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Dimethyltryptamine Levels in Blood of Schizophrenic Patients and Control Subjects

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Abstract. A gas chromatographic-mass spectrometric determination of blood N,N-dimethyltryptamine in normal controls and schizophrenic patients was carried out with a sensitivity limit of 0.05 ng/ml whole blood. Although the results appear to suggest that the mean DMT level was higher in the total patient group, those patients with acute psychosis, female patients and patients with suspiciousness scores on the BPRS of 4 or over, the differences were not statistically significant.

Key words: Dimethyltryptamine – DMT – Blood levels – Schizophrenia – Assay.

The possible relationships between N,N-dimethyltryptamine (DMT) and schizophrenia have been investigated extensively and the supporting evidence has been reviewed by Wyatt et al. (1973, 1974). These authors also discussed the various reports on the occurrence of DMT in blood and urine of schizophrenic patients and pointed out that in some cases the methodology used to analyze DMT in body fluids lacked the appropriate sensitivity and specificity. They further concluded that a major deficiency in the DMT hypothesis has been the inability to demonstrate unequivocally that this hallucinogen is present in elevated amounts in the majority of psychiatric patients evaluated (Wyatt et al., 1974; Mandel, 1975).

The development of a highly specific and sensitive assay for DMT (Walker et al., 1973) gave impetus to continue the studies on the measurement of DMT in whole blood samples of psychiatric patients and normal subjects. Three studies utilizing the gas-chromatographic–mass spectrometric (GC-MS) isotope dilution procedure have been reported to date. Wyatt et al. (1973) found no differences among normals, patients with psychotic depression and chronic schizophrenics. One psychotic depressive patient had a high level of DMT (10.6 ng/ml) during a period of severe agitated depression. Bidder et al. (1974) examined 24 h urine samples from 44 individuals (15 acutely, psychotic, 10 with psychotic depression, 4 manic depressives, 10 with non-psychotic psychiatric illness and 5 normal volunteers) and found detectable DMT levels in 7 cases, one of whom had an active psychotic illness. The same investigators found detectable DMT levels in the blood of two of 38 psychiatric patients, 34 of whom were acutely psychotic. Lipinski et al. (1974) measured DMT levels in whole blood and plasma of 39 subjects (6 chronic schizophrenics, 11 patients in hepatic coma, 11 patients with acute schizophreniform psychoses, and 11 normal controls) and found detectable levels in two patients – both with acute schizophreniform psychoses. The data to be presented here add to these studies and utilize a modified GC-MS isotope dilution assay for DMT with a sensitivity of 0.05 ng/ml whole blood.

METHODS

The patient group studied were inpatients on the NYU Neuropsychopharmacology Research Unit and consisted of the following: (1) 13 acute schizophrenics undifferentiated, catatonic, paranoid or affective types. Such patients were defined by a recent onset or exacerbation of symptoms and relatively well preserved affect when not symptomatic. (2) 5 patients diagnosed as chronic undifferentiated schizophrenia. These had less clear cut recent worsening of symptoms and poorly preserved affect. (3) 1 alcoholic with endogenous depression. (4) 1 asymptomatic schizophrenic. (5) 1 ex amphetamine abuser with mild hypomania – not amphetamine induced.

Twenty-three specimens were collected from these 21 patients. (The asymptomatic schizophrenic had a second sample collected after developing an acute exacerbation of symptoms and the amphetamine abuser had a second sample taken after 90 mg *d*-amphetamine was administered on the ward in divided doses over 4 h.)

Patients were drug free or on placebo prior to initiation of the studies for from 2 days to (in one case) 14 days; blood was drawn in a non-fasting state. Control blood samples were taken from

Table 1. Diagnosis, sex, BPRS pathology scores, and DMT levels (ngm/ml) in 23 psychiatric patients

