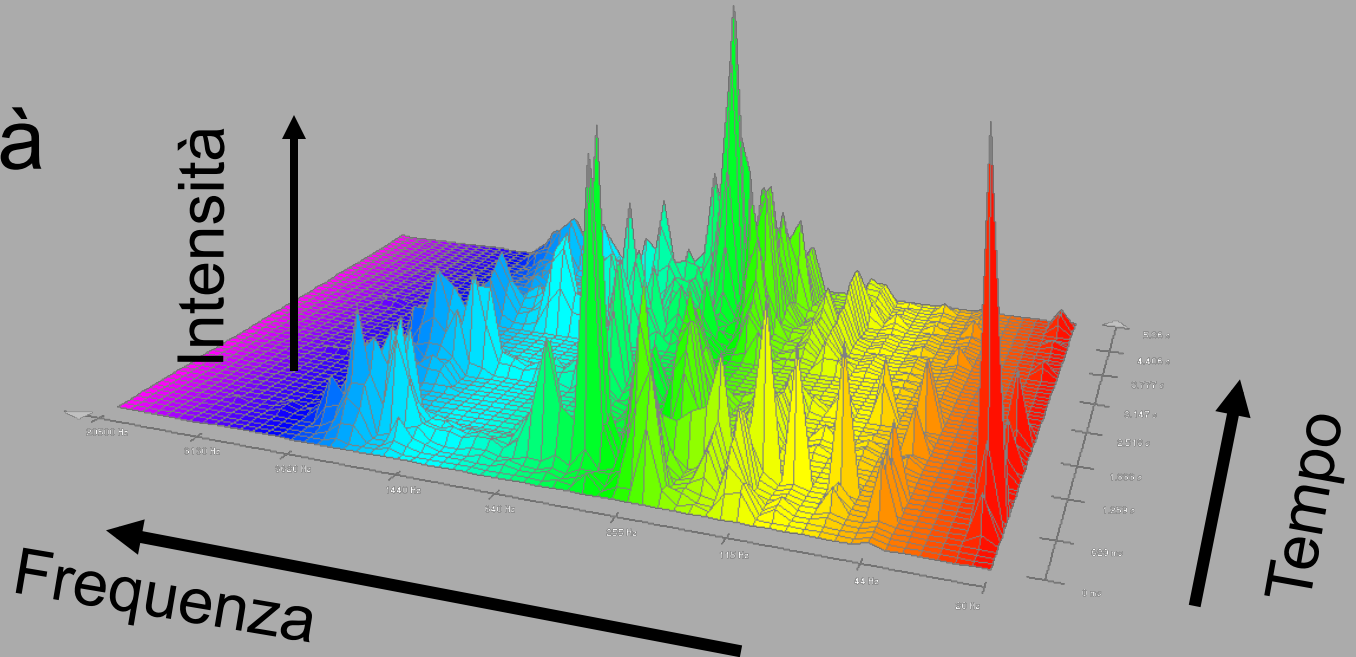
Ridotta discriminazione vocale

Solo un problema di soglia uditiva ?



Patologia cocleare

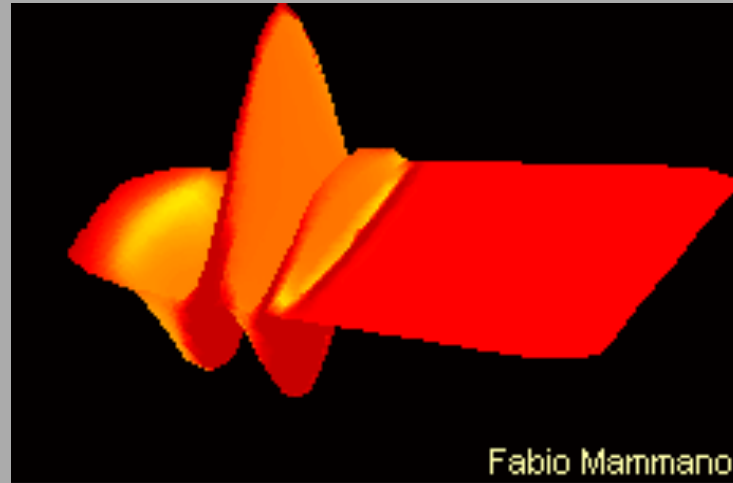
- Innalzamento della soglia uditiva
- Alterata risoluzione in
 - ✓ frequenza
 - ✓ tempo
 - ✓ intensità



