Reduced levels of SNAP-25 increase PSD-95 mobility and impair spine morphogenesis

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Synapses are highly specialized and plastic structures allowing communication between neurons.
Nowadays, it is known that different neurological and psychiatric disorders have their etiology in an alteration of the synapse. SNAP-25 is a SNARE protein that is involved in the regulation of synaptic vesicles exocytosis and modulates voltage-gated calcium channels. Recent evidences have suggested that SNAP-25 is involved in different neuropsychiatric disorders, like ADHD, schizophrenia and epilepsy. Since lower SNAP-25 expression has been detected in different brain areas of psychiatric patients we set out to determine whether lower SNAP-25 levels affect glutamatergic synaptogenesis. Using cultured hippocampal neurons from heterozygous SNAP-25 mice, we demonstrate that lower SNAP-25 levels are associated with alterations in postsynaptic maturation. These defects manifest as reduction in synapse number and immature spine morphology, resulting from a direct impairment of postsynaptic properties. Consistently, reduction of SNAP-25 results in increased PSD-95 mobility and reduced spine formation upon overexpression of PSD-95. Of note, spine defects are also detectable in the hippocampus of SNAP-25 heterozygous mice. These data provide new mechanistic insights into the involvement of SNAP-25 in pathologies that go beyond the protein's known roles in presynaptic function and open the possibility to new therapeutic targets.