may be mediated by synthesis of some RNA species. We performed a few experiments with smooth muscles dissected from stomach and blood vessels of 8- to 10-day chick embryos. In the presence of the active salivary-gland fraction the myoblasts lost their characteristic spindle shape and became round; sharp decrease in their eosinophilia was most likely caused by loss of myosin—as with the striated muscles.

The effect of the salivary-gland fraction on cartilage tissue was studied by culturing vertebrae of 10-day chick embryos for 48 to 72 hours, after which time cartilage fragments in control cultures remained well preserved. Similar fragments in the experimental culture showed sharp decrease in susceptibility to metachromatic staining of the intercellular matrix and changes in the morphology of the cells, which progressively reverted to more undifferentiated types.

Our observations on muscle and cartilaginous tissues indicate a process of dedifferentiation of these tissues as an effect of the salivary-gland fraction. It was therefore of interest to study possible effects of the same fraction on precursors of the same tissues. Rows of somites from chick embryos at stages 14 to 17 (*4*) were dissected together with fragments of neural tube, or without nerve tissue if explanted from older embryos at stages 27 to 28. The explants consisting of 5 or 6 somites were cultured in plasma clot or in Puck liquid media with 15 percent calf serum for 5 to 6 days; control and experimental cultures were then fixed, stained, and examined. Nodules of cartilage and striated muscle fibers were numerous in control cultures, among mesenchymal cells—which constituted the bulk of the explants. Experimental cultures consisted of a homogeneous cell population, with no differentiative marks evident in the many explants examined. It is significant that neither the stimulatory effect on mesenchymal tissue nor the dedifferentiative effect on mesodermal derivatives was obtained with extracts of organs such as thymus, liver, kidney, and pancreas.

The question now is how this salivary-gland fraction produces the marked morphological changes described. These effects may be due to the proteolytic activity that appears to be consistently associated with the active fraction throughout all purification steps. If so, the biologic effects may result from liberation of active peptides from a larger protein molecule, as well as from direct action of the enzyme on the cell surface.

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Mescaline, 3,4-Dimethoxyphenylethylamine, and Adrenaline: Sites of Electroencephalographic Arousal

Abstract. *Transections of the brain of rabbit reveal that electroencephalographic arousal produced by injections of adrenaline takes place at the midbrain level, while mescaline and 3,4-dimethoxyphenylethylamine induce such arousal lower in the brainstem, at the medullary level.*

It has been shown (*1, 2*) that psychotomimetic indole amines such as psilocin, bufotenin, and lysergic acid diethylamide have a site of electroencephalographic (EEG) arousal below the midbrain and above the first cervical segment of the spinal cord, while their nonpsychotomimetic congeners evoke EEG alerting at the midbrain level. Moreover the chemical constituents of the psychotomimetic congeners have an *N*-dimethyl or *N*-diethyl configuration, while their nonpsychotomimetic congeners lack such configurations.

Other workers (*3*) have found 3,4-dimethoxyphenylethylamine (DMPEA) in the urine of schizophrenic patients. Friedhoff and Van Winkle (*4*) have implicated this amine as an endogenous psychotomimetic substance because homogenates of liver obtained by biopsy from schizophrenic patients were capable of *O*-methylating both *O*-hydroxy groups of dopamine, whereas liver samples obtained from normal subjects induced no such reaction. DMPEA exhibited a catatonic effect similar to that produced by mescaline in cats (*5*); it is closely allied in chemical structure to mescaline, both being *O*-methylated catecholamines.

Eighty-six adult New Zealand albino rabbits weighing 2.5 to 3.0 kg were tracheotomized under ether and local anesthesia, curarized, and artificially respired. For monopolar recordings of an electroencephalogram, coaxial electrodes were placed superficially on motor and on limbic cortical areas, and also deeply in the head of the caudate nucleus, hippocampus, amygdala, and reticular formation, according to the map of Sawyer *et al.* (*6*). Blood pressure was monitored by means of a mercury manometer connected to a femoral artery. Intravenous and intracarotid injections of drugs were made through a polyethylene cannula inserted in a femoral vein and a T-shaped cannula connected to a common carotid artery. Transections of brain were performed (i) at the precollicular, prepontine plane, just above the midbrain; (ii) at the postcollicular, postpontine plane, just below the midbrain; and (iii) through the first segment of the cervical spinal cord (*1*).

In nine intact animals, 20 to 30 seconds after intracarotid injection of 50 to 150 mg of DMPEA, the EEG resting pattern changed from high voltage and slow waves to one consisting of decreased voltage and fast waves in the motor and limbic cortical areas, caudate nucleus, amygdala, and reticular formation, and of waves of predominantly large amplitude, 4 to 6 cy/sec, in the hippocampus. Arousal was also induced by intravenous injection of mescaline (10 to 40 mg/kg) into six intact animals and by intracarotid injection of 2 to 10 μg of adrenaline in five intact animals. Duration of the arousal produced by these drugs depended on the doses. Larger doses of DMPEA and mescaline produced protracted arousal lasting for more than 30 minutes. Arousal obtained by adequate doses of DMPEA and mescaline persisted even after first

cervical transection in each of four rabbits, but alerting did not occur in any of four other animals after postcollicular, postpontine transection.

As shown in Fig. 1, *a* and *b*, DMPEA and mescaline also produced arousal in four animals previously transected at the first cervical level, while in the animals previously transected at postcollicular, postpontine level the EEG pattern did not change even after large doses of both drugs. In contrast, injections of adrenaline produced arousal in each of four postcollicular, postpontine transected animals (Fig. 1*c*), but failed to do so in three of four precollicular, prepontine transected animals.

