REVIEW ARTICLE

CONTENTS

Significance of the γ-aminobutyric acid and FKBP5 genes polymorphisms in the risk of post-traumatic stress disorder developing

Bogdan S. Bozhuk[1], Yaroslav V. Kudiievskyi[1, 2], Anastasiya V. Kundiieva[1]

[1]STATE INSTITUTION «KUNDIIEV INSTITUTE OF OCCUPATIONAL HEALTH OF THE NATIONAL ACADEMY OF MEDICAL SCIENCES OF UKRAINE», KYIV, UKRAINE

[2]BOGOMOLETS NATIONAL MEDICAL UNIVERSITY, KYIV, UKRAINE

ABSTRACT

Aim: To analyse and interpret international and domestic literature regarding the potential relationship between the risk of developing post-traumatic stress disorder (PTSD) and the presence of single-nucleotide polymorphisms (SNPs) in the γ-aminobutyric acid (GABA) and FKBP5 genes.

Materials and Methods: The literature search was conducted in the following databases: PubMed, Web of Science, DOAJ, Scopus, Medline, Google Scholar, as well as on the official websites of the Ministries of Ukraine, libraries of higher medical institutions, the World Health Organization (WHO), and general Google search resources. The search period covered the years 2015–2025. To more comprehensively achieve the research objective, several historical scientific publications were also taken into account. The search keywords included PTSD, SNP, GABA gene, and FKBP5. The search encompassed scientific sources in English, Ukrainian, German, and French addressing issues related to PTSD and SNPs. Studies concerning the treatment of PTSD or single-nucleotide polymorphisms other than those of the FKBP5 and GABA genes were excluded. The initial article pool comprised 100 publications, of which 40 were included in the final analysis.

Conclusions: Early detection of PTSD within specific population groups allows the implementation of timely preventive measures aimed at reducing the incidence, severity, and duration of the disorder, thereby accelerating the restoration of psychological balance and resilience. The combination of genetic and epigenetic factors with neurotransmitter dysfunction constitutes the basis for the development of stress-related disorders. In particular, determining the frequency of GABA and FKBP5 gene SNPs may serve as a diagnostically significant biomarker of the pathophysiological mechanisms underlying PTSD.

KEY WORDS: post-traumatic stress disorder, single-nucleotide polymorphism

Wiad Lek. 2025;78(11):2471-2480. doi: 10.36740/WLek/214799 DOI

INTRODUCTION

The consequence of the Russian Federation's full-scale invasion of Ukraine and the ensuing large-scale military operations is a complex set of significant negative social, economic, environmental, sanitary-epidemiological, and psychological impacts. The combined effect of these factors is the main cause of stress-associated mental disorders, in particular post-traumatic stress disorder (PTSD) [1].

Traumatic events such as military conflict, accidents, natural disasters, or sexual violence, when witnessed or experienced by psychologically unprepared individuals, can cause profound and often critical negative changes in their psycho-emotional state [2]. Most people who experience such events suffer from considerable psychological distress but eventually recover without external assistance. However, there are individuals who, in similar situations, develop a wide range of mental health disorders–such as PTSD, depressive, and anxiety disorders–that may persist for several months or even years. Each of these disorders alone can significantly affect a person's health and quality of life, and their combination amplifies these negative effects [3].

Under direct and prolonged exposure to traumatic events, especially in wartime, PTSD is considered the most critical disorder because it is directly associated with traumatic experiences, characterised by the chronic nature of its symptoms, its impact on a person's ability to function, and the combination of

specific manifestations (flashbacks, nightmares, severe anxiety, emotional detachment, etc.), social isolation, and the possibility of collective trauma [4].

When referring to war as a traumatic event, mental trauma is common among a large portion of the population, and PTSD can become a "norm" for many, as numerous individuals may experience similar symptoms due to shared experiences. This increases the significance of PTSD as a social phenomenon. In such circumstances, it is essential to recognise that not only individuals but also entire communities may require psychological support and treatment. This underscores the importance of educating the Ukrainian population about the manifestations of PTSD [1–4].

Among other aspects, the relationship between genetics and PTSD is also of particular importance, especially in facilitating timely diagnosis through genetic testing aimed at determining the frequency of single nucleotide polymorphisms (SNPs) in the γ-aminobutyric acid (GABA) and FKBP5 genes. Such testing may support the early implementation of social and preventive programmes directed at restoring mental health [5].

AIM

The analysis and interpretation of international and domestic literature sources regarding the potential relationship between the risk of developing PTSD and the presence of single-nucleotide polymorphisms (SNPs) in the γ-aminobutyric acid (GABA) and FKBP5 genes.

MATERIALS AND METHODS

The literature search was conducted in the following databases: PubMed, Web of Science, DOAJ, Scopus, Medline, Google Scholar, as well as on the official websites of the Ministries of Ukraine, libraries of higher medical institutions, the World Health Organization (WHO), and general Google search resources. The search period covered the years 2015–2025. To more comprehensively achieve the research objective, several historical scientific publications were also taken into account.

The search keywords included PTSD, SNP, GABA gene, and FKBP5. The search encompassed scientific sources in English, Ukrainian, German, and French addressing issues related to PTSD and SNPs. Studies concerning the treatment of PTSD or single-nucleotide polymorphisms other than those of the FKBP5 and GABA genes were excluded. The initial article pool comprised 100 publications, of which 40 were included in the final analysis.

