

Effect of d-Lysergic Acid Diethylamide on Spinal Reflexes. (24287)

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The alterations in mental function induced by d-lysergic acid diethylamide (LSD) are, presumably, paralleled by modifications of the activity of cells or synapses within central nervous system, whether cortical, subcortical or spinal. LSD, when administered to spinal cats, in doses as small as 10 $\mu\text{g}/\text{kg}$ i.v. was found to augment polysynaptic withdrawal and crossed extensor reflexes(1). At higher doses (40-80 $\mu\text{g}/\text{kg}$) depression of the flexion

reflex was found. The monosynaptic knee jerk was less consistently affected. After administration of LSD in doses sufficient to cause mental symptoms increased activity of stretch reflexes has, however, been a consistent clinical observation(2). In the following experiments, the effects of LSD were evaluated by measurement of changes in magnitude of the reflex volley in ventral roots rather than by recording of muscular contraction.

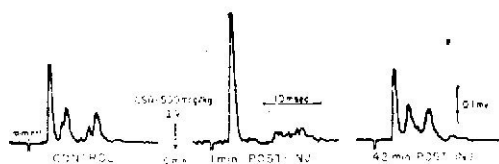


FIG. 1. Oscilloscopic tracing of response in 6th lumbar ventral root in response to stimulation of peroneal nerve.

Methods. The upper cervical spinal cords of adult cats were sectioned through the atlanto-occipital membrane under ether anesthesia. Peripheral nerves and ventral roots were prepared for stimulation and recording utilizing standard technics(3,4). In these experiments a gastrocnemius, tibial or peroneal nerve was stimulated with single square wave stimuli 0.08-3.0 volts intensity and 0.1-0.4 msec. duration. The stimuli were repeated at 2 or 3 second intervals. Temperatures of the animal and the pool of oil surrounding the cord were maintained at 36° and 34°C, respectively. Only those preparations whose baseline responses over a 30 minute control period varied less than 10% are considered in this report (20 out of 37). The criterion of significant change in amplitude of the monosynaptic spike was 20% and the change in area of the polysynaptic complexes, estimated visually, was 50%. Blood pressure was recorded from a common carotid artery with a strain gauge recorder. Thirty-six injections of LSD-25 (Sandoz) dissolved in sterile physiological saline, were administered through a cephalic vein in 20 preparations. Dosage ranged from 4-1000 $\mu\text{g/kg}$. The usual injection time was 10 seconds. Rate of injection did not influence the results.

Results. The characteristic modification of reflex activity observed in this study is shown in the figure. Increased height of the monosynaptic response was observed after 11 of 16 injections of doses greater than 200 $\mu\text{g/kg}$. Below this dose only 1 of 20 injections resulted in facilitation. Four instances of failure to respond to doses of LSD greater than 200 $\mu\text{g/kg}$ occurred in cats which had received another dose of LSD less than 2 hours previously. Only one such failure was observed among cats receiving more than 200 $\mu\text{g/kg}$ as the first dose. Increased amplitude of the

monosynaptic spike became apparent within 15 seconds after completion of injection and lasted from 4 minutes to 3 hours. Maximum facilitation was observed with 250-300 $\mu\text{g/kg}$. Higher doses tended only to prolong this effect, but no consistent relation of duration of effect to dose level was observed. For these reasons quantitative analysis of the dose-response relations were not possible. Polysynaptic activity was observed in several preparations where nerves to flexor muscles were stimulated. With one exception, depression of polysynaptic activity accompanied facilitation of the monosynaptic reflex. After injection of doses higher than 100 $\mu\text{g/kg}$ a significant increase in blood pressure was found but facilitation of the monosynaptic spike did not necessarily parallel the hypertensive effects.

Discussion. The foregoing experiments and those previously published on evaluation of LSD action on spinal monosynaptic and polysynaptic pathways(1) are not directly comparable. In the previous studies, muscle reflexes were recorded. In addition to an effect on the central pathway, reflex activity may have been modified by the action of LSD on peripheral structures. Of significance in this respect is the direct peripheral vasoconstriction which LSD induces similarly to its analogue, ergonovine(5). Resulting interference with muscle perfusion may influence contractility and modify the activity of proprioceptive reflexes.

The observation that larger doses were required to produce effects in this series than those reported in previous studies(1) is consistent with the observation of Elder *et al.* (6) that reproducible LSD intoxication in cats is obtained only with intravenous injection of 400 $\mu\text{g/kg}$ or greater.

The magnitudes of the reflexes reported here are dependent primarily upon the integrity and the excitability of motoneurons and, in turn, upon the facilitatory and inhibitory tone of the internuncial systems. Since LSD may act upon any of these components, more precise localization of site of action of LSD is required before interpretation of a central mechanism of action is feasible. At present

significant comparisons can be made, however, with the action of LSD upon other central pathways. Purpura(7) has postulated that those cortical tracts which have predominantly axosomatic synaptic connections are facilitated by LSD. Since the connections of muscle afferents with spinal motoneurons are principally axosomatic(8) facilitation of the monosynaptic spike is to be expected.

Also pertinent is the concept that certain cortical association tracts(9), midbrain reticular pathways(10) and spinal reflexes(11) contain adrenergic links. The present study shows that LSD modifies spinal reflexes in a manner analogous to that of epinephrine(12). Similar evidence has been presented in experiments on the transected preparation(9). LSD may, therefore, interact with proposed adrenaline-like transmitters.

Summary. The amplitude of the monosynaptic reflexes recorded from the ventral roots of unanesthetized spinal cats was found to be increased after i.v. injection of LSD in doses greater than 200 $\mu\text{g}/\text{kg}$. Polysynaptic activity was depressed coincidentally with facilitation of the monosynaptic spike.

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