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LIPID PEROXIDATION AND ANTIOXIDANT DEFENSE SYSTEM INDICATORS IN ADOLESCENTS WITH TENSION HEADACHE

DOI 10.25789/YMJ.2025.91.02

UDC 616.857+371.7:577.115

The aim of the study was to investigate the characteristics of changes in the indicators of the lipid peroxidation (LPO) system and antioxidant defense (AOP) in blood plasma and erythrocytes in adolescents with tension-type headache (TH). Materials and methods: 104 individuals (boys and girls) aged 12-17 years were examined, including 64 adolescents with TH (main group) and 40 without TH (comparison group). The content of LPO-AOP system parameters was determined using spectrophotometric detection methods. The obtained data were processed in the Statistica 12 program. Results: adolescents with TH had higher plasma MDA levels and lower plasma and erythrocyte SOD activity. A large number of individuals with high plasma MDA concentrations and low plasma and erythrocyte SOD activity were found in adolescents with a history of TH episodes. Statistically significant intragroup differences were revealed for most parameters of the LPO-AOP between their gradations: “normal level” and the level “above normal” and/or “below normal”. Discussion: considering the significant role of the imbalance of the LPO-AOP system parameters in the development of oxidative stress, the increase in MDA and decrease in SOD activity that we have identified are ambiguous in terms of their interpretation: on the one hand, they can be regarded as metabolic markers of the presence of TH, on the other hand, their role as predictors of the development of this pathology is highly probable. This assumption can be confirmed or rejected by the results of further studies. Conclusions: Adolescents with TH are characterized by a higher MDA content and lower SOD activity, which indicates that they have a greater severity of oxidative stress. In the group with TH, the number of adolescents with the above shifts in the LPO-AOP system is higher than in the group without TH.

Keywords: adolescents; tension headache; lipid peroxidation; antioxidant protection

For citation: Kostyuchenko Yu.R., Evert L.S., Smirnova O.V., Sinyakov A.A. Lipid peroxidation and antioxidant defense system indicators in adolescents with tension headache. Yakut medical journal. 2025; 91(3): 8-14. https://doi.org/10.25789/YMJ.2025.91.02

Introduction. Tension headache (TH) and migraine are common neurological disorders among adolescents and young adults, significantly affecting their quality of life. The problem of headache occupies a special place in pediatric practice, its frequency in adolescent populations is 18-25%, reaching a peak in adolescence [7]. One of the most common forms of primary cephalgia among adolescents is tension headache. Its prevalence varies depending on the geographic region, ethnicity, age, gender and socioeconomic conditions.

In recent decades, the role of oxidative stress (OS) in the pathogenesis of headaches has attracted the attention of researchers [4]. A number of relevant studies have been conducted on changes in the lipid peroxidation (LPO) and antioxidant defense (AOD) system parameters in adolescents and young adults with TH and migraine [1]. Changes in the LPO-AOP system parameters confirm the hypothesis of its role in the pathogenesis of TH and migraine. The LPO-AOP system reflects the balance between prooxidant and antioxidant processes. Disruption of this balance can contribute to the development and progression of pain syndromes, including TH [12].

The focus of research has shifted to the study of the molecular mechanisms underlying these conditions, among which the imbalance of the LPO and AOP system plays a key role [13]. A number of researchers have analyzed changes in LPO-AOP indices in blood plasma and erythrocytes, characteristic of TH and migraine, and assessed their potential as biomarkers of cephalgia [5, 11, 13]. The problem of comorbidity of pain in internal organs and headache is discussed [9]. However, the role of changes in LPO-AOP indices as risk factors or chronicity of headaches, especially in adolescents, remains controversial.

Numerous recent studies have been devoted to the study of various aspects of migraine [8], while very little attention has been paid to the study of similar problems in tension-type headaches [10, 11, 12], especially in adolescents and young adults. To date, the pathophysiology of headache has not been clearly established. A study by S. Vurucu et al. (2013)

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found that the average activity of erythrocyte superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPO), as well as malondialdehyde (MDA) levels were significantly higher in adolescents with chronic daily headache (CDH) than in the control group without headache ($p < 0.001$). The results of this work indicate that oxidative stress may play a causal or indirect role in children with CDH [11].

The small number and inconsistency of the results of studies of the parameters of the oxidant-antioxidant system in children and adolescents with tension-type headache, the need to clarify their role in the pathogenesis of this pathology, served as the basis for our study, **the purpose** of which was to study the features of changes in the parameters of the lipid peroxidation system and antioxidant protection in blood plasma and erythrocytes in adolescents with tension-type headache.

