



# Coronavirus Syndrome: COVID-19 World Psychotrauma

Nadezhda V Solov'eva<sup>1</sup> , Ekaterina V Makarova<sup>2\*</sup> and Irina V Kichuk<sup>3</sup>

<sup>1</sup>General Director, Psychiatrist, JCS "Scientific Center of Personalized Medicine", Russia

<sup>2</sup>Research Scientist of Somatic Rehabilitation, Anti-Aging and Reproductive Health Department of FSBI "National Medical Research Center of Rehabilitation and Balneology" of Ministry of Health of Russian Federation, Russia

<sup>3</sup>PhD, Associate Professor, Department of Neurology of Neurosurgery and Medical Genetics of the Medical Faculty of the N.I. Pirogov Russian National Research Medical University, Russia



## Abstract

Coronavirus syndrome is a mental disorder that is a response to the COVID-19 pandemic, which will affect up to 10% of the population. We can already observe acute stress reactions to the spread of the infection and changes in people's customary lifestyle. However, the most severe symptoms will be seen 6 months after the beginning of the catastrophe and will be similar to the clinical picture of post-traumatic stress disorder. The danger of coronavirus syndrome is that it will reduce the population's working capacity precisely when it will be crucial for economic recovery. The risk groups are health care workers who treat patients with COVID-19; people with a severe form of the disease; people who have lost their loved ones; and those who have suffered significant financial losses and lost their jobs. The timely prevention of coronavirus syndrome, consisting of pharmacotherapy and psychotherapeutic support, is critical.

## Keywords

COVID-19, Post-Traumatic Stress Disorder, Social Stress Disorder, Mental Health, Prophylaxis, Perspectives

## Introduction

Coronavirus infection is a new global issue that caught humanity completely unprepared. We can say that there have been no events in the world with such a powerful and all-encompassing resonance like this since the end of World War II.

The new viral infection has a number of significant features, such as the global scale, ultra-fast rate of spread, quite a high mortality rate, significant social and economic consequences disrupting people's customary style of life, drastic and rapid changes in the normative rules of life [1,2]. This phenomenon is called "pandemic", which implies the involvement of everyone on the planet. The meaning of the word "παν" (Greek for "all", "across the board") highlights the global nature of what is happening.

In his recent interview, the psychoanalyst Murray Stein called the COVID-19 problem a "World Shadow" [3]. There is probably not a single person on our planet who have not been touched by the coronavirus now or will not be touched by it in future. This is a critical historical period, which cannot but affect global mental health, perhaps even to a greater extent than somatic health as, even though there is a chance not to get sick, there is no way to protect ourselves from the flow of information and live as we lived before.

The actual impact and scale of the problem will, of course, be fully understood only after the catastrophe is over. Mental disturbances caused by the coronavirus will have large variations in time and space. Most people will experience acute stress disorder, some will experience post-traumatic stress disorder (PTSD), but a number of people will face a deeper legacy of what they have been through: depressive episodes, neurotic disorders and personality deformities. Thus, referring to mental disorders triggered by the COVID-19 pandemic, we can talk about "coronavirus syndrome".

The historical analogy would be the "Lost Generation" described by Ernest Hemingway, Francis Scott Fitzgerald, Erich Maria Remarque and other writers. The term refers

**\*Corresponding author:** Dr. Ekaterina Makarova, FSBI 'National Medical Research Centre of Rehabilitation and Balneology' of the Ministry of Health of Russian Federation, 121099 Russia, Tel: +7(915)-111-41-37

**Received:** September 17, 2020

**Accepted:** October 28, 2020

**Published online:** October 30, 2020

**Citation:** Nadezhda VS, Makarova EV, Kichuk IV (2020) Coronavirus Syndrome: COVID-19 World Psychotrauma. Ann Public Health Reports 4(1):78-83

to the generation of people who reached their eighteenth birthday before or during World War I. After the end of hostilities such people often could not adapt to peaceful life: They drank, went crazy, committed suicide [4].

