ASSESSMENT OF BLOOD CATECHOLAMINE AND SEROTONIN LEVELS IN ANXIETY AND DEPRESSIVE DISORDERS

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In psychiatric practice, there is a need to develop simple, pathogenetically substantiated biomarkers for prediction of the patient's current affective status and his/her status short-term perspective. The study aimed to analyze the association of the affective status of patients with mood disorders with the peripheral blood catecholamine and serotonin levels. The Hospital Anxiety and Depression Scale (HADS) was used for affective status evaluation. Concentrations of catecholamines (adrenaline, norepinephrine, and dopamine) in blood plasma and serotonin in blood serum were assessed by high-performance liquid chromatography (HPLC). The study included 114 individuals with affective disorders, the average age was 34.57 (SD = 10.36) years, the share of females was 64%. We revealed no significant prognostic effects of peripheral blood neurotransmitter levels relative to the current affective status. The serotonin/norepinephrine ratio, the increase in which significantly decreases the risk of clinical depression according to HADS-D considering the patient's sex and age ($p = 0.059$), turned out to be the only marker at the level of trends. In patients diagnosed with recurrent depressive disorder or depressive episode, a slight decrease in serotonin levels ($p = 0.068$) compared to the patients diagnosed with the disorders beyond the category of mood disorders is reported. In the same group a negative correlation has been found between the HADS-A scores (anxiety) and norepinephrine levels (Rs = –0.410, $p < 0.05$). The findings suggest that it will be possible to confirm the preliminary results obtained and acquire new data in the expanded clinically homogenous samples.

Keywords: depression, anxiety, non-psychotic mental disorders, catecholamines, serotonin, biological markers

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Compliance with ethical standards: the study was approved by the Ethics Committee of the Joint Stock Company "Scientific Centre of Personalized Medicine" (protocol No. 33 dated 1 December 2025). The subjects' personal data were hidden during the study. All the subjects submitted the informed consent for participation in the study.

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ОЦЕНКА УРОВНЯ КАТЕХОЛАМИНОВ И СЕРОТОНИНА В КРОВИ ПРИ ТРЕВОЖНО-ДЕПРЕССИВНЫХ РАССТРОЙСТВАХ

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В психиатрической практике существует необходимость разработки простых, патогенетически обоснованных и надежных биомаркеров для прогноза аффективного статуса пациентов в текущий момент и в ближайшей перспективе. Целью работы было провести анализ ассоциации аффективного статуса пациентов с непсихотическими расстройствами с уровнями катехоламинов и серотонина в периферической крови. Для оценки аффективного статуса использовали Госпитальную шкалу тревоги и депрессии (HADS). Концентрацию катехоламинов (адреналина, норадреналина и дофамина) в плазме и серотонина в сыворотке крови оценивали методом высокоэффективной жидкостной хроматографии (ВЭЖХ). В исследование вошли 114 человек с непсихотическими расстройствами, средний возраст составил 34,57 (SD = 10,36) лет, доля женщин — 64%. Мы не выявили достоверных прогностических эффектов уровней нейромедиаторов в периферической крови в отношении текущего аффективного статуса. Единственным маркером на уровне тенденции оказалось соотношение «серотонин / норадреналин», повышение значения которого снижает риск статуса клинической депрессии по HADS-D с учетом пола и возраста пациентов ($p = 0,059$). У пациентов с диагнозом рекуррентное депрессивное расстройство или депрессивный эпизод отмечено небольшое снижение уровня серотонина ($p = 0,068$) по сравнению с пациентами с диагнозами вне категории аффективных расстройств. В этой же группе обнаружена отрицательная корреляция между баллами по HADS-A (тревога) и уровнем норадреналина (Rs = –0,410, $p < 0,05$). Полученные результаты дают основания предполагать, что на расширенных клинически гомогенных выборках будет возможность подтверждения полученных предварительных результатов и получения новых данных.

