RIVISTA ITALIANA DI RICERCHE MEDICHE E CHIRURGICHE

ITALIAN REVIEW OF MEDICAL AND SURGICAL RESEARCHES

Medical Dr's Researches

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ESTRATTO
Pagg. 5 - 14
MARZO 1996 - ANNO IV - VOL.4 - N°1
RIVISTA TRIMESTRALE

Dr's REVIEWS NAPOLI

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GLI ADRENOGRAMMI SECONDO IL METODO DI VASSILIEV NELLA CLINICA DELLE MALATTIE NERVOSE.

Riassunto

L'autore illustra il metodo degli adrenogrammi da lui stesso brevettato e il suo significato per la biocorrezione, sempre secondo il metodo Vassiliev, di un ampio spettro di malattie nervose con eziologia dopaminica. Il metodo ha acquistato particolare importanza dopo la scoperta, grazie ad esso, della sindrome Shoshina-Vassiliev, soprattutto tra gli ammalati di paralisi cerebrale, e della sindrome Vassiliev, soprattutto tra i pazienti di malattie demielinizzanti, momento in cui è stato evidenziato il ruolo fondamentale della dopamina nella eziologia e patogenesi di tali malattie e la possibilità di guarigione da esse al 100%. Solo mediante gli adrenogrammi si riescono a scoprire i meccanismi interni di alterazione del funzionamento del SAS, a fare un'obiettivizzazione del paziente, a fornire elementi di prognosi sul suo stato, a calcolare microdosi rigorosamente individualizzate di preparati contenenti L-DOPA secondo il principio della "chiave giusta per ogni serratura" nel rispetto della cronoterapia e a effettuare diagnosi differenziali, e di evidenziare nuove funzioni della dopamina.

Alla base del metodo degli adrenogrammi c'è l'analisi di più di 1.500 persone clinicamente sane, di età e sesso diversi, in condizioni di relativo riposo e di vario stress, nelle ore del giorno e della notte, e di più di 8.000 pazienti con più di 30 nosologie dal 1968 al 1995.

Parole chiave: adrenogramma - metabolismo della dopamina - biocorrezione - prova diagnostica con L-DOPA

The discovery of the Shoshina-Vassiliev syndrome, common in patients with cerebral palsy (CP) (the first cases were discovered in 1968 and it was registered in 1985)[7-9], and of the Vassiliev syndrome among patients with demyelinating diseases (DD) (the first cases were discovered in 1975 and it was registered in 1990)[10,12,13,16] with 100% effectiveness, as well as the successful development of a wide range biocorrection of nervous disease with an effectiveness of no less than 50-70%, depending on the disease, has put fresh light on the fundamental role of dopamine levels in etiology and pathogenesis and highlighted some new functions[4,7-10,15,17,18].

All this has been made possible by the use of the adrenogram method, developed and patented by the author. This method was first employed in the assessment of healthy individuals of different ages and sex, in the selection of personnel in stressful occupations involving shift work, identifying periods of tiredness and recovery (operators, controllers, pilots, astronauts, etc.), to define physical stress (sport), in the differential diagnosis of mental illness and, in particular, to distinguish schizophrenia from neurosis, in the assessment and prognosis of patients along with the determination of the effectiveness of treatment (especially in neurotic cases) of physiotherapeutic and psychotherapeutic methods and mathematic models, etc.[1-3,5,6,10,11,16]

The method proved to be universal, compatible with electrocardiogram, electroencephalogram, etc., with tomography and with magnetic resonance, often actually proving superior due to the extent of detection and the possibility to calculate personalised doses of the compounds administered according to the "right-key-for-the-right-lock" principle in relation to cronotherapy.

The adrenogram method (the term was introduced officially by the author in the seventies) is based on the regular functioning of the sympathetic andrenergic system (SAS) present in 1,500 clinically healthy patients aged between 1 and 85 years, over day and night, in conditions of relative rest and under various conditions of stress and in 8,000 patients affected by more than 30 different diseases (Vassiliev V. 1968-1995)[1,5,11].