Patients and diagnosis	Sex	BPRS			Forrest test	DMT level
		Total	SUSP.	Halluc.		
1–SAPT	Female	53	5	1	Negative	0.29
2–SCUT	Male	41	3	4	Negative	0.07
3–SAPT	Female	46	6	1	Trace	0.29
4–SAPT	Female	49	4	4	1	0.13
5–SAUT	Female	58	4	1	2	0.10
6–SAATD	Female	32	3	3	Negative	0.11
7–SCUT	Female	57	5	6	Negative	< 0.05
8–SCATD	Male	45	3	4	Negative	0.13
9–ALC and DEP	Male	32	3	1	Negative	< 0.05
10–SAUT	Female	37	1	6	–	< 0.05
11–SAPT	Female	38	6	1	–	< 0.05
12–SCT(A)	Female	52	1	1	–	< 0.05
13–S-LAT	Male	19	1	1	–	< 0.06
14–Hypomanic	Male	29	1	1	–	0.15
15–SAPT	Male	40	4	6	Negative	0.07
16–SAUT*	Male	44	4	5	Negative	< 0.06
17–Hypomanic**	Male	39	1	1	Negative	0.11
18–SAATE	Female	67	5	4	–	< 0.05
19–SCT(A)	Female	unable to rate			–	0.79
20–SCUT	Male	33	2	1	–	< 0.05
21–SAUT	Female	40	5	6	–	0.05
22–SCUT	Female	26	1	3	Negative	< 0.05
23–SCUT	Male	67	6	4	Negative	0.06

SAPT–Schizophrenia, acute, paranoid type; SCUT–Schizophrenia, chronic, undifferentiated type; SAUT–Schizophrenia, acute, undifferentiated type; SAATD–Schizophrenia, acute, affective type, depressed; SAATE–Schizophrenia, acute, affective type, excited; SCT(A)–Schizophrenia, acute, catatonic type; S-LAT–Schizophrenia, latent, asymptomatic; Hypomanic–Mildly hypomanic state, ex-amphetamine abuser, not on amphetamine; ALC and DEP–Chronic alcoholic, with endogenous depression; SCATD–Schizophrenic, chronic, affective type, depressed.

* Same patient as no. 13, after acute onset of psychotic symptoms.

** Same patient as no. 14, after 90 ngm amphetamine over 4 h.

members of the staff of the NYU Neuropsychopharmacology Research Unit. The specimens were drawn directly into a vacutainer containing heparin, coded and frozen until analyzed. Analyses for DMT were done without knowledge of the subjects' psychiatric status. At the time bloods were drawn, patients were rated with the BPRS. In 14 of the 23 patients, urine was also collected and a Forrest test for phenothiazines performed (Forrest et al., 1961).

The method used for DMT analysis was a modification of the procedure of Walker et al. (1973). The original limit of sensitivity, 0.5 ng/ml blood, has been increased to 0.05 ng/ml in a 10 ml sample. If the volume of the sample is less than 10 ml the sensitivity decreases, for example the lower limit of sensitivity of a 7 cm^3 sample is approximately 0.07 ng/ml. This approximately 10-fold improvement in sensitivity was achieved by certain procedural refinements. A marked reduction in background response was realized by the elimination of the trimethylchrososilane originally used in the derivatization medium. The procedure has also been modified to include the use of undiluted deutero DMT rather than an 85/15 deutero/protio mixture as a carrier, as the absence of background interference now permits the measurement of low insensity MS signals. More stringent control of solvent used in the isolation procedure is maintained to keep the background response to a minimum. Minor improvements in isolation efficiency permits the use of 200 ng, rather than 400 ng, of the carrier/internal standard per assay, still giving sufficient sample for multiple injections. Instrumental stability has been improved by preconditioning of the magnet at the desired amperage, to permit attainment of thermal equilibrium. All these factors contribute towards the increased sensitivity of 50 pg/ml for a 10 ml blood analysis.

RESULTS

The DMT levels in whole blood found in the patient group, together with the clinical data (sex, diagnosis, total BPRS pathology score) and results of the forrest test when carried out are shown in Table 1. Because DMT is known to cause paranoid states (Wyatt et al., 1974) and is hallucinogenic (although not characteristically inducing schizophreniform hallucinations), the BPRS scores for suspiciousness and hallucinations are also specifically noted. The DMT concentrations in the whole blood samples of the 17 control subjects are presented in Table 2.

From the findings in Tables 1 and 2 means were calculated for several groups with values below the limits of sensitivity of the analysis arbitrarily considered zero. Statistical comparisons (independent t tests) were then made between the mean DMT levels of the following groups:

Table 2. Sex and DMT levels (ng/ml) of control subjects

Subject	Sex	DMT (ng/ml)
1	male	0.09
2	male	< 0.05
3	male	0.09
4	female	0.09
5	female	0.11
6	female	< 0.05
7	female	0.06
8	female	< 0.05
9	female	0.17
10	male	< 0.06
11	male	< 0.06
12	male	< 0.08
13	female	< 0.07
14	male	0.22
15	male	< 0.06
16	female	< 0.06
17	male	< 0.07

1. All patients samples ($N = 23$) mean (0.102 ng/ml) vs. all controls ($N = 17$) mean (0.049 ng/ml); not significant ($t = 1.19$, $df = 38$, $P = 0.10$).

