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Finger cooling test and psychometric analysis in thyroid auxiliary diagnostics

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Hypothyroidism is a fairly common disease. The signs and symptoms of thyroid hormone deficiency are non-specific and under certain conditions its diagnosis may be rather difficult. The aim of the study was to make an analytic comparison of several psychometric indices with rheological parameters of extremity microcirculation in patients with subclinical or overt hypothyroidism and in healthy controls. Serum levels of thyrotropin and of free thyroxine were measured. A psychometric analysis was carried out using the Mittenecker and Thoman test. The finger cooling test evaluated by eye verification and the systolic–diastolic index (SDI) was determined by means of planimetric photoplethysmography. An increase in SDI was found in the patients with subclinical and overt hypothyroidism, correlating with psychometric indices and hormonal levels. The results obtained indicate that an evaluation of rheological parameters of the finger cooling test and psychometric parameters may be very useful in the auxiliary screening of hypothyroidism.

Key words: thyroid hypothyreosis, biochemical diagnostics, finger cooling test, computer planimetric photoplethysmography, microcirculation, computer psychometric tests

1. Introduction

Hypothyreosis is a common chronic illness which appears throughout the country. Chronic illnesses of the thyroid gland appear in 5% of men and 15% of women in the adult population. There are 140 million people at risk of thyroid diseases due to iodine deficiency of which, in Europe, 97 million of reported cases are diagnosed with thyroid goitre [1]. The examination of the thyrotropin TSH level and free thyroxine fT4 level, determined by means of RIA, IRMA and ELISA tests [2]–[5], play a key role in the diagnosis of disorders in thyroid activity. However, there is a group of chronic illnesses of the thyroid gland which have drug-induced, toxic [6] or inflammatory – bacterial (kidney, prostate or sinus chronic infection, tooth caries, paradontosis) or immunological etiology [7]–[10]. They are rheumatoid arthritis, systemic sclerosis, MCDT and reactive arthritis (Reitter, Lymme, SARA syndrom), and the correlation between levels of concentration of the mentioned hormones in the blood and the intensity of clinical symptoms in such cases is lower [11]–[17]. In chronic illnesses of this kind, immunoglobulins or some chemical compounds may disturb peripheral conversion T4–T3, may influence expression and accessibility of the tissular receptors to T3 or may modify accessibility of hormones in serum albuminous buffers. Such states are called *subclinical hyperthyreosis* or *hypothyreosis* [18]–[21]. *Subclinical biochemically* seems to be a purposeful supplement to these terms, suggesting clinical symptoms in spite of near-normal hormone levels [22], [18]. The main problem in hypothyreosis symptomatology is temperature tolerance, especially skin sensitivity to cold. Each patient with diagnosed hypothyreosis complains of body freezing, especially of the hands and

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feet (Raynaud phenomenon). Based on this observation investigators have tried to expand thyroid diagnostic tests applying unspecific measurements, such as skin electroimpedance [23], [24] or microcirculation evaluation [25]–[27], which are particularly effective and assume a high level of correlation with the intensity of clinical symptoms. The next clinical consequence of a dwindling metabolism is a change in the sensitivity of the neuronal system, which leads to depression, vegetative, antisocial, and sometimes even psychotic trends, which can be measured by psychological tests.

This examination may be helpful as an inexpensive screening test used for supplementary diagnostics and for the monitoring of thyroid therapy [25]. Cardiologic [28]–[30] and neurological–psychiatric [31]–[37] disturbances are known issues existing alongside thyroid diseases. Their estimation may also be an unspecific marker in the evaluation of some disturbances in thyroid function.

2. The aim of the work

Finding correlations with the traditional hormone criteria of hypothyreosis was the focus of the investigation. Comparative analyses of selected psychopathological features, evaluated by the Mittenecker and Toman's computer test [38], and rheological changes of microcirculation in the finger cooling test, evaluated by planimetric computer photoplethysmography [39]–[41], [25] in a group of individuals suffering from subclinical (C) and biochemically evident hypothyreosis (B), compared with healthy controls (A) are the aim of the study. Some of the previously proposed modifications include:

1. Constructing a narrow-angled sensor and taking measurements in a small finger venous area that is particularly sensitive to cold (in the cooling test).
2. Using computer and electronic systems to convert the signal from analogue to digital which allows for a quick recording and accurate drawing of the results on the screen enabling immediate calculation.
3. Creating and clinical use of the computer version of the Mittenecker and Thoman's test.
4. Calculating the results of cooling and psychological tests using the indices of relative change of selected parameters and correlating them with thyreotropin (TSH) and free thyroxine level (fT4) in the groups A, B, C.

