

Interest of 5-hydroxytryptophan (5-HTP) as a neuroendocrine marker in depressive illness*

A negative report

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ABSTRACT

Among 8 primary depressives, 4 schizophrenics, 4 manics and 4 normal controls, 5-hydroxytryptophan (5-HTP), the precursor of serotonin (200 mg p.o.), appears devoid of any stimulating activity on the liberation of growth hormone (GH). So, 5-HTP test can not be useful as a specific neuroendocrine marker of serotonergic metabolism in depressive patients [Acta psychiat. belg., 83, 50-56, (1983)].

Key words: 5-HTP, neuroendocrine test, depression.

Introduction

Various arguments suggest that there is a disturbance of monoaminergic metabolism in depression, particularly that of noradrenaline and/or serotonin (5-HT) (for review, see van Praag, 1980a and 1980b).

A specific disturbance in the serotonergic transmission seems to exist in certain types of depression, notably « vital depression ». Arguments supporting this conclusion are as follows.

1. *Post mortem* brain studies revealed that the concentration of 5-HT and its principal metabolite (5-HIAA) may be subnormal in suicide victims (Lloyd *et al.*, 1974) as well as depressive patients deceased from natural causes (Birkmayer and Riederer, 1975).

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2. CSF studies revealed a decrease of baseline 5-HIAA in a subgroup of depressive patients (Åsberg *et al.*, 1976a) ; after probenecid, which inhibits the transport of 5-HIAA from the CNS to the bloodstream, the accumulation of 5-HIAA is decreased in about 40 % of the patients (van Praag and Korf, 1971 ; van Praag *et al.*, 1973 ; Post and Goodwin, 1978).
3. Plasma concentration of free tryptophan is decreased in relation to that of other neutral aminoacids such as leucine and isoleucine (Møller *et al.*, 1976 ; Coppen and Wood, 1978). In ventricular CSF, tryptophan is lower in vital depressive patients (Bridges *et al.*, 1976).
4. Antidepressants like zimelidine are specific reuptake inhibitors of 5-HT (Ögren *et al.*, 1980).
5. 5-HTP possesses antidepressant properties, especially in the subgroup with low CSF 5-HIAA values (van Praag, 1977).
6. 5-HTP can also possess prophylactic properties in recurrent unipolar and bipolar depressive patients with low CSF 5-HIAA values (van Praag and De Haan, 1980).
7. CSF 5-HIAA values in vital depression are negatively correlated to suicidal tendencies, especially to violent suicide (Åsberg *et al.*, 1976b ; Banki *et al.*, 1981 ; Träskman *et al.*, 1981).
8. In healthy subjects, low CSF 5-HIAA values were found to correlate positively with the incidence of depression in the family (Sedvall *et al.*, 1980).

TABLE

Tryptophan → 5-hydroxytryptophan → 5-hydroxytryptamine

(5-HTP)

Serotonin

(5-HT)

↓

5-hydroxyindoleacetic acid

(5-HIAA)

5-HTP is the direct precursor of 5-HT ; but, unlike 5-HT, it passes the blood brain barrier (table). It is therefore thought to possess neuroendocrine activity, and indeed, three studies have reported for it a stimulating activity on the liberation of growth hormone (GH) in normal subjects :

1. Yoshimura *et al.* (1973), with a dose of 200 mg of 5-HTP p.o. in 7 normal subjects eliciting a plasma GH response between 7 and 18.8 ng/ml ;

2. Imura *et al.* (1973), with 150 mg p.o. in 8 normal subjects obtaining 6 responses higher than 5 ng/ml (mean = 15.1 ± 3.6 ng/ml) ;

3. Lancranjan *et al.* (1977), with 200 mg I.V. in 11 subjects (in association with a peripheral decarboxylase inhibitor benserazide) giving a response in 9 subjects (mean = 40.4 ± 9.9 ng/ml).

However, two studies found no stimulating activity :

1. Müller *et al.* (1974) with oral administration of doses as elevated as 150 mg/kg in 7 subjects ;

2. Benkert *et al.* (1973) with doses of 75, 100 and 150 mg. I.V. (administered with benserazide) in 8 subjects.

In depressed patients, Takahashi *et al.* (1973) found a stimulating activity of 5-HTP (200 mg p.o.) on the liberation of GH in 4 bipolars in the manic phase ; on the contrary, 3 bipolars in the depressive phase did not respond. Among 5 unipolars, 3 demonstrated a liberation of GH while 6 « protracted » depressives failed to show a GH response.

Westenberg *et al.* (1982), however, did not find any stimulating activity of oral 5-HTP in 14 depressives and 12 normal controls, with association of a decarboxylase inhibitor (carbidopa).

The aim of this study was to evaluate the interest of the 5-HTP test as a neuroendocrine marker of serotonin metabolism. If a decrease in the GH response could be expected in certain depressives which would demonstrate a specific disturbance of 5-HT metabolism in these patients, then the 5-HTP test could be used to predict a favorable response to specific uptake inhibitor antidepressants such as zimelidine.