Materials and methods of the study. The object of the study were 104 adolescents (boys and girls) with TH (the main group, n=64, including 39 boys and 25 girls) and without TH (the comparison group, n=40, including 24 boys and 16 girls). The criterion for inclusion in the main group was the presence of such a clinical form of primary cephalgia as episodic frequent TH in adolescents. The presence of episodic rare TH in adolescents was not a reason for their hospitalization, and was regarded by us as a criterion for non-inclusion in the study. The parameters of the LPO-AOP system were considered as the subject of the study. The presence of tension headache was assessed using a questionnaire that included the criteria of the International Classification of Headache Disorders (ICHD) for this type of cephalgia [6].

LPO-AOP indicators were assessed in venous blood samples from pediatric patients, collected from their cubital vein in the morning on an empty stomach in Vacutainer tubes with sodium heparin solution (5 U/ml), using spectrophotometric detection methods [3].

The set of laboratory parameters included determination of the parameter of secondary products of free radical oxidation (FRO) of lipids and proteins – malondialdehyde (MDA, μmol/1 g protein). Evaluation of the non-enzymatic link of the activity of the endogenous antioxidant defense system included determination of reduced glutathione (GSH, μmol/1 g Hb). The enzymatic link of the endogenous AOP system was assessed by the activity of superoxide dismutase (SOD, U/min/1 g protein), glutathione peroxidase (GPO, μmol/1 g Hb), catalase (CAT, μmol/s/1 g protein), glutathione-S-transferase (GST, mmol/min per 1 g Hb) and determination of ferroxidase activity of ceruloplasmin (CP, mg/l). The complex of laboratory studies also included determination of hemoglobin content (Hb, g/l) and total blood protein.

All procedures performed in this study complied with the ethical standards of the Biomedical Ethics Committee and the principles of the World Medical Association Declaration of Helsinki (as amended in 2013). The study design was reviewed and approved at a meeting of the Ethics Committee of the Federal State Budgetary Scientific Institution, the Scientific Center of the Siberian Branch of the Russian Academy of Sciences (protocol No. 3 dated March 16, 2020). Before inclusion in the study, all patients aged 15 years and older, as well as parents (or legal representatives) of patients under 15 years of age, were informed about the goals and methods of the work and

Table 1

Quantitative indicators of the LPO-AOZ system in adolescents with and without tension headaches

Indicators	Groups	M	N	Me	Mo	25‰	75‰	p1-2 (по MU)
In blood plasma								
Protein (norm 65-85)	1.without HT 2. with HT	70.32 63.41	34 58	68.50 61.50	85.00 53.00	60.00 54.00	84.00 71.00	0.0140
Malondialdehyde (MDA, μmol/1g protein)	1.without HT 2. with HT	0.38 1.35	34 58	0.35 1.14	multiple multiple	0.18 0.78	0.52 1.53	<0.0001
Superoxide dismutase (SOD, units/min/1g protein)	1.without HT 2. with HT	190.59 132.17	34 57	190.08 136.24	197.14 no mode	152.73 94.43	245.32 169.41	<0.0001
Catalase (CAT, μmol/s/1g protein)	1.without HT 2. with HT	0.04 0.06	34 58	0.03 0.04	0.01 0.03	0.01 0.02	0.08 0.07	0.1048
Ceruloplasmin (CP, mg/l)	1.without HT 2. with HT	278.76 268.16	34 58	253.00 254.50	multiple 187.00	209.00 200.00	311.00 332.00	0.9195
In erythrocytes								
Hemoglobin (Hb, g/l)	1.without HT 2. with HT	93.16 93.03	40 64	96.94 93.91	no mode 61.23	81.12 81.27	110.04 104.97	0.6836
Malondialdehyde (MDA, nmol/1g Hb)	1.without HT 2. with HT	0.24 0.25	37 62	0.16 0.19	0.17 0.14	0.10 0.12	0.29 0.27	0.5773
Catalase (CAT, mmol/s/1g Hb)	1.without HT 2. with HT	14.68 14.55	40 64	13.16 13.06	no mode 12.28	10.84 11.55	16.09 15.89	0.8779
Glutathione peroxidase (GPO, μmol/1g Hb)	1.without HT 2. with HT	0.26 0.25	40 64	0.19 0.21	0.06 0.18	0.11 0.15	0.30 0.32	0.3997
Reduced Glutathione (GSH, μmol/1g Hb)	1.without HT 2. with HT	6.87 7.48	35 61	6.06 6.80	4.67 no mode	4.58 4.41	8.32 9.97	0.3731
Superoxide dismutase (SOD, units/min/1g Hb)	1.without HT 2. with HT	206.58 103.80	40 64	231.65 95.64	no mode multiple	129.29 78.02	274.60 125.62	<0.0001
Glutathione S-transferase (GST, mmol/min/1g Hb)	1.without HT 2. with HT	10.91 10.51	40 64	9.54 10.02	5.47 7.08	6.73 5.68	13.28 14.47	0.6665

signed a written voluntary informed consent to participate.