ETHICS

Publicly available sources were used. The authors adhered to the ethical principles of the World Medical Association Declaration of Helsinki and international standards for publications in medical journals, including the ICMJE guidelines. Plagiarism and data fabrication are excluded. All sources of information are appropriately cited and properly formatted.

FRAMEWORK

The study was conducted as a fragment of the scientific project of the Department of Occupational Epidemiology, Laboratory of occupational hygiene and physiology of State Institution «Kundiiev Institute of Occupational Health of the National Academy of Medical Science of Ukraine» under the R&D direction «Analysis of the frequency of distribution of single nucleotide polymorphisms in the FKBP5 and gamma-aminobutyric acid genes for the detection of PTSD in military personnel and workers in hazardous professions» (state registration number 0124U003776; term: 2025-2027).

REVIEW AND DISCUSSION

THE HISTORY OF PTSD BEFORE THE OFFICIAL TERM WAS RECOGNIZED

Concerning the symptoms of PTSD, individual observations were recorded by Herodotus, Hippocrates, Xenophon, and other notable figures of antiquity, as well as in even earlier reports describing combat-related mental disorders from the era of the Assyrian Empire (circa 1300 BC) [6]. However, the specific symptoms of the disorder have been more clearly described over the past few centuries. For instance, during the American Civil War (1861–1865), surgeon Jacob Mendes da Costa identified a syndrome later referred to as somatoform autonomic dysfunction (also known as Da Costa's syndrome or soldier's heart) [7]. In 1888, the neurologist Hermann Oppenheim proposed the term traumatic neurosis [8], and around the same time, Pierre Marie Félix Janet observed that victims of psychological trauma repeatedly re-enacted the behaviours, emotions, and bodily sensations experienced at the moment of trauma [9].

During the First World War, the recognition of military post-traumatic stress disorder as a disease allowed veterans in England, France, and Germany to claim pensions and receive treatment. Approximately 80,000 cases of post-traumatic disorders were registered, including soldiers who lost their memory, sight, hearing, smell, taste, or ability to walk. At that time, the principal diagnosis became the so-called shell shock (Fig. 1), a term introduced by psychiatrist Charles Samuel Myers [10].

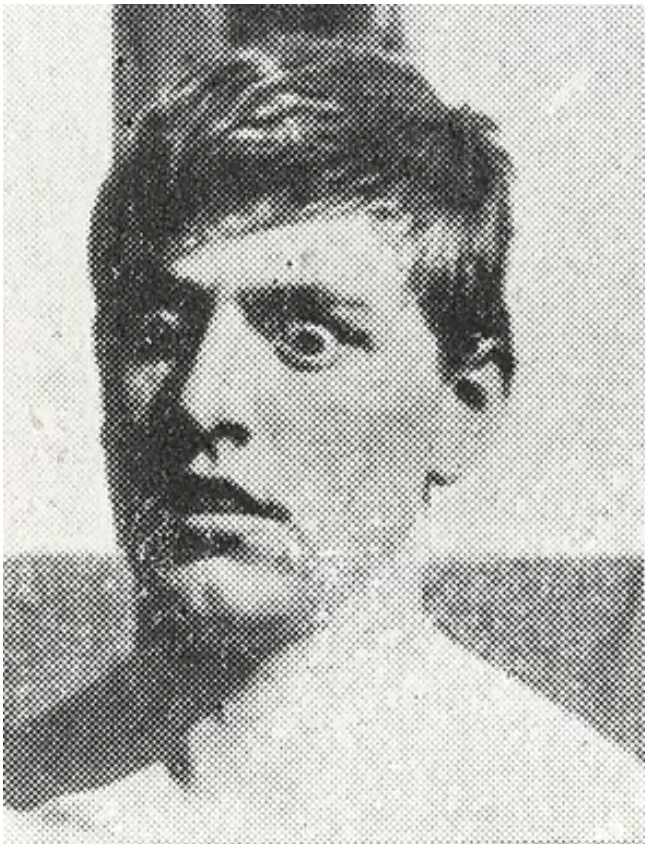

Fig. 1. Characteristic signs of shell shock: stunned facial expression and an immobile, frozen gaze
Source: compiled by the authors based on [10]

In 1940, psychologist Abram Kardiner studied World War I veterans and concluded that post-traumatic psychological disorder has distinct symptoms, with the development of "war neurosis" largely resulting from the maladaptation of combatants to post-war conditions [11].

During the Second World War (1939–1945), Soviet psychiatrists and neurologists used the term concussion (mild traumatic brain injury) to describe servicemen exhibiting various manifestations of combat stress [12]. Moreover, during World War II, post-traumatic symptoms were identified not only among military personnel but also among concentration camp prisoners. These individuals developed a form of PTSD characterised by an overwhelming sense of guilt for having survived extreme events (e.g., accidents, terrorist attacks, riots, natural disasters, epidemics, wars, genocides, or concentration camps) while many others perished. This condition became known as concentration camp syndrome (KZ-syndrome, from Konzentrationslager in German), survivor guilt syndrome (Das Überlebenden-Syndrom in German), or Holocaust syndrome. The extreme psychological stress endured in the camps resulted in the syndrome developing in more than 75% of victims [4, 13, 14].

