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Poor Memory Performance in Aged Cynomolgus Monkeys with Hippocampal Atrophy, Depletion of Amyloid Beta 1-42 and Accumulation of Tau Proteins in Cerebrospinal Fluid

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Abstract. *Background: Due to their similarities in behavior and disease pathology to humans, non-human primate models are desirable to complement small animals as models for the study of age-related dementia. Materials and Methods: Based on their performance on delayed response task (DRT) tests of memory, aged cynomolgus monkeys were divided into two groups to compare high-performing (n=6) and low-performing (n=6) subjects. Both groups were tested for biomarkers related to Alzheimer's disease and their brains were scanned using structural magnetic resonance imaging. Results: The subjects with poor DRT performance had evidence of atrophy in the hippocampus and cortical areas, significantly lower cerebrospinal fluid levels of amyloid beta amino acid 1-42 ($p<0.001$) and higher cerebrospinal fluid total tau levels ($p<0.05$) compared with the group performing well on the DRT tests. Conclusion: These findings suggest that old, memory-impaired cynomolgus monkeys may be useful as a spontaneous non-human primate model for investigations of age-related neurodegenerative diseases.*

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Key Words: Neurodegenerative disease, non-human primate, memory, biomarkers, magnetic resonance imaging.

As one of the first neurodegenerative diseases to be characterized (1, 2), models of Alzheimer's disease (AD) has been studied extensively using many different animal models (3, 4), including animals genetically modified to develop the pathological hallmarks of AD, such as amyloid beta (Aβ) plaques and neurofibrillary tangles (NFTs) (5, 6).

An ideal model of AD in animal must exhibit the current criteria established by the National Institute of Neurological and Communicative Disorders and Stroke and Alzheimer's disease and Related Disorders Association. These characteristics include cognitive impairments and biomarker profiles similar to those seen in patients with AD (7, 8). A major advantage provided by non-human primate (NHP) models of age-related dementia is the observation that these animals exhibit signs of disease that mimic the signs seen in humans, especially cognitive decline (9, 10). Particularly if a proportion of the aged population spontaneously develops age-associated dementias, NHPs may represent extremely valuable spontaneous models.

In an animal model, progression from mild cognitive impairment (MCI) to AD-like dementia should be confirmed