Cariprazine-induced obsessive-compulsive symptoms in a patient with bipolar II disorder: A case report

SUWANAN PORNLERTKOCHAKORN and KRITTISAK ANUROJ

Department of Psychiatry, Faculty of Medicine, Srinakharinwirot University, Nakhon Nayok 26120, Thailand

Received March 7, 2026; Accepted May 18, 2026

DOI: 10.3892/br.2026.2168

Abstract. Drug-induced obsessive-compulsive (OC) symptoms have been described for clozapine and several second-generation antipsychotics, whereas reports involving cariprazine remain scarce. The present report describes the case of a 28-year-old Thai female patient with bipolar II disorder who had premorbid, subclinical counting compulsion, which had remained stable since its onset in adolescence. After 3 days of cariprazine treatment during a regimen switch for bipolar disorder, the pre-existing counting compulsion worsened and additional patterns of OC symptoms emerged. At seven days after discontinuation of cariprazine, the newly emerged symptoms were fully resolved, while the counting compulsion returned to its baseline subclinical severity. The present report highlights the need for clinical vigilance regarding OC symptom exacerbation with cariprazine treatment as a part of comprehensive follow-up of the mental health and wellbeing of psychiatric patients. Potential mechanistic considerations involving serotonergic and dopaminergic systems are discussed. The literature review of drug-induced OC symptomatology in the present study also identified limited documentation of premorbid OC symptomatology and age-at-onset phenotypes. Future reports incorporating detailed phenotypic characterization may improve the identification of patients at risk of symptom exacerbation.

Correspondence to: Dr Krittisak Anuroj, Department of Psychiatry, Faculty of Medicine, Srinakharinwirot University, 62, Moo 7, Ongkharak, Nakhon Nayok 26120, Thailand
E-mail: thymelancille@gmail.com

Abbreviations: OC, obsessive-compulsive; OCD, obsessive-compulsive disorder; 5-HT_{1A}, serotonin 1A; 5-HT_{2A}, serotonin 2A; 5-HT_{2B}, serotonin 2B; SSRI, selective serotonin reuptake inhibitor

Key words: cariprazine, atypical antipsychotics, drug-induced, medication-induced, OC symptoms, OCD, bipolar disorder, adverse drug reaction, adverse effect, psychopharmacology

Introduction

Obsessive-compulsive (OC) symptoms comprise obsessions (recurrent, intrusive, unwanted thoughts, images, or urges causing anxiety or distress) and compulsions, which are repetitive behaviors or mental acts performed in response to these obsessions to reduce distress or prevent feared outcomes (1,2). These symptoms are understood to be distributed along a right-skewed continuum, with subclinical manifestations common in the general population, and individuals at the extreme end of the spectrum meeting criteria for obsessive compulsive disorder (OCD) (3-5). The pathophysiology of OC symptoms involves the cortico-striato-thalamo-cortical loop and modulatory inputs from limbic regions (6,7). The integrity and functioning of the circuits, which in turn shape susceptibility and symptom expression, could be influenced by multiple interacting factors, including genetic, perinatal and neurodevelopmental liability, as well as subsequent interactions with biopsychosocial circumstances (8-12). Pharmacological agents capable of disrupting the delicate neurotransmitter balance of the systems may, in susceptible individuals, precipitate new-onset OC symptoms or exacerbate pre-existent ones (13,14). Well-documented clinical examples include dopaminergic agonists used in Parkinson's disease, such as pramipexole and ropinirole, which have been associated with dose-dependent emergence of impulsive-compulsive behaviors, which phenomenologically overlap with the OC spectrum (15-17). Another agent widely recognized to precipitate or aggravate classical OC symptoms is clozapine, the first second-generation antipsychotic, which exerts complex effects on dopaminergic and serotonergic neurotransmissions (18). Among other second-generation antipsychotics, a small number of case reports have described the precipitation or aggravation of OC symptoms with olanzapine, risperidone and quetiapine (19-22). Notably, conflicting evidence also exists regarding potential therapeutic effects of some of these agents in OCD (23-25).

Cariprazine is an atypical antipsychotic approved for the treatment of schizophrenia and bipolar disorder, and is increasingly utilized in bipolar depression and mixed presentations (26-30). The agent acts as a partial agonist at the serotonin 1A (5-HT_{1A}) receptor and at dopamine D_2 and D_3 receptors, with a high affinity for the dopamine D_3 receptor (28,31). Cariprazine also acts as an antagonist at serotonin 2A (5-HT_{2A}) and serotonin 2B (5-HT_{2B}) receptors (27,28). Cariprazine is

generally well tolerated, with commonly reported adverse effects including akathisia, insomnia, and extrapyramidal symptoms (32,33). However, as with other second-generation antipsychotics, unexpected neuropsychiatric adverse effects have been observed, although specific reports on worsening or emergence of OC symptoms remain limited (34-37). An analysis of post-marketing data has also suggested that its adverse effect profile may be more diverse than that observed in clinical trials (38). The present report describes a patient with bipolar II disorder who developed marked exacerbation of OC symptoms shortly after a medication switch to cariprazine.

Case report

A 28-year-old female patient with bipolar II disorder presented with marked emergence of OC symptoms shortly after cariprazine was added to her treatment regimen. All clinical encounters described in this case report were under the care of the same treating psychiatrist and took place in 2025 at HRH Princess Maha Chakri Sirindhorn Medical Center, a university-affiliated hospital in Nakhon Nayok Province, Thailand. A summary of the clinical timeline is provided in Table I.

The patient reported premorbid OC symptoms characterized by urges to count during goal-directed activities, such as counting steps while walking or counting numbers while preparing food, accompanied by a compulsion to restart the activity if the counting was not performed correctly. These symptoms were reportedly infrequent, occurring approximately once per week since the age of 14 years, remained stable in frequency and intensity over time, and did not cause significant distress or functional impairment. Consequently, the patient never sought treatment. The patient reported no childhood history of attention-deficit/hyperactivity disorder or tic disorder, and displayed no features suggestive of intellectual disability or autism spectrum disorder.

