The impact of environmental problems on biotechnology associated with humoral predictors of the formation of chronic abnormal conditions

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Abstract. The article assesses the nature of the impact of environmental problems on biotechnology associated with changes in humoral factors (level of neuron-specific enolase in association with hormonal factors) during the formation of chronic abnormal conditions in conditions of environmental trouble. The possibility of using neuron-specific enolase as a predictor of these conditions has been proved. The quantitative values of neuron-specific enolase for predicting the risks of developing chronic abnormal processes in the presence of ecological problems have been established. The connection of these processes with the formation of endocrine dysfunction against the background of an increase in the level of neuron-specific enolase has been proved.

1. Introduction
It is known that the level of an environmental-dependent problem is determined by the complex influence of environmental and hygiene factors with a predominance of the sanitary-hygienic component and related environmental parameters, such as chemical pollution of the territories of settlements (soil, air, water bodies) [1]. So, according to V.A. Shashel (2018), in territories with a conditionally unfavorable ecological situation compared with a conditionally favorable - the prevalence of chronic abnormal conditions is significantly higher - 318.4 ± 28.12 and 411.9 ± 15.07 ‰, respectively (p <0.01) [2]. The share of the influence of environmental polluting factors on the frequency of occurrence of these conditions among those living in ecologically favorable territories, according to the same author, was 13.88%, on conditionally favorable - 19.75%, on unfavorable - 24.53%, with the prevailing influence of polluted air pool [3]. Therefore, the study of the impact of environmental problems on biotechnology associated with changes in humoral factors during the formation of chronic abnormal conditions is becoming relevant [4].

2. Statement of the problem
Taking into account the above-mentioned problems, conducting a further search for prognostic humoral factors in the formation of chronic abnormal conditions in conditions of environmental disadvantage remains relevant. For the diagnosis and prediction of the course of various abnormal states, it is important to determine specific humoral markers (neuron-specific enolase (NSE) in relation to hormonal factors) as predictors of the development of these conditions [5].
3. Research questions

The role of endocrine factors in the development of chronic abnormal conditions is still of interest. There are works proving the protective effect of such hormones as somatotrophic hormone (STH), insulin, estradiol, triiodothyronine (T3) [6 - 9].

Other studies show that thryotrophic hormone (TSH), cortisol, have the opposite effect [10].

But there are works that do not confirm the unambiguous anabolic or catabolic effects of these hormones. For example, in the studies of L.P. Filaretova, (2009) and P.Yu. Bobysheva (2009) proved not the catabolic, but the gastroprotective role of cortisol [11, 12].

Therefore, requirement for the specification of the role of various hormones in the development of chronic abnormal conditions is still relevant.

It should also be noted that in recent years there has been a significant increase in interest in the determination of neuron-specific enolase (NSE) [13]. This is a special enzyme found in the cells of the APUD system.

In the scientific literature, only few studies of NSE in the aspect of triggers for the development of chronic abnormal conditions have been found [14, 15].

Therefore, it seems appropriate to study the role of NSE in the development of chronic abnormal conditions, taking into account the special role of the endocrine system in this process in order to expand the prospects for the early detection of these conditions in terms of the potential of biotechnologies associated with humoral predictors.

The purpose of the study: to assess the nature of changes in the level of neuron-specific enolase in relation to hormonal factors in chronic abnormal conditions in conditions of environmental trouble; to prove the possibility of using neuron-specific enolase as a predictor of these conditions.

4. Materials and research methods

The level of neuron-specific enolase was determined by enzyme-linked immunosorbent analysis by kits of Can Ag Diagnostics (Sweden) under standardized conditions. ELISA results were recorded and evaluated using a SUNRISE photometer manufactured by TECAN (Austria). The study of hormone levels was also carried out by enzyme-linked immunosorbent analysis for estradiol by kits of firm R & D (USA); testosterone, thyroid-stimulating hormone, triiodothyronine, cortisol - sets of the company "Alcor Bio" (Russia); insulin kits from Monobind Inc. (USA); growth hormone - sets of company DRG (USA); cholecystokinin - sets of company PENINSULA LABORATORIES INC (USA) also under standardized conditions.

Statistical processing of the research results was carried out with the help of the STATISTICA 7.0 software packages using nonparametric statistics methods (Mann-Whitney, Fisher test, Spearman correlation coefficient), taking into account that the distribution of NSE values did not comply with the normal distribution law. Data are presented as median (Me), as well as 25 and 75 quartiles [25% - 75%]. Significantly, the significance level was p≤0.05. The relationship between the various indicators was assessed using analysis of variance and correlation. The diagnostic efficacy of screening tests was being evaluated by analyzing ROC curves and determining the area under the ROC curve (AUC).

5. The results of the study and their discussion

It was found that the level of neuron-specific enolase in the main group (study group) was significantly higher than in the control group: 10.50 (9.05-12.37) μg / L and 9.8 (4.85-11.93) μg / L, respectively (p≤0.01), which probably indicates a possible relationship between changes in NSE concentrations and the formation of chronic abnormal states.