This phenomenon drew attention of doctors in the 80's of the 20<sup>th</sup> century. That is when the concept of PTSD was also developed in the USA and the term "Vietnam syndrome" to describe mental symptoms and personality changes observed in veterans of the Vietnamese war was introduced [5]. In medical practice of Russian psychiatrists, similar conditions were observed in the participants of wars in Afghanistan and Chechnya, and are known as "Afghan" and "Chechen" syndromes [6-8].

Participation in battles is not the only thing that can cause psychological trauma and lead to a stress disorder. We know of numerous descriptions of psychological consequences of catastrophes [9], natural disasters (for example, earthquakes [10] and hurricanes [11]), terrorist attacks (September 11, 2001 [12]). Economic and social phenomena affecting a large number of people also lead to large-scale mental changes, an example of which is the widely known "Great Depression" developed in the 30's of the 20<sup>th</sup> century in the USA during the economic crisis.

Russian publications include the concept of Social Stress Disorder (SSD) to describe how the change in the political system of the government affected mental health of the population. In Y.A Aleksandrovskiy's opinion [13], while PTSD develops in people who have survived dangerous and traumatic situations, SSD is typical of people who have fallen under the influence of macrosocial group-wide psychogenic factors. The phenomenology of SSD does not essentially differ from the disorders observed in people who have gone through extreme conditions, but it is caused by common reasons and develops simultaneously in a large number of people.

## Clinical Signs of Stress Disorders

The clinical picture of PTSD develops on average from 30 days to 6 months after the first episode takes place and affects up to 10% of the trauma-exposed individuals [14].

This pathology manifests itself in psychological maladaptation (psychobiological dysfunction) and is accompanied by the variety of intra- and interpersonal conflicts, reinterpretation or loss of meaning in life, the collapse of long-established ideals and loss of faith in a successful future, in other words, some level of existential crisis [15].

The clinical traits include [16-21]:

- Recurrent memories of stressful events;
- Accentuation of personality traits;
- Reduced social activity, distrust in other people;
- Thought disorder, development of pathological ideas and attitudes;
- Development of obsessions and compulsions;

- Affective symptoms associated with high emotional excitement, aggression, irritability or oppression, apathy and depression;
- Refusal to accept reality;
- Alcoholism, drug abuse, deviant behaviour;
- Difficulties in concentration, cognitive deficit;
- Sleep disturbances in the form of poor sleep quality, difficulty falling asleep, nightmares or hypersomnia.

The heavier the trauma, the more likely the disorder is to develop, however, it does not occur in all people, no matter how serious the trauma is. Thus, there are a number of factors that determine a person's vulnerability and ability to recover quickly. Moreover, Frueh, et al. found that after the war PTSD occurred in many of those who had never took part in battles [22].

Studies aimed at finding morphological and biochemical deviations in PTSD have revealed reductions in hippocampal volume [23,24] (however, this phenomenon may be a prerequisite to the development of maladaptation in response to the trauma) and specific neurotransmitter changes (dysfunctions in monoaminergic systems [25], g-amino butyric acid receptor dysfunctions [26,27]) and reduction of cortisol concentration in blood plasma due to induction of negative feedback on hypothalamic-pituitary-adrenal axis [28].

As a matter of fact, mental and/or somatic responses to stressful events are absolutely natural. Not every manifestation of such responses should be regarded as pathological; moreover, a certain level of stress will, on the contrary, enhance adaptive capacities of an organism in future [29]. According to psychologists, emotional outbursts, re-experiencing and talking about one's fears, anger and irritation, followed by the analysis of the negative experience, promote integration of the trauma and a faster compensation of one's mental condition [30,31]. A stress disorder that lasts more than three months is considered chronic [32], however, normal parameters in this matter are always patient-specific, and the doctor, in his or her turn, should pay attention to the manifestations of maladaptation, the degree of decline in the patient's working capacity and quality of life, and the presence of criticism of the patient to his or her condition.

## Coronavirus Syndrome as a Special Case of Social Stress Disorder

Coronavirus syndrome is a mental disorder, which represents the body's reaction to the COVID-19 pandemic. We can now only hypothesize how the situation will develop, since it will certainly take time (at least six months from the beginning of the catastrophe) for coronavirus syndrome to be more clearly defined.