The obtained material was processed using the nonparametric statistics module of the program “Statistica 12” [2]. The normality of the distribution of quantitative indicators was assessed using the Kolmogorov-Smirnov Test and the Shapiro-Wilk Test. The results of the analysis of quantitative features are presented as median (Me) values and its interquartile range (Q25–Q75). The form of presentation of qualitative (binary) features were the values of % share and the boundaries of the confidence interval (CI) determined by the Wilson method. The significance of differences (p) for quantitative features was assessed by the Mann–Whitney U-test, for binary features – by the Pearson χ2 criterion. Values of p ≤ 0.05 allowed us to consider the differences in indicators obtained between the groups statistically significant.

Results and discussion. According to the International Classification of Headache Disorders (ICHD) criteria for frequent episodic tension-type headache [6], adolescents with a frequency of cephalgic episodes from 1 to 15 per month were considered to be persons with this clinical form of cephalgia. Evaluation of the frequency of headache attacks showed that episodes of cephalgia 2 days per week (d/wk) were observed in 13.8% of our patients, 34.5% had headaches 3 days/wk, 20.7% had headaches 4 days/wk, 17.2% had headaches 5 days/wk, and 6.9% each accounted for the number of adolescents with a frequency of cephalgia 6 and 7 days per week. Pain intensity was assessed using a visual analogue scale (VAS) and expressed as points. The average score on this scale in adolescents of the main group (with TH) was 5.7 (CI 4.9-6.6) points. The average duration of the presence of cephalgic episodes in the anamnesis was 3.9 (CI 3.3-4.8) years in adolescents of the main group.

To correctly assess the level of indicators of the LPO-AOP system in the blood plasma and erythrocytes of the examined patients, we preliminarily determined internal standards for each quantitative indicator by verifying their percentile values in adolescents of the control group - without TH. The norm was considered to be the values of each of the indicators in adolescents without TH, which were in the range of ≥ 25‰ and ≤ 75‰. The level above the norm was considered to be the value of the indicator > 75‰, below the norm - the value < 25‰.

The quantitative values of the LPO-AOP system indicators in adolescents with and without tension-type headache (TH) are reflected in Table 1.

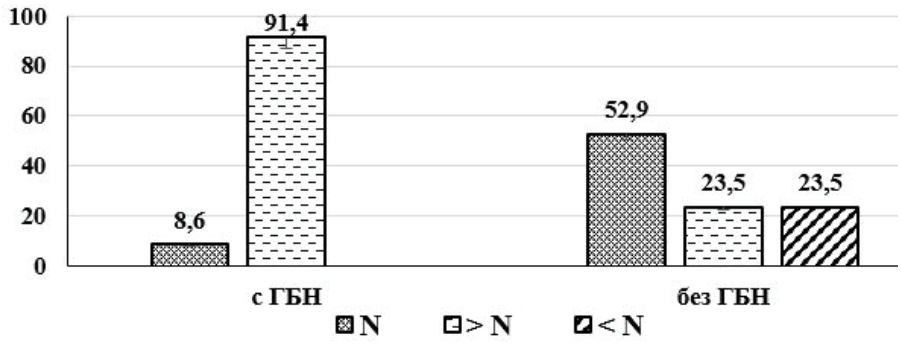

Fig. 1. Distribution of adolescents in the compared groups by the level of malondialdehyde (MDA) in blood plasma, in %. Note: Statistical significance of differences (p) in the comparison groups for the indicator "MDA Level N" p1-2 <0.001, x2=22.46; for the indicator "MDA Level > N" p1-2 <0.001, x2=44.17; for the indicator "MDA Level <N" p1-2|<0.001, x2=14.95

