ISSN NO: 2771-8840
Date of Publication: 28-04-2023

General Description of Serotonin Theory

Yusra A. Radeef[1], Zahraa Ali Abdullah[2]
[1,2]Department of Biology, College of Science, Babylon University,Babylon, Iraq.
sci.yusra.ali@uobabylon.edu.iq

Abstract
This research review sheds light on an overview of serotonin and its relationship with cases of depression. The chemical activity of serotonin has been addressed, as serotonin acts as chemical messengers that act on cells throughout the human body, which starts from the calculus of early development and during puberty. In this research, we discuss how to increase serotonin through the use of drugs, which is an important field in psychiatric and biological research. We determine the normal range of serotonin in the blood through a simple blood test. The functions of serotonin, which is considered as a direct-acting neurotransmitter that is commonly stored in presynaptic vesicles. And we define the side effects and the expected results of reducing the natural ratio of serotonin in the human body.

Keywords: Serotonin, 5-hydroxytryptamine (5-HT), nervous system

Introduction

Serotonin:

The idea that depression is the result of abnormalities in brain chemicals, particularly serotonin (5-hydroxytryptamine or 5-HT), has been influential for decades, and provides an important justification for the use of antidepressants. A link between lowered serotonin and depression was first suggested in the 1960s [1], and widely publicised from the 1990s with the advent of the Selective Serotonin Reuptake Inhibitor (SSRI) antidepressants [2,3,4]. Although it has been questioned more recently [5, 6], the serotonin theory of depression remains influential, with principal English language textbooks still giving it qualified support [7, 8], leading researchers endorsing it [9,10,11], and much empirical research based on it [11,12,13,14]. Surveys suggest that 80% or more of the general public now believe it is established that depression is caused by a 'chemical imbalance' [15, 16]. Many general practitioners also subscribe to this view [17] and popular websites commonly cite the theory [18].

It is often assumed that the effects of antidepressants demonstrate that depression must be at least partially caused by a brain-based chemical abnormality, and that the apparent efficacy of SSRIs shows that serotonin is implicated. Other explanations for the effects of antidepressants have been put forward, however, including the idea that they work via an amplified placebo effect or through their ability to restrict or blunt emotions in general [19, 20]. Despite the fact that the serotonin theory of depression has been so influential, no comprehensive review has yet synthesized the relevant evidence. We conducted an 'umbrella' review of the principal areas of relevant research, following the model of a similar review examining prospective biomarkers of major depressive disorder [21]. We sought to establish whether the current evidence supports a role for serotonin in the a etiology of depression, and specifically whether depression is associated with indications of lowered serotonin concentrations or activity

Chemistry of serotonin

Serotonin or 5-hydroxytryptamine (5-HT) is a chemical messenger which acts on cells throughout the human body, beginning in early development and throughout adulthood[22]. 5-HT acts as both a neurotransmitter and a hormone that regulates blood vessel constriction and intestinal motility [22]. In the central nervous system, 5-HT is released from presynaptic neurons where it diffuses across the synaptic space and binds to 5-HT receptors, promoting downstream signaling and activating postsynaptic neurons[23,24]. Thus, 5-HT is a master regulator of circuits, physiology and behavioral functions including the sleep/wake cycle, sexual interest, locomotion, thermoregulation, hunger, mood, and pain[22]. 5-HT is cleared from synapses and taken into presynaptic neurons by the serotonin transporter (SERT), thus terminating serotonergic signaling[23,24,25]. SERT resides in the plasma membrane of neurons and belongs to a family of neurotransmitter sodium symporters (NSSs) which also includes the dopamine (DAT) and norepinephrine transporters (NET)[23,24, 25]. NSSs are

ISSN NO: 2771-8840
Date of Publication: 28-04-2023

twelve trans membrane spanning secondary active transporters which utilize sodium and chloride gradients to energize the transport of neurotransmitter across the membrane [25,26,27].

