Regulation of dendritic spine plasticityby actin binding proteins

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Changes in the shapes of dendritic spines, driven bydynamic actin filaments in the spine cytoplasm, may contribute to morphologicalplasticity of excitatory synapses in central nervous system circuits. Usingtime lapse recording of GFPÐactin in cultured hippocampal neurons we have foundtwo activity-dependent mechanisms, operating on different time-scales, thatsuppress actin dynamics and stabilize spine morphology. Activation of AMPAreceptors produces an immediate blockade of spine motility which is reversed assoon as the stimulus is withdrawn. By contrast, blockade of spine motility viaNMDA receptors requires 30 min to develop and persists for hours after thestimulus is withdrawn. To understand the regulatory mechanisms underlying theseeffects we have studied the influence of various actin binding proteins thatare enriched in dendritic spines. Profilin shows activity-dependent targetingto spine heads which depends on activation of NMDA receptors and which can beinduced by patterns of electrical stimulation associated with both LTP and LTD.Concomitantly with profilin accumulation, actin dynamics are suppressed andspine motility is blocked for several hours. Profilin accumulation can beprevented by expressing in neurons a polyproline-rich peptide corresponding to thecore of its binding domain in surface proteins of the VASP/MENA family.Expressing the blocking peptide destabilizes spines which becomemorphologically irregular and highly motile, suggesting that binding ofprofilin to a VASP-like surface protein regulates spine plasticity. Spinemorphology is also destabilized by overexpressing in neurons the actin-bindingprotein drebrin or just its short actin binding domain. Coincidentlyalpha-actinin, with which drebrin is known to compete for binding to actin filaments,is displaced from spine heads where it is usually concentrated, suggesting thatcompetition between drebrin and actin filament cross-linking proteins likealpha-actinin is also involved in the stabilization of spine structure.Together with other examples of actin binding proteins to be presented thesedata suggest that several distinct receptor-dependent mechanisms regulate thedynamics of spine actin and hence morphological plasticity at excitatorysynapses.

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