Besides a clinical assessment, a necessary component in the evaluation of sympathetic-adrenergic activity in man is the study of the dynamics of the excretion of adrenaline (A), noradrenaline (NA), dopamine (DA) and their common precursor, DOPA, in the urine through the use of functional tests developed by the author with L-DOPA. Originally, besides studying the excretion of free forms of those substances, the excretion of bound forms was also studied, in particular sulphates and in some cases metabolites (metanephrine, normetanephrine, homovanillylic and vanillylmandelic acid) and MAO

Rivista Italiana di Ricerche Mediche e Chirurgiche - 1:5-14, 1996; (L'articolo in lingua originale è riportato a pag. 11) ***Pervenuto in redazione*** *il 05/03/96;* ***Alla correzione*** *19/03/96;* ***Corretto e revisionato*** *il 03/04/96;* ***Indirizzo per corrispondenza****: Prof. Vassiliev Vitali - P.co S. Vincenzo - 81022 Casagiove (CE) - Tel. 0823/494855.*

activity. In some cases a concentration in the blood of A and NA was found. To identify certain mechanisms a contemporary determining factor is the content of corticosteroids, histamine, serotonin and other substances in blood and urine.[1,5]

In SAS activity controlling organs and mechanisms which regulate the activity of the system are usually found. Controlling organs include the central and periphery rings for whose activity biosynthesis, storage, secretion, interaction with receptors and hormonal metabolism are important. The central rings of the SAS are represented by the dopaminergic and noradrenergic systems while the adrenergic system represents the periphery rings.

The mechanisms which regulate SAS activity are found mainly in the hypothalamus and in the mesencephalic reticular formation which, in turn, is also controlled by the periphery nerves. On the basis of the generally accepted pattern of the synthesis of catecholamines (CA) we have: tyrosine (phenylalanine)-dopa-dopamina-noradrenaline-adrenaline.

Tyrosine and phenylaline are vital aminoacids. The aminoacid dopa is a precursor of CA and in particular of DA and others. It is not physiologically active.

It is known that DA is the neuro-transmitter of the 4 dopaminergic systems of the central nervous system (CNS) (nigrastriatal, mesolimbic, tuberoinfundibolar, mesocortical) which, through various upward and downward paths, cover practically all the central regulating spheres of the CNS.

DA is the direct precursor of NA which is a widely represented mediator in the CNS. It is important to note that in the stem and the structure at the base of the brain, besides dopaminergic and noradrenergic paths, there are also serotinergic and histominergic paths. All these systems are united by the presence of common enzymes in the chain of their biosynthesis and metabolism. By this we mean monoxidase, decarboxylase, methyltransferase. Thus, a change or modification of the activity of any one of the above mentioned enzymes may cause an abnormality of the metabolism and of many other systems, leading to a distortion in the intersystemic balance.

Following the study of clinical and laboratory findings relating to biocorrection in more than 800 patients affected by nervous disease with paralysis, and of 4,500 patients with neurosis, the authors were able to demonstrate the fundamental role of a distortion of the metabolism of DA and its direct role in the etiology and pathogenesis of a series of nervous diseases: CP, DD, myopathia, various types of atrophy and others, and to highlight new functions, as well as the possibility to recover (correct) its metabolism, which gives the possibility:

- in cases of epilepsy, epileptic attacks, convulsions and a tendency to convulsions, to eliminate such conditions;
- in cases of strabismus (pupillary divergence), in 60-70% of cases, to remove the defect;
- in cases of language defect (anarthria, dysarthria and others), to correct the disability in a time span from a few days to a few months. After 5-7 days the appearance of "flowing speech" may be observed in patients aged between 5 and 17 years, with CP and Shoshina-Vassiliev syndrome. In the adrenogram the language defect is often accompanied by acute paroxysms, the elimination of which removes vocal spasms;
- to regain or improve sight, especially in patients with multiple sclerosis, even in cases of atrophy of the optic nerves in upto 40% of cases;
- to improve hearing, especially in MS patients, even after unsuccessful stereotaxis in cases of head injury, meningocephalitis and in other cases. Improvement was observed in the hearing of a 24 year old patient with the diagnosis of CP and deaf-mutism;
- to restore or stimulate menstruation: with the administration of a compound containing L-DOPA menstruation becomes regular; to restore erection and potency in males;
- to bring back to normal thermoregulation which assumes particular characteristics in patients with MS and myopathia: febricola is eliminated, the temperature of the lower and upper limbs is brought back to normal;
- to normalise micturition and evacuation, especially in patients affected with MS, myopathia, post-traumatic illness and others; pelvic organ functions often return to normal a few weeks after the beginning of biocorrection;
- to normalise weight in cases of obesity or, conversely, in cases of breakdown reaching cachexy. In patients, especially those with MS and myopathia, gradually, over a few months, muscular tissue is strengthened with a reintegration of its innervation. Significant weight loss may be observed in cases of CP, hydrocephalitis and other pathologies which lead to obesity, and the elimination of hypothalamic attacks. Diet therapy increases the effectiveness of treatment;
- to obtain a change and often the normalisation of intellectual development in patients who, in many cases, have been diagnosed as having psychiatric illness such as a breakdown in mental development, oligophrenia, idiocy, a mental handicap and others.