Fig. 2. "A Look at Two Thousand Yards". The thousand-yard stare
Source: compiled by the authors based on [16]

Similar symptoms were observed among survivors of the atomic bombings of Hiroshima and Nagasaki on August 9, 1945. Approximately one-third of the survivors of the Hiroshima attack (Japanese: hibakusha – "those who survived the explosions") experienced profound feelings of guilt that developed into a psychological complex. Around 10% of the victims of the bombings suffered from post-traumatic stress disorders [4]. In studies of World War II veterans, a syndrome resembling PTSD was referred to as gross stress reaction [15]. In the United States in 1945, the colloquial expression "the thousand-yard stare" (Fig. 2) was used to describe the vacant, unfocused gaze commonly seen in soldiers who had suffered psychological trauma in combat [16].

During the Vietnam War (1959-1975), the development of dependencies in those who were in combat was added to the list of already known symptoms. According to statistics, 700,000 American veterans were diagnosed with post-traumatic symptoms. Mental disorders with these characteristics were previously undescribed in psychological literature and, thus, were named "Vietnam syndrome." Approximately 25% of participants in combat operations in Vietnam suffered personality changes due to psychological trauma [4]. Research of the problem led to the introduction of the term "traumatic neurosis" in a new version of the Diagnostic and Statistical Manual of Mental Disorders (DSM). In 1968, this term was replaced by "post-traumatic stress disorder" (PTSD). This term

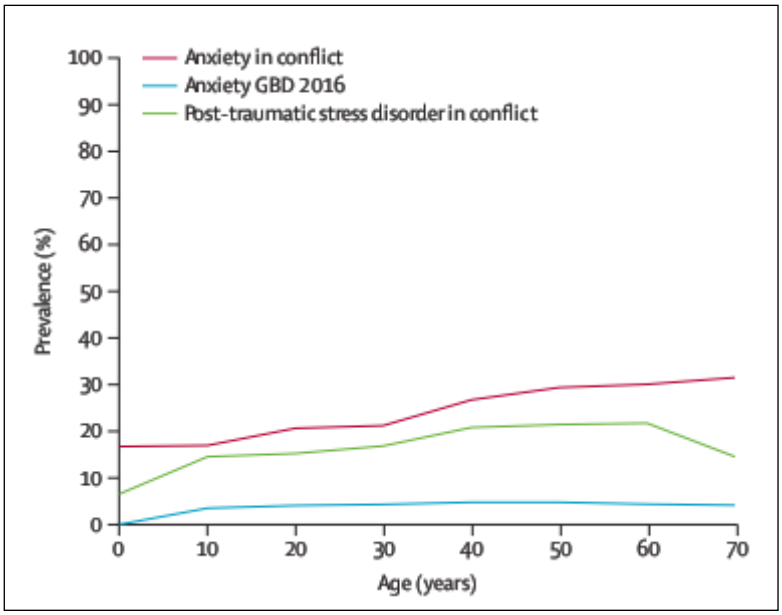

Fig. 3. Age prevalence (average) of depression, any anxiety, and PTSD in conflict-affected populations GBD —Global Burden of Disease
Source: compiled by the authors based on [1]

Fig. 4. The map of the number of global scientific studies on PTSD from 1980 – 2017
Source: compiled by the authors based on [1]

was officially recognized by the American Psychiatric Association in 1980 in the third edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III) [17].

CONTEMPORARY INSIGHTS INTO PTSD AND THE IMPORTANCE OF IDENTIFYING THE PROBLEM, ESPECIALLY IN UKRAINE

According to WHO estimates, as of May 2024, 3,9% of the world's population suffers from PTSD [3]. In conflict situations, tendencies towards depression and anxiety increase with age, and conversely, the average prevalence of post-traumatic stress disorder in older age groups decreases (Fig. 3).

The likelihood of developing PTSD varies depending on the type of traumatic event experienced. According to Fiona Charlson, one in five people living in post-conflict environments suffer from depression, anxiety disorder, PTSD, bipolar disorder, or schizophrenia. Moreover, PTSD rates are more than three times higher (15,3%) among individuals who have experienced conflict accompanied by violence or war [1]. The highest prevalence of disaster-related PTSD is observed among survivors (30%–40%) and first responders (10%–20%), compared to the general population (5%–10%) [2].

According to WHO data, the number of psychiatric epidemiological studies has increased significantly in countries affected by military conflicts and other emergencies. Between 2000 and 2017, comprehensive scientific studies on PTSD were conducted in only 34 countries worldwide, with almost none performed in Ukraine (Fig. 4).

However, just after the start of the full-scale invasion of Ukraine, there has been a significant increase in the diagnosis of PTSD among Ukrainians. According to the National Health Service of Ukraine (NHSU), in 2021, 3167 patients were officially diagnosed with PTSD, in 2022 – 7051 people, in 2023 the number of Ukrainians diagnosed with PTSD increased to 12494, and in just the first two months of 2024 (as of March 6, 2024), 3292 cases have already been diagnosed

