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CHANGES IN NEURONAL TRACE RESPONSES OF THE SENSOMOTOR CORTEX AND PUTAMEN INDUCED BY HALOPERIDOL

L. A. Zhavoronkova and E. V. Rusinova

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Mechanisms of action of haloperidol are mainly studied in behavioral experiments on animals during conditioning [3, 5] and also on models such as amphetamine stereotypy, rotatory responses to electrical stimulation of the caudate nucleus, etc. [7]. However, there is no information on the effect of haloperidol on the ability of neurons of different structures to form and preserve trace responses.

The aim of this investigation was to compare the action of haloperidol on formation and reproduction of conditioned trace responses by neurons of the putamen and sensomotor cortex. The reasons why these brain structures were chosen were, first, that the basal ganglia and, in particular, putamen are the point of application of the action of haloperidol [2], and second, that the putamen and neocortex have many direct connections [1, 6].

EXPERIMENTAL METHOD

Experiments were carried out on 25 waking, unimmobilized rabbits. Trace activity of 122 neurons in the putamen and 121 neurons in the sensomotor cortex was analyzed during formation and reproduction of a conditioned reflex to time. Motor conditioned reflexes to time were formed by combinations of an acoustic stimulus (conditioned stimulus – clicks: 10/sec) with electrodermal stimulation – EDS (unconditioned stimulus – square pulses: 40/sec, 4-6 V) applied at a constant 30-sec interval, and reproduction of these responses was tested with omissions of combinations at assigned intervals. Clicks were applied for 2 sec, whereas EDS was applied after isolated action of the acoustic stimuli for 1.5 sec, and it continued for 0.5 sec [4]. Unit activity was recorded during 10 combinations, a series of 15 omissions of stimuli, and a repeated series of combinations and omissions in intact animals and in animals receiving haloperidol. Haloperidol was injected intravenously in a dose of 0.2 mg/kg into animals to which about 40-50 combinations had been presented. The significance of differences in responses of the cells was determined by the Wilcoxon–Mann–Whitney U test.

EXPERIMENTAL RESULTS

Changes in trace activity of neurons in the putamen and sensomotor cortex under the influence of haloperidol were diametrically opposite in character. In the putamen the number of neurons exhibiting trace responses after injection of haloperidol increased by 21% whereas

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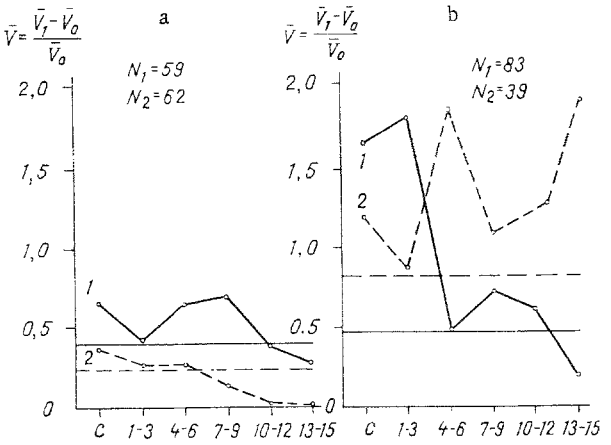

Fig. 1. Curves of reproduction of neuronal trace responses of sensomotor cortex (a) and putamen (b) before and after injection of haloperidol. 1) Neuronal responses before injection of haloperidol, 2) the same after injection of haloperidol. N) Number of neurons analyzed. Abscissa: C) response to combination, numbers denote trace responses averaged for three consecutive omissions; ordinate, relative magnitude of trace response, averaged for number N of neurons analyzed, where V_0 denotes mean spontaneous discharge frequency in 0.5 sec, V_1 mean frequency in 0.5 sec during omissions of combinations. Horizontal lines: continuous — level of significance for trace responses before, broken line — after injection of haloperidol.

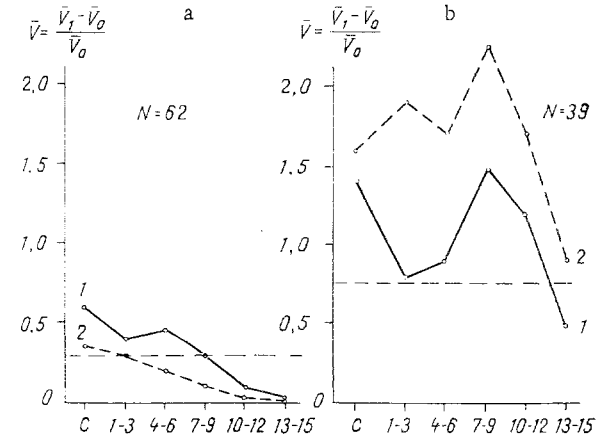

Fig. 2. Curves showing changes in conditioned and unconditioned components of neuronal trace responses of sensomotor cortex (a) and putamen (b) after injection of haloperidol. 1) Unconditioned component of neuronal responses, 2) conditioned component of neuronal responses. Remainder of legend as to Fig. 1.

in the sensomotor cortex it decreased by 15%. Analysis of the dynamics of neuronal trace activity in the two structures showed that haloperidol significantly changes the intensity and duration of trace responses. After injection of haloperidol significant trace plastic changes in unit activity were observed during 13-15 omissions, compared with 10-12 omissions before injection of haloperidol (Fig. 1b); in the sensomotor cortex these changes were observed during only 2-4 omissions, compared with 10-12 omissions before injection of haloperidol (Fig. 1a). Injection of haloperidol increased the intensity of neuronal trace responses in the putamen (Fig. 1b, 2) and the intensity of the response increased with the course of time. Incidentally the curve reflecting the trend of trace responses in the putamen after injection of haloperidol was a mirror image of the corresponding curve showing the trend of trace responses before injection of haloperidol. In the sensomotor cortex, however, the in-

tensity of trace responses was reduced after injection of the drug (Fig. 1a, 2) and the curve showing the trend of trace processes roughly repeated the trend of trace responses of the neurons before injection of haloperidol. Analysis of the character of changes in the conditioned and unconditioned components of trace responses of neurons of the two structures showed that injection of haloperidol causes changes in both components in the same direction both in the sensomotor cortex (Fig. 2a) and in the putamen (Fig. 2b), except the first three omissions. The conditioned component of trace responses of both structures exhibited greater sensitivity under these circumstances to the action of haloperidol than the unconditioned component.

Haloperidol thus weakens the ability of sensomotor cortical neurons to form trace responses considerably, and their ability to reproduce and preserve trace responses even more; this is probably due to increased intensity of these processes in the putamen. Evidence of this is given by the negative correlation obtained between changes in neuronal trace activity in the putamen and sensomotor cortex. Worsening of conditioned reflex formation, observed at the behavioral level, with preservation of motor responses and orienting reflexes [5] under the influence of haloperidol, may probably be a result of inhibition of the conditioned component of trace responses of sensomotor cortical neurons due to disturbance of dopaminergic transmission in the substantia nigra — neostriatum chain. It can be postulated that the dopaminergic system participates directly in interaction between neostriatum and sensomotor cortex and in the formation of trace activity of these structures.

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