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ANXIETY, DEPRESSION, DYSFUNCTION OF THE AUTONOMIC NERVOUS SYSTEM AND THEIR CORRELATIONS DURING COVID-19 PANDEMIC

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The purpose of the study was to explore correlations between psychological and regulatory mechanisms in the development of autonomic nervous system dysfunction in response to stressors during the COVID-19 pandemic. 133 students were examined. HADS, PSS-10, State-aR questionnaires were used. Dysfunction of the autonomic nervous system was determined according to A.M. Wein and based on heart rate variability analysis. 37.0 % of respondents had symptoms of anxiety, 38.1 % had subclinical and clinical symptoms of depression, 99.1 % had a moderate and high level of subjective stress. Altered heart rate variability was noted in individuals with subclinical and clinical signs of depression. There were positive correlations between levels of anxiety and depression ($R=0.50$, $p<0.001$), anxiety and stress ($R=0.28$, $p<0.01$), anxiety and ANS dysfunction index ($R=0.23$, $p<0.01$), depression and ANS dysfunction index ($R=0.30$, $p<0.005$), negative correlations – between levels of anxiety and the total index of autonomic regulation aR ($R=–0.45$, $p<0.001$), depression and the total index of autonomic regulation aR ($R=–0.29$, $p<0.01$).

Key words: stress, anxiety, depression, autonomic nervous system, COVID-19 pandemic, international students

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ВЗАЄМОЗВ'ЯЗОК ТРИВОГИ, ДЕПРЕСІЇ ТА ДИСФУНКЦІЇ АВТОНОМНОЇ НЕРВОВОЇ СИСТЕМИ ПІД ЧАС ПАНДЕМІЇ COVID-19

Метою дослідження було вивчення взаємозв'язку психологічних і регуляторних механізмів розвитку дисфункції автономної нервової системи у відповідь на стресові фактори під час пандемії COVID-19. Було обстежено 133 студента. Використовували опитувальники HADS, PSS-10, State-aR. Дисфункцію автономної нервової системи визначали за А.М. Вейном та на основі аналізу варіабельності серцевого ритму. Серед когорти обстежених у 37,0 % відмічались прояви тривоги та 38,1 % мали субклінічні та клінічні прояви депресії. Помірний та високий рівень суб'єктивного стресу мали 99,1 % опитаних. У осіб з субклінічними та клінічними ознаками депресії відзначалась змінена варіабельність серцевого ритму. Прямі зв'язки були між рівнями тривоги та депресії ($R=0,50$, $p<0,001$), тривоги та стресу ($R=0,28$, $p<0,01$), тривоги та показника дисфункції АНС ($R=0,23$, $p<0,05$), депресії та дисфункції АНС ($R=0,30$, $p<0,005$), зворотні – між рівнем тривоги та сумарного показника автономної регуляції aR ($R=–0,45$, $p<0,001$), між рівнем депресії та сумарного показника автономної регуляції aR ($R=–0,29$, $p<0,01$).

Ключові слова: стрес, тривожність, депресія, автономна нервова система, пандемія COVID-19, іноземні студенти

The study is a fragment of the research project "Study of the role of exogenous and endogenous factors in the regulation of protective and adaptive systems of the body", state registration No 0118U004460.

Since the beginning of the COVID-19 pandemic, there has been a deterioration in people's mental health. The prevalence of such symptoms as stress, anxiety, and depression increased by 25 % in the first year of the pandemic, according to the World Health Organization's (WHO) data [12]. During the pandemic, people faced numerous stressors, such as social isolation, restrictions on work, and communication with loved ones. Being alone, feeling a constant fear of infection, the suffering

and death of loved ones, grief after a loss, and financial problems are also significant stressors that lead to anxiety and depression. The pandemic has had the greatest impact on young men's and women's mental health [2, 3]. There is evidence that women are more affected than men, and people who already have chronic diseases, such as asthma, cancer, and heart disease, are more likely to have symptoms of mental disorders [12].