NA is a central neurotransmitter directly involved in the development of neuro-muscular pathology. It is a pressor hormone which acts more softly but at the same time lasts longer than A and has a spastic action. A is a hormone of the surrenal glands which also has a pressor and spastic action. These amines have a vasoactive effect and are regulators of both the circulation of blood in the brain and blood flow in the organism (as a whole).

It is important to specify the polyhedral biological effect of the amines which have a direct influence on

a change in the metabolism of glucose, on the activation of the lipolytic, proteinic, electrolytic and other processes.

All these properties of biogenous amines can favour an improvement of trophia and a reduction in the level of destruction of the nervous system, thanks to an improvement in the blood supply to the brain and a reduction of the processes of free radicals. In this way they are useful in recovering the structural integrity of the receptors and of the cellular membranes, and in regulating potassium and sodium ion transfer which improves the conductivity of the action potential.

Furthermore, biogenous amines, in so far as they influence various factors of the hypothalamic sphere, are neuromodulators of the level and physiological effects of the hormones and various neuropeptides.

For this reason, subsequent to a change in the metabolism of biogenous amines, do neuroendocrine changes appear. The level of destruction of the focus point of the lesion, its position, just as a modification of neurohumoural regulation, together with a modification of the biophysical and biochemical constants of the brain determines the multiform nature of the clinical manifestation of the disease and the complexity of the pathogenesis.

Among the various biological liquids of man (blood, saliva, tears, sweat, encephalospinal liquid, etc.) the most accessible and informative is urine collected at various times for the analysis of the metabolism of CA's.

Despite the fact that free CA's in the urine make up 4-5% of the total undergoing metabolism in the organism, modification of their content reflects the activity, tone and reactivity of the SAS and, with the adoption of a functional test with L-DOPA, also the prognostic possibilty of the working of this system.[1,5]

Our research on blood, saliva, tears, sweat and encephalospinal liquid have convinced us that for a number of reasons (difference between tests on the right vein and the left, the non-physiologicity of the samples, time limits, high percentage of method errors, continuous fluctuation of CA content (every second), these tests are complimentary. Urine is a collector of CA content and does not present the above mentioned defects. It is known that SAS activity is subordinate to daily, seasonal and annual cycles. The circadian rhythm, for example, is characterised by peak activity in the morning (8-12) and in the evening (16-22) and by an afternoon low (12-16) and a sharp drop in CA content during the night (22-8)[1,5].

Furthermore, it has been established that the circadian rhythm reflects the level of adaptability towards certain conditions, and in the presence of a pathology a change is noted which manifests itself in the absence of a fall or even an abnormal increase in the excretion of CA in diurnal and, in particular, nocturnal hours or in monotony(inversion) in the course of 24 hours. It has been observed that together with a clinical improvement there was a recovery of the circadian rhythm of SAS. Thus, circadian rhythm is an important indicator of man's adaptability and resistance under stress[1,5].

The term "adrenogram" indicates a clinical interpretation of the study of the dynamics of CA excretion in relation to biorhythym and with the introduction of the prognostic clinical test with 0.5g. of L-DOPA and diagnostic test with 0.1g. of L-DOPA[1-8]. In 1987, the USSR Health Minister recommended the author's method for wide clinical use[9].

Graphically, the adrenogram is constructed in such a way that time intervals (8-12-morning, 12-16-afternoon, 16-22-evening, 22-8-night) are placed on the horizontal axis while the numerical content of A, NA, DA and DOPA (in ng/min) is placed on the vertical axis. On the adrenogram clinical data are compared, in relation to age and sex, with those of healthy subjects (norm), also in graphic form.

