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USF Researchers Receive $9 Million to Develop Strategies to Treat Age-related Hearing Loss

Boosting the hormone aldosterone and developing brain/ear-training sounds to improve hearing are two keys to five-year research project

TAMPA, Fla. (March 21, 2016) – Researchers in the University of South Florida's Global Center for Hearing and Speech Research (GCHSR) ((http://www.gchsr.usf.edu/), recognized as the world's top research center for age-related hearing loss, have received a five-year, $9 million grant from the National Institutes of Health's (NIH) National Institute on Aging to study two unique ways to treat age-related hearing loss (ARHL).

Because the age-related decline in the hormone aldosterone is a factor in ARHL, the researchers will boost the aldosterone levels in aging mice to see if it improves their hearing. Also, they will develop and use a variety of unique and pleasant sounds to directly target known deficits of ARHL with a goal of shaping how the human ear and brain process sound to overcome the hearing deficits associated with ARHL.

According to Robert Frisina, Jr, PhD, director of the GCHSR, ARHL, also called "presbycusis," is the number one communication disorder and most common neurodegenerative condition affecting older Americans and AHRL affects more people than other neurodegenerative diseases, such as Alzheimer's disease or Parkinson's disease.

Frisina explained that hearing loss can occur from many environmental reasons, but their focus is on age-related hearing loss, which they are trying to better understand perceptual, neural, cellular, and molecular levels where the changes occur with age.

"Permanent hearing loss, including ARHL, is estimated to affect 10 percent of the U.S. population," said Frisina, who is also a professor of biomedical engineering in USF's College of Engineering. "Currently, there are no U.S. Food and Drug Administration-approved treatments for permanent hearing loss, including ARHL, despite its prevalence. While ARHL directly and negatively affects quality of life for older people, severe ARHL has also recently been linked to the earlier onset of dementia."

GCHSR researchers are focusing on the key hormone "aldosterone" because it regulates a number of aspects of the body's function, particularly functions where sodium and potassium are especially important in normal physiology. Reduced aldosterone levels have been linked to hearing loss and the hope is that boosting aldosterone may improve hearing for those with ARHL.

"Having the proper levels of aldosterone is good for a number of systems in the body, not just hearing, so boosting its level may have other benefits," added Frisina. "Most hormone levels decline with age, so it is likely that with correct timing and dosage, hormonal intervention could slow or prevent the progression of ARHL. Our first goal is to use animal models to determine if boosting aldosterone has a positive effect on hearing loss."

In that phase of the study, laboratory mice will receive aldosterone boosts in the form of subcutaneous, time-release pellets. If successful, the research will move from animal testing to clinical trials with human volunteers with ARHL. It is also likely that the eventual intervention with aldosterone will be accompanied by adjunct treatments as well, potentially making a "drug cocktail" with multiple benefits for other age-related issues in addition to ARHL.

Joseph Walton, PhD, a professor in the College of Behavioral and Community Science's Department of Communication Sciences and Disorders, with a joint appointment in the College of Engineering in Chemical and Biomedical Engineering, is the project leader for the animal behavior and neurophysiology components of the grant. Using sensors that record brain activity during sound stimulation, Walton's lab investigates the neural bases of hearing behavior of mice, correlating the perceptual abilities of mice to their brain's encoding of sound. The goal, says Walton, is to uncover the neural underpinnings of improved sound perception.

"Over the next several years, our lab will investigate the neural machinery of brain plasticity following one form of intervention - exposure to enriched auditory environments," explained Walton. "The brain is very plastic, even the aged brain, and auditory training can improve auditory processing ability, especially in difficult listening situations. The key is to understand the neural mechanisms. A big breakthrough has come with our ability to understand the how the timing of the neural code for sound is altered in aging. The goal is to get neurons to improve their ability to synchronize their response with the sound signal."

Walton's group has already discovered that long-term treatment with aldosterone in a mouse model of ARHL improves neural processing in a key brain region. They also found that the neural properties allowing the auditory system to separate one sound from another dramatically improved in treated mice versus those receiving a placebo. Their future work will investigate various combinations of therapeutics.

"An advantage of the program project grant format is that it brings together several scientific disciplines in both human and animal behavior and neurophysiology and molecular biology to attack a major health issue," concluded Walton.

According to David Eddins, PhD, associate director of GCHSR, the first step in human studies will include monitoring aldosterone levels in humans with ARHL five times over a four-year period.

"During this time, we will measure a number of critical hearing abilities and indices of central auditory function," said Eddins, who is a professor in both the College of Behavioral and Community Science's Department of Communication Sciences and Disorders and the College of Engineering's Department of Chemical and Biomedical Engineering. "This will allow us to better understand the relations among aldosterone and known deficits associated with ARHL."

It is well known that ARHL creates hearing difficulties and the most common complaint is increased difficulty hearing in background noise. Older listeners have a significant disadvantage when listening to speech or music in the presence of background competition, as one might experience in a crowded, noisy restaurant.

According to Eddins, in addition to difficulty hearing in background noise, older listeners typically have difficulty hearing soft sounds. One component of this difficulty is in understanding the consonants, such as "b" and "p," involved in 'phoneme,' perception, which provide changes in meaning or - when they are not accurately heard - misunderstandings.

"As we age, we also experience changes to our perception of the loudness of sounds, and this makes it challenging for hearing aids to make soft sounds audible without making loud sounds too loud," explained Eddins. “Another hallmark of ARHL is a loss of the fine timing needed to encode the details that give sounds clarity and a rich quality. This timing deficit can also make it difficult to accurately hear certain sounds and separate them from background noise.”

Accordingly, the researchers are also aiming to “augment the acoustic environment” in parallel animal and human studies. As explained by Eddins, the strategy will be to induce and “steer” plasticity in the central auditory system.

“To do this, we will present low-level background sounds that can be played over a personal computer or ear-level hearing instruments,” said Eddins. “The first step is to determine how plastic the older auditory system is relative the younger auditory system. Then, we will present sounds intended to target the age-related deficits noted above – loudness perception, perception of the fine timing details of sound, and separating speech from background noise.”

According to Frisina, they will be working on devising pleasant, enjoyable sounds, possibly musical sounds, to which people with ARHL can listen. “A major focus of the experiments will be the link between ARHL and nerve cell inhibition and excitation changes that take place in the aging brain,” he said.

If successful, such treatments may help slow or prevent the progression of ARHL by re-training the ear/brain connections. Dr. Eddins noted that the team, including his co-investigator and wife, Ann Clock Eddins, PhD, co-director of the Auditory and Speech Sciences Laboratory, will begin recruiting approximately 150 older individuals later this spring to participate in the various studies. Persons interested in participating can contact the Auditory & Speech Sciences Laboratory which is affiliated with the GCHSR at USF. (www.usf.edu/cbcs/csd/labs/assl/)

The grant is a $1.8 million per-year extension of their previous NIH grants related to ARHL research and runs from 2016 to 2021.

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