CAA Webinar

Understanding Cases of Tinnitus with a Normal Audiogram: Is Hearing Loss Undetected

Speaker: Brandon Paul, PhD., Sunnybrook Health Sciences Centre

Host: Melissa Polonenko
June 9, 2020

CAA Canadian Academy of Audiology Heard. Understood.
Académie canadienne d'audiologie Entendus. Compris. ACA

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Canadian Academy of Audiology is a professional association dedicated to enhancing the role of audiologists as primary hearing health care providers through advocacy, education and research.

Melissa Polonenko - Host

Melissa Polonenko is Co-Chair of the CAA Science and Education Committee and is a Clinician Scientist.

Currently she is a postdoctoral associate at the University of Rochester Medical Center, studying new methods to test hearing function such as ABRs to ongoing stories, as well auditory-visual perception of space in adults with blindness from a stroke.

She completed her PhD at the University of Toronto in the Cochlear Implant Lab at SickKids Hospital in Toronto, studying bilateral development in children with asymmetric hearing loss who use both a cochlear implant and contralateral hearing aid (bimodal hearing). Melissa worked as a clinical audiologist at the Glenrose Rehabilitation Hospital in Edmonton, Alberta, where she worked with infants to the elderly.

Speaker: Brandon Paul, PhD.

Brandon Paul is a Postdoctoral Fellow at Sunnybrook Research Institute and the Department of Otolaryngology within Sunnybrook Health Sciences Centre in Toronto. His research interests concern tinnitus, cochlear implant outcomes, cognitive consequences of hearing loss, and neuroimaging using electroencephalography (EEG). His research has been funded by the Natural Sciences and Engineering Council (NSERC) of Canada, and the American Tinnitus Association.

Understanding Cases of Tinnitus with a Normal Audiogram: Is Hearing Loss Undetected?

Brandon Paul, PhD
Sunnybrook Research Institute & Department of Otolaryngology
Sunnybrook Health Sciences Centre

Sunnybrook
RESEARCH INSTITUTE

Webinar for the Canadian Academy of Audiology
09 June 2020

Overview of the talk

- Discuss *chronic, subjective* tinnitus with and without observable hearing loss
- Consider threshold shifts in audiogram that are missed with conventional testing
- Consider damage to the ear that does not affect audiogram
- "Deep dive" into *cochlear synaptopathy* and its relationship to tinnitus

Tinnitus, Conceptual Artwork poster by Bill Sanderson

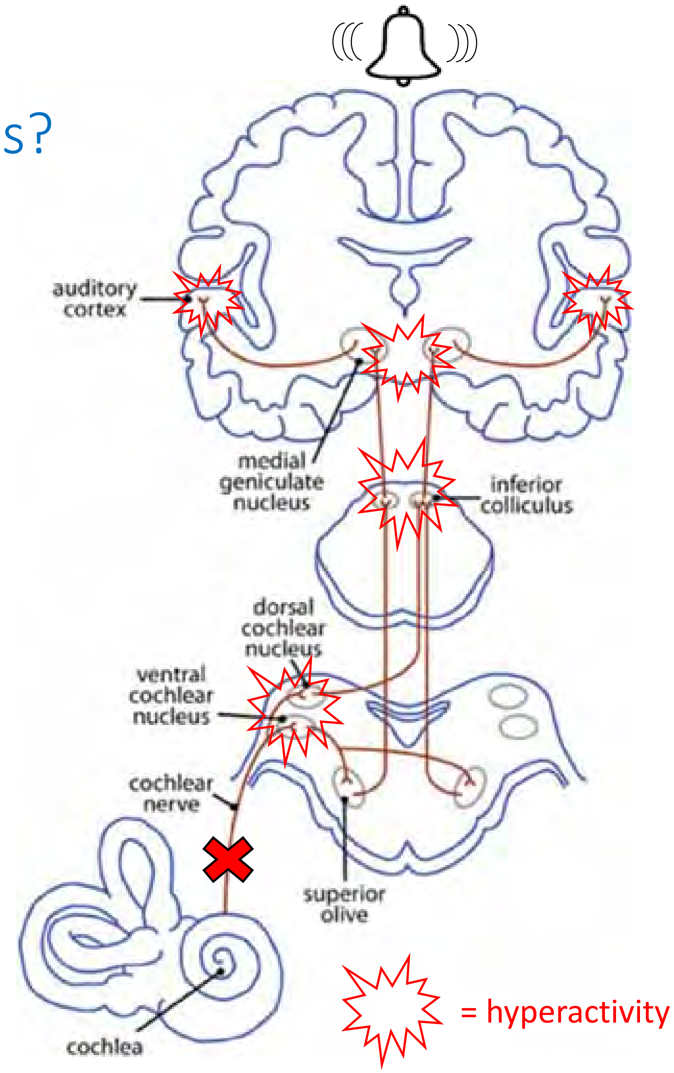
How might we get tinnitus from hearing loss?

1. Cochlear damage
   (after noise exposure/aging)

2. Central auditory neurons lose connection to ear, become hyperactive

3. Hyperactivity perceived as tinnitus

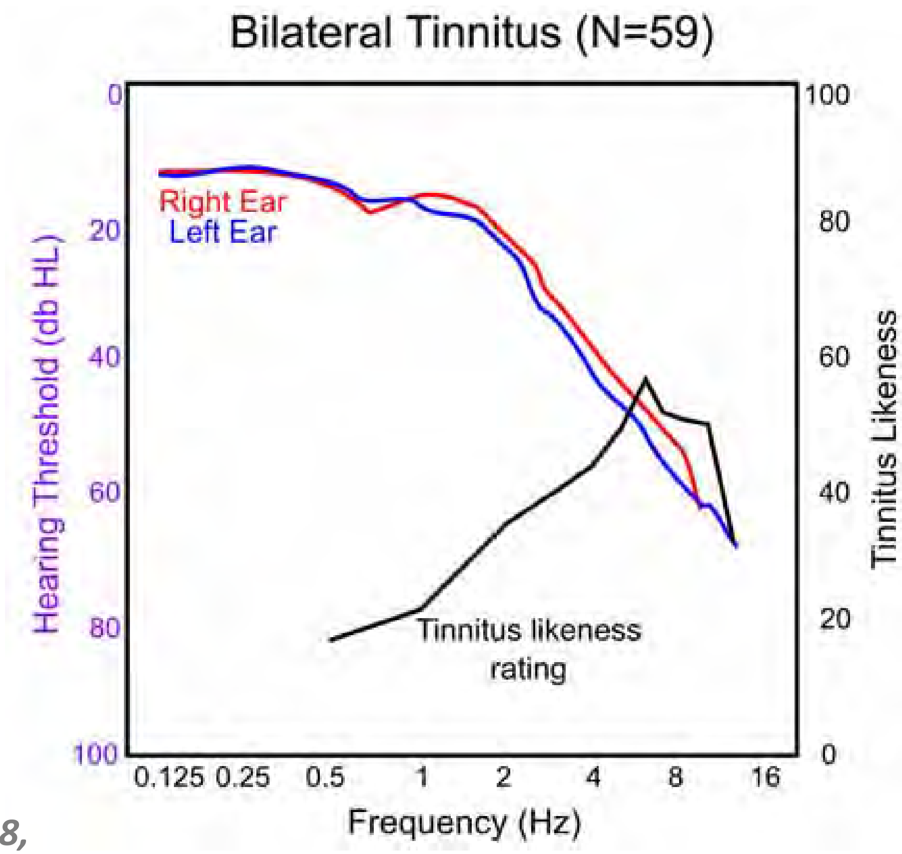
4. Involvement of non-auditory brain areas
   (emotion, cognitive function)



http://humanphysiology.academy/Neurosciences%202015/Chapter%203/A.3p%20Thalamus.html

Tinnitus and hearing loss are (typically) related

- Hearing loss remains the largest risk factor for tinnitus (age, noise, drugs, other trauma)
- 85-90% of individuals with tinnitus also exhibit threshold shifts in the audiogram
- In many cases, tinnitus is experienced where there are threshold shifts**

