An essential feature of Alzheimer's disease (AD) is the accumulation of amyloid-\(\beta\) (A\(\beta\)) peptides in the brain, many years to decades before the onset of overt cognitive symptoms. We suggest that during this very extended early phase of the disease, soluble A\(\beta\) oligomers and amyloid plaques alter the function of local neuronal circuits and large-scale networks by disrupting the balance of synaptic excitation and inhibition (E/I balance) in the brain. The analysis of mouse models of AD revealed that an A\(\beta\)-induced change of the E/I balance caused hyperactivity in cortical and hippocampal neurons, a breakdown of slow-wave oscillations, as well as network hypersynchrony. Remarkably, hyperactivity of hippocampal neurons precedes amyloid plaque formation, suggesting that hyperactivity is one of the earliest dysfunctions in the pathophysiological cascade initiated by abnormal A\(\beta\) accumulation. Therapeutics that correct the E/I balance in early AD may prevent neuronal dysfunction, widespread cell loss and cognitive impairments associated with later stages of the disease. This article is part of the themed issue 'Evolution brings Ca\(^{2+}\) and ATP together to control life and death'.

Jahr: 2016
Band: 371
Heft / Issue: - page 1 -