3. Material and method

3.1. Groups of patients

The study was performed among patients of the Thyroid Clinic for Outpatients and Nuclear Medicine Laboratory in Cieszyn. The control group (A) consisted of healthy medical workers: 12 women aged 38.6 ± 4.2 years, 8 men – 36.5 ± 3.4 years. The first test group (B) with biochemically positive hypothyreosis was comprised of 24 subjects (17 women aged 44.6 ± 6.2 years and 7 men aged 46.3 ± 5.8 years). The second study group with biochemical subclinical hypothyreosis consisted of 25 patients: 15 women aged 42.1 ± 4.8 years and 10 men aged 40.6 ± 3.8 years. Patients in groups B and C met positive clinical and laboratory criteria (based on the Thyroid Association list of criteria). In both groups, all subjects were evaluated using a visually verified cooling test and computer photoplethysmography as well as the Mittenecker–Thoman, fT4 and TSH tests.

3.1.1. General excluding criteria

The following subjects were excluded from the study: those who smoked more than 10 cigarettes a day, had a positive history of arterial hypertension, diabetes, coronary heart disease, arteriosclerosis or collagen disease, those taking any vasoactive drugs and those who had suffered from any hand, shoulder or neck injury.

3.2. Testing methods

3.2.1. Hormonal tests

The blood for the tests was taken from the patients' right elbow vein (5 cm^3), and then, after cloting, was spin-dried and frozen (–5 °C). The material was transported to laboratory freezed as it was necessary to do so. Tests were carried out only on the completed samples which were already in a liquid state and had a room temperature (about 20 °C) in the Nuclear Medicine Laboratory in Cieszyn using (1) the "Farmos" TSH-IRMA system and the (2) "Cis" fT4 RIA system.

3.2.2. Psychometric test

A computerised version of the author's modification of the Mittenecker and Thoman's test, for the diagnosis of depression, psychosis, vegetative lability and antisocial tendency scale was used for the research. The study was performed in a cosy room furnished with a comfortable armchair, computer desk and display. Patients were requested to answer 214 questions shown on the computer display (for about 2 h). The temperature in the surgery room was approx. 20–22 °C.

for 5 minutes. The hands tested were protected before immersion using thin polypropylene gloves, which due to their tenuity, exerted no pressure on the skin. Afterwards it was assessed whether distinct areas of whiteness were visible on the index finger. The temperature of the measurement room was 20 °C. Patients participating in the test had been given 10 minutes to acclimatise. They were forbidden to smoke or drink

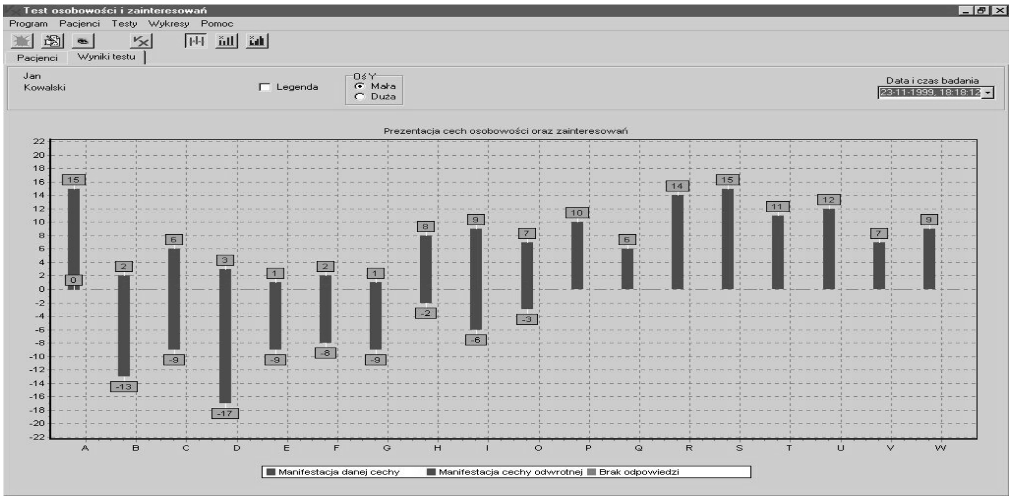


Fig. 1. Screenshot – the Mittenecker–Thoman test window. The columns whose ranges are from negative to positive values on the *y*-axis represent ambivalent tendencies (social–antisocial), while the columns whose ranges are positive represent individual, psychological patient's skills

3.2.3. Statistical tests

Statistical analysis: average value, standard deviation, correlation factor, *t*-Student's test.