How to increase serotonin

For the last 4 decades, the question of how to manipulate the serotonergic system with drugs has been an important area of research in biological psychiatry, and this research has led to advances in the treatment of depression. Research on the association between various polymorphisms and depression supports the idea that serotonin plays a role, not only in the treatment of depression but also in susceptibility to depression and suicide. The research focus here has been on polymorphisms of the serotonin transporter, but other serotonin-related genes may also be involved.[28,29,30,31,32]. In the future, genetic research will make it possible to predict with increasing accuracy who is susceptible to depression. Much less attention has been given to how this information will be used for the benefit of individuals with a serotonin-related susceptibility to depression, and little evidence exists concerning strategies to prevent depression in those with such a susceptibility. Various studies have looked at early intervention in those with prodromal symptoms as well as at population strategies for preventing depression [33,34,35,36,37,38]. Obviously, prevention is preferable to early intervention; moreover, although population strategies are important, they are ideally supplemented with preventive interventions that can be used over long periods of time in targeted individuals who do not yet exhibit even nonclinical symptoms. Clearly, pharmacologic approaches are not appropriate, and given the evidence for serotonin's role in the etiology and treatment of depression, nonpharmacologic methods of increasing serotonin are potential candidates to test for their ability to prevent depression.

Another reason for pursuing nonpharmacologic methods of increasing serotonin arises from the increasing recognition that happiness and well-being are important, both as factors protecting against mental and physical disorders and in their own right [39,40,41].

Normal range

Doctors measure serotonin levels in the blood with a simple blood test. Typical serotonin blood levels range between 101to 283 Nano grams per milliliter.

Serotonin levels in the brain cannot be measured. There is no evidence that the level of serotonin in your blood reflects the level of serotonin in your brain.

As a result, researchers are not exactly sure what the right levels are and how these levels might vary for different people.

Function

Serotonin is a direct-acting neurotransmitter that is commonly stored in presynaptic vesicles. Upon activation of the nerve by adjacent nerve impulses, serotonin is released into the synaptic cleft, where it can bind to postsynaptic receptors[42]. These postsynaptic serotonin receptors, also known as 5-hydroxytryptamine receptors, either act as G-couple protein receptors or ligand-gated ion channels. This activation ultimately allows activation of a second intracellular messenger cascade producing either an excitatory or inhibitory response[43] .

An estimated 90% of the serotonin in the human body is stored in enterochromaffin cells located in the gastrointestinal tract. Upon luminal and basolateral secretion, the compound is absorbed by circulating platelets. Once activated, serotonin functions to mobilize intestinal contraction and direction via the stimulation of my enteric neurons[43,44]. Although only 10% of serotonin is produced by neurons located in the central nervous system, it is for its function in the brain for which it is better known. The various functions of serotonin in the central nervous system include sleep, hunger, mood, memory, and learning management.

When excessive serotonin is released from the enterochromaffin cell, it frequently is introduced to the bloodstream, where it interacts with blood platelets. The platelets absorb the serotonin and store it until clot forms. However, once a clot forms, the serotonin is re-released in the blood, where it can regulate hemostasis and blood clotting[45]. At elevated levels, serotonin functions by contracting vascular smooth muscle cells leading to vasoconstriction. However, at lower levels, serotonin facilitates endothelial class to release nitric oxide leading to vasodilation[45].

Side effect

They include: nausea and vomiting, restlessness and agitation, indigestion, diarrhea or constipation, weight or appetite loss, increased sweating, dizziness, blurred vision, sleepiness or insomnia, feeling shaky, dry mouth, headache, low sex drive, erectile dysfunction, suicidal thoughts.

ISSN NO: 2771-8840
Date of Publication: 28-04-2023

Serotonin deficiency results

Depression, Anxiety, Panic Attacks, Insomnia, Irritable bowel, PMS/Hormone dysfunction, Fibromyalgia, Obesity, Eating disorders, Obsessions and Compulsions, Muscle pain, Chronic Pain, Alcohol abuse, Migraine Headaches.