However, M.Daly, E.Robinson in a meta-analysis of longitudinal cohort studies showed a sharp increase in mental health symptoms at the beginning of the pandemic and a significant decrease in symptoms with time. These symptoms were indistinguishable from pre-pandemic symptom profiles. They showed that the so-called psychological adaptation took place [6].

It is known that depression is associated with pronounced autonomic nervous system disorders. Patients with depression had elevated plasma catecholamines levels and other autonomic nervous system (ANS) dysfunction markers. Heart rate variability (HRV) reflects sympatho-vagal balance and is considered an important marker of autonomic function. There is substantial evidence that low HRV precedes the onset of risk factors, whereas high HRV indicates a lower risk profile. [7]. We noted a small number of studies that would study the interaction of psychological and regulatory (vegetative) mechanisms in the development of maladaptive reactions to stress factors during the COVID-19 pandemic. In our opinion, it is important to detect the pre-morbid condition in time in persons affected by the stress factors of the pandemic, which will provide an opportunity to provide them with careful observation and treatment.

The purpose of the study was to explore the correlation of psychological and regulatory (vegetative) mechanisms in the development of autonomic nervous system dysfunction and the formation of premorbid conditions in response to stressors during the COVID-19 pandemic.

Materials and methods. The research was carried out as part of the scientific project "Study of the role of exogenous and endogenous factors in the regulation of the body's protective and adaptive systems", State No. 0118U004460 at the Poltava State Medical University during the COVID-19 pandemic, from November 2020 to the end of January 2021. 133 foreign students of different ethnic groups and from different regions (from the countries of central and northern Africa, the Middle East, Pakistan and India) voluntarily participated in the study. The sample included 78 boys and 55 girls; the age of the interviewees was 20.6±0.2 years. The sample did not include persons with diseases of the cardiovascular system, persons who had psychiatric diseases in the past or at the moment, or those who took psychotropic drugs. According to individual types of questionnaires, the number of responses was from 95 (71 %) to 110 (82 %). This study was conducted with the appropriate understanding of the participants and with their written consent in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the Poltava State Medical University (Protocol No. 189).

The Hospital Anxiety and Depression Scale (HADS) questionnaire by Zigmond and Snaits (1983) was used to assess depression and anxiety symptoms caused by the COVID-19 pandemic. The Perceived Stress Scale (PSS-10) questionnaire was used to assess the level of subjective stress according to Cohen (1983). The state of autonomic regulation was assessed using the State-aR questionnaire with three subscales (orthostatic-circulatory, rest/activity and digestion regulation) [9] and the presence of autonomic nervous system (ANS) dysfunction was determined according to Wein (1998). Neuroticism, individual and psychological focus and the level of socially acceptable answers were assessed according to the questionnaire of H.Eysenck EPi (1963). A separate questionnaire also included a number of questions that assessed life satisfaction (on an 11-point scale from -5 to +5), lifestyle, physical activity, presence or absence of meteotropic reactions.

The study of the state of the ANS based on the analysis of heart rate variability (HRV) was carried out using the hardware ECG systems CARDIOLAB of XAI-MEDICA (Ukraine). The research was carried out in accordance with the International Standard of the European Working Group (1996). HRV indices were calculated using the software of CARDIOLAB HRV/ANS of XAI-MEDICA (Ukraine) and analyzed [1].

For statistical analysis, quantitative indices were expressed as Mean±SEM, ordinal indices were presented in frequency tables. The analysis of the normality of the distributions of indices was carried out using the one-sample Kolmogorov-Smirnov test. Because some measures were not normally distributed, data were compared using the Mann-Whitney U-test. Spearman's rank coefficient of pairwise correlation R was calculated to analyze the relationship between indices. The limit of statistical significance was considered to be $p<0.05$.

