How Amyloid Beta Reduces Plasticity Related to Synaptic Signaling

December 30, 2009 |

The early stages of Alzheimer's disease are thought to occur at the synapse, since synapse loss is associated with memory dysfunction. Evidence suggests that amyloid beta (Aβ) plays an important role in early synaptic failure, but little has been understood about Aβ's effect on the plasticity of dendritic spines.

These spines are short outgrowths of dendrites (extensions of neurons) that relay electrical impulses in the brain. A single neuron's dendrite contains hundreds of thousands of spines, providing memory storage and transmission of signals across the synapse – the junction where such nerve impulses occur. Plasticity of these spines, or the ability to change and grow, is essential for the transmission of signaling in the brain.

Researchers led by Roberto Malinow, MD, PhD, professor of neurosciences and Shiley-Marcos Endowed Professor in Alzheimer's Disease Research at the University of California, San Diego School of Medicine, have shed more light on how Aβ's destructive effects on the brain are related to its impact on the plasticity of dentritic spines. Their study was published on December 27 in the journal *Nature Neuroscience.*

The researchers have shown that if Aβ is over-produced by either the pre-or post-synaptic side of the axon, it can cause destructive effects. Secondly, these effects are over a distances of about 10 microns of the neuron – affecting thousands and thousands of synapses.

"We found that amyloid beta affects structural and not just functional, plasticity," said Malinow. "Normally, plasticity can be induced, which makes synapses stronger and bigger, but amyloid beta prevents this."

According to Malinow, it also appears that continuous release of Aβ is required to prevent plasticity. "Even a short window of 30 to 60 minutes without Aβ secretion is enough to permit plasticity to occur," he said. As Aβ's effect on the dendritic spines – critical for memory – had been thought to be irreversible, this shows that there is a hope of change if scientists learn how to stop the secretion of Aβ at synaptic sites."

"Our results show that the continuous production of Aβ at dendrites or axons acts locally to reduce the number and plasticity of synapses," Malinow concluded.

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The study was supported by the National Institutes of Health, the Cure Alzheimer's Fund and the Leslie C. Quick Fellowship.

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