PEPTIDES AND RAT BRAIN MEMBRANE PHOSPHOPROTEINS

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Behaviorally active peptides derived from ACTH inhibit *in vitro* the phosphorylation of at least five protein bands from rat brain synaptic plasma membranes (SPM), as separated on SDS-polyacrylamide slab gel electrophoresis (Zwiers *et al.*, 1976). A direct interaction of ACTH with SPM-protein kinase(s) is likely to be responsible for the effect on phosphorylation (Zwiers *et al.*, 1978). The structure-activity relation found, closely resembles that observed for the effect of these peptides on grooming behavior in the rat (Gispen *et al.*, 1975).

Under similar *in vitro* conditions cAMP stimulates the phosphorylation of three other SPM protein bands with higher molecular weight whereas cGMP is without effect. Attention is focussed on one ACTH-sensitive SPM protein band (B-50, M.W. 48,000), in particular, and on a procedure to isolate the native protein kinase responsible for the phosphorylation of that protein. Treatment of SPM with 0.5% Triton X-100 in 75 mM KCl solibilized 80% of the protein. In this solubilized fraction ACTH again inhibits the endogenous phosphorylation of band B-50. The inhibition is Mg-dependent but not dependent on the presence of Ca. Exogeneously added B-50 obtained after preparative SDS-polyacrylamide gel electrophoresis and extraction of B-50 out of the gel, is also phosphorylated by the SPM extract. Column chromatography using DEAE cellulose and a K-phosphate gradient yields endogenous B-50 phosphorylating activity at about 150 mM K-phosphate. Presumably the B-50 phosphorylating activity resides in a complex of B-50 and protein kinase which after application on Biogel P200 runs in the void volume.

Preliminary data on the effects of various fragments of β-LPH (endorphins) are shown.

If SPM protein phosphorylation is involved in certain types of synaptic transmission (Greengard, 1976) then the present data support the notion that behaviorally active peptides may act as modulators of neurotransmission.

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