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Discrimination of Idiopathic Pain Syndromes from Neurogenic Pain Syndromes and Healthy Volunteers by Means of Clinical Rating, Personality Traits, Monoamine Metabolites in CSF, Serum Cortisol, Platelet MAO and Urinary Melatonin

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Summary. The aim of the present study was to investigate the discriminative power of a series of variables (including determination of depressive symptomatology by means of a visual analogue scale, determination of personality traits by means of the Karolinska Scales of Personality, determination of monoamine metabolites in CSF, platelet MAO activities, serum cortisol before and after dexamethasone suppression and urinary melatonin) in differentiating (a) chronic pain patients from healthy subjects, and (b) patients with idiopathic pain syndromes from patients with neurogenic pain syndromes. Separately each of the measures gave a significant but often low contribution to the discrimination, while a combination of several measures gave a complete discrimination both between healthy subjects and patients with chronic pain syndromes and between patients with idiopathic and neurogenic pain syndromes, respectively.

Key words: Chronic pain – Idiopathic pain – Neurogenic pain – Visual analogue scale – Personality traits – KSP – 5-HIAA – HVA – Cortisol – MAO – Dexamethasone – Melatonin – Discriminant analysis

Introduction

The clinical diagnosis of patients with chronic pain syndromes is often a difficult task. In long standing pain syndromes, the clinical picture usually changes over time and the clinical profile becomes similar to that seen in patients with depressive syndromes (Sternbach 1974; von Knorring 1975). Sometimes a somatic lesion is found, sometimes not, and even if a lesion is found it is difficult to decide if the lesion is an adequate explanation for the presence of the chronic pain syndrome (Merskey and Spear 1967; Sternbach 1974).

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In some of the patients, no somatic lesion is found despite long standing efforts, in other patients it seems obvious that the clinical picture cannot be explained by the lesions found. It has been suggested that the patients have a distinct psychobiological disorder – the pain prone disorder – with characteristic clinical, psycho-dynamic, biographic and genetic features (Blumer and Heilbronn 1982). Williams and Spitzer (1982) criticised the name – the pain prone disorder, and suggested the term „idiopathic pain syndrome", as used in the present study.

In a series of studies, we have compared patients with idiopathic pain syndromes with healthy volunteers and patients with defined neurogenic pain syndromes and been able to demonstrate pronounced differences as concerns depressive symptomatology (Almay 1986), personality traits (von Knorring et al. 1986), 5-hydroxy indole acetic acid (5-HIAA) and homovanillic acid (HVA) in CSF (Almay et al. 1986b), platelet in monoamine oxidase (MAO) activity (Almay et al. 1986a), serum cortisol and response to dexamethasone suppression of serum cortisol (Almay et al. 1986c) and melatonin in serum and urine (Almay et al. 1986d). Usually, the patients with idiopathic pain syndromes deviate from healthy volunteers in the same way as patients with depressive syndromes, and it has been suggested by Blumer and Heilbronn (1982) that the idiopathic pain syndrome is a variant of depressive disease. However, usually the patients with neurogenic pain syndromes also deviate from the healthy volunteers, often in the same direction as the patients with idiopathic pain syndromes and thus, the clinical delineation between patients with idiopathic pain syndromes and patients with somatic lesions is still a difficult task.

There are some reports indicating the possibility of differentiating patients with idiopathic pain syndromes from patients with defined somatic lesions using clinical variables (Blumer and Heilbronn 1982), serum cortisol determinations (Shenkin 1964; Lascelles et al. 1974; Johansson 1982a) and endorphins, fraction I (Almay et al. 1978; von Knorring et al. 1983). However, there are still several questions unanswered.

Thus, the purpose of the present study was to determine to what extent patients with chronic pain syndromes can be discriminated from healthy volunteers and to what extent patients with idiopathic pain syndromes can be discriminated from patients with neurogenic pain syndromes, and to determine which of the variables – depressive symptomatology, personality traits, serum cortisol determinations, dexamethasone suppression, monoamine metabolites in CSF, platelet MAO and urinary melatonin – are the most important in such a discrimination.