When studying the hormonal status, it was found that the level of GH in the study group had lower values compared to the control group (1.91 ± 0.40 and 2.30 ± 0.52 ng / ml, respectively, p = 0.05) (table 1). Similar changes were found in the study of insulin concentration (7.57 ± 0.34 and 8.45 ± 0.47 μU / ml, respectively, for the main group and the control group, p = 0.05) (table 1).

A higher level of cortisol was found in the main group compared with the control group (553.78 ± 23.05 and 477.64 ± 24.62 nmol / L, respectively, p = 0.05) (table 1).
When conducting a study of the level of sex hormones, an increased content of estradiol was found in the study group in comparison with the control (p <0.05) (table 1).

**Table 1.** The level of hormones in the main group and control group.

| Indicators          | Main group (N=154) | Control group (N=56) |
|---------------------|---------------------|----------------------|
|                     | M±m            | Me       | [25; 75] | M±m         | Me       | [25; 75] |
| Insulin (mkmEd/ml)  | *7.57±0.34      | 7.40     | 6.40;8.20 | 8.45±0.47     | 7.90     | 7.30;9.00 |
| Cortisol (nmol/ml)  | *553.78±23.05   | 500.0    | 450.00;538.00 | 477.64±24.62 | 488.00   | 398.50;514.50 |
| STH (ng/ml)         | *1.91±0.40      | 0.50     | 0.30;1.36 | 2.30±0.52     | 1.08     | 0.50;2.90 |
| Progesterone(nmol/l)| 2.61±0.28       | 2.15     | 1.00;3.50 | 2.52±0.38     | 2.10     | 1.25;3.00 |
| Testosterone (ng/ml)| 1.97±0.40       | 0.15     | 0.05;0.80 | 1.52±0.55     | 0.31     | 0.11;0.93 |
| Estradiol(pg/ml)    | *24.88±2.43     | 20.0     | 15.20;24.00 | 18.24±3.38   | 16.00    | 5.50;21.50 |
| TSH(mkME/ml)        | 1.95±0.11       | 1.80     | 1.30;2.20 | 1.83±0.16     | 1.80     | 1.30;2.20 |
| T3 (nmol/l)         | 2.05±0.04       | 2.10     | 1.80;2.20 | 1.99±0.10     | 1.95     | 1.70;2.20 |
| T4(nmol/l)          | 113.95±1.71     | 114.0    | 103.0;126.0 | 111.11±4.16  | 113.50   | 99.50;126.0 |
| Gastrin (pmol/l)    | 2.37±0.38       | 1.61     | 0.50;3.21 | 2.66±0.70     | 1.69     | 0.46;4.06 |
| Cholecystokinin (mkg/l) | 31.11±1.58   | 27.60    | 25.15;30.50 | 29.65±2.89   | 26.72    | 23.72;30.89 |

Note: * - statistically significant differences, p <0.05.

The analysis revealed a direct correlation between neuron-specific enolase and cortisol (r = 0.24; p <0.05), neuron-specific enolase and thyroid-stimulating hormone (r = 0.33; p <0.006), neuron-specific enolase and cholecystokinin (r = 0.25; p <0.04) in the study group, which probably can indicate the unidirectional effects of the studied humoral factors in the formation of chronic abnormal conditions. In the main group, inverse correlations were also found between NSE and insulin (r = -0.37; p <0.003), NSE and estradiol (r = -0.29; p <0.016), NSE and triiodothyronine (r = -0.30; p <0.014), which may indicate alternative effects of these hormones and neuron-specific enolase in the development of chronic abnormal conditions. In the control group, such ratios of the presented indicators were not revealed. That is, the obtained data indicate the probability of the existence of a single interaction system, including hormones and a neuron-specific enolase, which is an intracellular enzyme and is related to the APUD system. This set of humoral factors, of course, can be considered as an important component in the formation of chronic abnormal conditions in conditions of environmental trouble.

In order to assess the prognostic significance of the neuron-specific enolase in the formation of chronic abnormal conditions, the ROC curve was analyzed. It was revealed that the diagnostic model had good and satisfactory quality with a sensitivity of 95.5% (90.9-98.2) and a specificity of 64.3% (50.4-76.6) (figure 1). In this regard, an increase in neuron-specific more than 8 μg / l suggests the presence of a chronic abnormal condition, as well as an increase in the risk of developing this condition by 2.7 times (p <0.0001).
6. Conclusions
The study using the capabilities of biotechnology associated with humoral factors has proved the association of a chronic abnormal state with the formation of endocrine dysfunction, characterized by a decrease in insulin and STH levels against the background of increased values of cortisol and estradiol in the blood.

The revealed high level of neuron-specific enolase in chronic abnormal conditions indicates the possible participation of this factor in the formation of these processes.

Unidirectional changes in neuron-specific enolase in the form of a direct correlation with TSH, cortisol, cholecystokinin in chronic abnormal conditions indicate a probable synergism of these factors in the development of these processes.

The opposite dynamics of changes, confirmed by the inverse correlation between NSE and insulin, NSE and estradiol, NSE and triiodothyronine, probably proves the effects alternativeness of these humoral factors (hormones and neuron-specific enolase) in the formation of chronic abnormal conditions.

To identify the risk group for the formation of chronic abnormal processes, it is advisable to use quantitative indicators of neuron-specific enolase > 8 mkg/l, which can be regarded as possible predictors of these conditions.

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