

## ACTION OF NEUROLEPTICS (CHLORPROMAZINE, STELAZINE, AND HALOPERIDOL) ON SINGLE UNIT ACTIVITY

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Unit activity in the sensorimotor cortex and mesencephalic reticular formation of rabbits was studied against the background of administration of chlorpromazine, stelazine, and haloperidol. Chlorpromazine was found to reduce, and stelazine and haloperidol to increase the number of neurons responding to electrodermal stimulation. It is concluded that the role of the reticular formation during development of the response differs in character depending on which of the tested drugs is given.

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The mechanism of action of chlorpromazine has frequently been studied from the beginning of its clinical application. Experiments have shown that after administration of chlorpromazine unit activity is considerably reduced in the cortex and reticular formation [1, 3-6]. Many aspects of the mechanism of action of stelazine and haloperidol are still unexplained.

The object of this investigation was to compare changes in responses of neurons of the sensorimotor cortex and mesencephalic reticular formation to afferent stimulation after administration of chlorpromazine, stelazine, and haloperidol.

### EXPERIMENTAL METHOD

Neither general anesthesia nor curarization of the animals was used in the experiments. By means of a micromanipulator with two electrode holders (designed by A. M. Melekhova [2]) activity of two neurons in different parts of the brain could be recorded simultaneously. Glass microelectrodes with impedance of 5-15 MΩ were used. Electrodermal stimuli (pulses of 10-15 V, 1-5 msec) were applied to the animal's hind limb. The drugs were injected intramuscularly in the following doses: chlorpromazine 0.5 mg/kg, stelazine 0.1-0.2 mg/kg, haloperidol 0.02-0.01 mg/kg. Unit activity was analyzed at each stage of the investigation for a period of 1 sec in 10 chosen combinations. Altogether the activity of 673 cortical neurons and 584 neurons of the reticular formation was analyzed.

### EXPERIMENTAL RESULTS

Most cells of the sensorimotor cortex discharged at a frequency of 2-10/sec, mean  $8.7 \pm 0.4$ /sec. The frequency spectrum of the neurons of the reticular formation had wider limits (from 1 to 56/sec) and its mean frequency was  $16 \pm 3.7$ /sec.

In the character of their responses to electrodermal stimulation, the spontaneously discharging neurons were divided into 3 groups. The first group consisted of cells whose firing rate was unchanged or was altered by less than 10%. Group 2 included neurons whose firing rate was increased by stimulation by more than 10%. Group 3 consisted of neurons whose firing rate was reduced by more than 10% under the influence of stimulation. The same principle was used to divide into groups those neurons whose activity was recorded in the interval from 30 to 60 min after injection of one of the tested drugs. After injection of chlorpromazine the number of neurons in the cortex and, in particular, in the reticular formation responding to afferent stimulation was reduced, while after administration of stelazine and haloperidol, the number of responding neurons was increased (Fig. 1).

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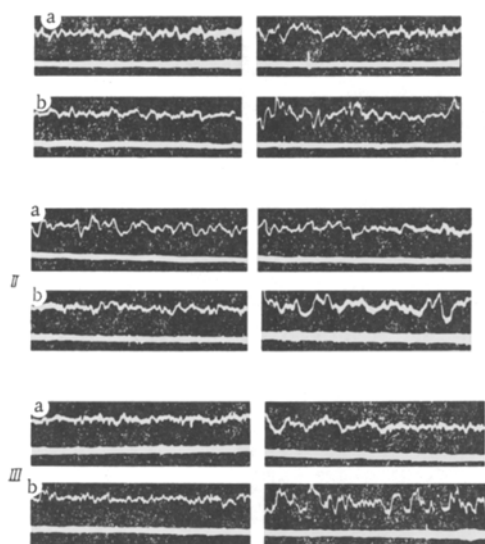


Fig. 1. Record of global electrical activity (upper curves) and single unit activity (lower curves) before (on the left) and 30 min after (on the right) injection of neuroleptics. I) Test with chlorpromazine; II) test with stelazine; III) test with haloperidol; a) sensorimotor cortex; b) mesencephalic reticular formation.

TABLE 1. Results of Investigation of Activity of Different Groups of Neurons after Administration of Neuroleptics (in %)

Group of neurons	Background		Chlorpromazine		Stelazine		Haloperidol	
	sensorimotor cortex	reticular formation	sensorimotor cortex	reticular formation	sensorimotor cortex	reticular formation	sensorimotor cortex	reticular formation
1	42.5	33.1	64.3	52.7	15.5	8.7	5.5	7.9
2	48.1	63.4	23.6	38.1	50.4	60.9	16.3	54.3
3	9.4	3.5	12.1	9.2	34.1	30.4	78.2	38.8

The results obtained in these experiments (Table 1) show that, unlike chlorpromazine, stelazine and haloperidol have no inhibitory action on the principal component of the ascending activating system. This may explain the stimulant effect of these drugs during treatment of patients. On the other hand, their neuroplegic action is evidently connected with their predominantly inhibitory effects on other brain structures.

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