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Mental health, depressive disorder and its management: A review

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Abstract

Mental health is a state of mental well-being that enables people to cope with the stresses of life, realize their abilities, learn well and work well, and contribute to their community. India's mental health struggles are largely due to societal stigma and inadequate healthcare access.

Depression is a major cause of disability worldwide and contributes greatly to the global disease burden. Depression is characterized by persistent sadness, hopelessness, irritability, guilt, loss of interest, fatigue, difficulty concentrating, sleep disturbances, changes in appetite, physical aches, and thoughts of death or suicide. Symptoms can also include increased anger, restlessness, withdrawal, impulsivity, alcohol or drug use, isolation, and difficulties with sexual desire and performance. Major depressive disorder (MDD) is one of the most common types of depression. It is characterized by changes in neuronal structure and function, which are accompanied by several biochemical changes. It is caused by a variety of biological, psychological, and environmental factors. This review will cover depression, its signs and symptoms, risk factors, mechanisms, and management. The management of depression includes various types of medication, therapies, counselling, stimulation, and strategies to combat depression.

Keywords: Mental Health; Depression; Depressive disorder; Antidepressants; Psychotherapy.

1 Introduction

Mental health is a condition of mental well-being that allows people to cope with life's stressful events, realize their strengths, study and work effectively, and add value to their society. Mental health encompasses more than just the absence of mental diseases. Mental illnesses and psychosocial disabilities, as well as other mental states linked with considerable suffering, disability in functioning, or risk of self-harm, are examples of mental health issues. A clinically significant impairment in an individual's cognition, emotional regulation, or behavior characterizes a mental disorder. It is often associated with anxiety or problems in vital areas of functioning.

In 2019, one in every eight individuals, or 970 million people worldwide, suffered from a mental disorder, with anxiety and depression being the most frequent. Because of the covid-19 epidemic, the number of persons living with anxiety and depression illnesses increased dramatically in 2020.

There are two main reasons for increasing mental health disorders in India. First of all, India's mental health struggles are largely due to societal stigma and limited healthcare access. People often view mental health issues as taboo, leading to isolation and shame. As societies transition to nuclear families, stress and social isolation have increased, causing an increase in mental health issues. The second most important reason for the country's poor mental health is a lack of mental health specialists.

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There are various mental disorders like Anxiety disorders, Depression, Bipolar disorder, post-traumatic stress disorder, Schizophrenia, Disruptive behaviour and dissocial disorders, Neurodevelopmental disorders, eating disorders etc.

Depression and anxiety are two of the most frequent mental health problems. This review will cover depression, its signs and symptoms, risk factors, mechanisms, and management.

1.1 Two main reasons for poor mental health in India

1.1.1 Lack of awareness in society

India's mental health issues are largely due to societal stigma and inadequate healthcare infrastructure. The country's nuclear families have increased stress and anxiety levels, leading to an increase in mental health problems. Governments and social institutes need to educate about mental health issues and remove misconceptions, as they have successfully addressed diseases like polio, leprosy, and typhoid. This will help reduce the cycle of shame, suffering, and isolation experienced by those suffering from mental health issues.

1.1.2 Shortage of mental health professional

The Indian Union Ministry of Health and Family Welfare reports that the country needs around 13,000 psychiatrists, but currently has only 3500, which is one psychiatrist for over 2 lakh people. Other mental health professionals, such as clinical psychologists, social workers, and nurses, also face shortages. Many psychiatrists leave India for better opportunities abroad due to limited awareness and stigma associated with mental illness, making it difficult for them to match other medical specialties in terms of income and recognition.

2 Depression (Depressive disorder)

Depression is a very frequent mental illness. It is distinguished by continuous unhappiness and a loss of interest or pleasure in formerly rewarding or pleasurable activities. It can also impact with appetite and restful sleep. Tiredness and lack of attention are common symptoms. Depression's consequences can be long-lasting or recurring, and they can have a significant impact on a person's capacity to function and live a fulfilling life. It is believed that 5% of adults worldwide suffer from the illness. Depression is one of the biggest causes of disability worldwide, contributing significantly to the global illness burden.

Depression is caused by complex interplay between social, psychological, and biological variables. Childhood hardship, loss, and unemployment all contribute to and may hasten the onset of depression.

