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Some Observations on Psilocybin, a New Hallucinogen, in Volunteer Subjects

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IT IS IRONIC that interest in hallucinogens like LSD-25 and mescaline has been recently heightened not by the published reports of a scientist, but of a banker. Gordon Wasson[16] described the use of the "magic mushroom," *psilocybe mexicana heim,* by the priestesses or "curanderas" of certain remote Indian tribes in Southern Mexico. Wasson acquired his love of mushrooms from his late wife; with her he gained the confidence of these secretive people and was invited to participate in their solemn religious rituals. During these ceremonies, which outsiders had never before witnessed, the Wassons observed and experienced various hallucinatory phenomena. Subsequently, Hofmann[9] was able to isolate the active psychotropic principle from these mushrooms, which he named "Psilocybin."

Psilocybin is a most interesting substance. It is a hydroxytryptamine derivative, closely related to serotonin. Much has been written in recent years of the latter's possible role in brain function and mental illness.[4,18,19] Psilocybin also contains the indole ring structure found in many other hallucinogens (fig. 1).

This paper describes our initial pilot study of clinical effects; in addition, we make a comparison between these observations and the findings of our previous experience with other hallucinogens.[8,11,12] Isbell[10] and Delay[2] had already reported briefly on Psilocybin but had not used more than 8 and 10 mg., respectively, in any of their subjects. We decided to start with these levels as our lower limits and study the effects of higher dosages. We chose paid volunteers rather than patients for these studies in order to get a clearer picture of drug action unobscured by an overlay of previously existing and overtly manifest neurotic or psychotic symptomatology. The studies were not done in double blind fashion since we wanted first to familiarize ourselves with the drug and then to determine an optimal dosage level at which double blind studies could best be carried out. The subjects and attending nurses were not aware, however, whether an active hallucinogen or a placebo was to be administered, or whether the hallucinogen, if administered, would be LSD-25, one of its derivatives, or Psilocybin.

MATERIAL AND METHOD

Fourteen student volunteers were chosen for the study after a psychiatric screening interview. All were paid for their services. Among the criteria for selection were freedom from previous mental illness, adequate adaptive functioning in their present life situa-

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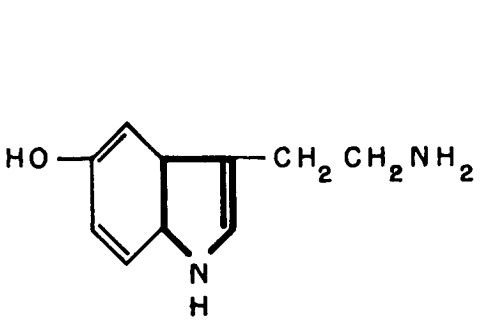

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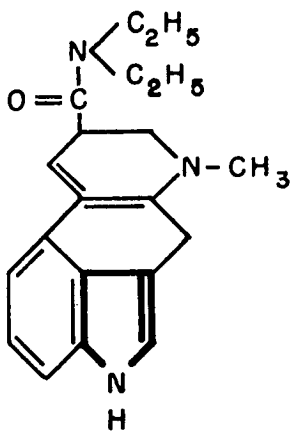

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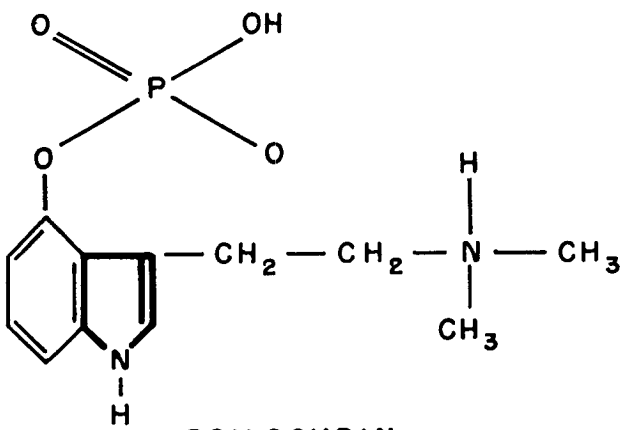

PSILOCYBIN

Fig. 1.—Substances containing the indole nucleus (indole nucleus shown in heavy black outline).

tions, and the absence of overt evidence of neurosis or psychosis. Twelve men and two women, ranging in age from 20 to 27 years, comprised the series. The median age was 22.5 years. The volunteers selected were told only that they might receive a substance which could produce temporary changes in perception and bodily feelings, or an inert substance.

