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Mescaline and LSD-25 in Activation of Temporal Lobe Epilepsy

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In a previous report,[1] the effects of mescaline and d-lysergic acid diethylamide (LSD-25) on 24 physician volunteers were summarized. As seen in tables 1 and 2, there is a striking resemblance between the action of the two drugs in their widespread psychic effects and to analogous phenomena which occur in the so-called functional psychoses. In general, the affective reactions and the distortion of ideational content seem to be patterned on a frame of reference colored by previous life experiences. For instance, one volunteer related much of his mescaline-induced experience in such a form as: "I have proprioceptive changes in my feet, legs, and perineum. I feel that my feet are wiggling . . . the only way to affect it is to move the muscles."

In another volunteer haptic hallucinations developed: "My face is being touched." This same volunteer experienced colored visual synesthesias of flaming crosses and waterfalls in his homolateral visual fields when figures were traced on his outstretched palm. He claimed that he was unable to perceive the touch sensation, but he envisaged it correctly. Other examples were numbness of the lower lip and auditory hallucinations of growling dogs. Another volunteer reported a feeling of contemplation and philosophic omniscience.

It was also noted that the reactions to LSD-25 were productive of uncontrollable laughing and giggling, whereas reactions to mescaline more frequently resembled the stuporous state. Two volunteers who took both mescaline and LSD-25 at different times had experiences essentially the same as those reported by Mátéfi.[2] They became withdrawn and rather catatonic after receiving mescaline, whereas they were inappropriately silly and affected by giggles when LSD-25 was used. Their drawings and autographs showed the same effects as did Mátéfi's. In no instance was there any clouding of consciousness when these drugs were used, although a subjective sense of timelessness existed for all. As an example of an intact intellect, one polylingual volunteer translated a paper on electroencephalography from Italian to French to English.

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TABLE 1

PSYCHIC DISTURBANCES IN 11 NORMAL VOLUNTEERS AFTER THE ADMINISTRATION OF MESCALINE

Disturbance	*Volunteer*										
	1	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*
Affect											
Anxiety (fear, apprehension)			+	+		++				+	++
Depression (somatization, facies, etc.)			+			++					+
Manic symptoms (expansive, euphoria)		++		++	+						
Withdrawal (indifference)	++				+		+	+	++	++	+++
Suspicion (facies, ideas of influence, heightened significance of objects)				+	++			++			
Sensory											
Vision (hallucinations, macropsia, micropsia, polyopia, illusions, after-images)	++	+++		+	+	++	+	+	++	++	+
Hearing (hallucinations hyperacusis)					++			++			
Body image (depersonalization, floating, unreality)	++	++	+	++	+	++	+	+++	+	++	++
Synesthesias (visual hearing, somesthetic vibrations)	+++	+++		+++	+++		+++	++	+	++	+
Motor											
Catatonia (stupor)		+		+			+	+		+	++
Thought											
Blocking (deprivation)						+	+	+	+	++	+
Loosening of associations	+	+		++	+						
Neologisms							+				
Pressure		+	+	++							

\+ = present ++ = marked +++ = very marked

In many instances the maximal effects of mescaline and LSD-25 occur after some acute stress such as exercise. One volunteer was convinced that, aside from nausea, the mescaline had no effect. However, four hours after the ingestion of 400 mg. of mescaline he took a brisk walk that precipitated his "floating back" to the laboratory, where pronounced visual hallucinations and depersonalization phenomena ensued.

