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A History of Temporary Threshold Shift (TTS) Research

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We all have experienced the loss of hearing sensitivity upon exposure to loud sounds that resolves over hours or days. It is probable that those during the early days of man also experienced temporary threshold shifts. The advent of electronics in the early 20th century allowed for reproducible presentation of a sound stimulus. This sound stimulus level could be manipulated allowing for reliable measurement of Temporary Threshold Shifts (TTS) and Permanent Threshold Shifts (PTS) and ultimately led to the clinical audiometer. Electronics also allowed for noise exposures to be presented in the loudness range where TTS and PTS could be carefully studied in the laboratory.

As purposely creating PTS in humans is unethical, studies of TTS and Asymptotic Threshold Shift (ATS, a TTS that grows over 6-12 hours of noise exposure) became the foundation for rules and regulations designed to prevent Permanent Threshold Shift. This research was later used to develop occupational and environmental noise limits. Later studies indicated that TTS was not a good predictor of PTS, and the research fell out of favor. Recently, TTS research has experienced a resurgence, as advanced imaging techniques allow study of specific underlying mechanisms and challenge previous assumptions about threshold shift. This poster will review seminal research on TTS beginning with World War II.

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Variation Analysis of Transcriptome Data Reveals Candidate Genes for Further Investigation of Individual Variation in Cochlear Responses to Acoustic Trauma

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Introduction
Individuals display different susceptibility to acoustic trauma. Although this variation has been linked to multiple biological events, its molecular basis is still not clear. One strategy to address this question is to identify the genes that contribute to the individual variation. Given the presence of a large number of genes expressed in the cochlea, selecting candidate genes for an in-depth investigation is a research challenge. In this investigation, we analyzed the expression variation of cochlear genes using RNA-sequencing (RNA-seq) data to identify the genes that potentially contribute to individual variation.

Methods
C57BL/6J mice were exposed to a broadband noise at 120 dB SPL for 1 hour. The cochlear sensory epithelia were collected at 1 day post-noise exposure for RNA-seq. The RNA-seq data were analyzed to identify the genes showing an increased expression variation after the acoustic trauma. The functional relevance of these identified genes were defined using two bioinformatic tools: the database of annotation, visualization and integrated discovery (DAVID) and Ingenuity pathway analysis (IPA). To verify the results, we examined the change in expression of 84 genes responsible for mitochondrial function using qRT-PCR in animals showing different levels of cochlear dysfunction after acoustic overstimulation.

Results
Control samples without acoustic trauma displayed diverse levels of variation in FPKM values across individual genes. This variation was significantly increased for some genes, but remained unchanged or decreased for others after acoustic trauma. Bioinformatics analyses revealed that the genes with increased variation were related to the molecular pathways of apoptosis, cell damage and defense. By contrast, the genes that were stable were functionally related to basic biological processes. Further screening of the genes responsible for mitochondrial function revealed three genes showing a damage-level dependent expression change. All these genes displayed increased individual variation in their expression levels measured by RNA-seq after the noise injury, suggesting that the genes with the increased expression variation are likely to contribute to individual variation in the cochlear response to acoustic trauma.

Conclusion
Variation analysis of RNA-seq data is a valuable strategy for identification of candidate genes for further investigation into the molecular basis of individual variation in the cochlear response to acoustic overstimulation.

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9-methyl-beta-carboline: Protection against Cisplatin-Induced Toxicity in vitro and Pharmacokinetics following Intratympanic Injection

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Previous studies have demonstrated that 9-methyl-beta-carboline (9MßC) promotes cell survival and neuroregeneration through mechanisms that include: 1) increased performance of the respiratory chain; 2) increased transcription and expression of the neurotrophins; 3) reduced levels of ROS; 4) decreased apoptosis and; 5) the reduced expression of inflammatory modulators. We hypothesized that these properties may also protect hair cells from the burden of ototoxicity caused by a range of chemicals including the chemotherapeutic agent cisplatin. Therefore, we investigated the effect of 9MßC in an *in vitro* model of cisplatin-induced toxicity in the human neuroblastoma cell line SH-SY5Y.

Association for Research in Otolaryngology

38TH Annual MidWinter Meeting

Saturday, February 21 –
Wednesday, February 25, 2015

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