

EXTRACELLULAR CALCIUM BINDING PROTEINS MEDIATE PLASTICITY OF NEURONAL NETWORKS IN REGENERATION AND MEMORY CONSOLIDATION

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Antibodies directed against specific proteins of the goldfish central nervous system (ependymins) interfere with (i) activity-dependent sharpening of the regenerating retinotectal projection after optic nerve crush (J.Schmidt and Shashoua, *Neuroscience*, 1987, 22, S254), (ii) retention of a vestibulomotoric swimming skill, and (iii) consolidation of long-term memory following associative learning of an active avoidance response, when infused (regeneration study) or injected (learning experiments) into brain ventricles during a critical time period after acquisition of the task. These results suggest a functional role in neuronal plasticity of the antigen molecule, either at neuronal cell surfaces or in the extracellular compartment. Ependymin-like immunoreactivity has been localized to pyramidal cells of the optic tectum and also to axons and growth cones of explanted retinal ganglion cells. Radioactive labelling studies and radioimmunoassay measurements revealed secretion of ependymins into the brain extracellular fluid, in accordance with the presence of a cleavable N-terminal signal sequence in ependymin precursors typical of secretory proteins. Both, synthesis and secretion of ependymins, are stimulated by the vestibulomotoric and the classical conditioning. Isolated ependymins are responsive to their ionic environment: They bind radioactive calcium, may be co-purified with an EDTA-sensitive metalloprotease activity, and polymerize in the absence of calcium ions (compare Shashoua and Holmquist, *J. Neurochem.*, 1986, 47, 738).

It is suggested that the concentration of extracellular calcium in the synaptic cleft induces conformational changes of secreted ependymin molecules, thereby regulating their interaction with synaptic membranes. (Supported by the Deutsche Forschungsgemeinschaft)