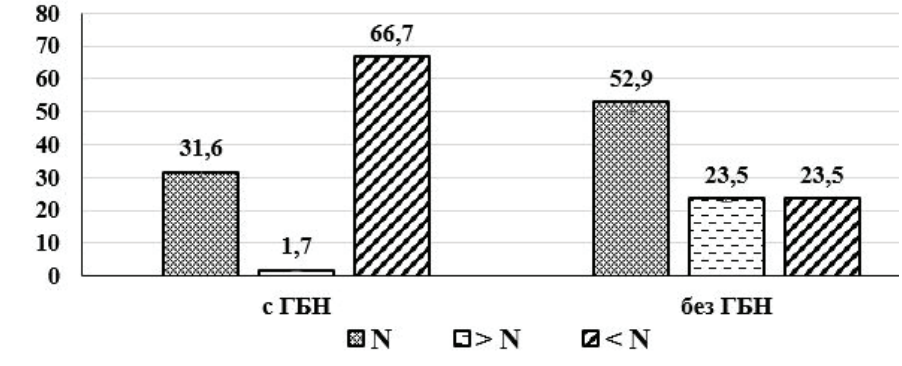

Fig. 2. Distribution of adolescents in the compared groups by the level of superoxide dismutase (SOD) in blood plasma, in %/ Note: Statistical significance of differences (p) in the comparison groups for the indicator "SOD Level N" p1-2 = 0.044, χ2 = 4.06; for the indicator "SOD Level > N" p1-2 <0.001, x2 = 11.33; for the indicator "SOD Level <N" p1-2 <0.001, x2 = 15.85

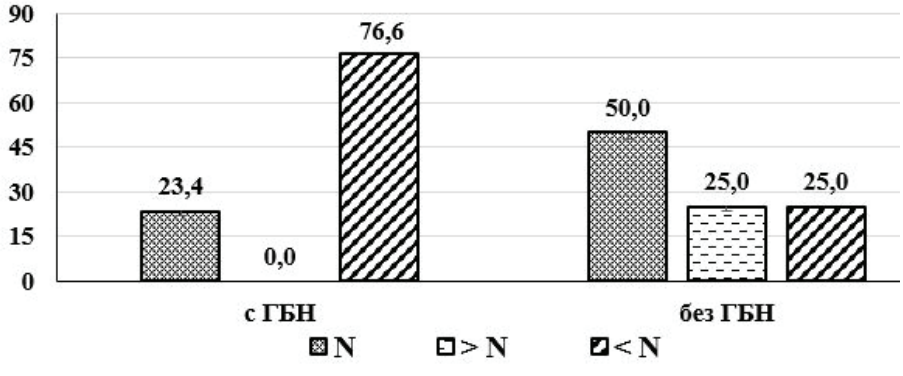

Fig. 3. Distribution of adolescents in the compared groups by the level of superoxide dismutase (SOD) in erythrocytes, in % Note: Statistical significance of differences (p) in the comparison groups for the indicator "SOD Level N" p 1-2=0.006, chi * 2 = 7.78 for the indicator "SOD Level > N" p 1-2<0.001, chi * 2 = 17.7 ; for the indicator "SOD Level < \mathbb{N} ^ prime prime p1-2<0.001, chi * 2 = 26.66 .

As follows from the above table 1, adolescents with TH had significantly higher levels of malonic dialdehyde in their blood plasma and lower plasma concentrations of the enzyme superoxide dismutase (p1-2 <0.0001). The content of this enzyme was also lower in the erythrocytes of those examined with TH (p1-2 <0.0001). The metabolic shifts detected in adolescents with TH indicate that they have manifestations of oxidative stress.

The distribution of the examined adolescents with and without TH depending on the level of malondialdehyde in the blood plasma is presented in Fig. 1.

According to statistical analysis, it was established that among those examined with TH, there were significantly more adolescents with a high content of malondialdehyde (p1-2 <0.001), significantly fewer with a level of the indicator within the normal range (p1-2 <0.001), and there were no individuals with a dialdehyde level below the norm among those examined in this group (p1-2 <0.001) (Fig. 1).

Figure 2 illustrates the distribution of adolescents in the compared groups by the level of superoxide dismutase (SOD) in blood plasma.

In the group with TH, there were significantly fewer adolescents with normal and elevated levels of plasma superoxide dismutase, and the proportion of individuals with low values of this indicator was higher. While the comparison group (without TH) had a larger number of individuals with normal and above-normal levels of superoxide dismutase, this group had significantly fewer adolescents with low levels of this enzyme.

Figure 3 shows the results of a comparative analysis of the distribution of adolescents by the level of superoxide dismutase in erythrocytes in groups with and without TH.

As follows from the data presented in Fig. 3, the trend in the distribution of those examined by the level of SOD in erythrocytes was similar to that noted for this indicator, but determined in blood plasma.

In addition to the analysis of intergroup differences, we analyzed intragroup differences in the indicators in each of the compared groups. The results obtained are included in Tables 2 and 3.

In the overwhelming majority of cases, statistically significant intragroup differences were observed between such gradations of the analyzed characteristics as "normal level" and "level above normal", as well as between the gradation "normal level" and "level below normal". Only in isolated cases were the differences between the gradation "level above normal" and "level below normal" statistically significant; such a pattern was characteristic of almost all indicators and all compared groups (Tables 2 and 3).

The percentage ratio of the number of adolescents with normal, elevated and reduced levels of the LPO-AOP system indicators both in plasma and in erythrocytes did not have statistically significant differences. The exception was a smaller number of individuals with high plasma protein concentration in blood plasma and a larger proportion of individuals with high plasma protein content among adolescents with TH (Table 2).

