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Levels of Total and Free Tryptophan in the Plasma of Endogenous and Neurotic Depressives

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Summary. The levels of total and free tryptophan were determined in the plasma of 34 endogenous depressives, 20 neurotic depressives and 25 healthy volunteers. Whilst the levels of total tryptophan were not different in the three groups, the level of free tryptophan was reduced in both endogenous and neurotic depressives. No difference could be found between endogenous and neurotic depressives.

Key words: Total tryptophan – Free tryptophan – Endogenous depression – Neurotic depression

Zusammenfassung. Gesamt- und freies Tryptophan wurde im Plasma von 34 endogen Depressiven, 20 neurotisch Depressiven und 25 gesunden Kontrollpersonen bestimmt. Während beim Gesamttryptophan kein Unterschied zwischen den drei Gruppen festgestellt werden konnte, war das freie Tryptophan bei endogen Depressiven und neurotisch Depressiven signifikant erniedrigt. Zwischen endogen und neurotisch Depressiven fand sich kein Unterschied.

Schlüsselwörter: Gesamt- und freies Tryptophan – Endogene Depression – Neurotische Depression

Introduction

Over the past two decades, biochemical research has provided evidence for the role of biogenic amines in affective disorders. One biogenic amine that has received much attention together with its metabolites is 5-hydroxytryptamine (serotonin). To date, a significant reduction of 5-hydroxyindolaceticacid (5-HIAA) has been found, which is one of the principal metabolites of serotonin in the CSF of depressives [1, 3, 12]. Furthermore, post-mortem studies have shown that in some

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areas of the brain of suicidal patients with endogenous depression a significant reduction in serotonin and 5-hydroxyindolaceticacid is found [8, 15]. Van Praag found, in a tryptophan loading study, a reduced serotonin turn-over in the CSF of depressives [16]. These findings suggest a possible deficiency in the serotonin (5-hydroxytryptamine) metabolism in the brain of depressive patients, which has led to therapeutic trials using l-tryptophan and 5-hydroxytryptophan, the precursors of serotonin. The level of tryptophan in the plasma of depressives has also been reported to be reduced, though there have been conflicting reports [4, 5, 13, 17]. Less controversy, however, exists over the reduction of free tryptophan in the plasma of depressive patients. Free tryptophan is the non-albumin bound portion of tryptophan which, alone, is thought capable of crossing the blood–brain barrier. Of interest in this context is the report of Fiori [7], who found that in contrast to the reduced levels of total and free tryptophan in the plasma of five endogenous depressive patients, neither total nor free tryptophan was reduced in the plasma of five neurotic depressives. This difference may provide the means for differentiating between both types of depressive disorders. The purpose of the present study was to apply these ideas to a larger patient population, and to test the feasibility of this method as a means of differentiating between endogenous and neurotic depression.

Patients and Methods

Blood samples were collected from 54 depressive patients residing in a psychiatric hospital. Of these, 34 suffered from endogenous depression (13 males, 21 females), and 20 from neurotic depression (8 males, 12 females). The diagnostic classification was based on the data of standard psychiatric interviews and case histories, requiring the agreement of at least two psychiatrists on the diagnosis. The diagnostic criteria for endogenous depression were those mostly used in the classical German school of psychiatry [9, 14]. The criteria for neurotic depression were adequate conflicting situation, long duration and lack of the typical clinical characteristics of endogenous depression. It was also taken into account that there are endogenous depressions released by

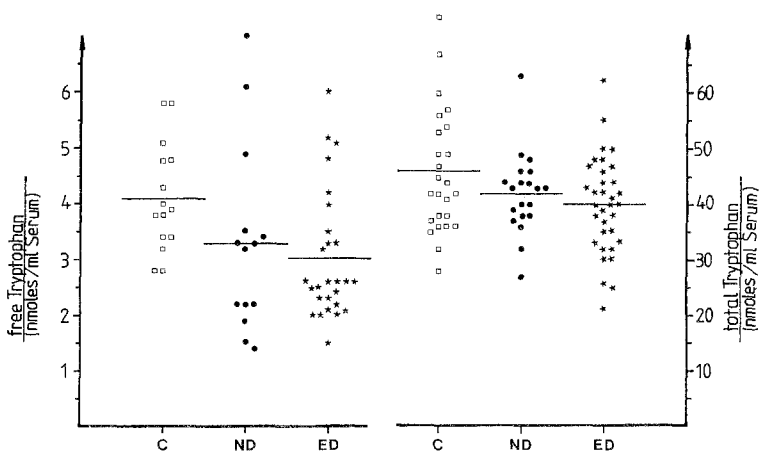

Fig. 1. Single values in nmol/ml of free and total tryptophan for controls (*C*), neurotic depressives (*ND*) and endogenous depressives (*ED*). Bar indicates mean