Half a year have passed since the first cases of COVID-19 infection in Wuhan were registered, and now people are experiencing only first stages of acute stress reactions. But it is now when it is important to pay attention to prevention of the development of coronavirus syndrome, because in six months, when the society is fully aware of what has happened

and global mental health is particularly vulnerable, it will be critical to preserve the working capacity of the population to intensively restore the economy and let people maintain their own resources as well. Forewarned is forearmed.

## Epidemiology

Coronavirus syndrome is expected to affect up to 10% of the world's population affected by the pandemic, similar to PTSD frequency [33]. This tenth of the population includes people exposed to a combination of psychosocial and biological stress-vulnerability factors.

The following categories of people can be considered as high-risk groups:

- Medical workers and especially doctors who help patients with COVID-19 under the conditions of overload, lack of information about the disease, lack of vaccines and specific medicines, lack of medical equipment and personal protective equipment;
- People of other professions who have to continue working during the epidemic, putting themselves at risk of infection;
- COVID-19 patients, especially if hospitalized with a severe form of the disease;
- People who have lost their loved ones;
- People who have lost their jobs and suffered financial losses;
- Psychoactive substance abusers;

In addition, there are biochemical stress-vulnerability factors associated with PTSD. One of the biological factors is the genetic profile of an individual, which is related to his or her mental flexibility. The polymorphism of the gene encoding the enzyme catechol-o-methyltransferase (COMT) can be mentioned among the most studied ones. Its function is to decompose the adrenal hormones produced during stress. The rate of recovery of the human mental health depends on the rate of the decomposition of these hormones. The variant of the genotype G/G (rs4680 Val158Val) with a high rate of decomposition of stress hormones allows mobilizing, making quick decisions, ignoring external stimuli under stressful conditions [34].

The risk of coronavirus syndrome is low in such individuals. The variant of genotype G/A (rs4680Val158Met) with a lower rate of decomposition of stress hormones does not allow mental health to recover as quickly, lingering on stressful situations occurs; such people may be exposed to coronavirus syndrome in combination with other risk factors. The variant of genotype A/A (rs4680Met158Met) with low rate of utilization of stress hormones is associated with high risk of development of anxiety disorders, development of dependent behavior; coronavirus syndrome possibility in such patients is high [35].

Another biological factor is the history of hazards, which make the patient's mind less flexible to changes. These hazards include hypertension, diabetes, obesity, atherosclerosis

of brain vessels, thyroid disease, imbalance of sex hormones, history of craniocerebral injuries, comatose states, neuroinfections, intoxications (with alcohol, drugs, carbon monoxide, various toxic chemicals), shortage of nutrients, vitamins, micro and macro elements of various genesis, etc. [36].

Among personal and psychological features, the following factors increase the risk of PTSD development: Childhood traumas, history of psychiatric diseases in the patient and his or her family, low level of education, lack of support from relatives, high base level of stress, propensity for avoidant behaviour and passive response to stress [37,38].

## Anticipated Symptoms of Coronavirus Syndrome

In the case of coronavirus syndrome, the clinical picture is likely to be similar to the one of SSD, like the one observed in Russia during "perestroika". The cause of mental disorders in this case is not a specific traumatic event localized in time, but long-term neurotizing experiences that go beyond normal experience, changes in social bonds and life plans, instability and uncertainty of the future, and a large amount of unconstructive disturbing information in mass media.

The picture of mental manifestations of coronavirus syndrome can be divided into several stages, by analogy with reactions to other types of stressful events [15-17,32,33].

### Stage 1. Acute reaction to stress

This reaction lasts for the whole period of the existence of the threat. It can already be observed now and will decline when the epidemiological situation improves and the quarantine measures are lifted. Acute reaction manifests itself by the spectrum from panic and exaggeration of the problem to its denial (some people buy up buckwheat and toilet paper, others go to barbecues in parks).

There are several variants of the body's response to stress. In the current situation one type of people reacts with a mental block, narrowed consciousness, sluggishness in mind, negative predictions. The other type demonstrates an energetic, talkative, hypomanic and excited behaviour.

One can clearly see the coronavirus unity in social networks, the abundance of humorous and joking content, at the same time many people experience anxiety, associated with fear of infection and fear of death. In some cases, people's critical thinking is reduced and the events are interpreted from the perspective of mysticism and conspiracy theories. All of these are signs of psychological defense in the face of the disaster.

Many people note a distorted sense of time (one day seems to last forever) and sleep disorders (difficulties falling asleep, interrupted sleep, nightmares), decreased motivation and a sense of lostness. In people with a history of mental diseases, exacerbations are likely to occur. In the absence of strict life regulations, the percentage of substance and alcohol use gets higher, increasing cases of conflicts and fights. Vegetative and psychosomatic manifestations (stress ulcers) can be expected [32].

In a significant number of people this stage will be limited to the mobilization of inner forces, accompanied by specific biological changes in their body, without any clinical manifestations. First of all, gamma-aminobutyric acid (GABA) receptors become less sensitive to GABA affinity mediator due to the excessive load [26]. Then the functioning of the whole monoaminergic system changes, which subsequently leads to dysfunction of serotonin, dopamine, noradrenaline [25,39,40], and cortisol concentration in blood plasma decreases (due to the induction of negative feedback on hypothalamic-pituitary-adrenal axis) [28].

## Stage 2. Transition stage

This stage will start only after the real threat disappears and will depend on the degree of change in the dynamic stereotype of life, patient's lifestyle and the extent of biological changes occurred during the first stage. Some people will experience it subacutely, with inner emotional tension, changes in eating habits and sleep disorders. Others may develop depression or anxiety disorder.

## Stage 3. Post-traumatic stress disorder

This stage will develop after the society as a whole and its separate individuals recognize the reality of the problem. It is a delayed reaction to stress that develops a month or six months after the end of the pandemic. It can also develop in people who did not show any mental disorders during the first two stages.

We can assume the following clinical traits:

- Personal and social disorientation, a sense of loss of meaning;
- Irritability, emotional lability;
- Sharpening of personality traits;
- Depression, apathy, low muscle tone and decreased efficiency, or manic manifestations with low productivity;
- Increased psycho-emotional tension, excessive vigilance, especially to everything that seems threatening to health, personal space, financial well-being; aggravated sense of self, up to egocentrism.

At this stage, the most frequent complaints will be: Attention disorders, difficulties in remembering and keeping this or that information in mind, and difficulties in reproducing it. This is not directly related to memory disorders, but rather to the fact that patients' attention will be fixed on their past experiences, they will not devote enough attention to everyday life and will be unable to switch over. This will have a negative impact on their working capacity and everyday activities. Their suggestibility will increase, enhancing risks of falling victim to fraud. Everything reminding of the infection or isolation, or the strict discipline measures, will preserve tension.

Clinical manifestations may be more serious in doctors working with COVID-19, people who have lost family members and friends, their place of work or business. This group is much more likely to perceive the situation as a personal trauma and, therefore, is at a greater risk of developing a full-

scale clinical picture of PTSD with such serious symptoms as:

- Haunting and depressing memories of the traumatic events, re-experiencing of the highlights of the epidemic over and over again, sometimes flashbacks (sudden, vivid, recurrent experiences) of business collapse, family breakdown, loss of a loved one, etc. It can be difficult to distinguish flashbacks from reality, patients may show mental aberrations, sometimes demonstrating aggression;
- Re-experiencing of loss, feeling weak and powerless;
- Distressing dreams, difficulty in falling asleep with an influx of unpleasant memories, night awakenings and early awakenings in a state of anxiety;
- Fear that the traumatic event will happen again, phobic/panic attacks;
- Significant decrease in working capacity and apathy, or the development of hyper-asthenia, to the extent of destructive unreasonableness;
- Personality changes.

At this stage low mood is observed, there is no interest in any new or previously important activities, the view of the future is pessimistic; it is difficult for the patient to see the prospects of development, which causes irritability and outbursts of anger; patients tend to search for the guilty side or try to determine the degree of their own guilt, up to starting self-blaming. Somatic abnormalities are frequent. There is a high risk of alcohol and cannabinoids abuse and the use of other psychoactive substances.

## Biological changes

With increased pathological brain activity at this stage can be seen on the electroencephalogram in the form of increased power spectrum and decreased coherence between temporal, temporoparietal and parietofrontal brain regions [41], and in the form of overall tendency to desynchronization: Increased power of beta rhythm, decreased relative representativity of alpha range [42-44].