It seemed interesting to us to analyze the features of the quantitative values of the indicators of the POL-AOP system among the examined adolescents depending on their gender. The results of the comparative analysis of these indicators are presented in Table 4.

As the analysis showed, statistically significant gender differences were revealed only in relation to the content of the enzymatic component of the AOP – erythrocyte glutathione peroxidase: girls with TH had a higher content of this en-

Table 2

Intergroup and intragroup differences in the indicators of the LPO-AOP system in adolescents with and without TH

Groups of those surveyed	Indicators of the LPO-AOP system						P (Pearson's χ2)
	(a) norm		(в) above normal		(c) below normal		
	abs.	% (DI)	abs.	% (DI)	abs.	% (DI)	
Plasma protein (g/l)							
1 gr. without TH (n=34)	19	55.9 (39.5-71.1)	7	20.6 (10.3-36.8)	8	23.5 (12.4-40.0)	ав=0.003 ас=0.007 вс=0.770
2 gr. with TH (n=58)	28	48.3 (35.9-60.8)	4	6.9 (2.7-16.4)	26	44.8 (32.7-57.5)	ав<0.001 ас=0.710 вс<0.001
Total (n= 92)	47	51.1 (41.0-61.6)	11	12.0 (6.8-20.2)	34	37.0 (27.8-47.2)	ав<0.001 ас=0.054 вс<0.001
p1-2; χ2	0.482; 0.50		0.051; 3.82		0.042; 4.17		
Catalase (CAT) of blood plasma (μmol/s/1 g protein)							
1 gr. without TH (n=34)	20	58.8 (42.2-73.6)	7	20.6 (10.3-36.8)	7	20.6 (10.3-36.8)	ав=0.002 ас=0.002 вс=1.000
2 gr. with TH (n=58)	40	69.0 (56.2-79.4)	13	22.4 (13.6-34.7)	5	8.6 (3.7-18.6)	ав<0.001 ас<0.001 вс=0.041
Total (n= 92)	60	65.2 (55.1-74.2)	20	21.7 (14.5-31.2)	12	13.0 (7.6-21.4)	ав<0.001 ас<0.001 вс=0.120
p1-2; χ2	0.325; 0.97		0.838; 0.04		0.100; 2.71		
Ceruloplasmin (CP) in blood plasma (mg/l)							
1 gr. without TH (n=34)	18	52.9 (36.7-68.5)	8	23.5 (12.4-40.0)	8	23.5 (12.4-40.0)	ав=0.013 ас=0.013 вс=1.000
2 gr. with TH (n=58)	27	46.5 (34.3-59.2)	16	27.6 (17.8-40.2)	15	25.9 (16.3-38.4)	ав=0.035 ас=0.021 вс=0.834
Total (n= 92)	45	48.9 (38.9-59.0)	24	26.1 (18.2-35.9)	23	25.0 (17.3-34.7)	ав=0.002 ас<0.001 вс=0.866
p1-2; χ2	0.555; 0.35		0.669; 0.18		0.804; 0.06		
Malondialdehyde (MDA) (nmol/1g Hb)							
1 gr. without TH (n=37)	20	54.1 (38.4-69.0)	9	24.3 (13.4-40.1)	8	21.6 (11.4-37.2)	ав=0.009 ас=0.005 вс=0.783
2 gr. with TH (n=62)	41	66.1 (53.7-76.7)	11	17.7 (10.2-29.0)	10	16.1 (9.0-27.2)	ав<0.001 ас<0.001 вс=0.811
Total (n= 99)	61	61.6 (51.8-70.6)	20	20.2 (13.5-29.2)	18	18.2 (11.8-26.9)	ав<0.001 ас<0.001 вс=0.719
p1-2; χ2	0.233; 1.43		0.431; 0.62		0.494; 0.47		

zyme than a similar group of boys (0.30 and 0.22 μmol/1 g Hb, respectively) (Table 4). As illustrated by the data presented in Table 4, significant differences in the content of both plasma and erythrocyte concentrations of the LPO-AOP system indicators depended mainly on the presence or absence of TH, and not on gender. Both boys and girls with TH were characterized by a higher content of MDA in both plasma and erythrocytes, in contrast to their peers without TH. In contrast, adolescents without TH, regardless of gender, had a higher content of the SOD enzyme (Table 4). No significant differences were found in the comparison groups for other indicators of the LPO-AOP system - catalase (CAT), ceruloplasmin (CP), reduced glutathione (GSH), and glutathione-S-transferase (GST) (Table 4).