On the day of the study the volunteers reported at 8 a.m. without breakfast. A baseline EEG, mental status and check list of symptoms were completed before the drug was administered. A previous publication describes the check list in detail.[11] This list contains an enumeration of autonomic, affective, cognitive and perceptual changes frequently observed after hallucinogen administration with provision for quantification of these modalities. The drug was administered orally. The experiment was conducted in a semidarkened room. A nurse, doctor or both were constantly in attendance. Verbatim statements of the subject's productions, as well as blood pressure, pulse and respiration were recorded by the nurse. Every fifteen minutes the psychiatrist rated the subject's responses on the check list and conducted a mental status examination. A second EEG was recorded at the height of the drug action, usually 2 to 2 1/2 hours after ingestion. Observations were terminated between 3 and 5 p.m., depending on the subject's condition. Volunteers were told that they might

Table 1.—*Dosage Range of Psilocybin*

Dosage (mg.)	No. of Volunteers Receiving Dosage
8	1
14	1
16	1
20	1
25	1
30	3
32	2
35	3
36	1
	Total 14

be required to remain in the hospital for 24 hours, but in only two instances was this necessary. Within 24 to 48 hours following the procedure, the volunteers returned for a follow-up interview and were encouraged to write reports of their experiences. Several of the volunteers were requested to return for additional follow-up interviews from which further psychodynamic material was obtained.

The dosage of Psilocybin administered ranged from 8 to 36 mg. Table 1 lists the dosage range in detail.

Results

A. *Perceptual Responses*

1. *Visual Hallucinations.* By visual hallucinations we mean a visual perception with eyes open or closed for which no external stimulus was present. Twelve of the fourteen subjects reported visual hallucinations. They consisted predominantly of abstract colored forms. Four subjects reported seeing conventional colored objects. One of these subjects reported "a scene like a Gauguin painting with green hills and a primitive ox cart moving slowly along a road." Another reported "a circus or carnival scene with animated objects like candy canes, waves of toys changing in kaleidoscope fashion, and presided over by a little elf. It was The Nutcracker ballet suite with vivid reds, yellows, oranges and blues." This same subject also saw "fields of waving red, green and blue flowers like poppies." A third subject reported a scene "like the fun house at a carnival with mirrors and the face of a laughing clown all in brilliant red and luminous fuchsia." Of the subjects listed in table 1, only those receiving 8 and 20 mg. of the drug, respectively, did not develop visual hallucinations.

2. *Illusions.* By illusion we mean a distorted or misinterpreted sense perception of an existing stimulus. Two types were observed: visual and auditory. Nine subjects reported visual illusions. These were usually seen in patients receiving higher levels of the drug, 30 mg. or above. Typical comments were, "People's faces appeared as if they had 6 or 8 eyes." "The nurse's face looked as if it were covered with green and blue pimples." Two subjects seemed to see their legs disconnected from their bodies. Two experienced auditory illusions. One heard a "calliope-like sound" when a siren sounded in the vicinity; the other heard his own rhythmic breathing which sounded like a waterfall. The latter might also be considered a form of hyperacusis.

3. *Body Image Distortions.* Many of these were combinations of depersonalization and derealization with somatic delusions of distortions in body shape and size. Ten subjects reported these phenomena. All had received the drug in the 14 to 36 mg. range. One subject described his body as "feeling heavy, like the gravitational pull from a ride in an amusement park." Another stated, "I felt like I was floating on a heavy but soft mass, like mercury. My body felt peculiar." Another commented, "My body felt different. I almost forgot I had one. It was as if I had just stepped out of my body." Other comments were, "I felt as if my legs were detached from my body." One subject felt his legs were shorter; another that they were longer. Another subject described the room as "unreal and different, like a strange and unfamiliar basement."

4. *Temporal Distortions.* Five subjects misjudged time by estimating the hour as 2 to 3 hours later than it actually was, but none were disoriented for date, place or person.

B. *Affective Responses*

The predominant affective responses were *euphoria, anxiety* and *depression,* in that order. Ten subjects developed euphoria. In three, the reaction was marked; in five, moderate, and in two, slight. One euphoric response was followed by anxiety. Nine subjects developed anxiety. In three, the reaction was marked; in two, moderate, and in four, slight. In five subjects, the anxiety reactions were followed by euphoria. Depression of slight to moderate intensity developed in four subjects after the euphoria had subsided. One subject became withdrawn and noncommunicative following a period of marked anxiety that had been characterized by near panic and sharp self reproach.

