Annual meeting CAA 2018. Niagara Falls. October 2018

Towards an Improved Sub-Classification of SNHL Spectrum Disorder

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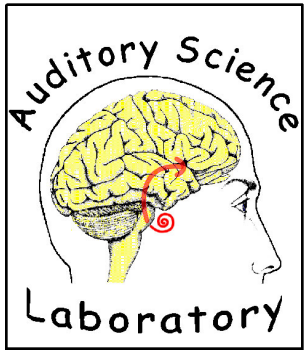

SickKids®

An evolution of thought?

University of Toronto, Otolaryngology – HNS, Grand Rounds March 2018

Making Clinical Sense of New Knowledge on Inner Ear Pathology

Mediterranean Society for Otology and Audiology, Jerusalem May 2018

The pathogenesis of hearing loss; things we can learn from animal models

Sound Wave Symposium, San Diego, October 2018

SNHL- Understanding the cause is important for treatment

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Towards an Improved Sub-Classification of SNHL Spectrum Disorder

Learning Objectives:

To explore the anatomical damage to the cochlea and associated functional deficits in a range of animal models of sensorineural hearing loss (SNHL).

To provide a greater understanding of different sub-types of SNHL based on structural deficits and on etiology.

To encourage the development and clinical use of a sub-classification scheme for SNHL

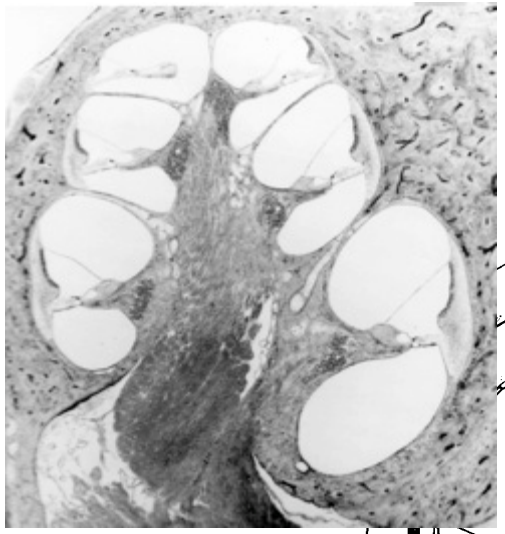
My own studies of animal models of hearing loss include:

- Drug ototoxicity
- Acoustic Trauma
- Endolymphatic hydrops
- Cochlear hypoxia
- Autoimmune disease
- Cochlear ablation
- Genetic mutations
- Auditory deprivation
- Ageing
- Infection

These all result in what we call "sensorineural hearing loss" but are very different in terms of anatomical lesions and functional impairment. These differences are largely depending on ETIOLOGY

OVERALL THESIS: If we pay more attention to etiology we can distinguish classes or types of SNHL. This in turn will narrow our focus on treatment and rehabilitation strategy and provide more accurate prognosis

Cochlear areas of maximum vulnerability



Stria vascularis

hypoxia, ischemia
loop diuretics (Lasix)
metabolic inhibitors
old age
viral infection
genetic mutation
(sometimes reversible)

Haircells

ototoxic drugs
e.g. aminoglycosides
old age
acoustic trauma
genetic mutation
(not reversible)

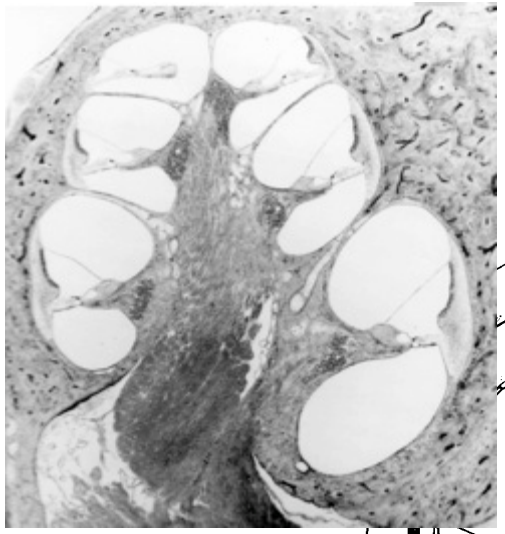
Spiral ganglion cells

loss of inner haircells
Glutamate excitotoxicity
Sensorimotor neuropathy
Hidden hearing loss?

