Noise Pollution

Current Status & Future Directions

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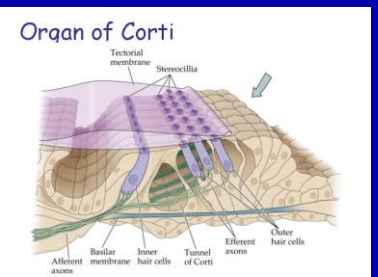


Noise Pollution

- Increasingly recognized as a public health problem
- 1.3 billion affected by hearing loss globally (2010)
- 10% of the world's population is exposed to sound pressure levels that could cause NIHL (WHO estimate)

- With the modern world so dependent on noise-producing and noise-related technology – industries, automobiles, aircraft, motorcycles, amplified music, car stereo systems - the ambient noise level is rapidly accelerating
- Of all types of environmental pollutants, noise is the most prevalent and insidious with deleterious physiological and psychological effects

Effects of Noise

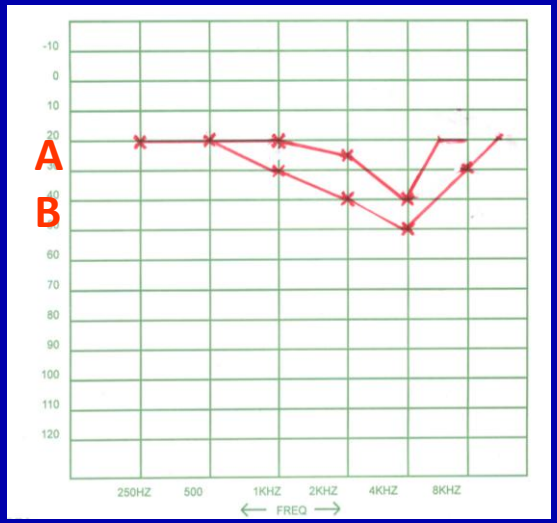
Noise effects are both health and behavioral in nature - by increasing stress hormones like adrenaline, noradrenalin, and cortisol

- Hypertension
- High stress levels
- Sleep disturbances
- Trigger for heart disease, immunity problems, stroke

- Annoyance, Aggression
- Irritability
- Depression, Insomnia
- Fatigue
- Decreased work capacity
- Increased usage of sedatives, antacids and CVS drugs
- Feeling of isolation
- Paranoia
- Erosion of self confidence

Auditory Effects of Noise Pollution

- Tinnitus
- Hearing loss
- Ear pain
- Paracusis
- Hyperacusis
- Binaural Diplacusis
- Speech Misperception
- Vertigo



Noise Pollution

- An increase of 10 dB indicates a doubling of loudness, and an increase of 20 dB represents a sound that is four times louder
- Whispers - 20 dBA
- Normal conversation - 50 to 60 dBA
- Shouting - 85 dBA
- Traffic noise in busy junction - 90 dB
- Loud music - over 120 dBA
- Jet takeoff - 130 dB
- Continuous exposure to sounds over 85 dBA may cause permanent hearing loss

- An estimated 1.1 billion young people (between 12 & 35 yrs) are at risk of developing hearing loss due to recreational noise

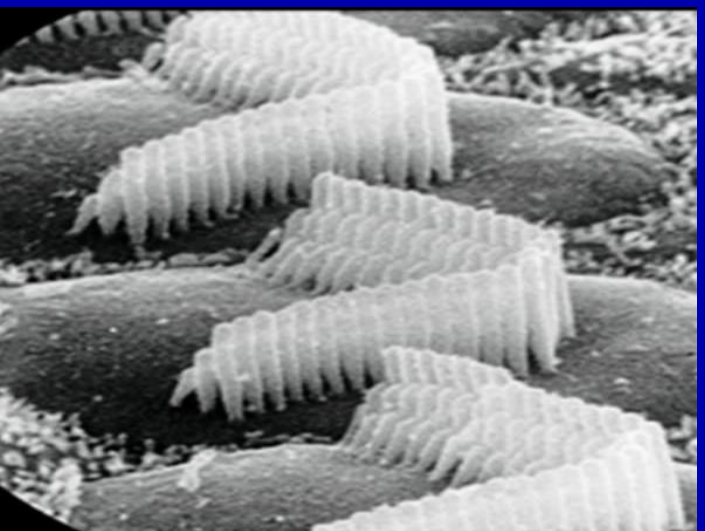
Noise in Hospitals

"Unnecessary noise is the most cruel absence of care which can be inflicted either on the sick or well "

Florence Nightingale (1859)

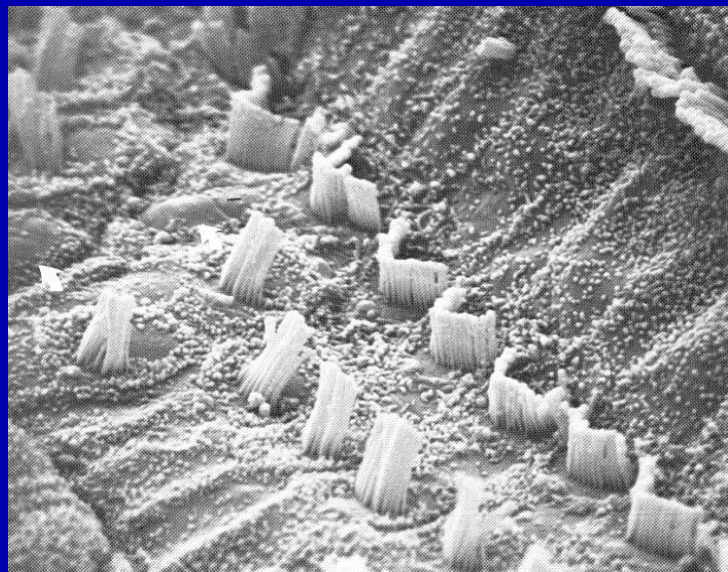
Pathophysiology

- Outer hair cells - more susceptible to noise exposure than inner hair cells
- Temporary threshold shifts - anatomically correlated with decreased stiffness of the stereocilia of outer hair cells
- Stereocilia become disarrayed and floppy