For the HADS questionnaire, the anxiety scale Cronbach's alpha coefficient was α=0.80, the depression scale – α=0.79; for the PSS questionnaire – α=0.67; for the autonomic nervous system dysfunction questionnaire – α=0.78; for the State-aR autonomic regulation questionnaire, Cronbach's alpha coefficient was α=0.73 (orthostatic and circulatory regulation subscale), α=0.64 (rest-activity regulation subscale) and α=0.23 (digestion regulation subscale) in the examined group. The statistical analysis was performed using JASP 0.16.

Results of the study and their discussion. Our surveys showed that according to the anxiety scale (HADS questionnaire), the mean level of anxiety among boys was 6.35±0.60 points, and among girls – 6.83±0.61 points, there was no statistically significant difference. In total, 65.3 % of students had no pronounced manifestations of anxiety, and 37.7 % had manifestations of anxiety of varying severity.

According to the depression scale (HADS questionnaire), the mean level of depression in boys was 6.86±0.57 points, in girls – 6.04±0.69 points, there was no statistically significant difference. In total, 61.9 % of students did not have pronounced manifestations of depression, while 38.1 % of the respondents had subclinical and clinical manifestations of depression.

According to PSS questionnaire, the level of subjective stress was found 29.8±0.7 points in boys, and 31.4±0.7 points in girls. 66.7 % of boys and only 40.4 % ($p<0.05$) of girls had a moderate level of subjective stress. 59.6 % of girls and only 31.5 % ($p<0.05$) of boys had high subjective stress. Only 1 of the interviewees did not show signs of stress. At the same time, the index of life satisfaction was positive: for boys +3.0±0.4 points, and for girls +2.9±0.3 points.

Further, an analysis of indices of psycho-emotional state and autonomic regulation was carried out in persons without anxiety symptoms (62 students) and in persons with subclinical and clinical symptoms (combined group, 33 persons, including 13 persons with subclinical and 20 with clinical symptoms of anxiety) (Table 1).

Table 1

Indices of psycho-emotional state and autonomic regulation in students without anxiety symptoms and with subclinical and clinical anxiety symptoms

Index	Without pronounced signs of anxiety		With subclinical and clinical signs of anxiety		p
	M±m	n	M±m	n	
Anxiety index, points	4.06±0.24	62	11.33±0.51	33	<0.001
Depression index, points	5.13±0.49	60	9.06±0.79	32	<0.001
Subjective stress, points	27.8±0.7	60	32.1±.0	31	<0.02
Index of autonomic dysfunction, points	22.04±2.21	56	29.29±3.15	28	>0.05
Individual and psychological focus, points	10.5±0.4	59	11.00±0.6	31	>0.05
Neuroticism, points	11.2±0.6	59	15.10±0.9	31	<0.002
Total index of regulation on the aR scale, points	2.41±0.04	60	2.16±0.06	31	<0.001
Index of orthostatic regulation aR, points	2.52±0.05	61	2.24±0.08	31	<0.005
Index of rest-activity regulation aR, points	2.31±0.06	61	2.13±0.08	31	<0.02
Index of digestion regulation aR, points	2.32±0.05	61	2.10±0.09	31	>0.05

Note: p is an index of the statistical significance of the difference between the indices of groups without pronounced signs of anxiety and with subclinical and clinical signs of anxiety.

In the first group (without signs of anxiety) there were 53 % of young men, in the second group (with manifestations of anxiety) 46 % of young men, there was no statistically significant difference between the distribution by gender. The mean level of anxiety in the first group was 4.1±0.2 points, in the second – 11.3±0.5 points ($p<0.001$). The mean level of depression symptoms in the second group was also higher (9.1±0.8 points vs. 5.1±0.5 points in the group without anxiety, $p<0.001$). The stress level was also higher in the group with anxiety symptoms (33.8±0.7 points vs. 30.3±1.0 points, $p<0.05$), as was neuroticism (15.1±0.9 points vs. 11 ,2±0.6 points, $p<0.002$).

