A?1-42 stimulates actin polymerization in hippocampal neurons through Rac1 and Cdc42 Rho GTPases

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A number of psychiatric and neurodegenerative disorders, such as Alzheimer's disease, are characterized by abnormalities in the neuronal cytoskeleton. Here, we find that the enhancement in actin polymerization induced by fibrillar amyloid-beta peptide (A?) is associated with increased activity of Rac1/Cdc42 Rho GTPases. Rac1 upregulation involves the participation of Tiam1, a Rac guanine-nucleotide exchange factor, where A? exposure leads to Tiam1 activation by a Ca2+ -dependent mechanism. These results point to Rho GTPases as one of the targets in A?-induced neurodegeneration in Alzheimer's disease pathology, with a role in mediating changes in the actin cytoskeletal dynamics.