References

1. Coppen, A. The biochemistry of affective disorders. Br J Psychiatry. 1967;113:1237–64.
2. American Psychiatric Association. What Is Psychiatry? 2021. https://www. psychiatry.org/patients-families/what-is-psychiatry-menu.
3. GlaxoSmithKline. Paxil XR. 2009. www.Paxilcr.com (site no longer available). Last accessed 27th Jan 2009.
4. Eli Lilly. Prozac - How it works. 2006. www.prozac.com/how_prozac/ how _it _works .jsp ? req NavId=2.2. (site no longer available). Last accessed 10th Feb 2006.
5. Healy, D. Serotonin and depression. BMJ: Br Med J. 2015;350:h1771.
6. Pies, R. Psychiatry's New Brain-Mind and the Legend of the "Chemical Imbalance." 2011. https://www.psychiatrictimes.com/view/psychiatrys-new-brain-mind-andlegend-chemical-imbalance. Accessed March 2, 2021.
7. Geddes, J.R., Andreasen, N.C., Goodwin, G.M. New Oxford Textbook of Psychiatry. Oxford, UK: Oxford University Press; 2020.
8. Sadock, B.J., Sadock, V.A., Ruiz, P. Kaplan & Sadock's Comprehensive Textbook of Psychiatry. 10th Editi. Lippincott Williams & Wilkins (LWW); 2017.
9. Cowen, P.J., Browning, M. What has serotonin to do with depression? World Psychiatry. 2015;14:158–60.
10. Harmer, C.J., Duman, R.S., Cowen, P.J. How do antidepressants work? New perspectives for refining future treatment approaches. Lancet Psychiatry. 2017;4:409–18.
11. Yohn, C.N., Gergues, M.M., Samuels, B.A. The role of 5-HT receptors in depression. Mol Brain. 2017;10:28.
12. Hahn, A., Haeusler, D., Kraus, C., Höflich, A.S., Kranz, G.S., Baldinger, P., et al. Attenuated serotonin transporter association between dorsal raphe and ventral striatum in major depression. Hum Brain Mapp. 2014;35:3857–66.
13. Amid far M, Colic L, Kim MWAY-K. Biomarkers of major depression related to serotonin receptors. Curr Psychiatry Rev. 2018;14:239–44.
14. Albert, P.R., Benkelfat, C., Descarries, L. The neurobiology of depression—revisiting the serotonin hypothesis. I. Cellular and molecular mechanisms. Philos Trans R Soc Lond B Biol Sci. 2012;367:2378–81.
15. Pilkington, P.D., Reavley, N.J., Jorm, A.F. The Australian public's beliefs about the causes of depression: associated factors and changes over 16 years. J Affect Disord. 2013;150:356–62.
16. Pescosolido, B.A., Martin, J.K., Long, J.S., Medina, T.R., Phelan, J.C., Link. B.G. A disease like any other? A decade of change in public reactions to schizophrenia, depression, and alcohol dependence. Am J Psychiatry. 2010;167:1321–30.
17. Read, J., Renton, J., Harrop, C., Geekie, J., Dowrick, C. A survey of UK general practitioners about depression, antidepressants and withdrawal: implementing the 2019 Public Health England report. Therapeutic Advances in. Psychopharmacology. 2020;10:204512532095012.
18. Demasi, M., Gøtzsche, P.C. Presentation of benefits and harms of antidepressants on websites: A cross-sectional study. Int J Risk Saf Med. 2020;31:53–65.
19. Jakobsen, J.C., Gluud, C., Kirsch, I. Should antidepressants be used for major depressive disorder? BMJ Evidence-Based. Medicine. 2020;25:130–130.
20. Moncrieff, J., Cohen, D. Do antidepressants cure or create abnormal brain states? PLoS Med. 2006;3:e240.
21. Kennis, M., Gerritsen, L., van Dalen, M., Williams, A., Cuijpers, P., Bockting, C. Prospective biomarkers of major depressive disorder: a systematic review and met analysis. Mol Psychiatry. 2020;25:321–38.

