

Complete text

VI LSD No.181 (\$102a)

M 3 cortex

mescaline (\$102b)

adrenaline (\$68d)

serotonin (\$90a)

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Evoled cortical responses under the influence of hallucinogens and related drugs.

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Mescaline is characterized clinically by the production of marked visual hallucinations in man and disturbances in conduct in the cat. It is of interest, therefore, that adrenaline, which is closely related chemically, had been shown by the authors to produce cortical synaptic inhibition in the cat and that this effect could be demonstrated in the optic pathways. Evoking responses in the optic cortex through the transcallosal pathway by stimulation of the symmetrical point in the contralateral cortex serves as a convenient index of synaptic activity and, because of volume conductor properties, the electrical activity recorded at the cortex reflects the inflow and corresponding synaptic response. The differential changes in these are interpreted as signs of synaptic actions, which were most readily elicited by the

introduction of the drugs in the common carotid artery ipsilateral to the recording electrodes. In keeping with the structural similarity noted, mescaline produces the same type of change or synaptic inhibition and this may underlie the visual hallucinations it produces. Lysergic acid diethylamide (LSD 25), which is an even more potent hallucinatory agent, was also found to have the same effect in minute doses. A chemical link between LSD 25 and adrenaline, amphetamine and mescaline, all of which can produce mental disturbances with varying effectiveness, is afforded by adrenochrome which is derived from adrenaline. Like LSD 25 it is an indole, though chemically much less complex, and like LSD 25 it has been claimed to have reproduced a schizophrenic syndrome in man. Difficulties in obtaining pure material have prevented us from adequately testing adrenochrome, but tests with serotonin, another relatively simple indole derivative naturally present in the brain, show that it also produces synaptic inhibition in the visual cortex on intracarotid injection, and in fact does so in doses of 1 to 2 gamma. This shows that serotonin can successfully traverse the blood-brain barrier but does not support the notion that serotonin could offset LSD 25 induced psychoses or that serotonin deficiency could be the cause of schizophrenia. On the other hand, the high potency raises the question of the possible relation of this substance, occurring naturally in the brain, to neurochemical synaptic inhibitory mechanisms. The data suggest that a disturbance of adrenergic or related cerebral neurohumoral mechanisms is implicated in the actions of the hallucinogens studied. The resulting imbalance in the reciprocal relation between adrenergic inhibition and cholinergic excitation in the most susceptible cerebral synapses might be an underlying mechanism in mental disturbance.