Psychotropic Drugs

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With regard to the latter eventuality (which would be the principal line of action), we may say that few drugs exist that exercise a selective, stimulating action on the sole functions of the Ego. We have, however, noted that (although only in the embryonal state) a relatively new central acting drug, Ritalin, does have this effect.

We injected 23 patients, i.v. with a dose of 40 μ diluted in 2 cc water. Judging by the therapeutic results (not always present), the patients felt more lucid and active, thought was facilitated, and attention augmented; all these being signs of a strengthening of the Ego. Using the Toulouse Pieron test, carried out by Dr. VELLA, we noted an increase in the exactness of the responses, together with a diminution in their quantity. This shows a strengthening of attentive concentration, which is an indication of the strengthening of numerous other functions that are dependent upon voluntary attention, functions that exactly characterize the Ego. In no case were compromises to the sympathetic nervous system observed (or rather, expressed in terms of psychodynamic fact, there were no accentuations of subconscious dynamisms), in contrast to what happens in the case of other stimulating central acting drugs, such as simpamina, methedrine, etc.

We are of the opinion that the future of psychopharmacology is not to be sought in selective, sedative drugs, but rather in those medicaments that have a stimulating selective action on what we consider the functions, the contents of the Ego. Only thus will pharmacotherapeutical psychiatry be able to play, not the merely consolidating part as at present, especially in psychoneurotic disturbances, but the part of elective therapy: psychotherapy. Only thus will it one day be raised to the ranks of essential therapy, with all the ensuing advantages on the clinical and social plane.

Rome (Italy) G. F. TEDESCHI

Dimethyltryptamine (DMT) experiments with psychotics

Experimental trials with DMT have been carried out in 24 female patients at our department, a single dose of 1 mg/kg being administered in every case. In 3 cases the experiment was repeated with single doses of 1.5 mg/kg. The age of the patients varied from 24 to 53 years. The majority of the test subjects had been suffering from chronic schizophrenia for 3 to 20 years (20 cases). Also included in the trials were 2 cases of oligophrenia, 1 case of psychopathy, and 1 case of conversion hysteria.

The differences in the manifestations of the DMT psychosis between normal and psychotic experimental subjects may be outlined as follows:

(1) It was remarkable that, as compared with the normal test subjects and the 4 non-schizophrenics, the schizophrenic patients developed the vegetative symptoms about 3 to 4 minutes later. There was no such difference between the normal test subjects and the patients suffering from mental diseases other than schizophrenia. Even this relatively small difference in time seems to be a highly important feature, in view of the rapid onset and course of the DMT effect.

(2) In schizophrenics the vegetative symptoms were less marked and 4 patients showed no such symptoms at all. In the latter cases, behaviour suggested no pathological experience, either.

(3) Except for a sensitive borderline case, schizophrenics did not respond to DMT with hallucinations, whereas all the 4 non-schizophrenics did.

(4) Changes in the affective state and behaviour did not reveal any after-effect in the cases of schizophrenia, neither were pertaining subjective experiences related by the patients.

In both groups the experimental psychosis resulted in already existing normal or pathological personality features becoming more pronounced, although such manifestations were somewhat suppressed by self-criticism in normal subjects. The latter appears to be responsible, at least in part, for the fact that in normal individuals no contents related to sex were brought to the surface, though it is also true that normal subjects suffered much more from the experimental psychosis than the psychotic individuals, who had also less marked vegetative symptoms, as has been mentioned already. Also, the disturbances of perception represented more strain for the normal subjects than for the psychotics, who, even if they had pathological experiences of this kind in response to DMT, were apparently more "crusty", *i.e.* indifferent, toward them or found them to be less alien to their psychotic personality.

On the basis of all that has been elaborated beforehand, it can be stated that schizophrenics are apparently less sensitive to DMT. This fact suggests that the cause of the difference may be a metabolic disturbance of the nervous system in the background of the psychic process of schizophrenia, as has been assumed by CONDRAU on the grounds of the evidence derived from his LSD experiments. The claim that schizophrenia may be due to a disturbance in metabolism is as old as the disease itself, because as early as 1896 KRAEPELIN suggested an autointoxication of endocrine nature to be the cause of the disease entity outlined under the term "dementia praecox".

