Toxic Alzheimer's protein spreads through brain via extracellular space

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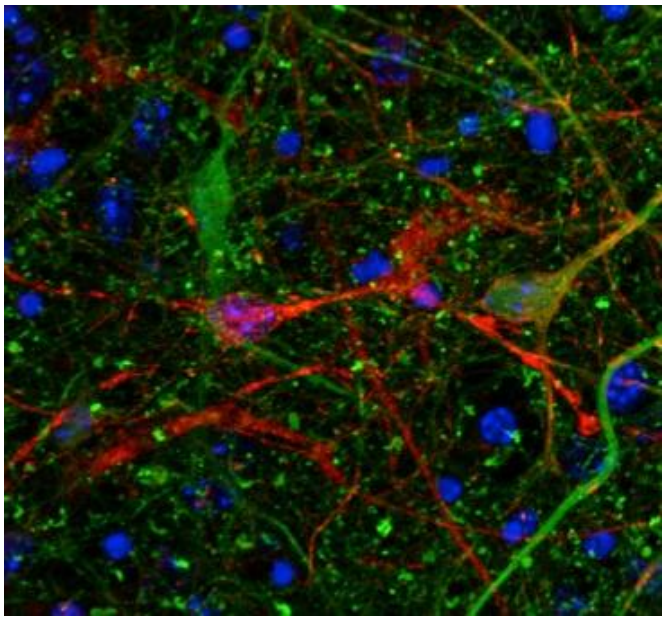

Orange indicates where tau protein has traveled from one neuron to another. Credit: Laboratory of Karen E. Duff, PhD, Columbia University Medical Center

A toxic Alzheimer's protein can spread through the brain—jumping from one neuron to another—via the extracellular space that surrounds the brain's neurons, suggests new research from Columbia University Medical Center.

The study has been published online in *Nature Neuroscience*.

The spread of the protein, called tau, may explain why only one area of the brain is affected in the early stages of Alzheimer's but multiple areas are affected in later stages of the disease.

"By learning how tau spreads, we may be able to stop it from jumping from neuron to neuron," said Karen Duff, PhD, professor in the department of pathology and cell biology (in the Taub Institute for Research on Alzheimer's Disease and the Aging Brain) and professor of psychiatry (at New York State Psychiatric Institute.) "This would prevent the disease from spreading to other regions of the brain, which is associated with more severe dementia."

The idea the Alzheimer's can spread through the brain first gained support a few years ago when Duff and other Columbia researchers discovered that tau spread from neuron to neuron through the brains of mice.

In the new study, lead scientist Jessica Wu, PhD, a former post-doctoral researcher at the Taub Institute who is currently at Massachusetts Institute of Technology, discovered how tau travels by tracking the movement of tau from one neuron to another. Tau, she found, can be released by neurons into extracellular space, where it can be picked up by other neurons. Because tau can travel long distances within the neuron before its release, it can seed other regions of the brain.

"This finding has important clinical implications," explained Dr. Duff. "When tau is released into the extracellular space, it would be much easer to target the protein with therapeutic agents, such as antibodies, than if it had remained in the neuron."

A second interesting feature of the study is the observation that the spread of tau accelerates when the neurons are more active. Two team members, Abid Hussaini, PhD, and Gustavo Rodriguez, PhD, showed that stimulating the activity of neurons accelerated the spread of tau through the brain of mice and led to more neurodegeneration.

Although more work is needed to examine whether those findings are relevant for people, "they suggest that clinical trials testing treatments that increase brain activity, such as deep brain stimulation, should be monitored carefully in people

with neurodegenerative diseases," said Dr. Duff.

The study is titled, "Neuronal activity enhances tau propagation and tau pathology in vivo."

More information: Jessica W Wu et al, Neuronal activity enhances tau propagation and tau pathology in vivo, *Nature Neuroscience* (2016). DOI: 10.1038/nn.4328