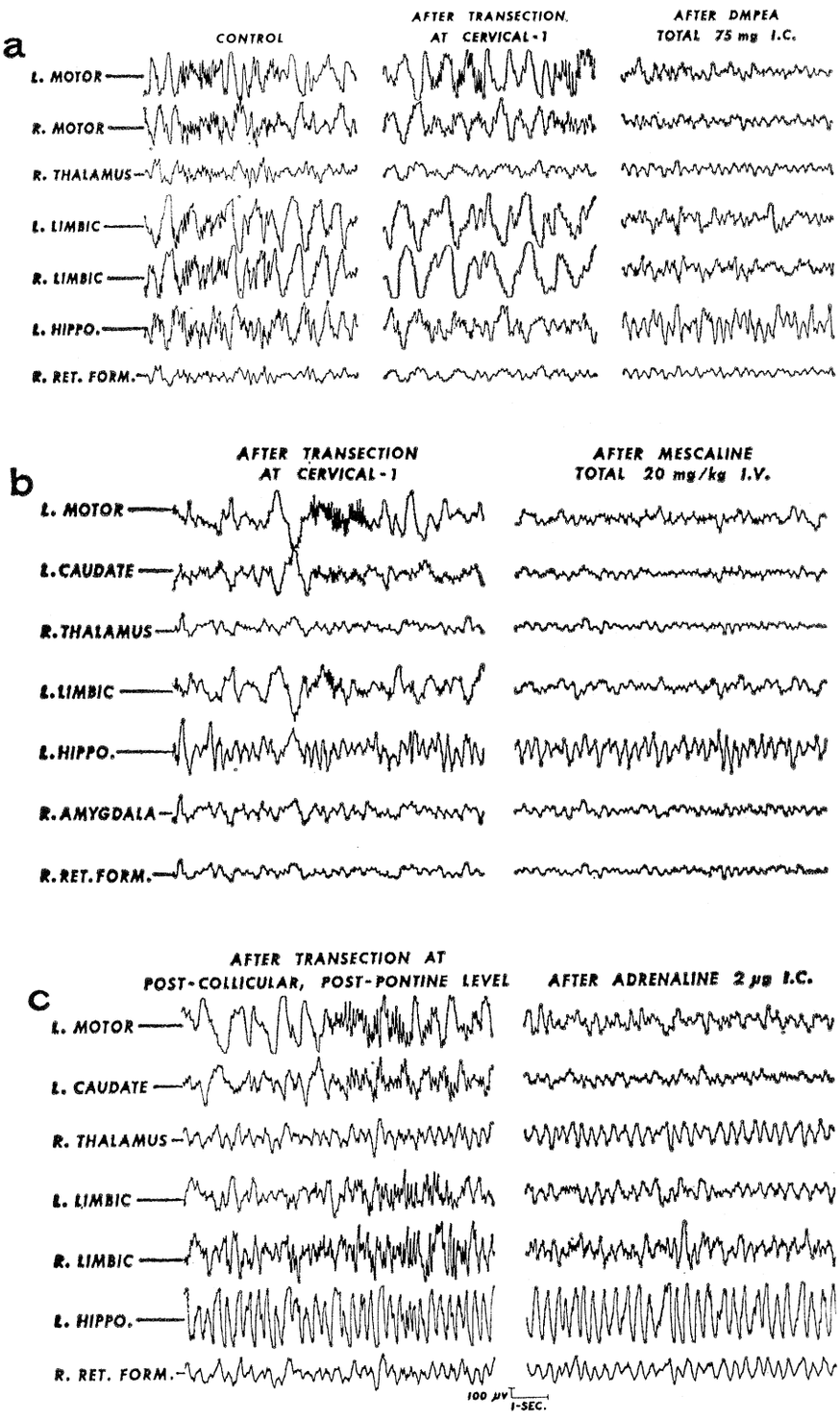

Fig. 1. EEG arousal induced by: 3,4-dimethoxyphenylethylamine (DMPEA) (*a*) and mescaline (*b*) in rabbit transected at first cervical level; adrenaline in rabbit transected at postcollicular, postpontine level (*c*).

Changes of cerebral blood flow due to increases in blood pressure induced by injections of adrenaline are associated with EEG activation (*7*). In our experiments, however, the EEG arousal patterns induced by adrenaline had a delayed onset that was not necessarily related to the pressor responses. Moreover, the EEG alerting reactions induced by DMPEA and mescaline persisted even after blood pressure returned to normal. Probably the DMPEA-induced EEG arousal did not involve peripheral receptors, because it still occurred in animals in which the vagal nerves were cut in the neck region and the nerves of the carotid sinus and carotid body were inactivated by 10 percent formalin. The requirement of a considerably larger dose of DMPEA than of mescaline to produce the EEG response may reflect either relatively poorer permeability of DMPEA through the blood-brain barrier or more rapid rate of inactivation by the enzyme monoamine oxidase.

Our results show that DMPEA and mescaline have a main site of EEG arousal caudad to the midbrain and cephalad to the first cervical segment, whereas adrenaline has a site of EEG activation at the midbrain level. The finding that the durations of DMPEA- and mescaline-induced EEG arousals were shorter in the first cervical-transected preparations than in intact animals suggests that both drugs also sensitize the input from the lemniscus as lysergic acid diethylamide does in the cat (*7*).

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