Inner haircell synapse

some drugs e.g. aspirin
chronic hypoxia
anti cancer drugs – carboplatin
noise exposure
(sometimes there is recovery)

Cochlear areas of maximum vulnerability



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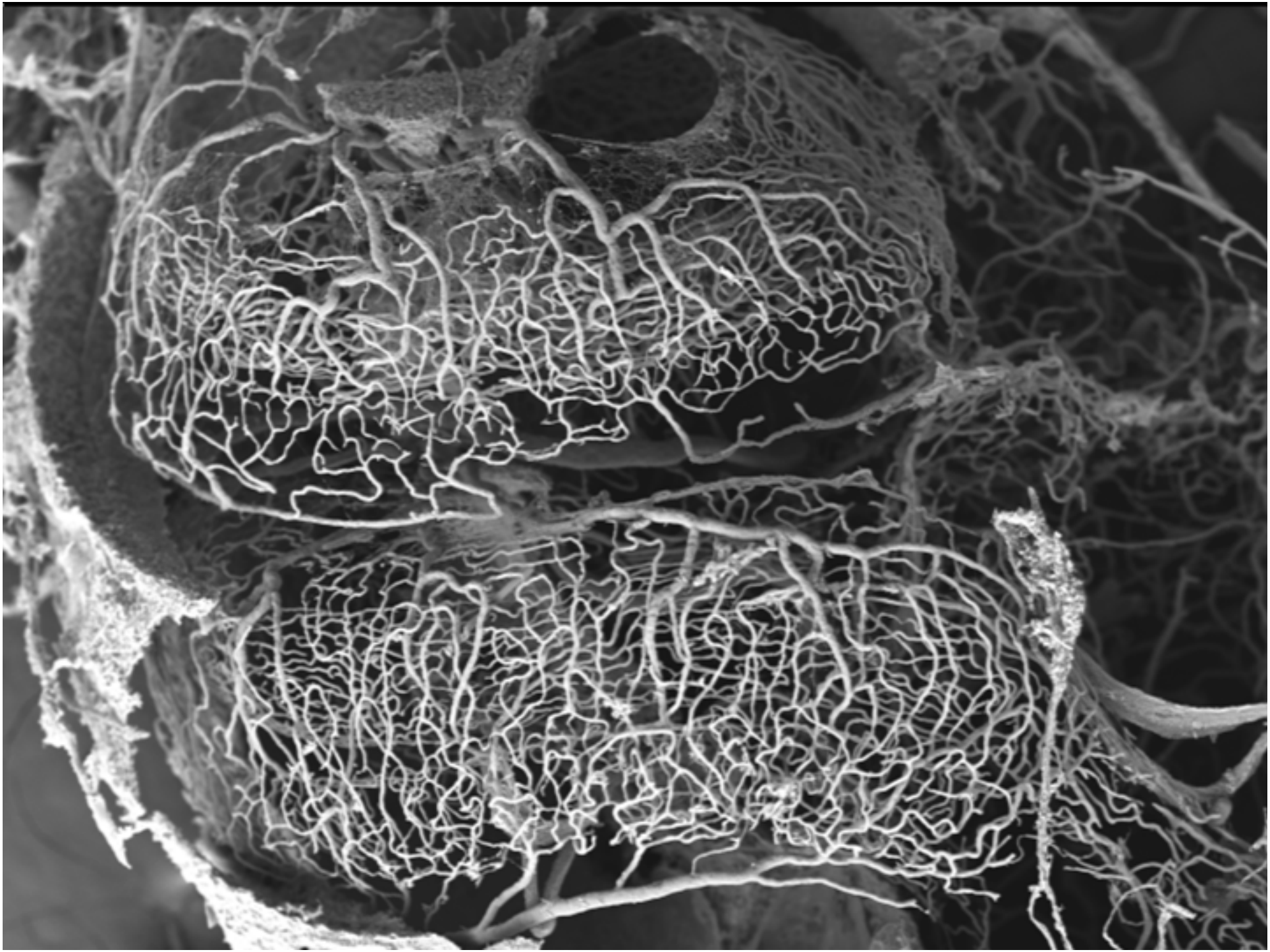
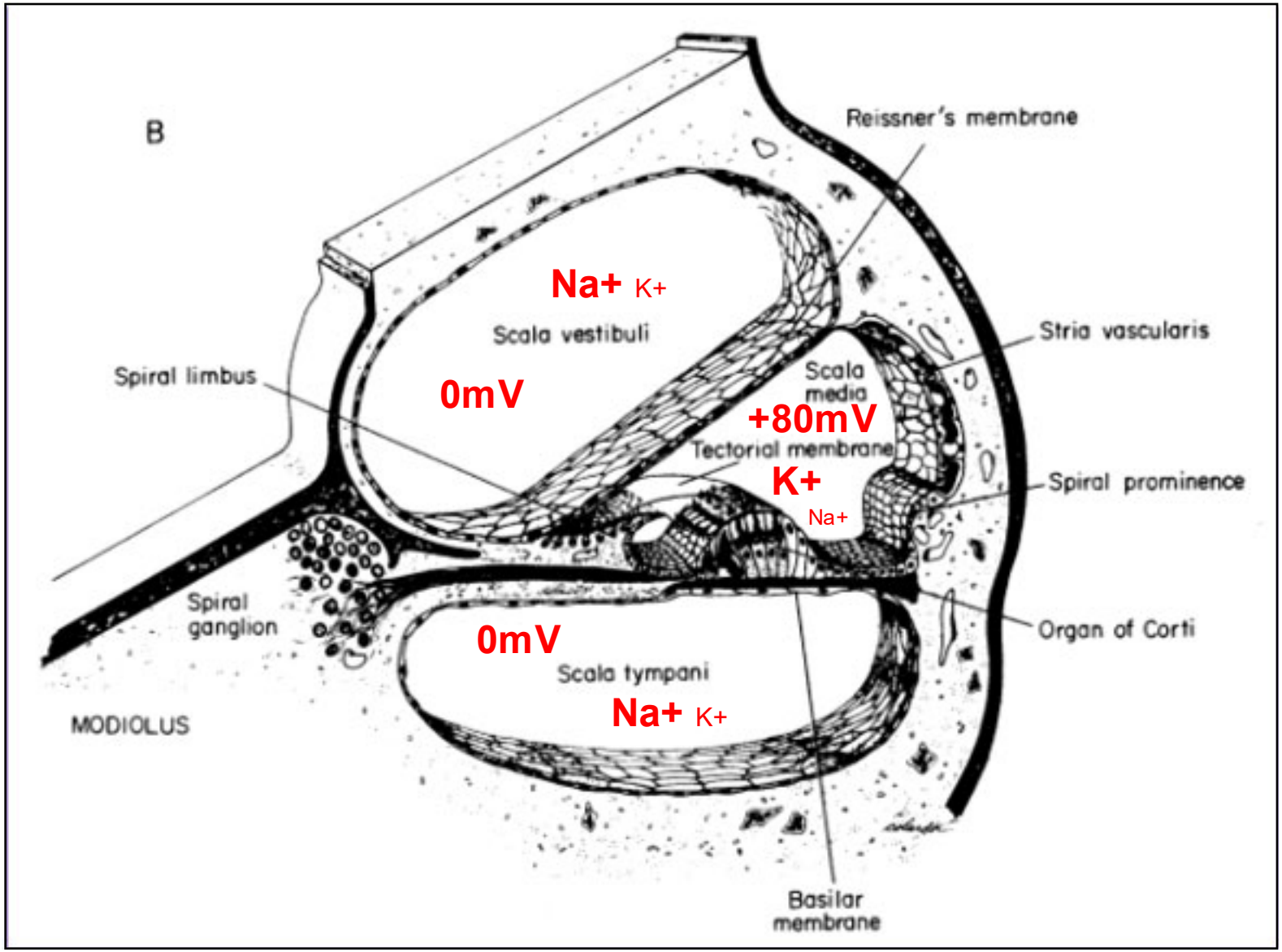
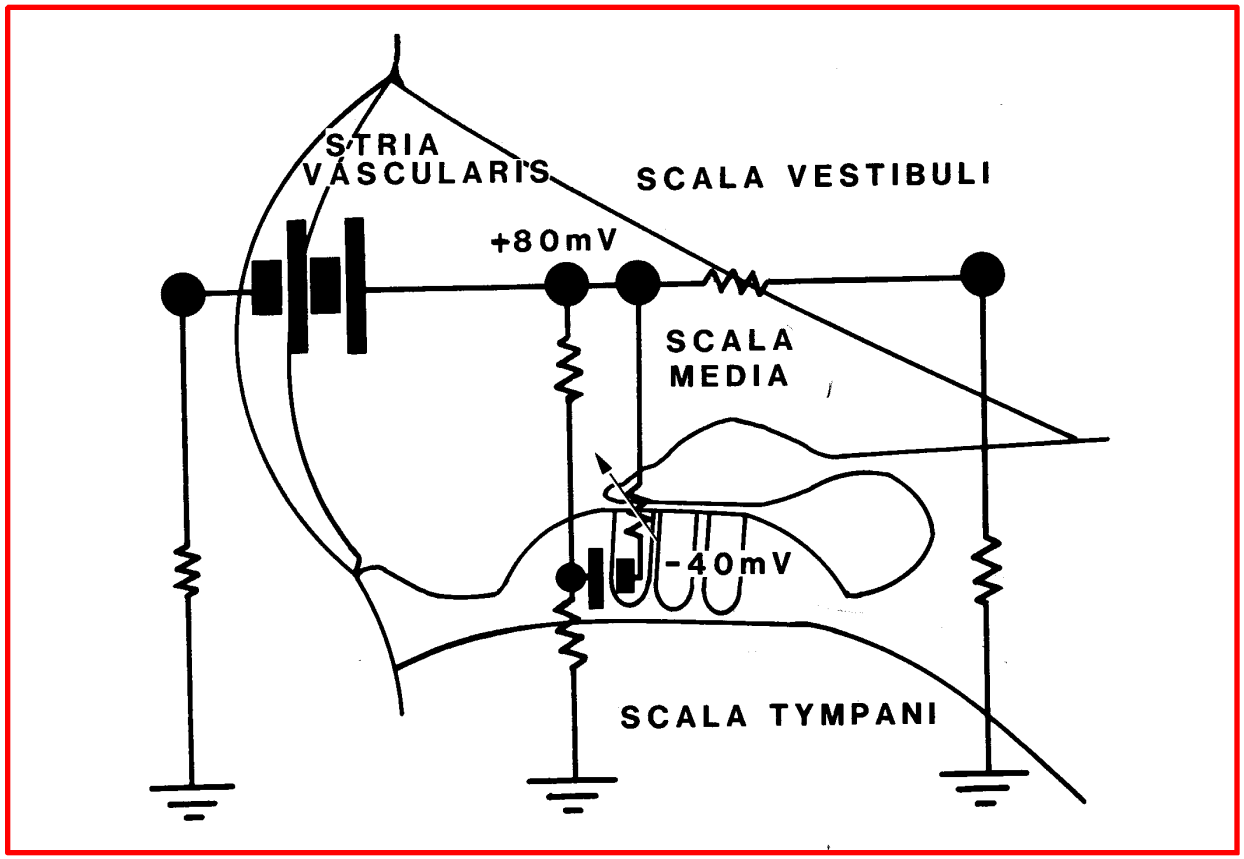


