

APP -- Good, bad or both?

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New data about amyloid precursor protein, or APP, a protein implicated in development of Alzheimer's disease, suggests it also may have a positive role -- directly affecting learning and memory during brain development. So is APP good or bad? Researchers at Georgetown University Medical Center say both, and that a balance of APP is critical.

Alzheimer's disease, the fourth leading cause of death in the United States, is characterized by neuronal cell death and a progressive loss of functioning in the brain. Symptoms of Alzheimer's (AD) include memory loss and impaired judgment. Abeta is one of many proteins found to be associated with the disease. It is released when APP, a larger protein, is cut by several enzymes. Research suggests this occurs when APP is abnormally processed, possibly due to trauma, cholesterol levels or oxidative stress. When Abeta is released, it can form plaque, a contributing factor in AD. Thus, Abeta and APP are involved in the early process of AD development.

APP is also known to be present at the synapses between neurons though its molecular action is not understood. Synapse loss is thought to be one of the main contributors to the cognitive decline seen in AD.

In a presentation at the 39th annual meeting of the Society for Neuroscience, Georgetown University Medical Center researchers say that while APP is negatively associated with AD, it appears to play a critical role in brain development.

Many studies have elucidated the importance of synapses and dendritic spines, the protrusions that allow communication between [brain neurons](#), in [learning](#) and [memory](#). In this new research, the GUMC scientists found decreased spine density in mice that have been genetically modified to not produce APP. The scientists then looked at four-week-old mice that over produced APP and found a significant increase in spine density. At one year old, however, these mice have Abeta plaques, as well as a decrease in spine density due to the effect of Abeta, which is known to be neurotoxic.

"Our work suggests that APP balance is critical for normal neuronal development, connection of synapses, and dendritic spine development, all of which have implications for the extensive synapse loss and cognitive decline seen in Alzheimer's disease," explains the study's author, Hyang-Sook Hoe, PhD, a research scientist in the department of neuroscience. "One strategy to counteract development of Alzheimer's disease is to maintain balance in APP protein expression in order to prevent production of Abeta."

Source: Georgetown University Medical Center ([news](#) : [web](#))

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