Depression and related mental diseases can have a significant impact on all parts of life, including academic achievement, work productivity, relationships with family and friends, and ability to participate in community activities. There are also strong links between depression and physical health, such as TB and cardiovascular disease, according to research. Depression affects people of all ages, affluent and poor, and in all countries. Women are more prone than men to suffer from depression.

2.1 Statistics on Global and Indian Mental Health: The Effects of Depression on Population and Mortality

Globally, the total number of people suffering from depression was predicted to exceed 300 million in 2015, accounting for 4.3% of the worldwide population. According to the national mental health survey 2015-16, over 15% of Indian adults require active intervention for one or more mental health conditions, and one in every twenty Indians suffers from depression. It is projected that over 258 000 suicides occurred in India in 2012, with the age group 15-49 years being the most afflicted.

Depression is the most prevalent cause of global disability (7.5% of all years lived with disability in 2015). At its worst, depression can lead to suicide; each year, over 800,000 people commit suicide. It is the second biggest cause of death among people aged 15 to 29.

3 Signs And Symptoms of Depression

If you have been experiencing some of the following signs and symptoms, most of the day, nearly every day, for at least 2 weeks, you may be suffering from depression:

- Persistent sad, anxious, or “empty” mood

- Feelings of hopelessness or pessimism
- Feelings of irritability, frustration, or restlessness
- Feelings of guilt, worthlessness, or helplessness
- Loss of interest or pleasure in hobbies and activities
- Decreased energy, fatigue, or feeling slowed down
- Difficulty concentrating, remembering, or making decisions
- Difficulty sleeping, waking early in the morning, or oversleeping
- Changes in appetite or unplanned weight changes
- Physical aches or pains, headaches, cramps, or digestive problems that do not have a clear physical cause and do not go away with treatment
- Thoughts of death or suicide or suicide attempts

Not every person who is depressed exhibits all of these symptoms. Some people have only a few symptoms, while others have several symptoms. Depression symptoms interfere with daily functioning and cause severe distress for the person experiencing them.

Other changes in mood or behavior that can accompany depression include:

- Increased frustration or irritation
- Feeling anxious or on edge
- being withdrawn, negative, or detached
- Increased participation in high-risk activities
- Higher impulsivity
- Rise in use of alcohol or drugs

Exclusion from family and friends

- Inability to fulfill work and family responsibilities or ignoring other significant duties
- Issues with sexual desire and performance

Men and women handle depression in different ways. Although men, women, and people of all genders can experience depression, how they exhibit those symptoms and the coping methods they employ may differ. Some men (and women) may exhibit symptoms other than melancholy, such as being angry or irritated. And, while increasing use of alcohol or drugs can be a coping mechanism for anybody suffering from depression, men may be more likely to do so.

4 Risk Factors for Depression

Depression is a prevalent mental disorder influenced by genetic, biological, environmental, and psychological factors. It can occur at any age, but typically begins in adulthood. It is also present in children and adolescents, with children often expressing more irritability than sadness. Chronic mood and anxiety disorders in adults often begin with high levels of anxiety in childhood. Depression can co-occur with other serious medical illnesses, such as diabetes, cancer, heart disease, and Parkinson's disease, making these conditions worse. The Centres for Disease Control and Prevention (CDC) has acknowledged that certain mental disorders, including depression and schizophrenia, can increase the risk of severe illness from COVID-19. Physical health problems or medications can also contribute to depression, and a healthcare provider experienced in treating these complex illnesses can help develop the best treatment strategy.

Other risk factors for depression include:

- Personal or family history of depression
- Major negative life changes, trauma, or stress
- biological (genetic, chronic diseases, terminal illness)
- Psychological
- Social (familial, relationships, violence, disasters)
- Cultural (religion, caste, beliefs, attitudes)
- Economic
- Consumption of alcohol and drugs can further aggravate the condition.

5 Types of Depression (Depressive disorder)

There are many different types of depression, some of which are caused by events in your life, and others by chemical changes in the brain.