C. *Cognitive Alterations*

Four of the fourteen subjects exhibited marked impairment in verbalizing their thoughts with resultant *blocking.* Seven others suffered varying degrees of *disorganized thinking,* ranging from mild to severe. This was often expressed as "trouble concentrating." *Distractibility, loosening of associations, pressure of speech* and *flight of ideas* were noted, with *clang associations.* One example follows: "Doctor, where have you been? I'm Alabama bound! I'm carbamino bound. I suggested that to Bruce to use it in the show. Bruce-Brust. That's breast in German. Yeah. Bard Hall. Bard Hall. Leon M. Bard. Loeb. Loeb. Kuhn Loeb. I was at the Jewish Museum yesterday and all those people had medallions. Jones of microbiology used to say, 'No levity in the autopsy room.' I love to play tennis. Tennis. Tennis. Six love, love six. I love you!" Concrete responses to proverbs with *inability to abstract* after receiving the drugs were noted in several patients. Before the drug, in response to "a stitch in time saves nine," one subject paraphrased it with the statement, "If a situation is getting worse, you should clear it up before it gets much worse." After the drug he said, "It's about sewing. I'm confused. What time is it? I'm mixed up about time." Another subject, in response to "People in

glass houses shouldn't throw stones," said, before the drug, "You shouldn't point out faults in others that might exist in yourself." After the drug he said, "At who? That depends on a lot of things." Then he blocked. Another subject who had given a satisfactory response before the drug to "A rolling stone gathers no moss," replied after the drug, with obvious euphoric overtones, "A wandering we will go!"

Some subjects felt that their thinking was slowed down; others that it was speeded up. One expressed it as, "My thoughts were racing at an incredible speed." Another stated, "My thoughts were uncontrollable. They came in such a rapid sequence I couldn't keep up with them." Another said, "They just seemed to flow."

Four subjects gave definite evidence of *paranoid ideation.* One was grandiose, felt "very important" and thought that the study "was the most important thing going on at the hospital and everyone should be paying attention to it."

One subject felt that his lunch was drugged and that he was being watched to see if he ate it. Another felt we were trying to prove he was "crazy" and consequently decided not to answer some of the questions since he felt they were geared to "test my sanity."

One volunteer felt that the doctor was trying to trick him when he corrected one of the subject's distorted perceptions, and that the nurse was attempting to seduce him.

D. *Fantasy Material*

Fantasies were often of the wish fulfilment type and frequently could be understood in terms of individual psychodynamics. One subject fantasied lying passively on a tropical beach surrounded by attentive servants; another that he was the ruler of a tropical island, regally entertaining his appreciative fiancee. Only three admitted to sexual fantasies but it is interesting that all three related an associated lack of physical feeling or desire. This was succinctly described by one subject: "It was all in my thoughts. I knew I couldn't do anything. My body wasn't up to it." One subject described sexual fantasies about the nurse. Another fantasied having fellatio performed on him by a girl, and had homosexual fantasies as well.

E. *Autonomic Responses*

1. *Pupillary Dilatation.* All fourteen subjects showed pupillary dilatation beginning 30 minutes after ingestion of Psilocybin and lasting throughout the entire procedure, a period of 6 or more hours.

2. *Nausea.* Six subjects complained of slight to moderate nausea usually beginning 30 minutes after ingestion and lasting from 15 minutes to one and a quarter hours. There was no associated vomiting.

3. *Dizziness.* Six subjects complained of slight to moderate dizziness but only when changing suddenly from a prone to a sitting or standing position.

4. *Flushing.* Four subjects developed slight flushing of the face within 30 minutes to one hour and 15 minutes after receiving the drug, which persisted for 45 minutes to 3 hours.

5. *Abdominal Complaints.* Three subjects complained of "cramping," "tightness" and "fullness" in the lower abdomen. One further described a pain extending into the groin and another into the base of his penis and scrotum. These complaints developed after 15 minutes to one hour and 30 minutes, were of slight to moderate severity and lasted from 1 to 2 hours and 30 minutes.

6. *Blood Pressure and Pulse Changes.* Only three of the fourteen subjects showed any significant change in these modalities. In all three cases, the changes developed during a period of increased anxiety and motor activity. Two subjects showed temporary elevations of 20 to 40 mm., both systolic and diastolic. One subject's pulse increased from 60 to 110 per minute and then gradually returned to its baseline as his anxiety diminished.