Thus, our study has established the presence of activation of LPO-AOP processes in patients with TH, confirmed by a higher content of malondialdehyde and manifestations of imbalance in antioxidant protection indicators in the form of significantly lower activity of plasma and erythrocyte SOD. We attempted to analyze the features of changes in oxidant-antioxidant status indicators and assess the significance of its imbalance in the genesis of TH in adolescents. The importance of studying these aspects is due to the need to determine the role of these disorders as one of the probable pathogenetic mechanisms for the transformation of this type of cephalgia into chronic forms of psychosomatic pathology, the importance of their early diagnosis and the feasibility of pathogenetically substantiated correction.

The antioxidant defense system plays a critical role in maintaining the balance between the formation of reactive oxygen species and protecting the body from oxidative stress. Components of the antioxidant defense system (SOD, GPx, CAT, GST, GSH, CP) are crucial in protecting the body from oxidative stress, playing an important role in the pathogenesis of TH and migraine in adolescents. Studying changes in the levels of these indicators allows developing prevention and treatment strategies aimed at restoring the antioxidant balance and improving the quality of life of adolescents with TH and migraine.

Over the past decade, the key role of LPO-AOP imbalance in the pathogenesis of migraine and TH in young people has been proven. For a deeper understanding of these aspects, multicenter studies with unified protocols are needed. In our opinion, a promising direction for further research is the identification of highly informative predictors and diagnostic markers of LPO-AOP system disorders for the purpose of early diagnosis of oxidative stress in adolescents and young adults with recurrent cephalgia for effective prevention, personalized antioxidant therapy and improved prognosis for these types of pathology.

Table 3

Intergroup and intragroup differences in the indicators of the LPO-AOP system in adolescents with and without TH (continued)

Groups of those surveyed	Indicators of the LPO-AOP system						P (Pearson's χ2)
	(a) norm		(в) above normal		(c) below normal		
	abs.	% (DI)	abs.	% (DI)	abs.	% (DI)	
Catalase (CAT) of erythrocytes (mmol/s/1g Hb)							
1 gr. without TH (n=40)	20	50.0 (35.2-64.8)	10	25.0 (14.2-40.2)	10	25.0 (14.2-40.2)	ав=0.021 ac=0.021 вс=1.000
2 gr. with TH (n=64)	38	59.4 (47.1-70.5)	16	25.0 (16.0-36.8)	10	15.6 (8.7-26.4)	ав<0.001 ac<0.001 вс=0.188
Total (n= 104)	58	55.8 (46.2-64.9)	26	25.0 (17.7-34.1)	20	19.2 (12.8-27.8)	ав<0.001 ac<0.001 вс=0.317
p1-2; χ2	0.350; 0.88		1.000; 0.00		0.238; 1.39		
Glutathione peroxidase (GPO) of erythrocytes (μmol/1 g Hb)							
1 gr. without TH (n=40)	20	50.0 (35.2-64.8)	10	25.0 (14.2-40.2)	10	25.0 (14.2-40.2)	ав=0.021 ac=0.021 вс=1.000
2 gr. with TH (n=64)	37	57.8 (45.6-69.1)	18	28.1 (18.6-40.1)	9	14.1 (7.6-24.6)	ав<0.001 ac<0.001 вс=0.052
Total (n= 104)	57	54.8 (45.2-64.0)	28	26.9 (19.3-36.2)	19	18.3 (12.0-26.8)	ав<0.001 ac<0.001 вс=0.136
p1-2; χ2	0.437; 0.61		0.727; 0.12		0.161; 1.97		
Reduced glutathione (GSH) of erythrocytes (μmol/1g Hb)							
1 gr. without TH (n=35)	19	54.3 (38.2-69.5)	8	22.9 (12.1-39.0)	8	22.9 (12.1-39.0)	ав=0.007 ac=0.007 вс=1.000
2 gr. with TH (n=61)	24	39.3 (28.1-51.9)	21	34.4 (23.7-47.0)	16	26.2 (16.8-38.4)	ав=0.274 ac=0.123 вс=0.325
Total (n= 96)	43	44.8 (35.2-54.7)	29	30.2 (21.9-40.0)	24	25.0 (17.4-34.5)	ав=0.037 ac=0.005 вс=0.420
p1-2; χ2	0.157; 2.01		0.235; 1.41		0.714; 0.13		
Glutathione-S-transferase (GST) of erythrocytes (mmol/min/1g Hb)							
1 gr. without TH (n=40)	20	50.0 (35.2-64.8)	10	25.0 (14.2-40.2)	10	25.0 (14.2-40.2)	ав=0.021 ac=0.021 вс=1.000
2 gr. with TH (n=64)	23	35.9 (25.3-48.2)	19	29.7 (19.9-41.8)	22	34.4 (23.9-46.6)	ав=0.454 ac=0.854 вс=0.570
Total (n= 104)	43	41.3 (32.4-51.0)	29	27.9 (20.2-37.2)	32	30.8 (22.7-40.2)	ав=0.042 ac=0.113 вс=0.648
p1-2; χ2	0.157; 2.01		0.605; 0.27		0.314; 1.02		

Conclusions:

1. Adolescents with headaches have higher plasma malondialdehyde concentrations and lower plasma and erythrocyte superoxide dismutase activity.