3.2.4. Cooling test

The cooling test shows distortions in blood distribution between nutrition and thermoregulatory microflows (figure 2). The test was performed by inserting a patient's hand in a mixture of water and ice and evaluating microcirculation after a 5-minute exposure. A visual evaluation of fingers after the test, with attention focused on their whitening, can detect only advanced forms of the Raynaud phenomenon. Many attempts at rendering the cooling tests more objective have been carried out so far by retrieving the data directly from the microflow. Various kinds of plethysmography (isotope, electro-impedance, ultrasound, laser), photoplethysmography, and capillaroscopic planimetry have been used for this purpose.

Initial condition. The cooling test was performed by inserting the right hand of a patient in a mixture of water and ice at a temperature of 15 °C neither any caffeine nor alcohol from the day before the measurement (until after the measurement). Before the cold test, the patients' blood pressure was examined (mmHg by the automatic "OMRON" system – data was exported to an EXCEL table). Only patients with pressure lower than 140/90 had been allowed to take the cold test. An eye evaluation was performed immediately after cooling (two examiners), with the computer measurement coming a few seconds later.

Physiology basis. A normal microvascular bed (the fingers) consists of various forms of nutrition capillary nets (70%) and thermoregulation anasthomoses (Sequet–Hoyer canals). Blood flow steered by sympathetic nerves controls the sphincters of these vessels (figure 2). The normal, nutritional microflow of blood increases after cooling and stabilises the temperature of finger tissue (with small efficiency). When the temperature continues to decrease, nutritional flow closes and takes on a strong flow through the Sequet–Hoyer canal.

The flow described above increases the curve area as can be seen in the diagram (figure 5). Patients with hypothyreosis show pathological reactions. Their nutrition microflow is similar to that of healthy