Material and methods

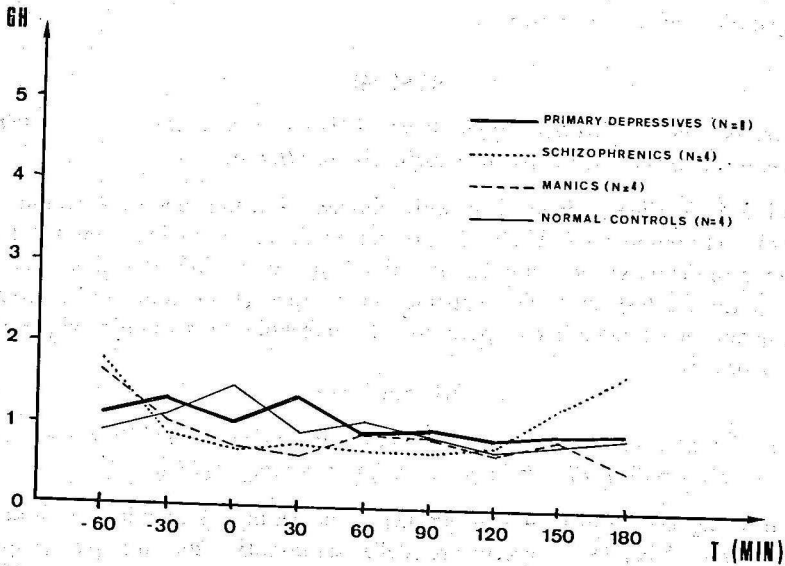
A group of 8 unipolar primary depressive patients (4 male and 4 female, age 30-60, mean = 45.7), hospitalized at the Psychopharmacology Unit of the University Hospital « de Bavière », Liege, Belgium, were included in the study. They met Research Diagnostic Criteria and had a score greater than as equal to 21 in the Hamilton Depression Scale. As a control, a group of 4 schizophrenics (2 male and 2 female, age 19-52, mean = 25.5), 4 manics (3 male and 1 female, age 40-52, mean = 46.7) and 4 normal subjects (3 male and 1 female, age 28-38, mean = 32.5) were also included. All patients met Research Diagnostic Criteria (Spitzer *et al.*, 1978). In addition, all patients (the test group as well as the controls) had been free of any medication for at least 2 weeks at the time of study.

The test was conducted following the same procedure as Takahashi *et al.* (1973). The patients fasted overnight and at 7 a.m. a catheter was inserted into a forearm vein. Blood was taken at 30 minutes intervals for 1 hour before and 3 hours after administration of 200 mg of 5-HTP. No decarboxylase inhibitor was associated. After the blood collections, the arterial pressure, pulse rate, psychic modifications and untoward effects were noted. GH was measured by radioimmunoassay (Franchimont, 1968).

Results

1. Primary depressives.

No stimulating activity of 5-HTP on GH resulted in any of the patients in this group. There was also no modification of blood pressure, pulse or psychic state. In one case, the patient presented transient nausea.



2. Schizophrenics.

No stimulating action of 5-HTP on GH; no modification of arterial pressure, pulse or psychic state; no untoward effects.

3. Manics.

No stimulating action of 5-HTP on GH; no modification of blood pressure, pulse or psychic state; no untoward effects.

4. Normal controls.

No stimulating action of 5-HTP on GH; no modification of blood pressure, pulse or psychic state; no untoward effects.

Discussion and conclusion

Based on the results of this methodological procedure, the 5-HTP test appears to be devoid of any interest as a neuroendocrine marker. Contrary to the report of Takahashi *et al.*, none of the patients (primary depressives, schizophrenics or manics) have shown an increase of GH after the intake of 5-HTP. Moreover, the stimulating activity of serotonin on the liberation of GH under these conditions has not been confirmed.

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RESUME

Intérêt du test au 5-hydroxytryptophane (5-HTP) en tant que marqueur neuroendocrinien dans les états dépressifs. Un résultat négatif.

Chez 8 déprimés primaires, 4 schizophrènes, 4 maniaques et 4 témoins, le 5-hydroxytryptophane (5-HTP), le précurseur de la sérotonine (200 mg p.o.), se montre dépourvu de toute activité stimulante sur la libération d'hormone de croissance. Le test au 5-HTP apparaît donc dépourvu de toute utilité comme marqueur neuroendocrinien spécifique du métabolisme sérotoninergique chez les déprimés.

RIASSUNTO

Ricerca sull'eventuale interesse del 5-idrossitriptofano (5-HTP) come marcatore endocrino degli stati depressivi. Un risultato negativo.

In 8 depressi primari, 4 schizofrenici, 4 maniacali e 4 campioni, il 5-idrossitriptofano (5-HTP), il precursore della serotonina (200 mg p.o.), appare sprovvisto di qualsiasi attività sulla liberazione dell'ormone della crescita. Il test al 5-HTP non appare quindi di alcuna utilità come marcatore endocrino specifico del metabolismo serotoninergico nei depressi.

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