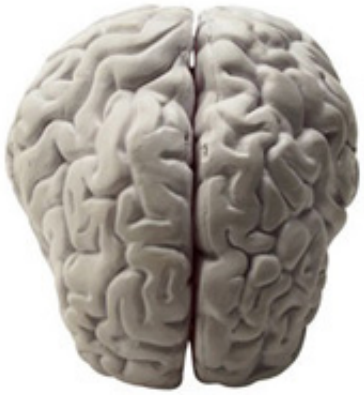
Team combats memory loss by enhancing brain function

20 October 2015



A new study, led by scientists at The Scripps Research Institute (TSRI), the Veterans Affairs San Diego Healthcare System (VA) and University of California (UC) San Diego School of Medicine shows that increasing a crucial cholesterol-binding membrane protein in nerve cells (neurons) within the brain can improve learning and memory in aged mice.

"This is a novel strategy for treating neurodegenerative diseases, and it underscores the importance of brain cholesterol," said Chitra Mandyam, associate professor at TSRI and co-first author of the study with Jan M. Schilling of UC San Diego and the VA.

Senior author Brian Head, a research scientist with the VA and associate professor at UC San Diego, added, "By bringing back this protein, you're actually bringing cholesterol back to the cell membrane, which is very important for forming new synaptic contacts."

The study, published recently online ahead of print in the journal *Biological Psychiatry*, focuses on a specific membrane protein called caveolin-1 (Cav-1) and expands scientists' understanding of neuroplasticity, the ability of neural pathways to grow in response to new stimuli.

Previous work by Head's group at the VA and at UC San Diego had shown that raising Cav-1 levels supported healthy "rafts" of cholesterol involved in neuron growth and cell signaling; however, it wasn't clear if this new growth actually improved brain function or memory.

To find out, the researchers delivered Cav-1 directly into a region of the brain known as the hippocampus in adult and "aged" mice. The hippocampus is a structure thought to participate in formation of contextual memories—for example, if one remembers a past picnic when later visiting a park.

In addition to improved neuron growth, treated mice demonstrated better retrieval of contextual memories—they froze in place, an indication of fear, when placed in a location where they'd once received small electric shocks.

Mandyam and Head believe that this type of gene therapy may be a path toward treating age-related memory loss. The researchers are now testing this gene therapy in mouse models of Alzheimer's disease and expanding it to possibly treat injuries such as spinal cord injury and traumatic brain injury. Mandyam said this new understanding of Cav-1 and neuroplasticity could also be relevant to memory loss due to alcohol and drug use.

"We're very interested in studying whether we can manipulate Cav-1 in other areas of the brain," Mandyam said.

More information: *Biological Psychiatry*, www.biologicalpsychiatryjourna … (15)00817-3/abstract

Provided by The Scripps Research Institute