A clinical interpretation of the data obtained is reported beneath the graph:

Case type: adrenergic (type A), noradrenergic (type NA), mixed (type A + NA).

Emotive tension: morning, afternoon, evening, night.

Syndrome: hysterical, neurasthenic, phobic (obssession), hypothalamic involvement (compensation, heightening, type of crisis, breakdown) and the possibility of seasonal heightening: winter, spring, summer, autumn, hypothalamic involvement.

Attacks: adrenergic, noradrenergic, mixed (acute, average, weak) and times (morning, afternoon, evening, night).

Paroxysms: acute, average, weak (morning, afternoon, evening, night).

SAS asthenia: (morning, afternoon, evening, night).

Sleep: within normal limits, disturbed, very disturbed.

Circadian rhythm: within normal limits, disturbed, very disturbed.

Therapeutic action (cronotherapy) to be taken with reference to: morning, afternoon, evening, night.

Deciphering the adrenogram:

In the examination of patients with neurosis and other diseases, that is to say, hyper- or hypo-emotive, accompanied by hyper- or hypo-secretion of CA, as well as clinically healthy subjects, the most fruitful approach is the subdivision in biotypes. It is important to note the coincidence of such divisions with clinical data.

Biotyping is made by calculating the prevalent excretion, types A, NA or A+NA, which in many cases derives genetically or is the result of a disease or of taking some substances (drugs, alcohol and others).

Thus, type A corresponds to an anxious subject (phobic), type NA to a hyperchondriac subject (hysterical), and the leader type, type A+NA to a hyperactive subject (hyperemotivity).

In the case of SAS exhaustion, when the excretion of CA is low, the test with 0.1g. of L-DOPA makes it possible to establish accurately the biotype in relation to the predominant increase in the synthesis of one or another CA.

Recently we managed to demonstrate that the biotypes may be distinguished one from the other from an immunological, haemo-chromocytometrical and biochemical point of view.[1,5].

Adrenogram analysis of neurotic cases highlighted a significant difference regarding the types mentioned in relation to sex. In males, for example, type A is met 7.7% times as much and accounts for 37.8%, while type NA is found 9.1% times less compared with females and accounts for 17%. Type A+NA accounts for 34.2% of males and only 22.8% of females.

Biotyping is useful in professional selection, patient assessment, the solution of psychological problems of a family or social nature (to create, for example, a pleasant atmosphere at home or work). Clinically speaking, it is important to take into consideration the fact that two equal biotypes clash and neglecting this fact leads to the onset of neurosis, a worsening of the treatment, etc.

An analysis of the adrenograms of cases of neuroses highlighted the correlation between the main forms of neuroses and certain types of functional activity of the SAS.

Our data demonstrate convincingly that the adrenogram of type A is found more often in the neuroses of obsessive states, type Na is found in hysterical neuroses and type A+NA in female neuvrasthenia. In all three forms of neuroses type A and type NA have reliably distinguishable adrenograms. In the study of basic forms of neuroses substantial changes in the circadian rhythm of CA and DOPA excretion may be observed, with a higher retention in cases of hysterical neuroses, a fact which testifies to the significant compensatory biological possibilities in those cases.

Furthermore, on the basis of adrenograms, attacks may be divided into adrenergic (A) and noradrenergic (NA). A attacks occur particularly in situations of mental trauma. On objective examination tachycardia, dyspnoea, palpitations and increased systolic blood pressure are recorded. In addition, patients complain of precordialgia, suffocation and, rarely, of headache, dizziness and tremors. As a rule, anxiety and fear complete the picture in A. Similar attacks last from a few minutes to an hour and disappear as soon as circumstances temporarily resolve the pathogenic situation. The presence of type A attacks served as a basis for the formation of a phobic symptomatology, in particular, of cardiophobia.

NA attacks manifest themselves in the form of psycho-emotive tension with unjustified anxiety, interior restlessness and tension without somato-vegetative disturbances.

Sympathetic-adrenergic attacks (SA) in females occur particularly in the evening and, as a rule, in the course of 24 hours not one, but two or more SA attacks may be observed. In males, SA attacks occur much less frequently compared with females and tend to occur mainly in the first half of the day and fluctuate significantly, particularly in their development, between 12h. and 16h. In males, NA attacks may also be observed which, in their clinical manifestation pass more easily than a type A attack.