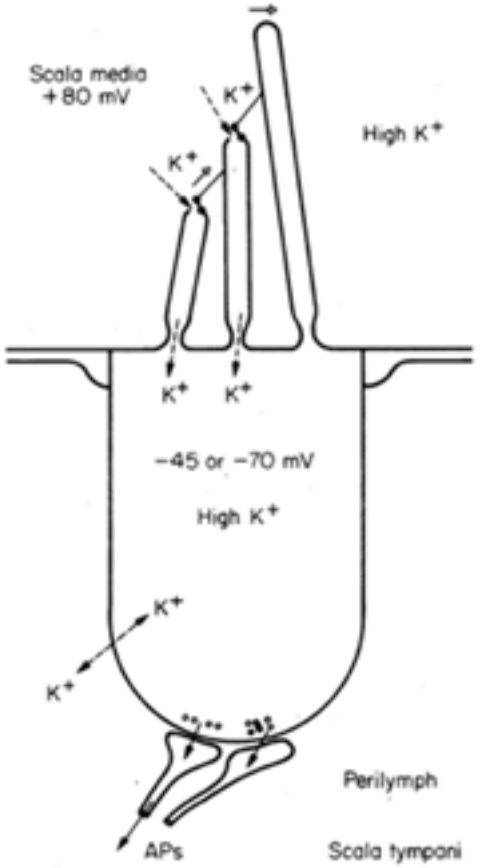
CARRARO M, PARK A, **HARRISON RV**. (2016)
Partial corrosion casting to assess cochlear vasculature in mouse models of presbycusis and CMV infection.
Hearing Research. 332 95-103.

