CHARACTERIZING AD-RELATED NETWORK DYSFUNCTION WITH THALLIUM AUTOMETALLOGRAPHY

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It is increasingly recognized that network dysfunction may be a mechanism underlying Alzheimer related cognitive decline. Pathogenic beta amyloid assemblies have been shown to induce multifaceted neuronal impairments, e.g. alteration of neuronal signaling pathways, structural and functional synaptic disruption and changes in neuronal morphology and plasticity. All these beta amyloid mediated neuronal alterations likely cause dysfunction of neuronal network activity. However, little is known about the characteristics and properties of AD-related network dysfunction in vivo. One reason is that the investigation of network function is challenging, as appropriate methods are severely limited.

We investigated the Alzheimer mouse model 5xFAD by analyzing patterns of neuronal activity during normal behaviour with single-cell resolution mapping of neuronal activity by thallium autometallography. That novel method is based on the tight coupling of neuronal activity and potassium uptake. Potassium-analogues like the heavy metal ion thallium can be used, therefore, as tracers for imaging neuronal activity. We observed significant changes of network activity within the cortex and subcortical areas. Interestingly, the functional alteration of network activity precede neuronal cell death and correlates with the beginning of behavioural deficits suggesting that network dysfunction may be the entry point for AD-related cognitive decline.