Normal

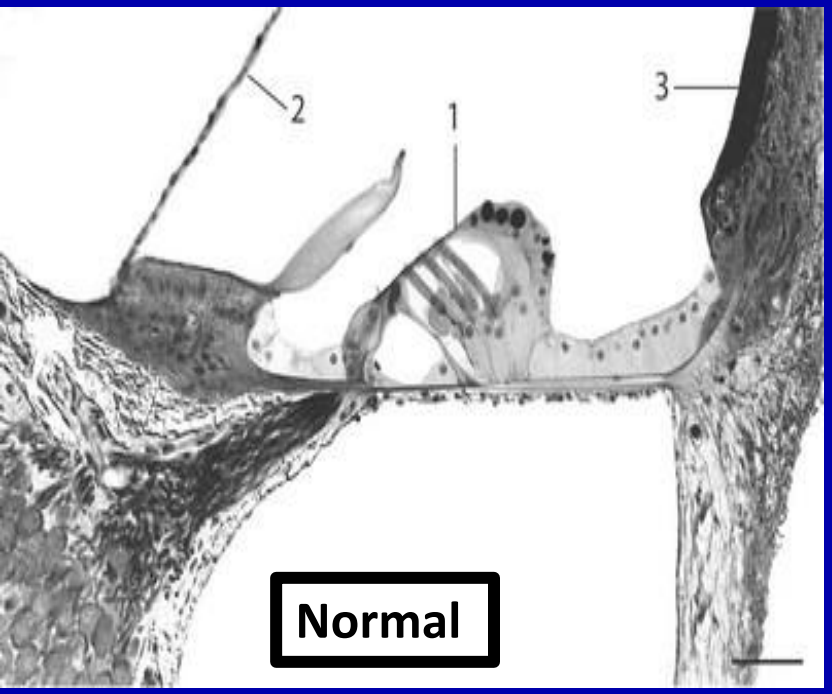
NIHL

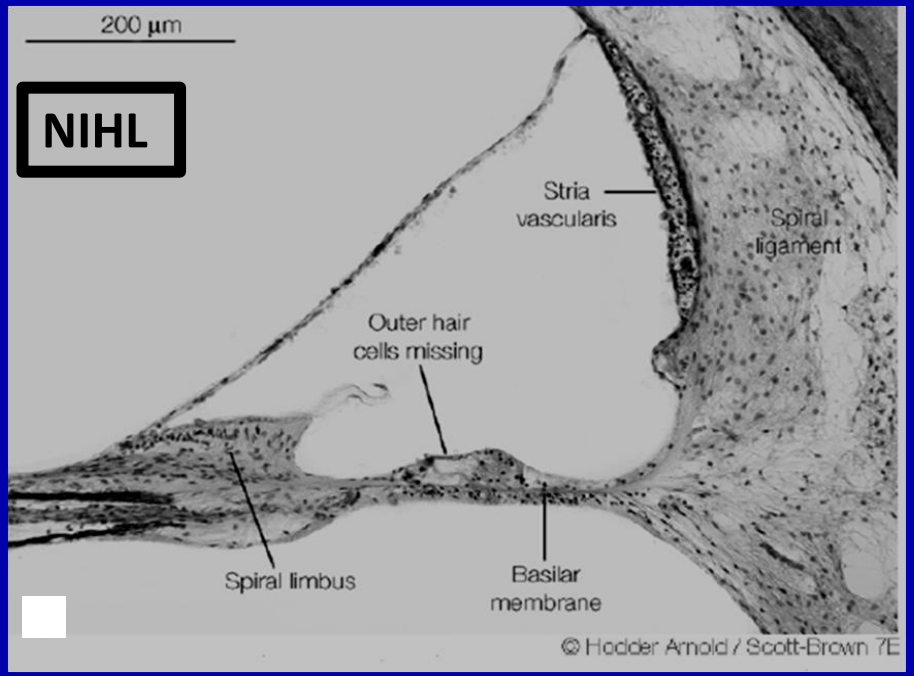


Temporary threshold shifts

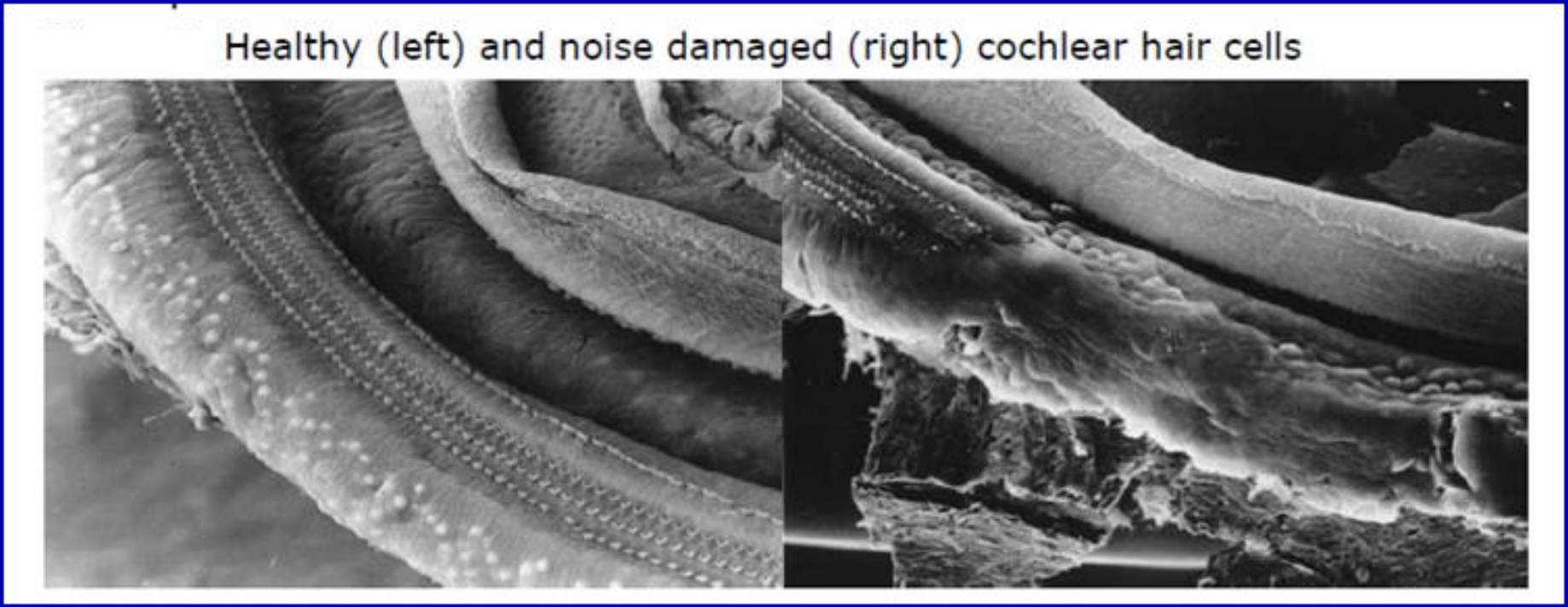
- Activity of the ion transporters Na,K-ATPase and Ca-ATPase (role in generating the endocochlear potential) decreases, while free radicals are increased, in the cochlear lateral wall after TTS inducing noise