The earliest visual experiences associated with the use of both drugs were similar to the visions obtained by photic stimulation alone; for instance, inanimate objects such as multicolored geometric forms were gradually recognized as Aztec art, tapestries, medieval stained-glass windows, and kaleidoscopes. Later, interpretations became more personalized, in the form of Tibetan mountain shrines, castles along the Rhine, and Nijinsky's war mask. One volunteer, who was both blue-yellow and red-green color blind, was convinced that LSD-25 had greatly relieved this defect until he was given the pseudoisochromatic plates for the testing of color perception. Other less

TABLE 2
PSYCHIC DISTURBANCES IN 13 NORMAL VOLUNTEERS AFTER THE ADMINISTRATION OF LSD-25

Disturbance	Volunteer												
	1	2	3	4	5	6	7	8	9	10	11	12	13
Affect													
Anxiety		+	+		+	++		+	++				+
Depression													
Manic symptoms (laughing, giggling)	+	++	++	++	+++	+++	+++	++	++		++	+	
Withdrawal									+	+	+		+
Suspicion				++					+				
Sensory													
Vision	+	+	+	+	++	++	+	++	+	+		+	++
Hearing										++	+		
Body image	+	+	++	+	++		++	+	++		++	+	+++
Synesthesias					++								
Motor													
Catatonia (stupor)	+	++		+			+			+		+	+
Thought													
Blocking	+	+	+						+				
Loosening of associations				+	+	++	+++	+	++			+	++
Neologisms					+								
Pressure					+								

\+ = present ++ = marked +++ = very marked

frequent visual phenomena included distortions in size, shape, and movement, such as the illusion of writhing snakes on a brick wall, micropsia, macropsia, and polyopia.

Associated with these perceptual distortions were the changes in affect. One volunteer said: "I feel indifferent; I don't care; I sit here, yet the feeling doesn't concern me; it's nirvana. I don't care to talk; but wish to be left in peace."

In one volunteer, who was outgoing and garrulous before he received mescaline, suspicious facies developed and he went into a trancelike state. He sat aware of his surroundings, yet gave no sign of recognition of his wife when she entered the room.

Another volunteer expressed his situation as, "I feel that everyone in the room is taking notes. Each glance is meant for me. They're evaluating my situation. I'm a goldfish in a bowl. All noises are intensified. I have a feeling of being different, and that my behavior might not be socially acceptable."

Another volunteer, in whom a mildly agitated depression developed, said: "I feel miserable, restless and jumpy, cold, and out of touch. It's a state of being just about to pass out, yet you stay that way."

Many of these reactions came in waves when the symptoms increased greatly, and they were commonly associated with increased nausea or vomiting or both, in addition to other autonomic changes. Rinkel[3] reported an effect of recurrent phases of dreamy confusion, with *déjà vu* and distorted bodily sensations, produced by LSD-25. Whereas mescaline seemed to cause detached reactions of suspension in the present, LSD-25 seemed to be more productive of fantasies and reveries connected with previous meaningful life experiences. Al-

though all volunteers were capable of conjuring erotic visions, all felt the action of both drugs as physically anaphrodisiac. One volunteer said he was unable to obtain an erection while under the influence of mescaline. With the exception of one volunteer, no one had any typical vestibular dreams. The one dream produced by mescaline consisted of colored three-dimensional railroad tracks winding in and out, and a microcephalic dog with pink eyes.

Hughlings Jackson's[4] classic description of the paroxysmal dream state, with the associated psychic symptoms of hallucinations, perceptual illusions, affect disturbances, forced thinking, and automatisms occurring in the presence of a relatively clear sensorium, is reminiscent of the manifold effects of LSD-25 and mescaline. Many of Jackson's classic comments, and more recently the descriptions provided by Penfield and Kristiansen[5] and Mulder,[6] are suggestive of some common substrates for both temporal lobe epilepsy and the effects of mescaline and LSD-25. For instance, Mulder mentioned the complex visual and auditory hallucinations, the strange feeling states in which the patient complains of being different or transferred back to some early memory, and the illusions of distortion of size or shape of objects. The various affect states such as terror, dread, and euphoria that are paroxysmal in temporal lobe epileptic persons all occur when mescaline and LSD-25 are employed

