

MEDICAL INTELLIGENCE

EXPERIMENTAL PSYCHIATRY. V — PSILOCYBINE, A NEW PSYCHOTOGENIC DRUG*

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PSILOCYBINE (Fig. 1), the phosphoric ester of 4-hydroxytryptamine, has been established by Hofmann et al.¹⁻⁴ as the active principle of the Mexican mushroom family *Psilocybe mexicana* Heim. The chemists emphasize the fact that this chemical is the only phosphorylated indole compound that is known to occur in nature and that it is remarkable in that it is an indole substituted at the fourth position.

The *pharmacology* of psilocybine⁵ in animal experiments has been summarized by Cerletti as follows:

2. In the intact animal, it produces pupillary dilatation, pilo-erection, tachycardia, tachypnea, hyperthermia, hyperglycemia, blood pressure increase, contraction of nictitating membrane. The majority of these effects seems to be secondary to a central stimulation, affecting mainly the sympathetic system. The arousal pattern of the EEG produced by psilocybine, as well as the facilitation of spinal

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reflexes, points to central sites of action. In contrast to these findings, the motor behavior is not stimulated but rather retarded.

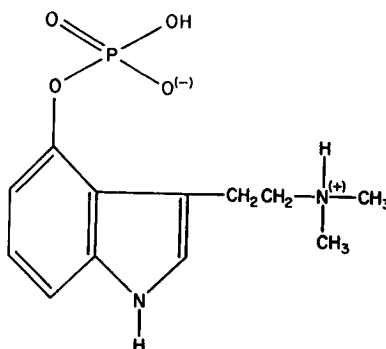


FIGURE 1. Chemical Structure of Psilocybine.

It has low toxicity. Up to 200 mg. per kilogram of body weight injected intravenously in mice had no lethal effect. The absolute toxicity in terms of the LD₅₀ could not as yet be determined because of the limited supply of the drug.

MENTAL EFFECTS

Two publications report on the psychologic effects of psilocybine. Hofmann et al. reported that in man the effects of the mushroom and of psilocybine are alike. The oral administration of 4 to 8 mg. of psilocybine is followed, after about forty-five minutes, by a state of inebriation ("*Rauschzustand*"), with physical relaxation and clearly observed mental alterations. This state lasts for several hours and leaves no after-effects. The symptoms vary in individuals and are somewhat similar to those of mescaline and lysergic acid diethylamide (LSD).

Delay et al.⁶ administered 10 mg. of psilocybine sublingually to 4 normal subjects and 14 mentally ill

patients. According to the summary heading this report, psilocybine caused hallucinations, dreamlike states, reliving of emotionally charged experiences and modifications of mood. These manifestations varied from subject to subject. The name "psychodysleptic" was suggested for the action of this type of psychotropic drug.

PRESENT EXPERIMENTS

Psilocybine was supplied in 2-mg. tablets that have a sweetish taste (not unpleasant) and dissolve rather slowly under the tongue. We gave from 5 to 10 mg. sublingually to 4 male volunteers whose pre-experimental physical and mental condition was well known. Three of the volunteers had taken psychotropic drugs in previous experimental situations; for 1 this was his first experience. The experiments were carried out in a quiet room (with the venetian blinds drawn) at the Massachusetts Mental Health Center, under the observation of 1 psychiatrist and 3 psychologists. This pilot study was limited to the observation of mental and behavioral changes; some psychologic tests were given to make the observations objective, and neurologic changes were recorded when noted.

RESULTS

First of all, it may be stated that our observations confirmed that the drug is active. The first effects appeared between thirty and forty-five minutes, with the acme about one hour after the administration of the drug, and lasted about three or four hours. The return to the pre-experimental state was gradual and took about sixteen hours, although after six to eight hours the subjects felt competent to go about their routine activities. No untoward aftereffects were observed or reported by the subjects. The psychologic effects were generally mild and varied in number and

intensity from subject to subject; however, all 4 manifested increased irritability and attempts at over-control. All were fully oriented in time, space and person.

Hallucinations

None of the subjects had hallucinations, and only 1 reported illusions, consisting of pictures of light rays on the wall that formed themselves into geometric patterns, specifically a spider web. The reality of the pattern was so marked that there was only a slight distortion in the perceptually stimulated phantasy.

Mood

All subjects experienced changes in mood, characterized by euphoria or dysphoria. They appeared to be overcontrolled even at the height of the reaction. One subject admitted to anger toward the observers, but did so only after the major effects had worn off.

Behavior

Two subjects felt more relaxed and sleepy, having difficulty keeping their eyes open; the other 2, on the contrary, had difficulty in closing their eyes, wanting to move and to be active, and 1 of these said that he felt jumpy, slightly manic and tense. One subject, a musician, insisted on playing the piano; he was buoyant but felt unnatural. While playing the piano, he was unable to sustain the tempo, missed notes and slurred passages. He felt always as though he were two measures ahead of himself. He gave up playing, after less than ten minutes, feeling annoyed at himself.

Speech

Speech was either slow, and at times slurred, or rapid and resembled push of speech.

Thinking

No distortions of thinking, fragmentation or disconnections were observed. The thought processes seemed logical but slowed down. Two subjects were asked to write essays; 1 wrote, although with effort, a short essay with logical sequence associations, and the other, who rejected a suggested topic and selected one for himself, gave up the problem after a few unsuccessful attempts and stated that he could not concentrate.

Concentration and attention were disturbed in all subjects.

Perception was only moderately disturbed. Time perception was experienced as too fast or too slow. In 1 subject it was not disturbed.

Depersonalization was observed in 1 subject, who felt himself very tall and at another time very small; he also thought that his legs were detached from his body.

Somatic Symptoms

Only in 1 subject the pupils became maximally dilated; the pupils of the other subjects did not change materially. Other somatic symptoms reported by the subjects were as follows: feeling of light-headedness, nausea, pressure in the back or front of the head; photosensitivity; and feeling of weakness in the legs, which the subjects described as rubberlike, plastic or waxy.

Psychologic Tests

On block design tests all 4 subjects had difficulty, and all showed what Kurt Goldstein has referred to as a "catastrophic response." Their performance during the height of the drug reaction was considerably more impaired than the performance of similar volunteers during experimentation with LSD.

DISCUSSION

Psilocybine is an active chemical that, like LSD and mescaline, has psychotogenic effects. Regarding the dose needed to bring about observable effects in adult human beings the order is as follows: LSD, 70 microgm.; mescaline, 500,000 microgm.; and psilocybine, 5000 to 10,000 microgm. The experiments with psilocybine did not produce true hallucinations in 8 normal subjects (our own group and those described by Delay). Delay and his associates reported the presence of "true hallucinations" only in 1 case, in a patient suffering from melancholia, who saw herself surrounded by terrifying figures. Many pertinent factors do materially influence the course and outcome of such experiments: the personality and attitudes of the observer; the rather artificial setting of the experiment (in contrast to the native's accustomed environment and ceremonies); the lighting and climatic condition of the experimental setting (air conditioned, temperature, humidity); the dosage and route of administration; the purity of the product (it has been argued that the impurities of the natural plant may account for the dramatic effects reported by explorers); the time and duration of observation; the emotional state and expectancy of the subject before administration of the drug; previous drug experiences; and the personality pattern and motives of the subjects who undergo the experiment.

We are indebted to Dr. Harry C. Solomon, Massachusetts Commissioner of Mental Health, and Dr. Jean Delay, professor of psychiatry, Paris, France, for suggesting this research and providing us with the chemical.

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