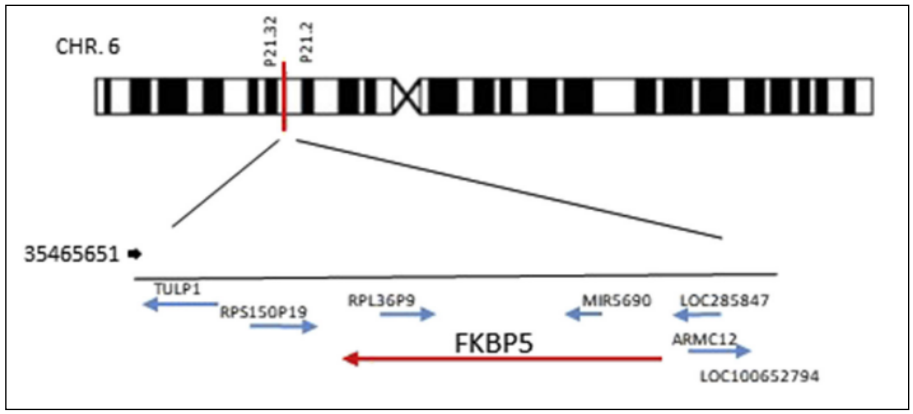

Fig. 5. The schematic diagram of FKBP5 location on chromosome 6 (6p21.31). The FKBP5 gene spans 154 kilobase pairs (kbp) from 35541362 to 35696360 on the reverse strand
Source: compiled by the authors based on [36]

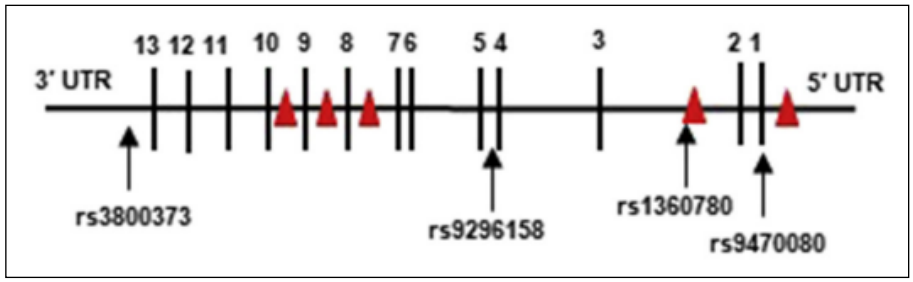

Fig. 6. Schematic diagram of polymorphism locations around the FKBP5 gene and glucocorticoid receptor sites
Label: ▲ – hormonal response element
Source: compiled by the authors based on [36]

[5]. In Ukraine, the prevalence of PTSD diagnosis varies depending on many factors, but undoubtedly the greatest risk of developing the disorder is present in individuals who are directly exposed to a stressor, and there is an interdependence between the probability of PTSD occurrence and the severity, duration, and scale of the traumatic event. This correlation can be traced by comparing the prevalence of PTSD before and after the full-scale invasion of Ukraine – if during the Anti-Terrorist Operation (2014-2018 years) PTSD was diagnosed in 27,7% of the military personnel who participated in it [18], then as of the end of 2024, that increased to 53,3% [19].

According to WHO data, the prevalence of mental disorders, including PTSD, is significantly higher for displaced persons and other war-affected individuals than for the general population [1]. In Ukraine, according to the Ministry of Social Policy, as of April 23, 2025, there were more than 4,5 million (4 594 270 people) officially registered internally displaced persons (IDPs) [20]. According to N. Masik et al., signs of PTSD were more often found in IDPs (83,33%) compared to civilians (10,0%). Moreover, IDPs predominantly exhibited symptoms of avoidance (76,67%), negative cognition (76,67%), and hyperarousal (88,33%), which emphasized the significant role of emotional reactions and possible influence on other PTSD symptoms [30].

THE DIAGNOSTIC CRITERIA FOR GENETIC MARKERS FOR INCREASED RISK OF DEVELOPING PTSD

The influence of genetics on PTSD has been insufficiently studied due to the inherent limitations of genetic research on mental disorders. Nevertheless, it is well established that genetic factors play a significant role in the development of PTSD [21].

Analysis of the frequency of single-nucleotide polymorphisms (SNPs) in various genes is an important tool in exploring the genetic basis of PTSD, as it enables a deeper understanding of the primary genetic and subsequent biological mechanisms underlying this disorder. An SNP is a variation in deoxyribonucleic acid (DNA) in which a single nucleotide – the basic unit of DNA (adenine, thymine, cytosine, or guanine) – is substituted for another at a specific location in the genome. In other words, it represents a point polymorphism, where different bases occur at a given locus of the genome across individuals or populations. SNPs constitute the foundation of population diversity and are the most common type of polymorphism in the human genome, occurring on average once every 1,000 nucleotides in human DNA [22, 23].

Studies of specific nucleotide polymorphisms in genes associated with central nervous system metabolism make it possible to identify various risks and mechanisms of PTSD development, which, in turn, may inform the creation of targeted preventive measures.

THE ROLE OF SNPS IN THE GABA AND FKBP5 GENES IN THE RISK OF DEVELOPING PTSD

THE ROLE OF GABA GENE POLYMORPHISMS

Changes in the activity of GABA gene are of particular importance in the neurobiological mechanisms that

