EFFECT OF LSD ON SINGLE UNIT ACTIVITY IN CERTAIN PARTS OF THE BRAIN

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The background firing rate of neurons on the mesencephalic reticular formation is about three times higher than that of hippocampal neurons. Under the influence of LSD, the background firing rate in these parts of the brain is modified, showing that the mesencephalic reticular formation and hippocampus possess unit responses in these parts of the brain to LSD can be expressed by activation and by inhibition of spike activity. The character of the response of these neurons to LSD is independent of their background activity.

Elucidation of the mechanism of action of LSD is interesting because of the psychotomimetic properties of this compound. Investigations have shown that the central point of action of LSD in the brain stem [4, 7].

Work in the author's laboratory has shown that the mesencephalic reticular formation (MRF) and hippocampus are specifically sensitive to LSD. In these parts of the brain, the effect of LSD on functions of both serotoninergic and adrenergic elements has been demonstrated [1]. These observations have also been confirmed by the histochemical investigations of Khristolyubova [2], who established the definite action of LSD on metabolism of the biogenic amines of the brain. She observed that LSD acts selectively on particular cell groups in the MRF region.

To continue the study of the mechanism of action of LSD, it was decided to investigate the effect of this compound on functions of single units in brain regions specifically sensitive to LSD; the MRF and hippocampus.

EXPERIMENTAL METHOD AND RESULTS

Experiments were carried out on male albino rats weighing 200-300 g anesthetized with urethane (1-1.3 g/kg body weight). Unit activity was recorded on a dual-beam CRO (Disa Electronic) with motion-picture camera. Discharges from units of the MRF and dorsal hippocampus was recorded extracellularly by means of glass microelectrodes with a tip 1-2 μ in diameter, filled with 3 M NaCl solution. The coordinates of the brain structures were determined from the stereotaxic atlas of Fifkova and Marsala [3]. Activity of 25 MRF units and 20 hippocampal units was recorded.

The records of background unit activity of rats anesthetized with urethane showed that dorsal hippocampal neurons discharge at the rate of 2-10/sec; neurons of the MRF discharge at a considerably higher rate, from 5-30/sec.

Subcutaneous injection of LSD (0.5 mg/kg body weight) caused changes in the background activity of the neurons after 4-7 min.

The results given in Table 1 show that most neurons of the hippocampus and MRF respond to LSD. This response may take the form of a decrease or increase in the frequency of the initial unit activity,

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TABLE 1. Responses of Hippocampal and MRF Neurons to LSD

Part of brain	Number of neurons	Response to LSD		
		neurons with slowing of activity	neurons with quickening of activity	neurons with no change in firing rate
Hippocampus	20	13	4	3
Mesencephalic reticular formation	25	12	9	4

TABLE 2. Relationship between Character of Unit Responses to LSD and Their Background Firing Rate

Part of brain	Number of neurons	Initial firing rate of neurons (spikes/sec)	Response to LSD		
			neurons with slowing of activity	neurons with quickening of activity	neurons with no change in firing rate
Hippocampus	11	2-4	6	2	3
	5	5-6	4	1	0
	4	7-10	3	1	0
Mesencephalic reticular formation	11	5-10	4	5	2
	8	11-20	4	2	2
	6	21-30	4	2	0

and under these circumstances LSD may change the background firing rate by as much as 2-3 times. It must also be pointed out that the hippocampal neurons respond much more often by inhibition than by excitation; in most cases their inhibitory response took the form of the complete cessation of activity (in 10 of 13 neurons). The MRF neuron responded both by activation and by inhibition of activity in about equal numbers of cases, but total inhibition of spontaneous activity was observed less frequently than in the hippocampal neurons (in 5 of 12 neurons).

An attempt was also made to discover whether the character of the unit response to LSD depends on the frequency of their initial activity (Table 2).

As the results given in Table 2 show, no definite relationship was established between the original firing rate of the neurons and the character of their response to LSD. Whatever the background firing rate, hippocampal neurons in most cases responded by inhibition. MRF neurons, with a low initial firing rate (5-10/sec) responded about equally often by inhibition and by activation, while those with a moderately high (11-12/sec) or high (21-30/sec) firing rate responded somewhat more frequently by inhibition.

The effects of LSD on unit activity in the MRF and dorsal hippocampus obtained in these experiments thus agreed with those of other investigators [1, 5, 6] who observed specific sensitivity to LSD in these brain structures. However, the results of the present experiments differ significantly from those of Sailer et al. [6], who found that LSD inhibits hippocampal neurons, and with those of Foote et al. [5], who found that LSD activates MRF neurons. The present investigation showed that responses of the hippocampal and MRF neurons to LSD are not simply of one type, but may take the form of both activation and inhibition of spike activity. The initial background activity of the neurons is evidently not a decisive factor. It can be postulated that the reasons for the differences in the character of the responses of units in the same brain structure to LSD may be either that these neurons belong to different functional systems, in which the neurons tested could be exposed to reflex influences, or that they differ in their neurochemical nature.

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