

Understanding the Genetic and Environmental Contributions to Depression

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Depression is a mood disorder and a psychiatric disorder that negatively affects a person's quality of life. Depression usually manifests with symptoms such as sadness, hopelessness, guilt, anxiety, loss of energy, loss of appetite, sleep disturbance, and trouble focusing. According to data from the World Health Organization (WHO) and the World Bank, it is predicted that the prevalence of depression, which is a common mental disorder in society, will increase in the future and may be seen as the second most common disease after cardiovascular diseases.^[1,2] As it can be understood from this, despite different opinions, the idea that the future will not bring happiness to people and the necessity to investigate and identify the causes.^[3]

A single risk factor is not sufficient for the emergence of the disease.^[4] Genetic and environmental factors exceeding a certain threshold and timing are essential.^[5] In many studies, genetic inheritance,^[6] educational level, unfavorable living conditions, migration,^[7] being a woman, diseases, and their treatments have been suggested as risk factors for major depression.^[8,9]

While biological and genetic influences play a more critical role in severe cases of depression,

ABSTRACT

Depression, classified as a psychiatric disorder, manifests as an individual's incapacity to adhere to their typical daily routines, accompanied by a prevailing sense of despondency, anxiety, and diminished energy levels. Its prevalence is noteworthy in contemporary society. Depression encapsulates an emotional state characterized by a pervasive feeling of melancholy, accompanied by a decline in functional and vital activities. Etymologically rooted in 'depress,' signifying a state of lowness or suppression, depression can arise from genetic predispositions or be triggered by environmental and hormonal factors. The clinical landscape of depression encompasses various subtypes, some posing challenges in terms of accurate diagnosis and effective treatment. This review aims to provide an overview of the genetic and environmental determinants contributing to depression.

Keywords: Depression, environmental factors, genetics, hereditary, mood disorder

environmental influences play a more important role in mild cases.

There are subtypes of depression. Major depression is defined as chronic depression when symptoms are present for two or more years, while affective disorder is defined when symptoms of depression are observed and improve at specific periods. If the symptoms start within four weeks after the birth, it is defined as postpartum depression. Depression with psychotic features is defined as depression if, during episodes of depression, impressions in the form of hallucinations produced by imagination and thought are observed.^[10]

The genetic epidemiology unit defines the relationship between disease and genetic structure and determines risk groups and treatment methods. Many factors can cause depression, but generally, biological factors include genetic predisposition, imbalances in brain chemistry, hormonal imbalances and medical conditions. Psychological factors may include a person's loss of thoughts, adverse life events,

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and personal experiences. Social factors include life events such as loneliness, job loss, divorce, and family problems.^[11]

Depression is one of the most prevalent psychological disorders. Epidemiologic data show that 13% of women and 8% of men are depressed in any given year. The Türkiye mental health profile study reported a prevalence of depressive episodes of 2.3% in men and 5.4% in women, with an overall perfect prevalence of 4%. As can be seen, this rate is twice as high in women.^[12] Three out of every 100 men and six out of every 100 women suffer from depression.^[13] The reasons why women are more likely to suffer from depression than men are as follows:^[14]

- women are more likely to be subjected to sexual abuse, violence, and harassment, and the long-term trauma caused by these situations

- incidence of mental disorders in young people

- women are subjected to socio-cultural pressure and violence by society

- increase exposure to and struggle with adverse life circumstances and harsh conditions

- hormonal processes and factors

- postpartum depression

- perimenopausal period

Depression can be treated with various approaches, including medication, therapy, and lifestyle changes. Early diagnosis and treatment can help reduce symptoms and prevent further disease development. Psychological intervention, cognitive behavioral, interpersonal, and supportive therapy are commonly used psychological treatments.^[15]

Pharmacotherapy remains the primary medical way to treat depression. Continuous progress in recent years has led to the availability of many influential and well-tolerated medications.^[16] However, the various side effects of pharmacotherapy have led the scientific community to consider alternative treatment modalities. After psychotherapy and pharmacotherapy, the new plan includes nutrition. Studies have shown that fruits/vegetables, seeds, fish, vitamins A, B, C, D, C, E, magnesium and zinc minerals, omega-3, and some phytochemicals positively affect cognitive functions and mood.^[17]

Diagnostic Criteria of Depression

Depression can manifest itself in different ways in patients. Clinically, there are different criteria for the

diagnosis of depression. According to the Diagnostic and Statistical Manual of Mental Disorders-V, five or more of the following symptoms must be present within two weeks, and at least one of the symptoms must be seğressiveness, loss of interest, and loss of pleasure (anhedonia). The diagnostic criteria for major depressive disorder are as follows:^[18]

- the emergence of sleep disorders

- lack of enjoyment of activities and life

- pessimism

- despair

- slowing of speech, behavior and thoughts, thinking of death scenarios

- anxiety

- decreased number of selves

- fatigue, exhaustion, weakness, and loss of energy

- loss of appetite, weight loss, weight gain

- decreased sexuality and lack of activity

- feeling guilty/ responsible for situations, shame, and feeling worthless

GENETIC AND ENVIRONMENTAL FACTORS IN DEPRESSION

Genetic Factors

Depression has a biological process involving genetics, neurotransmitters, and the endocrine immune system. The broad picture of the neurobiology of depression is not fully understood.^[19]