More recently, FABING revived this theory on a modern basis, when stating that schizophrenia is based on a disturbance of enzyme systems acting on the cerebral synaptic connexions, which, in turn, is caused by the formation of hallucinogenic indol compounds in the body. According to FABING, the favourable effect of the new ataraxics is due to an elimination by them of some of these metabolic disturbances. If we knew the role played by serotonin in normal cerebral function, we could subject this assumption, also, to a more detailed and realistic analysis.

On the basis of our own experiments we could make statements concerning this theory only if we had succeeded in demonstrating substantial differences in the breakdown of DMT between normal individuals and patients with schizophrenia. Unfortunately, we have carried out but a few experiments in this direction, and these cannot yet be evaluated.

Budapest (Hungary)

Z. BÖSZÖRMÉNYI
G. BRUNECKER

Crossed tolerance between LSD-25 and mescaline

The rapid establishment of tolerance to the effects of LSD-25 when repeated doses of the drug are given has been recently observed in man by ISBELL *et al.*[3] and confirmed by CHOLDEN *et al.*[2] and by ABRAMSON *et al.*[1]. The last-named authors seem to have also observed, in one case, the way in which habituation to BOL-148 does not induce tolerance to LSD-25. CHOLDEN *et al.* affirm that subjects inured to LSD-25 are also tolerant to LAE and BOL-148, but not to mescaline.

Our tests were carried out (in collaboration with D. FONTANARI) on three subjects (two psychoneurotics, one schizoid psychopathic personality). Increasing the dosage progressively, for 3, 4, and 5 days, respectively, a good tolerance was set up for the psychic and, partly, for the vegetative effects of fairly elevated doses (200–250 γ per os) of LSD-25. The next day 0.5 g i.v. mescaline sulphate was injected. The effect in the psychic and vegetative field was very mild, inferior to that obtained with the last administration of LSD-25.

A control experiment with the same dosage of mescaline was carried out, in one case 4 days before the tolerance experiments, and in the other two cases 5 and 8 days, respectively, after the last tolerance trial was ended .Very marked reactions (nausea, vomiting, midriasis, emotional variations, disorders of hallucinatory and illusional type) were observed in all cases.

We cannot discuss here the negative findings of CHOLDEN *et al.*, since the authors did not give us the dosages and the number of tests, but, in any case, we know that they gave LSD-25 for only two days. There seems to be some evidence for an acquired tolerance to the autonomic effects of mescaline in the dog (WOOD *et al.*[4]).

Our findings seem to supply evidence of a new example of crossed tolerance, to be enumerated among others already described regarding substances having different chemical structures but an analogous action on the C.N.S.. It is, for instance, known that an individual having acquired tolerance to morphine is also very much less sensitive to synthetic analgesics (meperidine, methadone). Something similar happens with various barbiturates. It is also well known that an inveterate alcoholist resists the action of hypnotics such as ether, chloroform, and avertine.

The problem of drug tolerance has been discussed, especially in the field of analgesics, where it is also related to the pathogenesis of the withdrawal syndrome. To-day, it is admitted that, at least as regards the analgesics themselves, the body adapts itself to the presence of the drug through chemical modifications at a cellular level (theories of TATUM, SEEVERS AND COLLINS, and of SEEVERS AND WOODS) or by the intervention of homeostatic mechanisms of an autonomic nature (theory of HIMMELSBACH). It is, however, difficult to say whether the tolerance develops as regards the chemical structure or only as regards the pharmacological effect.

This difficulty is particularly evident in connection with the phenomena of crossed tolerance. They are, indeed, easy enough to explain, on a chemical basis, in the field of the barbiturates, alcohol, and aliphatic narcotics, given the evident structural analogy among these various compounds. The problem becomes much more difficult when we pass to the analgesics and, as at present, to the hallucinogens. We should like to stress the paralellism between what happens as regards morphine, meperidine, and methadone, and what we are now observing with LSD-25 and mescaline. The theoretical possibility of a similarity between the chemical structure of the three analgesics appears to be sustained also by the observation that N-allylmorphine can antagonize all three compounds. Such a possibility exists, too, in the field of hallucinogens, inasmuch as we know, for instance, that the indolic group, which appears in LSD-25 and in other compounds having similar effects, may perhaps be obtained from mescaline by closing its lateral chain.

Our present results seem to uphold any hypothesis based on a chemical similarity between the two compounds. It should be stated, however, that the C.N.S. seems to react in a peculiar way after protracted administration of certain drugs, apart from considerations of a chemical order. For instance, the "extrapyramidal" syndrome provoked, after prolonged administration only,