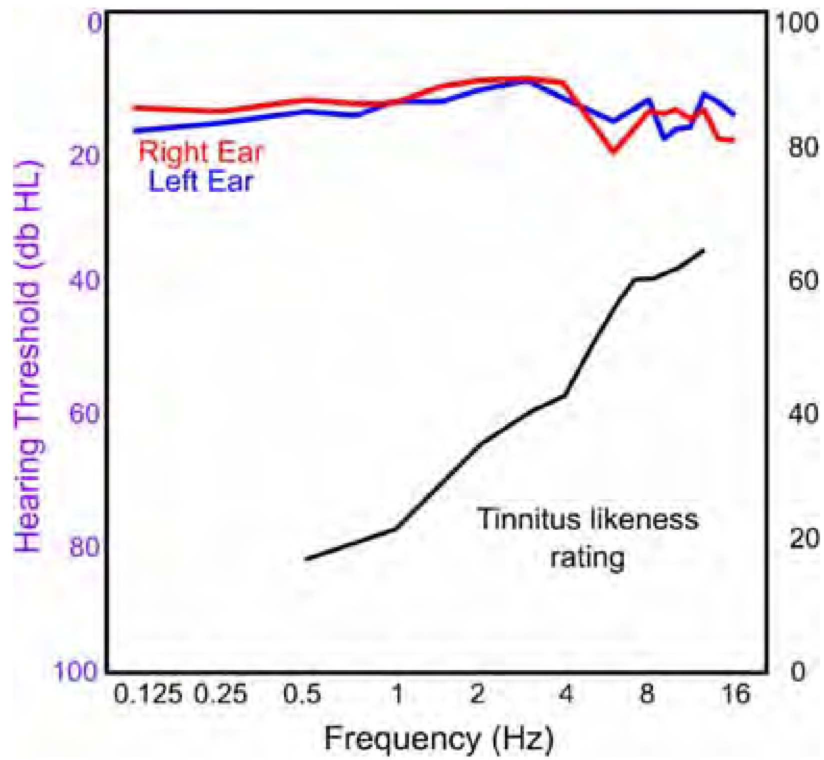


Roberts et al. 2008,
J. Assoc Research Otolaryngol

When threshold shifts and tinnitus are NOT related

- Estimated 8 to 15 % of tinnitus cases show normal thresholds

Henry et al., 2005; J. Speech Lang Hearing
Barnea et al. 1990; Int. J Audiol.



Paul et al. 2017
Hearing Research

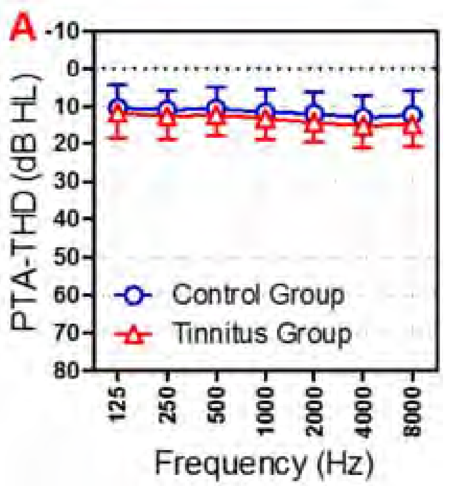
Possible reasons why tinnitus occurs with normal audiograms

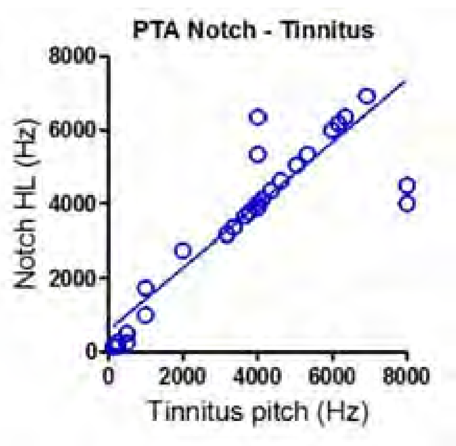
- Tinnitus cases that are unrelated whatsoever to hearing damage

- Conventional tests "miss" hearing loss
  - Low precision in audiometry
  - Hearing damage "hidden" from the audiogram or otoacoustic emissions (OAEs)

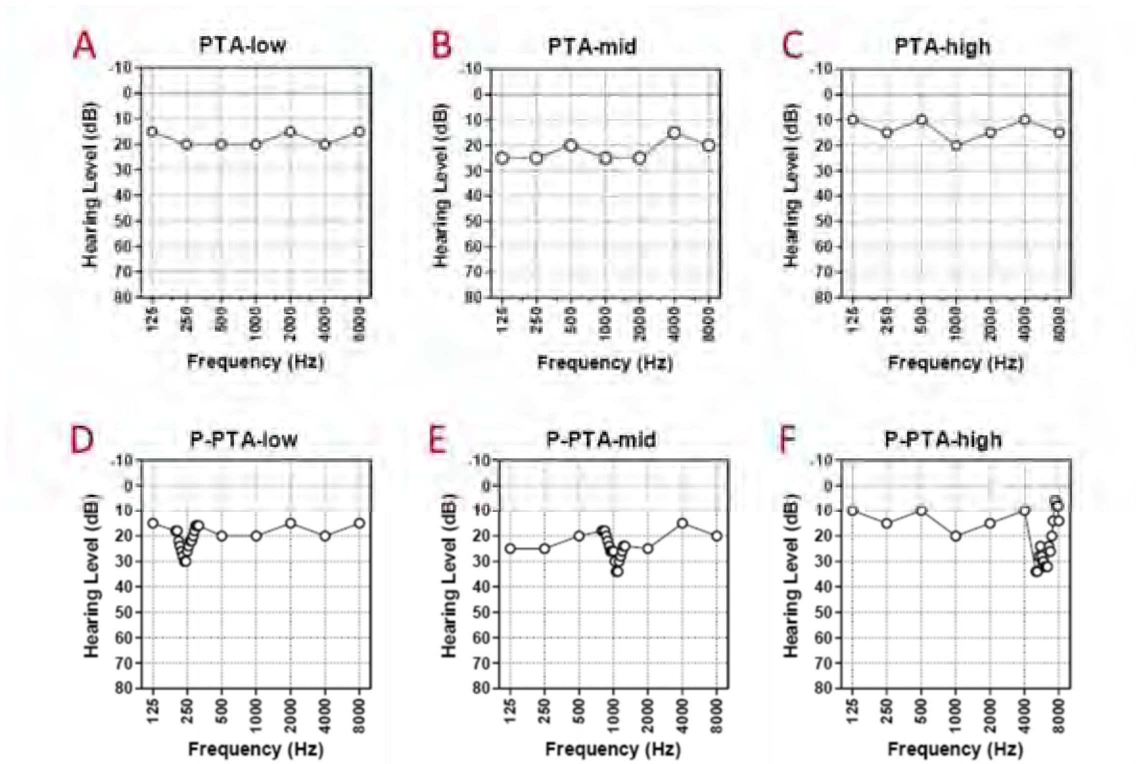
Unknown artist

Does conventional audiometry miss threshold shifts that relate to tinnitus?





Thresholds in ¼ octave steps around tinnitus pitch



- **52 out of 106 patients showed notches**
- **Notch “trough” correlated with tinnitus pitch**

Xiong et al. 2020
Hearing Research

Does conventional audiometry miss threshold shifts that relate to tinnitus?

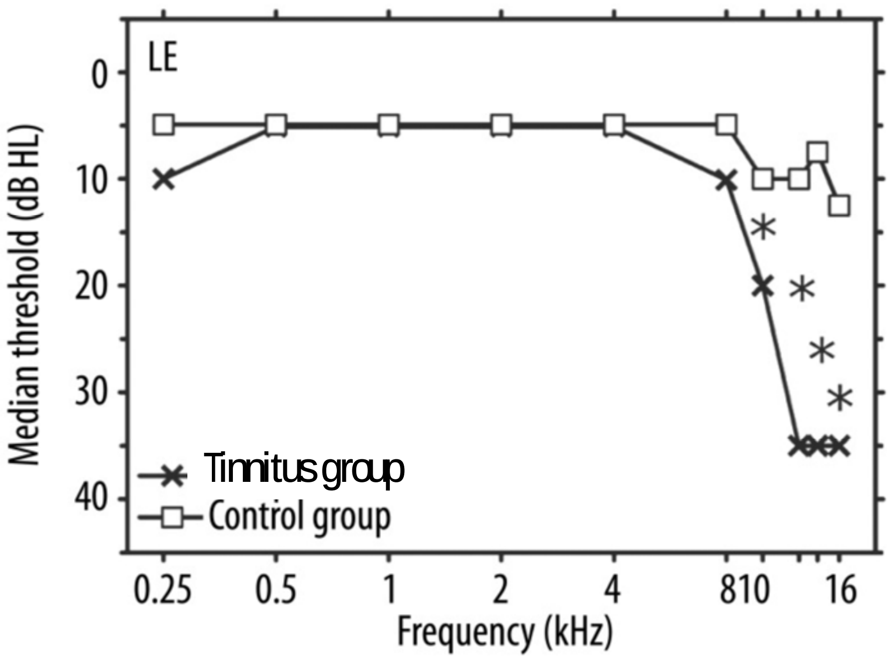
- Threshold shifts above 8 kHz may reveal hearing loss in tinnitus sufferers

- Severity of tinnitus has been found to correlate with degree of shift > 8 kHz

Vielsmeier et al. 2015
Biomed Research International

- This is not a rule; many studies show no differences in thresholds > 8 kHz between tinnitus and non-tinnitus groups