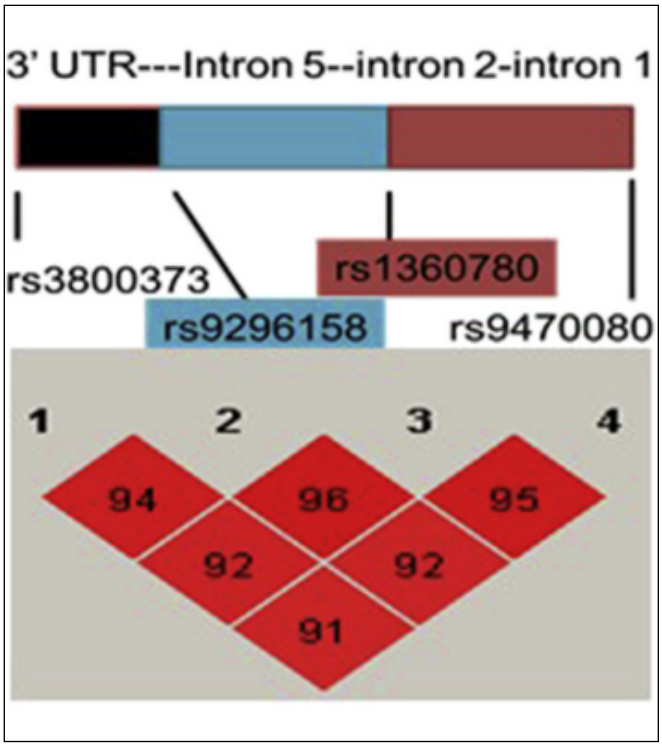

Fig. 7. Relative position of FKBP5 polymorphisms and their haplotype block structure. Numbers in squares refer to one block of strong pairwise linkage disequilibrium (r = 0,91–0,96)
Source: compiled by the authors based on [36]

determine the body's response to stress and traumatic events. GABA is the main inhibitory neurotransmitter in the central nervous system. When GABA is released into the synaptic cleft, it activates the ion channels of GABAA- and GABAC-receptors, leading to the inhibition of nerve impulses. Under the influence of GABA, brain energy processes are also activated, tissue respiratory activity increases, glucose utilization by the brain improves, and blood supply improves. In extreme conditions with a large energy deficit, GABA is oxidized in the brain by an oxygen-free pathway, releasing a lot of energy and normalizing the content of histamine and serotonin in the brain. Since the main physiological role of GABA is to ensure a stable balance between excitatory and inhibitory systems, normalize sleep, and provide the brain with energy and its resistance to hypoxia, as well as other harmful influences, including distress, a decrease in GABA levels disrupts the balance of excitatory and inhibitory neurons, leading to neurotransmission dissonance, impaired neuroendocrine regulation, and, as a consequence, hypothalamic dysfunction. Stress-limiting systems are capable of limiting the activity of the stress system and excessive excitatory reaction at the central and peripheral levels of regulation [24]. At the same time, P. Hepsomali's research has shown that the consumption of natural and biosynthetic GABA can positively affect stress levels and sleep [25].

However, after prolonged stress, there is a decrease in synthesis and depletion of GABA due to the activation of GABA-transaminase, and nerve impulse transmission in neurons is disrupted with an increase in glutamate (an excitotoxic amino acid), leading to cell apoptosis and neuronal death, and increased excitation with impaired Krebs cycle and worsening cognitive functions of the body. Against the background of chronic stress and decreased GABA synthesis, the main physiological role of GABA – the formation of a stable balance between excitatory and inhibitory systems – is disrupted. Thus, with a deficiency or blockade of GABA synthesis, thinking productivity decreases and memory worsens, other cognitive functions are impaired, anxiety and irritability increase, aggression appears, resistance to hypoxia, stressors, and body endurance decreases, the sleep cycle is disrupted, and, consequentially, the circadian rhythm of hormones [24]. GABA receptor ligands are considered potential agents for the treatment of various mental and central nervous system disorders, including sleep disorders (insomnia, narcolepsy), epilepsy, Parkinson's and Alzheimer's diseases [26]. Genes associated with its synthesis, receptors, and metabolism may have SNPs that affect neurotransmission and neuroplasticity. Such variations may be associated with the risk of developing mental disorders such as depression, anxiety disorders, and schizophrenia. A study by K. Skelton et al. showed a significant correlation between three polymorphisms in the gene of the GABA receptor alpha-2 and the severity of childhood trauma, which is important for predicting PTSD in adults. According to the study, people with a certain genotype of G-protein signaling 2 (RGS2), a protein that reduces G-protein-coupled receptor signaling, experience high levels of stress due to environmental factors in adulthood and have a significant predisposition to PTSD throughout their life. This was especially true for adults with previous trauma and low social support [21].

THE ROLE OF FKBP5 GENE POLYMORPHISMS

The FKBP5 gene (FK506 binding protein 5) (Fig. 5) encodes a protein that regulates the activity of glucocorticoid receptors (GR), which are an important component of cellular stress response mechanisms, regulate numerous physiological processes, including metabolism, immune reactivity, and affect the body's stress response [27-29].

Assuming that one of the key systems mediating the long-term consequences of stress and PTSD is the glucocorticoid receptor (GR) system of the hypotha-

lamic–pituitary–adrenocortical (HPA) axis, individuals with PTSD may exhibit either heightened sensitivity to stress or, conversely, less severe symptoms, depending on molecular anomalies in the signaling pathways involved in GR stimulation. As a transcription factor – that is, a protein that binds to specific DNA regions and regulates the expression of target genes – the glucocorticoid receptor is activated upon binding to its ligand (e.g., cortisol) and translocates from the cytosol to the cell nucleus, where it interacts with DNA sequences to modulate gene expression. This process is regulated by a large molecular complex that includes the *FKBP5* protein [30, 31].