2. Schizophrenic patients ($N = 20$) mean (0.105) vs. all controls ($N = 17$) mean (0.049); not significant ($t = 1.17$, $df = 35$, $P = 0.25$).

3. Acute patients ($N = 13$) mean (0.141 ng/ml) vs. all controls ($N = 17$) mean (0.049 ng/ml); not significant ($t = 1.62$, $df = 28$, $P = 0.10$).

4. Female patients ($N = 13$) mean (0.135 ng/ml) vs. all controls ($N = 17$) mean (0.049 ng/ml); not significant ($t = 1.51$, $df = 28$, $P = 0.10$).

5. Female patients ($N = 10$) mean (0.135 ng/ml) vs. female controls ($N = 8$) mean 0.054 ng/ml); not significant ($t = 1.00$, $df = 19$, $P = 0.25$).

6. Patients with total BPRS pathology scores of over 50 ($N = 6$) mean (0.075 ng/ml) vs. all controls ($N = 17$) mean (0.049 ng/ml); not significant ($t = 0.67$, $df = 21$, $P = 0.40$).

7. Patients with BPRS suspicion scores of 4 or over ($N = 11$) mean (0.155 ng/ml) vs. all controls ($N = 17$) mean (0.049 ng/ml) not significant ($t = 1.23$, $df = 26$, $P = 0.25$).

8. Patients with hallucination scores on BPRS of 4 or over ($N = 10$) mean (0.051 ng/ml) vs. all controls ($N = 17$) mean (0.049 ng/ml); not significant ($t = 0.08$, $df = 25$, $P = 0.25$).

9. Female schizophrenic patients ($N = 13$) mean (0.135 ng/ml) vs. male schizophrenic patients ($N = 7$) mean (0.047 ng/ml); not significant ($t = 1.02$, $df = 18$, $P = 0.25$).

Examination of these data reveals 4 of 23 patients with DMT levels greater than or equal to 0.15 ng/ml.

Table 3. Highest DMT levels and psychiatric status

DMT level (ng/ml)	Status
0.79	female, catatonic stupor
0.29	female, acute paranoid schizophrenia
0.29	female, acute paranoid schizophrenia
0.22	male, normal control
0.17	female, normal control
0.15	male, hypomanic state

In the control group of 17 subjects, 2 showed DMT levels of this magnitude. The psychiatric status and DMT level of these 6 individuals are presented in Table 3.

Since withdrawn behavior has been described after DMT administration (Wyatt et al., 1974), it was of interest to note that the highest level observed was in a female with catatonic stupor. Another female catatonic patient, however, who was not completely stuporous but withdrawn and manneristic, had a DMT level of 0.05 ng/ml.

DISCUSSION

This study is similar in design and results to three published previously (Wyatt et al., 1973; Bidder et al., 1974; Lipinski et al., 1974). It was undertaken for several reasons:

1. The floridness of pathology of some patients in this institution might maximize the chances of significant differences from controls.

2. The housing of patients on a separate research unit meant that we could guarantee some "wash out" period of neuroleptics, albeit brief in some florid cases.

3. Rating patients with the BPRS at the time blood was drawn provided an opportunity to correlate DMT levels with total pathology scores as well as subscores for suspiciousness and hallucinations.

4. The assay methodology had a sensitivity limit of 0.05 ngm DMT/ml blood, a 10-fold improvement over that in earlier studies.

Our findings are in accord with the three studies published previously. No statistically significant differences between psychiatric patients and control subjects were found. However, the results suggested that the mean DMT value was higher in the total patient group, patients with acute psychosis, female patients and patients with suspiciousness scores on the BPRS of 4 or over.

Wyatt et al. (1974) summarized the evidence implicating DMT in schizophrenia. While the present results could be interpreted as negating the DMT

hypothesis, single measurements of DMT levels in venous blood may not be the most fruitful approach to validate the hypothesis. It has been demonstrated that DMT is metabolized very rapidly in man (Wyatt et al., 1974). Therefore, venous blood levels may not reliably reflect concentrations of this psychotogen in the CNS particularly if DMT is produced and released episodically rather than continously. Frequent blood sampling from the same patient could be a better experimental approach than the occasional sampling procedure we have used. Alternatively, it may be more relevant to utilize cerebrospinal fluid for the DMT analyses.

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