Association of N-cadherin levels and downstream effectors of Rho GTPases with dendritic spine loss induced by chronic stress in rat hippocampal neurons

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 Chronic stress promotes cognitive impairment and dendritic spine loss in hippocampal neurons. In this animal model of depression, spine loss probably involves a weakening of the interaction between pre- and postsynaptic cell adhesion molecules, such as N-cadherin, followed by disruption of the cytoskeleton. N-cadherin, in concert with catenin, stabilizes the cytoskeleton through Rho-family GTPases. Via their effector LIM kinase (LIMK), RhoA and ras-related C3 botulinum toxin substrate 1 (RAC) GTPases phosphorylate and inhibit cofilin, an actin-depolymerizing molecule, favoring spine growth. Additionally, RhoA, through Rho kinase (ROCK), inactivates myosin phosphatase through phosphorylation of the myosin-binding subunit (MYPT1), producing actomyosin contraction and probable spine loss. Some micro-RNAs negatively

control the translation of specific mRNAs involved in Rho GTPase signaling. For example, miR-138 indirectly activates RhoA, and miR-134 reduces L