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Research Briefs at Dalhousie: Genes, Noise and Dementia

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1. Noise-Induced Cochlear Damage and Gene-Therapy for Cochlear Protection against Traumatizing Factors

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Background

Noise is a common pollution in modern society, not only in industrial settings, but also in our living environments due to traffic, loud music and other recreational noise. Cochlear structures are vulnerable to noise mainly at two loci: outer hair cells (OHCs), which

provide the cochleae with good sensitivity to soft sounds; and the synapses between inner hair cells (IHC) and auditory neurons, which constitute the information pathway from the ear to the auditory brain. Noise can damage and/or kill OHCs and therefore elevate hearing thresholds. Noise can also damage the synapses, which makes the auditory neurons die slowly and reduces and distorts the information reaching the brain. Since the sensorial cells and neurons in the inner ear are terminally differentiated (i.e., special), the lost cells cannot be naturally replaced and there is no effective medical treatment to cure NIHL after it happens.

Our Research in Cochlear Gene Therapy

The goal of our gene therapy research is to prevent the cell death from happening. Previously, we reported some success by over-expression of a gene in a cell-death pathway called apoptosis: the X-linked inhibitor to apoptosis protein. Currently, we are regulating multiple genes simultaneously in three different cell-death pathways. Through this research, we are investigating methods to improve gene regulation (over-expression and knockdown) by using viral vectors through different approaches (including round-window membrane after ultrasound treatment to increase permeability of the membrane).[1]

Our Research in Noise Induced Synaptopathy

If noise exposure is limited in certain doses, the noise may not damage OHCs, but only damage synapses. In this case, hearing thresholds may not be elevated but information sent to the auditory brain may be reduced and distorted. Since there is no threshold shift, the damage cannot be detected by routing audiometric thresholds tests. Therefore, the functional deficits associated with this synaptic damage and loss have been called noise-induced hidden hearing loss (NIHHL). Our research in this area has been focusing on several aspects: (1) synaptic damage caused by noise of different levels and durations, (2) mechanisms dominating synaptic damage, (3) methods for preventing synaptic damage and promoting synaptic repair, (4) the consequences of synaptic damage on signal coding, (5)

the molecular and structural bases for coding deficits in damaged and repaired synapses, (6) methods for detecting coding deficits associated with NIHHL that can be translated to human subjects; (7) NIHHL in human subjects.

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2. Noise-Induced Hidden Hearing Loss in Military and Industrial Populations

S. Aiken, M. Bance, H. Dajani, P. Van Roon, M. Sharpe and J. Wang

Noise-induced hidden hearing loss (i.e., synaptopathy) is difficult to study humans, since noise exposure cannot be experimentally controlled and synapses cannot be directly studied. Human studies have generally used non-invasive measures (e.g., electrocochleography) to search for evidence of synaptopathy in people with high reported noise-exposure, but such evidence has been elusive. Our team is working on this problem by employing a suite of behavioral and physiological (electrophysiological and middle-ear muscle reflex) measures in people with well-defined noise exposure histories. The first project, led by PhD student Patricia Van Roon, is investigating hidden hearing loss in industrial workers in Nova Scotia. The second, in collaboration with colleagues at Cambridge University, is investigating hidden hearing loss in a highly occupationally exposed population in the United Kingdom. This study involves measures before and after occupational exposure involving impulse noise exposure (with standard hearing protection), as well as longitudinal measures and measures in people chronically exposed to high noise levels.

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3. The impact of hearing loss on dementia and potential

mechanisms

S. Aiken, A. Newman, R. Brown and J. Wang

Hearing loss is a risk-factor in the development of dementia in the elderly, independent of many other risk factors such as age, gender, metabolic disorders and cardiovascular disorders. Structural and functional changes in subjects with hearing loss have been documented in the human brain using various imaging methods. Our team has been working in animal models exploring how hearing loss impacts the function of the hippocampus, one of the few brain regions in adult mammals where new neurons are generated throughout the life span. This is called neurogenesis, which is critical for the functions of learning and memory formation. Neurogenesis is normally increased by learning. However, we have found that learning appears to be less effective for promoting neurogenesis in mice with hearing loss. We are now investigating whether and how hearing loss changes the expression of learning/memory related genes. We are also beginning to explore whether learning-promoted brain plasticity is reduced in human subjects with hearing loss.

References

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