In the first group, there were higher indices of autonomic orthostatic-circulatory regulation of aR (score of 2.5±0.1 in persons without anxiety versus 2.2±0.1 in persons with signs of anxiety, $p<0.005$) and rest-activity regulation aR (score 2.3±0.1 in persons without anxiety versus 2.1±0.1 in persons with signs of anxiety, $p<0.02$).

The level of autonomic dysfunction according to Wein had no statistically significant differences: the first group had 57.1 % of people with dysfunction, in the group with anxiety – 78.6 % ($p<0.05$).

Neuroticism was by 35 % higher in the subclinical and clinical anxiety group (p<0.002).

According to the level of individual psychological orientation and the sincerity of the answers, no statistically significant difference was found between individuals with different levels of anxiety according to the HADS (Fig. 1).

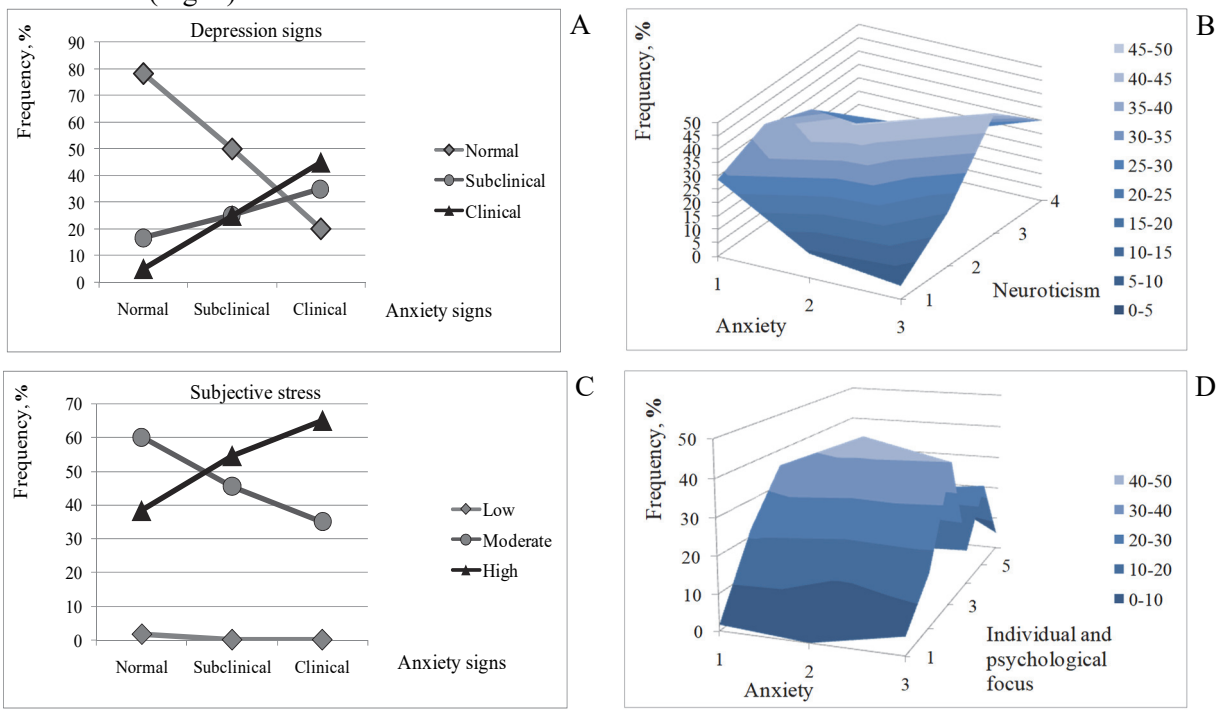

Fig. 1. Manifestations of depression (A), levels of subjective stress (C) and distributions of neuroticism (B) and individual psychological orientation (D) in students with different levels of anxiety. Markings. Anxiety: 1 – norm; 2 – subclinical manifestations; 3 – clinical manifestations. Neuroticism: 1 – low, 2 – medium, 3 – high, 4 – very high. Individual psychological orientation: 1 – hyperintrovert, 2 – introvert, 3 – potential introvert, 4 – ambivert, 5 – potential extrovert, 6 – extrovert.