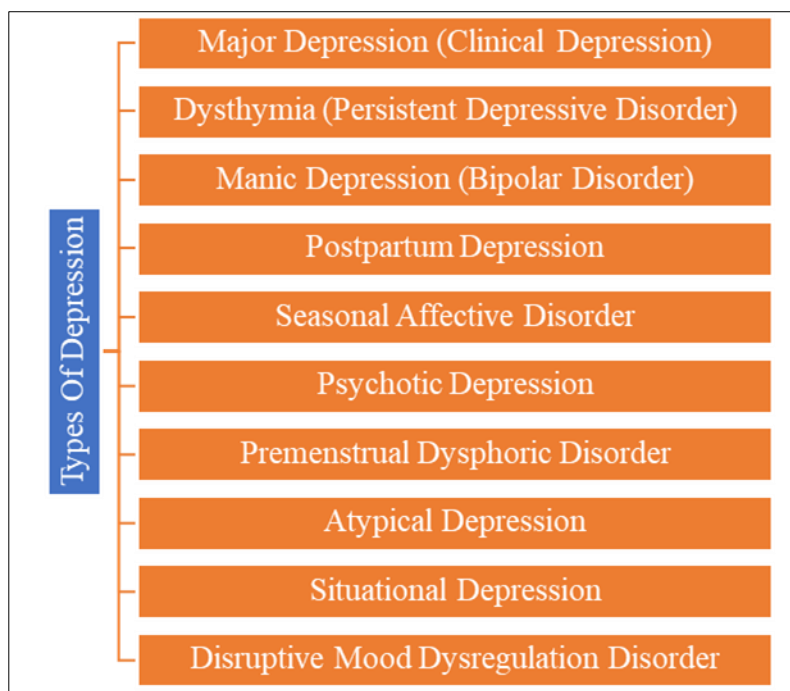


Figure 1 Types of depressive disorder

6 Mechanism of depression

There are five different theories of pathophysiology of depression:

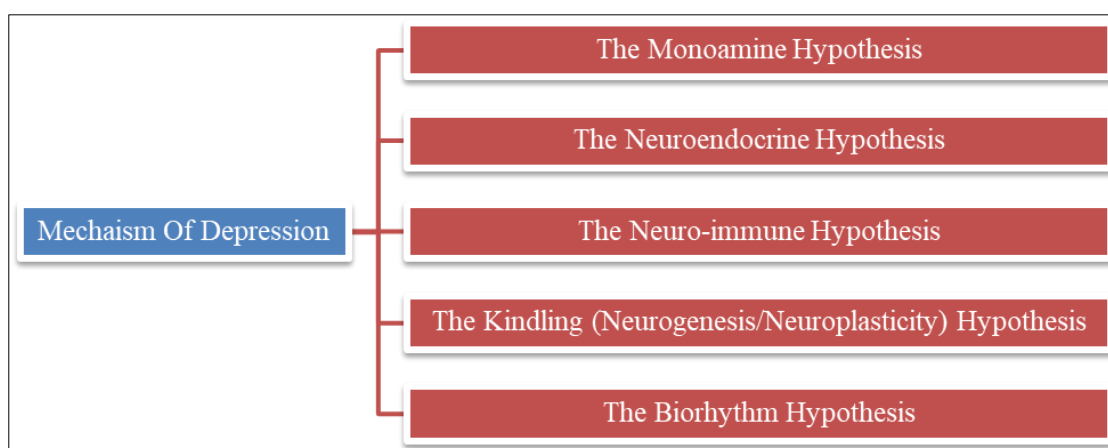


Figure 2 Mechanism of depression

6.1 The Monoamine Hypothesis

The monoamine hypothesis, developed in the 1960s and 1970s, suggests that depression is caused by dysfunction in adrenergic or serotonergic neurotransmission. Two observations based on this theory include the depletion of monoamine neurotransmitters in the brain by antihypertensive drug reserpine and the modification of norepinephrine and serotonin levels by antidepressant drugs. Iproniazid, an antimycobacterial agent, improved mood in tubercular patients with depression and was found to inhibit monoamine oxidase, preventing the degradation of serotonin and

norepinephrine. Later studies showed that cerebral spinal fluid levels of monoamines and their metabolites were different in patients with depression compared to individuals without depression. The monoamine hypothesis proposes that there is a depletion in the level of serotonin, norepinephrine, and/or dopamine in the central nervous system, which is more important for neuropsychopharmacologists than major or minor neurotransmitter systems.