ISSN NO: 2771-8840
Date of Publication: 28-04-2023

22. Berger, M., Gray, J.A., Roth, B.L. The expanded biology of serotonin Annual Review of Medicine.2009; 60:355–366.
23. Gether, U., Andersen, P.H., Larsson, O. M., Schousboe, A. Neurotransmitter transporters: molecular function of important drug targets Trends in Pharmacological Sciences.2006; 27:375–383.
24. Kristensen, A.S., Andersen, J.J., ørgensen, T.N., Sørensen, L., Eriksen, J.. Loland, C.J., Strømgaard, K., Gether, U. SLC6 neurotransmitter transporters: structure, function, and regulation Pharmacological Reviews 2011;63:585–640.
25. Rudnick, G., Krämer, R., Blakely, R. D., Murphy, D.L., Verrey, F. (2014) The SLC6 transporters: perspectives on structure, functions, regulation, and models for transporter dysfunction P flügers Archiv - European Journal of Physiology.2041;466:25–42.
26. Navratna, V., Gouaux, E. Insights into the mechanism and pharmacology of neurotransmitter sodium symporters Current Opinion in Structural Biology.2019;54:161–170.
27. Yamashita, A., Singh, S. K., Kawate, T., Jin, Y., Gouaux, E. (2005) Crystal structure of a bacterial homologue of na+/Cl--dependent neurotransmitter transporters Nature.2005;437:215–223.
28. Li, D., He, L. Meta-analysis supports association between serotonin transporter (5-HTT) and suicidal behavior. Mol Psychiatry. 2006;12:47-54.
29. Neumeister, A., Young, T., Stastny, J. Implications of genetic research on the role of the serotonin in depression: emphasis on the serotonin type 1A receptor and the serotonin transporter. Psychopharmacology (Berl) 2004;174:512-24.
30. Anguelova, M., Benkelfat, C., Turecki, G. A systematic review of association studies investigating genes coding for serotonin receptors and the serotonin transporter: II. Suicidal behavior. Mol Psychiatry 2003;8:646-53.
31. Anguelova, M., Benkelfat C, Turecki G. A systematic review of association studies investigating genes coding for serotonin receptors and the serotonin transporter: I. Affective disorders. Mol Psychiatry 2003;8:574-91.
32. Gutknecht, L., Jacob, C., Strobel, A., et al. Tryptophan hydroxylase-2 gene variation influences personality traits and disorders related to emotional dys regulation. Int J Neuropsychopharmacol 2007;10:309-20.
33. Schoevers, R.A., Smit, F., Deeg, D.J.H., et al. Prevention of late-life depression in primary care: do we know where to begin? Am J Psychiatry 2006;163:1611-21.
34. van 't Veer-Tazelaar, N., van Marwijk, H., van Oppen, P, et al. Prevention of anxiety and depression in the age group of 75 years and over: a randomized controlled trial testing the feasibility and effectiveness of a generic stepped care program me among elderly community residents at high risk of developing anxiety and depression versus usual care. BMC Public Health 2006;6:186.
35. Barrett, P.M., Farrell, L.J., Ollendick, T.H., et al. Long-term outcomes of an Australian universal prevention trial of anxiety and depression symptoms in children and youth: an evaluation of the friends program. J Clin Child Adolesc Psychol. 2006;35:403-11.
36. Schotte, C.K.W., Van Den Bossche, B., De Doncker, D., et al. A bio psychosocial model as a guide for psych education and treatment of depression. Depress Anxiety. 2006;23:312-24.
37. Whyte, E.M., Rovner, B. Depression in late-life: shifting the paradigm from treatment to prevention. Int J Geriatr Psychiatry. 2006;21:746-51.
38. Jorm, A.F., Griffiths, K.M. Population promotion of informal self-help strategies for early intervention against depression and anxiety. Psychol Med. 2006;36:3-6.
39. Delamothe, T. Happiness. BMJ 2005;331:1489-90. [PMC free article]
40. Wellbeing: an idea whose time has come. Lancet 2005;366:1412.
41. A sensible 10-year plan for mental health. Lancet 2006;367:86.
42. David, D.J., Gardier, A.M. The pharmacological basis of the serotonin system: Application to antidepressant response]. Encephale. 2016 Jun;42(3):255-63.
43. Smith, C., Smith, M,, Cunningham, R., Davis, S. Recent Advances in Antiemetics: New Formulations of 5-HT3 Receptor Antagonists in Adults. Cancer Nurs. 2020 Jul/Aug;43(4):E217-E228.
44. Kitson, S. L. 5-hydroxytryptamine (5-HT) receptor ligands. Curr Pharm Des. 2007;13(25):2621-37.

ISSN NO: 2771-8840
Date of Publication: 28-04-2023

45. Ivetic, N., Arnold, D.M., Smith, J.W., Huynh, A., Kelton, J.G., Nazy, I. A platelet viability assay (PVA) for the diagnosis of heparin-induced thrombocytopenia. Platelets. 2019;30(8):1017-1021.