Eight months prior to the index visit, at the age of 27 years, the patient first sought psychiatric care at HRH Princess Maha Chakri Sirindhorn Medical Center (Nakhon Nayok, Thailand) for depressed mood, and was diagnosed with major depressive disorder. The symptoms responded poorly to fluoxetine (no partial response at 20 mg/day after 1.5 months) and sertraline (minimal response at doses of 50-100 mg/day after 3 months). Aripiprazole was later added as augmentative agent to sertraline at a dose of 2.5 mg/day for 1 month. A hypomanic episode subsequently emerged, prompting diagnosis revision to bipolar II disorder, discontinuation of sertraline, up-titration of aripiprazole to 5 mg/day, and initiation of clonazepam at 0.5 mg/day to control aripiprazole-related akathisia. The regimen adequately controlled the hypomanic symptoms but not depressive symptoms. Augmentation with lamotrigine was briefly attempted at doses of 25-50 mg/day over a 1-month period; however, a generalized allergic skin reaction occurring a week after dose titration to 50 mg/day led to its discontinuation. As aripiprazole-induced akathisia, first observed 3 months earlier at doses between 2.5-5 mg/day and required adjunctive clonazepam for symptom control, limited further dose titration, a switch in antipsychotic treatment was considered. The patient declined quetiapine because of metabolic concerns, and cariprazine was selected. Notably, throughout the 7 months of treatment prior to cariprazine initiation, the counting compulsion of the patient remained at baseline.

At 14 days before the index visit, aripiprazole dose was reduced to 2.5 mg/day for four days before discontinuation. On the same day that the dose of aripiprazole was reduced, cariprazine treatment was initiated at 1.5 mg/day. After 3 days on cariprazine, two new forms of OC symptoms emerged. The first consisted of intrusive thoughts involving desecration of, or uttering profanities toward, religious objects. The second involved recurrent intrusive, fear-provoking mental images of catastrophic accidents affecting the family of the patient, in the absence of any relevant traumatic or separation-threatening events. Concurrently, the preexistent counting compulsion worsened in frequency and intensity, along with a development of a new undoing compulsion (engaging in self-pinching when the counting was not properly conducted). In contrast to its previously benign nature, the exacerbated counting compulsion started to become distressing and functionally impairing. However, insights into the irrationality of these OC phenomena were preserved. Focused clinical assessment did not identify any recent psychosocial stressors. There were no concurrent symptoms of infection, other clinical features suggestive of an immune-mediated exacerbation of OC symptoms, concurrent medical illnesses, or other new psychiatric symptoms. The patient was not concurrently on any other medications.

At the index visit, the patient reported these OC symptoms and additionally complained of weight gain. The treatment regimen was switched back to aripiprazole at a dose of 5 mg/day, and sertraline was reinitiated at 25 mg/day to manage the persistent depressive symptoms. Within 7 days after discontinuing cariprazine, the two newly emerged OC symptom clusters that had appeared 3 days after cariprazine initiation were completely resolved, while the counting compulsion returned to its baseline, subclinical severity. Rechallenge with cariprazine was not pursued due to the patient's refusal.

At subsequent follow-up visits up to 1.5 months later, the counting compulsion remained at baseline. Persistent akathisia was reported at the 2-week follow-up visit, while minor work-related stress was reported at the 1.5-month follow-up visit. Clonazepam was switched to propranolol (30 mg/day) to manage aripiprazole-associated akathisia, and sertraline was increased to 50 mg/day for depressive symptom control.

Discussion

The present report describes marked exacerbation of OC symptoms in a patient with bipolar II disorder undergoing a medication switch. No proximal psychosocial stressors were identified based on clinical assessment at the time of symptom onset, reducing the likelihood of acute stress-related symptom exacerbation, although unrecognized or unreported stressors cannot be entirely excluded as assessment could have been limited in routine clinical settings. Nevertheless, the temporal association with cariprazine, including symptom emergence 3 days after its initiation and resolution 7 days after its discontinuation, was suggestive of a medication-related phenomenon.

The patient had been on aripiprazole for 4 consecutive months, without any sign of OC symptom fluctuation. Therefore, direct aripiprazole-induced phenomena were considered relatively unlikely. However, symptom onset

Table I. Timeline of the patient's history and clinical course.

Timing	Symptoms/events	Management
14 years prior	Infrequent counting compulsion; non-distressing; stable; no impairment; no other neurodevelopmental conditions; did not seek treatment	N/A
8-5 months prior	Sought treatment for depressive symptoms; counting compulsion stable	Antidepressant trials: fluoxetine 20 mg/day for 1.5 months, then sertraline 50-100 mg/day for 3 months
4 months prior	Diagnosis revised to major depressive disorder with atypical features; counting compulsion stable	Sertraline maintained at 100 mg/day; aripiprazole started at 2.5 mg/day
3 months prior	Akathisia; hypomania; diagnosis revised to bipolar II disorder; counting compulsion stable	Sertraline discontinued; aripiprazole increased to 5 mg/day; clonazepam started at 0.5 mg/day for akathisia
2-1 months prior	Somnolence from clonazepam; persistent depression; counting compulsion stable	Aripiprazole maintained at 5 mg/day; clonazepam reduced to 0.25 mg/day; lamotrigine trial (25-50 mg/day; discontinued due to rash)
14 days prior	Worsened depression; counting compulsion stable	Aripiprazole tapered to 2.5 mg/day for 4 days then discontinued; cariprazine started at 1.5 mg/day; clonazepam maintained 0.25 mg/day
11 days prior (3rd day on cariprazine)	Baseline counting compulsion worsened; new OC symptoms emerged (religious blasphemous thoughts and catastrophic images of harm occurring to family members)	N/A
Index visit (14th day on cariprazine)	Persistent OC symptoms; distressing but insight preserved; mood stable; complained of weight gain; refused medication rechallenge	Cariprazine discontinued; aripiprazole restarted at 5 mg/day; sertraline restarted at 25 mg/day; clonazepam maintained at 0.25 mg/day
7 days post-cariprazine discontinuation	Counting compulsion returned to baseline; new OC symptoms resolved	N/A
2 weeks post-cariprazine discontinuation	Counting compulsion stable at baseline; akathisia	Aripiprazole maintained at 5 mg/day; sertraline maintained at 25 mg/day; clonazepam discontinued; propranolol started at 30 mg/day
1.5 months post-cariprazine discontinuation	Counting compulsion stable at baseline; reported work stress and mood changes	Aripiprazole maintained at 5 mg/day; sertraline increased to 50 mg/day; propranolol maintained at 30 mg/day