The next step was to analyze the indices of psycho-emotional state and autonomic regulation in people without signs of depression (the first group, 60 people) and in people with subclinical and clinical signs of depression (the combined second group, 37 people, including 22 people with subclinical and 15 with clinical signs of depression) (Table 2).

Table 2

Indices of psycho-emotional state and autonomous regulation in students without signs of depression and with subclinical and clinical signs of depression

Index	Without pronounced signs of depression		With subclinical and clinical signs of depression		p
	M±m	n	M±m	n	
Anxiety index, points	4.96±0.40	57	9.34±0.76	35	<0.001
Depression index, points	3.72±0.28	60	10.95±0.51	37	<0.001
Subjective stress, points	29.7±0.7	60	32.2±0.9	34	<0.02
Index of autonomic dysfunction, points	20.96±2.08	55	32.03±3.49	30	<0.01
Individual and psychological focus, points	11.3±0.5	59	9.85±0.53	34	>0.05
Neuroticism, points	11.3±0.6	59	14.3±1.0	34	<0.01
Total index of regulation on the aR scale, points	2.38±0.04	59	2.27±0.06	34	>0.05
Index of orthostatic regulation aR, points	2.51±0.05	59	2.32±0.08	35	>0.05
Index of rest-activity regulation aR, points	2.31±0.05	59	2.18±0.09	35	>0.05
Index of digestion regulation aR, points	2.25±0.06	59	2.24±0.08	35	>0.05

Note: p is an index of the statistical significance of the difference between the indices of groups without pronounced signs of depression and with subclinical and clinical signs of depression.

In the first group there were 47 % of young men, in the second 62 % of young men, the difference between the distribution by gender was not statistically significant. The mean level of symptoms of depression in the second group was 11.0±0.51 points against 3.7±0.3 points in the group without depression, p<0.001). The mean level of anxiety in the first group was 5.0±0.4 points, in the second –

9.3±0.8 points (p<0.001). The level of stress did not have a statistically significant difference between these groups. Neuroticism was higher in the group with depression (14.3±1.0 points vs. 11.3±0.6 points, p<0.01).

The indices of autonomic orthostatic-circulatory regulation aR, rest-activity regulation aR and digestive regulation aR had no significant differences.

But the level of autonomic dysfunction according to Wayne differed significantly. In the first group, there were 56.4 % of people with dysfunction, while in the group with depression – 80.0 % (p<0.05). Complaints about the presence of meteotropic reactions increased with the severity of depressive symptoms: 37.9 % of students without clinical symptoms of depression, 54.5 % of students with subclinical symptoms and 60.0 % of students with clinical symptoms (R=0.31, p<0, 05).

Neuroticism was higher by 26 % in the group with subclinical and clinical manifestations of anxiety (p<0.01).

According to the level of individual psychological orientation and the sincerity of the answers, no statistically significant difference was found between individuals with different levels of anxiety according to the HADS (Fig. 2).

The index of ANS dysfunction according to A. Wein was higher in those interviewed with complaints of meteotropic reactions (R=0.37, p<0.02). In the group without dysfunction, 16.7 % of respondents had such complaints, in the group with dysfunction – 57.7 %.

A number of correlations were observed between the studied indices. There were direct relationships between levels of anxiety and depression (R=0.50, p<0.001), anxiety and stress (R=0.28, p<0.01), depression and stress (R=0.24, p <0.05), anxiety and the index of ANS dysfunction (R=0.23, p<0.05), depression and ANS dysfunction (R=0.30, p<0.005), the inverse – between the level of anxiety and the total index of autonomic aR regulation (R=–0.45, p<0.001), between the level of depression and the total index of aR autonomous regulation (R=–0.29, p<0.01).

