



Neurological Paper on Depression

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Abstract

This paper attempts to discuss depression. It will explain what defines clinical depression. It will list the common symptoms associated with depression. It will explain the brain areas and neurotransmitters involved in this disorder. It will also describe some of the treatment options available – both medical and alternative to manage depression.

Keywords: depression, neurotransmitters, clinical depression

Definition of Depression

The National Institute of Mental Health (NIMH), in its article on *Depression*, defines it as “a common but serious mood disorder. It causes severe symptoms that affect how a person feels, thinks, and handles daily activities, such as sleeping, eating, or working” [1]. Depression ranges in seriousness from mild, temporary episodes of sadness to severe, persistent depression. Mayo Clinic, in its article *Clinical Depression: What does it mean?* defines it as “a more-severe form of depression, also known as major depression or major depressive disorder (MDD). It isn't the same as depression caused by a loss, such as the death of a loved one, or a medical condition, such as a thyroid disorder” [2]. The symptoms of depression should persist for at least two weeks for a doctor to diagnose them as clinical depression.

Types of Depression

Depression can manifest itself in different forms. NIMH makes the following classifications [3] –

- **Major depression** includes symptoms of depressed mood or loss of interest, most of the time for at least 2 weeks, that interfere with daily activities.
- **Persistent depressive disorder** (also called dysthymia or dysthymic disorder) consists of less severe symptoms of depression that last much longer, usually for at least two years.
- **Perinatal depression** is depression that occurs during pregnancy or after childbirth. Depression that begins during pregnancy is prenatal depression, and depression that begins after the baby is born is postpartum depression.
- **Seasonal affective disorder** is depression that comes and goes with the seasons, with symptoms typically starting in the late fall or early winter and going away during the spring and summer.

- **Depression with symptoms of psychosis** is a severe form of depression in which a person experiences symptoms of psychosis, such as delusions (disturbing, false fixed beliefs) or hallucinations (hearing or seeing things others do not hear or see).

Symptoms of Depression

Depression can manifest itself in many ways. These can be broadly classified as Psychological symptoms, Physical symptoms, and Social symptoms [4].

1. Psychological Symptoms:

- a. continuous low mood or sadness
- b. feeling hopeless and helpless
- c. having low self-esteem
- d. feeling tearful
- e. feeling guilt-ridden
- f. feeling irritable and intolerant of others
- g. not feeling motivated or interested in things
- h. finding it difficult to make decisions
- i. not getting any enjoyment out of life
- j. feeling anxious or worried
- k. having suicidal thoughts or thoughts of harming yourself

2. Physical Symptoms

- a. moving or speaking slower than usual
- b. changes in appetite or weight (usually decreased, but sometimes increased)
- c. constipation
- d. unexplained aches and pains

- e. lack of energy
- f. disturbed sleep – for example, finding it difficult to fall asleep at night or waking up very early in the morning.

3. Social Symptoms

- a. avoiding contact with people and taking part in fewer social activities
- b. neglecting your hobbies and interests
- c. having difficulties in your home, work, or family life

Causes of Depression

Depression is a very complex neurological disorder, and several factors can cause it [5] –

- Imbalance of chemical neurotransmitters
- Faulty mood regulation by the brain
- Nerve cell connections, nerve cell growth, and functioning of the synapses
- Genetic vulnerabilities
- Stressful life events