Because of the gross analogy between the phenomena seen in temporal lobe epilepsy and the phenomena seen in the mescaline and LSD-25 psychoses, such as unusual memory states, various degrees of depersonalization, illusions, and the like, it seemed valid to inquire into the locus of action of these by an attempt to trigger seizures by means of drugs. This could be done by the use of certain drugs which express their effects by way of these channels in much the same way that an exploring electrode can trigger off a temporal lobe focus, producing a stereotyped, repetitive picture. Although the electroencephalographic changes occurring after the administration of mescaline and LSD-25 are minimal and difficult to interpret,[1,7,8] concomitant electroencephalographic tracings were made from three patients who had temporal lobe epilepsy. An eight-channel, Grass electroencephalograph was used, and 15 electrodes were applied in a standard manner.

REPORT OF CASES

Case 1.—A 44 year old farmer was first seen at the Mayo Clinic on August 20, 1954, with a two week history of three to ten seizures a day. He had an aura of a faraway feeling, followed by a "peculiar taste, not unpleasant, and then a smell of natural gas." On a few occasions he had a vivid hallucination of a "Japanese wrestler on television." During the seizure the patient was conscious and able to respond to questions and commands. After one minute the patient swallowed several times and took a deep breath, and the attack apparently was terminated. Occasionally he noted the sensation that his lower lip and chin were twice as large as normal, "like going to the dentist."

Results of complete physical and neurologic examinations, including the ocular fundi and visual fields, were negative. A roentgenogram of the skull revealed an intracerebral calcification in the right temporal region. The routine electroencephalogram was reported as disclosing nothing abnormal.

Activation with pentylenetetrazol (Metrazol) was carried out and, after a total dose of 250 mg. had been administered, a typical automatism developed, as previously described. It lasted one minute. Associated with this seizure was an initial, generalized discharge of four to three cycles per second that finally tended to lateralize to the right, particularly in the

sylvian area. These findings, together with the absence of aphasia, were interpreted as indicative of a lesion of the right temporal lobe. Accordingly, anticonvulsant medication was prescribed and the patient was advised to return in three months.

On December 1, 1954, the electroencephalogram showed a minimal, right sylvian frontal delta. The patient had an automatism with a "faraway" aura on hyperventilation. In an attempt to activate the hallucinatory phenomena accompanying his seizure, he was given 500 mg. of mescaline by mouth and was observed over a period of six hours. A mescaline reaction of stupor and inaccessibility developed. He had mescaline-induced visions of multicolored geometric forms and kaleidoscopic effects, but at no time did anything arise reminiscent of his aura, either directly or in the nature of a screen memory. The electroencephalogram showed only minimal and rather nonspecific changes associated with mescaline. However, the photic drive response was increased in amplitude by 50 per cent. Examination of the cerebrospinal fluid gave negative results. Ventriculography revealed shift of the lateral horns and third ventricle to the left. The patient underwent craniotomy. A brain tumor (oligodendroglioma, grade 3) was found deep in the right temporal lobe.

Case 2. A 21 year old woman came to the clinic on January 10, 1955. Birth had been precipitous and unattended, and an injury to the head had occurred at the age of three. The injury was followed by grand mal seizures, which disappeared when anticonvulsant medication was administered. At the age of eight years the patient had episodes of "blanking out," lasting approximately 30 seconds and occurring three to 30 times a day. She believed the spells were more likely to occur when she was fatigued or immediately before the menses. She said that as long as she could remember, the episodes had been ushered in with an aura of a vision. The visions have consisted of "knights in battle and beautiful gardens." Although the patient said she dreamed considerably, she maintained that the visions were very real and were different from her dreams.

Results of neurologic examination and funduscopic examination of the optic disks were normal. The electroencephalogram was interpreted as showing moderate dysrhythmia, bisylvian in location, and a focal sharp discharge in the left sylvian region. Because of the uncertainty in the differential diagnosis between temporal lobe epilepsy and petit mal seizure, activation with Metrazol was carried out. Typical attacks of petit mal with associated three per second, spike-and-wave discharges developed after the injection of a total of 350 mg. of Metrazol.