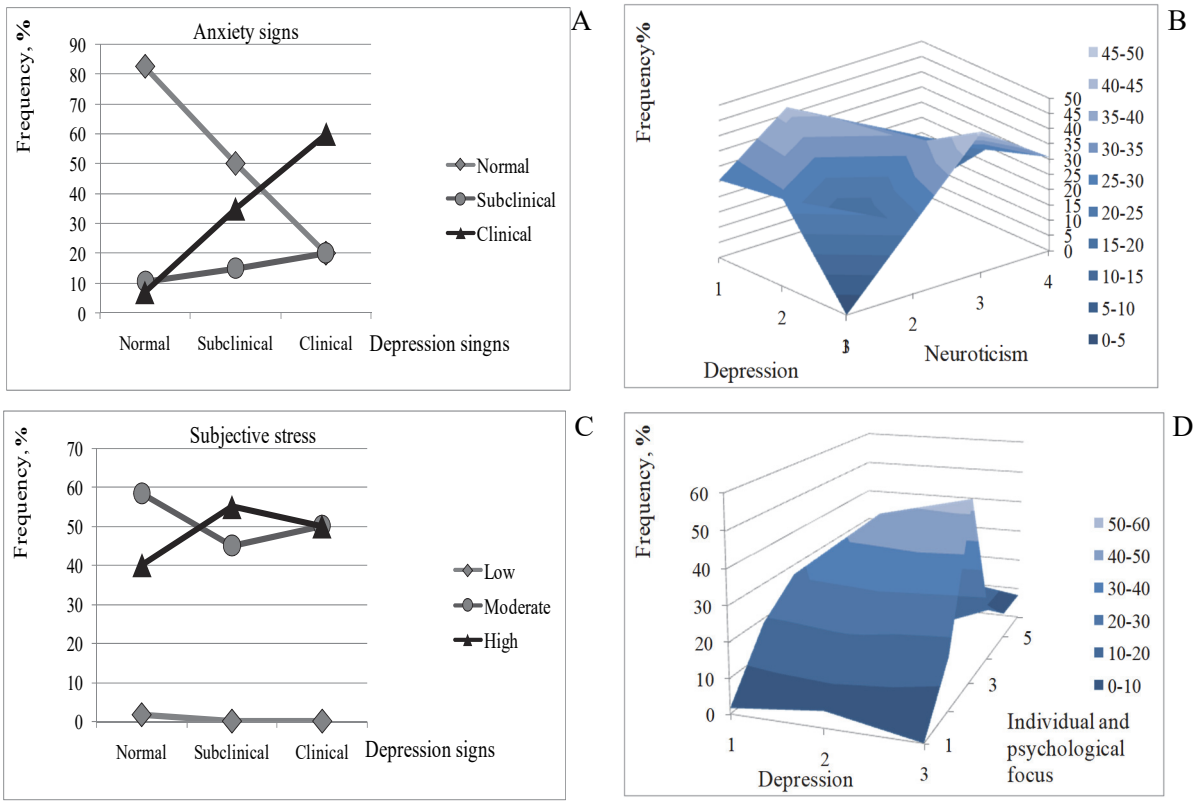

Fig. 2. Manifestations of anxiety (A), levels of subjective stress (C) and distributions of neuroticism (B) and individual psychological orientation (D) in students with different levels of depression. Markings. Depression: 1 – norm; 2 – subclinical manifestations; 3 – clinical manifestations. Neuroticism: 1 – low, 2 – medium, 3 – high, 4 – very high. Individual psychological orientation: 1 – hyperintrovert, 2 – introvert, 3 – potential introvert, 4 – ambivert, 5 – potential extrovert, 6 – extrovert.

