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Unusual biochemistry of changes in neuron membrane permeability evoked by cAMP

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Influence of different metabolic poisons on cAMP-evoked neuron membrane permeability is investigated Drugs preventing cAMP binding with R subunits of protein kinase decrease the cAMP-evoked current, but the inhibitor of the C subunit, H8, has no effect The cAMP-dependent current is increased by uncouplers and decreased by inhibitors of glycolysis and oxidative phosphorylation The mechanism of cAMP action on neuron permeability is discussed

cyclic AMP, Neuron permeability, Protein kinase, Glycolysis, Oxidative phosphorylation, (*Helix lucorum*)

1. INTRODUCTION

It was shown that intracellular injection of cyclic AMP evoked a generator potential [1] increasing Na^+ permeability and decreasing K^+ permeability [2]. It was generally believed that cAMP changes neuron activity by way of protein kinase activation and neuron membrane protein phosphorylation. However, the C subunit of protein kinase did not imitate the cAMP-dependent increase in Na^+ permeability [3,4] described by us. The delay of the cAMP response is so short that cAMP cannot be transported during this time from the electrode tip placed at the neuron center to the neuron membrane with the usual diffusional process [5]. Experiments described in this paper show that the biochemistry of the cAMP-dependent system controlling generator potential is not usual.

2. MATERIALS AND METHODS

Experiments were performed on neurons of suboesophageal ganglia of the land snail, *Helix lucorum* The ganglia were isolated and placed in bath solution containing 80 mM NaCl, 4 mM KCl, 7 mM $CaCl_2$, 5 mM $MgCl_2$, 5 mM Tris-HCl buffer (pH 7 5) Neurons were impaled by 3 microelectrodes filled with testing drugs such as 0 1 M adenosine 3' 5 -cyclic monophosphate (cAMP), 0 5 M ATP, 0 1 M N^6,O^2-dibutyryl adenosine 3'-5 -cyclic monophosphate (dibutyryl cAMP), 0 3 M tolbutamide, 10 mM *N*-[2-(methylamino)ethyl]-5-isoquinolinesulfonamide dihydrochloride (H8), 0 25 mM TTFB, 0 3 M iodoacetate, 0 3 M 6-deoxy-D-glucose

Some drugs were added to the bathing solution in the following final concentrations 1 mM sodium metavanadate, 1-5 mM potassium arsenate, 0 06-0 12 M dinitrophenol (DNP), 20 μg/ml oligomycin, 10 μg/ml antimycin A, 10^{-8} M *p*-trifluoromethoxycarbonyl cyanide phenylhydrazone (FCCP), 4×10^{-9} M 3,5-di-*tert*-butyl-4-hydroxybenzylidenemalononitrile (SF 6847), 6×10^{-6} M rotenone, 10 mM sodium azide

Measurement of the neuron electric activity and intracellular injection were made with a Nova 3D compu er as described previously [6] Computer simulation of cAMP-evoked current was achieved as shown in [7]

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3. RESULTS AND DISCUSSION

The dibutyryl analog of cAMP penetrating through a cell membrane is often used to study the cAMP effect. However intraneuronal injection of this drug did not cause the quick ionic current as in the cAMP case (fig.1A). When there are two electrodes in the neuron, one with cAMP and the other with dibutyryl cAMP, the neuron response to

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