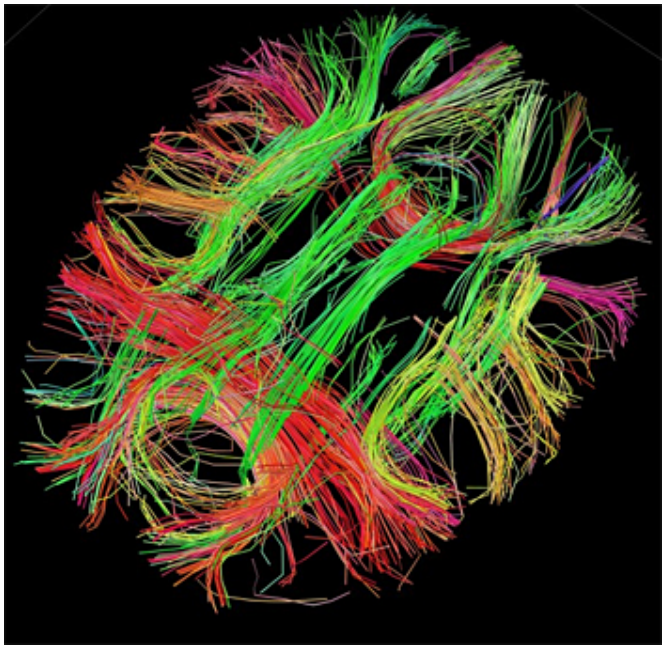
Protein linked to high risk of Alzheimer's can be removed from brain without hindering learning

4 October 2016



White matter fiber architecture of the brain. Credit: Human Connectome Project.

A protein linked to higher risk of Alzheimer's can be removed from the brains of mice without hindering memory and learning, according to a study that addresses whether potential therapeutics targeting this protein would have detrimental side effects.

The study from the Peter O'Donnell Jr. Brain Institute also showed, however, that the protein's absence in other parts of the body hinders brain function as blood cholesterol levels rise. This result substantiates previous research that indicated cardiovascular health affects the brain.

Researchers focused on the removal of apolipoprotein E (ApoE), which in a certain form can support the buildup of toxic plaques in the brains of Alzheimer's patients. Studies elsewhere have sought to determine whether reducing ApoE could be an effective treatment in preventing the disease, but a lingering question has been whether the protein is necessary for healthy brain function.

The study found that mice can maintain their learning and memory when virtually all ApoE is removed from the brain but kept present in the liver to filter cholesterol. Mice that lacked ApoE in both the brain and liver experienced unhealthy cholesterol levels and lost cognitive function.

More research is needed to determine what causes the cardiovascular issues to affect the brain, said Dr. Joachim Herz, the study's Principal Investigator and Professor of Molecular Genetics, Neuroscience, Neurology and Neurotherapeutics at the O'Donnell Brain Institute at UT Southwestern Medical Center.

But the findings, published in *The Journal of Neuroscience*, add support to the belief that reducing ApoE in the brain could eventually be a viable therapeutic option for treating Alzheimer's.

"This approach still holds potential," said Dr. Herz, holder of the Thomas O. and Cinda Hicks Family Distinguished Chair in Alzheimer's Disease Research and Director of the Center for Translational Neurodegeneration Research.

ApoE has several roles in the body, including transporting cholesterol and related molecules such as ?-amyloid that form plaques in the brains of Alzheimer's patients if not properly filtered or removed.

The type of ApoE produced by the ApoE gene determines how effectively the amyloid is removed

from the brain. ApoE2 is the most effective, ApoE3 is in the middle and ApoE4 is the most likely to allow for the buildup of amyloid plaques. People whose genes produce ApoE4 are at high risk of developing Alzheimer's.

Studies are ongoing at UT Southwestern and elsewhere to further understand the various effects that ApoE4 removal has on brain and body function.

Provided by UT Southwestern Medical Center