USF Researchers Discover Novel Drug Therapy to Slow Down Progression of Age-related Hearing Loss

The novel findings could pave the way for translational drug development toward the first medication to prevent the progression of ARHL.

Researchers in the University of South Florida's Global Center for Hearing and Speech Research (GCHSR), recognized as a top international research center for age-related hearing loss (ARHL), have discovered a novel drug therapy to slow down the progression of ARHL.

Dr. Robert Frisina, senior author and director of the GCHSR announced the study was recently published in *Hearing Research*, the No. 1 ranked journal in the Otolaryngology/Hearing Loss/Deafness journal category. In addition, the companion paper has been accepted for publication in the journal *Aging* in an upcoming issue.

While the auditory perceptual dysfunction is well understood the knowledge of the biological basis of ARHL is still somewhat lacking. Surprisingly, there are no FDA-approved drugs for treatment of ARHL.

Age-related hearing loss (ARHL) – presbycusis – is the most prevalent neurodegenerative disease and No. 1 communication disorder in the aged population, affecting hundreds of millions of people worldwide. Its prevalence is close to that of cardiovascular disease and arthritis, and can be a precursor to dementia. The auditory perceptual deficits are fairly well understood, but knowledge of the neural underpinnings of ARHL is still somewhat mysterious.

Based on their previous studies of human subjects, where they discovered relations between serum aldosterone levels and the severity of ARHL, the researchers treated middle age mice with aldosterone, a hormone which normally declines with age in all mammals. They found that hearing thresholds and suprathreshold responses significantly improved in the aldosterone-treated mice compared to the non-treatment group.

In terms of cellular and molecular mechanisms underlying this therapeutic effect, additional experiments revealed that inner ear spiral ganglion cell survival was significantly improved, mineralocorticoid receptors were upregulated via post-translational protein modifications, and age-related intrinsic and extrinsic cochlear cell death (apoptotic) pathways were blocked by the aldosterone therapy.

Taken together, these novel findings pave the way for translational drug development toward the first medication to prevent the progression of ARHL.

The majority of persons over the age of 60 suffer from some degree of ARHL. This progressive loss of auditory sensitivity and perceptual capability results in significant declines in workplace productivity, quality of life, and abilities to communicate effectively with family, friends and co-workers.

In addition to Frisina, other researchers and contributors include: Senior author Dr. Joseph Walton, professor of communication sciences and disorders and chemical and biomedical engineering, and associate director GCHSR; Dr. Bo Ding, research assistant professor of communication sciences and disorders and GCHSR; Dr. Xiaoxia Zhu, senior bioscientist, chemical and biomedical engineering and GCHSR; Ashley Hinton, USF doctoral candidate in audiology; Dr. Joshua Halonen, former post-doctoral researcher, GCHSR; and project administrative support: Shannon Salvog M.S., GCHSR administrator, Dept. of Chemical & Biomedical Engineering

In March 2016 the GCHSR received a five-year, $9 million grant from the National Institutes of Health's (NIH) National Institute on Aging to study unique ways to treat age-related hearing loss (ARHL).

Frisina^, R.D., Ding^, B., X. Zhu, J.P. Walton. (2016– In Press) Age-Related Hearing Loss: Prevention of Threshold Declines, Cell Loss and Apoptosis in Spiral Ganglion Neurons. *Aging.* [Impact Factor ~7] ^equal 1st authors.

Halonen, J., Hinton, A., Frisina, R.D., Zhu, X., Walton, J.P. (2016 – In Press) Long-term Treatment with the Mineralocorticoid Aldosterone Slows Down the Progression of Age-Related Hearing Loss Measured Behaviorally. *Hearing Res.* [Impact Factor ~4] Note: this is the leading, 1st ranked journal in the "Otolaryngology/Hearing Loss/Deafness" journal category.

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