NEUROSCIENCE

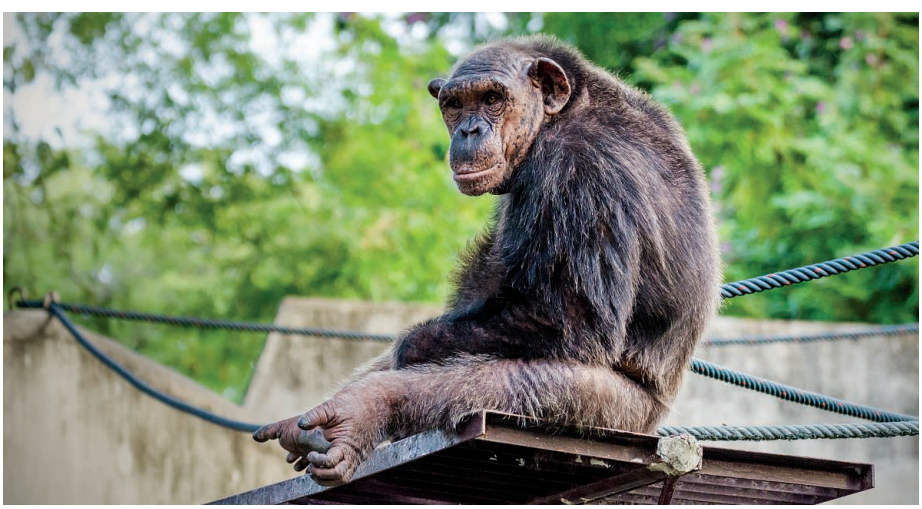
Elderly chimps may get Alzheimer's disease

Hallmark plaques and tangles found in the largest analysis yet of old chimp brains

By **Ryan Cross**

Researchers have discovered tell-tale signs of Alzheimer's disease in 20 elderly chimpanzee brains, rekindling a decades-old debate over whether humans are the only species to develop the debilitating condition. Whether chimps actually succumb to Alzheimer's or are immune from symptoms despite having the key brain abnormalities is not clear. But either way, the work suggests that chimps could help scientists better understand the disease and how to fight it—if they could get permission to do such studies on these protected animals.

A definitive diagnosis of Alzheimer's includes dementia and two distortions in the brain: amyloid plaques, sticky accumulations of misfolded pieces of protein known as amyloid β peptides; and neurofibrillary tangles, formed when proteins called tau clump into long filaments that twist around each other. Many other primates including rhesus monkeys, baboons, and gorillas also acquire plaques with aging, but tau tangles are either absent in those species or don't fully resemble those seen in humans.



A chimp's brain may degenerate with age, but whether the animals develop dementia is unknown.

In the new study, researchers led by biological anthropologist Mary Ann Raghanti at Kent State University in Ohio turned to our closest relative, chimpanzees. In 2015, the U.S. Fish and Wildlife Service declared all U.S. chimps endangered, effectively ending all invasive research on them. But thanks to a new center that collects brains from chimps that die at zoos or research centers, the team was able to examine the brains of 20 chimps aged 37 to 62—the oldest recorded age for a chimp. Of these chimps, 13 had amyloid plaques, and four also had the neurofibrillary tangles seen in more advanced stages of Alzheimer's in humans, the team reports this week in *Neurobiology of Aging*.

"I am not surprised by it at all," says Lary Walker, a neuropathologist at Emory University's Yerkes National Primate Research Center in Lawrenceville, Georgia, who was not involved in the new study. In 2008, Walker led a team that found both plaques and tangles in a study of a single, 41-year-old chimp that died from stroke, although that chimp's distribution of plaques and tangles didn't resemble those in human brains with Alzheimer's. Walker says the new study makes him "certain that the chimp we observed previously wasn't an outlier of some sort."

But so far, only humans are known to show the Alzheimer's trifecta of plaques, tangles, and dementia. Raghanti says that the 20 chimps whose brains she studied had not been tested for cognitive or behavioral changes. As a result, "we can't say these chimps had Alzheimer's, but we can say for sure that they are the only other species with its pathologic hallmarks."

Some scientists aren't persuaded that the chimp brains match those of human Alzheimer's patients. Caleb Finch, a neurobiologist who studies Alzheimer's at the University of Southern California in Los Angeles, points out that in human brains, amyloid plaques are associated with neuron death, which wasn't measured in the new study. "Until we get data on cell numbers and do more studies on cognition, I am happy to be agnostic."

Raghanti and colleagues plan to go back to the same chimp brains to calculate neuron death, but proving that chimps develop dementia will require research on living animals. Few studies, "some very old and all inconclusive," have probed how cognition changes in aging chimps, says behavioral neuroscientist Agnès Lacreuse at the University of Massachusetts in Amherst. Her own 3-year study of 38 female chimps found that the oldest four—all over 50—got progressively worse at a spatial memory test as they aged. But, Lacreuse says, "there is much more research to do." Studies investigating memory loss, disorientation, sleeping disorders, and socially inappropriate behavior in chimps could point to the cognitive deficits that accompany Alzheimer's in people, she says.

"We could design a number of studies to tax their memory now," says William Hopkins, a co-author of the study and a neuroscientist at Georgia State University in Atlanta and the Yerkes center. Even better, he says, would be to combine MRI scans with behavioral studies, because the scans would allow scientists to follow chimps whose brains appear to be on track for Alzheimer's.

Lacreuse worries, however, that because "there are so many limitations on chimp research … it will only become more and more difficult to do these kinds of studies." Kathy Hudson, a science and policy consultant in Washington, D.C., and former deputy director for science, outreach, and policy at the National Institutes of Health, agrees. "I don't think there is anything here that is going to cause a fundamental reconsideration of where we are," she says. Hudson notes that noninvasive, behavioral studies of chimps are now allowed, but as for brain imaging: "That's not going to happen," she says. "Doing MRI on consenting humans who understand what's going on is stressful enough."

Primate Products President Thomas Rowell in Immokalee, Florida, who is a former director of the New Iberia Research Center in Louisiana, which still houses 192 chimpanzees, is also doubtful. "The time for accessing chimpanzee models for any type of research has passed." ■

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