Barnea et al. 1990
Int. J. Audiology



Fabijańska et al 2012
Medical Science Monitor

Damage to the ear that goes undetected in the audiogram

Normal audiogram ≠ normal hearing

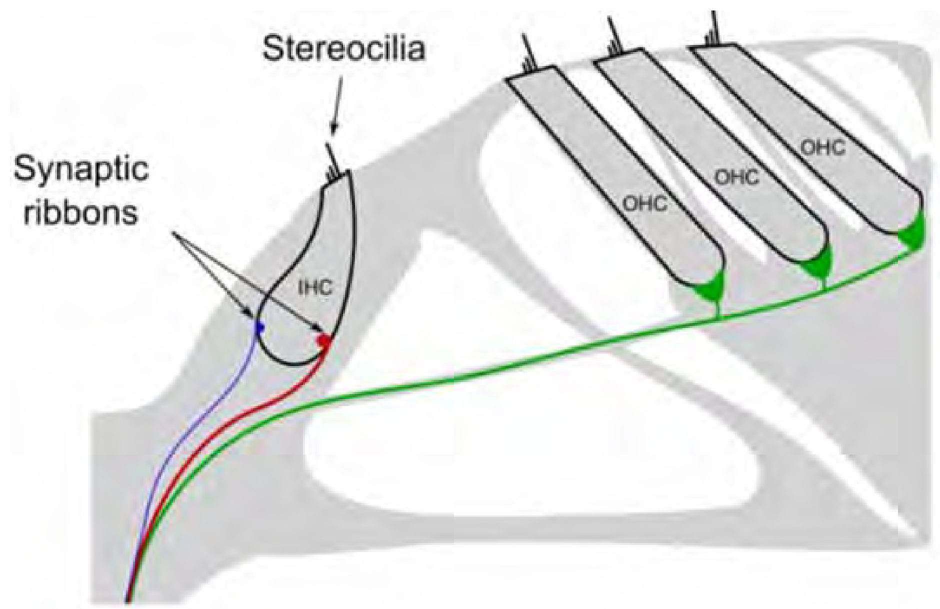
Carhart & Tillman, 1970; Archives of Otolaryngol

~5% of adults and children < 60 with normal thresholds have listening difficulty

Hind et al. 2011, Int J. Audiol

Several configurations of damage to the elements of the inner ear that are undetected by conventional audiometry

Pienkowski, 2017
Ear & Hearing



It takes a lot to elevate thresholds…


Hearing Research 302 (2013) 113–120

Contents lists available at SciVerse ScienceDirect

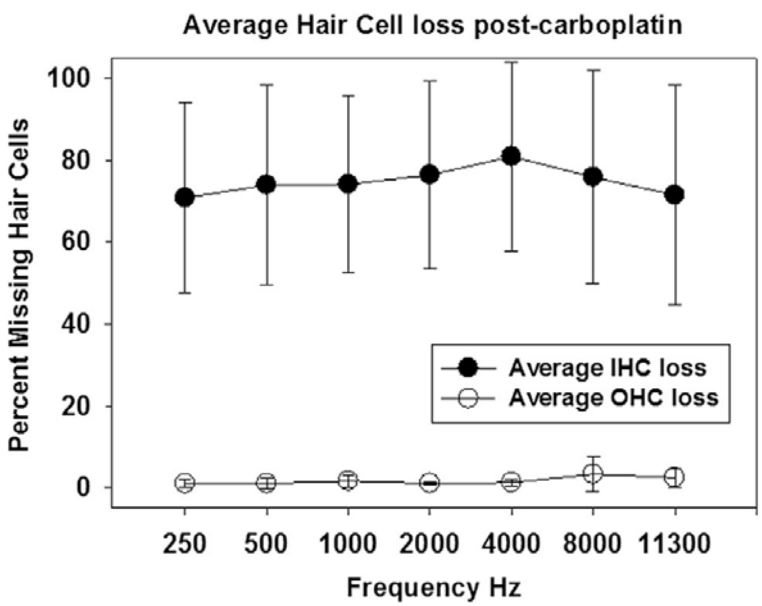
Hearing Research

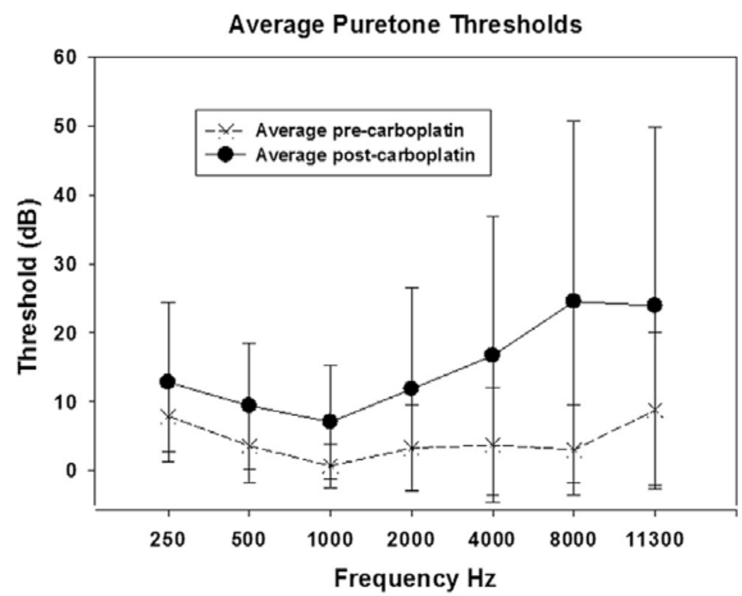
journal homepage: www.elsevier.com/locate/heares

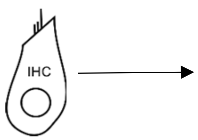
Research paper

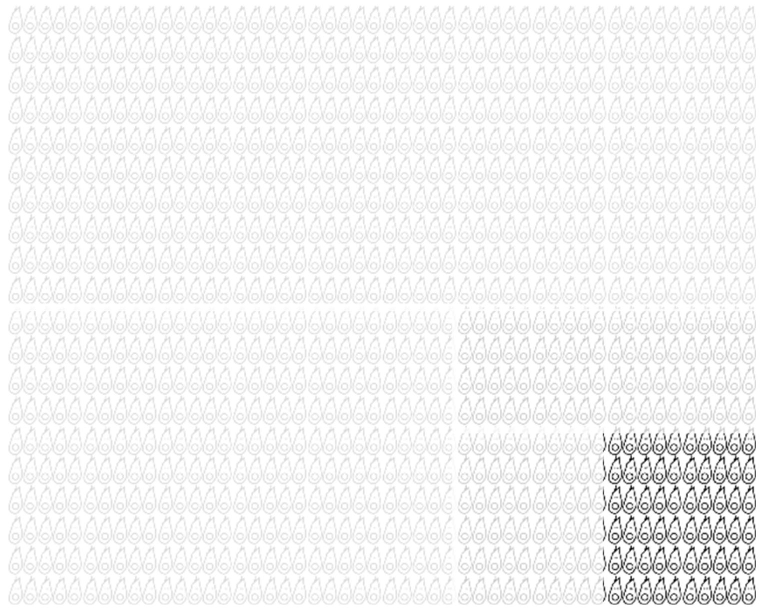
Insensitivity of the audiogram to carboplatin induced inner hair cell loss in chinchillas

Edward Lobarinas [a,*], Richard Salvi [b], Dalian Ding [b]









normal
audiogram

Lobarinas et al., 2013; Hear Res 302:113-20
Chambers et al., 2016; Neuron 89:867-79

