IS LONG-TERM MEMORY FORMATION COMPREHENSIBLE AS A MICRO-EVENT IN STRUCTURAL AND FUNCTIONAL DIFFERENTIATION OF NEURONAL CONNECTIONS?

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Glycoproteins are known to guide migration of neurectodermal cells, to promote neuronal regeneration and to support adhesion of neurites in vitro. During behavioural adaptations metabolism of some glycoproteins is enhanced in the CNS. Ependymin is such a CNS-specific glycoprotein. Synthesis of ependymin is increased after optic nerve crush, and anti-ependymin antibodies interfere with the sharpening of receptive fields during functional regeneration of the retinotectal projection. The same glycoprotein displayed increased synthesis and secretion after various learning tasks. Quantitative in situ hybridization revealed a rapid and pronounced increase in ependymin mRNA expression 1 hour after acquisition of an active avoidance conditioning. Increased translation and secretion of ependymin were demonstrated by radioactive precursor incorporation studies and by quantitative radioimmunoassay measurements. Inactivation of secreted ependymin by intracerebroventricular injection of antibodies interfered with memory consolidation, but neither with acquisition nor performance, and indicated that ependymin exerts its physiological function after secretion at targets away from its site of synthesis in reticular cells of the leptomeninx. This interpretation is in accordance with ultrastructural immuno-localization of ependymin.

The primary structure of ependymin precursors, as deduced from cDNA cloning, exceeds the mature molecule by a N-terminal signal sequence typical of secretory proteins. Two N-glycosylation sites give rise to mono- and bi-N-glycosylated variants of 31 and 37 kDa, respectively. Ependymin sugar moieties comprise terminal 3-sulfated glucuronic acid, an epitope characteristic of cell adhesion molecules (e.g., N-CAM and MAG). Also ependymin provides a good substrate for the outgrowth of retinal ganglion cell axons in vitro. Changes in the calcium concentration of the medium, that are known to regulate the conformation of ependymin molecules, may alter the cell adhesion properties and provide the mechanism for structural modifications of the micro-environment in the sequel of neuronal activity.

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