## Possible complications and personality changes that coronavirus syndrome can lead to

Possible complications and personality changes that coronavirus syndrome can lead to will be associated with a change in a patient's world view and understanding of his or her place in the world. The complications are dangerous not only by reducing quality of life and social functioning of a person, they can also cause persistent disability and provoke the conversion of the neurotic disorder into an organic one.

The complications are associated with the prolongation of the stress response, personality neurotization and psychopathization, as well as the conversion of the neurotic disorder into an organic one (especially when using psychoactive substances). Patients do not only risk losing flexibility of communicative abilities and the ability to adapt to what is happening to them, not only facing sharpening of their personality traits (developing explosive, hysterical, demonstrative or schizoid traits) but also becoming cynical, prone to antisocial behavior

or inertia, limiting their communication to “fellow sufferers” only, often against the background of alcohol and/or drug abuse. There is also the risk of suicide.

## Prevention and Treatment

All specialists note that PTSD treatment is a complicated and time-consuming task. The National Institute for Health and Care Excellence (NICE) offers the following principles in its standards of care for patients with stress disorders (2018) [17]:

- Support (provided by health care professionals, specific support groups), providing all relevant information;
- Creating safe environment; - involving family and friends in the problem;
- Actively interacting with the patient during the process of treatment planning;
- Actively monitoring the patient’s condition.

It is very important to start therapy in patients with acute stress disorder on time to prevent the development of a chronic PTSD. Studies show that treatment is much more successful in the acute period [32,33]. However, not everyone realizes having any problems or considers it necessary to see a psychiatrist or psychotherapist during this period.

The following preventive measures can be used:

1) Psychotherapy: Cognitive behavioral therapy with narrative and exposure techniques can be considered as the most effective one. Therapy should be aimed at helping to accept COVID-19 and its consequences as an inevitable reality, at desensitisation and reprocessing of the psychological trauma, developing future perspectives and new patterns of behaviour. Pharmacological therapy is aimed at relieving anxiety, restoring sleep, treating depression and other mental disorders;

2) Pharmacotherapy: Pharmacotherapy if necessary to relieve acute symptoms (antidepressants, antipsychotics, sedatives and anxiolytics).

In case PTSD develops, treatment approaches remain similar, however, the work with a psychotherapist may take much longer and requires prescription of stronger medicinal drugs [45].

The purpose of treatment is to help patient’s mind to adapt, to help restore social activity, efficiency, improve mental and physical quality of life. Treatment can take from 6 to 12 weeks or more. For some people it takes even much longer [16-18].

## Conclusions

Coronavirus syndrome is a mental disorder that is a response to the COVID-19 pandemic, which will affect up to 10% of the population. We can already observe acute stress reactions to the spread of the infection and changes in people’s customary lifestyle. However, the most severe symptoms will be seen 6 months after the beginning of the catastrophe and will be similar to the clinical picture of PTSD.

The danger of coronavirus syndrome is that it will reduce the population’s working capacity precisely when it will be crucial for economic recovery. The risk groups are health care workers who treat patients with COVID-19; people with a severe form of the disease; people who have lost their loved ones; and those who have suffered significant financial losses and lost their jobs.

The timely prevention of coronavirus syndrome, consisting of pharmacotherapy and psychotherapeutic support, is critical.

## Authors Contributions

NV: Idea and concept of the review, informational support; EM: Bibliographical search, writing the text of the article; IV: Scientific consultant.

## Acknowledgments

The Authors thank colleagues of the Department of Neurosciences, University of Padova, Italy and of the A & C M-C Foundation for Translational Myology, Padova, Italy for discussions and critical readings.

## Funding

None.

## Conflict of Interest

The authors declare they have no financial, personal, or other conflicts of interest.