6.2 Neuro Endocrine Hypothesis

The neuro-endocrine hypothesis suggests that depressive disorders are caused by dysregulation of the endocrine system, with at least three subsystems playing important roles in the pathogenesis. The thyroid gland and endocrine gonads are two subsystems that are known to function improperly in mood disturbances. Cortisol plays a multifaceted role in mood disorders, with patients being resistant to the feedback action of exogenous glucocorticoids and having elevated basal cortisol levels. Impaired corticosteroid receptor function may be the key mechanism in the pathogenesis of depression, leading to dysfunctional stress hormone regulation. Studies have shown that abnormal functions can be detected at the level of the hypothalamus in depression. Corticotrophin-releasing hormone is secreted from hypothalamic paraventricular cells, stimulating the pituitary gland to produce adrenocorticotrophic hormone, which stimulates the cortex of the suprarenal glands to secrete cortisol into the general circulation. However, elevated cortisol levels do not correct the levels of corticotrophin-releasing hormone and adrenocorticotrophic hormone.

Cortisol is an important component of the complex emotional response initiated and controlled by the hypothalamus and is an intracerebral neurotransmitter and/or neuromodulator. It is secreted from the adrenal glands in hourly pulses and can penetrate the brain, having multiple effects depending on the concentration. High cortisol levels facilitate the emotional response and inhibit the cognitive response to stress, while also protecting central nervous system nerve cells against potential damage due to uncontrolled, heavy activity.

6.3 Neuro-Immune Hypothesis

Depression is a chronic inflammatory disorder characterized by changes in neuronal structure and function. The neuro-immune hypothesis for the genesis of depression focuses on the inhibition of hippocampal function. Neurotrophic factors are produced by a variety of immune cells and have pleiotropic effects (multiple actions and multiple targets), including important effects in the central nervous system (CNS). These cytokines are produced in the periphery by different immune cells, including activated monocytes, macrophages, T cells, B-cells, natural killer cells, and fibroblasts, in response to different stimuli, including pathogen-associated molecules, danger signals, and stress. These pro-inflammatory factors are primarily produced by immune-competent cells and are involved in the elaboration of the central component of the acute phase inflammatory response. In the central nervous system, inflammatory factors have a significant impact on brain development and neuroplasticity, including the emergence of structural changes that can be considered neurodegenerative, and this condition may progress into Alzheimer's disease and other dementias. Thus, antidepressant drugs may protect neurons from detrimental changes by promoting repair and construction or reconstruction of neural networks.

6.4 The Kindling (Neurogenesis/Neuroplasticity) Hypothesis

The amygdala-kindling model is used to investigate the emergence of clinical seizure disorders (e.g., temporal lobe epilepsy) as well as the emergence of behavioral disorders (especially bipolar mood disorders). According to the kindling hypothesis, a similar trend occurs in depressive illnesses, where first episodes are triggered by psychosocial stresses, but after enough repetition, they also begin to develop spontaneously. The endocrine system is expected to play a major role in the emergence of kindling seizures, which are accompanied by a number of biochemical alterations including classical neurotransmitters, neuropeptides, cytokines, and neurotrophic factors. Furthermore, the hippocampus/amygdala complex is thought to have a role in the pathophysiology of depression. In this review, we provide a possible explanation for the pathogenicity of depression, which may be mainly related to its anti-manic activity, and its anti-depressive effects may occur elsewhere.

6.5 The Biorhythm Hypothesis

Depression is a condition characterized by a malfunction in the biological clock, leading to sleep disturbances, disrupted sleep architecture, and irregular biorhythms. Symptoms can fluctuate over the day, with some experiencing seasonal patterns. Psychiatric hypnograms show irregular sleep phases and abnormal sleep sequences. The endogenous biological clock is regulated by genes, including the circadian pacemaker in the brain. The biological clock of the suprachiasmatic nucleus requires daily entrainment signals, called "Zeitgebers," triggered by daylight and melatonin. The interaction between daylight, melatonin, and the circadian rhythm is complex, but a simplified model suggests that the biological clock is reset by full exposure to daylight. Melatonin, a hormone secreted by the pineal gland during sleep, enhances sensitivity to daylight entrainment, affecting the biorhythms of patients with dysfunctional retinas. The

biorythm hypothesis postulates that depressive symptoms are caused by a dysfunction in the spinal cord that affects the generation of a correct circadian rhythm.

7 Management of Depression

Even the most severe symptoms of depression are treatable. Treatment is more successful the earlier it is started. Psychotherapy, stimulation therapy, medicine, and counseling are the usual treatments for depression.

