CHANGES IN REACTIVITY OF SOMATOSENSORY CORTICAL NEURONS DUE TO NEMBUTAL

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Comparison of the character of changes in focal responses of the somatosensory cortex and in single unit responses indicates the high sensitivity of the neuron systems of the projection cortex to barbiturates. Administration of nembutal shortens the duration of the unit responses, impairs rhythm binding to high-frequency stimulation, and gives rise to periodic fluctuations of excitability. Similar changes in the high-frequency components of focal responses and discharges of a particular group of cortical neurons confirmed the view that they are causatively interconnected.

Contrary to the established view that barbiturates act mainly on the reticular formation of the brain stem, investigations in recent years have demonstrated the high sensitivity of cortical neuronal systems to barbiturates [1-6, 10, 12]. To study the direct action of nembutal on cortical evoked activity the writers used interzonal focal reactions arising in a somatosensory area of the cortex in response to stimulation of another somatosensory area [2]. Analysis of the changes in the individual components of these responses showed that nembutal blocks the late high-frequency components and also prolongs their recovery cycle. However, before these results could be interpreted, it was necessary to compare the character of the changes in the high-frequency components and the single unit discharges.

The object of the present investigation was to examine changes in the response of cortical neurons during activation of the thalamo-cortical and interzonal pathways by means of nembutal.

EXPERIMENTAL METHOD

Experiments were carried out on cats. The animals received a preliminary injection of nembutal in a dose of 15-20 mg/kg; they were then immobilized with listhenon or tubocurarine and maintained on artificial respiration. The points of fixation of the animal in the stereotaxic apparatus and the tissues of the scalp were infiltrated with 0.5% procaine. Focal evoked potentials from the cortical surface and single unit responses to stimulation of the posteroventral nucleus of the thalamus and the first somatosensory area (CI) were recorded from the second somatosensory area (CII). The action of nembutal, when injected intravenously, was observed at the earliest 5-6 h after the beginning of the experiment.

EXPERIMENTAL RESULTS AND DISCUSSION

Comparison of the focal thalamo-cortical and interzonal responses with single unit responses in unanesthetized animals and in animals anesthetized with nembutal showed a clear relationship between the period of onset of the high-frequency components of the responses from the cortical surface and the duration of discharges of cells responding to a synchronous stimulus by a primary high-frequency discharge. Under nembutal anesthesia the number of high-frequency waves in the phase of development of the focal responses

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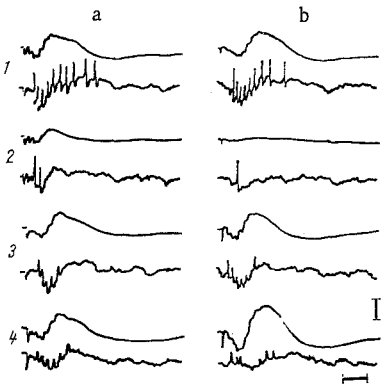

Fig. 1

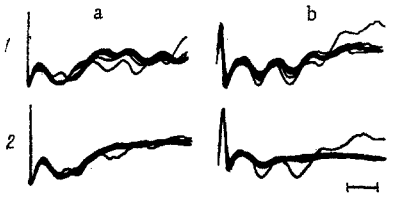

Fig. 2

Fig. 1. Effect of nembutal on electrical responses in area CII of the cortex: a) stimulation of cortical area CI; b) stimulation of posteroventral nucleus of thalamus; 1) before injection of nembutal; 2) 20 min after injection of nembutal in dose of 7 mg/kg; 3) 1 h, and 4) 2 h after injection. Calibration of amplitude 0.25 mV, time 10 msec.

Fig. 2. Effect of nembutal on high-frequency components of primary focal responses: a) stimulation of posteroventral nucleus of thalamus; b) stimulation of area CI at 30/sec; 1) before injection of nembutal; 2) before injection of nembutal in dose of 15 mg/kg. Time marker 2 msec; frequency band of amplifier clipped below.

and the number of discharges in the primary unit responses did not exceed two or three. In the unanesthetized cats or in animals recovering from anesthesia the high-frequency components could accompany the development of the entire primary focal response. The period of unit discharge was lengthened correspondingly. Bioelectrical responses in CII to single stimulation of cortical area CI (a) and of the thalamus (b) in an animal which received the initial dose of nembutal 9 h before the beginning of recording are shown in Fig. 1:1. Both primary responses were accompanied by high-frequency waves not only during the initial positive wave, but also throughout the period of development of the negative wave of the focal cortical responses. Responses of the neuron to both stimuli took the form of a high-frequency grouped discharge, more than 20 msec in duration. Such a lengthy primary response of the cortical neuron, as well as the time of onset of the high-frequency components of the focal responses, indicated a relatively weak process of after-inhibition, following the initial discharge of the cortical cells.

After injection of nembutal in a dose of 7 mg/kg (Fig. 1:2), the neuron still maintained its moderate background activity. The amplitude of both focal primary responses was considerably reduced, and the unit response contained fewer discharges because the later ones were blocked. The number of high-frequency waves in the focal response was correspondingly and sharply reduced. These effects were not due to a decrease in excitability of the cortex or nucleus at the site of stimulation, for with an increase in the intensity of the stimuli the amplitude of the primary focal responses increased only very slightly without any lengthening of the phase of unit discharges. Recovery of the responses of this neuron could be followed for a long time (Fig. 1:3 and 4). During recovery, a relationship was observed between the duration of the unit discharges and the period of manifestation of the high-frequency components.

These facts confirm the earlier hypothesis regarding the nature of the high-frequency components of the primary responses of the projection cortex and their connection with discharges of a particular group of cortical cells [7, 8].

As a result of administration of repeated small doses of nembutal, the recovery cycle of the cortical unit discharges also was increased. In the stages of superficial barbiturate anesthesia, the after-changes in excitability of the cortical neurons were phasic in character, with the appearance of secondary bursts of discharges. During deep anesthesia these phasic changes of excitability disappeared and the recovery cycle of the neurons increased progressively in length.

Ability to reproduce the frequency of stimulation, and changes in rhythm binding following the action of nembutal were largely determined by the latent period of the unit responses. Nembutal considerably

depressed responses to high-frequency stimulation even in short-latency neurons. Meanwhile the early high-frequency components of the focal responses were completely suppressed (Fig. 2). Before administration of nembutal the high-frequency components were able to reproduce a frequency of stimulation of 30/sec with hardly any decrease in amplitude. Under the influence of nembutal, only the response to the first stimulus remained. In all subsequent responses, at the same frequency, all waves except the first were blocked.

Analysis of the changes in the high-frequency components of the focal responses of the unit discharges showed a decrease in the level of cortical unit excitability even after administration of subnarcotic doses of nembutal. These results confirm the earlier hypothesis that nembutal acts in stages on the thalamic and cortical projection systems of neurons. By analogy with the mechanism of action of nembutal on the relay neurons of the ventrobasal complex of the thalamus, it can be postulated that the restriction of rhythm binding of the cortical neurons in the subnarcotic stages of barbiturate action and the prolongation of the recovery cycle with the formation of phasic secondary after-discharges are due to strengthening of the postsynaptic inhibitory action cutting off the unit discharges beyond a certain range of frequencies. During deep barbiturate anesthesia, the discharges of the short-latency neurons persist, although the cyclic after-changes in excitability disappear. This can evidently be attributed to the greater sensitivity of cortical interneurons responsible for the development of after-inhibition on the pyramidal neuron to the action of nembutal than to the excitatory postsynaptic action which develops primarily [11].

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