EFFECT OF PSYCHOSTIMULANTS ON THE AVOIDANCE REACTION TO STIMULATION OF THE CAUDATE NUCLEUS

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Chronic experiments on cats showed that caffeine (10-30 mg/kg) facilitates the emotional manifestations of the avoidance reaction to mesencephalic or diencephalic stimulation. Caffeine does not change the inhibitory effects of stronger stimulation of the neostriatum. Meanwhile, subthreshold stimulation of the caudate nucleus, evoking restful activity in control experiments, inhibits the defensive behavior by a weaker degree in conjunction with the action of caffeine. Amphetamine (1-3 mg/kg) depresses the emotional manifestations of defensive responses. It abolishes the effect not only of threshold, but also of subthreshold stimulation of the caudate nucleus on spontaneous motor activity and defensive behavior arising in response to hypothalamic or mesencephalic stimulation.

Some authorities [5, 7, 11] consider that stimulation of behavior by caffeine and amphetamine is due partly to a disturbance of the function of inhibitory mechanisms of the brain. One structure effectively depressing behavior is the caudate nucleus [1, 3, 9].

It was therefore decided to study the effect of caffeine and amphetamine on caudate inhibition of defensive responses.

EXPERIMENTAL METHOD

Electrodes were implanted into various structures of the hypothalamus, mesencephalon, and caudate nucleus of 14 cats. The caudate nucleus was stimulated at 10/sec and the hypothalamus and mesencephalon at 100/sec. In experiments with combined stimulation, the caudate nucleus was stimulated first (60 sec), after which the hypothalamus and caudate nucleus were stimulated simultaneously for 20 sec. In the course of the experiment, the latent period of the components of the mesencephalic response, the composition of its various manifestations, and the biological significance of behavior were analyzed. Caffeine (10-30 mg/kg) and amphetamine (1-3 mg/kg) were injected intraperitoneally.

EXPERIMENTAL RESULTS

Defensive behavior evoked by threshold stimulation of the lateral hypothalamus and central gray matter of the mesencephalon (25 points) included alerting, investigation of the chamber, and occasional mewing and growling. The response usually ended with running out of the chamber (if the door was left open) or with attempts to open the door. With an increase in the strength of brain stimulation the animals exhibited restlessness, mewed, and tried to leave the chamber.

Low-frequency stimulation of the head of the caudate nucleus (47 points) evoked a response of restraint. This was manifested as cessation of spontaenous movement and, occasionally, with rotation of the head. During this period the orienting reactions to stimuli of any modality disappeared. Against this back-

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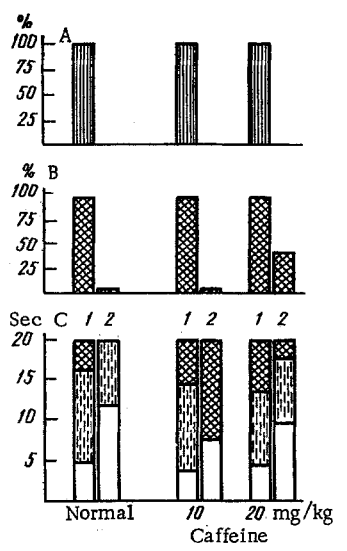

Fig. 1

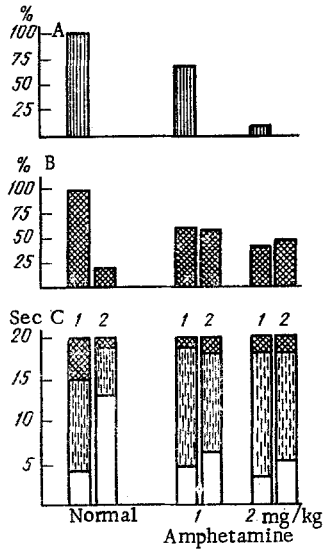

Fig. 2

Fig. 1. Effect of caffeine on inhibition of the avoidance reactions to stimulation of the caudate nucleus: A) caudate response of restraint; B) running from the chamber evoked by meso-diencephalic stimulation in control (1) and accompanying threshold stimulation of caudate nucleus (2); C) dynamics of defensive behavior in response to meso-diencephalic stimulation in control (1) and accompanying threshold stimulation of caudate nucleus (2). Ordinate: graphs A and B) probability of restraint response (A) and flight response (B) (in percent of initial level), graph C) duration of meso-diencephalic stimulation (in sec). Columns in graph C represent individual components of defensive behavior: unshaded – alerting, broken lines – investigation, cross-hatched – running from the chamber.