Ключевые слова: депрессия, тревога, непсихотические психические расстройства, катехоламины, серотонин, биологические маркеры

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According to the World Health Organization (WHO) data on mental health, more than a billion people in the world suffer from mental disorders. Moreover, a significant proportion of mental disorders are mood (affective) disorders, which include both depressive and anxiety disorders [1].

Depression is a chronic recurrent mental disorder manifesting most often in young and middle age that significantly affects the patients' quality of life and social functioning. Among mental disorders, depression plays the most important role in the structure of global burden of diseases. According to the WHO prognosis, it will become one of the leading causes of disability and mortality by the year 2030 [2]. These predictions are based on high prevalence of depression: the disorder is reported in 19% of the general population during life; in general, more than 350 million people all over the world are affected [2]. Furthermore, 30–50% of healthy people experience subclinical depression that does not meet the diagnostic criteria of mood disorders, but nevertheless is associated with the risk of developing the clinically significant disorder later in life [3].

In aggregate, life expectancy in patients with depression is reduced by more than 10 years [4].

Depression is associated with high risk of suicide, the second most common cause of death at the age of 15–29 years. About 800,000 people die from suicide worldwide annually [2]. The WHO data suggest that 2/3 of people, who had made suicide attempts, showed manifestations of depression. A total of 21% of patients suffering from depressive disorders make suicide attempts, a significant proportion of which are completed [5].

Symptoms of depression being an important element of many mental disorders constitute a significant part of clinical features, although these may not reach a clinically significant diagnostic level. Depression and anxiety tend to cluster in families and often overlap, which is also supported by the results of current genome-wide studies. From a clinical perspective, the combination of depression and anxiety is associated with a more severe course and a worse response to antidepressant therapy [6].

In real clinical practice, when treating patients with non-psychotic disorders, the patient's current affective status becomes a priority for the psychiatrist. There is a clear need to develop simple, pathogenetically substantiated and reliable biomarkers, the use of which could provide the physician with stable guidelines for predicting affective status in the near future [7].

Such markers may include levels of catecholamines and serotonin, assessed peripherally, for example, by analyzing the patient's blood.

It is believed that serotonin and catecholamines play an important role in the pathogenesis of depression and anxiety [8–10]; these are associated with the disease course severity [10]. Serotonin and catecholamines also modulate the response to therapy for mood disorders [11].

We have previously analyzed the relationship between serotonin levels and the clinical status of patients with depression [12, 13].

Considering the transdiagnostic nature of the depression and anxiety symptoms [14], as well as the important role of catecholamines and serotonin in the pathogenesis of most mental disorders, it seems appropriate to analyze the relationship between the current affective status and neurotransmitter levels. Most of the studies are focused on the analysis of neurotransmitter levels as the therapy efficacy markers [11, 15], as well as markers of the disease status within the framework of case-control studies [16, 17] and the development of the well-known kynurenine hypothesis of the etiology and pathogenesis of mental disorders [18].

In this study we assumed that peripheral blood neurotransmitter (catecholamine and serotonin) levels can be associated with the current affective status of patients with non-psychotic mental disorders, these can be used as biomarkers of the anxiety and depression symptom severity and for prediction of the patient's actual affective status.

The study aimed to analyze the association of the affective status of patients with mood disorders with the peripheral blood catecholamine and serotonin levels.

METHODS

Patients

The study involved patients with non-psychotic mental disorders aged 18–65 years, who contacted the Scientific Centre of Personalized Medicine (Moscow) seeking outpatient care. Inclusion criteria: the fact of having a disorder diagnosed within the last month in accordance with the ICD-10 criteria by a psychiatrist: bipolar affective disorder, current episode mild or moderate depression (F31.3), depressive episode (F32), recurrent depressive disorder (F33), dysthymia (F34.1), Other recurrent mood (affective) disorders (F38.1), other anxiety disorders (F41), obsessive-compulsive disorder (F42), somatoform disorders (F45). Exclusion criteria: schizophrenic spectrum disorders, psychotic level of bipolar affective disorder, psychoactive substance addiction, exacerbation of chronic disorder, history of seizures.