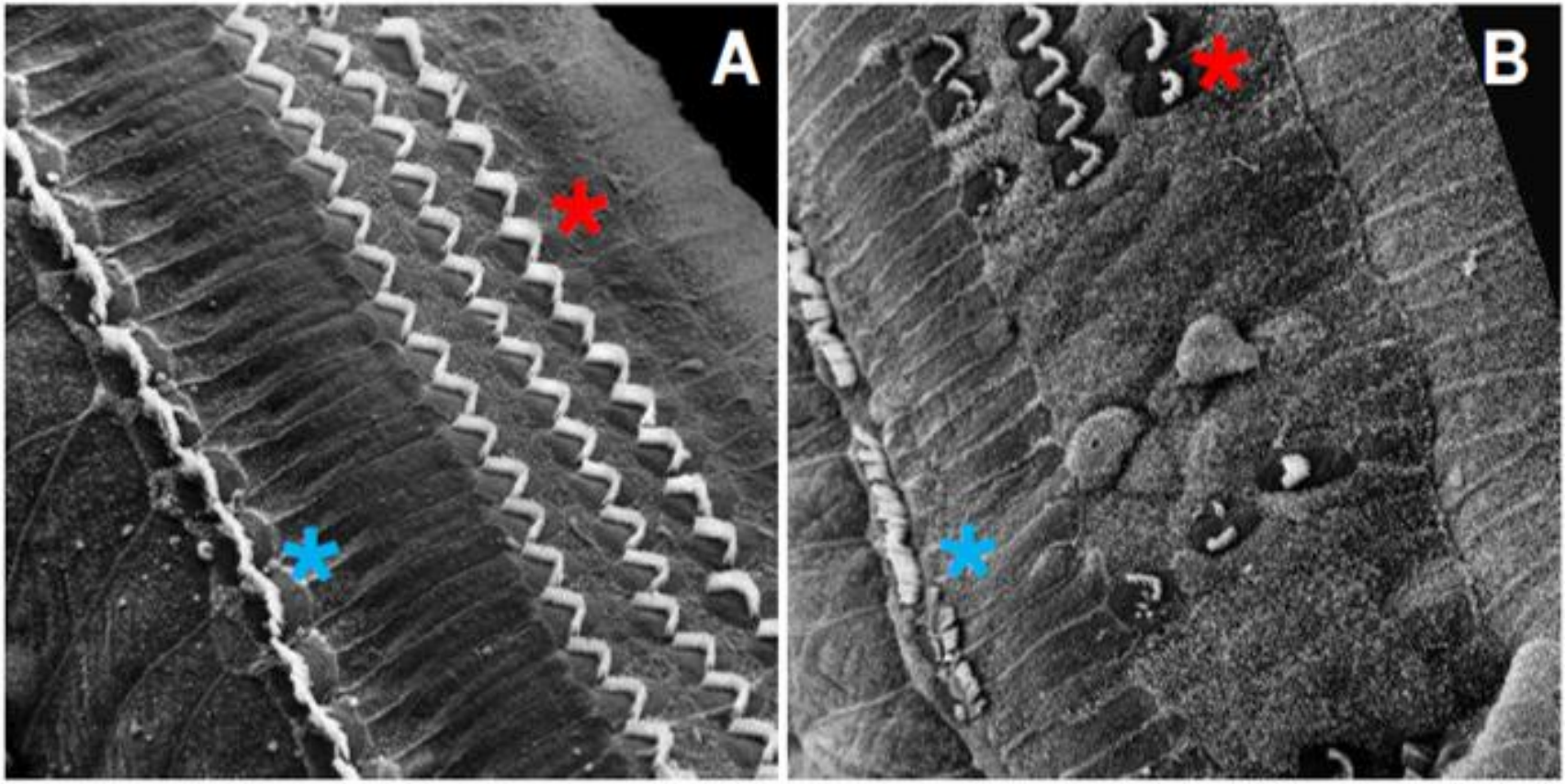
- Permanent threshold shifts - associated with fusion of adjacent stereocilia and loss of stereocilia
- More severe exposure - loss of adjacent supporting cells, complete disruption of the organ of Corti
- Progressive Wallerian degeneration and loss of primary auditory nerve fibers





- Basal region of the organ of Corti - more vulnerable to noise injury compared to the low-frequency apical region