The selection of parameters used in the study, was based on variables that were easily and generally accessible and often showed deviances in patients with depressive disorders.

Depressive symptomatology was determined by means of self-rating on a visual analogue scale (VAS). The method has been proven to have a high validity and a high reliability (Johansson 1982b).

The personality traits were determined using the Karolinska Scales of Personality (KSP). The scales have been proven to be fairly independent of the state of the subjects (Perris et al. 1979), and patients with depressive disorders have been demonstrated to have a special response pattern (Perris et al. 1984). In a discriminant function analysis where healthy subjects were separated from depressed patients by means of KSP, 81.3% of the subjects were correctly classified (von Knorring et al. 1984).

In patients with depressive disorders, disturbances in the serotoninergic systems have been claimed to be of importance in the pathogenesis (Coppen 1967; van Praag et al. 1973). If so, the concentrations of the serotonin metabolite 5-HIAA in CSF should be reduced, and results in favour of the hypothesis have been reported by Åsberg et al. (1984). However, they also found a reduction in the concentrations of the dopamine metabolite HVA in CSF (Ågren 1981). Thus, determinations of both 5-HIAA and HVA in CSF were included in the present study.

5-HIAA in CSF has been demonstrated to be a rather state dependent marker of the turnover in the serotoninergic systems (Åsberg et al. 1984). However, in healthy volunteers, a significant positive correlation exists between the concentrations of 5-HIAA in CSF and the activity of MAO in platelets (Oreland et al. 1981). Platelet MAO activities are under strong genetic control (Revely et al. 1983). Thus, if low concentrations of 5-HIAA could be demonstrated with normal platelet MAO activities, the disturbances in the serotoninergic systems could be regarded as related to the state of the patients, while low concentrations in both 5-HIAA in CSF and low platelet MAO activities would indicate a genetically determined low turnover in the serotoninergic systems. Furthermore, patients with depressive disorders with pain as a prominent symptom have been found to have low platelet MAO activities (von Knorring et al. 1984).

In patients with affective disorders, the most extensively reported neuro-endocrine abnormality is hyper-secretion of cortisol (Sachar 1975). Non-suppression to dexamethasone has also been suggested as a specific laboratory test for the diagnosis of melancholia (Carroll et al. 1981). Originally, the dexamethasone suppression test (DST) was reported to have a very high specificity (96%) and a lower sensitivity (67%) (Carroll et al. 1981). Abnormal dexamethasone suppression has since been reported in normal subjects (Hällström et al. 1983) and in a variety of psychiatric disorders (Coppen et al. 1983; Berger et al. 1984). Thus, both sensitivity and specificity of the test seem to be lower than originally reported but still hyper-secretion and dexamethasone non-suppression are common findings in patients with depressive disorders.

Another biological marker of great interest in patients with depressive disorders is melatonin in serum and urine (Wetterberg et al. 1979; Beck-Friis 1983; Brown et al. 1985). It has been demonstrated that a subgroup of depressed patients has low concentrations of serum melatonin and high concentrations of serum cortisol at 2 a.m. and low concentrations of urinary melatonin collected during the night (Beck-Friis 1983).

As the patient series collected so far is too small to permit subdivision to a criterion sample and a replication sample, in its present form, the study is hypothesis-generating rather than hypothesis-testing.

Methodology

The Series. The series consisted of patients with idiopathic pain syndromes fulfilling the criteria of Williams and Spitzer (1982), i.e. (a) preoccupation with severe pain of at least 6 months duration as the predominant disturbance, (b) the pain presented as a symptom is inconsistent with the anatomic distribution of the nervous system; after extensive evaluation no organic pathology or patho-physiological mechanism can be found to account for the pain; or when there is some related organic pathology, the complaint is grossly in excess of what would be expected from the physical findings, and (c) not due to somatization disorder or major depression.

