

From the University of Mississippi Medical Center Division of Public Affairs

BRAIN TRAINING REVERSES RATS' AGE-RELATED COGNITIVE DECLINE

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JACKSON, Miss. – Specialized brain training targeted at the regions of a rat's brain that process sound reversed many aspects of normal, age-related cognitive decline and improved the health of the brain cells, according to a new study from researchers at the University of California, San Francisco University and the University of Mississippi Medical Center.

The results indicate that people who experience age-related cognitive decline, including slower mental processing and decreased response to new stimuli, might also benefit from specially designed mental exercises.

"From middle age onward, there are universal changes in the brain affecting perceptual processing," said Etienne de Villers-Sidani, M.D., a neurologist and postdoctoral fellow with the UCSF Department of Otolaryngology who was the lead author on the study. "We used to think these were permanent changes and now are beginning to think maybe they're not."

The study found that intense auditory training greatly improved sound perception and processing among rats that had previously experienced normal, age-related sensory-processing degradation. Findings appeared online July 19 in the Proceedings of the National Academy of Sciences, at <http://www.pnas.org/content/early/2010/07/15/1007885107.full.pdf+html>.

Collaborators Drs. Rick C.S. Lin and Kimberly Simpson along with graduate student Loai Alzghoul at the University of Mississippi Medical Center (UMMC) documented physical changes in the brains of the trained, aging rats in the paper. They found that myelin density and neuron health improved in the primary auditory cortices to nearly the level seen in young rats.

"These results are encouraging because as Baby Boomers age, we'll have more and more elderly people," said Lin, a professor of anatomy at UMMC. "They indicate that you shouldn't just stick to your routine. Challenge yourself and don't stop doing something just because you might take longer at it."

The study builds upon extensive previous research in the laboratory of Dr. Michael M. Merzenich, UCSF professor of otolaryngology and physiology and senior author in the study. That research had demonstrated how cognitive training can powerfully rewire brain circuits. de Villers-Sidani said he and collaborators are in the first stages of designing programs and figuring out which training strategies will be most effective in humans.

For a month researchers spent an hour a day giving two groups of rats – young and old – intense auditory training. Two other groups of aging and young rats, used as controls, received no training. Aging rats between 26 and 32 months are equivalent to humans aged 65 to 85, de Villers-Sidani said, an age range at which cognitive and sensory processing have degraded.

Specifically, the researchers targeted the rats' primary auditory cortices, the sound-processing areas of their brains. In their training, rats heard a rapid sequence of six notes, five of the same pitch and one different, oddball pitch. The oddball note came at random on any one of the sequence's final four notes.

When a rat recognized the oddball note, it received a food reward. The researchers progressively upped the difficulty by stepping the oddball's pitch from a half-octave above the base note to ultimately only one-fiftieth an octave difference. Both young and aging rats steadily improved in their ability to distinguish the subtle difference.

At the end of the month, the researchers used electrophysiology to test for a range of characteristics related to auditory cortex response. In the trained aging rats, they found partial-to-complete recovery in the ability to discriminate between frequencies. That improvement held true across the entire frequency spectrum on which they had been trained.

Compared with the aging controls, the trained aging rats also showed an improved ability to process successive signals, suppress false-positive responses and suppress background noise while deciphering novel stimuli, a skill, for example, important to humans trying to hold a conversation in a noisy room.

"One of the most striking findings of this study is that every aspect of sound processing we examined in the aging primary auditory cortex was degraded and then substantially reversed with a simple training strategy," de Villers-Sidani wrote in the study's results.

Post-mortem analysis of the rat auditory cortices showed surprising physical changes in the aged-trained group.

Lin, who holds a co-appointment in the UMMC Department of Psychiatry and Human Behavior, said the cortices of trained aging rats showed not only an increased number of inhibitory neurons, specialized cells crucial for sensory perception and synaptic plasticity, but normal-looking inhibitory neurons that resembled those found in young rats.

The untrained aging rats showed on average 25 percent fewer inhibitory neurons compared with the untrained young rats. Training the aging rats partially reversed that trend. The aging trained rats showed an average 20 percent increase, while myelin density also improved.

"The neurons looked young again. They were full and robust. It's like a hose without water going through it appears collapsed. Run the water and it expands to its original size. Recovery happens," Lin said. "It indicates the brain is a lot more plastic. The training exercises reopen the hose and the rats recovered almost to the point of young rats."

de Villers-Sidani, who trained as a neurologist at McGill University, Canada, said he became interested in aging and dementia while doing clinical work at the UCSF Memory and Aging Center.

"Since I started my training, I saw hundreds of patients who had difficulty dealing with noisy situations. Almost everyone, if you measure it, experiences declines in visual and auditory-discrimination tasks. That's normal. That's universal," de Villers-Sidani said.

"They may be slower to process information or more sensitive to interference, like the patient who, as he aged, had trouble riding his motorcycle on the highway because he couldn't keep track of all the cars around him."

The scientific context was that these changes occur over time and may not be permanent, de Villers-Sidani said.

"We're arguing that if they're plastic, maybe they're reversible, rather than being permanent," he said. "If you're a violinist you have to practice to keep up your skills. You stop and everyone in the orchestra will notice if you haven't practiced for a year. It's the same with the brain. If you don't practice, your brain will degrade into a less precise machine, one less able to process signals."

Age-related cognitive decline is a big concern with people, de Villers-Sidani said.

"If we can sort out what normal brain aging is, then that will help us sort out pathological age-related diseases like Alzheimer's," he said.

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Co-author Xiaoming Zhou, in the School of Life Sciences, Institute of Cognitive Neuroscience, East China Normal University, Shanghai, China, also contributed to the paper.

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