Journal of Fundamentals of Mental Health

Mashhad University of Medical Sciences

Psychiatry and Behavioral Sciences Research Center

Letter to Editor **Open Access**

Obsessive-compulsive disorder and migraine: The "serotonin" connection

Adit Deshmukh

M.B.B.S; M.D. (Pharmacology), Hyderabad, India.

Abstract

Obsessive-Compulsive Disorder (OCD) is characterized by uncontrollable, intrusive and recurring thoughts (obsessions), resulting in repetitive behaviours (compulsions). Migraine is a debilitating neurovascular disorder characterized by recurrent throbbing one-sided headache. Several investigations suggest that both OCD and migraine are associated with serotonergic dysfunction.

OCD: The Cortico-Striatal-Thalamic-Cortical loop (CSTC) is considered the most important brain circuit involved in the pathophysiology of OCD, wherein serotonin is the principal neurotransmitter involved. Serotonergic medications act on specific circuits of CSTC leading to increased synaptic serotonin levels, which in turn help in amelioration of various symptoms of OCD.

Migraine: The serotonergic system present in the brainstem raphe nucleus has been most commonly attributed in migraine pathophysiology. Reduced brain 5-HT synthesis and, thereby, reduced 5-HT neurotransmission in migraineurs can dilate cranial blood vessels and initiate migraine. Triptans act as 5-HT1B/1D receptor agonists and mimic the role of serotonin in binding to its receptors in trigeminal nerve endings and blood vessels, leading to cranial vasoconstriction as well as decrease in the release of peptides like Calcitonin Gene-Related Peptide (CGRP) and substance P, which ultimately stops the headache.

There is a possible association between migraine and OCD. More research is warranted in this area to confirm this association. Considering the common role of serotonin in both these pathologies, there is a room for research on novel pharmacotherapy which can simultaneously act on the serotonergic pathways implicated in the pathology of both the disorders.

Keywords: Migraine, Obsessive-compulsive disorder, Serotonin

Please cite this paper as:

Deshmukh A. Obsessive-compulsive disorder and migraine: The "serotonin" connection. Journal of Fundamentals of Mental Health 2025 Nov-Dec; 27(6): 417-420. DOI: 10.22038/JFMH.2025.86406.3221

Introduction

Obsessive-Compulsive Disorder (OCD) is a disorder characterised by uncontrollable, intrusive and recurring thoughts (obsessions), resulting in repetitive behaviours (compulsions). People with OCD have debilitating and time-consuming symptoms that can cause significant disability and distress affecting the quality of life. It has a lifetime prevalence of 2−3%. (1,2). Migraine is a neurovascular disorder in which the patient has recurrent throbbing headache, which is often one-sided, occurs with aura or without aura, and is often associated with nausea and disturbed vision. Migraine is a disabling condition that may affect quality of life and professional performance as well (3,4).

Several investigations suggest that OCD may be associated with serotonergic dysfunction (5). Researchers have also suggested that serotonin

***Corresponding Author:**
Hyderabad, India.
deet.deshmukh@gmail.com
Received: Mar. 01, 2025
Accepted: Aug. 25, 2025

plays an important role in the pathophysiology of migraine (6,7). Since the pathogenesis of both the disorders involves the same neurotransmitter, it is intriguing to raise a question: Can the presence of one disorder lead to increased chances of development of other disorder in the same person? To answer this question, we need to dig deeper into the pathophysiologies of both the disorders.

OCD: OCD has a multifactorial basis, including genetic, environmental and biological, of which latter involves the role of neurotransmitters like serotonin. Genetic mutation can lead to defective regulation of SERT (Serotonin Transporter protein which acts as a transporter of serotonin from synaptic cleft back to the pre-synaptic neuron), which may contribute in the causation of OCD. The Cortico-Striatal-Thalamic-Cortical loop (CSTC) is considered the critical brain circuit involved in the pathophysiology of OCD. Among the different CSTC circuits, the ventral motivational/reward CSTC circuit is one of the important circuits involved in OCD, which consists of the neural pathway from OrbitoFrontal Ccortex (OFC) to Nucleus Accumbens (NA) to the thalamus (Figure 1) (8). Another brain circuit involved in OCD is the frontolimbic circuit, which extends from ventromedial prefrontal cortex to amygdala to thalamus (Figure 2) (8).