The series included 67 patients, 30 males and 37 females, with a mean age of 45.9 years. The mean duration of the pain syndromes was 70.7 ± 75.6 months. The mean age at onset of the pain syndrome was 40.1 ± 12.1 years. The localization of the pain syndromes were: head and face, $n = 10$, shoulder and upper extremities, $n = 11$, breast, $n = 3$, abdomen, $n = 2$, genitalia, $n = 6$, lower back pain and pain in lower extremities, $n = 19$, multiple, diffuse pain syndromes, $n = 16$. The series is described in detail elsewhere (Almay 1986). As there were several patients in which one or several of the included variables were missing, the number of subjects was different in the different analyses made. At each occasion the correct number is given.

A second series included 35 patients with clearly defined neurogenic pain syndromes in whom a somatic lesion was clearly present and in whom the pain syndrome presented seemed to be in agreement with what could be expected in relation to the lesion found. The series included 18 male and 17 female patients with a mean age of 44.1 ± 11.2 years. The mean duration of the pain syndrome was 68.2 ± 71.9 months. The localization of the pain syndromes was: head and face, $n = 9$, upper extremities, $n = 7$, lower back and lower extremities, $n = 19$. The series is described in detail elsewhere (Almay 1986). Due to missing data a smaller number of the subjects was usually included in each of the separate analyses.

The healthy volunteers comprised 137 subjects, 56 males and 81 females with a mean age of 35.3 ± 9.9 years. Most of them were staff at the University Hospital or their relatives. None of them had any symptoms or signs of a psychiatric or somatic disturbance at examination in relation to the experimental investigation. Most subjects did not complete all the different experiments and thus the number was considerably smaller in several analyses.

The clinical differentiation between patients with neurogenic pain syndromes and patients with idiopathic pain syndromes was made exclusively by means of the presence of pain of more than 6 months duration, the description of the pain, the physical findings and the results of extended investigations aiming at defining the presence of any somatic lesion.

The results of the experimental investigations were not known at the time when the clinical diagnosis was made. Most of the samples for determinations of platelet MAO, 5-HIAA, HVA and melatonin were kept in the freezer. The VAS, the personality inventory and the results of the cortisol determinations were kept separately until the diagnosis was made. Thus, the clinical diagnosis was not confounded in any way by the experimental results used in the discriminant analysis.

Visual Analogue Scale. A sheet with six separate VAS, each consisting of a 100-mm long horizontal line with definitions in the ends but with no marks in between was used. The six items covered were: sadness, bodily discomfort, inner tension, concentration difficulties, pain and memory disturbances. The item pain was not included in the discriminant analysis as this item was used in the clinical delineation of the groups. The VAS used is described in detail elsewhere (Johansson 1982b).

Personality Inventory. The personality inventory was constructed for research purposes at the Department of Psychiatry and Psychology of the Karolinska Institute in Stockholm to measure stable personality traits. The inventory is denoted KSP (Schalling and Edman 1986).

The inventory comprises 135 questions grouped in 15 scales: psychic anxiety, somatic anxiety, muscular tension, social desirability, impulsiveness, monotony avoidance, detachement, psychasthenia, socialization, indirect aggression, verbal aggression, irritability, suspicion, guilt and inhibition of aggression.

Most of the scales are based on hypotheses of biologically relevant temperament dimensions (Schalling et al. 1983). In most scales, items were primarily selected from rational-theoretical considerations rather than by factor-analytical or empirical techniques. The scale is described in more detail in von Knorring et al. (1984a).

Serum Cortisol. Serum cortisol was determined at 9 a.m. and at 4 p.m. under standardized conditions by means of a radioimmunoassay kit produced by Farmos Group Ltd, Finland. The methodology is described in more detail elsewhere (Johansson 1982a).

Dexamethasone Suppression Test. For the DST 1 mg of dexamethasone was given at 11 p.m. and serum cortisol was determined at 9 a.m. and 4 p.m. the day after.

5-HIAA and HVA in CSF. A lumbar puncture was performed after 12 h of rest with the patient in a lateral recumbent position. A 12 ml sample of CSF was withdrawn, carefully mixed and frozen at −80°C. The determination of 5-HIAA and HVA were made simultaneously using the method of Magnusson et al. (1980) with minor modifications. The method is based on HPLC with electrochemical detection.