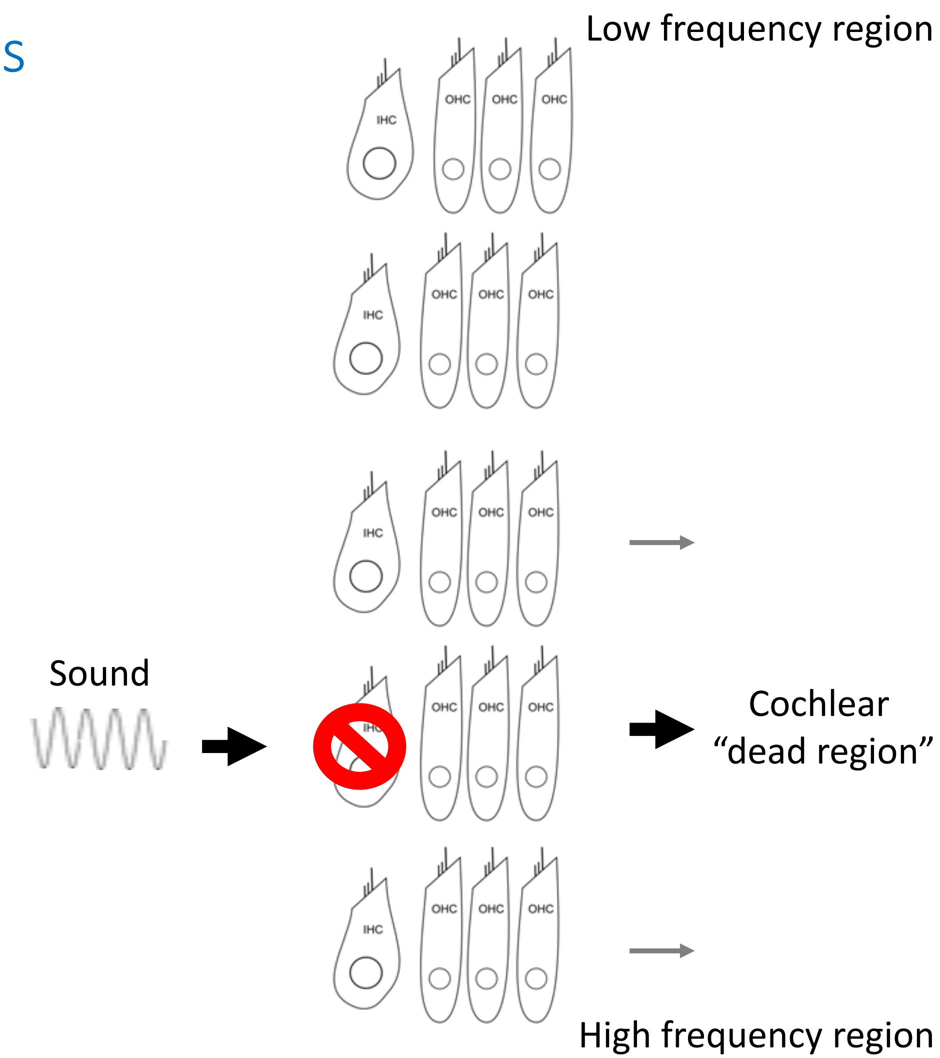
Does evidence of inner hair cell loss relate to tinnitus?

- One study suggested evidence of "dead regions" in tinnitus sufferers despite normal thresholds

Weisz et al. 2006; Hearing Research

- However, many replication failtures

Gilles et al. 2013; Noise & Health
Kiani et al. 2013; Hearing Research



Cochlear Synaptopathy

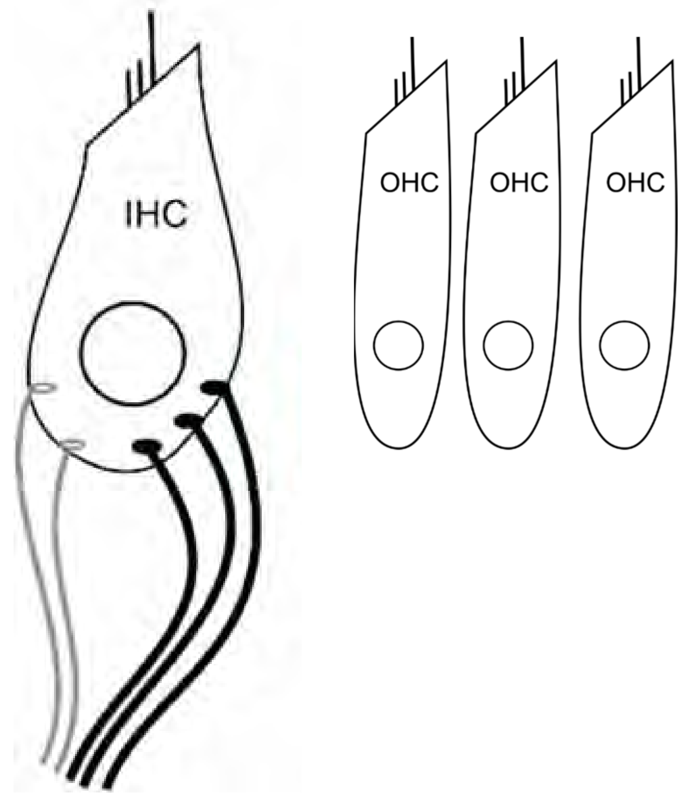
Noise exposure with temporary threshold shifts:

Irreversible damage to synapses connecting IHCs and auditory nerve

Kujawa & Liberman 2006; 2009

Cochlear synaptopathy with normal thresholds: a form of "hidden hearing loss"

Schaette & McAlpine, 2011



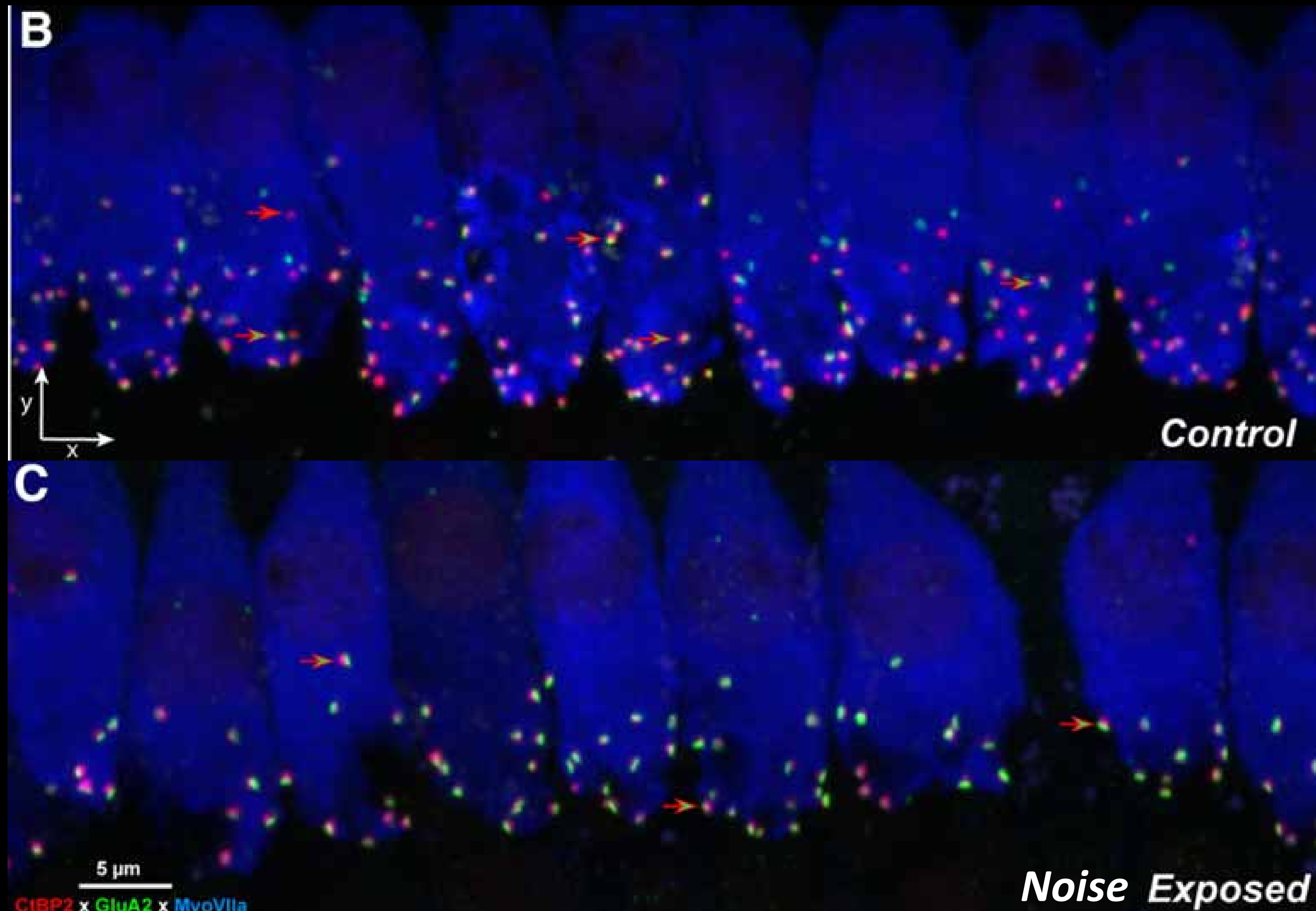
Blue: IHC

Green:
Postsynaptic side

Red:
Presynapic side

Fewer red dots =
More synapse loss

Fernandez et al.
J. Neurosci., May 13, 2015 35(19):7509 –7520



Special vulnerability of high-threshold (HT) synapses

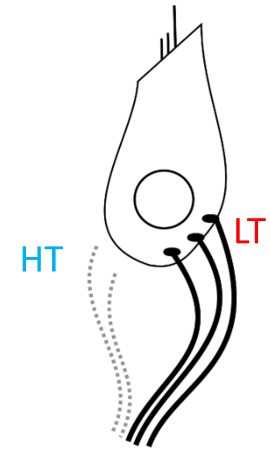
Moderate noise exposure targets synapses with
high firing thresholds
Furman et al 2013