N/A, not applicable; OC, obsessive-compulsive.

occurred on the third day after the dose was reduced from 5 to 2.5 mg/day. While a classical withdrawal effect appears less consistent given aripiprazole's long elimination half-life and the low tapering dose (39), a transient change in net dopaminergic signaling could have occurred as cariprazine and aripiprazole possessed different dopaminergic receptor affinities (27,40). The overlapping exposure therefore represents a limitation in attributing causality in the present case.

The patient was also concurrently taking clonazepam (0.25 mg/day). The onset of OC symptoms did not coincide with either clonazepam initiation (3 months prior) or dose reduction (2 months prior), making a direct temporal association less likely. However, as relatively prolonged benzodiazepine use can lead to tolerance or inter-dose withdrawal that may theoretically influence anxiety symptom fluctuations (41,42), clonazepam's contributory role cannot be definitively excluded.

Sertraline was initiated at the time of cariprazine discontinuation at a dose of 25 mg/day. However, because complete remission of the OC symptoms occurred within 7 days, contributory therapeutic effect of sertraline was considered unlikely given both the low dose and the timeframe preceding sertraline's typical onset of action in OCD (43,44).

Given the evidence that premorbid or subclinical OC symptoms confer increased vulnerability to the later development of clinically significant OCD (45-47), cariprazine exposure in the current case may have acted as a precipitating factor that shifted the patient's preexisting OC-related pathology from a subclinical to a clinically manifestable level.

The present study adds to the limited literature regarding OC symptomatology attributed to cariprazine. One previous report has described a 65-year-old female patient with bipolar disorder who developed repetitive door checking, excessive cloth washing, fear of physical illness, and chanting ritual shortly after the initiation of cariprazine monotherapy at 1.5 mg/day. The patient's symptoms gradually improved during a 6-week taper, and complete remission was observed ~2 months after cariprazine discontinuation (37). Another report described a 19-year-old male patient with schizophrenia who developed ritualistic and intrusive cleanliness-related compulsions while receiving cariprazine (3 mg/day) in combination with olanzapine (5 mg/day), although the emergence of OC symptoms coincided with the patient's exposure to extensive news coverage of the coronavirus disease 2019 pandemic. Nevertheless, as the cariprazine dose was reduced to 1.5 mg/day while olanzapine was maintained at the same dose, the OC symptoms improved within 1 week and continued to improve substantially over the subsequent 2 months (48). These observations were broadly consistent with the emergence of OC symptoms after cariprazine exposure in the present case.

Multiple mechanisms across glutamatergic, serotonergic, and dopaminergic systems could be relevant in explaining antipsychotic-induced OC symptoms. Within the serotonergic system, the 5-HT_{2A} receptor is of particular interest because it is highly expressed in the prefrontal cortex and modulates cortical glutamatergic output, while dysregulated glutamatergic signaling has been implicated in OCD (49-52). A positron emission tomography study in OCD has reported low postsynaptic 5-HT_{2A} receptor availability at the orbitofrontal and dorsolateral prefrontal cortices, which was associated with symptom severity (53). Increased receptor binding in the caudate nucleus in untreated patients, interpreted as a possible compensatory response to altered serotonergic tone, was also reported (54). Antagonism of 5-HT_{2A} receptors, shared by a number of antipsychotic agents, including cariprazine (40), may therefore contribute to disturbances in neurotransmitter systems implicated in OC symptoms. Notably, it has been remarked that the 5-HT_{2A} antagonistic potency of the antipsychotic agent tended to mirror the frequency of reported drug-induced OC symptoms (55).

Heterogeneity in the relationship between antipsychotic doses and the emergence of OC symptoms across different agents has been observed (13,18-22,36,55-59). Remarkably, clozapine was consistently reported to be capable of inducing OC symptoms at a wide dose range (36,18). Risperidone, in contrast, has been reported to trigger OC symptoms at moderate to high weight-adjusted doses (56,58,59), at levels associated with relatively greater D_2 receptor occupancy (60). These observations led to the hypothesis that the relative balance between 5-HT_{2A} and D_2 receptor antagonism may be another relevant factor contributing to the emergence of drug-related OC symptoms (57), although whether high degrees of D_2 antagonism contribute to the development of OC symptoms remains unclear (56,59,61,62). In the present case, cariprazine, a partial D_2 agonist, appeared to trigger OC symptoms at a low dose, at which strong net D_2 antagonism is less likely (27,40). Therefore, pathophysiological mechanisms involving marked D_2 receptor blockade are unlikely to be relevant to our patient.

Cariprazine also exhibits partial agonism at the 5-HT_{1A} receptor (27), a receptor more commonly implicated in mood and anxiety regulation than in OC symptom domains (63). In animal models, agonism at this receptor has been shown to facilitate repetitive and compulsive behaviors (64,65), whereas human studies on OCD have yielded inconsistent findings (66-68). Nonetheless, a pharmacovigilance analysis of antipsychotics found that higher 5-HT_{1A} receptor affinity was positively associated with increased reporting of OC symptoms, and that the 5-HT_{1A}/D_2 receptor affinity ratio may be relevant to this signal (69).

To the best of our knowledge, antagonism at the 5-HT_{2B} receptor, another serotonergic effect of cariprazine (27,40), has not been systematically implicated in the development of OC symptoms.

