Reprinted from: E. ROTHLIN (Editor), *Neuro-Psychopharmacology*, Vol. 2 (1961),
Proceedings of the 2nd International Meeting of the Collegium Internationale
Neuro-Psychopharmacologicum, Basle 1960

PSILOCYBIN AND DIETHYLTRYPTAMINE: TWO TRYPTAMINE HALLUCINOGENS

Z. BÖSZÖRMÉNYI

Central State Institute for Nervous and Mental Diseases, Budapest 27 (Hungary)

The interest devoted to model psychoses originates from anthropological, biochemical, pharmacological and clinical psychiatrical viewpoints, and is part of the enormous expansion of pharmacopsychiatry which is taking place before our eyes. The first task in the experiments with new psychotogenic drugs is to determine the symptomatology of the model psychoses to which they give rise, and from this draw some conclusions as to their potential use in therapy. The second step is to test these drugs on patients. In our own model psychosis experiments with dimethyl- and diethyltryptamine, as well as with psilocybin (more than 200 in number) we, too, followed this method.

The symptomatology was determined in volunteer test subjects, while in the therapeutic experiments neurotics and psychotics were involved. Although it is of theoretical importance, the dimethyltryptamine psychosis seemed to merit no further study because it produces violent vegetative symptoms and its effect subsides in less than 1 h. We have already described in detail the diethyltryptamine syndrome which is very reminiscent of a mescaline effect of medium severity and lasts for about 3 h: during the first 10 to 40 min vegetative symptoms predominate, the psychopathological symptoms, *e.g.* the pseudohallucinations, culminate during the second hour, while during the third hour the symptoms gradually diminish.

We have carried out 52 experiments with psilocybin; of these, 28 were made in normal test subjects, of whom 18 had been involved ½ to 1 year earlier in the diethyltryptamine (DET) series. Fifty per cent of the test subjects took the drug per os, the other 50% were treated by intramuscular injection in doses of from 6 to 11 mg, averaging 9 mg, in proportion to the body weight. Of the 24 patients, 16 were psychotics, 11 schizophrenics, 5 hysterics and 8 neurotics. Three of the psychotics and 3 of the neurotics had previously taken part in the DET experiments. The psilocybin syndrome has already been described by a number of authors, although the number of test subjects was relatively small and the doses were variable (in DELAY's series 4 normal and 14 psychotic test subjects, in RÜMMELE's 18 normal, and in ISBEL's 9 narcomaniac test subjects). On the basis of our own experiments we may outline the psilocybin syndrome as follows:

1. At 30 to 45 min following the peroral, or at 5 to 8 min following the intramuscular administration the vegetative symptoms appear, vary in intensity for 30 to 50 min and disappear about 2 h after their onset. The only difference between these vegetative symptoms and those elicited by mescaline, LSD-25 and DET is the common occurrence of temporary facial flushes, the development of bradycardia in some, and the increase of blood pressure in most subjects.

2. The psychical symptoms quickly follow the vegetative ones. Consciousness is moderately clouded, narrowed, together with disturbances of perception, eidetic phenomena, disturbances in the perception of space and development of illusions. Then elementary, and in about $^1/_3$ of the test subjects, scenic hallucinations present themselves, together with disturbances in the perception of the body scheme and depersonalisation phenomena. The associations loosen up, thinking and the behaviour as a whole show regression. The latter manifests itself in disinhibition, affective outbreaks (outbursts), and in an exaggerated demand for attention and love. This occurs particularly in the anxious test subjects. Only a few of the normal test subjects showed evidence of paranoid tendencies. Mostly there is dysphoria and although the dream-like experiences are enjoyed by many test subjects, lasting euphoria was produced usually only by the smaller and peroral doses.

3. The neurological symptoms included a diffuse increase of reflexes, paraesthesia, tremor, ataxia, muscular adynamia: these occurred in every subject given doses larger than 8 mg. The duration of the bodily and psychic symptoms was 3 ½ to 4 h.

4. The after-effects were similar to those noted after treatment with the other psychotogenics: fatigue with mental tension, insomnia, etc. The eidetic phenomena and the changes in mood may last 2 to 3 days.

Although most of the normal test subjects had undergone personality tests as well (RORSCHACH, TAT, LÜSCHER), no parallelism may be established at present between the results obtained and the psilocybin syndrome.

Our experiments thus seem to indicate that it appears to be possible to distinguish the action of DET from that of psilocybin, although both produce what may be called a collective reaction emerging over individual differences. The differences may be outlined as follows.

DET, besides its hallucinogenic-dysleptic effects, seems also to stimulate the cerebral structures responsible for the coordination of personality, self-control, critical faculties, etc., while psilocybin, in doses of 8 to 9 mg, seems to suspend this control activity, produces diffuse excitation, inhibits situative integration: thus, some of the normal test subjects forgot temporarily that they were involved in an experiment. Three of the test subjects were intravenously injected with 15 mg of amphetamine at the peak of the psilocybin effect; some measure of a normalisation was noted, the obsessional ideas of an obsessive neurotic recurred in response to amphetamine after they had ceased during the experiment, but the disturbances of perception continued. Thus, there seems to be a certain parallelism between the DET effect and the combined actions of psilocybin and amphetamine. This observation of ours is at variance with that made by BALESTRIERI, who applied amphetamine shock at the peak of the LSD and mescaline effects in 8 test subjects and found an aggravation of psychotic symptoms, and who claimed that amphetamine did not even qualitatively modify the pattern of symptoms.