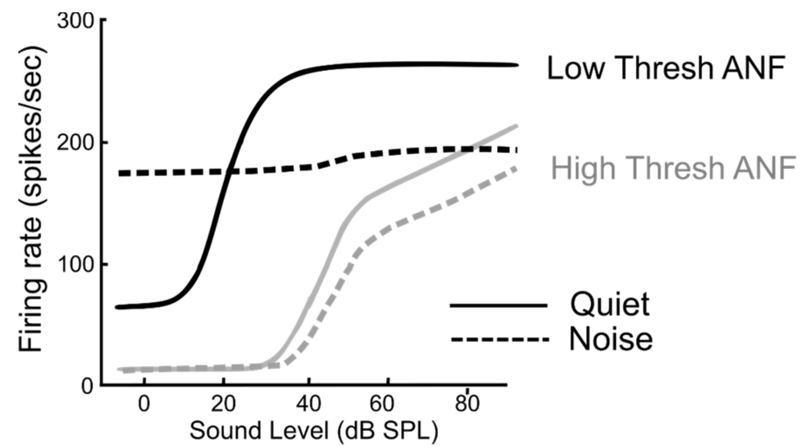
Consequence: normal perceptual thresholds, diminished *suprathreshold* listening ability

Bharadwaj et al 2014; Frontiers in Systems Neuroscience

HT nerve fibers: good at phase locking to sounds; robust in noise

Costalupes et al 1984





adapted from Bharadwaj et al., 2014, Front. Sys. Neurosci. 8 (26)
from data of Liberman, 1978

Robust evidence of synaptopathy in animals

Liu et al. 2012;
Int. J. Otolaryngol

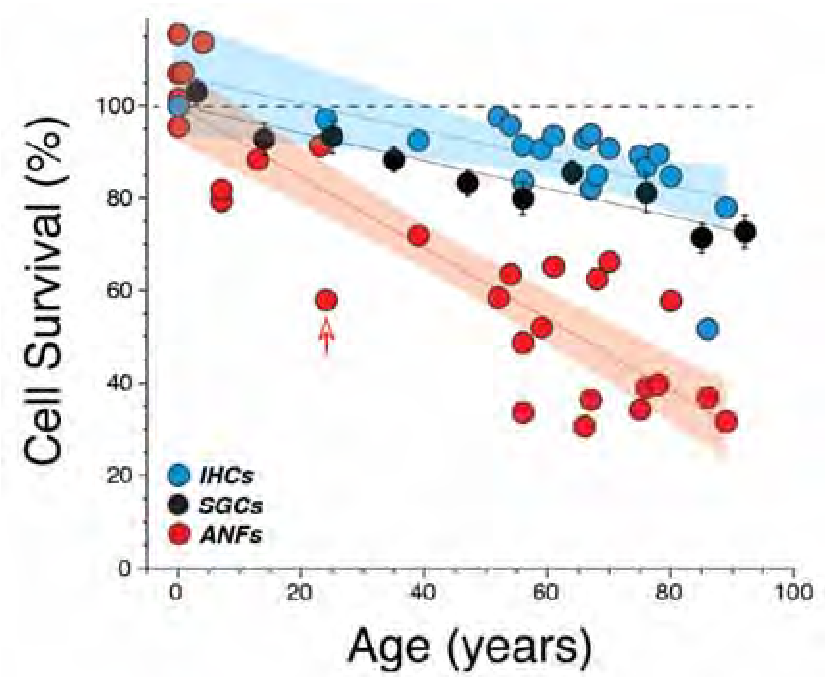
Kujawa & Liberman, 2009;
Journal of Neuroscience

Valero et al. 2017;
Hearing Research

Hickox et al. 2017;
Hearing Research

Hickox et al. 2017;
Hearing Research

There likely is synaptopathy in humans too...



Wu et al. 2020; Neuroscience

Human temporal bone study (N = 20)

3:1 loss of nerve fibers compared to hair cell loss with age

…but detecting it in practice is difficult

Hearing Research 377 (2019) 88–103

Contents lists available at ScienceDirect

Hearing Research

journal homepage: www.elsevier.com/locate/heares

Opinion paper

The search for noise-induced cochlear synaptopathy in humans: Mission impossible?

Naomi Bramhall[a,b], Elizabeth Francis Beach[c,d], Bastian Epp[e], Colleen G. Le Prell[f], Enrique A. Lopez-Poveda[g], Christopher J. Plack[h,i], Roland Schaette[j], Sarah Verhulst[k,l], Barbara Canlon[m,*]

[a] VA RR&D National Center for Rehabilitative Auditory Research (NCRAR), VA Portland Health Care System, Portland, OR, USA
[b] Department of Otolaryngology/Head and Neck Surgery, Oregon Health & Science University, Portland, OR, USA
[c] National Acoustic Laboratories, Macquarie University, Australia
[d] The HEARing CRC, Melbourne, Australia
[e] Hearing Systems Group, Department of Electrical Engineering, Technical University of Denmark, Denmark
[f] School of Behavioral and Brain Sciences, The University of Texas at Dallas, USA
[g] Instituto de Neurociencias de Castilla y Leon, Departamento de Cirugía, University of Salamanca, 37007, Salamanca, Spain
[h] Manchester Centre for Audiology and Deafness, The University of Manchester, Manchester Academic Health Science Centre, M13 9PL, UK
[i] Department of Psychology, Lancaster University, LA1 4YF, UK
[j] UCL Ear Institute, 332 Gray's Inn Road, London, WC1X 8EE, UK
[k] Hearing Technology @ Waves, Dept. of Information Technology, Ghent University, Belgium
[l] Technologiepark 15, 9052, Zwijnaarde, BE, Belgium
[m] Department of Physiology and Pharmacology, Karolinska Institute, Stockholm, 171 77, Sweden

Issues:

- E-phys measurement is “noisy”
- Unaware of noise exposure
- Hyperacusis can confound

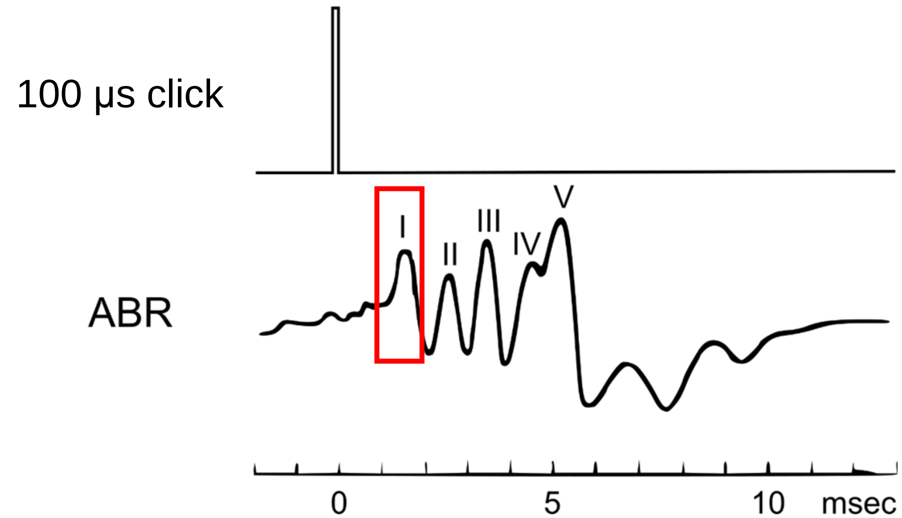
Three candidate measures:

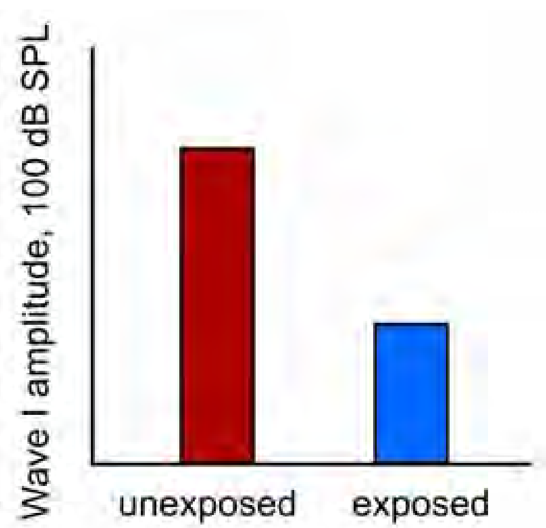
1) Auditory Brainstem Response
2) Envelope Following Response
3) Middle Ear Muscle Reflex

Cochlear Synaptopathy Diagnosis I: Auditory Brainstem Response Wave I

Wave I: synchronous firing of nerve fibers

Theoretically, an ideal non-invasive marker





Animal findings: Normal Wave I threshold but reduced ***suprathreshold*** amplitude

Kujawa & Liberman, 2009;
Journal of Neuroscience

Wave I responses in tinnitus subjects

Studies controlling for
age, biological sex, and audiograms:

Schaette & McAlpine, 2011 ✓
J Neurosci

Gu et al., 2012 ✓
J. Assoc. Research Otolaryng.