The partial agonism of cariprazine at the dopamine D_3 receptor may also be relevant. Preclinical and human studies have indicated that dopamine D_3 receptor activation modulates reward-related learning and reinforcement processes (70,71), which can influence the persistence of learned or conditioned behaviors. Although findings are limited and mixed, genetic studies have also reported associations between dopamine D_3 receptor variations and OCD (72-74). Despite being described separately and differing in underlying mechanisms, impulsive-compulsive behaviors observed in Parkinson's disease share some clinical features with obsessive-compulsive symptoms, such as repetitiveness, difficulty of controlling, and persistence despite apparent maladaptation and negative consequences (72-75). Such behaviors have been associated with antiparkinsonian agents possessing high dopamine D_3 receptor selectivity (such as pramipexole and ropinirole), and less frequently with levodopa; proposed mechanisms similarly involve dysregulated reward processing and decision-making (76-79).

Conversely, cariprazine has also been reported to be an effective augmenting agent in treatment-resistant OCD, predominantly in adolescent-onset patients, at a dose of 1.5 mg/day (80,81). Cariprazine has also been reported to be effective in a case of OCD comorbid with schizophrenia, as well as in another case of OCD comorbid with autism, as an augmentative agent at doses between 1.5 and 3 mg/day (82,83). Mirroring the conflicting reports regarding the OC-inducing potential and treatment efficacy observed in other antipsychotics (19-25), it could be hypothesized that cariprazine's combination of mechanisms of action may confer benefit in certain subgroups of OCD, given the heterogeneity of the biological underpinnings of OC symptoms (84,85). Nevertheless, direct comparative data on pathophysiological differences across various OC and OCD phenotypes remain limited (86).

OCD is recognized to have a bimodal age-at-onset, at which point the symptoms can emerge at subclinical levels (3). Although the precise age cutoffs remain inconsistent across studies (3,87,88), childhood-onset (or early-onset) OCD is more commonly linked with comorbidity such as tic disorders and neurodevelopmental disorders, whereas adult-onset (or late-onset) OCD more frequently co-occurs with mood and anxiety disorders (87,89-92). Structural and functional

neurological differences across these groups have been characterized (93-95). These two phenotypes also appear to respond differently to pharmacotherapy, with early-onset groups showing lower response rates to selective serotonin reuptake inhibitors (SSRIs), while responding more favorably to antipsychotics when comorbid tic disorder is present or when the disease is resistant to SSRIs (86,96-98). As their biological underpinnings and response profiles to serotonergic and dopaminergic agents differ, it can be inferred that the propensity for preexisting OC symptoms to be exacerbated by antipsychotics (especially ones that possess both serotonergic and dopaminergic mechanisms of action) may also vary by age-at-onset phenotypes. Numerous case reports and association studies of antipsychotic-associated OC symptoms have not systematically evaluated patient age at onset or the presence of premorbid symptoms (13,18-22,36,55-59). The observation that the same antipsychotic can both induce and alleviate OC symptoms at similar doses may be partly attributable to differences in age-at-onset OC phenotypes. This represents an important knowledge gap, and future case reports and observational studies would benefit from more detailed phenotypic characterization. Improved patient characteristic delineation may enhance the understanding of who may be at greater risk of OC symptom exacerbation or, alternatively, who may benefit from cariprazine treatment.

The present case should be considered as a probable case of cariprazine exacerbating preexisting adolescent-onset OC symptoms. The patient's age at onset (14 years) lies within the gray zone of commonly suggested age cutoffs (3,87,88), and the symptoms likely remained unevaluated because of their mild severity and sociocultural barriers related to emotion suppression, avoidant coping tendency, and mental health-related stigma (99-105). Clinicians should remain attentive to emerging reports of OC symptoms associated with cariprazine, particularly with regard to patient characteristics that may indicate vulnerability, to help inform treatment selection.

The present case report has several limitations. Symptom assessment was based on clinical interview and patient reports, without the use of standardized psychometric instruments such as the Yale-Brown Obsessive Compulsive Scale or structured interview (106), limiting objective quantification. Due to constraints inherent to real-world clinical practice, drug washout was not implemented. Rechallenge with cariprazine was not pursued due to patient refusal. Cross-titration was implemented in a relatively short period. Contributory effects of concurrently administered medications, including aripiprazole (either drug-related effects or withdrawal phenomena) and clonazepam, cannot be definitively excluded. All of these factors limited the ability to establish a confirmatory causal relationship, and the observed association between cariprazine and OC symptom exacerbation should be interpreted as suggestive rather than definitive. Alternative strategies, such as a slower cross-titration or more gradual exposure to cariprazine, were not explored in the present patient and may be considered in similar cases in the future.

The presence of premorbid, subclinical OC symptoms limited generalizability. The small possibility that the OC pathology worsened independent of pharmacological effects cannot be fully excluded.

The present report described the case of a 28-year-old female patient with premorbid, subclinical adolescent-onset OC symptoms, whose OC symptoms were exacerbated to the clinical level after cariprazine was introduced into the treatment regimen for bipolar II disorder. Mechanistic considerations involving serotonergic and dopaminergic systems have been discussed. Clinicians are advised to be cautious regarding the ability of cariprazine to induce OC symptoms in vulnerable cases. In particular, patients with pre-existing subclinical OC symptoms may benefit from close monitoring during the first week of treatment.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

The data supporting this case report are not publicly available due to Ethics Committee's restrictions but may be available from the corresponding author upon reasonable request and subject to Ethics Committee approval.

Authors' contributions

SP and KA conceptualized the study. SP contributed to data collection and review of electronic medical records. SP and KA confirm the authenticity of all the raw data. SP and KA wrote the original draft, and reviewed and edited the manuscript. All authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate

The case report was approved by the Human Research Ethics Committee of Srinakharinwirot University (approval no. SWUEC-693007; Srinakharinwirot University, Nakhon Nayok, Thailand). The patient was treated in accordance with the Declaration of Helsinki. Written informed consent was obtained from the patient for participation in this case report.