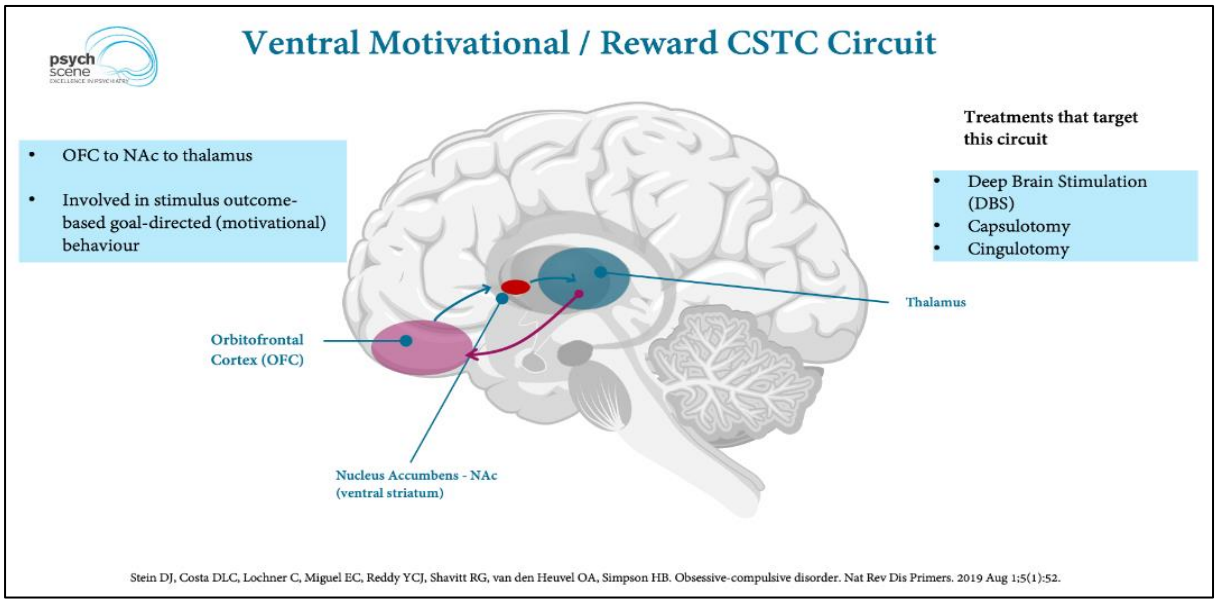

Figure 1. The ventral motivational/reward CSTC circuit

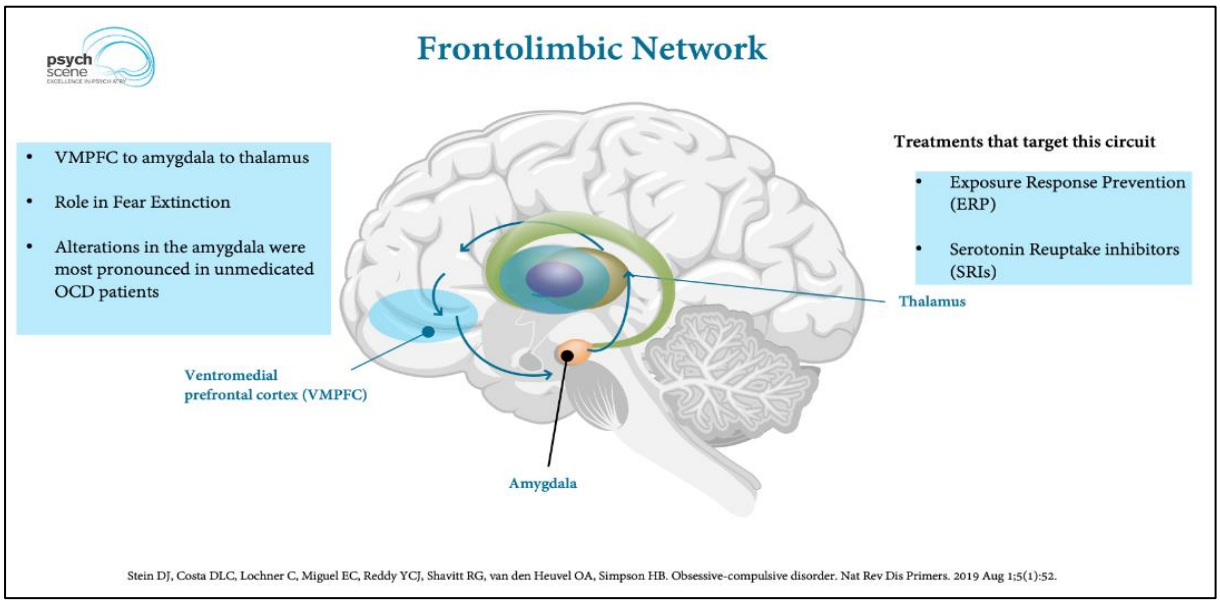

Figure 2. The frontolimbic circuit

Serotonin plays a crucial role in the neurotransmission via both these circuits and alterations within these circuits are linked to the symptoms observed during early phases of OCD. Serotonergic depletion in the OFC (ventral reward CSTC circuit) leads to increase in habitual responding at the expense of goal-directed behaviour. Therefore, serotonergic medications can help facilitate a shift from habitual to goal-directed behaviours by increasing serotonin (5-HT) activity in OFC (8). Similarly, serotonergic innervation to amygdala (frontolimbic circuit) is influenced by the drug class Selective Serotonin Reuptake Inhibitors (SSRIs), so that the increased serotonin levels by these drugs activate 5-HT2A receptors present on GABAergic neurons enhancing GABA release, which in turn inhibits NA neurons, which leads to positive change in the appraisal of emotions, fear extinction and abatement of compulsive behaviour (8).

