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Involvement of Secretory Calcium-Binding Glycoproteins in Neuronal Plasticity

Increasing intracellular calcium concentrations have been found to mediate homosynaptic plasticity like facilitation and habituation(1). The decreasing extracellular calcium concentration induced by synchronous activity of neuronal networks may provide an additional signal for hetero-synaptic mechanisms involved in long term sensitization, regeneration and associative learning.

Two calcium-binding glycoproteins derived from goldfish central nervous system have been biochemically characterized. They are preferentially synthesized and secreted into the extracellular matrix when the fish learn an operant(2) or classical task. Antibodies directed against these proteins (named ependymins) interfere with activity-dependent sharpening of the multiunit receptive fields during regeneration of retinotectal projections following optic nerve crush(3). They also prevent memory consolidation after vestibulomotoric training(2) or associative learning of an active avoidance response(4), when injected into brain ventricles during a critical time period after acquisition (0.2 - 24 hours). Screening of c-DNA libraries prepared from goldfish brain(5) revealed the presence of a cleavable N-terminal signal sequence in the ependymin precursor-molecule, typical of secretory proteins. Isolated ependymins are responsive to their ionic environment: They bind radioactive calcium, may be co-purified with an EDTA-sensitive metalloprotease activity(6), and polymerize in the absence of calcium ions(7).

It is suggested that the activity-dependent extracellular calcium concentration in the synaptic cleft regulates the conformation of secreted ependymin molecules. The induced modifications may ultimately lead towards ultrastructural changes of functional significance.

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