Both the index of orthostatic regulation and the index of rest-activity regulation (aR subscales) were inversely correlated with the anxiety index (R=–0.37, p<0.001 and R=–0.35, p<0.001, respectively), and with depression index (R=–0.26, p<0.02 and R=–0.23, p<0.05, respectively). But the stress index was correlated only with the index of orthostatic regulation aR (R=–0.22, p<0.05). The index of digestive regulation aR had correlation only with the rest/activity regulation aR (R=0.25, p<0.01) and with the total

index of autonomous regulation aR (R=0.44, p<0.001), and in a small group of 10 people who drank alcohol, there is a negative relationship with the frequency of its use (R=–0.64, p<0.05).

It should be noted that the way of life had connections with the severity of anxiety. Morning exercise frequency (number of days per week) and morning exercise duration were correlated with a lower anxiety score (R=–0.32, p<0.05 and R=–0.33, p<0.05, respectively). The frequency of morning exercise was also higher in persons with a lower level of stress (R=–0.35, p<0.02). Among those who practiced morning exercises, only 25 % and 31 % of students were in groups with subclinical and clinical manifestations of anxiety and depression, respectively (Fig. 3).

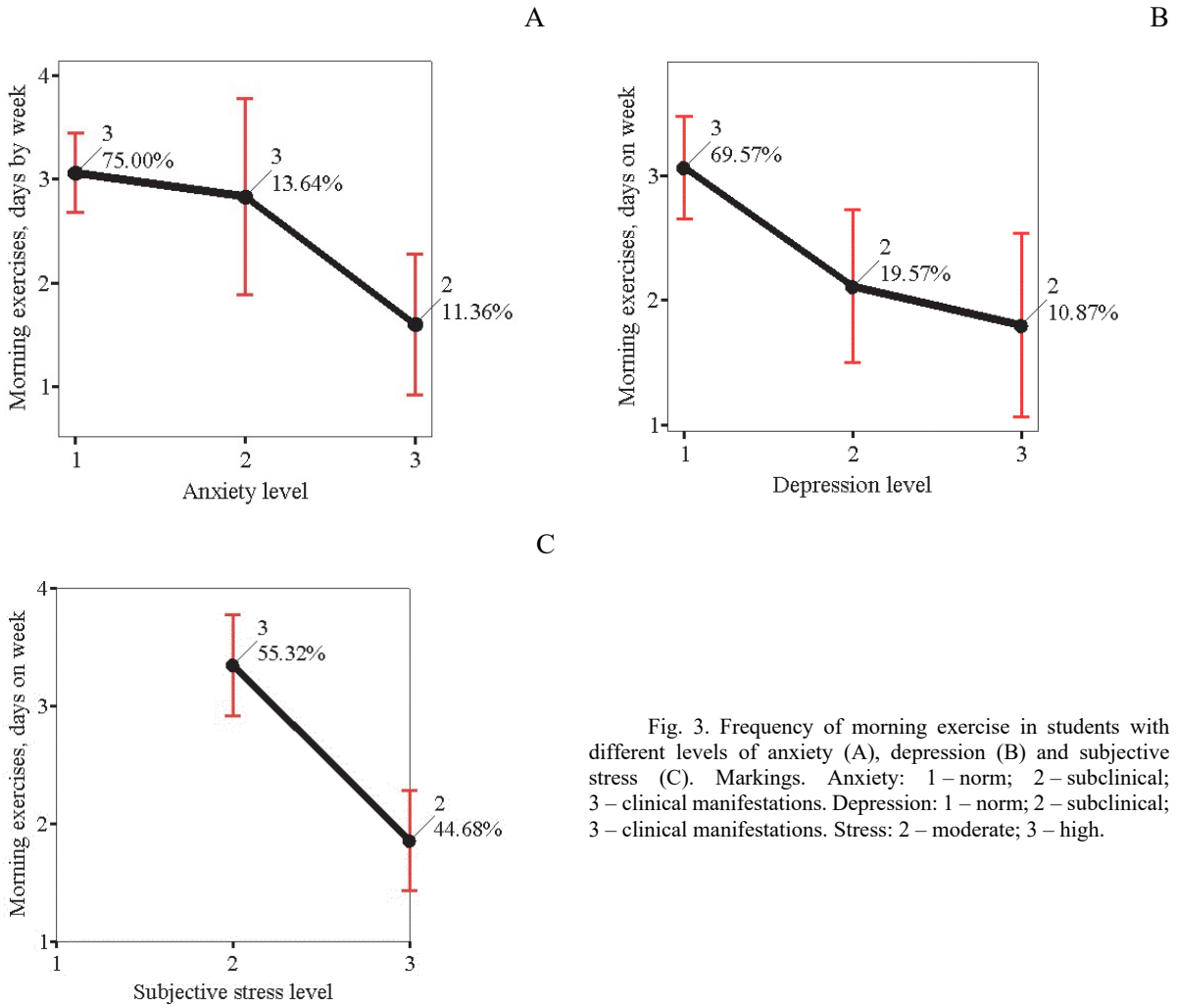

Fig. 3. Frequency of morning exercise in students with different levels of anxiety (A), depression (B) and subjective stress (C). Markings. Anxiety: 1 – norm; 2 – subclinical; 3 – clinical manifestations. Depression: 1 – norm; 2 – subclinical; 3 – clinical manifestations. Stress: 2 – moderate; 3 – high.

The life satisfaction index was inversely correlated with the severity of anxiety (R=–0.29, p<0.05), positively correlated with the frequency of morning exercises (R=0.30, p<0.05).

According to S.Cohen and D.Janicki-Deverts (2012), in this age group the stress level should be within the range of mean±SD 16.78±6.86, which is significantly lower than what we observed in the examined group [5]. A review of Harrison, L. et al. (2022) also found a high prevalence of depression and anxiety among children and adolescents during the COVID-19 pandemic [8] According to L.Brusaferri et al. (2022), since the beginning of the pandemic, the severity and prevalence of symptoms of psychological distress, fatigue, brain fog, and other conditions have increased significantly in the United States, including among people who were not infected with SARS-CoV-2 [4].