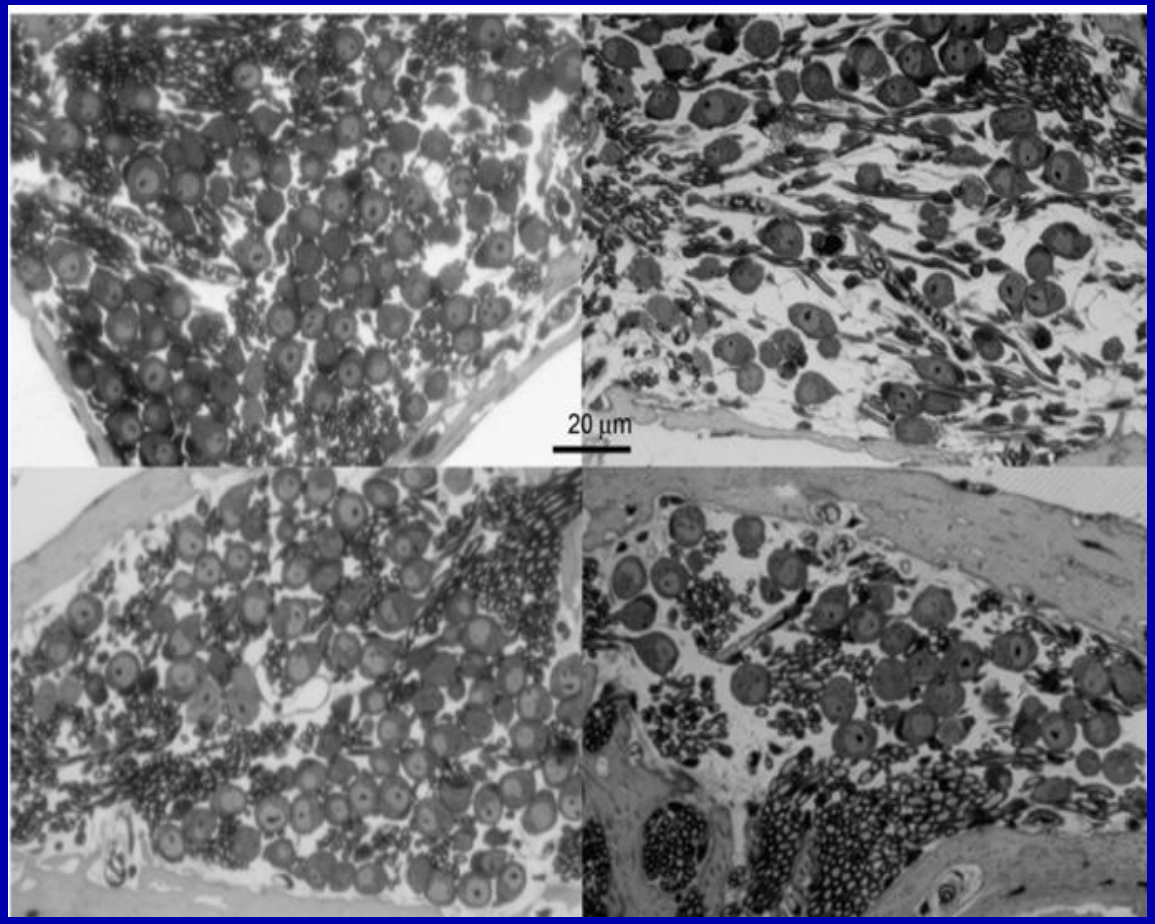




Electromicrographs of the Rat Organ of Corti. This figure highlights the IHCs (blue *) and OHCs (red *) before (A) and after (B) excessive noise exposure (taken from http://newsroom.hei.org/pr/hri/photo.aspx?fid=138451 &id=E0C32378).

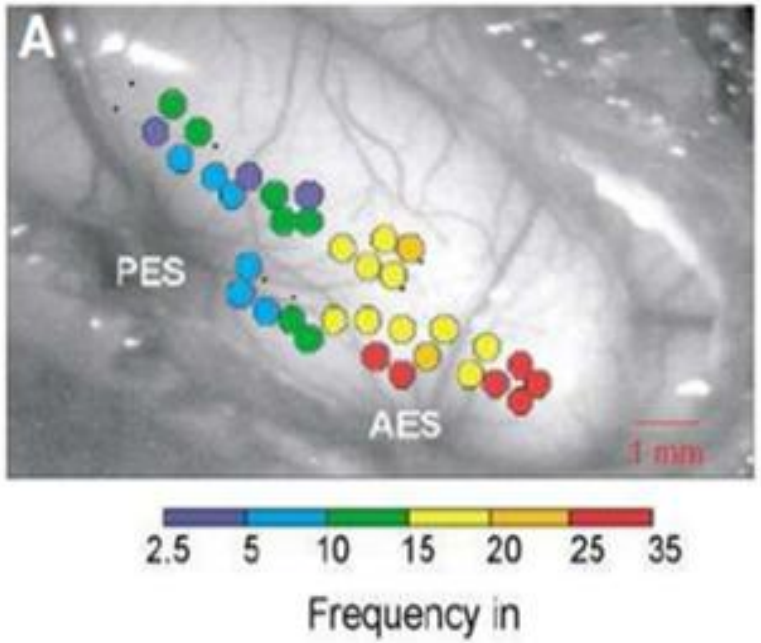
SGNs of Rosenthal's canal

Normal cochlea (Apical & Basal turn)

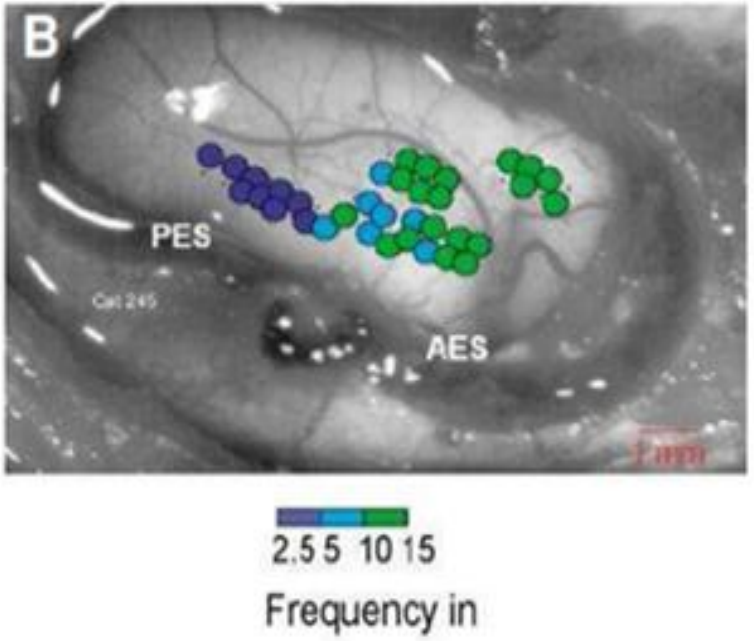


Noise-damaged cochlea (Apical & Basal turn)

Normal Auditory Cortex Tonotopic



Reorganized Cortical Map After



Normal and reorganized tonotopic maps in cat primary auditory cortex. The characteristic frequency at each recording site is colour-coded and overlaid on a photograph of the cortical surface for a control cat (A) and a cat with a noise induced hearing loss (B) (Eggermont and Roberts, 2004). Legend: AES = Anterior Ectosylvian Sulcus; PES = Posterior Ectosylvian Sulcus.