7.1 Medication for Depression

Prescription drugs known as antidepressants are often used to treat anxiety, obsessive-compulsive disorder, and depression. Antidepressants are medications that improve depression symptoms by boosting mood. Almost all antidepressants have some effect on monoaminergic transmission in the brain, and many of them also have other related characteristics.

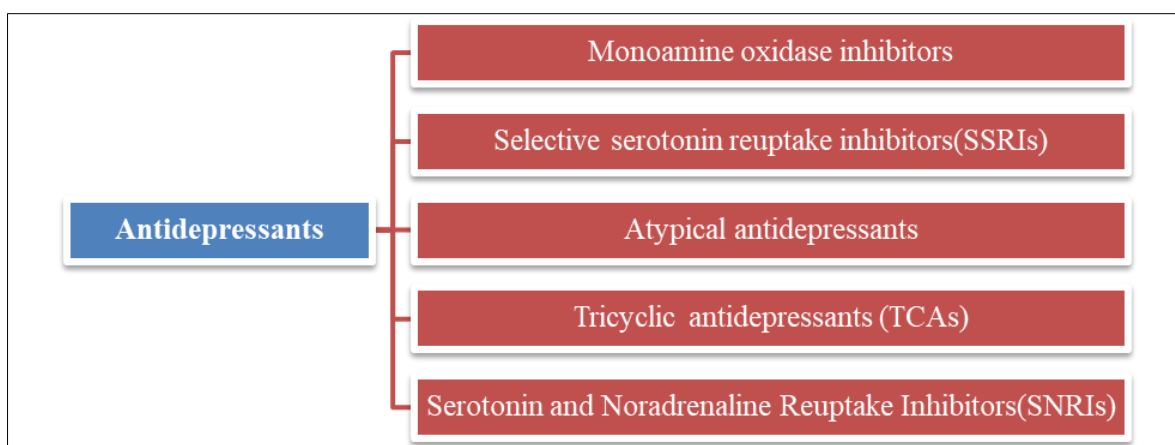


Figure 3 Types of Antidepressants

7.1.1 Monoamine Oxidase Inhibitors

The monoamine oxidase enzyme, which catabolizes dopamine, norepinephrine, and serotonin, is inhibited by MAOIs. The earliest antidepressants to be identified were monoamine oxidase inhibitors. Because of its side effects and potential for drug interactions, MAOIs are not recommended as a first-line treatment for depression.

7.1.1.1 Drugs

- Selegiline
- Moclobemide
- Tranylcypromine
- Isocarboxazid
- Phenelzine
- Clorgyline

7.1.1.2 Administration

Isocarboxazid	<ul style="list-style-type: none"> • The starting dose is 20 mg daily, and the usual maintenance dose is 20 to 60 mg daily.
Phenelzine	<ul style="list-style-type: none"> • The starting dose is 45 mg daily, and the usual maintenance dose is 60 to 90 mg daily.

Figure 4 Administration of monoamine oxidase inhibitors

7.1.3 Adverse effects

- Nausea
- Dizziness
- Headache
- Insomnia
- Rarely Excitement
- Liver Damage
- Potential for serotonin syndrome
- Sexual dysfunction

7.1.2 Selective Serotonin Reuptake Inhibitors (SSRIs)

A family of drugs called selective serotonin reuptake inhibitors (SSRIs) is most frequently administered to treat depression. Because of their safety, effectiveness, and tolerability, they are frequently used as first-line pharmacotherapy for depression and many other mental illnesses. The use of these in adult and pediatric patients is authorized.

7.1.4 Drugs

- Sertraline
- Fluvoxamine
- Fluoxetine
- Paroxetine
- Citalopram
- Escitalopram

7.1.5 Administration

Citalopram	<ul style="list-style-type: none"> • The starting dose is 20 mg daily, and the usual maintenance dose is 20 to 40 mg daily.
Escitalopram	<ul style="list-style-type: none"> • The starting dose is 5-10 mg daily, and the usual maintenance dose is 10 to 20 mg daily.