In spite of producing a sensation of mental tension, psilocybin, in contrast with DET, induced in most subjects a tendency to passive meditation, to introversion. However, this difference was marked only with the intramuscular administration, while the response to the peroral administration of psilocybin more closely resembled the DET effect and was definitely reminiscent of a prolonged dimethyltryptamine effect. This is not at all astonishing if we realize that the active component of psilocybin and psilocyn is apparently 4-hydroxy-dimethyltryptamine. Thus, the response to

the perorally administered psilocybin stands closer to the mescaline effect, while that to the intramuscularly administered drug in some way resembles the effect of LSD. We are unable to explain this difference in action, but differences in absorption might very well be responsible.

Psilocybin, as used in normal test subjects, seems to be more suitable for inducing a schizophrenia-like state because the depersonalisation and derealisation it produces are stronger, and the regression as well as the loss of self-control are more marked. For the latter reason it may prove useful in the treatment of obsessional neurotics as a psychotherapeutic adjuvant. We have found it to be so in two of our cases. In a few of the normal subjects who had exaggerated self-control and were "over-logical", psilocybin caused a remarkable "mellowing" and an increased affective resonance. DET is superior to psilocybin in breaking through a stupor. This has been found in a case of catatonic and in another of hysteric autism. These patients had shown no response to psilocybin (9 mg and 8 mg respectively), while the usual 0.8 mg/kg dose of DET successfully resolved psychotic mutism. It appears that in cases of neurosis, psilocybin may prove to be more useful for bringing suppressed, *i.e.* subconscious, contents to the surface and for what is called oneirosynthesis, although DET, too, markedly increases suggestibility in most test subjects.

These statements should, of course, be treated with reserve because it is just as difficult to assess the effectiveness of psychotogenic drugs as it is to assess other drugs. To diminish these difficulties, some workers treat the same test subjects with various preparations (FISHER, LEBOVITS *et al.*), while others condemn this practice (SOLMS, and others) because of an unconscious bias and an anticipation of earlier experiences by the subjects. We employed the former method, because it was thought that the reactions due to differences in personality represented a more serious source of error. This method permits reproduction of the pre-experimental atmosphere under the control of the same experimenter; moreover, we may learn how the test subject usually responds to stress situations and thus the changes in behaviour may in some measure become characteristic for the drug actually tested. This, of course, is true only to a limited extent because the pre-experimental life situation is of decisive importance as has been emphasized by many workers and also experienced by us. For example, one of the test subjects was involved in a DET experiment when he was in a serious existential situation: he "escaped" during the experiment into a reckless, disinhibited, paranoid-aggressive state. One year later, when his life had become normal again, he responded to the same experiment with a quiet euphoria, with the same degree and quality of disturbances of perception, and with marked vegetative symptoms, but without paranoid aggressivity. This case tends to confirm the validity of the statement made by SCHULZE-GÖRLITZ that every test subject is in his total constellation a unique individual who appears at every experiment with an unreproducible starting state.

In comparing the symptomatology of the pschotogenic drugs some workers (ISBELL) employ hourly answering to questionnaires, while others advocate the rating afterwards of certain statements or allegations, *i.e.* a method of selection similar to the MMPI test (DITMANN AND WHITTLESEY), although the shortcomings of such methods are admitted *e.g.* symptoms may be suggested, not every symptom is included, should be used with drugs of longer action in the first place, etc. We have tried to use a new method, consisting of a study of questionnaires after the experiment;

thus, the experimenter first filled the questionnaire modified according to JARVIK, on the basis of the protocol, tape recordings and the test subject's personal account, then he asked the test subject only such questions as remained unclarified. Thereby suggestibility was in some measure diminished. The disadvantages of the method are, it is time-consuming, can be applied exclusively to cultured (educated) test subjects in whom the response to the drug is not too violent, and the test should be completed within 2 or 3 days. Placebos were not used; instead, the test subjects were kept relatively uncertain by telling them before the experiment that the drug might prove to be ineffective, that individual variations in the response are extreme. Some test subjects were given very small doses intentionally. It should also be known that the reliability of the accounts given by the patients after the experiments varies with the various drugs. Such accounts (written statements) seem to be more objective following moderate doses of mescaline and DET, while after the LSD and psilocybin tests there is usually a tendency to confabulate.

All these difficulties do not, of course, diminish the theoretical and therapeutic significance of research in experimental psychosis, they may only stimulate further collection of data. The tryptamine hallucinogenics, because of their potential connexions with tryptophan or serotonin metabolism, are even more important targets of research than the other kinds of psychotogenic compounds.

Printed in The Netherlands