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AMPA receptor signaling in the CNS and interference by specific human autoantibodies

AMPA receptors are essential for fast excitatory transmission in the central nervous system. Autoantibodies to AMPA receptors have been identified in humans with autoimmune encephalitis and severe defects of hippocampal function. These patients suffer from severe memory deficits, confusion, and seizures. Here, we analyze how specific human autoantibodies against the AMPA receptor subunit GluA2 affect receptor function and composition, synaptic transmission, and plasticity. Using passive transfer of purified human pathogenic antibodies to mice, electrophysiology, and super-resolution imaging, we show that anti-GluA2 antibodies induce a distinct pattern of changes in synaptic AMPA receptor composition. GluA2 subunits are replaced by GluA1 resulting in synaptic scaling due to synaptic incorporation of AMPA receptors with increased single channel conductance and reduced inward rectification. With passive transfer of human pathogenic antibodies to mice, we show that anti-GluA2 antibodies impair synaptic plasticity and memory. Our results identify a specific immune-neuronal rearrangement of AMPA receptor subunits providing a novel framework to explain disease symptoms.

Date: **Friday, 10 November 2017**
Hour: **13:00**
Place: Aula 14, Medicine Faculty, Medicine Campus