2. The group with TH has a higher proportion of adolescents with high plasma MDA levels and low plasma and erythrocyte SOD activity.

Table 4

Content of POL-AOZ components in adolescents of different sexes with and without TH

Indicators	Groups of those surveyed		M	N	Me	Mo	25‰	75‰	Std. Dev.	P по MU
In blood plasma										
Protein (norm 65-85)	1rp	without TH (m)	69.90	20	68.50	60.00	82.50	12.58	1-2	0.9581
	2rp	without TH (d)	70.93	14	73.50	60.00	84.00	14.89	3-4	0.1653
	3rp	with TH (m)	61.17	36	60.50	54.50	67.00	10.35	1-3	**0.0105**
	4rp	with TH (d)	67.09	22	65.50	54.00	79.00	13.41	2-4	0.5156
Malondialdehyde (MDA, µmol/1g protein)	1rp	without TH (m)	0.34	20	0.26	0.13	0.61	0.27	1-2	0.1666
	2rp	without TH (d)	0.44	14	0.39	0.29	0.48	0.25	3-4	0.1492
	3rp	with TH (m)	1.52	36	1.27	0.80	1.60	1.52	1-3	**<0.0001**
	4rp	with TH (d)	1.06	22	1.08	0.68	1.33	0.40	2-4	**<0.0001**
Superoxide dismutase (SOD, units/min/1g protein)	1rp	without TH (m)	192.42	20	184.91	137.45	262.77	75.03	1-2	0.9860
	2rp	without TH (d)	187.97	14	197.14	168.57	228.58	67.50	3-4	0.7742
	3rp	with TH (m)	132.93	35	141.51	78.56	175.86	58.05	1-3	**0.0050**
	4rp	with TH (d)	130.96	22	126.50	96.46	159.25	38.75	2-4	**0.0016**
Catalase (CAT, µmol/s/1g protein	1rp	without TH (m)	0.05	20	0.03	0.02	0.08	0.04	1-2	0.3356
	2rp	without TH (d)	0.04	14	0.02	0.01	0.08	0.04	3-4	0.6193
	3rp	with TH (m)	0.06	36	0.04	0.02	0.07	0.07	1-3	0.5324
	4rp	with TH (d)	0.06	22	0.05	0.03	0.07	0.04	2-4	0.0797
Ceruloplasmin (CP, mg/l)	1rp	without TH (m)	257.40	20	238.00	208.00	314.50	67.72	1-2	0.5755
	2rp	without TH (d)	309.29	14	259.50	210.00	311.00	194.98	3-4	0.9744
	3rp	with TH (m)	267.58	36	250.50	214.00	320.50	74.66	1-3	0.6752
	4rp	with TH (d)	269.09	22	256.00	187.00	332.00	94.67	2-4	0.8077
In erythrocytes										
Hemoglobin (Hb, g/l)	1rp	without TH (m)	90.63	24	95.29	76.14	108.31	25.25	1-2	0.4814
	2rp	without TH (d)	96.95	16	98.89	86.41	111.17	20.12	3-4	0.2893
	3rp	with TH (m)	94.20	39	98.21	85.11	106.15	24.51	1-3	0.7023
	4rp	with TH (d)	91.20	25	90.31	80.36	102.77	16.46	2-4	0.2450
Malondialdehyde (MDA, nmol/1g Hb)	1rp	without TH (m)	0.28	22	0.17	0.11	0.37	0.31	1-2	0.2585
	2rp	without TH (d)	0.17	15	0.16	0.08	0.23	0.10	3-4	0.7035
	3rp	with TH (m)	0.28	37	0.18	0.12	0.27	0.37	1-3	0.9937
	4rp	with TH (d)	0.22	25	0.19	0.11	0.24	0.17	2-4	0.3559
Catalase (CAT, mmol/s/1g Hb)	1rp	without TH (m)	14.85	24	13.09	10.61	16.27	6.20	1-2	0.7719
	2rp	without TH (d)	14.42	16	13.35	11.50	15.61	5.04	3-4	0.0622
	3rp	with TH (m)	14.42	39	12.06	10.91	15.15	6.84	1-3	0.7129
	4rp	with TH (d)	14.76	25	14.53	12.28	16.92	3.45	2-4	0.3427
Glutathione peroxidase (GPO, µmol/1g Hb)	1rp	without TH (m)	0.27	24	0.16	0.10	0.31	0.31	1-2	0.5526
	2rp	without TH (d)	0.23	16	0.23	0.14	0.30	0.14	3-4	**0.0019**
	3rp	with TH (m)	0.22	39	0.17	0.11	0.24	0.20	1-3	0.8874
	4rp	with TH (d)	0.30	25	0.28	0.21	0.36	0.13	2-4	0.1177
Reduced Glutathione (GSH, µmol/1g Hb)	1rp	without TH (m)	7.14	20	6.23	4.28	8.79	4.49	1-2	0.8285
	2rp	without TH (d)	6.52	15	5.81	4.67	8.10	2.81	3-4	0.9706
	3rp	with TH (m)	7.45	37	6.80	4.36	10.05	3.92	1-3	0.5811
	4rp	with TH (d)	7.52	24	6.95	4.59	9.68	3.96	2-4	0.5348
Superoxide dismutase (SOD, units/min/1g Hb)	1rp	without TH (m)	195.89	24	207.33	119.54	274.60	76.46	1-2	0.3136
	2rp	without TH (d)	222.62	16	258.95	180.82	273.82	68.67	3-4	0.1044
	3rp	with TH (m)	108.86	39	106.18	83.87	135.78	32.43	1-3	**0.0001**
	4rp	with TH (d)	95.91	25	87.41	68.87	117.81	34.71	2-4	**<0.0001**
Glutathione S-transferase (GST, mmol/min/1g Hb)	1rp	without TH (m)	11.08	24	9.49	6.73	13.08	5.68	1-2	0.8038
	2rp	without TH (d)	10.67	16	9.54	6.78	13.28	5.99	3-4	0.9835
	3rp	with TH (m)	10.41	39	9.99	5.67	14.66	5.70	1-3	0.5475
	4rp	with TH (d)	10.68	25	10.04	7.08	14.16	6.57	2-4	0.9255