Coclea: tempo, frequenza, intensità

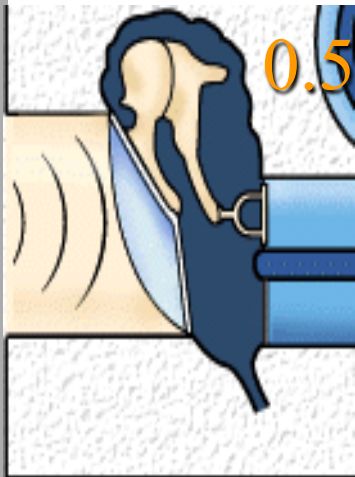


4 kHz

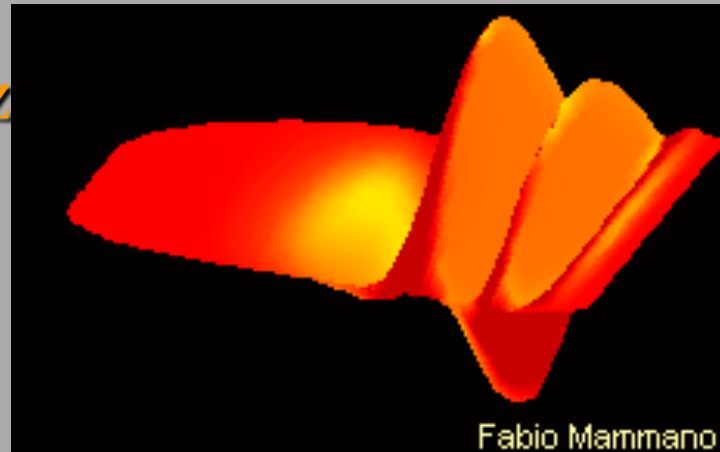


Fabio Mammano

exaggerated basilar membrane width

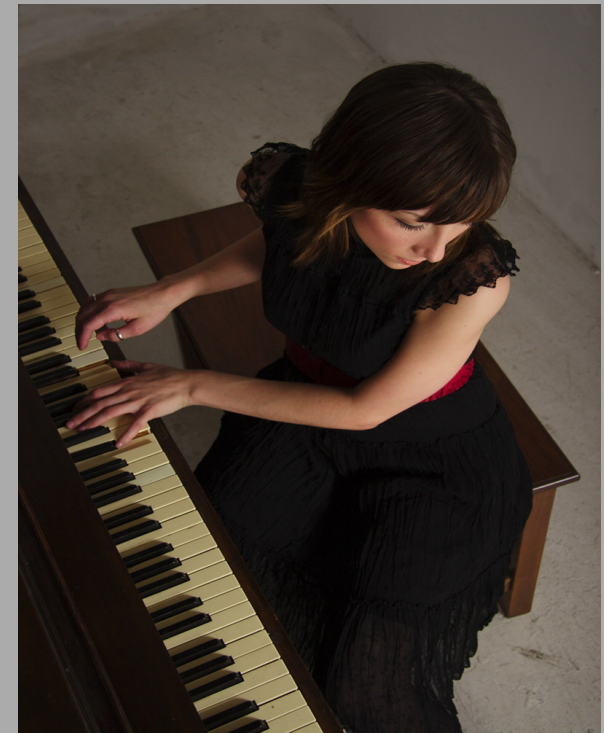


0.5 kHz



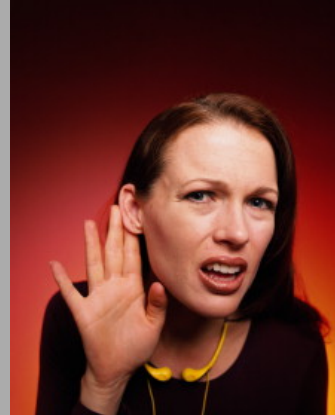
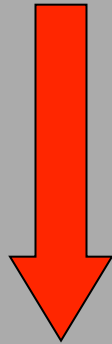
Fabio Mammano