Psychometric assessment

The subjects' current affective status was assessed using the Hospital Anxiety and Depression Scale (HADS) [19]; the HADS Russian version was used [20]. The scale has two independent subscales: depression symptoms (HADS-D) and anxiety symptoms (HADS-A). The scale gradations are as follows: score 0–7 баллов — no anxiety or depression symptoms, score 8–10 баллов — subclinical anxiety or depression manifestations, score 10 or more — clinical anxiety or depression manifestations. Based on individual HADS scores the patient's status was recorded in accordance with the gradations, along with the anxiety/depression (A/D) score ratio as a ratio of the anxiety score (HADS-A) to the depression score (HADS-D).

Biochemical testing

Concentrations of catecholamines (adrenaline, norepinephrine, and dopamine) in blood plasma and serotonin concentrations in blood serum were assessed by high-performance liquid chromatography (HPLC). Blood sampling was performed in the fasting state on the day of the questionnaire survey; the samples were transferred to the Chromolab laboratory (Moscow, Russia) for analysis. Both neurotransmitter levels itself and the ratios of those (serotonin/dopamine, serotonin/norepinephrine, serotonin/adrenaline, norepinephrine/dopamine, norepinephrine/adrenaline, adrenaline/dopamine) were used for analysis, which could be informative indirect indicators of the neurotransmission state.

Study design

The study was cross-sectional and comparative. All patient information was obtained during a single visit. To assess the association of the current affective status with neurotransmitter levels, groups were allocated in accordance with the current affective status based on the HADS-D and HADS-A scores,

Table 1. Comparison of patients with clinical anxiety based on HADS-A with other patients

	Clinical anxiety HADS-A			Other (normal and subclinical anxiety) HADS-A			*U*	*p*
	n = 92			*n* = 22				
	Mean value	SD	Me (Q_1; Q_3)	Mean value	SD	Me (Q_1; Q_3)		
Age (years)	35.53	10.036	33.5 (28; 43)	32.24	11.09	30 (23; 35)	797.5	0.123
Serotonin (SER), ng/mL	117.72	78.33	95.2 (56; 184.25)	95.68	65.99	81 (44.21; 125.1)	899.5	0.419
Dopamine (DA), ng/mL	44.31	56.69	34.62 (16.9; 53)	43.4	47.19	30 (15; 44.5)	860.5	0.525
Adrenaline (A), ng/mL	52.34	50.9	37.2 (23; 68.5)	43.18	39.55	33.39 (26.5; 46.2)	832.5	0.397
Norepinephrine (HE), ng/mL	346.56	183.21	319.6 (223; 432)	323.73	213.02	279 (186; 389)	811.5	0.315
Serotonin/Dopamine (SER/DA)	5.5	5.71	3.69 (1.57; 7.13)	6.3	10.96	2.93 (1.21; 7.36)	898	0.723
Serotonin/Norepinephrine	0.626	1.5	0.329 (0.18; 0.58)	0.357	0.24	0.29 (0.16; 0.63)	870	0.572
Serotonin/Adrenaline	4.015	4.73	2.41 (1.43; 5.48)	3.959	5.524	1.93 (1.06; 4.09)	857	0.508
Norepinephrine/Dopamine	16.57	16.92	9.27 (5.68; 20.91)	21.66	38.56	9.42 (6.53; 16.09)	930	0.91
Norepinephrine/Adrenaline	11.82	10.93	7.9 (3.94; 15.92)	11.48	9.45	7.98 (4.69; 18.68)	907	0.775
Adrenaline/Dopamine	2.17	1.75	1.34 (0.77; 2.36)	2	2.08	1.4 (0.78; 2.56)	940	0.97

Note: *p* — asymptote (bilateral), *U* — Mann–Whitney *U*-test.

regardless of the clinical diagnosis. These groups were compared with each other based on biochemical indicator levels. The correlation analysis was performed for the relationship between biochemical indicators and the HADS-D and HADS-A scores, along with the regression analysis for the estimated HADS-D and HADS-A scores predicted based on biochemical indicators.

