The Excretion of Dimethyltryptamine in Psychiatric Patients

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For many years research workers have been attracted by the idea that some endogenously produced psychotogen might be implicated in the etiology of schizophrenia. Unfortunately, lack of knowledge concerning the neurochemical mechanisms of normal behaviour has deprived investigators of a sound basis on which to plan their strategy, with the result that biochemical research into the condition has been mainly characterized by the accumulation of negative findings and discarded theories. However, recent advances in neurochemistry and in the standardization of psychiatric symptomatology and classification have facilitated the emergence of coherent testable hypotheses. One of these predicts that the abnormal metabolism of methylated indoleamines may be a factor in the genesis of some of the symptoms of schizophrenia (Domino 1975, Gillin *et al.* 1976).

Dimethyltryptamine (DMT) and Hollister's Criteria

The indoleamine hypothesis centres on NN-dimethyltryptamine, and its adequacy can best be examined in relation to the criteria which Hollister (1967) decreed should be satisfied before any agent can be considered as a possible endogenous cause of schizophrenia (Table 1). When injected in single doses to human volunteers DMT does include a short-lasting model psychosis in which some of the symptoms of schizophrenia can be discerned; repeated administration does not lead to a general loss of responsiveness to DMT (Gillin *et al.* 1976). The enzymatic machinery and substrates (tryptamine and S-adenosylmethionine) for the endogenous formation of DMT are present in animal and human tissues (Mandel 1975). DMT is thus not only the first human hallucinogen for which there is a known biosynthetic mechanism but, unlike for instance LSD, its effects do not subsequently diminish because of the development of tolerance. Current knowledge suggests that DMT at least partially satisfies the first five of the criteria in Table 1, but we have as yet no information on the effects of neuroleptic drugs on the metabolism of DMT. This paper will be mainly concerned with Hollister's remaining criteria, i.e. is DMT differentially synthesized or metabolized in schizophrenia?

Table 1

Criteria for an endogenous hallucinogen causative of schizophrenia (after Hollister 1967)

(1) The agent must be capable of mimicking clinical aspects of schizophrenia
(2) Repeated administration should not cause tolerance
(3) The agent should be found in man
(4) The precursor of the agent should be found in man
(5) The agent should be synthesized in man
(6) The agent should be differentially synthesized or metabolized in schizophrenia
(7) Neuroleptic drugs should be capable of inhibiting the synthesis, increasing the metabolism or antagonizing the behavioural effects of the agent

Clinical Studies

Several groups of workers have examined the blood of mentally ill subjects for dimethyltryptamine. Narasimhachari *et al.* (1971) claimed to find DMT more frequently in the blood of schizophrenics, but four other groups have failed to distinguish DMT levels in the blood of schizophrenics from those of other psychiatric patients and normal subjects (e.g. Angrist *et al.* 1976). However, not only are there methodological objections to these studies, but the rapid metabolism of DMT makes its appearance in blood very transitory. We, therefore, decided to use 24 hour urine specimens as a pool for total body DMT.

In an earlier study of 122 acute psychiatric patients (Rodnight *et al.* 1976) we detected DMT in the urine of 47% of those diagnosed by their psychiatrists as schizophrenic, 38% of those with 'other psychoses', 19% of neurotics, 13% of those with affective psychosis and 5% of normals. The use of a variety of operational definitions of psychosis failed to reveal any group more closely related to the detection of DMT than a hospital diagnosis of schizophrenia. But, an analysis of the symptomatology of these patients as assessed in a semi-standardized fashion using the Present State Examination (Wing *et al.* 1974) showed a general association between the excretion of detectable levels of DMT and psychotic symptoms; the symptoms most closely related to DMT detection were hypomania, sexual and fantastic delusions and auditory hallucinations.

Carpenter and his colleagues (1975) have carried out a similar though smaller study in which they failed to detect DMT more frequently in the urine of 12 acute schizophrenics than in that of 9 normal controls. The only way of resolving the discrepancy between their study and ours was to develop a quantitative rather than a qualitative method of estimating DMT. Such a technique has now been developed with a sensitivity limit of about 20 ng per 24 hour sample of urine, i.e. levels some 25 times lower than could be detected with our original method.

Using the new method we have now studied a further 68 subjects. These consisted of 54 recently admitted psychiatric patients and 14 normal controls. None of the subjects had received any

Table 2
Urinary dimethyltryptamine and psychiatric diagnosis

Diagnosis	*No. of subjects*	*Percentage > 500 ng/24 h*	*Mean excretion (ng/24 h)*
Mania	4	100	1717
Schizophrenia	15	53	1365
Psychotic depression	8	38	566
'Other psychoses'	12	58	810
Neurosis	15	13	226
Normal subjects	14	7	228

drugs other than benzodiazepines in the two preceding weeks, and the estimations were carried out in ignorance of the subjects' clinical condition. We detected DMT in the urine of all subjects, both patients and controls. The level of excretion ranged from 63 to 4500 ng per 24 hours, and the mean levels were much higher for psychotic patients than for neurotic and normal individuals (Table 2). The percentage of schizophrenics, 'other psychotics', neurotics and normals with an excretion of more than 500 ng per 24 hours was not dissimilar to that in our original study, but high values were also found this time in a group of 4 manic patients.

Potential Pitfalls

We have no evidence of the origin of urinary DMT. It may bear little relation to neurochemical events, and could be influenced by factors such as diet or bowel status. As failure to control for such factors has in the past led investigators into error (Wyatt *et al.* 1971) we have attempted to explore some of the potential pitfalls. One heroic volunteer lived entirely on Complan for five days without significant change in DMT excretion, thus excluding diet as a major influence on urinary DMT. Another possible source could have been gut bacteria, but 2 subjects had their guts sterilized with neomycin and still excreted DMT. Similarly, physical exercise and emotional stress had no effect on urinary DMT.

Conclusion

Our findings suggest that the excretion of DMT is not exclusively related to schizophrenia or even to mental illness. That all 14 normal subjects tested also excreted DMT raises the intriguing possibility that this hallucinogen has some physiological function. Nevertheless, we have now demonstrated in two separate studies that much higher levels are excreted by some acutely psychotic patients. These elevated levels do not seem to be the consequence of nonspecific factors such as diet, medication, bowel status, activity or stress. Exactly what mental or physical features of psychosis are particularly associated with increased excretion of DMT, and whether DMT excretion is a cause or consequence of these features are fascinating but unanswered questions.

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Depression During Renal Dialysis and Following Transplantation

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This paper discusses the general management of depressive reactions in people in end-stage renal failure and the specific difficulties in treating such patients with tricyclic antidepressants.

Depression is common and normal during the onset of the physical illness or when a treatment fails. It is less common and more difficult to treat when it coincides with an improvement in physical state. In addition to occurring at an unexpected stage, depression may be abnormal in its severity and in the mode of its expression. Numerous factors aggravate it, including a fear of the equipment and procedures, the conflict between obligatory dependence on the machine and learning to cope with procedures independently, reasonable fear of death and further physical illness, electrolyte imbalance, residual uræmia, anæmia, hypotensive medication, psychosexual problems, infertility, marital and family stress and economic difficulties.

Sensitive staff can help the patient to work through his depression and the feelings underlying it. This is important, since prognosis is poor

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