Phenylethylamine and Glucose in True Depression

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Introduction

The presence of phenylethylamine (PEA) in human urine was demonstrated by several investigators (Jepson et al., 1960; Perry, 1962; Oates et al., 1963; Fischer et al., 1968; Boulton and Mil-ward, 1971; Fischer et al., 1972; Mosnaim and Inwang, 1973; Schweitzer et al., 1975). Further, a decrease of PEA was reported in the urine of depressed patients (Fischer et al., 1972; Rodriguez Casanova and Fernandez Labriola, 1972; Boulton and Milward, 1971; Mosnaim et al., 1973), and an increase in schizophrenic patients (Fischer et al., 1972) and in a subgroup of migrainous patients (Sandler, 1972). It has been claimed that the administration of D or DL-phenyla-lanine for true depression has resulted in an improvement of their symptomatology (Yaryura-Tobias et al., 1974; Fischer et al., 1975; Nachon and Di Santo, 1974; Ipar et al., 1974; Spatz et al.,1975). Contrariwise, it has aggravated schizophrenics with symptoms of depression (Yaryura-Tobias et al., 1974).

The methodology utilized for the measurement of PEA in urine has been controversial, and some authors feel that PEA values are actually lower than that reported in human (Schweitzer et al., 1975) and in animal (Axelrod and Saavedra, 1974) experimentation.

A 24-hour urine collection seems necessary to avoid cyrcadian rhythm variations. So far, three main groups, true depressed, schizophrenics, and normal, show consistently urinary PEA/ 24-hour value differences. Thereby we may assume that even if the present methodology recovers other urinary amines in addition to PEA, group differences may indicate a biochemical trend if correlated to clinical symptomatology. Although a doubt may be cast on the role of PEA in the etiology of depression, related investigation indicates the need to reconsider and further explore this hypothesis.

For instance, the administration of tri-cyclical antidepressants (Fernandez Labriola and Rodriguez Casanova, 1973; Fernandez Labriola et al., 1974) and tetrahydrocannabinol (Sabellr et al.,

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1973) raises the level of urinary PEA in true depressed patients and in animal experimentation (Mosnaim and Sabelli, 1971; Fischer et al., 1972). Moreover, the administration of D-phenylalanine increases the level of urinary PEA in true depressed patients (Spatz et al., 1975). In addition, the most important evidence emanates from clinico-pharmacological experiments where true depressed patients have improved after D or DL-phenylalanine therapy.

Glucose disturbances have been empirically associated with depression by (a) depression being a symptom of glucose dysfunction, or (b) glucose disturbance a parameter of a depressive illness.

A glucose monoamine metabolic interaction has been shown by various investigators (McDaniel et al., 1973; Fernstrom and Wurtman, 1971; Randle et al., 1963) as well as a relationship between glucose metabolism and mental illness (Yaryura-Tobias and Neziroglu, 1975). Based on theoretical speculation we decided to study urinary PEA and oral glucose-tolerance tests in true depression. Further, we continued to study the therapeutic action of D-phenylalanine in true depression and schizophrenia.

METHODOLOGY

Twelve patients (nine female and three male) ages ranging from 28 to 58 (x = 41.66) were selected for this study according to the following criteria: Duration of illness (including remissions) was 1 to 25 years (x = 7.33). Patients manifested the following target symptoms for true depression: insomnia (waking up in the middle of the night, early awakening), anorexia, loss of balance, constipation, saburra, and worse, depressed symptomatology immediately after awakening, with evening improvement. At times, a seasonal or cyclical rhythm was reported.

In addition, previous forms of treatment, chemotherapy and ECT, usually failed to improve the symptomatology.

Pre-treatment 24-hour urinary PEA was measured by the method of Fischer et al. (1973). Medication, if any, was discontinued 72 hours previous to testing. All patients were placed on a 350 g carbohydrate load in addition to their regular diet during 72 hours previous to the test. A 50GTT was given after the administration of 100 g of a glucose solution. Plasma glucose level was measured by the orthotoluidine method (normal values, 60-100 mg/100), and curves were read according to the following criteria:

a. Normal—values return within the range at the end of the second hour.

b. Flat—an elevation of 20 mg percent or less above the fasting level, and then remaining within the range.

c. Hypoglycemic—values below the normal range.

d. Diabetic —the Wilkerson Point System (O'Sullivan, 1967).

e. Prediabetic—normal fasting and inability to return to normal at the end of the second hour.

f. High-low—a diabetic or prediabetic curve during the first two hours followed by a hypoglycemic response.