It is important to note that the clinical manifestation of SA attacks in patients often occurs slightly later than their appearance on the adrenogram.

Thus, we managed to demonstrate the progress of SA attacks in patients with neuroses and this is undoubtedly of great practical importance for the suppression of such states. Thanks to the analysis of adrenograms it is possible to localise the attacks in time, their manifestations and frequency which gives the doctor the chance not only to identify in good time the progress of an SA attack but also to begin carefully aimed specific therapeutic measures, the effectiveness of which is visible in the comparison between adrenograms made before and after treatment.

Clinically speaking, paroxysms call to mind SA attacks but their manifestation is much weaker. Paroxysms are characterised by the appearance of palpitations, dyspnoea, slight fluctuation of blood pressure, a sense of unease and, in many cases, the appearance of the so-called "free fluctuating" anxiety. The adrenogram often shows up hyperadrenalinuria in the wake of a sharp drop in NA secretion. The discharge of A during morning hours (8-12) and evening (16-22) accompanied by sleep disturbance is typical of the paroxysm; a discharge of NA may occasionally be observed.

In the course of paroxysms a separation of the hormonal rings and the SAS mediators is observed and this leads to a reduction in the value of the NA/A ratio as low as 1 or even 0. In healthy subjects of comparable age the value is equal to 3-4.

As a rule, typical of paroxysmal activity is the exhaustion of SAS reserves which manifests itself in a sharp reduction in the excretion of DOPA and DA. Paroxysms often transform themselves into SA attacks. The right overall treatment reduces the manifestations of paroxysms and regulates SAS activity which is strictly linked to clinical improvement.

In cases of hypothalamic syndrome arising from trauma, neuroinfection following chemotherapy or antibiotic therapy or other causes, a set of symptoms emerged characterised by a clinical picture of vegetative-endocrine-trophic disturbances.

Analysing the adrenograms we divided the cases of hypothalamic syndrome into two types. THe first type (multiform) is characterised by an NA attack in the wake of increased A excretion and by a sharp drop in the excretion of DOPA and, in particular, of DA. Differences due to sex and the season are present.

The second type (simple) is characterised by the separation of A and NA excretion in the wake of a sharp drop in DOPA and DA excretion. With an increase in the excretion of A (of 1.2-6 times and more) a sharp drop in NA excretion is observed, sometimes as far as complete exhaustion. Significant differences due to sex and season are also present[1,5].

On the basis of the study of adrenograms certain changes, among which sleep, which occur in mass are evident. In fact, in males sleep disturbances are present in 82% of cases and in females 79%. Furthermore, it is known that an increase in A excretion is accompanied by anxious dreams while an increase in NA is accompanied by dreams of an obsessive nature. The level of change in CA excretion is correlated to clinical observations relating to sleep disturbances in patients and this is of great practical importance.

In cases of nervous pathologies a significant composition is found in which there is an exhaustion of hormone rings or SAS mediators and, moreover, of DOPA and DA, and this may be considered as a hypofunction (exhaustion) of the system.

We found two types of exhaustion of SAS activity: 1) hyperactivation of A and NA excretion with a sharp drop in DA and DOPA; 2) a general hypoactivation (exhaustion of SAS and its rings-low excretion of all CA's and DOPA) as a separation of hyperemotivity of patients with a large deficit of its hormones and mediators.

It is vital to note that real exhaustion of the SAS comes to light not only on the basis of a low excretion of DOPA and DA (often as low as zero), but also thanks to the aid of the test with 0.1g. of L-DOPA with which a blocking of the synthesis of those precursors as well as bound forms (sulphates) of CA's are defined.

Test for clinical prognosis with 0.5g. of L-DOPA or 30mg. of SINEMET, NAKOM according to the Vassiliev method.

For a rapid clinical determination of DA deficit and any future effect of treatment as well as a prognostic means, a consistent test is used with the administration per os, accounting for age, of from 0.25 to 0.5g. of L-DOPA (or 15 or 30g. of SINEMET or NAKOM). After 30 minutes the clinical effect is evaluated according to the "three cross" rule. In the case of a rapid effect (signs of warming of the limbs, in particular, the lower limbs, significant fall in hyperkinesis and paresis, the appearance of or an increase in motor activity, etc.) one may speak of a positve prognosis.