In the second phase, the diagnostic groups of patients (depression, anxiety, other) were compared with each other based on biochemical indicator values to assess a possible relationship between the diagnosis and neurotransmitter levels. Regression models adjusted for sex and age were constructed when finding significant intergroup differences.

Statistical processing

Statistical analysis was performed using SPSS 23.0. The distribution of most test variables was non-normal (Kolmogorov–Smirnov test), therefore, nonparametric methods were used. The nonparametric Mann–Whitney *U*-test was used to compare the groups based on quantitative variables. To assess the factors for prediction of clinical depression/anxiety based on the HADS scores, the logistic regression (stepwise) method using a dependent binary variable (present/absent) adjusted for sex and age was used. Linear regression was applied to assess the possibility of predicting the HADS-D and HADS-A scores based on neurotransmitter levels.

Spearman's rank correlation was used in the common cohort and diagnostic groups to assess the correlations between the HADS-D and HADS-A scores, as well as between the A/D ratio and the concentrations of catecholamines and serotonin.

RESULTS

A total of 114 individuals were enrolled, the average age was 34.57 (SD = 10.36) years, the share of females was 64% (73 individuals). The average HADS-D score of the sample was 14.83 (SD = 4.752); the HADS-A score was 19.29 (SD = 7.397).

Current affective status

For further analysis the sample was divided into groups based on the presence of depression and anxiety according to HADS. It was found that in the sample there were only five subjects with the HADS-A scores below 7 (0–7) ("normal") and six subjects with the HADS-D scores below 7 (0–7) ("normal"). In this regard, further analysis was conducted in two comparison groups: "Clinical Depression/Anxiety" and "Other" (normal and subclinical depression/anxiety). The analysis was conducted independently for anxiety and depression.

Patients with clinical anxiety (HADS-A) accounting for 80.7% of the sample (92 individuals) did not differ from other patients in age, neurotransmitter levels and their ratios (Table 1).

Patients with clinical depression (HADS-D) accounting for 75.4% of the cohort (86 individuals) showed a trend towards lower average serotonin/norepinephrine ratio values (0.39 (0.38)) compared to the "Other" group (1.19 (2.66), $p = 0.084$) (Table 2).

Then a regression model was constructed to predict the clinical depression status, including the serotonin/norepinephrine ratio and the relationship with sex, clinical diagnoses, as well as age and sex as covariates, explaining 20.8% of variance (Nagelkerke R Square = 0.208) and predicting 78.2% of possible outcome. It has been found that the presence of depression symptoms based on the HADS-A score ($p = 0.011$) and the increase in serotonin/norepinephrine ratio values ($p = 0.059$, trend) reduce the risk of clinical depression status according to HADS-D independently, considering the patients' sex and age (Table 3).

Comparison of diagnostic groups

For further analysis the cohort of patients was divided based on the clinical diagnosis (depression, anxiety, and other). The pairwise comparison of the diagnostic groups based on biochemical indicators was conducted. The "Depression" diagnostic group (RDD, depressive episode) accounted for 29.8% of the sample (34 subjects), "Anxiety" (anxiety disorders) — 41.2% (47 subjects), "Other" (other diagnoses) — 28.9% (33 subjects).

No differences in neurotransmitter levels and their ratios between the "Depression" and "Anxiety" (Table 4) and "Anxiety" and "Other" (Table 5) groups were revealed. In the "Depression" group, the average serotonin levels show a downward trend ($p = 0.068$) relative to the "Other" group (Table 6), but this result has not been confirmed by the regression analysis.