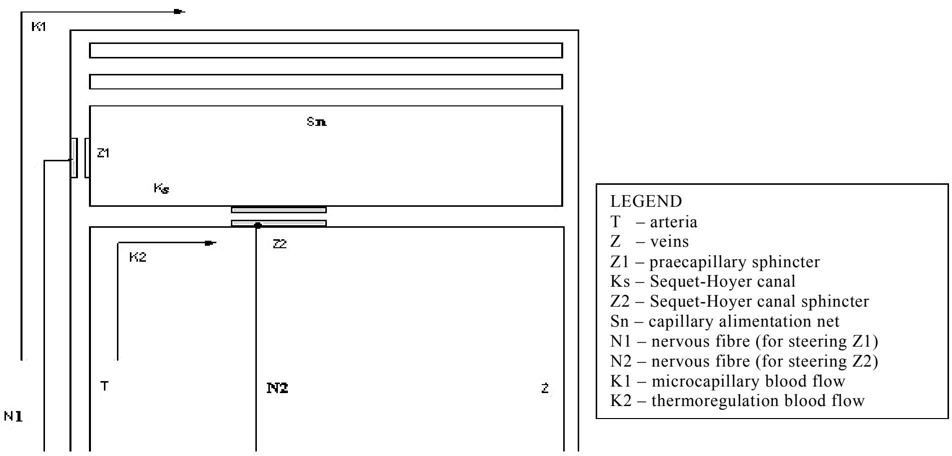


Fig. 2. Nutrition capillary net and thermoregulation anasthomoses

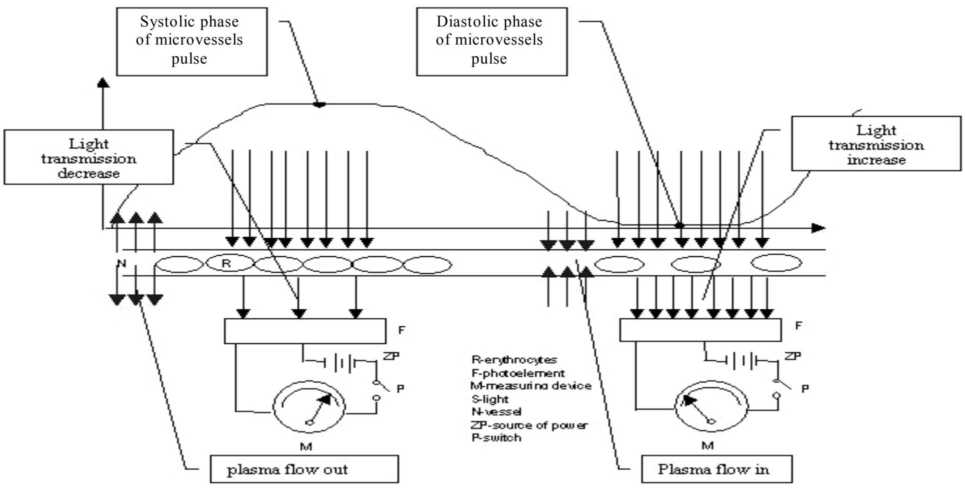
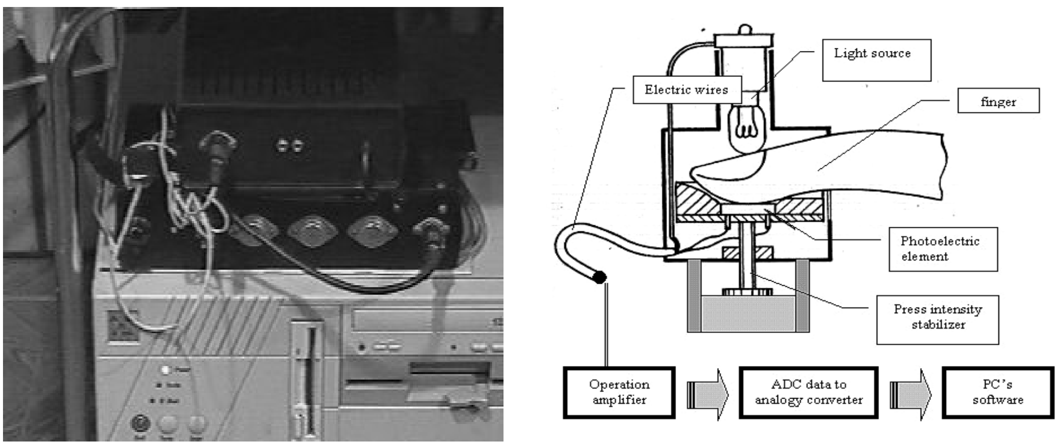


Fig. 3. Light transmission through finger plexus in the systolic and diastolic pulse phases

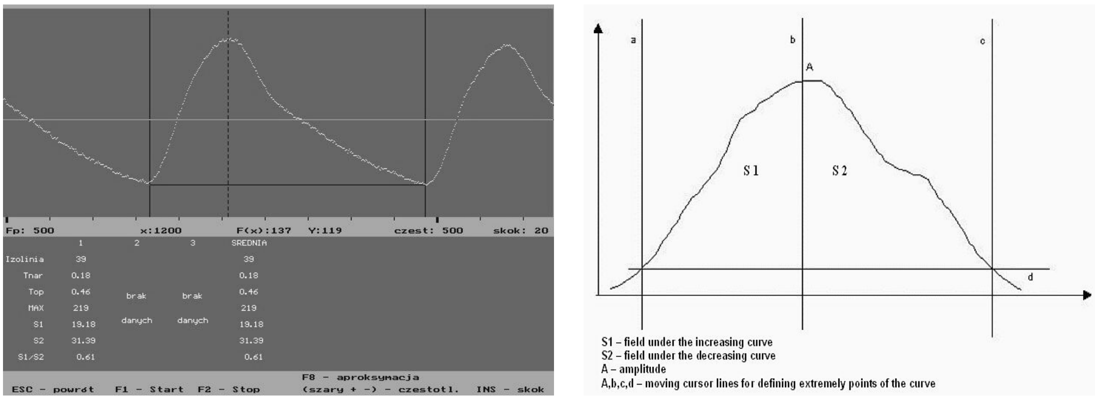


a b

Fig. 4. Computer photoplethysmograph prototype: picture (a), diagram of device structure (b)

people. After cooling, the nutrition flow closes, but the Sequet–Hoyer canal remains closed, as hypothyreosis changes the function of the nerve fibres, synapses and Pacinian receptors (which control this reflex).