Patient consent for publication

Written informed consent was obtained from the patient for publication of this case report and accompanying anonymized clinical information. The patient reviewed and approved the manuscript draft prior to submission.

Competing interests

The authors declare that they have no competing interests.

Use of artificial intelligence tools

During the preparation of this work, artificial intelligence tools (ChatGPT-4o) were used to improve the readability and

language of the manuscript, and subsequently, the authors revised and edited the content produced by the artificial intelligence tools as necessary, taking full responsibility for the ultimate content of the present manuscript.

References

1. Ayd FJ (ed): Lexicon of Psychiatry, Neurology, and the Neurosciences. Lippincott Williams & Wilkins, Philadelphia, New York, NY, 2000.
2. American Psychiatric Association: Diagnostic and statistical manual of mental disorders: DSM-5-TR. Fifth edition, text revision. American Psychiatric Association Publishing, Washington, DC, 2022.
3. Pinto A, Mancebo MC, Eisen JL, Pagano ME and Rasmussen SA: The brown longitudinal obsessive compulsive study: Clinical features and Symptoms of the sample at intake. J Clin Psychiatry 67: 703-711, 2006.
4. Zilhão NR, Smit DJ, Den Braber A, Dolan CV, Willemsen G, Boomsma DI and Cath DC: Genetic and environmental contributions to stability in adult obsessive compulsive behavior. Twin Res Hum Genet 18: 52-60, 2015.
5. Ravagnani Salto AB, Santoro ML, Hoexter MQ, Jackowski AP, Pan PM, Rosário MC, Belangero SI, Alvarenga PG, Doretto VF, Fumo AMT, *et al*: Obsessive-compulsive symptoms, polygenic risk score, and thalamic development in children from the brazilian high-risk cohort for mental conditions (BHRCS). Front Psychiatry 12: 673595, 2021.
6. Kaplan GB and Hammer RP (eds): Brain circuitry and signaling in psychiatry: Basic science and clinical implications. American Psychiatric Pub, Washington, DC, 2002.
7. Shephard E, Stern ER, van den Heuvel OA, Costa DLC, Batistuzzo MC, Godoy PBG, Lopes AC, Brunoni AR, Hoexter MQ, Shavitt RG, *et al*: Toward a neurocircuit-based taxonomy to guide treatment of obsessive-compulsive disorder. Mol Psychiatry 26: 4583-4604, 2021.
8. Moreso NV, Hernández-Martínez C, Val VA and Sans JC: Socio-demographic and psychopathological risk factors in obsessive-compulsive disorder: Epidemiologic study of school population. Int J Clin Health Psychol 13: 118-126, 2013.
9. Stavropoulos V, Moore KA, Lazaratou H, Dikeos D and Gomez R: A multilevel longitudinal study of obsessive compulsive symptoms in adolescence: Male gender and emotional stability as protective factors. Ann Gen Psychiatry 16: 42, 2017.
10. Murayama K, Nakao T, Ohno A, Tsuruta S, Tomiyama H, Hasuzawa S, Mizobe T, Kato K and Kanba S: Impacts of stressful life events and traumatic experiences on onset of obsessive-compulsive disorder. Front Psychiatry 11: 561266, 2020.
11. Strom NI, Burton CL, Iyegbe C, Silzer T, Antonyan L, Pool R, Lemire M, Crowley JJ, Hottenga JJ, Ivanov VZ, *et al*: Genome-Wide association study of obsessive-compulsive Symptoms including 33,943 individuals from the general population. Mol Psychiatry 29: 2714-2723, 2024.
12. Jagannathan N, Ginger EJ, Yu M, Chasson GS and Leventhal AM: A prospective longitudinal investigation of the trajectory of obsessive-compulsive symptoms during adolescence. Psychiatry Res 341: 116155, 2024.
13. Fonseka TM, Richter MA and Müller DJ: Second generation antipsychotic-induced obsessive-compulsive symptoms in schizophrenia: A review of the experimental literature. Curr Psychiatry Rep 16: 510, 2014.
14. Doobay M, Sharma V and Eccles H: Antiseizure medication-induced obsessive-compulsive disorder and tic disorder: A pragmatic review. Expert Rev Neurother 22: 721-731, 2022.
15. Hassan A, Bower JH, Kumar N, Matsumoto JY, Fealey RD, Josephs KA and Ahlskog JE: Dopamine agonist-triggered pathological behaviors: Surveillance in the PD clinic reveals high frequencies. Parkinsonism Relat Disord 17: 260-264, 2011.
16. Kelley BJ, Duker AP and Chiu P: Dopamine agonists and pathologic behaviors. Parkinsons Dis 2012: 603631, 2012.
17. Zhang G, Zhang Z, Liu L, Yang J, Huang J, Xiong N and Wang T: Impulsive and compulsive behaviors in Parkinson's disease. Front Aging Neurosci 6: 318, 2014.
18. Schirmbeck F and Zink M: Clozapine-induced obsessive-compulsive Symptoms in schizophrenia: A critical review. Curr Neuropharmacol 10: 88-95, 2012.