Platelet MAO Activity. Blood samples of 4.5 ml were taken, and about 1 ml of platelet rich plasma was obtained after sedimenation of the erythrocytes for 2–4 h at room temperature. The platelet count was performed using a Coulter Counter, and the plasma stored at −80°C until analysis. All samples were analysed in duplicate using beta-phenylethylamine and tryptamine as substrates. The methodology has earlier been described in detail (Eckert et al. 1980). In the present analysis, only MAO activities with tryptamine as a substrate were included due to the high correlation ($r = 0.94$) between results obtained using the different substrates.

Urinary melatonin. The subjects emptied their bladders at 10 p.m. and all urine produced from 10 p.m. to 8 a.m. was collected and frozen at −20°C. The analysis was performed using commercially available radioimmunoassays for melatonin (WHB, Box 19018, S-161 19 Bromma, Sweden), described in detail elsewhere (Beck-Friis 1983).

Statistics. All the statistical analyses were performed at the Umeå University Computer Center (UMDAC) by means of the Statistical Package for the Social Sciences (SPSS). In the present study a series of discriminant analyses were made, all by means of Wilk's method. A stepwise selection was used by means of the rule to reduce Wilk's lambda. Minimum tolerance level was 0.001, minimum F to enter 1.00 and maximum F to remove 1.00.

The aim of the study was to determine the discriminative power of the experimental procedures used and to determine the type of variables and the number of variables most useful in the discriminative procedure between healthy subjects and chronic pain patients, and between patients with neurogenic and idiopathic pain syndromes, respectively.

As the number of subjects was rather small when several experimental variables were introduced in the discriminant function analysis, and as the main aim of the study was exploratory, no division of the series was made in a criterion and a replication sample. Thus the results of the present study are to be replicated in later studies. Sensitivity was calculated as number of correctly classified healthy subjects/total number of healthy subjects × 100 and specificity as number of true classified pain patients/total number of pain patients × 100. The technique is described elsewhere (von Knorring et al. 1984a).

Results

Differentiation of Healthy Volunteers from Chronic Pain Patients

Depressive Symptomatology. By means of self-rating of depressive symptomatology by means of a VAS covering sadness, bodily discomfort, inner tension, concentration difficulties and memory disturbances, 85.1% of the subjects were correctly classified (Table 1). Only two items – bodily discomfort and memory disturbances – were selected (Wilks lambda = 0.50, $\chi^2 = 77.27$, $df 2$, $P < 0.001$). The sensitivity was high but specificity lower.

Personality Traits. By means of personality traits determined by means of KSP, 80.3% of the subjects were correctly classified. Of the scales 8 were included in the discriminant function – somatic anxiety, muscular tension, social desirability, monotony avoidance, psychasthenia, indirect aggression, suspicion and inhibition of aggression (Wilks lambda = 0.52, $\chi^2 = 94.93$, $df 8$, $P < 0.001$). Thus depressive symptomatology and personality traits distinguished chronic pain patients from healthy subjects to about the same extent (Table 1).

5-HIAA, HVA in CSF and Platelet MAO

By means of determinations of monoamine metabolites in CSF and platelet MAO, 69.0% of the subjects were correctly

Table 1. Discriminant analysis. Healthy volunteers versus patients with chronic pain syndromes. Nonstandardized canonical discriminant function coefficients

