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DEPRESSION-LIKE BEHAVIOUR IN NEURAL CELL ADHESION MOLECULE (NCAM) DEFICIENT MICE AND ITS REVERSAL BY AN NCAM-DERIVED PEPTIDE, FGL

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Neural cell adhesion (NCAM) plays important roles in the structural and functional plasticity in the CNS. Recent years much attention was put on the role brain plasticity in relation to depressive state. Mice deficient in NCAM molecule demonstrated signs of depression-like behavior in the tail suspension- and sucrose consumption tests. Analysis of hippocampal neurogenesis in NCAM deficient mice revealed a reduced survival of the newborn cells and their differentiation into calbindin-positive granule neurons. NCAM-deficient mice have also demonstrated reduction of CREB phosphorylation in the basolateral nucleus of amygdala, pre- and frontal cortex and CA3 regions of hippocampus. Since BDNF signaling system plays a significant role in the mechanisms of depression and in the effects of antidepressants, we measured the levels of BDNF and the level of phosphorylation of TrkB receptor in the brain of NCAM-/- mice. Experiments demonstrated a reduced BDNF signaling in the brains of NCAM-/- ice as a reduced level of phosphorylated Trk B receptor evidenced it. The depression-like signs in NCAM-/- mice were reversed by the NCAM-mimetic peptide FGL. In addition, repeated FGL administration enhanced survival of the newly generated cells in the dentate gyrus of NCAM-/- mice. Our data suggest that reduced brain plasticity due to deficiency in NCAM plays a role in the development of depressive state and NCAM mimetic peptide FGL might represent a new class of drugs with antidepressant activity.

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