Table 1. Mean, standard deviation and median are shown for free and total tryptophan for the three groups separately

		Endogenous depressive	Neurotic depressives	Controls
Free tryptophan	$\bar{x}$	3.02	3.29	4.1
	s	1.15	1.68	0.97
	n	27	14	15
	median	2.6	3.25	3.85
Total tryptophan	$\bar{x}$	39.9	42.0	45.8
	s	8.7	7.3	12.0
	n	34	20	25
	median	40.0	43.0	42.0

external events [11]. Blood samples were collected between 8.00 and 9.00 a.m. before breakfast. Patients had been without treatment for at least 3 days. Four of the endogenous depressive and eight of the neurotic depressive patients had received no psychopharmacological treatment for at least 1 month before the study. Two patients had received tryptophan as treatment.

Total and free tryptophan were measured by the method of Eccleston [6] with some modifications (Bloxan et al. [2]). The results were compared to a group of 25 healthy volunteers (17 males, 12 females).

Results

Our results showed a significant reduction in free tryptophan and a non-significant reduction in total tryptophan in the plasma of the two patient groups compared to the controls (Fig. 1 and Table 1). The difference in free tryptophan between the endogenous depressives and controls was significant ($P < 0.002$, Wilcoxon and Mann-Whitney tests), between neurotic depressives and controls somewhat less significant ($P < 0.05$). No significant difference could be shown between males and females in the groups of controls and neurotic depressives. In the endogenous depressive group males had significantly higher values for both total and free tryptophan (Table 2). By comparing males and females of the endogenous depressive and the control group separately, no difference could be shown between the males of the two groups, a significant difference ($P < 0.002$) was shown between the females of the two groups for free tryptophan, none for total tryptophan. The two patients who had received tryptophan as treatment did not show raised values (2.1 and 5.2 nmol/ml). Although the mean age of the three groups was different (controls $\bar{x} = 33$ years, neurotic depressives $\bar{x} = 43.5$ years, endogenous depressives $\bar{x} = 53$ years), no correlation could be shown between age and level of either total or free tryptophan for either of the three groups ($r < 0.2$ and $r > -0.3$). Furthermore no correlation existed between levels of free and total tryptophan for endogenous and neurotic depressives; however, a slight positive correlation was found for controls

		Endogenous depressives	
		Total tryptophan	Free tryptophan
Males	$\bar{x}$	45.9	3.84
	s	7.2	1.42
	n	13	8
Females	$\bar{x}$	36.1	2.7
	s	7.5	0.84
	n	21	19

Table 2. Mean and standard deviation of total and free tryptophan for the endogenous depressive group separated for sex

($r = 0.7$, $P < 0.05$). No difference could be shown between the two groups of neurotic and endogenous depressives for either total or free tryptophan, or the percentage free of total tryptophan.

Discussion

These results are in accordance with the reports of Coppen et al. [4, 5], who also found a reduction in free tryptophan in depressive patients, but not for total tryptophan. The differences of our results to the results of Fiori [7] may be due to differences in the diagnostic criteria or to sample size. The fact that the level of free tryptophan was reduced not only in endogenous depressives but also in neurotic depressives is surprising. Two explanations seem possible. (i) The reduction in free tryptophan in both neurotic and endogenous depressives may be not a cause but a consequence of depression. (ii) It cannot be excluded that our chronic neurotic depressive inpatients were in fact endogenous depressives. It is known since the investigations of Kinkelin [10] that prognosis and particularly the degree of remission of endogenous depression is not as favourable as it was believed at the time of Kraepelin. Huber [9] suspects that chronic endogenous depression with a blander clinical picture occur more frequently since the introduction of the antidepressant drugs. Our results might therefore indicate that tryptophan investigation might contribute to distinguish between true and apparent neurotic depression. Furthermore it should be taken into account that a further differentiation of neurotic and endogenous depression might be possible by investigation of additional biochemical parameters.

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