However, for a precise diagnosis it is necessary to construct an adrenogram, often with the 0.1g, L-DOPA test.

The diagnostic test with the administration of 0.1g. of L-DOPA according to the Vassiliev method.

Over the course of the first twenty four hours (control) urine is collected in the periods necessary for the adrenogram (8-12, 12-16, 16-22, 22-8). The second day, at 8h, 0.1g. of L-DOPA is introduced per os. Also on the second day urine is collected according to the time intervals indicated. Control data are equated to 100%, graphs are plotted of the dynamics of CA and DOPA excretion. Norm values are taken into account in the calculation. With this method it is possible to determine the amount of non-metabolised DOPA secreted, whether a block or synthesis of DA and other neuro-hormones occurs, a prognosis of the effectiveness of biocorrection can be made and, in particular, a diagnosis is established. On the basis of these data a personalised dosage is chosen, the exact moment of administration is determined and the length of treatment is established.

Figure 1 shows some specific aspects of the curve of DA synthesis depending on the pathology. Hyperactive synthesis is typical of multiple schlerosis (2) and of the Vassiliev syndrome (6), hypoactive synthesis of the Shoshina-Vassiliev syndrome (5), the specific curves of DA synthesis in myopathia (3), cerebral palsy (4) and encephalopathy (7) are specific compared with healthy subjects of the same age (1).

We present below an example of deciphering an adrenogram (fig.2).

Patient P., 17 years, type A+NA (anxious-hypochondriac), with morning and evening hyperemotivity, with hypothalamic syndrome and SA attacks of type NA in the morning and type A in the evening, with acute paroxysms in the afternoon, evening and at night with the possibility of heightening in spring and autumn, with a fall in DOPA and DA reserves, with asthenia, especially in the afternoon (12-16).

The possibility of biocorrection is demonstrated with a compound containing L-DOPA with a personalised dose and notes on administration times, physiotherapeutic measures to adopt with indications on the type and length of therapy.

The test made previously with 0.1g. of L-DOPA confirmed the diagnosis: progressive cerebral atrophy.

Thus, the adrenogram method makes it possible to assess the patient, to differentiate in many cases

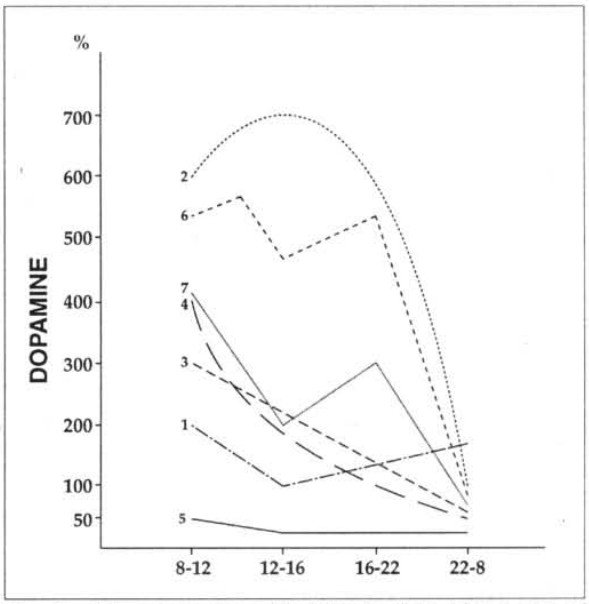


Fig. 1 - Diagnostic test with introduction of 0,1 gm of L-DOPA in accordance with the Vassiliev method.