Figure 5 Administration of selective serotonin reuptake inhibitors

7.1.6 Adverse effects

- Sexual dysfunction
- Headache
- QTc prolongation
- Nausea
- Vomiting
- Loose Motions
- Dizziness
- Occasionally Insomnia

7.1.3 Atypical Antidepressants

An atypical antidepressant is an antidepressant medication that acts in a manner that is different from that of most other antidepressants. Typical antidepressants include SSRIs, SNRIs, TCAs, and MAOIs, which act mainly by increasing the levels of the monoamine neurotransmitters, serotonin, and/or norepinephrine.

7.1.7 Drugs

- Trazodone
- Mianserin
- Mirtazapine
- Bupropion

- Amoxapine
- Tianeptine
- Amineptine

7.1.8 Administration

Bupropion	• The starting dose is 150 mg daily, and the usual maintenance dose is 300 mg daily.
Mirtazapine	• The starting dose is 15 mg daily, and the usual maintenance dose is 15 to 45 mg daily.

Figure 6 Administration of Atypical Antidepressants

7.1.9 Adverse effects

- Agomelatine- hepatotoxicity
- Mirtazapine-Sedation, Weight gain
- Bupropion- Seizures
- Trazodone - Arrhythmia
- Mianserin - blood dyscrasias, liver dysfunction

7.1.4 Tricyclic antidepressants (TCAs)

Tricyclic antidepressants (TCAs) constitute a class of medications used to manage and treat major depressive disorder (MDD). These medications function by inhibiting the reuptake of neurotransmitters, such as serotonin and norepinephrine, which can modulate mood, attention, and pain in individuals. TCAs are now regarded as second-line treatment options alongside selective serotonin reuptake inhibitors (SSRIs). They acquired the name "tricyclic" due to the presence of 3 rings in their chemical structure.

7.1.10 Drugs

- Amitriptyline
- Clomipramine
- Doxepin
- Imipramine
- Trimipramine
- Desipramine
- Nortriptyline
- Protriptyline
- Maprotiline
- Amoxapine

7.1.11 Administration

Amitriptyline	• The starting dose is 50 mg daily, and the usual maintenance dose is 100 to 200 mg daily.
Nortriptyline	• The starting dose is 25 mg daily, and the usual maintenance dose is 50 to 150 mg daily.

Figure 7 Administration of Tricyclic antidepressants

7.1.12 Adverse effects

- Dry mouth
- Urinary Retention
- Constipation

- QRS prolongation
- Seizures
- Orthostatic Hypotension

7.1.5 Serotonin and noradrenaline reuptake inhibitors (SNRIs)

The serotonin-norepinephrine reuptake inhibitors are a family of antidepressants that inhibit the reuptake of both serotonin and norepinephrine.

Serotonin and norepinephrine reuptake inhibitors (SNRIs) block serotonin and norepinephrine reuptake in the synapse, increasing postsynaptic receptors' stimulation. The affinity of SNRIs for the serotonin and norepinephrine transporters varies.

7.1.13 Drugs

- Venlafaxine
- Desvenlafaxine
- Duloxetine
- Milnacipran
- Levomilnacipran

7.1.14 Administration

Venlafaxine	<ul style="list-style-type: none"> • The starting dose is 75 mg daily, and the usual maintenance dose is 225 to 375 mg daily.
Desvenlafaxine	<ul style="list-style-type: none"> • The starting dose is 25 to 50 mg daily; the usual maintenance dose is 50 mg daily.

Figure 8 Administration of serotonin and noradrenaline reuptake inhibitors

7.1.15 Adverse effects

- Hypertension
- Headache
- Diaphoresis
- Bone resorption

7.2 Psychotherapy

Psychotherapy (also psychological therapy, talk therapy, or talking therapy) is the use of psychological methods, particularly when based on regular personal interaction, to help a person change behaviour, increase happiness, and overcome problems. Psychotherapy seeks to improve an individual's well-being and mental health by resolving or mitigating problematic behaviors, beliefs, compulsions, thoughts, or emotions, as well as improving relationships and social skills.