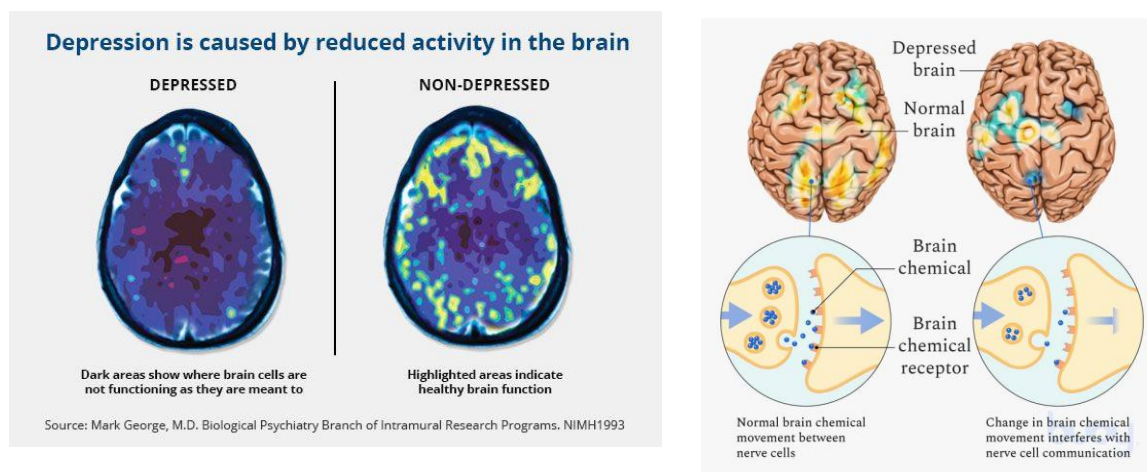
Brain Areas and Neurotransmitters Impacted

This section will describe how the different areas of the brain and neurotransmitters are affected in a depressed person when compared to a normal person. It will also describe other possible causes of depression. Understanding the causes of any disease is important to figure out the treatments and understand how the treatments would work.

1. **Imbalance of chemical neurotransmitters:** One of the most common causes of depression is the lack of reward neurotransmitters like serotonin and dopamine. Neurotransmitters are chemicals that relay messages from neuron to neuron. An antidepressant medication tends to increase the concentration of these substances in the spaces between neurons (the synapses).

In many cases, this shift appears to give the system enough of a nudge so that the brain can do its job better. Neurotransmitters that can result in feelings of depression if in imbalance are –

- a. Serotonin helps regulate sleep, appetite, and mood and inhibits pain. Research supports the idea that some depressed people have reduced serotonin transmission. Low levels of serotonin byproducts have been linked to a higher risk of suicide. *Therefore, low serotonin levels can result in depression* [6].
- b. Dopamine is essential for movement. It also influences motivation and plays a role in how a person perceives reality. Problems in dopamine transmission have been associated with psychosis, a severe form of distorted thinking characterized by hallucinations or delusions. *It is also involved in the brain's reward system; therefore, low levels of dopamine can result in depression, and on the other hand, extremely high levels of dopamine can cause extreme euphoria, hallucinations, and delusions, which in turn can cause depression when the stimulant is taken away* [7].
- c. Norepinephrine constricts blood vessels, raises blood pressure. It may trigger anxiety and be involved in some types of depression. It also seems to help determine motivation and reward. *Extremely high amounts of norepinephrine can cause anxiety and, therefore, depression* [8].
- d. Gamma-aminobutyric acid (GABA) is an amino acid that researchers believe acts as an inhibitory neurotransmitter. It is thought to help quell anxiety. *Therefore, very high amounts of GABA may result in extreme laziness or feeling of not doing anything and reduced movement, hence, depression* [9].
- e. Some researchers also suggest that imbalance in Acetylcholine and Glutamate can also result in feelings of depression.



Figures 1 and 2: These brain scans and diagrams show that in the depressed brain, there is less brain activity, less serotonin release, dopamine neurotransmitters, less neurogenesis, and less grey matter.

2. **Genetic variation:** that results in a lower number of serotonin receptors 5-HTT. Several researchers have shown a correlation between genetic variations that can result in a lower number of serotonin receptors 5-HTT and resulting depression. This is also why many people say that depression and bipolar disorders run in the family [10].
3. **Less gray matter in areas of the brain** – hippocampus, amygdala, cingulate cortex – this means a lesser number of dendrites to sense and for decision making, memory, and emotion.
4. **Shrinkage or enlargement in the parts of the brain**, which are related to decision making and emotional control, can result in depression [11].
 - a. **Amygdala:** The amygdala is part of a group of structures deep in the brain that is associated with emotions such as anger, pleasure, sorrow, and fear. Recalling an emotionally charged memory, such as a frightening situation, activates the amygdala.