- Significant milestones have been reached in the understanding of the cellular and molecular mechanisms of NIHL which can help in developing therapeutic strategies
- Complex interplay of genetic and environmental factors lead to oxidative stress at a molecular level

Noise-induced hearing loss

Metabolic mechanisms

- For noise exposure less than 115 dB
- Recovery from TTS - a role for metabolic mechanisms

Oxidative stress hypothesis for noise-induced cochlear injury

- Excessive generation of reactive oxygen species (ROS) and reactive nitrogen species (RNS) with acoustic overexposure
- They oxidize cell membrane lipids, intracellular proteins, and DNA, leading to injury and/or cell death and overwhelm cochlear antioxidant defenses [antioxidant enzymes, heat shock proteins, trophic factors, vitamins C and E, and glutathione (GSH)]

- Reactive oxygen species (ROS) can persist in the cochlea for 7 to 10 days after noise exposure, spreading from the base to the apex

- Excessive release of neurotransmitters – glutamate
- Increases in intracellular calcium
- Mitochondrial membranes become permeable and release respiratory enzyme molecules (e.g., cytochrome c) that activate cell death effector proteins (e.g., caspases)
- Programmed cell death pathways involve calpain, caspases, and JNK/c-Jun molecules
- Inflammation induced by DAMP (damage-associated molecular patterns) signaling - contributor to NIHL

Cell signaling networks - Mediators of HC damage

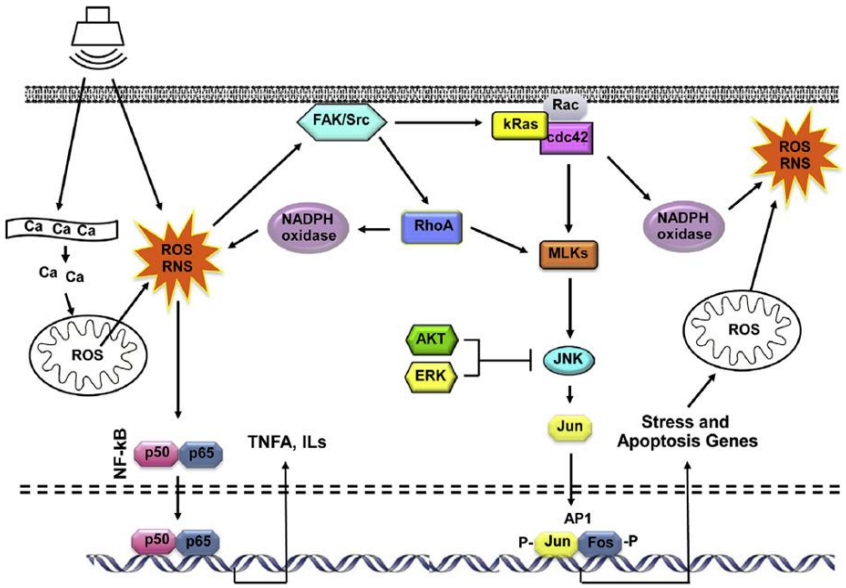


Fig. 1. Diagram illustrating damage processes and pathways thought to contribute to HC loss due to acoustic overexposure. Noise initiates the production of ROS via release of Ca^{2+} from the endoplasmic reticulum and/or entry from extracellular fluid, which induces release of ROS from mitochondria, and by activation of NADPH oxidases. ROS can activate NF-κB, leading to the production of pro-inflammatory cytokines, and also κRas/cdc42/JNK pathway leading to the expression of stress and apoptosis genes. Pro-apoptotic factors further increase mitochondrial membrane permeability, leading to the release of additional ROS. The JNK pathway can be inhibited by the ERK MAPK or AKT, signaling molecules that can be activated by growth factors.

Apoptosis

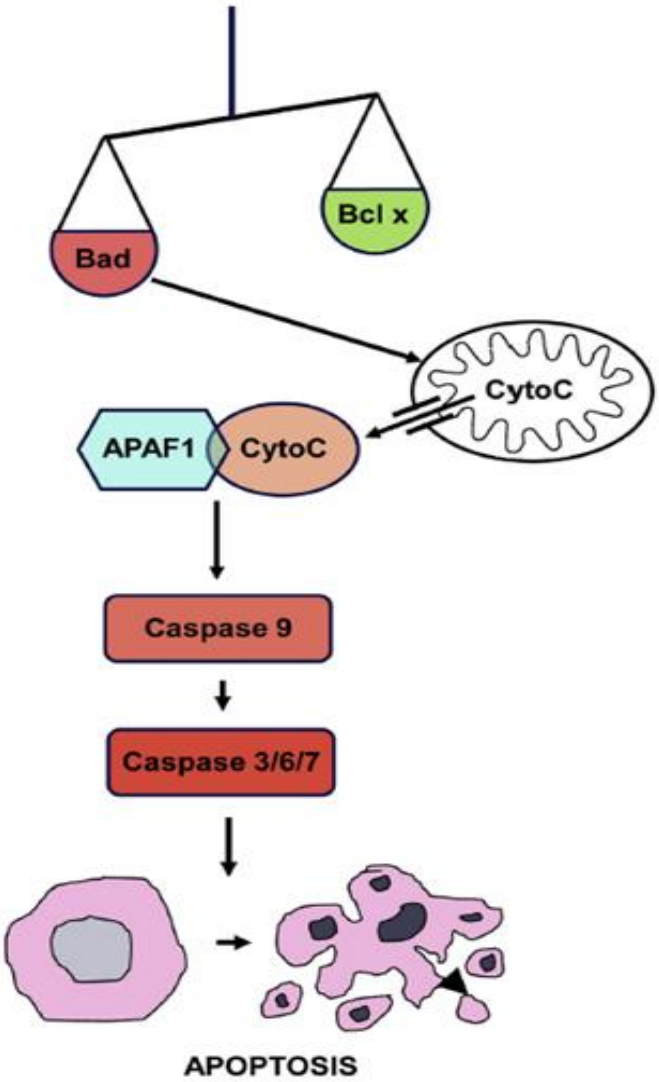


Diagram of the intrinsic pathway of apoptosis. Apoptosis can be initiated when pro-apoptotic proteins such as BAX or BAD which overwhelm anti-apoptotic proteins of the BCL family. This destabilizes mitochondrial membranes, releasing Cytochrome *c* into the cytoplasm. Interaction of Cytochrome *c* with APAF forms an apoptosome, which enzymatically cleaves pro-caspase 1 into its active form. This initiator caspase in turn cleaves executor caspases (3, 6 and 7), which mediate programmed death and orderly fragmentation of the cell.