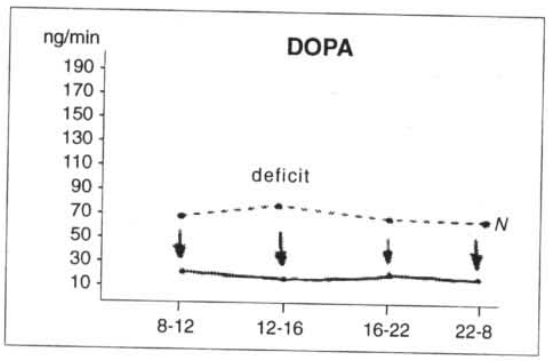
INITIAL DIAGNOSIS: **"PROGRESSIVE CERABRAL ATROPHY"**

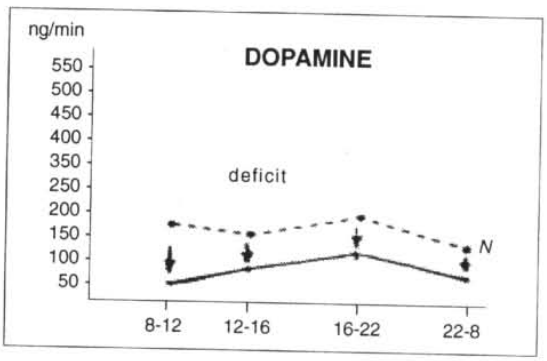
Date:_____ Surname, name, age: P. 17 years.

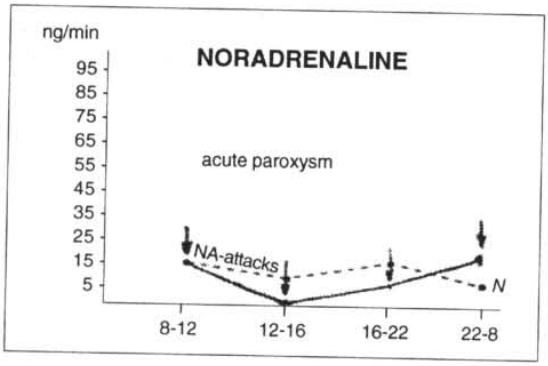
ADRENOGRAM of the V. Vassiliev method N°

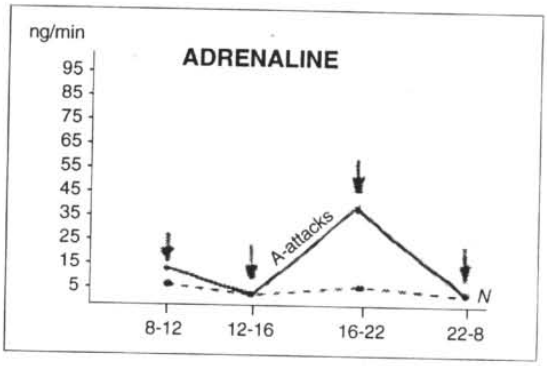
(urinary excretion in ng/min over a period of 24 hours)

	8.00 - 12.00 (morning)	12.00 - 16.00 (day)	16.00 - 22.00 (evening)	22.00 - 8.00 (night)
ADRENALINE	11.8	4.5	36.2	5.1
NORADRENALINE	14.2	0	3.7	17.6
DOPAMINE	24.8	71.2	83.4	46.4
DOPA	16.1	8.8	11.4	7.5









---------- N - norm (age, sex)

Fig. 2 - Initial diagnosis: progressive cerabral atrophy .

the diagnosis according to the principle of "finger prints", to calculate strictly personalised doses of compounds containing L-DOPA according to the "right-key-for-the-right-lock" principle. Subsequently, a prognosis can be made of the condition of the patient using mathematical models, in particular, of the situational model of the choice of rational recommendations on the basis of a simulation with susceptible integrals of modification[1,5,8].

Abstract

The adrenogram method (patented by the author) and its significance for the biocorrection of a broad range of nervous diseases with dopamine etiology is illustrated. This method acquired special importance after and thanks to the discovery of the Shoshina-Vassiliev syndrome, particularly among patients with cerebral paralysis, and the Vassiliev syndrome, especially among patients with demyelinizing diseases. At the same time the fundamental role of dopamine in the etiology and pathogenesis of

these diseases and their cure in the order of 100% has been highlighted. It is only through adrenograms that internal mechanisms of change in SAS functioning can be identified, objectification of the patient be made, prognostic elements of his/her condition be supplied, accurately personalised microdoses of the compound containing L-DOPA be calculated, according to the "right-key-for-the-right-lock" principle in relation to cronotherapy, differential diagnoses be conducted, and new applications of dopamine be highlighted.

Furthermore, his method of adrenograms is based on the analysis of more than 1500 clinically healthy individuals, of different age and sex, in conditions of relative stability and various forms of stress during the day and at night, and more than 8000 patients with more than 30 classified diseases.

Key words: adrenogram - dopamine metabolism - biocorrection - prognostic test with L-DOPA

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