Variables included	Function 1 A	Function 2 B	Function 3 C, E	Function 4 D	Function 5 A, B, C, E	Function 6 A, B, C, D, E, F
A. Depressive symptoms (VAS)						
Sadness						
Bodily discomfort	0.041				0.037	0.052
Inner tension					0.007	0.015
Concentration difficulties						
Memory disturbances	0.011					
B. Personality inventory (KSP)						
Somatic anxiety		0.085				
Psychic anxiety					0.055	
Muscular tension		−0.107				
Social desirability		−0.104			0.113	
Impulsiveness						
Monotony avoidance		0.142			−0.196	−0.241
Detachment						
Psychasthenia		−0.075			0.092	0.169
Socialization					0.057	0.101
Indirect aggression		0.098				
Verbal aggression						−0.282
Irritability						0.202
Suspicion		−0.065			0.169	0.202
Guilt					−0.123	−0.236
Inhibition of aggression		0.052			−0.080	−0.124
C. CSF						
5-HIAA			0.048		−0.013	−0.009
HVA			−0.012			
D. Serum Cortisol						
At 9 a.m.				−0.005		−0.002
At 4 p.m.				0.006		
After dexamethasone						
At 9 a.m.						0.004
At 4 p.m.				0.005		
E. Platelet MAO						
F. Urinary metatonin						
Constant	−1.850	0.160	−2.262	0.200	−4.682	−0.989
Healthy/pain patients *n/n*	28/86	137/90	35/65	26/86	19/54	15/32
Eigenvalue	1.01	0.92	0.12	0.14	4.12	9.15
Wilks lambda	0.50	0.52	0.89	0.88	0.20	0.10
χ^2	77.27	94.93	10.78	11.38	107.02	84.58
df.	2	8	2	3	11	13
P	<0.001	<0.001	<0.01	<0.01	<0.001	<0.001
Correctly classified	85.1%	80.3%	69.0%	64.4%	98.6%	100%
Sensitivity	100%	75.8%	68.6%	37.5%	100%	100%
Specificity	80.2%	83.3%	69.2%	74.2%	98.1%	100%

classified. Only 5-HIAA and HVA in CSF were included in the discriminant function (Wilks lambda = 0.89, $\chi^2 = 10.78$, $df2$, $P < 0.01$) (Table 1). Thus, as sole measures the determinations of monoamine metabolites in CSF and platelet MAO activity were less powerful for separating chronic pain patients from healthy volunteers than depressive symptomatology and personality traits.

Serum cortisol and DST. Cortisol in serum and cortisol in serum after dexamethasone were about equally effective as

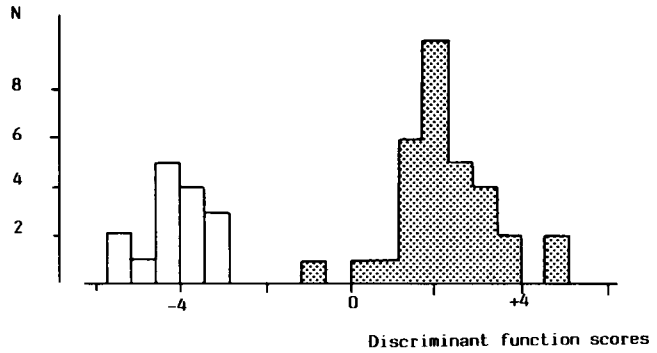

Fig. 1. Distribution of discriminant function scores in a discriminant analysis separating healthy volunteers from patients with chronic pain syndromes (□ healthy volunteers, $n = 15$; ▨ chronic pain patients, $n = 32$). The variables included in the discriminant function (function 6) are presented in detail in Table 1. Wilks lambda = 0.10, $\chi^2 = 84.58$, *df.* 13, $P < 0.001$. Correctly classified 100%

monoamine metabolites in CSF and platelet MAO activity in discriminating healthy subjects from chronic pain patients, with 64.4% of the subjects correctly classified (Table 1). Three items were selected in the discriminant function – serum cortisol at 9 a.m. and at 4 p.m. and serum cortisol at 4 p.m. after dexamethasone suppression (Wilks lambda = 0.88, $\chi^2 = 11.38$, $df3$, $P < 0.01$).

Depressive Symptomatology, Personality Traits, 5-HIAA in CSF, HVA in CSF and Platelet MAO Activity. When clinical symptomatology and personality traits were combined with measures reflecting monoamine turnover – 5-HIAA and HVA in CSF and platelet MAO activity, an almost complete discrimination was achieved, with 98.6% of the subjects correctly classified (Table 1). The items included in the discriminant function were – bodily discomfort, inner tension, psychic anxiety, social desirability, monotony avoidance, psychasthenia, socialization, suspicion, guilt, inhibition of aggression and 5-HIAA in CSF. Thus, the inclusion of CSF 5-HIAA increased the number of subjects correctly classified by means of depressive symptomatology and personality traits from 80%–85% to about 99%. Wilks lambda was 0.20, $\chi^2 = 107.02$, $df11$, $P < 0.001$.

Depressive symptomatology, personality traits, 5-HIAA in CSF, HVA in CSF, platelet MAO activity, serum cortisol, DST and urinary melatonin. When the number of variables included was extended with serum cortisol before and after dexamethasone suppression and urinary melatonin, a complete separation was achieved between the healthy subjects and the chronic pain patients. Included in the discriminant function were 13 variables covering depressive symptomatology, personality traits, 5-HIAA in CSF, serum cortisol at 9 a.m. both before and after dexamethasone suppression. Wilks lambda was 0.10, $\chi^2 = 84.58$, $df13$, $P < 0.001$ (Fig. 1).

Differentiation of Patients with Idiopathic Pain Syndromes from Patients with Neurogenic Pain Syndromes

Depressive Symptomatology. Depressive symptomatology was present in both patients with idiopathic pain syndromes and patients with neurogenic pain syndromes. A small but significant increase in separating ability was achieved by means of a discriminant function including only memory disturbances as the sole item. By means of this item 57.0% of the subjects were correctly classified. Wilks lambda = 0.95, $\chi^2 = 4.70$, $df1$, $P < 0.05$ (Table 2). Thus, it seems as if sadness and anxiety were about equally prominent in the two patient groups while items more related to inhibiton made a small contribution to the delineation between the two syndromes.

Personality Traits. By means of the personality traits covered by KSP 71.1% of the subjects were correctly classified. Thus, it is clear that personality is a much more powerful tool than clinical symptomatology in the differentiation between neurogenic and idiopathic pain syndromes. The discriminant function formed included 6 of the KSP scales (Table 2). Wilks lambda was 0.81, $\chi^2 = 17.51$, $df6$, $P < 0.01$.

5-HIAA in CSF, HVA in CSF and Platelet MAO Activities. The three values covering monoamine turnover gave a slightly better differentiation between the two groups than depressive symptomatology per se but also a weaker differentiation than the personality traits assessed by means of KSP, with 64.6% of the subjects correctly classified (Table 2). Only 5-HIAA was included in the discriminant function giving strength to the importance of serotonin turnover in patients with idiopathic pain disorders (Wilks lambda = 0.92, $\chi^2 = 5.05$, $df1$, $P < 0.05$).

Serum cortisol and DST. By means of determinations of serum cortisol both before and after dexamethasone suppression, approximately the same differentiation was achieved as with platelet MAO activities and monoamine metabolites in CSF as the included variables, with 64.4% of the subjects correctly classified (Table 2). In the discriminant function formed, 3 items were included – serum cortisol at 9 a.m. and serum cortisol at 9 a.m. and 4 p.m. after dexamethasone suppression (Wilks lambda = 0.88, $\chi^2 = 11.38$, $df3$, $P < 0.01$).

Depressive Symptomatology, Personality Traits, 5-HIAA in CSF, HVA in CSF and Platelet MAO Activities. When measurements covering depressive symptomatology and personality traits were combined with measurements covering monoamine turnover 81.5% of the subjects were correctly classified (Table 2). The discriminant function formed included 9 items covering depressive symptomatology, personality traits and 5-HIAA in CSF. Thus, as in the differentiation between healthy subjects and chronic pain patients, the clinical values combined with measurement of the serotonin metabolite 5-HIAA gave a satisfactory discrimination between patients with neurogenic and idiopathic pain syndromes, respectively (Wilks lambda = 0.54, $\chi^2 = 29.34$, $df9$, $P < 0.001$).

Depressive Symptomatology, Personality Traits, 5-HIAA in CSF, HVA in CSF, Platelet MAO Activities, Serum Cortisol, DST and Urinary Melatonin. When serum cortisol before and after dexamethasone suppression were included together with urinary melatonin a complete separation was achieved between patients with neurogenic and patients with idiopathic pain disorders (Table 2, Fig. 2). The discriminant function formed included 13 items covering depressive symptomatology, personality traits, HVA in CSF, serum cortisol after dexamethasone suppression and, as an important contributor, urinary melatonin (Wilks lambda = 0.13, $\chi^2 = 43.98$, $df13$, $P < 0.001$).

Discussion

The variables included in the present study were all primarly chosen on the basis that they have been shown to deviate in

Table 2. Discriminant analysis. Patients with neurogenic pain syndromes versus patients with idiopathic pain syndromes. Nonstandardized discriminant function coefficients

Variables included	Function 1 A	Function 2 B	Function 3 C, E	Function 4 D	Function 5 A, B, C, E	Function 6 A, B, C, D, E, F
A. Depressive symptom (VAS)						
Sadness					−0.201	−0.037
Bodily discomfort						−0.037
Inner tension					0.018	
Concentration difficulties					−0.027	
Memory disturbances	0.043					
B. Personality inventory (KSP)						
Somatix anxiety						0.126
Psychic anxiety						
Muscular tension		−0.124			−0.105	−0.259
Social desirability						
Impulsiveness					0.090	0.175
Monotony avoidance		0.159				0.562
Detachment						
Psychasthenia						
Socialization		0.054				
Indirect aggression		0.304			0.340	0.634
Verbal aggression		−0.207			−0.349	
Irritability					0.310	
Suspicion						−0.888
Guilt						
Inhibition of aggression		0.107				0.365
C. CSF						
5-HIAA			0.029		0.020	
HVA						0.006
D. Serum Cortisol						
At 9 a.m.				−0.004		
At 4 p.m.						
After dexamethasone						
At 9 a.m.				0.014		0.011
At 4 p.m.				−0.004		−0.007
E. Platelet MAO						
F. Urinary melatonin						−7.739
Constant	0.900	−7.938	−2.725	0.680	−3.881	−15.954
Neurogenic/idiopathic *n/n*	22/64	25/65	26/39	19/67	18/36	10/20
Eigenvalue	0.06	0.23	0.08	0.14	0.84	6.73
Wilks lambda	0.95	0.81	0.92	0.88	0.54	0.13
χ^2	4.70	17.51	5.05	11.38	29.34	43.98
df.	1	6	1	3	9	13
P	<0.05	<0.01	<0.05	<0.01	<0.001	<0.001
Correctly classified	57.0%	71.1%	64.6%	64.4%	81.5%	100%
Sensitivity	81.8%	64.0%	61.5%	37.5%	77.8%	100%
Specificity	48.4%	73.8%	66.7%	74.2%	83.3%	100%

patients with depressive disorders. The rationale behind such a selection was the pronounced clinical similarities between the chronic pain syndrome and the depressive syndrome (Pilowski and Bassett 1982) that have led to the conclusion that either the chronic pain syndrome and the depressive syndrome share a common patho-genetic mechanism (Sternbach 1974; von Knorring 1975) or that the chronic pain syndrome in fact is a variant of the depressive disorder (Blumer and Heilbronn 1982). As a result of the present study it can be demonstrated that measurements of monoamine metabolites in CSF (5-HIAA

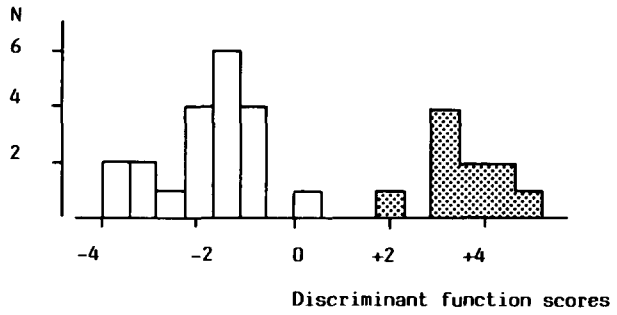

Fig. 2. Distribution of discriminant function scores in a discriminant analysis separating patients with neurogenic pain syndromes from patients with idiopathic pain syndromes (▨ patients with neurogenic pain syndrome, $n = 10$; □ patients with idiopathic pain syndromes, $n = 20$). The variables included in the discriminant function (function 6) are presented in detail in Table 2. Wilks lambda = 0.13, $\chi^2 = 43.98$, *df.* 13, $P < 0.001$. Correctly classified 100%