The analysis of the correlations between the HADS-D and HADS-A scores and neurotransmitter levels in the common cohort of patients revealed no significant correlations. The same analysis conducted separately in diagnostic subgroups

Table 2. Comparison of patients with clinical depression based on HADS-D with other patients

	Clinical depression HADS-D *n* = 86			Other (normal and subclinical depression) HADS-D *n* = 28			*U*	*p*
	Mean value	SD	Me (Q_1; Q_3)	Mean value	SD	Me (Q_1; Q_3)		
Age (years)	35.15	10.183	33 (27; 43)	34.12	10.727	31.5 (28.75; 40)	1097	0.481
Serotonin, ng/mL	111.16	75.15	88.11 (56; 178)	121.36	81.24	95.2 (48.57; 181.75)	1137.5	0.662
Dopamine, ng/mL	39.44	34.34	32.9 (17.1; 49.1)	59.5	94.56	30.65 (11.23; 58.73)	1074	0.829
Adrenaline, ng/mL	46.67	35.52	36.95 (24.4; 65)	63.49	77.9	36.5 (17.58; 79.75)	1071	0.813
Norepinephrine, ng/mL	354.96	177.54	315 (243.25; 470.57)	300.67	218.84	293.49 (140.6; 388.2)	885.5	0.126
Serotonin/Dopamine	4.9	5.28	3.35 (1.3; 6.1)	8.11	10.52	4.9 (1.73; 10.05)	922	0.203
Serotonin/Norepinephrine	0.39	0.38	0.3 (0.17; 0.52)	1.19	2.66	0.41 (0.22; 0.8)	857	0.084
Serotonin/Adrenaline	4.04	5.19	2.1 (1.47; 4.9)	3.89	3.65	3.14 (0.99; 5.98)	1082	0.873
Norepinephrine/Dopamine	16	16.13	9.93 (5.9; 17.7)	22.55	36.3	7.04 (4.4; 35.9)	1032	0.611
Norepinephrine/Adrenaline	12.39	11.07	8.77 (4.6; 16.1)	9.7	8.9	5.76 (3.4; 18.2)	889	0.133
Adrenaline/Dopamine	1.97	2.19	1.25 (0.7; 2.3)	2.71	3.59	1.59 (0.9; 2.6)	948	0.274

Note: *p* — asymptote (bilateral), *U* — Mann–Whitney *U*-test.

revealed only one correlation (HADS-A) — norepinephrine in the "Other" diagnostic group (Rs = –0.410, $p < 0.05$). According to the linear regression results adjusted for sex and age in the common cohort of patients, neurotransmitter levels and their ratios do not predict the HADS-A (F = 0.573, $p = 0.751$) and HADS-D (F = 0.434, $p = 0.854$) scores, as well as the A/D ratio (F = 0.814, $p = 0.561$).

DISCUSSION

The presence of platelet serotonin is the most reliable indicator of serotonin metabolism disorder in the central nervous system. Platelets are considered as an extracerebral model of serotonergic neurons. A highly significant correlation between serotonin levels in platelets and cerebrospinal fluid was found [22].

Serum serotonin is primarily platelet serotonin, and the changes in serum serotonin levels allow one to indirectly assess the activity of the brain serotonergic system. In this regard, we chose serum serotonin for the study.

In our study involving a small cohort of patients with non-psychotic mental disorders, we have revealed no significant prognostic effects of the peripheral blood neurotransmitter (catecholamine and serotonin) levels relative to the current affective status. At a trend level, the only marker was the serotonin/norepinephrine ratio, the increase in which reduced the risk of the clinical depression status according to HADS-D considering the patients' sex and age ($p = 0.059$). Furthermore, in the group of patients diagnosed with recurrent depressive disorder or depressive episode, there was a slight decrease in serotonin levels ($p = 0.068$) compared to patients

Table 3. Clinical depression prognosis (HADS-D) regression analysis results

	B	SE	Wald	Degree of freedom	*p*	Exp (B)	95% confidence interval for EXP(B)	
							Lower	Upper
Serotonin/Norepinephrine	–0.948	0.502	3.569	1	0.059	0.387	0.145	1.036
Clinical diagnosis of depression	–0.81	0.826	0.962	1	0.327	0.445	0.088	2.244
Clinical diagnosis of anxiety	–1.877	0.734	6.546	1	0.011	0.153	0.036	0.645
Constant	2.838	0.751	14.27	1	0	17.085		

Note: SE — standard error of the mean. Model characteristics: $X^2 = 16.398$, $p = 0.001$; –2 Log-likelihood=103.909.