19. Kulkarni G, Narayanaswamy JC and Math SB: Olanzapine induced de-novo obsessive compulsive disorder in a patient with schizophrenia. Indian J Pharmacol 44: 649-650, 2012.
20. Mishra DK, Singh UP, Kishore A and Niranjan V: Prevalence and pattern of olanzapine emergent obsessive-compulsive Symptoms: A cross-sectional study. Apollo Med 21: 159-162, 2024.
21. Saini RK and Pande V: Drug induced obsessive compulsive disorder in Schizophrenia. Med J Armed Forces India 64: 169-170, 2008.
22. Stamouli S and Lykouras L: Quetiapine-induced obsessive-compulsive Symptoms: A series of five cases. J Clin Psychopharmacol 26: 396-400, 2006.
23. Marazziti D and Pallanti S: Effectiveness of olanzapine treatment for severe obsessive-compulsive disorder. Am J Psychiatry 156: 1834-1835, 1999.
24. McDougle CJ, Epperson CN, Pelton GH, Wasylink S and Price LH: A double-blind, placebo-controlled study of risperidone addition in serotonin reuptake inhibitor-refractory obsessive-compulsive disorder. Arch Gen Psychiatry 57: 794-801, 2000.
25. Bogan AM, Koran LM, Chuong HW, Vapnik T and Bystritsky A: Quetiapine augmentation in obsessive-compulsive disorder resistant to serotonin reuptake inhibitors: An open-label study. J Clin Psychiatry 66: 73-79, 2005.
26. Keramatian K, Chithra NK and Yatham LN: The CANMAT and ISBD guidelines for the treatment of bipolar disorder: Summary and a 2023 update of evidence. Focus (Am Psychiatr Publ) 21: 344-353, 2023.
27. Stahl SM: Mechanism of action of cariprazine. CNS Spectr 21: 123-127, 2016.
28. Oldak SE, Chaparro MC and Jean-Paul LA: A brief review of cariprazine. Am J Psychiatry Resid J 19: 6-8, 2024. doi:10.1176/appi.ajp-rj.2024.190302.
29. Pejušković B, Munjiza Jovanović A and Pešić D: Exploring cariprazine as a treatment option for varied depression symptom clusters. Front Psychiatry 15: 1442699, 2024.
30. Citrome L, Li C, Yu J, Kramer K and Nguyen HB: Effects of cariprazine on reducing symptoms of irritability, hostility, and agitation in patients with manic or mixed episodes of bipolar I disorder. J Affect Disord 358: 353-360, 2024.
31. Koziej S, Kowalczyk E and Soroka E: Cariprazine in psychiatry: A comprehensive review of efficacy, safety, and therapeutic potential. Med Sci Monit 30: e945411, 2024.
32. Barabássy Á, Sebe B, Acsai K, Laszlovszky I, Szatmári B, Earley WR and Németh G: Safety and tolerability of cariprazine in patients with Schizophrenia: A pooled analysis of eight phase II/III studies. Neuropsychiatr Dis Treat 17: 957-970, 2021.
33. AbbVie Corporation: VRAYLAR®: PRODUCT MONOGRAPH INCLUDING PATIENT MEDICATION INFORMATION. 2024.
34. Heck J, Seifert J, Stichtenoth DO, Schroeder C, Groh A, Szycik GR, Degner D, Adamovic I, Schneider M, Glocker C, *et al*: A case series of serious and unexpected adverse drug reactions under treatment with cariprazine. Clin Case Rep 9: e04084, 2021.
35. Rodriguez Cruz J, Sahlsten Schölin J and Hjorth S: Case report: cariprazine in a patient with Schizophrenia, substance abuse, and cognitive dysfunction. Front Psychiatry 12: 727666, 2021.
36. Weise J, Schomerus G and Speerforck S: Add-on cariprazine in patients with long-term clozapine treatment and treatment resistant Schizophrenia: Two cases of psychotic deterioration and pisa Syndrome. Clin Psychopharmacol Neurosci 20: 398-401, 2022.
37. Pariwatcharakul P and Suthisisang C: Cariprazine-associated obsessive-compulsive Symptoms in a patient with bipolar disorder: Potential mechanisms of D3 receptors. J Clin Psychopharmacol 43: 79-80, 2023.
38. Zhu H, Qu Y, Du Z, Zhou Q, Shen Y, Jiang Y, Zhou Z and Zhou H: Mining and analysis of adverse event signals of Cariprazine based on the real-world data of FAERS database. J Affect Disord 347: 45-50, 2024.
39. Stahl SM (ed): Stahl's Essential Psychopharmacology: Prescriber's Guide. 8th edition. Cambridge University Press, Cambridge, 2024.
40. Meltzer HY and Gadaleta E: Contrasting typical and atypical antipsychotic drugs. Focus (Am Psychiatr Publ) 19: 3-13, 2021.
41. Krieger A: Benzos (as) needed: Research into as-needed and intermittent benzodiazepines for anxiety is required for comprehensive best prescribing practices. Front Psychiatry 16: 1569416, 2025.
42. Reid Finlayson AJ, Macoubrie J, Huff C, Foster DE and Martin PR: Experiences with benzodiazepine use, tapering, and discontinuation: An Internet survey. Ther Adv Psychopharmacol 12: 20451253221082386, 2022.