## Ethical Publication Statement

We confirm that we have read the Journal’s position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

## References

1. World Health Organization (2020) Coronavirus disease 2019 (COVID-19) Situation Report.
2. World Health Organization (2020) COVID-19 strategy update.
3. An interview with Murray Stein, Ph.D by Rev. Dr. Robert S Henderson (2020) A world shadow: COVID 19. Chiron publications.
4. Madsen Alex (2015) Sonia delaunay: Artist of the lost generation. Open Road Distribution.
5. Bremner JD, Southwick SM, Darnell A, et al. (1996) Chronic PTSD in Vietnam combat veterans: Course of illness and substance abuse. Am J Psychiatry 153: 369-375.
6. Soldatkin VA, Snedkov EV, Sukiasyan SG (2015) Vietnamky, Afghan, Chechen, Donbass syndrome. Evolution of views on the nature of post-traumatic stress. In: XVI Congress of Psychiatrists of Russia. All-Russian scientific-practical conference with international participation "Psychiatry at the stages of reform: Problems and prospects", 492.
7. Sharova NA (2014) Comparative analysis of the Vietnamese and Afghan syndromes. Nauka-Rastudent.ru 12: S6.
8. Leukhova MG, Manukyan GI, Hopiyainen OA (2004) Aggression: Chechen syndrome. In: VP Shchennikov, VI Krasikov, AA Ovcharov, Social Aggression. Third Kuzbass Philosophical Readings Materials of the International Conference, 95-98.