Finger photoplethysmography (figure 4) is a technique with a great potential in detecting vascular disorders caused by vibrations. The idea of photoplethysmography is based on the changes of light transmission



a b

Fig. 5. Sample curve wave chart and window of "Pletyzmograf 1.0" software (a), interpretation diagram – amplitude parameter (*A*) and area parameters (*S*1, *S*2) (b)

through a capillary finger plexus. Hydrostatic pressure in a systolic pulse phase of microvessels causes a plasma flow out from the microcapillaries. This process increases erythrocyte concentration in vessels and decreases light penetration (figure 3). In the diastolic phase, there is a blood plasma flow into the microcapillaries, diluting the erythrocytes, which increases light penetration.

Increased sensitivity and specificity of the method are the expected effect of the digital conversion of the pulse signal as well as a direct processing of files. We speculate that an objective computer analysis (figure 5a) of the tracings is likely to improve the clinical value of photoplethysmography after cold exposure.

The analog photoplethysmograph signal (figure 4a) was filtered in the preamplification stage, selectively, at 50 Hz (network frequency). The 8 bit ADC converter takes 1024 probes in 1 second (1 kHz) (figure 4a). The curve of the evolution of one pulse (pulse 75 = 1.25 Hz) consists of 752 points (figure 5a).

The files were then processed by means of "Pletyzmograf 1.0" software, which allows for the visualisation of the pulse wave and the parametric analyses of any chosen fragments which are then averaged. Parameterisation is performed using an interactive formula that requires defining the edge parameters of the curve with cursor lines. Defining the edge points of the pulse curves assures a precise definition of the area under the ascending and descending branches of the curve as well as a definition of the amplitude (figure 5b).

3.3. Estimation of curve parameters

The data is automatically analysed using area index (an increase or decrease in the curve area index defines a process associated with blood volume change of finger plexus after cold immersion).

$$ARI = \frac{AR_c - AR_b}{AR_b},$$

where:

AR_c – area index after cold exposure $AR_c = \frac{S_{1c} - S_{2c}}{S_{2c}}$,

AR_b – area index at baseline $AR_b = \frac{S_{1b} - S_{2b}}{S_{2b}}$,

S_{1b} – area under the ascending branch of the curve at baseline,

S_{2b} – area under the descending branch of the curve at baseline,

S_{1c} – area under the ascending branch of the curve after cold exposure,

S_{2c} – area under the descending branch of the curve after cold exposure.

4. Results

The study did not produce any positive results in the eye verification of the finger cooling test in the groups A, B and C, thus the results have not been included in table 1.

In the group of healthy patients, the average value of the SDI rate amounted to 0.351 and was significantly lower than these in the evident and biochemically subclinical hypothyreosis group (table 1). The TSH level in the group A amounted to 1.81 μg/dl, in the group B it was considerably higher and amounted to 8.21 μg/dl and in the group C it assumed a statistically insignificant value of 5.98 μg/dl. The fT4 level

Table 1. Biochemical, rheological and psychometric parameters

Groups	SDI	TSH	fT4	Depressive trends (D)	Psychotic trends (P)	Antisocial trends (A)	Vegetative instability (V)
Group A *n* = 20	0.351 ±0.044	1.81 ±0.14	18.7 ±1.23	–38.5%	–34.7%	–31.9%	–38.3%
Group B *n* = 21	0.625 ±0.069	8.21 ±0.81	7.1 ±0.63	41.2%	38.1%	35.7%	64.3%
Group C *n* = 25	0.491 ±0.085	5.98 ±0.61	11.5 ±0.86	39.4%	35.8%	34.9%	61.2%

Table 2. Statistical significance of the difference

A – B	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.01	P < 0.01	P < 0.001
A – C	P < 0.001	P < 0.01	P < 0.05	P < 0.001	P < 0.01	P < 0.01	P < 0.001
B – C	P < 0.001	P < 0.05	P < 0.05	P < 0.05	P < 0.05	P < 0.05	P < 0.05

Table 3. Biochemical and psychometric parameters correlation table from SDI

Group	SDI/TSH	SDI/fT4	SDI/ D	SDI / P	SDI/ A	SDI/ V
A	0.711	0.645	–0.665	–0.542	–0.511	–0.667
B	0.921	0.812	0.791	0.715	0.627	0.905
C	0.465	0.413	0.752	0.704	0.598	0.887

in the group A amounted to 18.7 μg/dl, in the group B 7.1 μg/dl and in the group C an insignificant value of 11.5 was noted. The expression level in the selected psychopathological features was significantly low in the group A and considerably higher in the groups B and C (tables 1, 2). SDI and hormone level correlation were high in the groups A and B and very low in the group C. SDI correlation and expression level of psychopathological features testified to a quite good correlation in all three groups (table 3).

