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Blood and Urine Levels of N,N-Dimethyltryptamine Following Administration of Psychoactive Dosages to Human Subjects

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Abstract. Psychoactive doses (0.7 mg/kg) of the hallucinogen N,N-dimethyltryptamine (DMT) were administered intramuscularly to 11 normal subjects. A gas chromatographic-mass spectrometric isotope dilution determination of DMT concentrations in whole blood and urine revealed that only a fraction of the injected dose was recovered and the blood DMT concentrations had a very similar time course o the subjectively reported "high".

Key words: N,N-Dimethyltryptamine — Psychotomimetic — Schizophrenia — Gas Chromatography — Mass Spectrometry.

Introduction

There has been interest in N,N-dimethyltryptamine (DMT) because it is an established potent psychotomimetic (Sai-Halasz, 1962; Sai-Halasz, Brunecker, and Szara, 1958; Szara, 1956), and it has been reported to be present in human blood and urine (Franzen and Gross, 1965; Narasimhaachari, Heller, Spaide, Haskovec, Meltzer, Strahilevitz, and Himwich, 1974; Rosengarten, Szemis, Piortowski, Romaszewska, Matsumoto, Stencka, and Jus, 1970; Tanimukai, Ginter, Spaide, Bueno, and Himwich, 1970; Walker, Ahn, Albers-Schonberg, Mandel, and VandenHeuvel, 1973). Moreover, an enzymatic mechanism for its synthesis exists in man (Mandell and Morgan, 1971; Mandel, Ahn, VandenHeuvel, and Walker, 1972; Saavedra and Axelrod, 1972; Wyatt, Saavedra, and Axelrod, 1973). DMT has been proposed as a candidate for the endogenous psychotogen in schizophrenia and differences in levels of DMT in urine and blood between psychotic patients and normals have been reported. Franzen and Gross (1965) reported the presence of DMT in 11 of 37 mixed subjects (patients and normals) in a concentration of 8 to 55 ng/ml in plasma and approximately 43 μg in 24-h urine

collections. Narasimhachari *et al.* (1971) found DMT in the serum in 15 of 22 acute schizophrenics but in only 2 of 20 non-schizophrenics. The same workers gave an MAO inhibitor (tranylcypromine) and cysteine to normal and schizophrenic subjects (Narasimhachari, Avalos, Fujimori, and Himmich, 1972). They reported an exacerbation of symptoms and an increase in urinary DMT in the schizophrenics while there were no changes in symptomatology and no DMT excretion in the controls. Wyatt, Mandel, Ahn, Walker, and VandenHeuvel (1973) were unable to demonstrate any difference in DMT plasma levels between groups of normals, chronic schizophrenics, acute schizophrenics, and psychotic depressives using a more sensitive and specific method. In fact, no DMT was detected at all in plasma except for one normal and one psychotic depressive. However, in two subsequent studies (Bidder, Mandel, Ahn, Walker, and VandenHeuvel, in press; Lipinski, Mandel, Ahn, VandenHeuvel, and Walker, in press) DMT was found in blood and urine in a limited number of cases from patients with psychotic illnesses.

The purpose of this study was to determine how accurately blood and urine levels of DMT correlate with a psychotomimetic response. In addition, we were interested in measuring how much of the administered dose could be recovered in blood and urine. This has bearing on whether blood levels or urine levels are reasonable parameters to compare between psychotics and normals as a test of the endogenous psychotogen hypothesis.

Methods

Eleven male (ages 21—28) experienced hallucinogen users, indicating a desire to continue their present rate of drug use, were used as subjects. Psychiatric interviews were conducted to eliminate subjects with a history of addictive drug use or who demonstrated severe psychopathology. Subjects were instructed to remain free of psychoactive drugs for one week and free of all drugs for 72 h prior to DMT administration.

DMT was obtained from Regis Chemical Company (Chicago, Illinois). It was prepared as a sterile powder for injection by the Pharmaceutical Development Service of the Clinical Center at the National Institutes of Health. Spectrophotometric analysis demonstrated the DMT to be $96.18 \pm 0.29\%$ of labeled strength. DMT was administered intramuscularly at a dosage of 0.7 mg/kg body weight.