It is known that SNPs in the *FKBP5* gene (Fig. 6) can alter stress sensitivity and affect the risk of developing mental disorders such as depression, anxiety, and PTSD, as well as other adverse psychological outcomes in which stress hormone regulation plays a critical role [32]. Moreover, identifying specific polymorphisms in this gene can inform personalised approaches to therapy and stress management strategies [30, 33].

Since FKBP5 is part of the FKBP/GR complex, which directly regulates GR sensitivity, its polymorphisms are associated with its functionality, which is caused by glucocorticoid action and GR sensitivity. According to P.D. Reynolds, FKBP5 plays a key role in intracellular ultrashort negative feedback with GR activity [34], which indicates the extremely important role of FKBP5 activity in the development of PTSD, given the cortisol-induced higher level of FKBP5 associated with PTSD [30]. K. Skelton's research points to the main polymorphisms of the FKBP5 gene, each of which has a special influence. The correlation between gene polymorphisms and the severity of childhood abuse predicts the severity of PTSD symptoms in adults. For example, the TT genotype of the FKBP5 gene is associated with the highest risk of PTSD among those who experienced abuse or other adversity in childhood, however, individuals with a similar genotype who did not experience childhood difficulties had the lowest risk of PTSD. Alcohol dependence interacts with FKBP5 polymorphism and stressful events in childhood, contributing to an increased risk of PTSD in these individuals. It has been proven that lower FKBP5 mRNA expression, which additionally occurs after trauma, including combat trauma, indicates greater severity of post-traumatic stress disorder symptoms [21].

A direct link is observed between parental mental trauma and the mental health of offspring; a greater intensity of reparative adaptive influences in parents increases the risk of developing stress disorders in offspring due to changes in FKBP5 gene methylation [35]. Childhood trauma is also a prognostic criterion for the risk of development and severity of PTSD in adults in the presence of four SNPs in the FKBP5 gene (rs9296158, rs3800373, rs1360780, and rs9470080) [30, 36, 37], especially rs9470080 [38]. Separate analysis of individual markers is less effective compared to statistical analysis based on haplotypes [39]. According to L. Zhang's study, probable PTSD subjects were significantly more likely to carry the A-allele of rs3800373, the G-allele of rs9296158, the C-allele of rs1360780, and the C-allele of rs9470080. In addition, the four SNPs were in one block of strong linkage disequilibrium (r = 0,91–0,96) (Fig. 7). Within the block, there were two main haplotypes CATT and AGCC (rs3800373-rs9296158-rs1360780-rs9470080), accounting for 99% of haplotype diversity. The distribution of the AGCC haplotype was significantly higher in patients with probable PTSD compared to patients without PTSD. Analysis based on diplotypes showed that AGCC carriers have a significant risk of developing PTSD [36].

FKBP5 expression levels are also associated with the size and functional capacity of several key brain structures, including the amygdala, hippocampus, and prefrontal cortex, and may influence therapeutic responses in PTSD. The amygdala plays a central role in the formation and persistence of fear, amplifying negative emotional reactions to traumatic cues. Stress hormones, in concert with neurotransmitters, modulate the functional activity of the amygdala, directly affecting the development and maintenance of PTSD [40].

CONCLUSIONS

1. Early identification of individuals or population groups at high risk of developing PTSD based on specific genetic variations enables the timely implementation of comprehensive preventive measures aimed at preventing the widespread occurrence of stress-related disorders, reducing their severity and duration, and accelerating the restoration of psychological balance and resilience.
2. The combination of genetic and epigenetic factors, along with neurotransmitter dysfunction, forms the basis for the development of PTSD. Determining the frequency of single-nucleotide polymorphisms (SNPs) in the GABA and FKBP5 genes represents a diagnostically significant approach for identifying pathophysiological changes underlying stress-related disorders.