Fig. 2. Changes in caudate inhibition of behavioral responses to amphetamine. Legend as in Fig. 1.

ground the course of the avoidance reaction was interrupted. For instance, during combined stimulation (caudate nucleus + hypothalamus) the animals turned their body and head chaotically. Purposive actions were absent. Discontinuing the stimulation of the caudate nucleus alone led to renewed attempts by the animal to run out of the chamber. It is interesting to note that at the end of combined stimulation the animals quickly became quiet, although in the control series a distinct after-effect was observed.

Subthreshold (for the restraint response) stimulation of the caudate nucleus as a rule led to quietening of the movements. Meanwhile sensory stimuli regularly evoked an alerting response. The animals were well oriented with respect to their surroundings.

The avoidance reaction to meso-diencephalic stimulation also was inhibited during subthreshold stimulation of the caudate nucleus. However, the inhibition of the behavioral responses was of a different character from that during the restraint response. The details given in Figs. 1 and 2 show that the latent periods of investigative activity and of running from the chamber were increased. In 92% of the experiments, stronger hypothalamic or mesencephalic stimulation was required to evoke running away. Meanwhile, no influence of the neostriatum on alerting could be found. In a few experiments with combined stimulation the latent period of the emotional component of the meso-diencephalic response (mewing, growling, agitated movements) was changed. If, despite neostriatal stimulation, the behavioral response ended in running from the chamber, this took place as soon as the door was opened.

Caffeine (10-30 mg/kg) stimulated spontaneous motor activity by a weak degree. However, under the influence of caffeine, facilitation of the defensive responses was observed in half of the animals. In particular, in 65% of the experiments, with meso-diencephalic stimulation of lower intensity, the animals attempted to leave the chamber ($P < 0.05$).

Caffeine had no effect whatever on the result of threshold stimulation of the caudate nucleus (Fig. 1). In particular, no significant changes in the restraint response were observed. Just as in the control, neostriatal activation was accompanied by cessation of the behavioral responses.

Injection of large doses of caffeine (20-30 mg/kg) usually abolished the quietening of movements evoked by subthreshold stimulation of the neostriatum. At the same time its effect on the avoidance reaction was weakened (Fig. 1). In the experiments with combined stimulation (caudate nucleus + hypothalamus) the latent periods of investigative activity and of running from the chamber were greatly lengthened. In 30% of cases an increase in the threshold of caudate inhibition of the defensive responses was observed ($P > 0.05$).

Consequently, caffeine slightly weakened the effects of subthreshold neostriatal stimulation. There was a parallel increase in the avoidance reaction.

Small doses of amphetamine caused a very slight increase in motor activity. Large doses (2-3 mg/kg) led to the appearance of stereotyped behavior. Starting with doses of 1 mg/kg, amphetamine suppressed some components of the avoidance reactions to mesencephalic and hypothalamic stimulation. Components of emotional expression (mewing, growling, increased attention to the door, after-effect) were chiefly inhibited. In 60% of experiments with amphetamine the animal did not run from the chamber ($P < 0.05$). Meanwhile, investigative activity became more intensive and the threshold of alerting was lowered.

In agreement with observations by other workers [2], amphetamine, in a dose of 2-3 mg/kg, significantly ($P < 0.05$) increased the threshold of the restraint response to stimulation of the caudate nucleus (Fig. 2). The neostriatum ceased to influence the avoidance reaction.

The effect of subthreshold stimulation of the caudate nucleus was abolished by a lower dose of amphetamine (1 mg/kg). The quietening of movements did not develop during caudate stimulation. With combined stimulation the latent periods of investigation and flight evoked by hypothalamic stimulation were not increased (Fig. 2). On the whole, the parameters of the avoidance reactions corresponded to those in the control.

Whereas threshold stimulation of the caudate nucleus inhibited simple and complex forms of behavior and interfered with the perception of stimuli, its subthreshold stimulation selectively inhibited investigation and flight, i.e., the behavioral components connected with the direction of motivation and with orienting and investigative activity. Systems of the paleocortex and neocortex are responsible for their integration [4, 8].

Caffeine stimulates these components of behavior and, at the same time, weakens their inhibition slightly during subthreshold stimulation of the neostriatum. This latter effect may be due to direct excitation at the cortical unit level [5, 6]. In the present experiments, amphetamine abolished the inhibitory effects of stimulation of the caudate nucleus, in harmony with its direct effects on neostriatal activity [10]. It is interesting to note that amphetamine abolished the animals' attempts to run away from the chamber but facilitated their orienting and investigative activity. The disturbance of the functions of the inhibitory mechanisms of the brain by amphetamine and caffeine is evidently connected with stimulation of only certain aspects of behavior.

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