Spiral modiolar artery (Branch of AICA)

- An important component of cochlear microcirculation
- Meets the lateral cochlear wall to form the stria vascularis
- Has been shown to constrict during and after noise exposure (Arpornchayanon et al., 2013)

Mechanical Damage

- With exposures of 115 to 125 dB
- Destruction of OHCs, disruption of Reissner's membrane, basilar membrane–cell junctions, damage to or loss of stereocilia bundles, disruption of subcellular organelles, such as the endoplasmic reticulum
- Persistence of PTS - due to structural changes

Glucocorticoid receptors

- Expressed in human cochlea
- Treatment with steroids helps improve hearing
- Pretreatment with glucocorticoid receptor antagonists exacerbates threshold shifts

Genetic susceptiblity to NIHL

- Advances in decoding the genetic predisposition for NIHL will facilitate early screening and aid the development of personalized NIHL prevention and treatment strategies

Genetic susceptiblity to NIHL

- Nox3- exclusively expressed in the inner ear - key gene for susceptiblity to NIHL (Rick A Friedmen, Keck school of medicine, USC)
- CDH 23 – encodes Cadherin 23 which is a component of stereocilia tip links - genetic variant may modify susceptibility toNIHL

Genetics in NIHL

- Include genes encoding proteins of the hair cell (Cdh23, Pmca2), oxidative stress (GRM7, GRHL2, Sod1; Gpx1), stress-activated heat shock factor (Hsf1) and potassium recycling (KCNE1 SNP and KCNQ4)
- Glutathione S-transferase Mu 1 and theta 1 (GSTM1 and GSTT1) deletion polymorphisms - found in noise-exposed workers

Genetic predisposition to NIHL

- Cochlear P2X2 receptor/ATP-gated ion channel signaling pathway – regulate sound transduction and auditory neurotransmission, outer hair cell electromotility, inner ear gap junctions, and K+ recycling - confers protection from NIHL
- Absence or mutation of P2X2 receptor increases susceptibility to NIHL

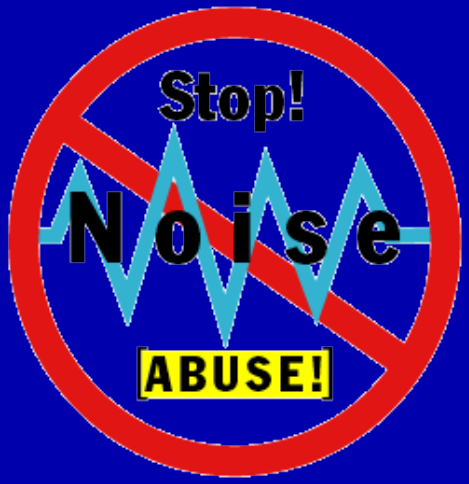
Genetics in NIHL

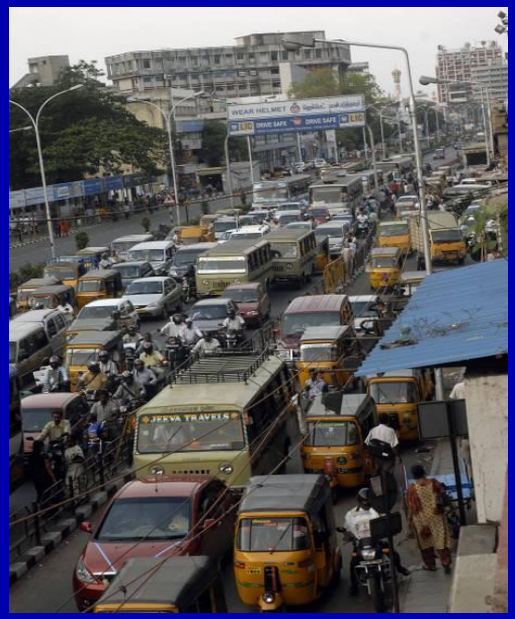
- Apoptosis is executed by a family of cysteine proteases called Caspases - significant role in noise-induced damage of the cochlea
- X-linked inhibitor of apoptosis (XIAP) - suppresses caspase-3 activity and may reduce NIHL

Genetics in NIHL

- Heat shock proteins (Hsps) are induced by noise (Lim et al, 1993)
- Hsps, when induced in response to moderate nontraumatic sound levels, can condition the ear to withstand effects of loud noise
- Genetic variation in the hsp70 genes - may contribute to the susceptibility to NIHL
- Haplotype analysis - Hap5 and Hap6 - significantly more frequent in NIHL

One-third of permanent hearing loss is preventable with proper hearing loss prevention strategies.





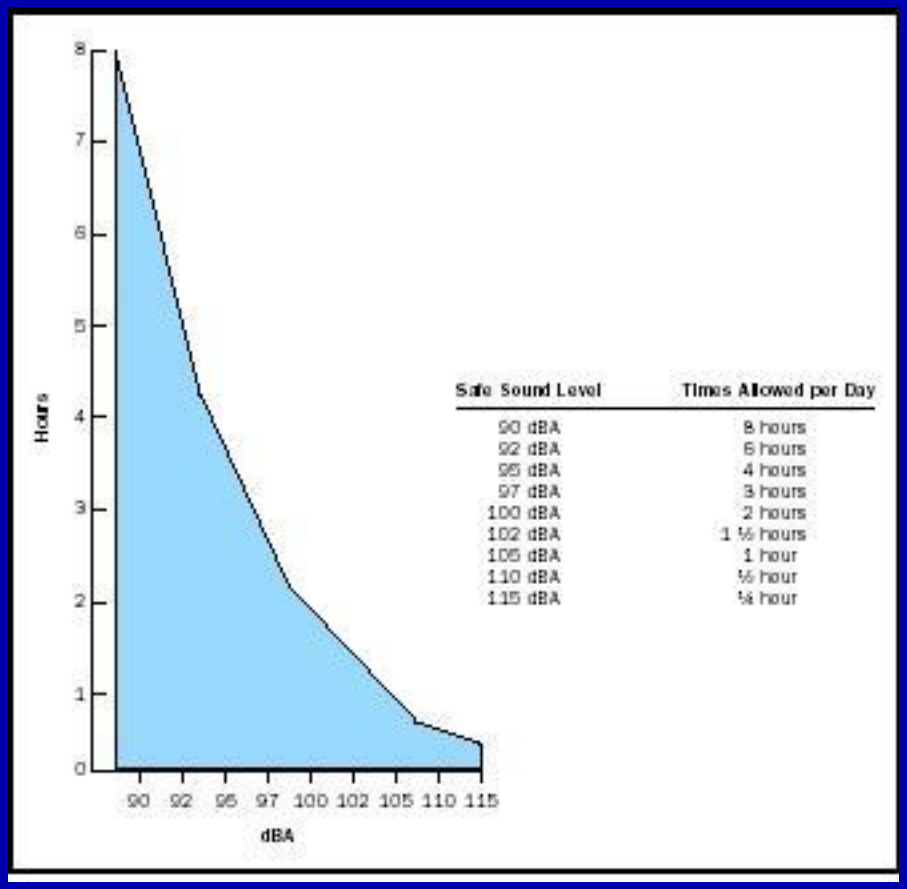
Reducing damage by Industrial Noise

- Exposure of workers to industrial noise has been addressed since the 1930s
- Redesign of industrial equipment
- Shock mounting assemblies
- Physical barriers in the workplace

