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Regulation of extrasynaptic glutamatergic signaling by polysialylated NCAM in health and disease

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Abstract: The neural cell adhesion molecule NCAM is known to mediate cell-cell and cell-extracellular matrix (ECM) adhesion via homophilic and heterophilic interactions. During brain development, NCAM and associated glycan, polysialic acid (polySia), play important roles in cell migration, proliferation, neurite outgrowth and fasciculation, and synaptogenesis. In the adult rodent brain, NCAM regulates synaptic plasticity, learning, and memory. Dysregulated cortical expression of NCAM and polySia have been found in Alzheimer's disease and schizophrenia. Our data demonstrate the essential role of polySia-NCAM in the balancing of signaling through synaptic/extrasynaptic NMDA receptors and highlight the therapeutic potential of short polySia fragments to restrain GluN1/GluN2B-mediated signaling in several animal models of neurological and psychiatric diseases.

Keywords: LTP; synaptic plasticity; polysialic acid; schizophrenia; Alzheimer's disease; NMDA receptor