43. Issari Y, Jakubovski E, Bartley CA, Pittenger C and Bloch MH: Early onset of response with selective serotonin reuptake inhibitors in obsessive-compulsive disorder: A meta-analysis. J Clin Psychiatry 77: e605-e611, 2016.
44. Kayser RR: Pharmacotherapy for treatment-resistant obsessive-compulsive disorder. J Clin Psychiatry 81: 19ac13182, 2020.
45. Fineberg NA, Hengartner MP, Bergbaum CE, Gale TM, Gamma A, Ajdacic-Gross V, Rössler W and Angst J: A prospective population-based cohort study of the prevalence, incidence and impact of obsessive-compulsive symptomatology. Int J Psychiatry Clin Pract 17: 170-178, 2013.
46. Frydman I, do Brasil PE, Torres AR, Shavitt RG, Ferrão YA, Rosário MC, Miguel EC and Fontenelle LF: Late-onset obsessive-compulsive disorder: Risk factors and correlates. J Psychiatr Res 49: 68-74, 2014.
47. Suñol M, Contreras-Rodríguez O, Macià D, Martínez-Vilavella G, Martínez-Zalacaín I, Subirà M, Pujol J, Sunyer J and Soriano-Mas C: Brain structural correlates of subclinical obsessive-compulsive Symptoms in healthy children. J Am Acad Child Adolesc Psychiatry 57: 41-47, 2018.
48. Koźmin-Burzyńska A, Matuszczyk M and Krzystanek M: Obsessive compulsive syndrome in a patient treated by cariprazine in the course of schizophrenia with predominantly negative symptoms. Pharmacotherapy in Psychiatry and Neurology/Farmakoterapia w Psychiatrii i Neurologii 37: 259-266, 2022.
49. Carlsson ML: On the role of prefrontal cortex glutamate for the antithetical phenomenology of obsessive compulsive disorder and attention deficit hyperactivity disorder. Prog Neuropsychopharmacol Biol Psychiatry 25: 5-26, 2001.
50. Mora S, Merchán A, Vilchez O, Aznar S, Klein AB, Ultved L, Campa L, Suñol C, Flores P and Moreno M: Reduced cortical serotonin 5-HT2A receptor binding and glutamate activity in high compulsive drinker rats. Neuropharmacology 143: 10-19, 2018.
51. Karthik S, Sharma LP and Narayanaswamy JC: Investigating the role of glutamate in obsessive-compulsive disorder: Current perspectives. Neuropsychiatr Dis Treat 16: 1003-1013, 2020.
52. Pastre M, Occéan BV, Boudousq V, Conejero I, Fabbro-Peray P, Collombier L, Mallet L and Lopez-Castroman J: Serotonergic underpinnings of obsessive-compulsive disorder: A systematic review and meta-analysis of neuroimaging findings. Psychiatry Clin Neurosci 79: 48-59, 2025.
53. Perani D, Garibotto V, Gorini A, Moresco RM, Henin M, Panzacchi A, Matarrese M, Carpinelli A, Bellodi L and Fazio F: In vivo PET study of 5HT(2)A serotonin and D(2) dopamine dysfunction in drug-naive obsessive-compulsive disorder. NeuroImage 42: 306-314, 2008.
54. Adams KH, Hansen ES, Pinborg LH, Hasselbalch SG, Svarer C, Holm S, Bolwig TG and Knudsen GM: Patients with obsessive-compulsive disorder have increased 5-HT2A receptor binding in the caudate nuclei. Int J Neuropsychopharmacol 8: 391-401, 2005.
55. Grillault Laroche D and Gaillard A: Induced obsessive compulsive symptoms (OCS) in Schizophrenia patients under Atypical 2 antipsychotics (AAPs): Review and hypotheses. Psychiatry Res 246: 119-128, 2016.
56. Alevizos B, Lykouras L, Zervas IM and Christodoulou GN: Risperidone-induced obsessive-compulsive symptoms: A series of six cases. J Clin Psychopharmacol 22: 461-467, 2002.
57. Lykouras L, Alevizos B, Michalopoulou P and Rabavilas A: Obsessive-compulsive symptoms induced by atypical antipsychotics. A review of the reported cases. Prog Neuropsychopharmacol Biol Psychiatry 27: 333-346, 2003.
58. Diler RS, Yolga A, Avci A and Scahill L: Risperidone-induced obsessive-compulsive symptoms in two children. J Child Adolesc Psychopharmacol 13 (Suppl 1): S89-S92, 2003.
59. Baker RW: Possible dose-response relationship for risperidone in obsessive-compulsive disorder. J Clin Psychiatry 59: 134, 1998.
60. Stahl SM: Stahl's Essential Psychopharmacology: Neuroscientific Basis and Practical Application. 4th edition. Cambridge University Press, Cambridge, 2013.
61. Ducasse D, Boyer L, Michel P, Loundou A, Macgregor A, Micoulaud-Franchi JA, Courtet P, Abbar M, Leboyer M and Fond G: D2 and D3 dopamine receptor affinity predicts effectiveness of antipsychotic drugs in obsessive-compulsive disorders: A metaregression analysis. Psychopharmacology (Berl) 231: 3765-3770, 2014.
62. Ramasubbu R, Ravindran A and Lapierre Y: Serotonin and dopamine antagonism in obsessive-compulsive disorder: Effect of atypical antipsychotic drugs. Pharmacopsychiatry 33: 236-238, 2000.
63. Lin J, Liu W, Guan J, Cui J, Shi R, Wang L, Chen D and Liu Y: Latest updates on the serotonergic system in depression and anxiety. Front Synaptic Neurosci 15: 1124112, 2023.
64. Seibell PJ, Demarest J and Rhoads DE: 5-HT1A receptor activity disrupts spontaneous alternation behavior in rats. Pharmacol Biochem Behav 74: 559-564, 2003.
65. Alvarez BD, Cavazos C, Morales CA, M Lopez S and Amodeo DA: Impact of specific serotonin receptor modulation on restricted repetitive behaviors. Front Behav Neurosci 16: 1078983, 2022.
66. Lesch KP, Hoh A, Schulte HM, Osterheider M and Müller T: Long-term fluoxetine treatment decreases 5-HT1A receptor responsivity in obsessive-compulsive disorder. Psychopharmacology (Berl) 105: 415-420, 1991.
67. Lesch KP, Hoh A, Disselkamp-Tietze J, Wiesmann M, Osterheider M and Schulte HM: 5-Hydroxytryptamine1A receptor responsivity in obsessive-compulsive disorder. Comparison of patients and controls. Arch Gen Psychiatry 48: 540-547, 1991.
68. Zohar J and Sasson Y: Obsessive compulsive disorder: Opportunities within and beyond the serotonergic domain. Acta Neuropsychiatr 9: 84-86, 1997.
69. Burk BG, DiGiacomo T, Polancich S, Pruett BS, Sivaraman S and Birur B: Antipsychotics and obsessive-compulsive disorder/obsessive-compulsive symptoms: A pharmacovigilance study of the FDA adverse event reporting system. Acta Psychiatr Scand 148: 32-46, 2023.
70. Osugo M, Wall MB, Selvaggi P, Zahid U, Finelli V, Chapman GE, Whitehurst T, Onwordi EC, Statton B, McCutcheon RA, *et al*: Striatal dopamine D2/D3 receptor regulation of human reward processing and behaviour. Nat Commun 16: 1852, 2025.
71. Kong H, Kuang W, Li S and Xu M: Activation of dopamine D3 receptors inhibits reward-related learning induced by cocaine. Neuroscience 176: 152-161, 2011.
72. Miguel EC, Leckman JF, Rauch S, do Rosario-Campos MC, Hounie AG, Mercadante MT, Chacon P and Pauls DL: Obsessive-compulsive disorder phenotypes: Implications for genetic studies. Mol Psychiatry 10: 258-275, 2005.
73. Kim SJ and Kim CH: The genetic studies of obsessive-compulsive disorder and its future directions. Yonsei Med J 47: 443-454, 2006.
74. Zai G, Zai CC, Burroughs E, Arnold PD, Kennedy JL and Richter MA: Dopamine D3 receptor gene is associated with obsessive-compulsive disorder and antidepressant response. Prog Neuropsychopharmacol Biol Psychiatry 140: 111428, 2025.
75. Theis H, Prange S, Bischof GN, Hoenig MC, Tittgemeyer M, Timmermann L, Fink GR, Drzezga A, Eggers C and van Eimeren T: Impulsive-compulsive behaviour in early Parkinson's disease is determined by apathy and dopamine receptor D3 polymorphism. NPJ Parkinsons Dis 9: 154, 2023.
76. Ahlskog JE: Pathological behaviors provoked by dopamine agonist therapy of Parkinson's disease. Physiol Behav 104: 168-172, 2011.
77. Napier TC and Persons AL: Pharmacological insights into impulsive-compulsive spectrum disorders associated with dopaminergic therapy. Eur J Neurosci 50: 2492-2502, 2019.
78. Shen H, Ma Z, Hans E, Duan Y, Bi GH, Chae YC, Bonifazi A, Battiti FO, Newman AH, Xi ZX and Yang Y: Involvement of dopamine D3 receptor in impulsive choice decision-making in male rats. Neuropharmacology 257: 110051, 2024.
79. Wolfschlag M, Espa E, Skovgård K, Halje P and Cenci MA: Impulsive-compulsive behaviours and striatal neuroactivity in mildly parkinsonian rats under D2/3 agonist and L-DOPA treatment. NPJ Parkinsons Dis 11: 142, 2025.
80. Bansal LR, Schafer D, Sood K, Abraham J, Kaushik A and Parikh P: Cariprazine augmentation to SSRIS in treating a case of treatment-resistant obsessive-compulsive disorder in an adolescent female. Int J Adv Res 12: 1648-1651, 2024.
81. Martiadis V, Pessina E, Martini A, Raffone F, Cattaneo CI, De Berardis D and Pampaloni I: Serotonin reuptake inhibitors augmentation with cariprazine in patients with treatment-resistant obsessive-compulsive disorder: A retrospective observational study. CNS Spectr: May 22, 2024 (Epub ahead of print).