7. *Inhibition of Urination.* One male subject described difficulty in starting to urinate, but during the follow-up interview described similar urinary difficulty in public toilets. In this case, the influence of prior conditioning and emotional factors may have played a greater role than any direct effect of the drug on the bladder musculature or sphincters.

F. *Electroencephalogram Findings*

Eight subjects had EEG's done before and during the drug administration. The second EEG was taken at the height of the subject's response, about 2 to 2½ hours after drug ingestion. Disc electrodes were applied to the scalp and 8 channel recordings were obtained from a Grass instrument. Four of the subjects showed no change. The other four showed increases in alpha frequency with a range of 0.5 to 3.0 c.p.s.

Our EEG findings were similar to those seen with LSD-25 by Gestaut et al.,[5] who observed an increase in alpha frequency of 0.5 to 4.0 c.p.s. with an accentuation of beta rhythms, and Rinkel et al.,[13] who confirmed these observations and also noted "a reduced response to hyperventilation probably on the basis of decreased subject cooperation." Similar findings have also been observed with mescaline. Wikler[17] noted either no change, or intermittent or continuous low voltage fast activity, or an increase in alpha frequency. Denber and Merlis[3] described an acceleration of alpha frequency with a decrease in percentage time alpha, including its disappearance, and nonspecific random beta activity.

G. *Miscellaneous*

1. *Paresthesias.* Five subjects complained of numbness and tingling in their extremities. One subject described "warm, pleasant tingling feelings in my arms and legs like one experiences just before an orgasm."

2. *Yawning.* Persistent yawning was observed in three subjects. In one the yawning was accompanied by drowsiness but in the other two it was not. We have reviewed the literature on this interesting phenomenon, going back over the last 20 years, and have found little information about its etiology, physiology or psychological significance. Anoxia has been reported as a common cause of yawning, as has suggestion. Yawning is associated with withdrawal from morphine. It may be that a more intensive study of yawning and related

symptoms which appear to involve a neurophysiologic substrate will offer additional clues as to the sites of action in the brain of Psilocybin and related hallucinogens.

3. *"Reality Testing" Behavior.* Four of our subjects displayed behavior which seemed to be a reparative device for holding on to reality. We have called this behavior "reality testing" because of its similarity to the reality testing employed by some schizophrenics. One volunteer clung to the headboard of his bed during intermittent attacks of panic and stated later, "I felt like I had to hold on to something. It was a way of anchoring myself. It seemed solid." Another subject began biting and gripping the side of the bed. Later he said, "I was having trouble distinguishing between what was real and what was not. This [the bed rail] was real." A third volunteer stood with his back to a radiator gripping it tightly during periods of extreme anxiety. "The radiator was something to hang on to." A fourth subject kept asking for water and stated later that the feeling of the glass in his hand and the water on his lips, both familiar objects from "the real world," were very reassuring.

H. *Duration of Drug Effects*

Most subjects began experiencing drug effects 30 to 60 minutes after ingestion. Peak response was usually reached in 1½ to 2½ hours. Rapid subsidence of symptoms therafter was common, with a few subjects symptom-free in five to six hours. The majority of subjects reported *post-drug* effects, however. Five volunteers complained of headache, three of drowsiness and lethargy, one of diarrhea and one of depression on the evening of the study or the following day. Wasson[15] reported no post-drug effects following the use of the whole mushroom in religious rituals. Characteristically, after 4 to 5 hours under the influence of the drug, the Indians are reported to fall into a deep sleep lasting two hours from which they awake "refreshed and ready for work." Delay[2] reported the usual length of the Psilocybin response as from 2 to 4 hours "with subtle disturbances occasionally remaining for several more hours and in rare instances for several days," but he does not elaborate on these side effects. Henze[7] reported that in the Sandoz Laboratories, "The effect wore off in 4 to 5 hours at reasonable dose levels." These were usually doses ranging from 4 to 8 mg. It is possible that our consistently higher dosage levels might account for our greater incidence of post-drug effects.

Discussion

Qualitatively, the reactions observed in our present subjects were similar to the responses we observed previously in subjects given LSD-25.[8,11,12] Both LSD-25 and Psilocybin volunteers showed a similar pattern of autonomic reactions, perceptual distortions, and affective variations. In the cognitive sphere, we noted a greater disturbance of thinking with Psilocybin, expressed as blocking, associational impairment and flight of ideas, but these results might have been either a factor of dosage or related to basic personality variations from subject to subject.

Stoll's[14] experience with LSD-25 after-effects resembles very much the post-drug symptoms we observed with Psilocybin. He reported somatic disturbances the day after LSD-25 ingestion consisting of "back pain, diarrhea and grippe-like symptoms," and in the psychic sphere, two cases of mild depression.

The lack of sexual desire seen in our present subjects has also been observed by us with LSD-25 and mescaline.[8] Stoll[14] reports a similar experience with LSD-25, and Guttman[6] commented on the anaphrodisiac qualities of mescaline in the Indians of the southwestern United States.

Our experience with Psilocybin reinforces our impression that hallucinogenic agents act in two ways simultaneously. On the one hand, they behave like toxic agents producing autonomic disturbances and predominantly visual perceptual distortions, without marked disorientation or clouding of consciousness. On the other hand, they act as nonspecific psychic stresses on the total organism, to which the individual responds in a manner dependent on his basic personality structure, his previous life experiences and the techniques of adaptation he has developed throughout his life to handle these experiences. The affective responses of the subject to the drug, and the total behavior pattern emerging under its influence may be related to this nonspecific stress effect. Thus, a schizoid individual might become more withdrawn and even appear to be temporarily schizophrenic when under the influence of a hallucinogen, while an individual with a cyclothymic temperament might act more euphoric and demonstrate less blocking and associational disturbance than the former. This viewpoint might explain why one investigator emphasizes that the hallucinogenic effects in his case material resemble closely a schizophrenic process, while another investigator using the same drug and dosage level finds little or no resemblance to schizophrenia in his subjects.

The stressing effect of hallucinogens is not limited to any single agent since, in addition to Psilocybin, we have seen it with LSD-25 and mescaline. The environmental setting in which the drug is administered also affects the emerging behavior pattern. This factor may also account for variations in results with different investigators. Our hospital setting, with the subject, a paid volunteer, receiving an unknown agent in an experimental framework surrounded by unfamiliar doctors and nurses, differs markedly from the mystical setting which Wasson observed, where the drug is part of a solemn religious ritual. Only one of our subjects reported what might be described as a transcendental experience resembling the religious ecstasies observed by Wasson. The differences in expectation and setting between these two grossly divergent groups may account in part for the disparity in their responses.

Recently, the use of hallucinogens, specifically LSD-25, as therapeutic agents in psychiatric disorders has been proposed.[1] We feel that such a usage of these drugs, especially in an out-patient setting, is fraught with danger and should be undertaken only with the greatest of caution. Psilocybin, LSD-25 and mescaline are extremely potent agents, capable of producing acute psychotic behavior in many individuals. Depression, with the ever present risk of suicide, may develop during or after their administration. Additional post-drug effects also occur. Once a patient has been entrusted with a hallucinogen, even when instructed to take the drug in small doses

below the hallucinogen threshold, we have no control over the numbers of pills he may take at any one time while at home. We believe that the use of hallucinogens should, for the present, be restricted to research in a hospital setting, where untoward reactions can be promptly managed with a maximum of safety. Further research is indicated regarding the site of action of hallucinogens, the relationship between personality, dosage level and total behavior pattern, and the possible prognostic value of these drugs in assessing the likelihood of future emotional decompensation in specific individuals.

Summary

Fourteen paid volunteers, screened by clinical interviews, received Psilocybin orally over a dosage range of 8 to 36 mg.

The perceptual, affective, cognitive, behavioral and autonomic responses observed were qualitatively similar to those previously described with d-LSD-25, but quantitatively, a greater impairment of cognition with Psilocybin was noted which may have been related to dosage or personality differences. EEG findings in four out of eight subjects were similar to those previously reported with d-LSD-25 and mescaline.

The use of psychotomimetic drugs as therapeutic agents in an out-patient setting may prove potentially hazardous. Acute states of excitement, depression with suicidal ideation and impairment of judgment may occur with these drugs, even in the most carefully supervised in-patient setting. With out-patients, the danger of self-administration and inadequate supervision could compound such occurrences.

Further research is indicated regarding the site of action of hallucinogens, the relationship between personality, dosage level and total behavioral pattern, and the possible prognostic value of such drugs in assessing ego strength in specific individuals.

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