The results of this study showed that stress and depression are associated with disorders of autonomic nervous regulation, affect HRV and shift the autonomic balance towards increased sympathetic tone and/or decreased cardiovagal activity. In persons with signs of depression, the standard deviation of the intervals from the norm to the norm was 68.2±4.5 ms (with the norm 59.8±3.8 ms), the mean square deviation of the difference of consecutive N-N intervals was 52.55±1.9 ms against 68.7±8.3 ms in persons without depression. All this indicated a sympatho-parasympathetic modulation of HRV and a decrease in the parasympathetic activity of the ANS. These baseline differences affected autonomic reactivity during

the orthostatic test, indicating dysfunction of autonomic regulation during long-term psychological stress and depression. According to Zsófia Ocsovszky, patients with major depressive disorder also had altered heart rate variability (HRV) [10].

This study once again showed the vulnerability of psychophysiological homeostasis and the possible development of post-traumatic stress syndromes during the COVID-19 epidemic. Understanding the regulation of psychophysiological processes is important for the development of effective systematic programs for the prevention of premorbid conditions and subsequent prevention and treatment.

Conclusions

1. Our research shows that among the examined cohort, 37.0 % had anxiety manifestations of varying severity, and 38.1 % had subclinical and clinical depression.

2. 99.1 % of respondents had a moderate and high level of subjective stress. Moreover, girls had a higher percentage of a high level of subjective stress.

3. Individuals with subclinical and clinical anxiety symptoms had higher mean levels of depression and stress symptoms. They had lower autonomic orthostatic-circulatory regulation and rest/activity regulation.

4. Stress and depression were correlated with autonomic nervous system disorders. Individuals with subclinical and clinical depression had higher baseline heart rate (HR) and altered heart rate variability (HRV), indicating altered autonomic balance due to increased sympathetic tone or decreased cardiovagal activity. These differences affected the autonomic reactivity during the orthostatic test.

5. Understanding the regulation of psychophysiological processes is important for the development of effective systematic programs for the prevention of premorbid conditions and their subsequent prevention.

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