Table 4. Comparison of patients with the clinical diagnoses of depression and anxiety based on biochemical indicators

	Depression *n* = 34			Anxiety *n* = 47			*U*	*p*
	Mean value	SD	Me (Q_1; Q_3)	Mean value	SD	Me (Q_1; Q_3)		
Age	34.5	11.67	32.5 (25.5; 39.5)	35.87	10.04	33.5 (28; 44.25)	705	0.368
Serotonin, ng/mL	100.81	70.31	76.84 (43.6; 171)	105.64	67.44	91.55 (50; 169.75)	748	0.625
Dopamine, ng/mL	44.32	49.82	30.5 (15.65; 46.84)	41.15	42.04	35 (18; 53)	685	0.604
Adrenaline, ng/mL	40.06	32.67	32.24 (25.25; 44.24)	61.76	66.14	47.1 (17.72; 76.5)	607.5	0.192
Norepinephrine, ng/mL	329.95	184.71	306.1 (207.1; 379.6)	341.05	196.75	310 (214.75; 422.5)	720	0.871
Serotonin/Dopamine	5.83	9.29	3.14 (1.12; 6.43)	4.75	4.53	3.45 (1.59; 7.13)	732	0.968
Serotonin/Norepinephrine	0.34	0.22	0.3 (0.16; 0.49)	0.64	1.84	0.28 (0.18; 0.52)	713	0.815
Serotonin/Adrenaline	4.11	4.94	1.95 (1.06; 6.08)	3.9	5.79	2.14 (1; 4.8)	723	0.895
Norepinephrine/Dopamine	20.37	32.8	10.03 (6.25; 16.4)	15.11	15.29	8.86 (5.65; 18.18)	697	0.692
Norepinephrine/Adrenaline	11.5	8.17	9.22 (4.58; 15.7)	11.6	11.6	6.78 (3.84; 17.87)	646	0.361
Adrenaline/Dopamine	1.84	1.96	1.16 (0.66; 2.27)	2.35	3.07	1.38 (0.79; 2.43)	666.5	0.48

Note: *p* — asymptote (bilateral), *U* — Mann–Whitney *U*-test.

Table 5. Comparison of patients with the clinical diagnoses of anxiety and "Other" based on biochemical indicators

	Anxiety $n = 47$			Other $n = 32$			U	p
	Mean value	SD	Me (Q_1; Q_3)	Mean value	SD	Me (Q_1; Q_3)		
Age	35.87	10.04	33.5 (28; 44.25)	34.19	9.38	33 (27.3; 42.8)	710	0.675
Serotonin, ng/mL	105.64	67.44	91.55 (50; 169.75)	134.99	90.43	103.79 (61.1; 194)	628.5	0.217
Dopamine, ng/mL	41.15	42.04	35 (18; 53)	49.33	74.4	36.87 (13.21; 56.5)	712	0.807
Adrenaline, ng/mL	61.76	66.14	47.1 (17.72; 76.5)	45.19	27.33	37.73 (25; 69.75)	695.5	0.681
Norepinephrine, ng/mL	341.05	196.75	310 (214.75; 422.5)	356.48	187.74	344 (208.48; 483)	685	0.604
Serotonin/Dopamine	4.75	4.53	3.45 (1.59; 7.13)	6.27	6.72	4.2 (1.59; 8.72)	654	0.405
Serotonin/Norepinephrine	0.64	1.84	0.28 (0.18; 0.52)	0.71	1.22	0.4 (0.19; 0.71)	641	0.335
Serotonin/Adrenaline	3.9	5.79	2.14 (1; 4.8)	4.04	3.26	2.55 (1.62; 6.17)	609	0.197
Norepinephrine/Dopamine	15.11	15.29	8.86 (5.65; 18.18)	17.59	18.72	8.36 (5.6; 30.8)	710	0.792
Norepinephrine/Adrenaline	11.6	11.6	6.78 (3.84; 17.87)	12.4	11.71	7.95 (4.02; 19.37)	692	0.655
Adrenaline/Dopamine	2.35	3.07	1.38 (0.79; 2.43)	2.04	2.38	1.43 (0.73; 2.5)	689.5	0.637

Note: p — asymptote (bilateral), U — Mann–Whitney U-test.