9. Sandifer PA, Walker AH (2018) Enhancing disaster resilience by reducing stress-associated health impacts. *Front Public Health* 6: 373.
10. Shinfuku N (2002) Disaster mental health: Lessons learned from the Hanshin Awaji earthquake. *World Psychiatry* 1: 158-159.
11. Pietrzak RH, Southwick SM, Tracy M, et al. (2012) Posttraumatic stress disorder, depression, and perceived needs for psychological care in older persons affected by Hurricane Ike. *J Affect Disord* 138: 96-103.
12. Neria Y, DiGrande L, Adams BG (2011) Posttraumatic stress disorder following the September 11, 2001, terrorist attacks: A review of the literature among highly exposed populations. *Am Psychol* 66: 429-446.
13. AlexandrovskyYu A (1996) Social stress disorders. *RMJ* 3: 117-126.
14. Stein DJ, Seedat S, Iversen A, et al. (2007) Post traumatic stress disorder: Medicine and politics. *Lancet* 369: 139-144.
15. Kuester A, Köhler K, Ehring T, et al. (2017) Comparison of DSM-5 and proposed ICD-11 criteria for PTSD with DSM-IV and ICD-10: Changes in PTSD prevalence in military personnel. *Eur J Psychotraumatol* 8: 1386988.
16. (2017) Clinical practice guideline for the treatment of PTSD in Adults. American Psychological Association.
17. NICE (2018) Post-traumatic stress disorder. National Institute for Health and Care Excellence.
18. Canadian Agency for Drugs and Technologies in Health (2015) Treatment for post-traumatic stress disorder, operational stress injury, or critical incident stress: A review of guidelines. CADTH Rapid Response Reports.
19. Fastovtsov GA, Sokolova EA (2012) PTSD and comorbid mental disorders. *Russian Psychiatric Journal*.
20. Tushkova KV, Bundalo NL (2011) Features of the manifestations of post-traumatic stress disorder of various severity in men and women. *Siberian Medical Review*.
21. Gilpin NW, Weiner JL (2016) Neurobiology of comorbid post-traumatic stress disorder and alcohol-use disorder. *Genes Brain Behav* 16: 15-43.
22. Frueh B, Elhia J, Grubaugh A, et al. (2005) Documented combat exposure of US veterans seeking treatment for combat-related post-traumatic stress disorder. *Br J Psychiatry* 186: 467-472.
23. Kitayama N, Vaccarino V, Kutner M, et al. (2005) Magnetic resonance imaging (MRI) measurement of hippocampal volume in post-traumatic stress disorder: A meta-analysis. *J Affect Disord* 88: 79-86.
24. Gilbertson MW, Shenton ME, Ciszweski A, et al. (2002) Smaller hippocampal volume predicts pathological vulnerability to psychological trauma. *Nat Neurosci* 5: 1242-1247.
25. Connor KM, Davidson JRT (1998) The role of serotonin in post-traumatic stress disorder neurobiology and pharmacotherapy. *CNS Spectrums* 3: 43-51.
26. Bremner JD, Innis RB, Southwick SM, et al. (2000) Decreased benzodiazepine receptor binding in prefrontal cortex in combat-related posttraumatic stress disorder. *Am J Psychiatry* 157: 1120-1126.
27. Harvey BH, Oosthuizen F, Brand L, et al. (2004) Stress-restress evokes sustained iNOS activity and altered GABA levels and NMDA receptors in rat hippocampus. *Psychopharmacology* 175: 494-502.
28. Yehuda R (2002) Current status of Cortisol findings in post-traumatic stress disorder. *Psychiatr Clin North Am* 25: 341-368.
29. Charney D (2004) Psychobiological mechanisms of resilience and vulnerability: Implications for successful adaptation to extreme stress. *Am J Psychiatry* 161: 195-216.
30. Brady F, Warnock-Parkes E, Barker C, et al. (2015) Early in-session predictors of response to trauma-focused cognitive therapy for posttraumatic stress disorder. *Behav Res Ther* 75: 40-47.
31. Mathew AR, Cook JW, Japuntich SJ, et al. (2015) Post-traumatic stress disorder symptoms, underlying affective vulnerabilities, and smoking for affect regulation. *Am J Addict* 24: 39-46.
32. Kessler RC, Sonnega A, Bromet E, et al. (1995) Posttraumatic stress disorder in the National Comorbidity Survey. *Arch Gen Psychiatry* 52: 1048-1060.
33. Bisson JI, Roberts NP, Andrew M, et al. (2013) Psychological therapies for chronic post-traumatic stress disorder (PTSD) in adults. *Cochrane Database Syst Rev* 13: CD003388.
34. Danzi BA, La Greca AM (2018) Genetic pathways to posttraumatic stress disorder and depression in children: Investigation of catechol-O-methyltransferase (COMT) Val<sup>158</sup>Met using different PTSD diagnostic models. *J Psychiatr Res* 102: 81-86.
35. Winkler EA, Yue JK, Ferguson AR, et al. (2017) COMT Val<sup>158</sup>Met polymorphism is associated with post-traumatic stress disorder and functional outcome following mild traumatic brain injury. *Journal of Clinical Neuroscience* 35: 109-116.
36. Malejko K, Abler B, Plener PL, et al. (2017) Neural correlates of psychotherapeutic treatment of post-traumatic stress disorder: A systematic literature review. *Front Psychiatry* 8: 85.
37. Brewin CR, Andrews B, Valentine JD (2000) Meta-analysis of risk factors for posttraumatic stress disorder in trauma-exposed adults. *J Consult Clin Psychol* 68: 748-766.
38. Di Gangi JA, Gomez D, Mendoza L, et al. (2013) Pretrauma risk factors for posttraumatic stress disorder: A systematic review of the literature. *Clinical Psychology Review* 33: 728-744.
39. Snyder K (2013) Stress, monoamines, and cognitive flexibility. Publicly Accessible Penn Dissertations p. 928.
40. Gesto M, López-Patiño MA, Hernández Soengas JL, et al. (2013) The response of brain serotonergic and dopaminergic systems to an acute stressor in rainbow trout: A time course study. *J Exp Biol* 216: 4435-4442.
41. Lee TW, Yu YW, Chen MC, et al. (2011) Cortical mechanisms of the symptomatology in major depressive disorder: A resting EEG study. *Journal of Affective Disorders* 131: 243-250.
42. Atlantis E, Fahey P, Cochrane B, et al. (2013) Bidirectional associations between clinically relevant depression or anxiety and chronic obstructive pulmonary disease (COPD): A systematic review and meta-analysis. *Chest* 144: 766-777.
43. Manna CB, Tenke CE, Gates NA, et al. (2010) EEG hemispheric asymmetries during cognitive tasks in depressed patients with high versus low trait anxiety. *Clin EEG Neurosci* 41: 196-202.
44. Mathersul D, Williams LM, Hopkinson PJ, et al. (2008) Investigating models of affect: Relationships among EEG alpha asymmetry, depression and anxiety. *Emotion* 8: 560: 572.
45. Markowitz S, Fanselow M (2020) Exposure therapy for post-traumatic stress disorder: Factors of limited success and possible alternative treatment. *Brain Sci* 10: 167.