Permissible noise exposures

Duration / day	Sound Level
8 hours	90 dB
4 hours	95 dB
2 hours	100 dB
1 hour	105 dB
1/2 hour	110 dB
1/4 hr or less	115 dB

OSHA standard for the maximum sound intensity tolerable over certain lengths of time (permissible exposure level)



Duration of 16 hours - 85 dBA

Duration of 8 hours - 90 dBA

Duration of 6 hours - 92 dBA

Duration of 4 hours - 95 dBA

Duration of 3 hours - 97 dBA

Duration of 2 hours - 100 dBA

Duration of 1.5 hours - 102 dBA

Duration of 1.0 hour - 105 dBA

Duration of 30 minutes - 110 dBA

Duration of 15 minutes - 115 dBA

- It is now accepted that the risk of hearing loss is negligible at noise exposure levels of less than 75 dB (A) Leq (8-hr)
- Many countries have adopted industrial noise exposure limits of 85 dB (A) +5 dB (A) in their regulations

Adequate hearing conservation program

- Baseline audiometry within 6 months of onset of exposure for all employees
- The audiogram must be obtained when the employee has not been exposed to hazardous noise for at least 14 hours
- Annual audiometric testing should be performed for workers whose TWAs equal or exceed 85 dBA
- Workers must have annual training about the effects of noise on hearing and the purpose of audiometric testing and hearing protective devices (HPDs)

Permissible decibel limits

Allowed decibel level	During day	During night
Industrial zone	75 dB(A)	70 dB(A)
Commercial zone	65 dB(A)	55 dB(A)
Residential zone	55 dB(A)	50 dB(A)
Silence zone (Not less than 100 m around Hospitals, educational institutions, courts)	50 dB(A)	40 dB(A)

Noise Pollution (Regulation & Control) Rules, 2000

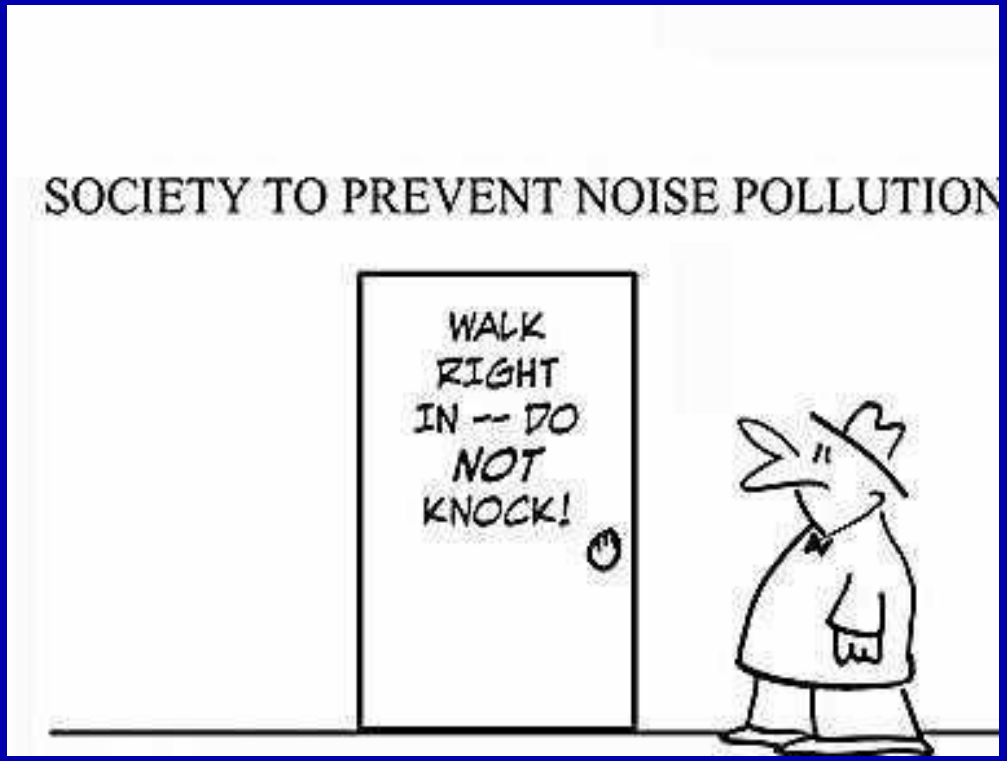
Mitigating roadway noise

- Noise barriers
- Limitation of vehicle speeds
- Alteration of roadway surface texture
- Limitation of heavy vehicles
- Traffic controls that smooth vehicle flow to reduce braking and acceleration
- Tire design

Sound Tube, Melbourne designed to reduce roadway noise

Measuring sound pollution caused by air-horns
The Hindu, Jan 12, 2013

Raise awareness about noise pollution



- Create, collect, and distribute information and resources regarding noise pollution
- Strengthen laws and governmental efforts to control noise pollution
- Establish networks among environmental, professional, medical, governmental, and activist groups working on noise pollution issues
- Assist activists working against noise pollution

TNPCB

Tamil Nadu Pollution Control Board

- Reduce noise exposure by honking less while driving
- Installing dual-paned windows
- Switching off the TV and not keep it constantly running

- According to The Noise Pollution (Regulation and Control) Rules, 2000, a loudspeaker or a public address system shall not be used except after obtaining written permission from the authority and the same shall not be used at night i.e. between 10.00p.m. and 6.00 a.m.
- The noise level at the boundary of the public place, where loudspeaker or public address system or any other noise source is being used shall not exceed 10 dB (A) above the ambient noise standards for the area or 75 dB (A) whichever is lower.
- The peripheral noise level of privately owned sound system shall not exceed by more than 5 dB (A) than the ambient noise standard specified for the area in which it is used, at the boundary of the private place.

In a landmark judgement in 2001, the Supreme Court ruled that the right to worship does not entitle anyone to the right to make noise

- The Supreme Court, in one of its judgment directed to put a complete ban on bursting of sound emitting fire crackers during night time (between 10 pm and 6 am)
- Ban on use of sound emitting instrument or any sound amplifier at night time except in public emergency and use of horn at night time except in exceptional circumstance have been ordered

In the year 2005, the Supreme Court banned bursting of sound-emitting crackers between 10 pm and 6 am during Deepavali

The Supreme Court dictates – But who's listening?