After one of the episodes the patient claimed she saw the vision of a "flower garden with the text, 'In God We Trust,' in which a fashion show was going on." It was also noted that the attacks could be triggered by flash stimulation at 15 per second.

The next day the patient received 50 gammas of LSD-25 by mouth. A reaction developed in which much inappropriate laughing and giggling were manifested and many visions were reported. In no instance was an episode of seizure induced, nor was there any electroencephalographic evidence of activation. The patient looked in a mirror and said, "My face looks too long and oval; too round; my mouth is over to the left." She said she saw "space ships, restaurants, crane hoists, waterfalls, and buildings." Much of the material was related to items in a magazine she had been looking at prior to taking LSD-25. However, she had no insight as to the significance of her associations and visions in relation to the previous experience. Throughout the period the patient looked perplexed and preoccupied. She asserted, "I'm in a dream, yet I'm not really here." Although she was a good subject for hypnosis, as determined in other studies, it was impossible hypnotically to influence any of the hallucinations produced by LSD-25.

Case 3. A 39 year old housewife came to the clinic on August 10, 1954, with a six month history of dream states with weak feelings that had occurred as frequently as once a day, just prior to her admission. The patient asserted that the attacks would last no more than a few seconds. About her dream she said, "It doesn't mean anything; it's not more than four to five sentences long. It's the very same dream over and over. It's simple. It's silly."

On one occasion the patient had a grand mal seizure, during which she bit her tongue. Results of the neurologic and funduscopic examinations were reported as normal. The electroencephalogram was interpreted as showing moderate dysrhythmia, generalized but maximal in the bitemporal areas, and suggestive of a disturbance of function of the temporal lobes.

LSD-25 in a dose of 50 gammas was given. It produced a reaction of uncontrollable crying and laughing. The patient became more pointed and direct in her speech. At times she would lapse into a trance, with fatuous facies, and giggled inappropriately to herself. However, nothing connected with the seizures was detected either clinically or electroencephalographically. Subsequently, a pneumoencephalogram and bilateral angiograms were made and were reported as essentially normal. Anticonvulsant medication was prescribed after the diagnosis of temporal lobe epilepsy had been made, and the patient was dismissed.

COMMENT

Judged on the basis of these three cases of temporal lobe epilepsy in which there were good histories of psychic aura, it would appear that mescaline and LSD-25, both powerful hallucinogenic agents, were ineffective as clinical activating agents. Hoch[9] has found mescaline capable of activating a manifest psychosis in a pseudoneurotic schizophrenic patient or in a patient with psychosis which had been relieved by prefrontal lobotomy. It would seem that the action of these drugs in producing the experimental psychosis might be a diffuse one, rather than one of selectively activating any single region, such as occurs in temporal lobe epilepsy. Although most of the thoughts of the model psychosis could be explained on experiential factors, it was surprising that virtually nothing was obtained that could be remotely linked with the auras. If the contents of the aura were conditioned by psychic factors, it would seem logical to be able to activate them or at least to produce some related associations with these drugs. Although mescaline and LSD-25 readily released other memories, visions, and the like, they could not precipitate the aura physiologically encapsulated in a damaged area and inaccessible to these drug stimuli. Although three cases are too few on which to base any conclusions, it would seem that the unraveling of the aura is more complex than has hitherto been believed. However, LSD-25 and mescaline might be useful in distinguishing a psychosis from a temporal epileptic syndrome. The psychosis presumably could be "activated," whereas the epilepsy would be refractive to these drugs.

SUMMARY

Mescaline and LSD-25, administered to three patients who had temporal lobe epilepsy, did not provoke psychic auras or any causally related material. The electroencephalographic changes were minimal and were associated with the action of mescaline and LSD-25, rather than as an activation of a focus.

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