BIOCHEMICAL PARTICIPATION OF GLYCOPROTEINS IN MEMORY CONSOLIDATION AFTER TWO DIFFERENT TRAINING PARADIGMS IN GOLDFISH

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The synthesis of three goldfish brain proteins, α, ß and γ (Mr 37 000, 32 000 and 26 000), is specifically enhanced when the animals learn to swim with a polystyrene float sutured close to their pectoral fins (1). ß and γ are glycoproteins. They have been isolated by affinity chromatography on Concanavalin A followed by SDS-PAGE and were used to immunize rabbits. The obtained antisera inhibit the consolidation of the newly acquired swimming behaviour, when injected into the IV. brain ventricle during a critical time period after training (2). The ß and γ proteins have been localized immunohistochemically to granule cells in the optic tectum and vagal lobes (3) and to cells of the periventricular gray of the ependymal layer (4) and therefore, they have been named "ependymins" . A very specific and sensitive radioimmunoassay has been developed for quantitative determination of ependymins (5). With the radioimmunoassay we demonstrated that ependymins are major constituents in the nervous tissue of untrained goldfish. They become secreted both, in vivo and in cell culture (6). Analysis of the amino acid composition, peptide mapping and pulse chacing experiments all indicate, that ependymins occur physiologically as dimeric molecules and that ependymin ß is proteolytically cleft by a protease activity of the extracellular brain fluid to become ependymin γ (7).

We have now applied the radioimmunoassay to analyse the regional and subcellular distribution of ependymins in goldfish brain. They are shown to be highly enriched in the cytoplasmic and extracellular compartments. After the float-training paradigm ependymin concentrations decrease temporarily in the extracellular brain fluid, before their steady state concentrations in the cytoplasm and the extracellular brain fluid increase over control values. Ependymin-like immunoreactivity has also been observed in cultured pyramidal neurons derived from embryonal rat brain hippocampus. Furthermore, the same anti-ependymin antisera which were shown to interfere with memory consolidation after the float-training also prevent long term memory formation after a classical avoidance conditioning: goldfish were trained in the "shuttle-box" to cross a barrier when a light comes on in one part of the training tank. When they were injected intraventricularly with anti-ependymin antiserum 0.5, 4.5 or 24 hours after the acquisition of the shuttle-box task and tested three days later, they were found unable to remember what they had learned on day one. The antiserum was without effect on memory consolidation, however, when injected 72 hours after training. Injection of neutral rabbit serum or of an antiserum from which the specific antibodies had been removed by adsorbance with ependymins were used as controls. Also the behaviour of goldfish that flee the light stimulus spontaneously was not influenced by the injection of anti-ependymin antiserum (active control group). - We assume that the antisera interfere with synaptic events during memory consolidation, since isolated ependymins possess substantial calcium binding capacity.

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