82. De Berardis D, Vellante F, Fornaro M, Orsolini L, Valchera A, Baroni G, Kim YK, Martinotti G and Di Giannantonio M: Rapid improvement of obsessive-compulsive disorder associated with schizophrenia with cariprazine add-on in a subject under paliperidone long-acting injection: A case report. Int Clin Psychopharmacol 35: 113-118, 2020.
83. Dolfi A and Tudose C: Obsessive-compulsive disorder in a woman with high-functioning autism. Dusunen Adam J Psychiatr Neurol Sci 37: 114-116, 2024.
84. C L and Dj S: Heterogeneity of obsessive-compulsive disorder: A literature review. Harvard review of psychiatry 11, 2003.
85. Proshina E, Gaidareva A, Beskhizhko M, Kazaryan G, Bainbridge E and Khayrullina G: Biomarkers of obsessive-compulsive disorder subtypes: A literature review. Int J Mol Sci 26: 8578, 2025.
86. Van Roessel PJ, Grassi G, Aboujaoude EN, Menchón JM, Van Ameringen M and Rodríguez CI: Treatment-resistant OCD: Pharmacotherapies in adults. Compr Psychiatry 120: 152352, 2023.
87. Anholt GE, Aderka IM, ven Balkom AJ, Smit JH, Schruers K, van der Wee NJ, Eikelenboom M, De Luca V and van Oppen P: Age of onset in obsessive-compulsive disorder: Admixture analysis with a large sample. Psychol Med 44: 185-194, 2014.
88. Burchi E and Pallanti S: Diagnostic issues in early-onset obsessive-compulsive disorder and their treatment implications. Curr Neuropharmacol 17: 672-680, 2019.
89. Sobin C, Blundell ML and Karayiorgou M: Phenotypic differences in early- and late-onset obsessive-compulsive disorder. Compr Psychiatry 41: 373-379, 2000.
90. de Mathis MA, do Rosario MC, Diniz JB, Torres AR, Shavitt RG, Ferrão YA, Fossaluza V, de Bragança Pereira CA and Miguel EC: Obsessive-compulsive disorder: Influence of age at onset on comorbidity patterns. Eur Psychiatry 23: 187-194, 2008.
91. Janowitz D, Grabe HJ, Ruhrmann S, Ettelt S, Buhtz F, Hochrein A, Schulze-Rauschenbach S, Meyer K, Kraft S, Ferber C, *et al*: Early onset of obsessive-compulsive disorder and associated comorbidity. Depress Anxiety 26: 1012-1017, 2009.
92. Torres AR, Fontenelle LF, Shavitt RG, Ferrão YA, Do Rosário MC, Storch EA and Miguel EC: Comorbidity variation in patients with obsessive-compulsive disorder according to symptom dimensions: Results from a large multicentre clinical sample. J Affect Disord 190: 508-516, 2016.
93. Kim T, Kwak S, Hur JW, Lee J, Shin WG, Lee TY, Kim M and Kwon JS: Neural bases of the clinical and neurocognitive differences between earlyand late-onset obsessive-compulsive disorder. J Psychiatry Neurosci 45: 234-242, 2020.
94. