EFFECT OF CAFFEINE ON NEOCORTICAL UNIT RESPONSES TO MESO-DIENCEPHALIC STIMULATION

É. B. Arushanyan, Yu. A. Belozertsev, and K. G. Aivazov

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Activity of sensomotor cortical neurons during high-frequency and single stimulation of the meso-diencephalon was recorded in acute experiments on anesthetized cats. Caffeine (20-40 mg/kg) increased the firing rate of the cells to some extent. Meanwhile the intensity of the activation shift gave stimulation of the reticular formation and the antero-medial and lateral hypothalamus was increased. The number of activation responses increased and are-active neurons were less frequent. At the same time no considerable changes were found in the inhibitory responses. Modulation of the cortical responses by caffeine is considered to be due chiefly to a change in the excitability of the cortical cells.

KEY WORDS: neocortex; meso-diencephalic structures; caffeine.

Caffeine acts simultaneously on subcortical structures and on the "neuronally isolated cortex" [2], but it does not change the EEG activation in response to stimulation of mesencephalic and diencephalic structures [6, 7]. However, by recording the potentials of single units the action of caffeine on the effects of subcortical stimulation can be demonstrated [3].

It was therefore interesting to study the effect of caffeine on single neocortical unit responses to meso-diencephalic stimulation.

EXPERIMENTAL METHOD

Experiments were carried out on 30 cats into which electrodes were inserted, using coordinates of Jasper and Ajmone-Marsan's atlas [4], into the brain-stem reticular formation (RF) and the antero-medial (AMH) and lateral (LH) hypothalamus. Single unit activity in the sensomotor cortex was recorded in curarized animals by the method described previously [1]. Caffeine in doses of 20-40 mg/kg was injected intravenously slowly. Significant indices of facilitation or inhibition of activity, determined by the formula $n-e/e$, where n is the mean number of discharges per second at the moment of stimulation and e is the number before stimulation, were used as the measures of the response to subcortical stimulation.

EXPERIMENTAL RESULTS

More than 150 neocortical neurons were tested, 25 of them before and after the injection of caffeine. In a dose of 20 mg/kg caffeine had no significant effect on the mean firing rate of the cells. With an increase in the dose to 40 mg/kg the firing rate increased.

In response to high-frequency (50-100/sec) meso-diencephalic stimulation most neocortical sensomotor neurons significantly changed their mean firing rate. The character of the effect (the ratio between

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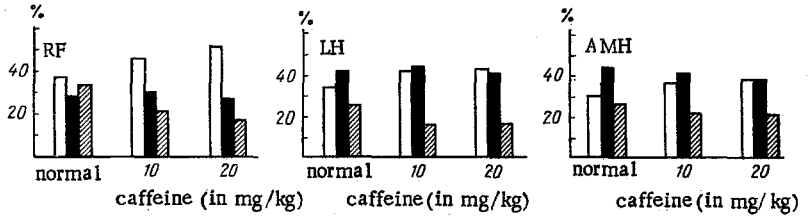

Fig. 1. Effect of caffeine on distribution of cortical unit responses to stimulation of RF, AMH, and LH. Ordinate, frequency (in %) of unit responses to high-frequency meso-diencephalic stimulation. Unshaded column represents activation of unit activity; black column – inhibition; obliquely shaded column – no response.

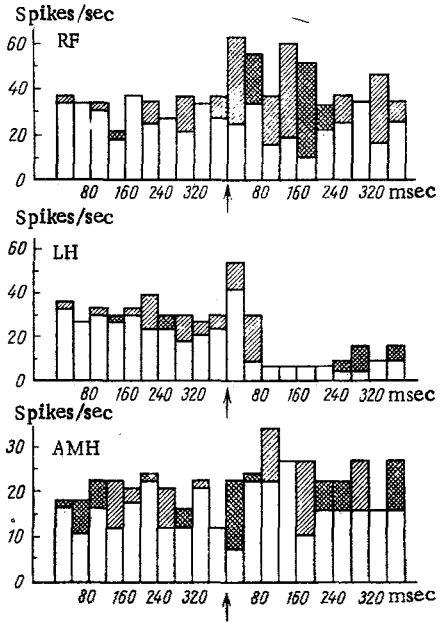

Fig. 2. Effect of caffeine on activation responses of cortical neurons during single stimulation of RF, LH, and AMH. Poststimulus histograms of activity of various units before and after application of a single stimulus (marked by arrow) to hypothalamus and mesencephalon. Obliquely shaded columns show effect of caffeine with an increase, and cross-hatched columns effect with a decrease in the original firing rate.

the number of responses of inhibition and activation) depended on the region of stimulation, although the intensity of stimulation was usually that which evoked orienting reactions in the animal before immobilization.

Stimulation of RF, as in the experiments of Krupp and Monnier [5], more often facilitated than inhibited neocortical unit activity (Fig. 1). Conversely, inhibitory unit responses occurred much more often after stimulation of LH and, in particular, of AMH.

Under the influence of caffeine (10-20 mg/kg) the changes in the indices of inhibition and facilitation recorded during reticular stimulation were reciprocal in character. The intensity of the facilitatory shift increased, but inhibition of the unit discharges weakened. It was noted that the structural reorganization of the cortical response under the influence of small doses of caffeine was accompanied by an increase in the number of cases of activation of unit activity. In the population studied, the number of areactive neurons was reduced by one-third. With an increase in the dose to 40 mg/kg, the changes became significant in degree ($P < 0.05$). The number of cells responding by inhibition remained constant during the action of the caffeine. Since the predominant response in the control experiments to an increase in the intensity of RF stimulation was slowing of the spontaneous rhythm, the action of caffeine was evidently not accompanied by any change in the thresholds of the reticular effects.

Responses to stimulation of LH and AMH changed similarly to the reticular responses under the influence of caffeine. The intensity of the activation shift during hypothalamic stimulation increased significantly, whereas inhibition of the original unit activity decreased slightly. During excitation of each part of the hypothalamus the number of cells responding by activation increased a little. Meanwhile a change in the number of areactive cells was recorded (Fig. 1).

The similarity between changes in the cortical responses during repetitive stimulation of the reticular and hypothalamic zones was confirmed by the study of the effect of caffeine on the response to single meso-diencephalic stimulation. Analysis of the poststimulus histograms (Fig. 2) shows that caffeine facilitated the increase in the initial firing rate of the cells regardless of which part of the brain was stimulated. In phasic responses to LH stimulation the intensity of activation, followed by a period of inhibition, was increased. A parallel increase was observed in the tonic responses to single stimulation of AMH or the mesencephalic part of RF. The pattern of the unit discharges in time was often rearranged, causing facilitation of evoked activity. On the whole the tendency was toward an increase in the number of activation responses.

Caffeine thus modifies cortical responses to single and repetitive stimulation of the mesencephalic RF and various zones of the hypothalamus. A characteristic feature of the action of caffeine is a change in the formation of the activation responses, but not the inhibitory responses, of the neocortical cells. The intensity of activation of unit activity and the number of neurons responding by an increase in the spontaneous firing rate both increased.

The fact that the changes induced by caffeine are in the same direction during stimulation of RF, LH, and AMH suggests that this modulation of the cortical responses is determined mainly by a change in the excitability of the cortical cells themselves.

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