15 cm^3 of whole venous blood were withdrawn into a Vacutainer tube containing ACD solution formula A (Becton-Dickinson Co., Rutherford, N.J.). Immediately after collection, the blood was frozen in dry ice. Samples were assayed for DMT using a gas chromatographic mass spectrometric isotope dilution method previously described (Walker *et al.*, 1973). Urine was collected, immediately frozen, then assayed using similar methods.

Subjective "high" was assessed by asking subjects how "high" they felt on a 0 to 10 scale where 10 was "higher than you have ever been", 9 was "as high as you have ever been" and 0 was "not high at all".

Results

Fig. 1 shows individual DMT levels for subjects including those with peak, minimal, and average levels. As can be seen there are considerable individual differences in the absolute levels; however, the time course for each subjects was quite similar. There was a rapid rise in blood level

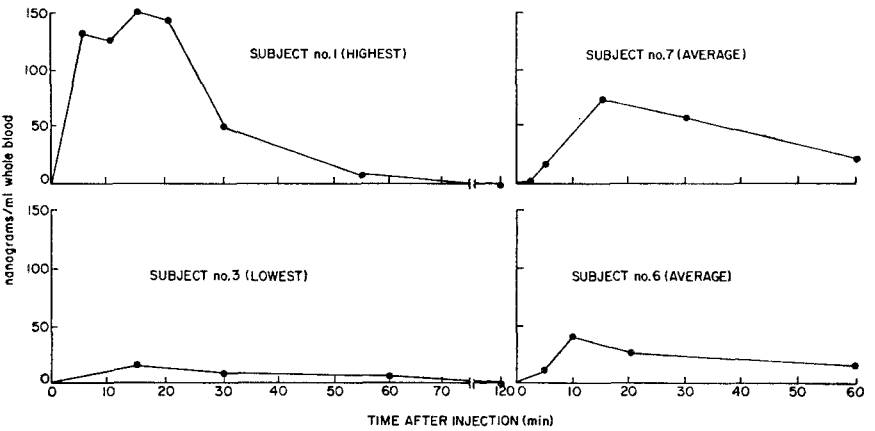

Fig. 1. Individual DMT blood levels

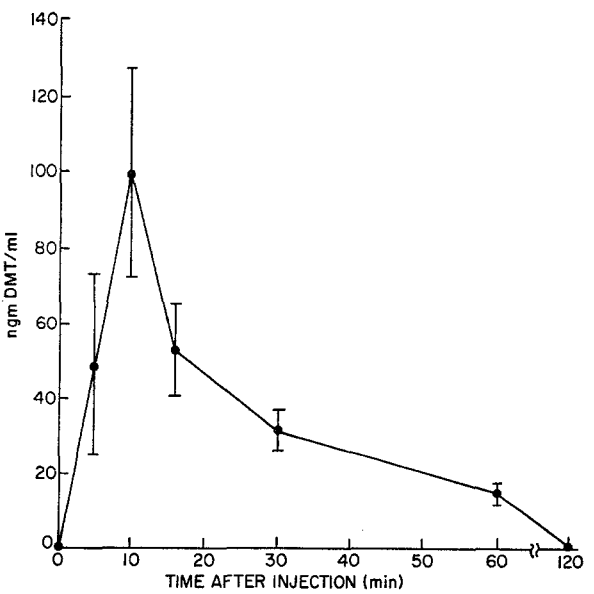

Fig. 2. Mean whole blood concentrations. Mean $\pm$ S.E.M. in ng/ml whole blood

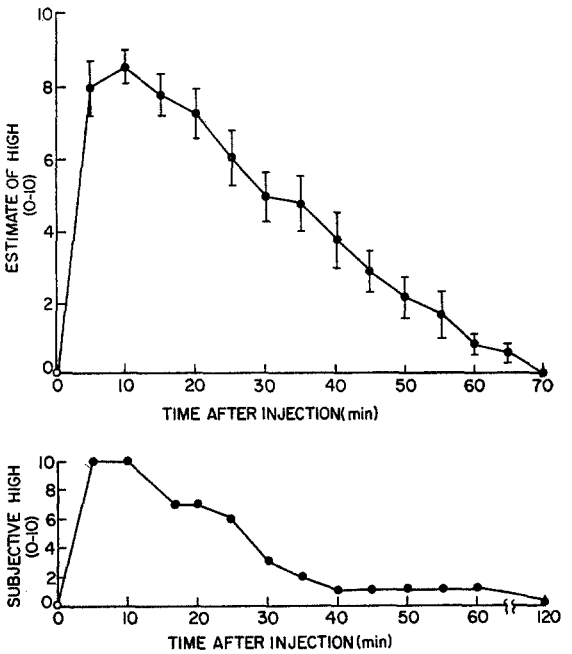

Fig. 3. a Subjective response time course. Mean ± S.E.M. Estimative "high". b Representative individual subjective response (subject no. 4)

Table 1. Urinary DMT (μg) recovered

Subject	Time		Subject	Time	
	0–2 h	2–6 h		0–2 h	2–6 h
1	24.5	10.3	8	82.6	0.40
2	9.4	0.33	9	3.35	0.81
3	59.9	0.17	10	4.18	0.65
4	36.8	0.79			

reaching a peak at 10–15 min. By 1 h, most of the DMT had disappeared. Fig. 2 shows the mean DMT concentration over time for the 11 subjects. The subjective time course was quite similar and the mean estimate of "high" over time for all the subjects as well as the curve for a typical subject is presented in Fig. 3. Table 1 presents the amounts of DMT recovered in the urine after DMT administration.

Discussion

The most striking aspect of the results was that the blood DMT levels and the subjective high appear to follow a similar time course. This and

the acuteness with the high was reached indicate that DMT's psychological effects are mediated by a mechanism requiring little or no metabolism of DMT. The intensity of the subjective experience is important since our dosage of 0.7 mg/kg has been described as just above the minimal dose necessary for psychoactivity (Sai-Halasz, 1962). However, most of these drug-experienced subjects rated the episode as "higher than they had ever been".