The stria vascularis is the power-house of the cochlea



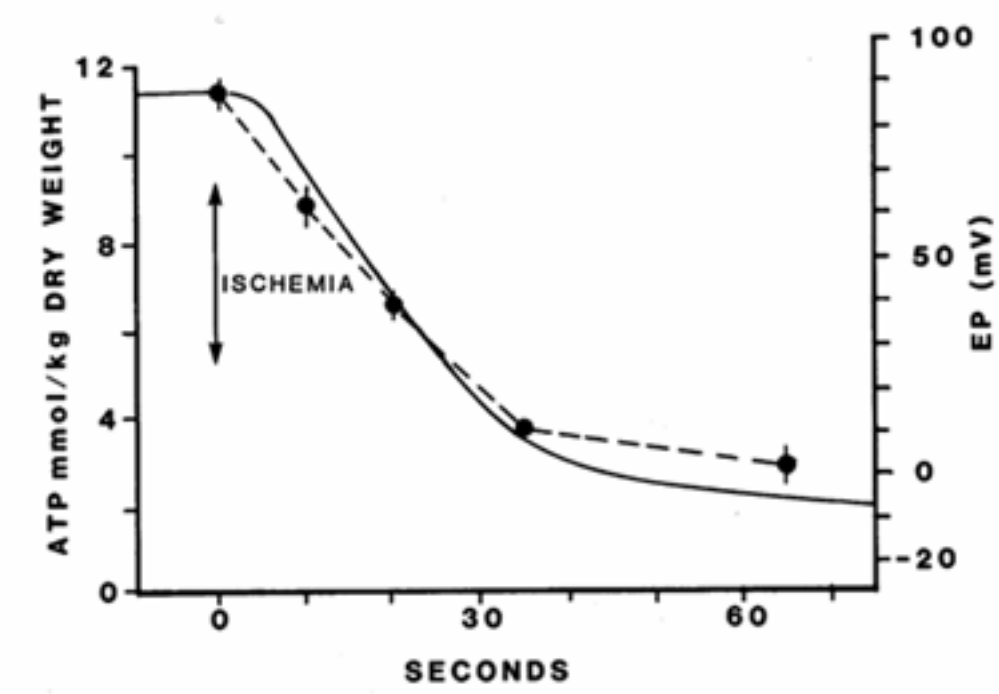
Impairment of strial function reduces electrical driving force for haircell activation



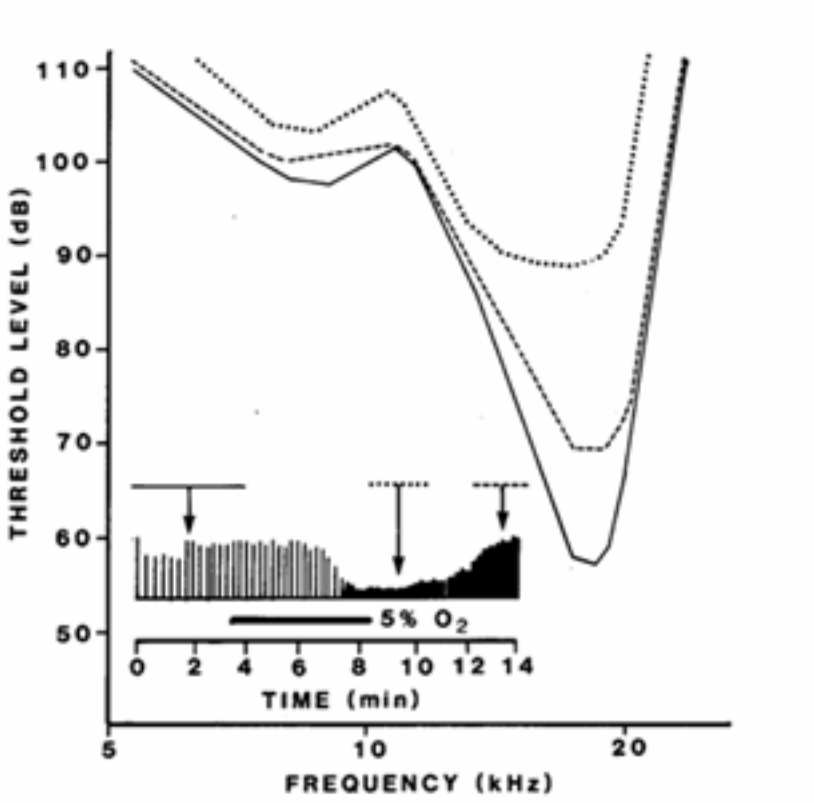


Standing cochlear potentials Davis' battery theory

Effects of hypoxia or ischemia on the strial function and the consequences on cochlear function