exaggerated basilar membrane width

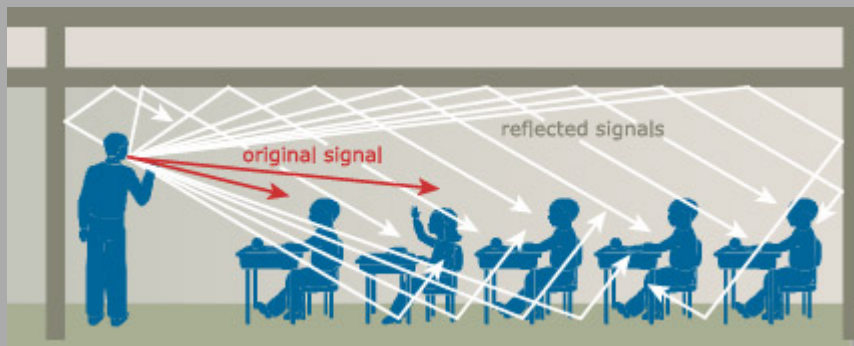


Patologia cocleare

- Innalzamento della soglia uditiva
- Alterata risoluzione in
 - ✓ frequenza
 - ✓ tempo
 - ✓ intensità



- ✓ Distorsione nella discriminazione vocale
- ✓ Distorsione nella percezione sonora (fastidio)



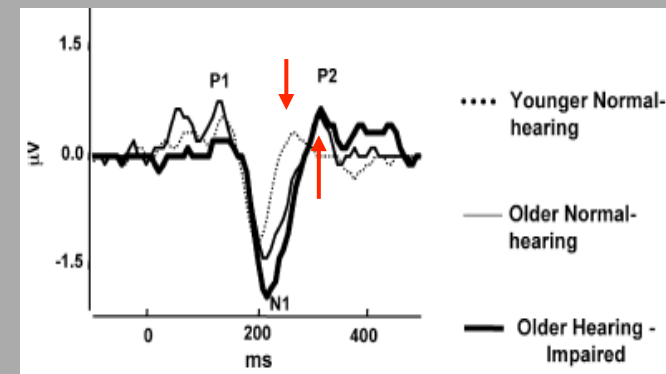
- Il danno della coclea e delle fibre del n. cocleare è in grado di spiegare le difficoltà nella percezione vocale in quiete e in presenza di rumore di fondo (*Humes, 1996*)
- In condizioni più sfavorevoli (es. suono riverberante, rumore di fondo variabile, stimoli vocali competitivi) il deficit di comprensione della voce può essere correlato anche alle difficoltà di risoluzione temporale legate all'età (*Turner et al, 1995; Wingfield et al, 2001*)

Deterioramento della capacità di risoluzione temporale

- La risoluzione temporale (per es. la percezione di un gap silente tra due suoni) è ridotta nell'anziano indipendentemente dalla soglia uditiva



- Aumento del periodo refrattario neurale, con conseguente ridotta sincronizzazione (*Tremblay et al 2007*)
- Riduzione fibre n.cocleare?
Alterata elaborazione centrale?

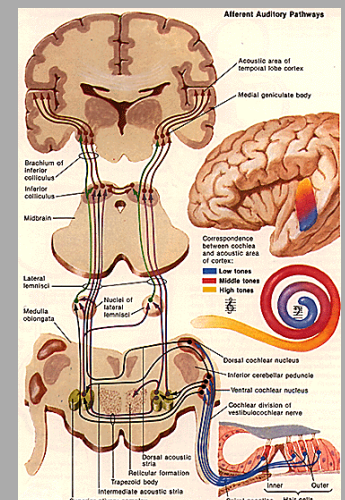


Presbiacusia Centrale ?

