Clusters of hyperactive neurons near amyloid plaques in a mouse model of Alzheimer's disease.

Abstract:
The neurodegeneration observed in Alzheimer's disease has been associated with synaptic dismantling and progressive decrease in neuronal activity. We tested this hypothesis in vivo by using two-photon Ca2+ imaging in a mouse model of Alzheimer's disease. Although a decrease in neuronal activity was seen in 29% of layer 2/3 cortical neurons, 21% of neurons displayed an unexpected increase in the frequency of spontaneous Ca2+ transients. These "hyperactive" neurons were found exclusively near the plaques of amyloid beta-depositing mice. The hyperactivity appeared to be due to a relative decrease in synaptic inhibition. Thus, we suggest that a redistribution of synaptic drive between silent and hyperactive neurons, rather than an overall decrease in synaptic activity, provides a mechanism for the disturbed cortical function in Alzheimer's disease.