5. Conclusions

1. A narrow-angled sensor for measurements in an index finger venous area, which was particularly more sensitive to cold (in the cooling test), used in correlation with eye verification was constructed (no positive results).

2. An electronic system and computer for analogue to digital conversion of the signal to enable a quick recording and calculation of the results were used.

3. Clinical use of the computer version of the Mittenecker and Thoman's test produced results much faster than a manual method (about 40 min. shorter). The study revealed a high correlation of rheological and psychometric parameters with thyroid hormone level in the cases with clinically evident hypothyreotic patients.

4. A correlation between psychological and rheological parameters evaluated in the cold test is comparable both among patients with evident and subclinical hypothyreosis. The subclinical hypothyreosis group, however, does not meet hypothyreosis criteria for hormone levels.

6. Discussion

One of the older methods for screening thyroid function was a basal metabolism ratio measurement based on a body's heat production; however, such an investigation was complex and could not be considered valid as a diagnostic criterium, due to the fact that measuring whole-body skin temperature depends largely on skin nutrition microvessels guided by non-peculiar stimuli (independent of thyroid function). More specific is the proportion of the finger nutritional microflow (at normal temperature) to the Sequet–Hoyer canal blood flow, registered at rest, particularly before and after cooling. Cooling test verification can be very difficult and challenging; there have been many attempts at verifying this test by scientists. The following methods have been used so far: laser-Doppler–flowmetry, radionuclide-plethysmography, electroimpedance-plethysmography, ultrasound, thermovision, multipoint thermometry and photoplethysmography. Analyses of examination results carried out to date have proven that specific measurements correlate with a small area on the fingertip plexus in which many arterio-venous anastomoses are present.

The observation field of our sensor does not exceed an area of 20 mm^2, thus it is incapable of including big vessels, and encompasses nutritive microflow only in a small scope, as thermoregulating arterio-venous junctions constitute a major part of the plexus [18], [19]. A combination of the photoplethysmography and computer methods allows for greater precision, making the parameterisation of the signal significantly quicker as well as renders mathematical calculations possible. It also simplifies the method and allows for using one-point measurements as a basis for calculations [8], [18]. The use of relative change indices to calculate the data has eliminated the difficult and time-consuming process of calibration of the investigation procedure [35], [41], [51], [52].

It has been concluded that computer photoplethysmography is highly specific and shows a greater sensitivity in detecting preclinical forms of the vascular type of heat production deficiency (the Raynaud phenomenon).

The average value the of SDI rate in healthy patients amounted to 0.351 and was significantly lower than in these with the evident (0.625) and biochemically subclinical hypothyreosis (0.491) group (table 1). The TSH level in the group A amounted to 1.81 μg/dl, in the group B a significantly higher value of 8.21 μg/dl was noted and in the group C it assumed a statistically insignificant value of 5.98 μg/dl. The fT4 level in the group A was 18.7 μg/dl, in the group B 7.1 μg/dl and in the group C it took a statistically insignificant value of 11.5 μg/dl. The expression level in the selected psychopathological features was particularly low in the group A and considerably higher in the groups B and C (tables 1, 2). SDI and hormone level correlation was high in the groups A and B, whilst being significantly low in the group C. SDI correlation and expression level of psychopathological features produced a relatively good correlation in all three groups (table 3).

A high correlation between unspecific rheological and psychometric parameter indices will surely enrich the clinical process of recognising subclinical and clinically evident forms of hypothyreosis with new differentiating criteria.

The value of the SDI rate was highly correlated with the amount and expression level of psychiatric symptoms in all the groups under examination. A high correlation with the hormone levels existed only in the clinically evident form. The fact that the research was conducted on a selected group of patients should be remembered, and the specification obtained could change on exposure to different environmental factors. Nevertheless its low costs and the fact that the method is non-invasive encourage consideration of its more widespread use. The results of the research indicate that neurological-psychiatric disorders may occur in the biochemically confirmed as well as in the biochemically non-confirmed cases of thyroid diseases. The diagnostic process described above can be carried out through use of the neuronal network. The results obtained seem to confirm some of the authors' reports concerning the generation of oligosymptomatic psychiatric syndromes by unrecognised, biochemically subclinical disorders of thyroid activities. The manifestation of masked depression, psychotic tendencies or antisocial attitudes is an evident premise to apply psychometric procedures in the treatment process.

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