Eps8 controls dendritic spine density and synaptic plasticity through its actin-capping activity

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Actin-based remodelling underlies spine structural changes occurring during synaptic plasticity, the process that constantly reshapes the circuitry of the adult brain in response to external stimuli, leading to learning and memory formation. A positive correlation exists between spine shape and synaptic strength and, consistently, abnormalities in spine number and morphology have been described in a variety of neurological disorders. In the present study, we demonstrate that the actin-regulating protein, Eps8, is recruited to the spine head during chemically induced long-term potentiation in culture and that inhibition of its actin-capping activity impairs spine enlargement and plasticity. Accordingly, mice lacking Eps8 display immature spines, which are unable to undergo potentiation, and are impaired in cognitive functions and sociability. Additionally, we found that reduction in the levels of Eps8 occurs in brains of patients affected by autism compared to controls. Our data reveal the key role of Eps8 actin-capping activity in spine morphogenesis and plasticity and indicate that reductions in actin-capping proteins may characterize forms of intellectual disabilities associated with spine defects. Dissecting the molecular mechanisms involved in synapse formation and plasticity could pave the way for the rational design of new therapeutic approaches for the treatment of intellectual disability.