Table 6. Comparison of patients with the clinical diagnoses of depression and "Other" based on biochemical indicators

	Depression $n = 34$			Other $n = 32$			U	p
	Mean value	SD	Me (Q_1; Q_3)	Mean value	SD	Me (Q_1; Q_3)		
Age	34.5	11.67	32.5 (25.5; 39.5)	34.19	9.38	33 (27.3; 42.8)	503	0.599
Serotonin, ng/mL	100.81	70.31	76.84 (43.6; 171)	134.99	90.43	103.79 (61.1; 194)	402	0.068
Dopamine, ng/mL	44.32	49.82	30.5 (15.65; 46.84)	49.33	74.4	36.87 (13.21; 56.5)	471	0.582
Adrenaline, ng/mL	40.06	32.67	32.24 (25.25; 44.24)	45.19	27.33	37.73 (25; 69.75)	438.5	0.324
Norepinephrine, ng/mL	329.95	184.71	306.1 (207.1; 379.6)	356.48	187.74	344 (208.48; 483)	441.5	0.344
Serotonin/Dopamine	5.83	9.29	3.14 (1.12; 6.43)	6.27	6.72	4.2 (1.59; 8.72)	447.5	0.386
Serotonin/Norepinephrine	0.34	0.22	0.3 (0.16; 0.49)	0.71	1.22	0.4 (0.19; 0.71)	411	0.175
Serotonin/Adrenaline	4.11	4.94	1.95 (1.06; 6.08)	4.04	3.26	2.55 (1.62; 6.17)	426	0.248
Norepinephrine/Dopamine	20.37	32.8	10.03 (6.25; 16.4)	17.59	18.72	8.36 (5.6; 30.8)	493	0.799
Norepinephrine/Adrenaline	11.5	8.17	9.22 (4.58; 15.7)	12.4	11.71	7.95 (4.02; 19.37)	477	0.638
Adrenaline/Dopamine	1.84	1.96	1.16 (0.66; 2.27)	2.04	2.38	1.43 (0.73; 2.5)	488	0.747

Note: p — asymptote (bilateral), U — Mann–Whitney U-test.

with psychiatric diagnoses that were beyond the category of mood disorders. It is interesting that it is this group, where the only correlation between the HADS-A scores (anxiety) and norepinephrine levels (Rs = –0.410, $p < 0.05$) has been found: the higher the anxiety score, the lower the norepinephrine level.

The study conducted is the first with such design; there is no possibility to directly compare the results with that of previous studies. The relationship between the anxiety severity and the functioning of stress response systems, in particular autonomic regulation with active involvement of noradrenergic mechanisms, is well known [21], and our results confirm these views. The serotonin/norepinephrine ratio may indirectly reflect, with known limitations, the interaction of autonomic mechanisms (norepinephrine) and emotional regulation systems (serotonin). The fact that we have received confirmation of the influence of this marker on affective status regardless of the formal psychiatric diagnosis may be a serious reason to continue research in this area using larger samples.

Study limitations

The reported pilot study involved small samples of subjects, which considerably limited the possibilities of data interpretation. The objective of the study was to assess the relationship between neurotransmitter levels and affective status. The affective status was assessed using the simple HADS screening self-report questionnaire, without the use of any clinical psychometric instruments. The HADS scale is successfully used for screening of anxiety and depression symptoms all over the world and in our country. The HADS scale was recently tested in a large online population-based study of depression in the Russian population [23], and a correct validation of this scale was carried out in the Russian general population [24].

CONCLUSIONS

The preliminary pilot study involving a mixed cohort of patients has revealed no significant associations between the patient's current affective status and peripheral blood catecholamine and serotonin levels. However, the effect of norepinephrine and the serotonin/norepinephrine ratio on the affective status of patients with clinical depression has been revealed. This suggests that in the next phase of the study involving larger and more homogeneous samples it will be possible to confirm preliminary results and obtain new data.

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