Migraine: Amongst the many neurotransmitters in the brain, the serotonergic system from the brainstem raphe nucleus has been most significantly attributed in migraine pathophysiology. There is evidence that serotonin vasoconstricts the nerve endings and blood vessels and in this way affects nociceptive pain. Therefore, reduced brain 5-HT synthesis and, thereby, reduced 5-HT neurotransmission in migraineurs can dilate blood vessels and initiate migraine (9). The vasodilation is accompanied by an increase in the concentration of Calcitonin Gene-Related Peptide (CGRP) and substance P that lower the pain threshold, which ultimately leads to the neuro-vascular headache of migraine (6).

Out of the 7 serotonin receptor types, 5-HT1 is involved predominantly in migraine. The antimigraine drug class, triptans, act as 5-HT1B/1D receptor agonists and mimic the role of serotonin in binding to its receptors in trigeminal nerve endings and blood vessels. This leads to cranial vasoconstriction as well as decrease in the release of peptides like CGRP and substance P, which ultimately stops the headache (10,11).

Future perspectives: Researchers have found that migraine is associated with some of the psychiatric disorders wherein serotonin dysfunction is predominantly implicated, such as OCD, major depressive disorder, generalised anxiety disorder, phobia, etc. (6). Some of the research articles have mentioned about the increased chances of development of OCD in patients suffering from migraine. However, more research is warranted in this area to confirm this association (6,12).

There is a large scope for research in the area of pharmacotherapy as well. Considering the common role of serotonin in both these pathologies, there is a room for research on novel pharmacotherapy which can simultaneously act on the serotonergic pathways implicated in the pathology of both the disorders. The drugs currently used for the treatment of OCD as well as migraine have their own set of limitations and adverse effects. Therefore, the novel drug class, which is able to target the pathological pathways of both the disorders simultaneously, will certainly benefit the patients who are suffering from both these disorders and also reduce the risk of development of adverse effects arising from the consumption of two separate classes of drugs for treating these disorders.

Conflict of Interest

The author reports there are no competing interests to declare.

Funding

No financial support was used for this study.

References

1. Carmi L, Brakoulias V, Arush OB, Cohen H, Zohar J. A prospective clinical cohort-based study of the prevalence of OCD, obsessive compulsive and related disorders, and tics in families of patients with OCD. BMC Psychiatry 2022; 22(1): 190.
2. Singh A, Anjankar V, Sapkale B. Obsessive-Compulsive Disorder (OCD): A comprehensive review of diagnosis, comorbidities, and treatment approaches. Cureus 2023; 15(11): e48960.
3. Rustom A, Audi F, Al Samsam H, Nour R, Mursi AM, Mahmoud I. Migraine awareness, prevalence, triggers, and impact on university students: a cross-sectional study. Egyptian journal of neurology, psychiatry and neurosurgery 2022; 58(1): 1-7.
4. Khan J, Al Asoom LI, Al Sunni A, Rafique N, Latif R, Al Saif S, et al. Genetics, pathophysiology, diagnosis, treatment, management, and prevention of migraine. Biomed Pharmacother 2021; 139: 111557.
5. Jalal B, Chamberlain SR, Sahakian BJ. Obsessive-compulsive disorder: Etiology, neuropathology, and cognitive dysfunction. Brain Behav 2023; 13(6): e3000.

6. Dinn WM, Dinn AA, Robbins NC, Harris CL. Migrane headache and obsessive-compulsive symptoms in a student sample. Bull Clin Psychopharmacol 2005; 15(4): 174-81.
7. Frimpong-Manson K, Ortiz YT, McMahon LR, Wilkerson JL. Advances in understanding migraine pathophysiology: A bench to bedside review of research insights and therapeutics. Front Mol Neurosci 2024; 17: 1355281.
8. Rege S. Obsessive compulsive disorder- neurobiology, diagnosis and treatment. [cited 2018]. Available from: https://psychscenehub.com/psychinsights/obsessive-compulsive-disorder-neurobiology-treatment/
9. Hamel E, Currents H. Serotonin and migraine: Biology and clinical implications. Cephalalgia 2007; 27(11): 1293-300.
10. Aggarwal M, Puri V, Puri S. Serotonin and CGRP in migraine. Ann Neurosci 2012; 19(2): 88-94.
11. Viudez-Martínez A, Torregrosa AB, Navarrete F, García-Gutiérrez MS. Understanding the biological relationship between migraine and depression. Biomolecules 2024; 14(2): 163.
12. Viticchi G, Falsetti L, Salvemini S, Bartolini M, Paolucci S, Buratti L, et al. Efficacy of onabotulinum toxin A on obsessive-compulsive traits in a population of chronic migraine patients. Brain Sci 2022; 12(11): 1563.