Gilles et al. 2016 X
PLoS ONE

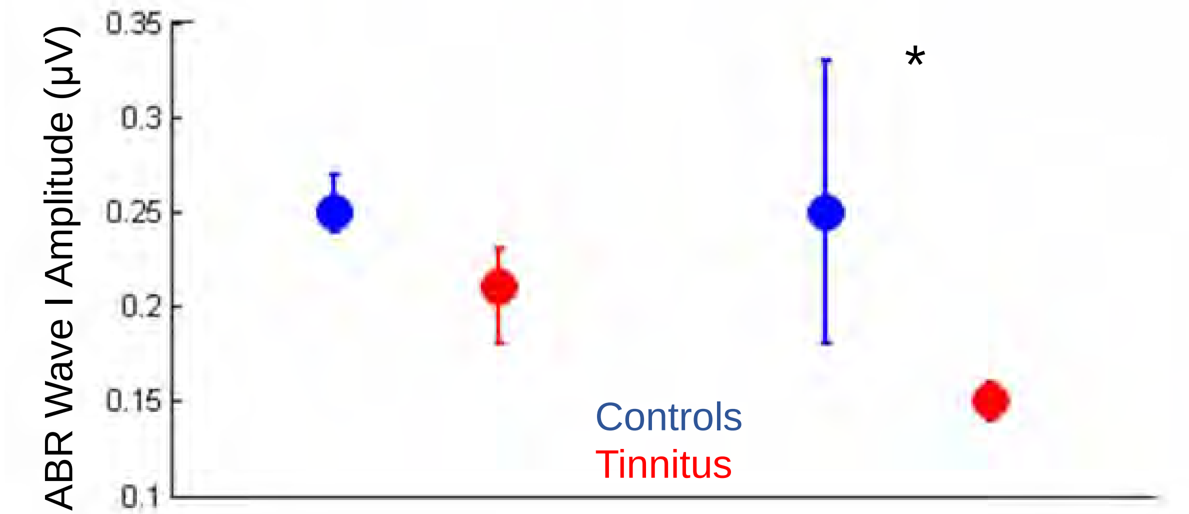
Guest et al., 2017 X
Hearing Research

Bramhall et al., 2019 ✓
J. Acoustical Soc. America

Milloy et al., 2017; Front. Aging Neurosci, 9:237
Meta-analysis of 19 human ABR studies

Normal thresholds

Threshold shifts



248 ears

105 ears

34 ears

831 ears

95% CIs overlap by 0.01 µV

*95% CIs do not overlap

Challenges in detecting synapse loss with ABR Wave I in humans

- Often difficult to record and measure with high precision
- Biological sex differences (head size) impact Wave I amplitude *Stamper & Johnson 2015a/b*
- Electrode montage choice (e.g., reference electrodes, tiptrodes)
- Difficulty to diagnose synaptopathy with concurrent OHC damage *Verhulst et al 2016*

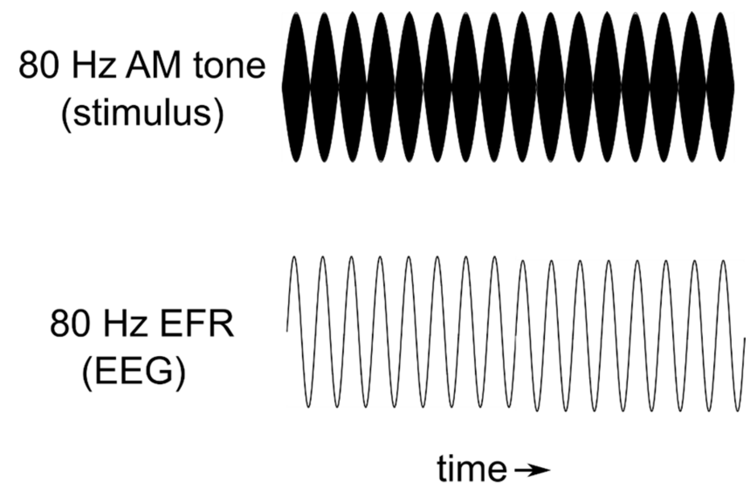
Result:

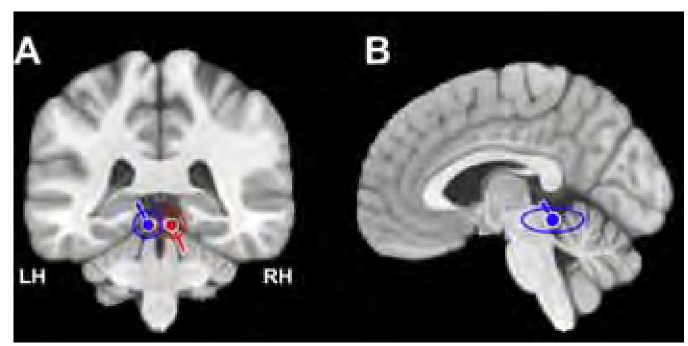
- Conflicting evidence of ABR Wave I amplitude relationship to noise exposure and putatively noise-related pathologies, such as tinnitus

Fulbright, 2016; Stamper & Johnson 2015b; Schaette & McAlpine, 2011; Gilles et al, 2016; Prendergast et al., 2017

Cochlear Synaptopathy Diagnosis II: Envelope Following Responses

- Brain response phase locked to envelope of amplitude modulated (AM) sound
- Composite response from population of brainstem neurons, *including ANFs*
- Stimulus modulation rates from 80-200 Hz generate responses strongly localized to midbrain





Bidelman et al 2015; Hearing Research

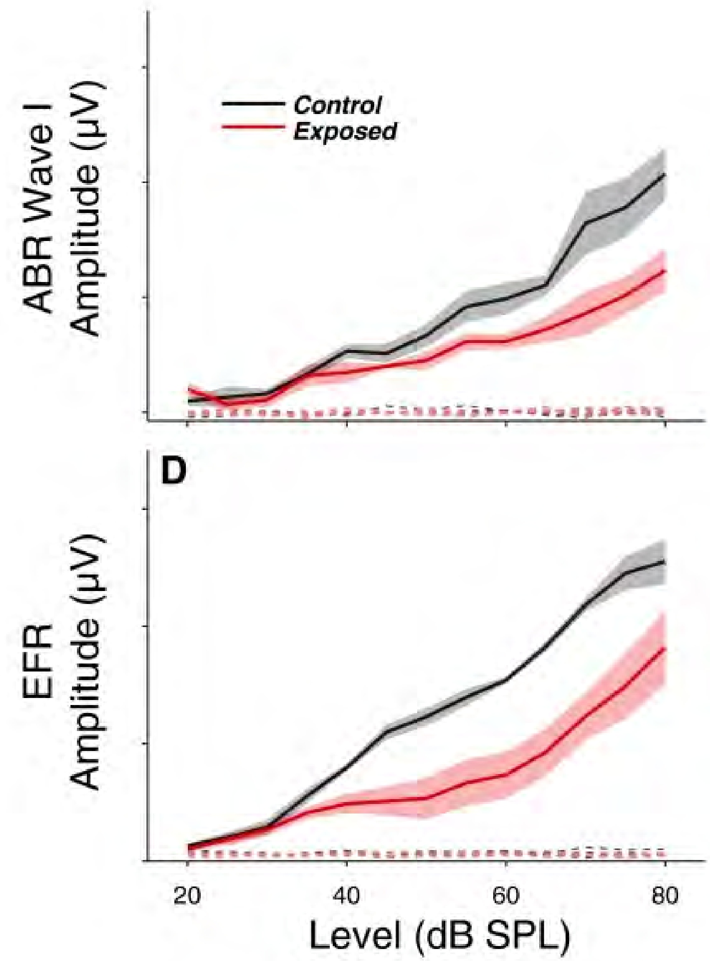
EFRs and synaptopathy

- HT nerve fibers (those targeted by noise exposure) adept at phase locking to stimulus envelope