REFERENCES

1. Charlson F, van Ommeren M, Flaxman A et al. New WHO prevalence estimates of mental disorders in conflict settings: a systematic review and meta-analysis. Lancet. 2019;394(10194):240–248. doi: 10.1016/s0140-6736(19)30934-1. DOI
2. Neria Y, Nandi A, Galea S. Post-traumatic stress disorder following disasters: A systematic review. Psychol Med. 2007;38(4):467–480. doi: 10.1017/s0033291707001353. DOI
3. WHO Post-traumatic stress disorder: Key facts. https://www.who.int/news-room/fact-sheets/detail/post-traumatic-stress-disorder [Accessed 27 August 2025]
4. Mykhalskyi AV, Tsariov YuO. Posttravmatychnyi stresovyi rozlad: istorychnyi ohliad. [Post-traumatic stress disorder: a historical overview]. Problemy suchasnoyi psykholohiyi. 2011;12:687–696. (Ukrainian)
5. Fischer S, Schumacher T, Knaevelsrud C et al. Genes and hormones of the hypothalamic–pituitary–adrenal axis in post-traumatic stress disorder: What is their role in symptom expression and treatment response? J Neural Transm. 2021;128(9):1279–1286. doi: 10.1007/s00702-021-02330-2. DOI
6. Hughes JH. Military Veteran Psychological Health and Social Care. New York: Routledge. 2017.
7. Da Costa JM. On Irritable Heart; a Clinical Study of a Form of Functional Cardiac Disorder and its Consequences. The American Journal of the Medical Sciences. 1871;121(1):17–52 doi: 10.1097/00000441-187101000-00001. DOI
8. Oppenheim H. Die traumatischen Neurosen, nach den in der Nervenklinik der Charite in den letzten 5 Jahren gesammelten Beobachtungen. [Traumatic neuroses, according to observations collected at the Charité neurology clinic over the last 5 years]. Berlin: Hirschwald; 1889. (German)
9. Van der Kolk B. Le corps n'oublie rien. Corps et esprit. Les influences réciproques. [The body forgets nothing. Body and mind. Reciprocal influences]. Sciences Humaines. 2023;(HS14):80-81. doi: 10.3917/sh.hs14.0080. (French) DOI
10. Myers CS. A contribution to the study of shell shock. Lancet. 1915;16(1):316–320. doi:/11.2021-99789283. DOI
11. Kardiner A. The Traumatic Neuroses of War. Washington: Martino Fine Books. 2012.
12. Shamrey VK, Kostyuk GP, Chudinovskikh AG, Sinenchenko AG. Organizatsiya psikhiatricheskoy pomoshchi i struktura psikhicheskikh rasstroystv voyennosluzhashchikh Krasnoy Armii v gody Velikoy Otechestvennoy voyny. [Organization of Psychiatric Care and the Structure of Mental Disorders in Red Army Servicemen during the Great Patriotic War]. Sotsial'naya i klinicheskaya psikhiatriya. 2010;20(4):146–153. (Russian)
13. Fimiani R, Gazzillo F, Dazzi N at al. Survivor guilt: Theoretical, empirical, and clinical features. International Forum of Psychoanalysis. 2021;31(5):1-15. doi: 10.1080/0803706X.2021.1941246. DOI
14. Niederland WG. Folgen der Verfolgung: Das Uberlebenden-Syndrom, Seelenmord. [Consequences of persecution: Survivor syndrome, psychological murder]. Frankfurt am Main: Suhrkamp.1980. (German)
15. Friedman MJ, Schnurr PP, McDonagh-Coyle A. Post-traumatic stress disorder in the military veteran. Psychiatr Clin North Am. 1994;17(2):265–277. doi: 10.1016/s0193-953x(18)30113-8. DOI
16. Greeley BM. The Two Thousand-Yard Stare: Tom Lea's World War II. College Station: Texas A&M University Press. 2008.
17. Friedman MJ. Finalizing PTSD in DSM-5: Getting Here From There and Where to Go Next. J Trauma Stress. 2013;26(5):548–556. doi: 10.1002/jts.21840. DOI
18. Chorna V, Serebrennikova O, Kolomiiets V et al. Posttravmatychnyi stresovyi rozlad pid chas povnomasshtabnoi viiny u viiskovosluzhbovtsiv. [Post-traumatic stress disorder during a full-scale war in servicemen]. Molodyy vchenyy. 2023;12(124):28–39. doi: 10.32839/2304-5809/2023-12-124-28. (Ukrainian) DOI
19. Masik N, Kylymchuk V, Masik O et al. Doslidzhennia chastoty vynyknennia ta oznak posttravmatychnoho stresovoho rozladu na etapi pervynnoi medychnoi dopomohy u viiskovosluzhbovtsiv i vymusheno peremishchenykh osib pid chas povnomasshtabnoho vtorhnennia. [Study of the incidence and signs of post-traumatic stress disorder at the stage of primary medical care in military personnel and forcibly displaced people during a full-scale invasion]. International Neurological Journal. 2025;21(1):1–8. doi: 10.22141/2224-0713.21.1.2025.1144. (Ukrainian) DOI
20. Derzhavne pidpryiemstvo «Informatsiino-obchisliuvalnyi tsent Ministerstva sotsialnoi polityky Ukrainy». [Vnutrishn'o peremishcheni osoby. State Enterprise «Information and Computing Center of the Ministry of Social Policy of Ukraine». Internally displaced persons]. https://www.ioc.gov.ua/analytics/dashboard-vpo [Accessed 23 April 2025]
21. Skelton K, Ressler KJ, Norrholm SD et al. PTSD and gene variants: New pathways and new thinking. Neuropharmacology. 2012;62(2):628–637. doi: 10.1016/j.neuropharm.2011.02.013. DOI
22. Stein MB, Jang KL, Taylor S at al. Genetic and environmental influences on trauma exposure and posttraumatic stress disorder symptoms: a twin study. Am J Psychiatry. 2002;159(10):1675–1681. doi: 10.1176/appi.ajp.159.10.1675. DOI
23. Landegren U, Nilsson M, Kwok PY. Reading bits of genetic information: Methods for single-nucleotide polymorphism analysis. Genome Res. 1998;8(8):769–776. doi: 10.1101/gr.8.8.769. DOI