Genetic factors are caused by specific genetic factors that may increase a person's risk of depression. Several neurochemical factors, primarily genetic factors, determine an individual's biological predisposition. Several epigenetic factors influence them, such as substance abuse, psychological stress, and trauma. In recent years, the adaptation of the brain when exposed to new biological and environmental conditions has been considered.^[20]

In studying psychiatric disorders concerning genetics, molecular genetics, cytogenetics, and neuroscientific studies are used to determine the individual's inheritance pattern and gene map. This is important to know the functions of the human body and the chromosome sequence map. Thus, psychoanalysis can be done at the molecular level. While social studies are conducted in this field, population genetics studies can give more precise

results. Research in this field focuses on families, twins, and adoptees. In family studies, relative risks are compared with the general population. In twin studies, genetic and environmental research is conducted between monozygotic (identical) and dizygotic (fraternal) twins. Since heredity is not a constant, environmental change can be seen in twins raised in different environments. In adopted individuals, if depression is genetic, the risk is still carried over. Also, if there are common psychological illnesses in the adoptive family, such as personality disorders or major depression, this can also be seen in the child.^[21]

Environmental Factors

Stressful life groups, traumas, substance abuse, and negative situations/losses in a person's life are among the environmental factors that cause depression, and they directly affect the person's quality of life and cause permanent or long-term depression and anxiety. It has been observed that the number of people who become depressed due to environmental factors is higher than the number of people who are genetically predisposed to depression. This situation can be an additional source of stress for an already depressed person. It leads to a loss of functioning. Since the loss of functionality may cause negative feedback from work or family life, it can contribute to the development of social anxiety disorder.^[22]

In December 2019, the Coronavirus disease 2019 (COVID-19) pandemic, which affected the whole world, negatively affected people's mental and physical health.^[23] During the pandemic, adverse effects on the mental states of individuals, depression, and anxiety symptoms were detected.^[24] In the COVID-19 pandemic, where protection and isolation were necessary, people's confinement to their homes led to an increase in mental disorders.^[25] While there was a decrease in anxiety and mental disorders with the decrease in the number of cases, people with anxiety due to COVID-19 anxiety were observed.^[26] In this process, where the flow of information is only through screens due to isolation, it has been found that the time spent in front of the screen affects the emotional state.^[27]

Stress

Stress is one of the most critical factors for depression.^[28] As a result of stress, one of the biggest problems of our day, cortisol, is secreted in the human body. Excessive cortisol secretion in long-term stress situations causes depression in the prefrontal lobe. The pathogenesis of major depressive disorder

and approaches to antidepressant therapies are directed toward intracellular targets that sustain cellular survival and neuroplasticity. Loss of synaptic plasticity and hippocampal atrophy are hallmarks of this common disorder. With a combination of environmental and genetic factors, hippocampal neurons become sensitive to stress. Experimental evidence has shown that stress can cause neuronal damage in the brain, particularly in hippocampal areas. Activation of glutamatergic transmission and its induction by stress can trigger neuronal cell death through excessive N-methyl-D-aspartic acid receptor stimulation. However, stress should not be simplified to just daily worries and work stress. Factors such as lack of sleep and overeating are sources of stress for the human brain.^[29,30]

However, patients who resorted to problem-oriented methods (acceptance, social support, expressing emotions, positive interpretation, holding back, coping religiously, and letting go) in stress situations had low rates of depression before and after the stress situation. There is a significant correlation between people who benefit from problem-oriented help and the level of depression.^[31] It has been found that the ability to develop appropriate responses to stressors and to cope with depression increases in people who are guided as a result of appropriate techniques.^[32]

The onset of depression is often influenced by life events, encompassing daily stressors, threats to one's physical well-being, and significant life experiences. Instances of physical and sexual violence, as well as the experience of losses and traumatic life events, contribute to the development of mental disorders.^[32,33]

The relationship between depression and somatization is essential. Somatization is a term that describes people who have somatic complaints that occur without any organic, physical body. Somatization is the tendency to experience and express physical discomfort without a pathological finding and to seek medical help with the possibility that it may be related to a physical disease.^[34]

Somatization is a different process in medicine that connects the physiology of discomfort with the psychology of symptom detection. Somatization starts with the realization of the reflection of the environmental relationship with body language since the first period of human life. It is seen that the process of desomatization begins with the expression of wants, needs, and discomforts with the language

of the price before the person starts to speak, and then with the use of words, but with the difficulties and problems encountered in life, transformations into a bodily language (resomatization) occur again. It is seen that these situations (desomatization, resomatization) occur with the shaping of the human lifestyle. Based on this statement, we see that somatization, like depression, is shaped by internal and external factors and is an adaptation process. As a result of a study conducted by the WHO with 5438 people in 14 countries, it was found that somatization varied between 7.3/36.8% and somatic symptoms and emotional disorders were largely interrelated, although there were variations in different regions.^[35]

