Integrins in synaptic excitability: relevance for neurodevelopmental disorders

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Integrins are cell adhesion receptors that serve as physical and functional link between the extracellular matrix and the intracellular cytoskeleton. They are expressed in nearly every cell type, and regulate diverse functions including migration, attachment and differentiation. In the brain, some integrins are enriched at synapses where they regulate synaptogenesis, synapse and dendrite maintenance, and synaptic plasticity. Further, some integrins have been implicated in diverse brain disorders from epilepsy to autism spectrum disorders [1, 2]. Although the physiological role of many integrins in the brain has been extensively studied, it is still unclear how dysfunctions in integrin-mediated cell adhesion alter structural and functional plasticity of dendritic spines, and behavior in mice. To elucidate the molecular and cellular mechanisms linking integrins to synaptic function, we performed morphological, protein chemistry, electrophysiological and behavioral experiments in mice deficient for the synaptic integrin αVβ3. Our results indicate that loss of integrin αVβ3 in neurons does not affect overall brain architecture and the dendritic arborization of neurons, but compromises selectively synaptic transmission, leading to behavioral abnormalities. Our findings support a model whereby integrin αVβ3 is necessary for the correct functioning of excitatory synapses.

[1] M. E. Kerrisk, L. A. Cingolani, and A. J. Koleske, Prog Brain Res 214 (2014) 101.

[2] A. Thalhammer and L. A. Cingolani, Neuropharmacology 78 (2014) 23.