Age-related central auditory processing disorder
(CAPD)

(Gates, 2005)

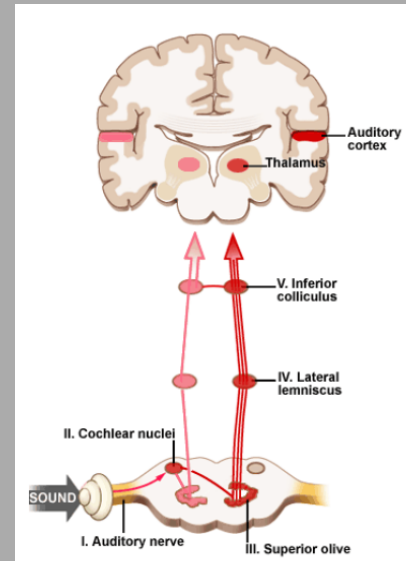
Associazione con l'età già prospettata nel 1948 da Gaeth che coniò il termine di “regressione fonemica” caratterizzata da una difficoltà alla discriminazione vocale superiore a quella prevedibile dalla soglia uditiva tonale



Funzione uditiva

3 livelli fondamentali

1. Periferia sensoriale (coclea, nervo cocleare): elaborazione del segnale
2. Vie uditive centrali: analisi ed elaborazione del codice neurale e percezione
3. Corteccia uditiva e associativa: processi cognitivi



(Willot et al, 2001)

Hearing in the Elderly—The Framingham Cohort, 1983–1985: Part II. Prevalence of Central Auditory Processing Disorders

J. C. Cooper, Jr., PhD; George A. Gates, MD

Ear and Hearing, Vol. 12, No. 5, 1991:304–311

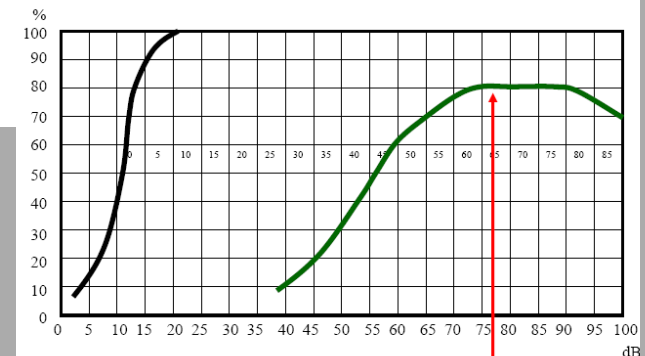
Table 3. Percent of subjects with indications of CAPD on any test followed by each test and the several test combinations.

Indication	Decade Age			Total
	64–69	70–79	80–89	
Any indication	11.80	22.89	46.53	22.59
Rollover ^a (RO)	0.31	1.30	4.23	1.38
PB-SSI ^b	10.89	18.45	46.58	18.14
SSW ^c	3.14	10.02	35.71	10.73
RO and PB-SSI	0.00	0.23	0.00	0.12
RO and SSW	0.00	0.20	0.00	0.11
PB-SSI and SSW	1.98	2.97	16.44	3.81
RO, PB-SSI, and SSW	0.00	0.00	0.00	0.00

^a Rollover index > 0.20.

^b PB-SSI difference > 20 percentage points.

^c Abnormal SSW category (adjusted when appropriate).



Abnormal results on any one index occurred in 22.6% of the subjects. Thus, we conclude that the prevalence of CAPD in the elderly is less common than previous studies would suggest. Furthermore, although the rate of CAPD increased with age, age accounted for no more than 15% of the variability of any of the three indices. Therefore, its presence is dominated by factors other than chronological age (Ear Hear 12 5:304–311).