D-phenylalanine was given in 50 or 100 mg capsules between 100 and 300 mg per day (x = 200 mg). This was an open study of two-week duration.

Clinical psychiatric and psychological evaluations were performed before, during, and after treatment. Family interviews were held to assess patients' improvement from their viewpoint. Patients were kept on their regular diets that in Buenos Aires usually consist of beef, salads, and fresh fruit. Alcohol intake and the use of any other medication was forbidden. Routine blood chemistry was done at pre- and post-treatment.

RESULTS

Results indicate values of urinary PEA to range from 12-76 mcg/24 hours (x = 38) (normal range: 130-350 mcg/24 hour).

50GTT has shown that 10 out of 12 presented a disturbance of glucose metabolism (see Table 1). Improvement was shown by the fifth day and good remission of symptoms by the second week. At times, four weeks was necessary to complete treatment (N = 2). In two cases, where improvement was not present, tricyclical medication (desipra-mine) enhanced DL-phenylalanine therapy. Side effects were few: mild headaches (N = 2), low blood pressure (N = 2), agitation (N = 1). In the latter, desipramine in conjunction with levothy-roxine and hydroxycobolamine controlled the depression. Three cases of schizophrenia not tabulated in this study became worse after the administration of D-phenylalanine. Routine blood work, CBC, SMA-12, urinalysis, remained within normal limits.

TABLE 1
PRE-TREATMENT PHENYLETHYLAMINURIA AND 50GTT VALUES IN TRUE DEPRESSION

NO.=12	AGE	DURATION/YEARS	URINARY PEA ug./24 HR. NORMAL VAL. (130-350)	50GTT									
				FAST	30 MIN.	1 HOUR	2 HOUR	3 HOUR	4 HOUR	5 HOUR	6 HOUR	TYPE	IMPROVEMENT
M.L.	58	3	31	80	80	80	100	80	80	100	100	F	VERY GOOD
M.S.	36	6	47	80	117	77	72	69	95	92	90	F	NEGATIVE
N.T.	41	12	46	80	119	110	79	69	70	81	85	F	NEGATIVE
CH.T	38	4	40	90	130	120	80	100	70	—	—	N	GOOD
M.S.	35	10	31	67	107	—	90	86	73	91	72	F	GOOD
M.D.	53	25	21	90	100	90	90	90	100	90	—	F	GOOD
C.V.	41	2	23	86	165	210	270	170	—	—	—	P_D	GOOD
L.M.	37	7	66	75	80	80	75	60	60	60	70	H	VERY GOOD
M.P.	28	3	76	84	84	70	56	72	72	70	70	H	MILD
Z.C.	58	1	12	80	140	130	110	100	80	70	—	F	NEGATIVE
G.D.	44	10	28	49	84	42	48	49	36	35	—	H	GOOD
H.A.	31	5	42	100	160	120	110	105	80	70	60	N	GOOD

N = NORMAL CURVE
F = FLAT CURVE
H = FUNCTIONAL HYPOGLYCEMIA
P_D = PREDIABETIC

DISCUSSION

The results of this study corroborate previous reports that suggest D and DL-phenylalanine as an antidepressant for true depression. So far, the main evidence to endorse PEA as a biochemical variable of true depression is indicated by clinical and biochemical observations. In this regard, some discrepancies are also observed. For example, not every experimenter reports the same period of time between onset of treatment, improvement, and duration of treatment. Also, positive results vary from 50 percent to 100 percent. It is difficult to accept an antidepressant that offers 100 percent of therapeutic efficacy (Nachon and Di Santo, 1974). It may be added that the action of D or DL-

phenylalanine to improve true depressed patients does not necessarily indicate a disorder of PEA metabolism, as long as we remember that the administration of one amino acid may throw off balance other amino acids. The presence of a glucose imbalance in our patient population may suggest a monoamine disorder. However, it should be remembered that poor dietary habits, anorexia, and stress are causes of glucose disturbance and they may also be present in true depression. Thus, to arrive at very conclusive statements is, at this stage, from the clinical viewpoint, premature.

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