The peak "high" coincides with a state when all subjects are incapable of much spontaneous speech and, therefore, an exact time estimate was impossible to elicit. We have confirmed earlier work which reported that the drug effects begin in 2—3 min and last approximately 1 h (Arnold and Hofman, 1957; Rosenberg, Isbell, and Miner, 1963; Sai-Halasz, 1962; Sai-Halasz *et al.*, 1957; Szara, 1956). The blood levels indicate that the short time course is due to the rapid sequestering or metabolism of the DMT. From studies in our Laboratory (Wyatt, Gillin, Kaplan, Stillman, Mandel, Ahn, VandenHeuvel, and Walker, 1973) as well as those of Cohen and Vogel (1972), it would appear that DMT's rapid disappearance is due to rapid metabolism.

The absolute amounts of DMT in blood and urine were quite small despite the extremely intense subjective effect. Only small fractions of the ingested dose were recoverable in either blood or urine. If the highest blood level we ever recorded (154 ng/ml) is considered and a blood volume of 6560 ml assumed for this subject, the percentage of the injected dose present in the blood at any one time is only 1.8%. Thus, if a small amount of endogenous DMT were to be produced in the brain, it would not be at all surprising if this were not detectable in the blood even if serendipitously the peak time were chosen.

If the blood levels were insensitive, the urine levels were even less indicative of DMT levels. During a pilot study, it was found that at least 97% of all DMT recoverable in the urine during a 24-h collection following DMT injection was recovered in the first 5.5 h. Accordingly, we measured urinary DMT in 7 subjects for 6 h. If the largest amount recovered is considered (83 μg), it represents only 0.16% of the injected dose. The mean recovery for the 7 subjects was 0.069 ± 0.02% of the injected dose. Hence, urinary levels of DMT would not appear to be a meaningful area for comparing psychotic and normal subjects, even if DMT were an endogenous psychotogen.

These data may explain why it is not feasible to demonstrate marked differences in DMT concentrations between patients and normals. While this study does not increase the probability that DMT is an endogenous psychotogen, it can explain why failure to find urinary or plasma DMT concentration differences would not eliminate its consideration. Searching for differences in DMT metabolites may have more utility.

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