In addition to the causes of depression, social and cultural factors play a role in shaping specific patterns and remedy-seeking behaviors. It has been reported that the vital difference observed between cultures in depression is that the expression of disturbed states and the way they are expressed are different.^[36] In the eastern region, depression is more likely to be expressed by physical reactions, whereas in the west, it is reported that feelings of guilt are more common. The role of religious structure in the ethnic and cultural differences of the findings is also noted to be very important.^[35]

PHYSICAL ILLNESS AND CONDITIONS

In recent epidemiologic studies, there has been an increased interest in examining physical and mental disorders together. It has been reported that depression-anxiety disorders are common in diseases such as cancer, diabetes, and respiratory diseases as a psychiatric relationship.^[36]

Chronic Illnesses

Chronic diseases cannot be cured on their own, and they are generally incurable, which people have to live with for the rest of their lives, and that affect their psychological and social lives along with physical symptoms.^[37,38]

People with chronic respiratory and heart disease find it very difficult to carry out daily routines and activities. Therefore, patients are affected psychologically and socially. As a result, the incidence of depression and anxiety increases.^[39]

Chronic pain is associated with all depressive disorders.^[40] In patients experiencing chronic pain, chronic pain conditions can be seen as a symptom of depressive disorder, while at the same time, as a physical disorder, it can cause mental collapse.

Chronic pain is a common health problem and the association with psychiatric symptoms is quite high. However, this relationship has not yet been fully explained.^[41] The known definition is that "depression increases pain and pain increases depression".^[42] While the prevalence of depression in the general population is 5-8%, the prevalence of depression in patients with chronic pain is 22-78%.^[43,44]

The risk of depression in people with pain problems increases in relation to the number of pain symptoms. In a follow-up of approximately 12 months, the incidence of depression was found to be twice as high in patients treated for headache, migraine, sinusitis, and joint pain.^[44]

In general, depression is expected to emerge in patients with chronic pain complaints as the duration increases. A link has been observed between the duration of pain and the level of depression.^[45]

Pregnancy

Pregnancy and childbirth is a period of significant biological variability. Various events and experiences experienced during early development may have been suppressed and may lead to a complex psychiatric process if they occur during pregnancy. During pregnancy and after delivery, the mother's getting used to and trying to accept the process of motherhood are factors that increase stress.^[46-49]

Postpartum depression is a type of depression that occurs in women after childbirth. Although the risk of severe depression is low during pregnancy, there is a marked increase in the incidence of psychiatric disorders in the postpartum period. Postpartum depression is reported to last for several months, years, or more. Without help, this process may continue for a long time and may end in hospitalization. Traumas that may have severe consequences can be experienced in the unsupported process. Therefore, early diagnosis is of great importance.^[50]

Cancer

In addition to being a disease that causes a lot of deaths in the world, cancer is also a disease with a high likelihood of mental disorders.^[49]

Major depression is an important psychiatric disorder that should be considered in individuals with cancer, and it affects self-care, quality of life, response to treatment, and the amount of cancer.^[51,52]

When an individual with cancer becomes depressed, unable to cope, distressed, and anxious due to the disease they are experiencing, it turns

into a process of depression. The ability to cope with cancer depends on many variables. Patient-specific characteristics (education, age, gender, various personality traits) and environmental factors (individuals who can receive social support, financial situation, etc.) create the effect of coping with cancer.^[53]

Cardiovascular Diseases

Depression and cardiovascular diseases have been discussed for a long time. The first scientific study was conducted by Frasure-Smith et al.^[54] In this study, depression was found to be an independent cause of death six months after acute myocardial infarction.^[52] According to the causal relationship, depression causes cardiovascular diseases and cardiovascular diseases cause depression.^[55-57]

Diabetes

Studies on psychiatric disorders in people with diabetes have focused especially on depression. This is because depression causes various problems in diabetic patients and is thought to harm diabetes treatment. Depression is thought to make it difficult to control the glycemic index in diabetic patients. In studies conducted on this subject, it has been reported that depression in diabetic patients is higher than in the normal population.^[58]

In a study published in 2001, 39 studies involving 20218 people were analyzed and it was found that the risk of depression was twice as high in people with diabetes compared to the normal population.^[59] Diabetes is a chronic disease, so hormonal changes are possible. For this reason, it is usual to have organic changes. In this respect, it is normal to establish a causal relationship with depression.

In conclusion, when the genetic and environmental factors that cause depression are considered, we can see the reasons for its prevalence today. Today, stressful conditions, heavy workloads, global epidemics, economic problems, and general anxiety about the future increase the incidence of depression. Especially in genetically susceptible individuals; these environmental factors are influential in developing depression. In addition, the inability of people to create their own private spaces and spare time for themselves also triggers the formation of depression. Depression has many negative effects on the formation of diseases and their treatment processes. Mental health is an important factor for physical health.

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