and HVA) and platelet MAO activity or the determination of serum cortisol before and after dexamethasone suppression increases the discrimination between healthy subjects from chronic pain patients from a chance value of 50% to about 65%–70%. The increase in discriminative power is significant but still of limited clinical value as a single diagnostic test. On the other hand, a standardized determination of depressive symptomatology by means of a short and rather simple VAS or a determination of stable personality traits by means of a standardized questionnaire such as KSP increased the discriminating capacity to about 80%–85% of the subjects correctly classified. It should also be noted that if these two clinical measurements were combined with a simple determination of the serotonin metabolite 5-HIAA in CSF, serum cortisol before and after dexamethasone suppression and melatonin in night urine, a complete discrimination was achieved, at least in this rather small criterion sample. Thus, even if a replication sample is needed before a final conclusion can be drawn about the optimal discrimination function to be used, it seems clear that the variables chosen, originally chosen due to their capacity to discriminate between healthy subjects and depressed patients were very relevant in the delineation between healthy subjects and patients with chronic pain syndromes.

It is also clear from the present results that a combination of clinical and biochemical measurements should be used as the sensitivity and specificity of most biochemical measurements is too low to make them clinically useful as single diagnostic tests, e.g. the DST has been suggested as a single method for discriminating healthy subjects and patients with depressive disorders (Carroll et al. 1981). Originally, the specificity was suggested to be very high while sensitivity was suggested to be around 65%. However, in later studies the specificity has also been suggested to be lower (Coppen et al. 1983). In the present context where the test was used to discriminate between healthy subjects and patients with chronic pain syndromes, the tendency was clearly the same: specificity was satisfactory while the sensitivity was very low and thus in total only about 65% of the subjects were correctly classified.

In the even more difficult delineation between patients with idiopathic pain disorders and patients with neurogenic pain disorders, the tendency in the present study was the same. The simple biochemical tests, either 5-HIAA and HVA in CSF and platelet MAO activity or serum cortisol before and after dexamethasone increased the number of correctly classified subjects to about 65%. The increase was significant but of limited clinical utility. However, in this delineation the use of clinical symptomatology, at least in the form of the symptoms covered by the present VAS, was of even more limited use and a clinically useful delineation cannot be made only by means of the presence of depressive symptomatology. Only 57% of the subjects were correctly classified. Instead, the best single measurement seemed to be a determination of stable personality traits by means of a standardized personality inventory such as KSP. However, still only about 70% of the subjects were correctly classified. The real increase in discriminative power was achieved when clinical measurements covering depressive symptomatology and personality traits were combined with determinations of monoamine metabolites in CSF, platelet MAO activity, serum cortisol, a DST and urinary melatonin. In the present, rather small, criterion sample the discrimination was complete which at least gives some strength to the selection of variables made in the present study.

In the final discriminant function formed, 5-HIAA in CSF was not included despite the great interest focused on the serotonin turnover in present hypotheses about idiopathic pain syndromes. However, in the earlier formed discriminant functions, 5-HIAA in CSF was included instead of HVA in CSF. 5-HIAA and HVA in CSF were highly intercorrelated and also correlated to several of the other variables included in the equation. Thus, the composition of the final discriminant function cannot be taken as a proof that the dopaminergic systems are of higher importance than the serotoninergic systems in idiopathic pain syndromes. It should also be noted that in the clinically difficult delineation between patients with idiopathic and neurogenic pain syndromes, respectively, a major contribution was made by determination of urinary melatonin, giving some support to the suggestion of Beck-Friis (1983) about a special low melatonin syndrome.

The fact that the variables chosen primarily because of their capacity to delineate the depressive syndrome also seemed to be very useful in a delineation of the idiopathic pain syndrome will give some strength to the suggestion by Blumer and Heilbronn (1982) that the idiopathic pain syndrome in fact could be variant of depressive disease.

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