  Bharadwaj et al 2014

- EFRs predict synaptopathy better in mouse model compared to ABR Wave I

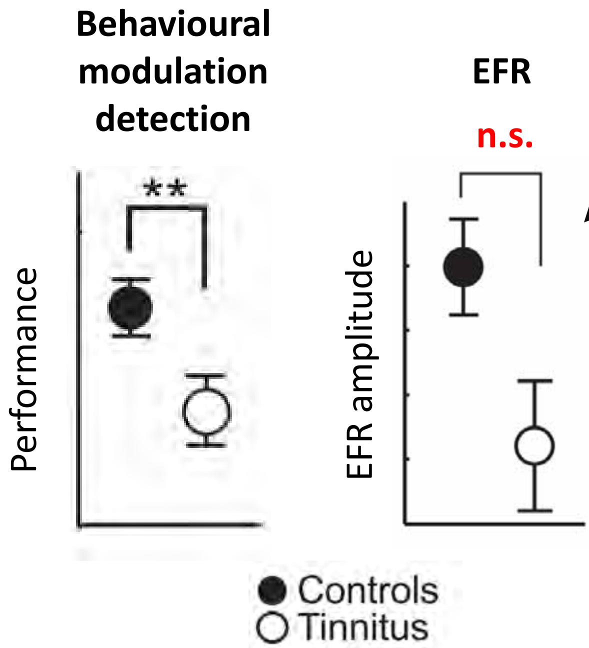
  Shaheen et al 2015



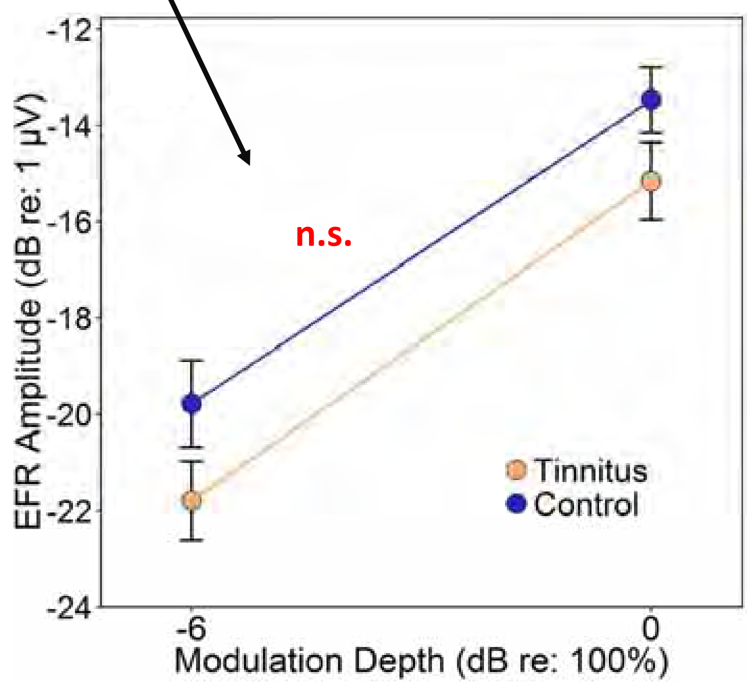
Shaheen et al 2015

EFRs in tinnitus

Lower EFR amplitude in tinnitus, but **not significant**

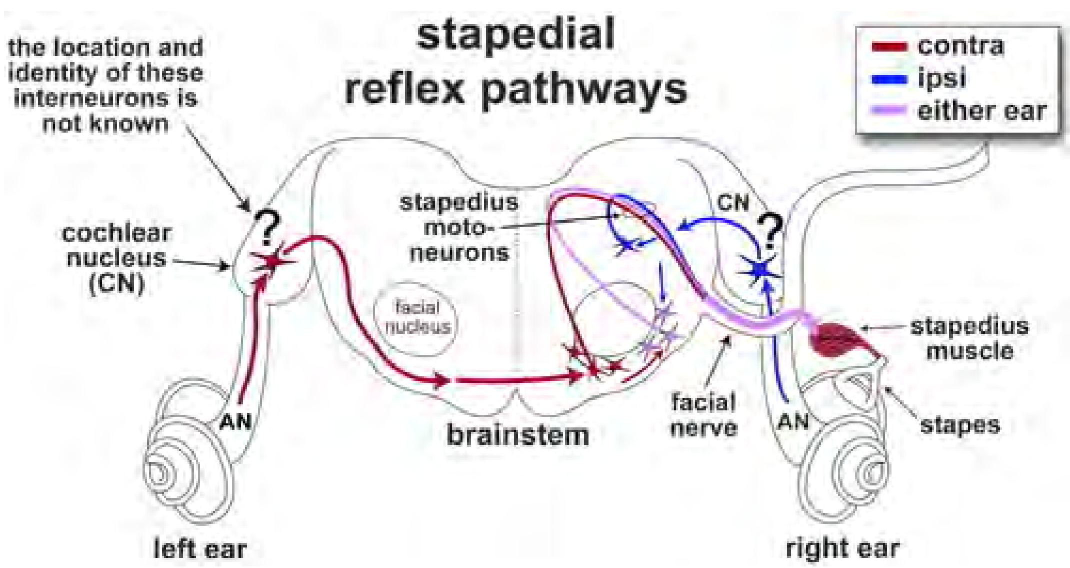


Paul et al. 2017; Hearing Research

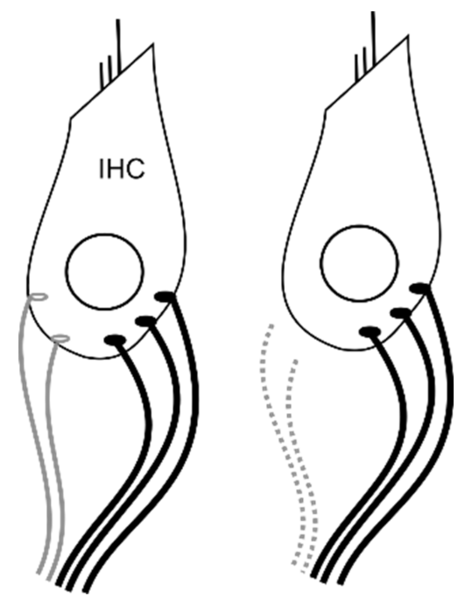


Guest et al. 2017; Hearing Research

Cochlear Synaptopathy Diagnosis III: The Middle Ear Muscle Reflex (MEMR)



- Stiffens stapes
- Deflects tympanic membrane inwards
- **Driven by high-threshold synapses**



Normal:
Strong MEMR

Synapse Loss:
Weak MEMR

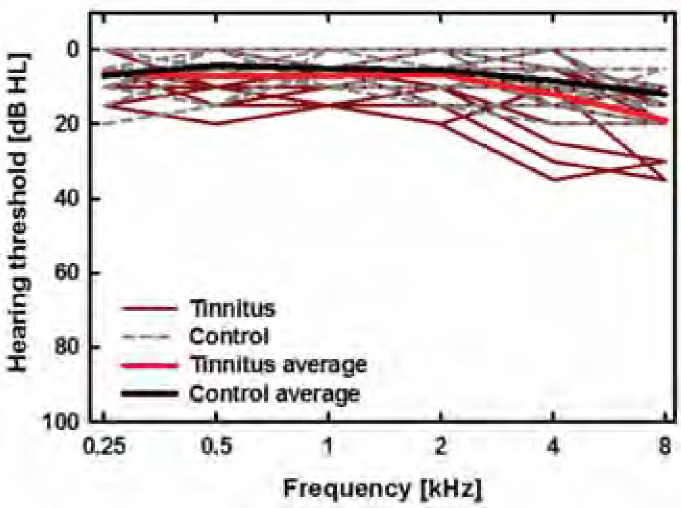
Research Article: New Research | Sensory and Motor Systems

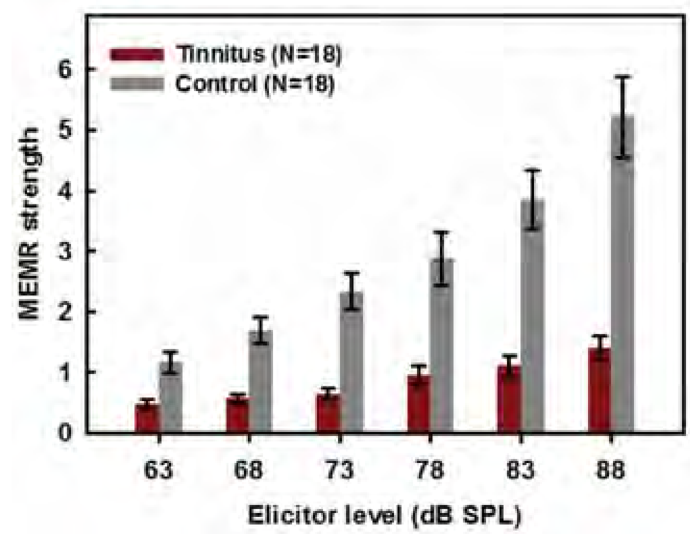
Weak middle-Ear-Muscle Reflex in Humans with Noise-Induced Tinnitus and Normal Hearing May Reflect Cochlear Synaptopathy

Middle-ear muscle reflex in humans with tinnitus

Magdalena Wojtczak, Jordan A. Beim and Andrew J. Oxenham

Department of Psychology, University of Minnesota, 75 East River Rd, Minneapolis, MN 55455, USA