3. There are statistically significant intragroup differences for most parameters of the LPO-AOP between their gradations: “normal level” and the level “above normal” and/or “below normal”.

4. The level of plasma and erythrocyte concentration of the LPO-AOP system indicators is associated to a greater extent with the presence or absence of TH than with the gender of adolescents.

5. Evaluation of the significance of altered levels of LPO-AOP system indicators as metabolic markers of the presence and/or risk of developing TH in adolescents is relevant and requires further study.

The authors declare no conflict of interest.

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COMPARATIVE ANALYSIS OF THE 5-HTTLPR POLYMORPHISM OF THE *SLC6A4* GENE IN RUSSIAN AND YAKUT POPULATIONS

DOI 10.25789/YMJ.2025.91.03

UDC 575.174.015.3

The 5-HTTLPR polymorphism of the *SLC6A4* gene plays a key role in the regulation of serotonergic transmission and may influence susceptibility to anxiety and depressive disorders. This study presents a comparative analysis of the distribution of genotypes and alleles of this polymorphism in representatives of the Russian (n = 250) and Yakut (n = 260) ethnic groups. A significantly higher prevalence of the S allele (77.7%) and the homozygous SS genotype (63.8%) was observed in the Yakut population compared to the Russian group (44.8% and 20.8%, respectively; p < 0.001). The Russian sample was characterized by a higher frequency of the L allele and the SL genotype. The identified differences reflect the high frequency of the S allele characteristic of the Indigenous peoples of Siberia and underscore the ethnic specificity of genetic factors involved in psycho-emotional regulation.

Keywords: 5-HTTLPR polymorphism, *SLC6A4* gene, genetic diversity, ethnic populations, serotonergic system.

For citation: Krylov A.V., Pavlova N.I., Bochurov A.A.. Comparative analysis of the 5-HTTLPR polymorphism of the SLC6A4 gene in Russian and Yakut populations. Yakut medical journal. 2025; 91(3): 14-17. https://doi.org/10.25789/YMJ.2025.91.03

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Introduction. Depressive and anxiety disorders constitute a significant burden of disease in global populations, affecting not only individuals but also their families and society as a whole, making them one of the key socio-economic challenges of the 21st century [11, 14]. In the context of this problem, modern genomics has laid the foundation for the transition from syndromic diagnoses to biologically based approaches in psychiatry, opening the way for personalized treatment strategies [12]. It is predicted that in the next decade, research into the genetic basis of behavioral patterns will take a central place in psychiatry: in-depth analysis of the relationships between genomic variations and neurobiological mechanisms will transform approaches to the study of mental health and optimize therapeutic strategies for anxiety and depressive disorders [5].