24. Pylypenko VM. Rol hama-aminomaslianoi kysloty v etiopatohenezi dysfunktsii hipotalamusa. Metody korektsii ta poperedzhennia neiromediatornykh porushen. [The role of gamma-aminobutyric acid in the etiopathogenesis of hypothalamic dysfunction. Methods of correction and prevention of neurotransmitter disorders]. Zdorov'ya Ukrayiny. Diabetolohiya, tyreoyidolohiya, porushennya obminu rechovyn. 2017;1(37):44–47. (Ukrainian)
25. Hepsomali P, Groeger JA, Nishihira J, Scholey A. Effects of Oral Gamma-Aminobutyric Acid (GABA) Administration on Stress and Sleep in Humans: A Systematic Review. Front Neurosci. 2020;14:1–13. doi: 10.3389/fnins.2020.00923. DOI
26. Alharbi B, Al-kuraishy HM, Al-Gareeb AI et al. Role of GABA pathway in motor and non-motor symptoms in Parkinson's disease: a bidirectional circuit. Eur J Med Res. 2024;29(205):1–13. doi: 10.1186/s40001-024-01779-7. DOI
27. Brandt J, Warnke K, Jorgens S at al. Association of FKBP5 genotype with depressive symptoms in patients with coronary heart disease: a prospective study. J Neural Transm. 2020;127(12):1651–1662. doi: 10.1007/s00702-020-02243-6. DOI
28. Halldorsdottir T. Evidence Mounting for Gene-by-Environment Interactions at the FKBP5 Locus Predicting Psychiatric Symptoms. Biol Psychiatry. 2016;80(11):89–91. doi: 10.1016/j.biopsych.2016.09.001. DOI
29. Suarez A, Lahti J, Kajantie E et al. Early Life Stress, FKBP5 Polymorphisms, and Quantitative Glycemic Traits. Psychosom Med. 2017;79(5):524–532. doi: 10.1097/psy.0000000000000439. DOI
30. Binder EB, Bradley RG, Liu W et al. Association of FKBP5 Polymorphisms and Childhood Abuse With Risk of Posttraumatic Stress Disorder Symptoms in Adults. JAMA. 2008;299(11):1291–1305. doi: 10.1001/jama.299.11.1291. DOI
31. Schmidt U, Buell DR, Ionescu LA at al. A role for synapsin in FKBP51 modulation of stress responsiveness: convergent evidence from animal and human studies. Psychoneuroendocrinology. 2015;52:43–58. doi: 10.1016/j.psyneuen.2014.11.005. DOI
32. Harnett NG, Goodman AM, Knight DC. PTSD-related neuroimaging abnormalities in brain function, structure, and biochemistry. Exp Neurol. 2020;330:113331. doi: 10.1016/j.expneurol.2020.113331. DOI
33. Fani N, King TZ, Shin J et al. Structural and functional connectivity in posttraumatic stress disorder: associations with FKBP5. Depression and Anxiety. 2016;33(4):300–307. doi: 10.1002/da.22483. DOI
34. Reynolds PD, Ruan Y, Smith DF, Scammell JG. Glucocorticoid resistance in the squirrel monkey is associated with overexpression of the immunophilin FKBP51. J Clin Endocrinol Metab. 1999;84(2):663–669. doi: 10.1210/jc.84.2.663. DOI
35. Frankova I, Chaban O, Petrenko H, Tokarchuk A. Kolektyvna travma naselennia Ukrainy: realii, perspektyvy ta mozhlyvist doslidzhennia transheneratsiinoho aspektu. Psykhosomatychna medytsyna ta zahalna praktyka. [Collective trauma of the population of Ukraine: realities, prospects and the possibility of studying the transgenerational aspect]. Psykhosomatychna medytsyna ta zahal'na praktyka. 2023;8(3):1–41. doi: 10.26766/pmgp.v8i3.442. (Ukrainian) DOI
36. Zhang L, Hu X-Z, Yu T et al. Genetic association of FKBP5 with PTSD in US service members deployed to Iraq and Afghanistan. J Psychiatr Res. 2020;122:48–53. doi: 10.1016/j.jpsychires.2019.12.014. DOI
37. Tamman AJF, Sippel LM, Han S et al. Attachment style moderates effects of FKBP5 polymorphisms and childhood abuse on post-traumatic stress symptoms: results from the National Health and Resilience in Veterans Study. World J Biol Psychiatry. 2019;20(4):289–300. doi: 10.1080/15622975.2017.1376114. DOI
38. Watkins LE, Han S, Harpaz-Rotem L et al. FKBP5 polymorphisms, childhood abuse, and PTSD symptoms: Results from the National Health and Resilience in Veterans Study. Psychoneuroendocrinology. 2016;69,:98–105. doi: 10.1016/j.psyneuen.2016.04.001. DOI
39. Fallin D, Cohen A, Essioux L at al. Genetic analysis of case/control data using estimated haplotype frequencies: application to APOE locus variation and Alzheimer's disease. Genome Res. 2001;11(1):143–151. doi: 10.1101/gr.148401. DOI
40. Gorbachenko VA, Olianin VV, Lukyanets OO. Fiziolohichni mekhanizmy stresu ta posttravmatychnyy stresovyy rozlad. [Physiological mechanisms of stress and post-traumatic stress disorder]. Fiziolohichnyy zhurnal. 2024;70(6):98–109. doi: 10.15407/fz70.06.098. (Ukrainian) DOI

CONFLICT OF INTEREST

The Authors declare no conflict of interest

CORRESPONDING AUTHOR

Anastasiia V. Kundiieva
Kundiiev Institute of Occupational Health of the
National Academy of Medical Science of Ukraine
75 Saksahanskyi St., 01033 Kyiv Ukraine
e-mail: av.kundiieva@gmail.com

ORCID AND CONTRIBUTIONSHIP
Bogdan S. Bozhuk: 0000-0002-8089-2840 A D E F
Yaroslav V. Kudiievskyi: 0000-0003-0282-0005 B D E
Anastasiya V. Kundiieva: 0000-0002-5988-4723 A D E F

A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article

RECEIVED: 16.05.2025
ACCEPTED: 10.10.2025