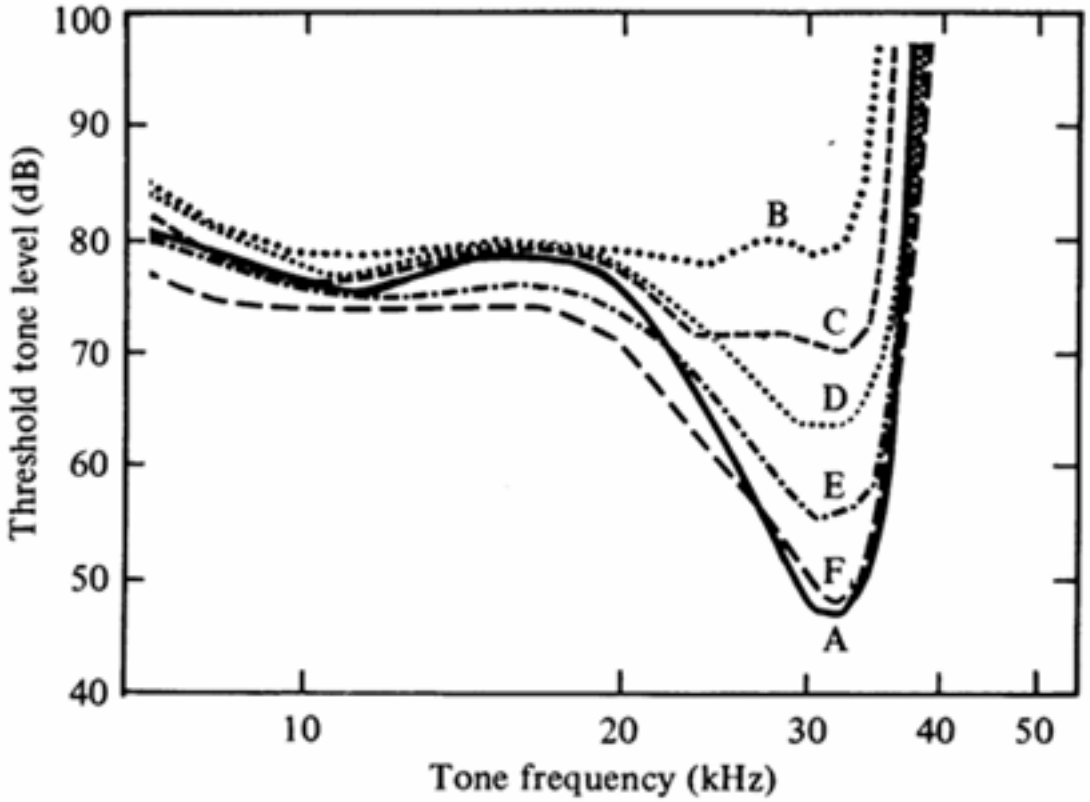


Thalmann et al. (1977) Noxious effects upon cochlear metabolism. Laryngoscope 87:699



Evans (1974) The effects of hypoxia on the tuning of single nerve fibers. J Physiol. 238:65

