MODULATION OF THE REACTION OF HIPPOCAMPAL NEURONS TO SENSORY STIMULI BY CHOLINERGIC SUBSTANCES*

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The influences of increasing endogenous acetylcholine (eserine) and its blockade (scopolamine) on the effects of sensory stimuli were analyzed through the extracellular recording of the activity of individual hippocampal neurons of awake rabbits. An increase in the level of acetylcholine, accompanied by the appearance of stable theta rhythm, leads to a substantial decrease in the reactivity of neurons, the suppression, attenuation, and inversion of the majority of inhibitory reactions and of a substantial proportion of activational reactions including on-responses of a specific type. At the same time, a limited group of activational reactions is intensified and extended against the background of eserine. Scopolamine, which blocks theta rhythm, does not change or intensifies inhibitory and some activational reactions, including on-responses. Tonic reactions are shortened; however, their gradual extinction disappears. The effects described are preserved in the hippocampus in the presence of basal undercutting of the septum which eliminates ascending brainstem pathways. These data make it possible to draw the conclusion that, under normal conditions, a new (significant) sensory stimulus elicits in the hippocampus an initial stoppage (reset) of activity with the coordinated triggering of theta rhythm and the passage against this background of signals along the cortical input in a specific phase relationship to it. The period of theta modulation switched on by the signal fosters its recording and the limitation of the passage of subsequent, interfering signals. The septohippocampal influences may thus support the mechanism of selective attention, as a necessary precondition for memory.

The functional significance of rhythmic theta modulation, organized in the medial septal region (MS-DB) and superimposed on the activity of hippocampal neurons in all situations associated with the processing of new and significant information (orienting—exploratory activity, attention, initial stages of learning), has been the object of the steady attention of investigators for a long time. Nevertheless, the specific contribution of influences supporting theta modulation to the processing of information by hippocampal neurons remains to a substantial degree an object of speculation. Despite the available evidences of the homology of the functions of the hippocampus (attention, memory) in man and animals, interest in the function of the theta rhythm has previously been limited to the existing opinion regarding its absence in the hippocampus of primates; this question has been reviewed currently [33]; this increases interest in the functional role of theta activity still further.

The septal influences supporting theta rhythm are, to a substantial degree, cholinergic. The death of cholinergic neurons in aging and in Alzheimer's disease leads to disturbances in attention and memory like the hippocampal injury syndrome [14, 22]. The blockade of cholinergic septohippocampal influences in animals and man reproduces the "hippocampal syndrome"; this points to their extreme importance for the hippocampus's effectuation of its functions in the organization of attention, memory, and learning [10, 12, 32].

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The present study was carried out to elucidate the role of "cholinergic theta rhythm" in the processing of sensory information by hippocampal neurons.

METHODOLOGY

The experiments were carried out on awake immobilized rabbits in chronic conditions. The operation and the conditions of the recording of the neuronal activity of the hippocampus, the remotely-controlled administration of eserine (0.1 mg/kg) and scopolamine (0.3-0.5 mg/kg) have been described in detail previously [3]. Two groups of animals were used in the experiments — intact and with complete basal undercutting of the septum, eliminating brainstem influences through the system of the medial forebrain bundle (MFB). The stimulating electrode was usually implanted into the basal part of the me-