Involvement of AMPA receptor endocytosis in Alzheimers disease: Examining memory and structural plasticity deficits in mouse models

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Research Abstract
Alzheimers disease (AD) was first described in 1906. Despite intense research in the intervening 100 years, there is no cure for AD and available treatments are far from ideal. Progressive memory loss is the defining feature of AD. The early stages of AD are characterized by inability to acquire new memories, often observed as difficulty in recalling recent events. The ability to remember older events is then disrupted. Symptoms gradually

worsen over time and many aspects brain function become affected. Although the precise cause(s) of AD remains elusive, b-amyloid (Ab), a small protein derived from amyloid precursor protein (APP), is widely implicated. Mutations in APP cause familial AD (FAD) and increase Ab levels. While high Ab may eventually trigger cell death, memory deficits are observed in AD patients before evidence of cell death, suggesting that high levels of Ab itself may interferes with the ability to acquire memories in the early stages of this disease. Indeed, recent findings in cells suggest that increased Ab decreases the surface expression proteins that are key players in memory formation. However, whether a similar process underlies the memory deficits in whole organisms such as mouse models of AD is unknown. Here we will test this prediction using mice genetically-designed to mimic AD. Importantly, these mice show memory deficits, similar to people with early-stage AD. Our exciting preliminary results suggest that interfering with the decrease in the surface expression of this key protein, indeed rescues the memory deficits in these mice designed to model AD. We will verify and extend this finding and explore possible ways to translate this finding into the clinic. Currently, there are few clinical therapeutic options for AD. Our results will not only increase our understanding of the neurobiological bases of AD, but may advance future treatments for AD.

Further information available at:

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