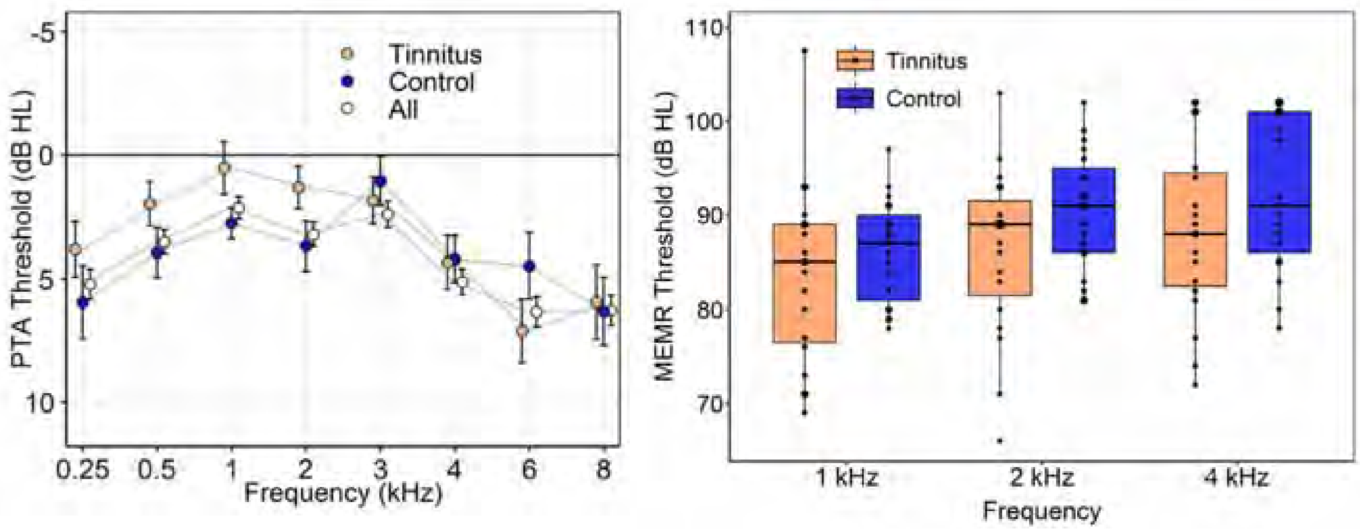




NEUROSCIENCE
RESEARCH ARTICLE
H. Guest et al. / Neuroscience 407 (2019) 75–82

Acoustic Middle-Ear-Muscle-Reflex Thresholds in Humans with Normal Audiograms: No Relations to Tinnitus, Speech Perception in Noise, or Noise Exposure

Hannah Guest,[a]* Kevin J. Munro[a,b] and Christopher J. Plack[a,c]
[a] Manchester Centre for Audiology and Deafness, University of Manchester, Manchester Academic Health Science Centre, UK
[b] Manchester University Hospitals NHS Foundation Trust, UK
[c] Department of Psychology, Lancaster University, UK



Do these methods reflect noise exposure history?

Hearing Research 344 (2017) 68–81

Contents lists available at ScienceDirect

Hearing Research

journal homepage: www.elsevier.com/locate/heares

Research Paper

Effects of noise exposure on young adults with normal audiograms I: Electrophysiology

Garreth Prendergast [a, *], Hannah Guest [a], Kevin J. Munro [a, b], Karolina Kluk [a], Agnès Léger [a], Deborah A. Hall [c, d], Michael G. Heinz [e], Christopher J. Plack [a, f]

[a] Manchester Centre for Audiology and Deafness, University of Manchester, Manchester Academic Health Science Centre, M13 9PL, UK
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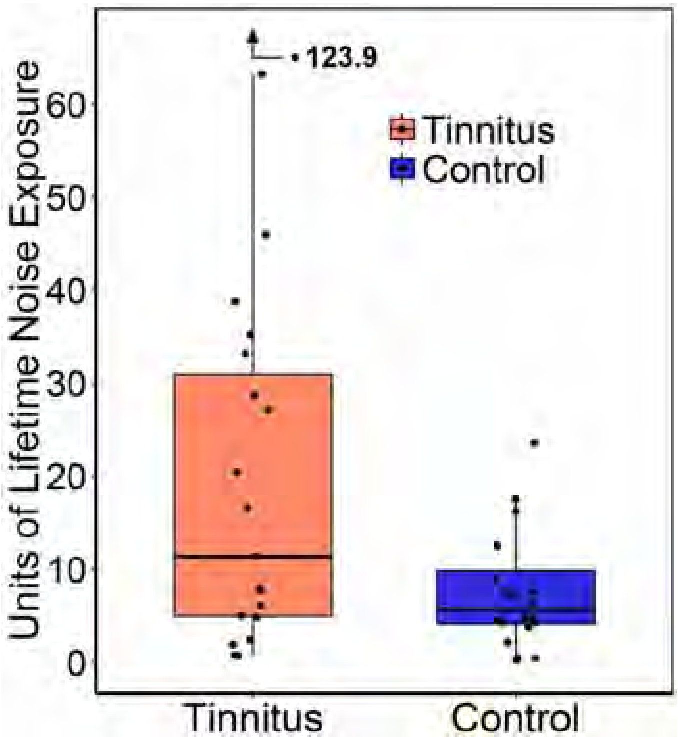
[c] National Institute for Health Research (NIHR) Nottingham Hearing Biomedical Research Unit, Nottingham, NG1 5DU, UK
[d] Otology and Hearing Group, Division of Clinical Neuroscience, School of Medicine, University of Nottingham, Nottingham, NG7 2UH, UK
[e] Department of Speech, Language, & Hearing Sciences and Biomedical Engineering, Purdue University, West Lafayette, IN 47907, USA
[f] Department of Psychology, Lancaster University, Lancaster, LA1 4YF, UK

The data have not been convincing…

Tinnitus and noise exposure

A critical piece of the puzzle



Guest et al. 2017; Hearing Research

Shargorodsky et al. 2010; Am. J. Medicine
N = 14,178

Occupational noise exposure:
tinnitus with threshold shift

Leisure-time noise exposure:
tinnitus without threshold shift

Summary

- Tinnitus cases with “normal” audiometry may be explained by:
  - Threshold shifts not seen in conventional testing
  - Hair cell loss not affecting audiogram
  - Potential loss of synapses that connect hair cells to nerve fibers
  - Causal factors outside of hearing
- Most efforts have focused on cochlear synaptopathy, measured by:
  - ABR Wave 1 amplitudes
  - Envelope Following Responses
  - Middle Ear Muscle Reflexes
- However, it is still unknown:
  - How to accurately measure cochlear synaptopathy
  - If cochlear synaptopathy relates to tinnitus

Art by George Michelsen Foy

Thank you for listening!

Special thanks to:

CAA Webinars on Demand

canadianaudiology.ca/webinars/

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Please keep your ‘thank you for attending email” for your record. More information on website.

UPCOMING WEBINAR: UNDERSTANDING CASES OF TINNITUS WITH A NORMAL AUDIOGRAM: IS HEARING LOSS UNDETECTED WITH BRANDON PAUL – JUNE 9TH, 2020 +

ARCHIVED WEBINAR: THE IMPORTANCE OF VESTIBULAR ASSESSMENT IN SPORT-RELATED CONCUSSIONS WITH JAMIE M. BOGLE, FEB 25, 2020 +

ARCHIVED WEBINAR: WHAT THE AUDITORY CORTEX DOES BEFORE AND AFTER HEARING LOSS WITH STEPHEN G. LOMBER (MAY 29TH, 2019) +

ARCHIVED WEBINAR: SPEECH UNDERSTANDING IN COMPLEX ENVIRONMENTS BY CHILDREN WHO ARE HARD OF HEARING – SEPT 25, 2019 +

COVID19 Resources

- Visit CanadianAudiology.ca
- Under Professional Resources
- COVID19

COVID19 HELPFUL LINKS

The Canadian Academy of Audiology would like to thank its members, associates and communities for all they are doing to manage the COVID19 efforts directed by the Federal, Provincial and Municipal governments together with their regulatory colleges.

We understand that this is a challenging time for you. Many have had major impacts on their ability to go to work and many have had to manage challenging communication with their patients. We know many of you also have stresses related to your personal and family life.

CAA will be monitoring ways we can support your needs within the scope of a professional association.

Facilitating your information needs:
We have provided a list of links to your regulatory college websites where you will find COVID19 messages and links. We have provided links to recommendations by other constituencies and some government health and business links.

We have also included links to the Employment Insurance website. We urge you to continue to monitor federal, provincial and municipal government websites to ensure that you are informed about the health and employment related mandates and policies.

Contact Information

- CanadianAudiology.ca
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