Loss of drebrin from dendritic spines in hippocampal neurons from Alzheimer's disease model mouse

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Alzheimer's disease (AD) is one of neurodegenerative diseases and the most common cause of dementia. Among pathology of AD, synaptic dysfunction has most correlation with cognitive dysfunction. Drebrin is an actin binding protein and stabilizes actin filaments. Drebrin-decorated stable actin filaments accumulate in dendritic spines and are thought to be crucial for synaptic plasticity but drebrin has been decreased at onset of dementia in AD. We therefore hypothesized that loss of drebrin, that is, loss of stable actin filaments from dendritic spines elicits synaptic dysfunction and causes dementia in AD. Here we used the *App* knock-in mouse model of AD (App^{NL-G-F} mouse), to analyze the details of abnormal synapse in AD. First we performed immunohistochemical analysis using App^{NL-G-F} mice brains. We focused on the cortex and found no drebrin immunoreactivity around amyloid plaques in the App^{NL-G-F} mice brains. We further used primary hippocampal cultured neurons derived from the App^{NL-G-F} mice (App^{NL-G-F} neurons) and evaluated synaptic status based on drebrin cluster number using high-content imaging analysis. Our data showed App^{NL-G-F} neurons had less drebrin clusters indicating low functionality of synapse. These data suggest that the loss of drebrin from the dendritic spine in AD brains causes synaptic dysfunction.