Activity in the amygdala is higher when a person is sad or clinically depressed, and this continues even after recovery from depression. This increase in activity may cause the amygdala to enlarge.

- b. Basal ganglia:** The basal ganglia are a related group of structures deep in the brain. They are connected to and interact with structures that are closer to the brain's surface. They may help facilitate movement and may be involved in memorizing, thinking, and emotional processing. *Some studies have found shrinkage and other structural changes in the basal ganglia in people with depression.*
 - c. Hippocampus:** The hippocampus plays a key role in processing long-term memory. Interplay between the hippocampus and the amygdala might account for the adage "once bitten, twice shy." It is this part of the brain that registers fear when you are confronted by a barking, aggressive dog, and the memory of such an experience may make you wary of dogs you come across later in life. *The hippocampus is smaller in some depressed people, and research suggests that ongoing exposure to stress hormones impairs the growth of neurons in this part of the brain.*
- 5. Brain plasticity:** Brain or neural plasticity is the change of synapses based on signaling responses. Neural plasticity, a fundamental mechanism of neuronal adaptation, is disrupted in depression. The changes in neural plasticity induced by stress and other negative stimuli play a significant role in the onset and development of depression [12].
- 6. Reduction in neurogenesis:** Neurogenesis is the formation of new brain cells. Studies have shown that neurogenesis, especially in the hippocampus, is reduced in depressed people. Creation of new neurons is linked to feelings of reward and well-being, and this gets impaired due to reduced neurogenesis in the hippocampus [13].

7. **High level of cytokines:** Researchers have shown that there is similarity between the “sickness behavior” – loss of appetite and fatigue, and depression. This led to studies that have shown a positive correlation between high levels of cytokines, which are produced during an anti-inflammatory response, and depression [14].

Treatment Options

Depression is something that humans have studied and tried to treat since ancient times. This section explores how depression has been treated from ancient times to the present day.

1. **Ancient Greeks and Romans:** Ancient medicine pioneers like Hippocrates have treated depression with exercise, music, hydrotherapy, and primitive forms of behavioral therapy. Probably the scientific idea behind this was to increase the release of serotonin and dopamine by doing activities that involved fun and relaxation, and reducing stress [15].
2. **Medieval Europeans:** Medieval Europeans, however, practiced some questionable forms of treatment, like leg irons, beating, imprisonment, drowning, starvation, and burning.
3. **Renaissance Europe:** Music, travel, herbal medicine, and marriage.
4. **Early 1900s:** Talk therapy was invented to help cure people with depression.
5. **Mid 1900s:** Focus started on the pharmacology of treating depression, and a drug used to treat tuberculosis was shown to show positive improvement in depressed people.
6. **Modern-day treatment options:**
 - a. *Antidepressant medications* – Selective serotonin reuptake inhibitors (SSRIs) – alter/increase the release of serotonin at the synapses [16].
 - b. *Antidepressant medications* – increase neurogenesis and brain plasticity – higher levels of BDNF, which promotes neurogenesis.
 - c. *Anti-inflammatory medications* – Ibuprofen – as cytokines are reduced.

- d. *SSRI, SNRI, tricyclic antidepressants* – increase serotonin and dopamine neurotransmitters.
 - e. *MAOI (monoamine oxidase inhibitors)* – block enzymes that break down neurotransmitters.
7. **Alternate treatment/therapy options:** Both dog and equine therapy have proven to show positive results in people suffering from depression.
- a. A psychiatric service dog can be trained to perform a wide range of tasks to help someone with depression. These include tasks related to assisting during a crisis, helping you cope with emotional overload, and providing treatment-related assistance.
 - b. Equine-assisted psychotherapy incorporates horses into the therapeutic process. People engage in activities such as grooming, feeding, and leading a horse while being supervised by a mental health professional.

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