Reversible effects of furosemide (lasix) on strial function

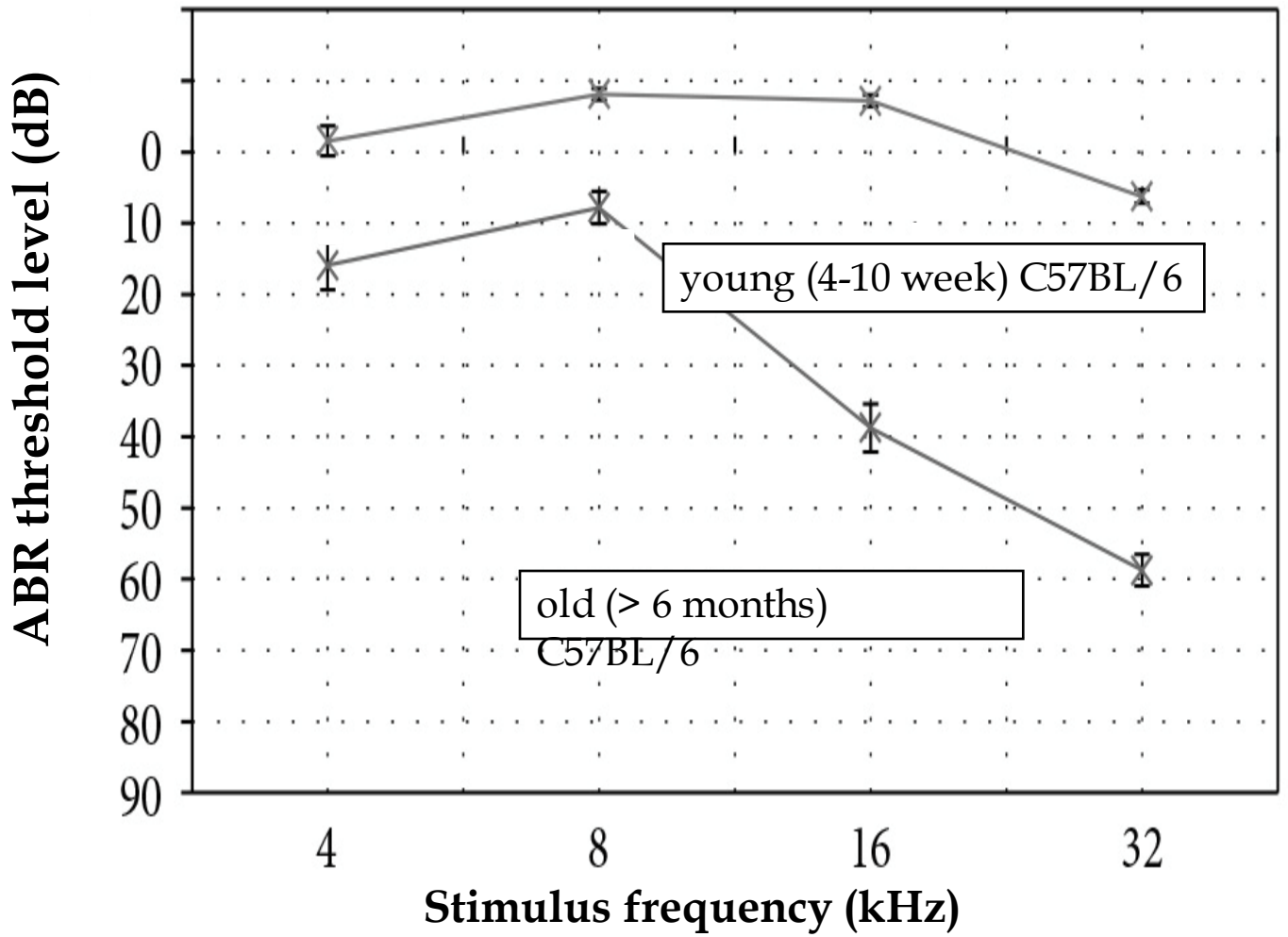


Threshold elevation (B) and subsequent recovery (C-F) of cochlear fibre responses

Evans and Klinke (1982) The effects of intracochlear and systemic furosemide on the properties of single cochlear nerve fibres in the cat. J Physiol 331:409