Psychotherapy can help you:

- Adjust to a crisis or other current difficulty
- Identify negative beliefs and behaviors and replace them with healthy, positive ones
- Explore relationships and experiences, and develop positive interactions with others
- Find better ways to cope and solve problems
- Identify issues that contribute to your depression and change behaviors that make it worse
- Regain a sense of satisfaction and control in your life and help ease depression symptoms, such as hopelessness and anger
- Learn to set realistic goals for your life
- Develop the ability to tolerate and accept distress using healthier behaviors

7.2.1 *Approaches to psychotherapy*

Approaches to psychotherapy fall into five broad categories:

7.2.2 *Psychoanalysis And Psychodynamic Therapies*

This approach focuses on changing problematic behaviours, feelings, and thoughts by discovering their unconscious meanings and motivations. A tight working connection between therapist and patient distinguishes psychoanalytically oriented therapies. Patients discover more about themselves through their interactions in the therapy partnership. While Sigmund Freud is closely associated with psychoanalysis, it has been developed and modified since his early formulations.

7.2.3 *Behaviour Therapy*

This approach emphasizes on the role of learning in the development of both normal and pathological behaviors.

Ivan Pavlov contributed significantly to behavior therapy by discovering classical conditioning, often known as associative learning. When Pavlov's famous dogs heard their dinner bell, they began drooling because they associated the sound with food.

"Desensitizing" is classical conditioning in action: A therapist may help a client with a phobia by repeatedly exposing him or her to whatever generates anxiety.

E.L. Thorndike, who discovered operant conditioning, was another influential thinker. To modify people's behavior, this sort of learning uses rewards and penalties.

Several versions have emerged since the introduction of behavior therapy in the 1950s. Cognitive-behavioral therapy, for example, focuses on both thoughts and behaviors.

7.2.4 *Cognitive Therapy*

Cognitive therapy focuses on what people think as opposed to what they do.

Cognitive therapists believe that faulty thinking is the source of dysfunctional emotions or behaviors. People can change how they feel and what they do by changing their thinking.

Albert Ellis and Aaron Beck are two major figures in cognitive therapy.

7.2.5 *Humanistic Therapy*

This approach emphasizes people's ability to make reasonable decisions and reach their full potential. Concern for others is another significant element.

This style of treatment was influenced by humanistic philosophers such as Jean-Paul Sartre, Martin Buber, and Sren Kierkegaard.

Three types of humanistic therapy are very effective. Client-centered treatment opposes the notion of therapists as experts on their clients' inner lives. Therapists instead assist clients in changing by stressing their concern, caring, and interest.

Gestalt treatment emphasizes "organismic holism," or the significance of being aware of the here and now and taking personal responsibility.

Existential therapy is concerned with free choice, self-determination, and the quest for meaning.

7.2.6 *Integrative Or Holistic Therapy*

Many therapists do not adhere to a single technique. Instead, they combine aspects from many approaches and personalize their treatment to the specific needs of each client.

7.3 Brain stimulation therapy

If medication or psychotherapy do not relieve depression symptoms, brain stimulation therapy may be an alternative to consider. There are now various types of brain stimulation therapy, some of which are FDA-approved for the treatment of depression.

Although brain stimulation techniques are less commonly utilized than medication and psychotherapy, they can be effective in treating persons with mental problems who have not responded to other treatments.

Brain stimulation therapies work by electrically activating or inhibiting the brain. Electricity is delivered either directly or indirectly through electrodes implanted in the brain or electrodes placed on the scalp. Applying magnetic fields to the head can also induce electricity.

The brain stimulation therapies with the largest bodies of evidence include:

- Electroconvulsive therapy
- Repetitive transcranial magnetic stimulation
- Vagus nerve stimulation
- Magnetic seizure therapy
- Deep brain stimulation

8 Conclusion

In conclusion, depression is a complicated mental disorder influenced by a variety of biological, psychological, and environmental factors. Changes in neurotransmitter systems, neuroendocrine function, and brain plasticity are all part of the pathophysiology of depression. An issue with the biological clock, which results in sleep disorders and irregular biorhythms, is the primary cause of depression. Antidepressants and psychotherapies are the foundations of an integrated approach to treating depression. Antidepressants reduce the symptoms of depression by regulating brain chemicals that regulate mood and emotions. On the other side, patients are given strategies and resources to deal with depressive thoughts and behaviors during psychotherapies. Both treatments have been proven effective, but their success largely depends on individual factors such as the severity of depression, the patient's personal circumstances, and their response to treatment. Therefore, a personalized treatment plan, often involving a combination of both methods, is typically the most effective way to treat depression, but if medication or psychotherapy does not reduce the symptoms of depression, then brain stimulation therapies can be considered as an alternative.

Compliance with ethical standards

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No conflict of interest to be disclosed.

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