- The Supreme Court also suggested to organize public awareness campaigns during festival seasons
- The Supreme Court also mandated an upper limit of 105 dB for fire crackers

Indian Penal Code

Noise pollution can be dealt under Sections 268, 290 and 291 of the Indian Penal Code, as a public nuisance

Smartphone technology (Apps) can be used to measure noise exposure levels and inform users about their risk for noise-induced hearing loss

The Chennai Scenario

- Study of noise levels by MERF-ISH at

  - Anna statue, Annasalai

  - Kathipara junction

  - Panagal Park, T. Nagar

- Noise levels ranged from 100 – 130 dB on a typical working day during rush hour

Management of NIHL

- Hearing aids and cochlear implants - currently available management strategies
- Pharmacological and molecular therapies for NIHL can ameliorate or repair injury to the cochlea
- Gene therapies and post noise otoprotective strategies may be available in the future

Intratympanic Steroids

- Dexamethasone, delivered to the round window membrane, has been shown to reduce hearing loss after noise (Harrop-Jones et al., 2016).
- Zhou et al. (2013) treated patients suffering recently (3 days to two weeks) from NIHL with systemic plus intratympanic dexamethasone, and compared them to patients receiving systemic steroid alone.

  The patients receiving intratympanic treatment showed significantly more improvement in thresholds.

Probable Interventions for NIHL in the Future

Intervention strategies for noise-induced damage

- Antioxidant methods to suppress reactive oxygen species – replenish cochlear GSH
- Antioxidant - adenosine A1 receptor agonist adenosine amine congener (ADAC)
- Long term omega 3 fatty acid supplementation - prevents expression changes in homocysteine metabolism in mice (Molinez-vega et al)
- Mitochondrial protectants (e.g., Acetyl-l-carnitine ALCAR) preventing mitochondrial-induced apoptosis

Intervention strategies for noise-induced damage

- Reducing glutamate excitotoxicity - glutamate receptor antagonist (Carbamathione)
- Calcium channel blockers or agents to prevent noise-induced cochlear vasoconstriction
- TNFa inhibitor etanercept - reduces noise-induced threshold shifts in animals

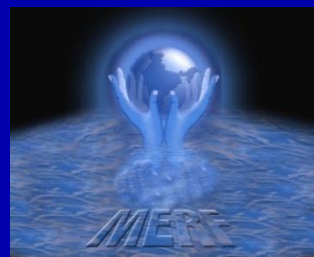
- Genes important for the genesis of hair cells in mammals, including *Notch*, *Math 1*, *Brn3.1* have been discovered

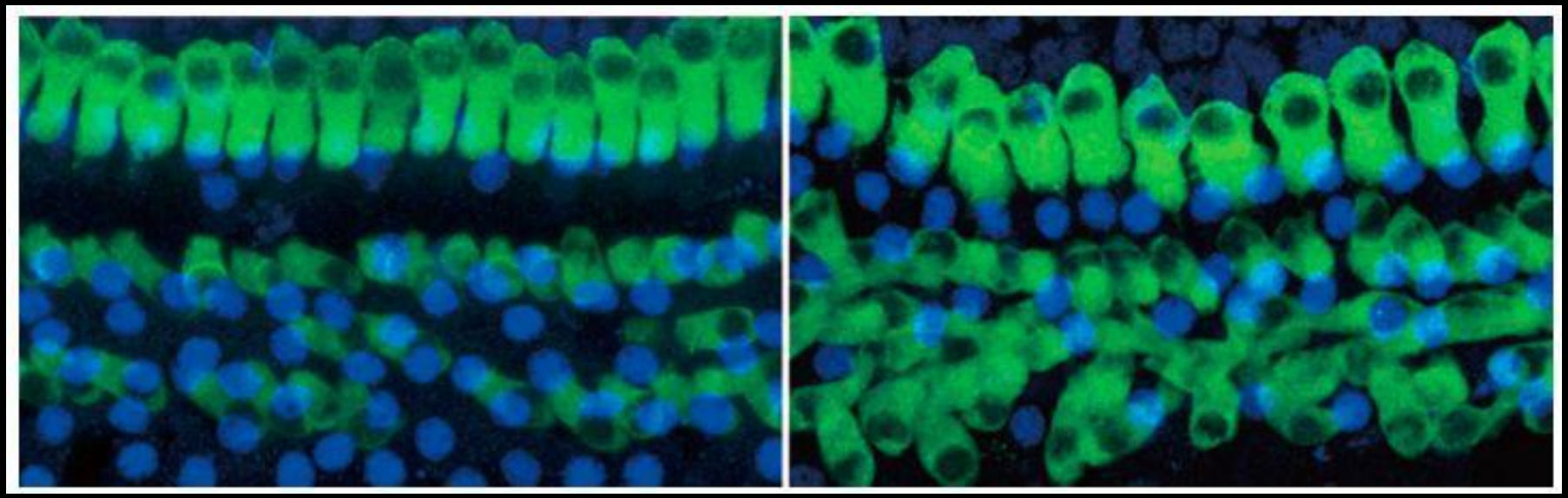
Gene therapy for NIHL

- Gene therapy – to increase endogenous expression of Neurotrophic factors and their receptors (development and maintenance of SGN)
- Cochlear inoculation of a viral vector carrying Atoh1 (Math 1) to regenerate stereocilia (Izumikawa *et al)*
- Gene therapy to over-express antioxidant enzymes in the cochlea

- Supporting cells - stimulated to become new hair cells resulting in partial recovery of hearing in mouse ears damaged by noise trauma

  Notch inhibition induces cochlear hair cell regeneration and recovery of hearing after acoustic trauma. Kunio Mizutari, Masato Fujioka et al, Neuron. 2013; 77(1): 58 – 69.





Mice with inner ear damage due to noise (left) recover hearing with drug treatment (right) that can prompt the regrowth of sound-sensing hair cells (green) (Mizutari et al./Neuron, 2013)

- Prevention of the release of cytochrome c from damaged mitochondria by preventing pore formation (e.g., overexpression of Bcl-2 or Bclxl via a gene therapy vector)

Sound conditioning

- The olivocochlear system may help protect against acoustic trauma
- Moderate-level sound exposures daily to reduce injury from a subsequent high-level noise exposure

Future Research

- Improved understanding of pathological mechanisms of NIHL, genetic susceptibility, etc
- Better understanding of sound conditioning may protect against the adverse effects of future sound exposure
- Advances in drug therapy to protect against or reverse the effects of noise exposure
- Advances in hair cell regeneration

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