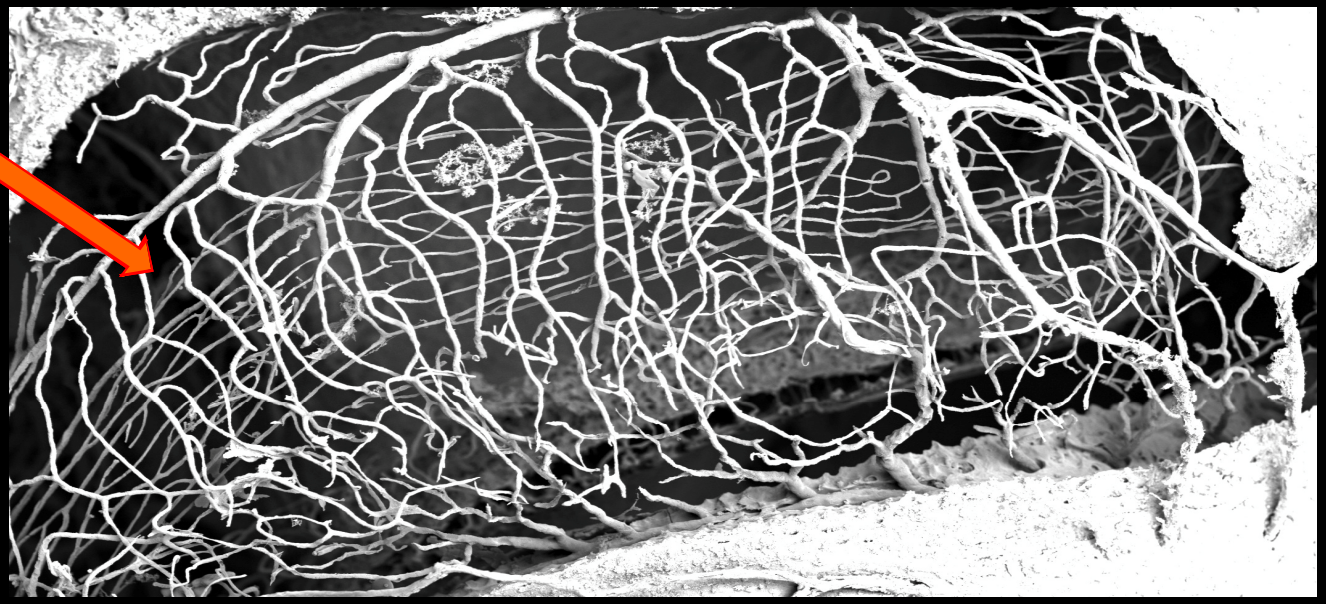

500um

ABR audiograms in a mouse model of presbycusis

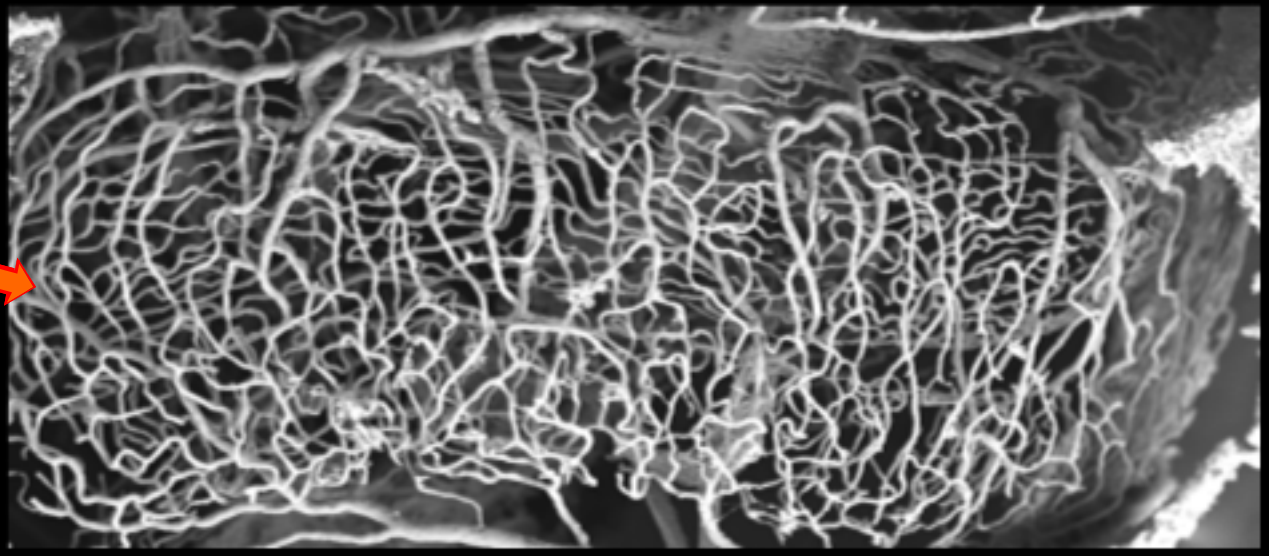


CLINKARD D, AMOODI H, KANDASAMY T, GREWAL AS, CHEN S, QIAN W, CHEN JM, HARRISON RV, LIN VY. (2013) Changes in the cochlear vasculature and vascular endothelial growth factor and its receptors in the aging C57 mouse cochlea. ISRN Otolaryngol. 2013 Jun 27;2013:430625.

Basal turn stria vascularis in age related hearing loss (mouse C57BL/6)



Basal turn of control (young) mouse



CARRARO M, **HARRISON RV**. (2016) Degeneration of stria vascularis in age-related hearing loss; a corrosion cast study in a mouse model. Acta Otolaryngol. 136(4):385-390