Researchers discover how West Nile virus triggers memory loss

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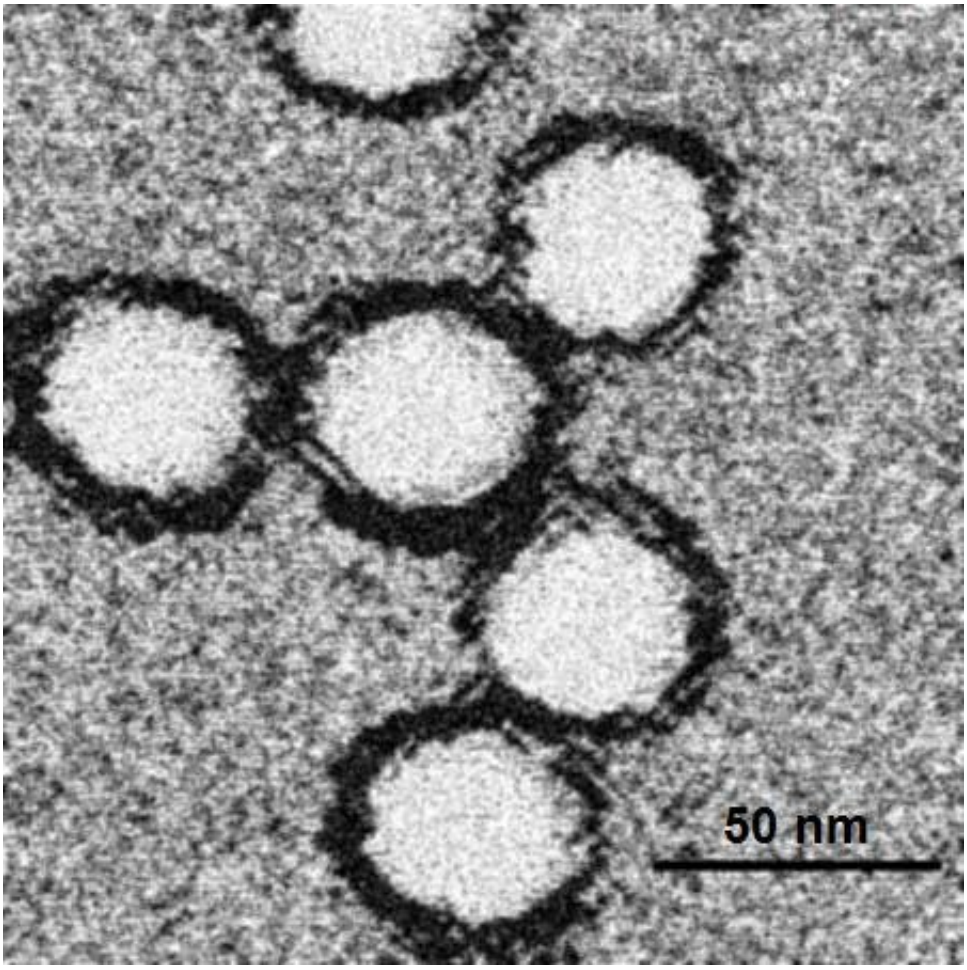

Electron microscopy of West Nile virus. Credit: PhD Dre, Wikipedia/CC BY-SA 3.0

Researchers at the University of Colorado Anschutz Medical Campus

have discovered how the most severe forms of West Nile virus cause memory loss and mood disorders, opening the door to potential new treatments for the mosquito-borne illness.

The study, published in the journal *Nature*, says 50 percent of patients who survive the most damaging kind of West Nile infection often go on to develop memory loss, learning difficulties, a lack of concentration and irritability.

Exactly why this happens has been a mystery until now.

Researchers discovered that the virus doesn't kill off neurons but sparks inflammation that prunes synapses, the connections that carry messages between nerve cells.

"What we found in mice, and later confirmed in humans, is that it's not the death of cells that causes memory loss, it's the loss of nerve cell connections," said study co-author Kenneth Tyler, MD, chairman of the department of neurology at the University of Colorado School of Medicine. "The viral infection activates microglial cells and complement pathways which are helping to fight the infection but in turn end up destroying synapses."

Bette K. DeMasters, MD, professor and head of neuropathology at CU Anschutz, also co-authored the study.

The researchers found that mice infected with West Nile had a difficult time negotiating their way out of a maze that healthy mice figured out much faster. They later discovered that the infected mice suffered significant damage to their synapses. The scientists examined brain tissue from humans who had died from West Nile and found the same phenomenon.

Tyler said West Nile is the leading cause of acute viral encephalitis in the U.S. though still relatively rare. Only about one in 100 people infected with the disease develop the most severe form, he said.

West Nile appeared in the U.S. during the late 1990s and has remained a persistent threat. Last year, California had 730 cases, Texas 252 cases and Colorado 101cases.

In Colorado, that number included 57 neuro-invasive cases, the most serious kind, and two deaths.

"This discovery opens up the opportunity to test therapies and medications on mice as a precursor to humans," Tyler said. "We already have some drugs that might be good candidates for treating this condition."

The best way to avoid West Nile is to wear long sleeves, use mosquito repellant and steer clear of standing water. The mosquito that carries the virus is most active at dusk and dawn.

More information: A complement-microglial axis drives synapse loss during virus-induced memory impairment, *Nature*, nature.com/articles/doi:10.1038/nature18283

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