Why Do We Feel Sad? Neurotransmitter Systems, Effects of Genetic Factors, Neurological Conditions Associated with Sadness and Treatment

Bennu Elbasioglu

Abstract
Sadness is one of the fundamental emotions humans experience. This paper examines sadness and explores its importance for survival, its relation with the emotion anger, serotonergic, dopaminergic, noradrenergic neurotransmitter systems' roles in sadness with the help of serotonin receptor 5-HT, effects of environmental and genetic factors, depressive disorder related to sadness and treatment for this conditions including antidepressants and psychotherapy.

Introduction
Sadness is one of the basic human emotions associated with sorrow, disappointment and grief. Sadness can usually be recognized from expressions like gloomy mood, crying and quietness.

Despite being a negative emotion, it is essential for our survival. Sadness is the way humans cope with grief and guides the way through pain. Experiences of sadness inform social judgment by seeing potential harm. This knowledge helps protect individuals from recurring pain, they know who and what to be careful of.

Sadness is closely related to one of the fundamental emotions: anger. Anger is like a defense mechanism of sadness, it's a shield. Anger covers the pain sadness causes when it's needed. It's a secondary response to sadness.

Neurotransmitter Systems and Receptors
Serotonergic, dopaminergic and noradrenergic neurotransmitter systems are involved in the emotion sadness. Serotonergic neurons are located in the raphe nuclei of the brain stem. Serotonin is the primary neurotransmitter in the serotonergic system. Serotonin is important for mood, sleep, digestion, nausea, wounding, learning and memory. Low levels of serotonin lead to sadness which can cause depression and anxiety. Serotonin firstly gets synthesized from the amino acid L-tryptophan, then the tryptophan gets converted to 5-HT by the enzymes tryptophan hydroxylase and amino acid decarboxylase.
Serotonin is stored in the synaptic vesicles of the presynaptic neuron, when an action potential reaches, serotonin gets released into the synaptic cleft by exocytosis. After its release, it binds to receptors post-synaptic or pre-synaptic receptors. The main receptors involved in the mood are 5-HT1A and 5-HT1B. Finally, serotonin is removed by SERT, a serotonin transporter from the synaptic cleft back to the presynaptic neuron so it can be recycled or degraded. This is the healthy serotonergic pathway in which the emotions of pleasure and well-being are produced. If the receptors that play a role in mood regulation have malformation, it will affect serotonin signaling which can cause sadness. Another factor of this system that can cause sadness is the serotonin transporter, reduced function of SERT can reduce the availability of serotonin which eventually leads to sadness.

Dopaminergic system and noradrenergic system also influence sadness. One of dopamine’s roles is motivation meaning that low levels of dopamine can result in sadness because of lack of motivation. Additionally low levels of norepinephrine are connected with low motivation, energy, mood and concentration.

**Depression, Environmental and Genetic Factors**

Depression is a mental disorder with the symptoms of lack of motivation and concentration, hopelessness, loss of pleasure and interest, disrupted sleep, feelings of low self-worth and energy. 7% of adults in the U.S. are estimated to have depression every year and 16% of adults in the U.S. are estimated to suffer from depression at some point in their life. 4.4% of children in the U.S have depression however these numbers can be higher in reality because not everyone who has depression gets medical help. Medical conditions, trauma, divorce, marriage, loss of a loved one, isolation, work, school, bullying are some environmental factors that can cause depression. 50% of the causes of depression are these physical or psychological ones. The other 50% is inherited by genes. A person who has a first-degree relative who suffered from depression is more likely to have depression. There is 1.5 to 3% higher chance to have depressive disorder than the general population. Low levels of SLC6A4 (Serotonin Gene Transporter) lead to low levels of serotonin in the synaptic cleft. 5-HTTLPR is a region in SLC6A4 that is crucial for depression. The short allele for this gene (SS) have lower serotonin transporter efficiency causing higher risk of depression. An extra gene linked to depression is BDNF. Low levels of BDNF gene decreases the resilience of stress and increases the vulnerability of depression.

![Figure 2: Depression](https://thewrightinitiative.com/misc/where-is-serotonin-produced-in-the-brain.html)
Treatment of Depression

Regular exercise, quality sleep, healthy diet and avoiding alcohol are things people can do on their own to manage depression symptoms. Fortunately depression is one of the most treatable disorders. Psychotherapy, also known as talk therapy, is one of the treatments. Talking with a mental health professional helps people improve their psychological well being and change unhealthy thoughts. The most popular psychotherapy is cognitive behavioral therapy (CBT). Medication prescribed by healthcare providers is another treatment for depression. Antidepressants change brain chemicals to regulate mood and affect neurotransmissions like serotonin, dopamine and norepinephrine.

Conclusion

This paper analyzed the emotion sadness, the reasons why we feel it and health conditions linked to it. Sadness is important for survival as it’s a part of recovery. Serotonergic, dopaminergic and noradrenergic systems are the main neurotransmitter systems related to sadness, low levels of the primary neurotransmitters in these systems results in sadness. Some malfunctions in systems also lead to this emotion. The source of mental health condition, depressive disorder’s source is sadness. The roots of this condition is related to genetics as much as environmental factors. Stressful life events and trauma can trigger depression. The genes 5-HTTLPR and BDNF play a role in depression. Depression can be managed with self-care strategies and cured through psychotherapy with the help of medication. Sadness serves important functions even though it’s a negative emotion and understanding it is crucial for developing treatments.

References

rt#:~:text=5%2DHTTLPR%20is%20a%20polymorphism. Accessed 13 July 2024.
Cleveland Clinic. “Antidepressants.” Cleveland Clinic, 1 Mar. 2023,
my.clevelandclinic.org/health/treatments/9301-antidepressants-depression-medication.

---. “Depression Symptoms, Causes, & Treatment .” Cleveland Clinic, 13 Jan. 2023,
my.clevelandclinic.org/health/diseases/9290-depression.

Forgas, Joseph P. “Four Ways Sadness May Be Good for You.” Greater Good, 4 June
2014,
greatergood.berkeley.edu/article/item/four_ways_sadness_may_be_good_for_you.

“Happy or SAD: The Chemistry behind Depression.” The Jackson Laboratory,

Hasler, Gregor. “Pathophysiology of Depression: Do We Have Any Solid Evidence of
Interest to Clinicians?” World Psychiatry, vol. 9, no. 3, 1 Oct. 2010, pp. 155–161,
www.ncbi.nlm.nih.gov/pmc/articles/PMC2950973/#:~:text=The%20monoamine%20deficiency%20theory%20posits,

Sangkuhl, Katrin, et al. “Selective Serotonin Reuptake Inhibitors Pathway.”
Pharmacogenetics and Genomics, vol. 19, no. 11, Nov. 2009, pp. 907–909,
www.ncbi.nlm.nih.gov/pmc/articles/PMC2896866/,
https://doi.org/10.1097/fpc.0b013e32833132cb.

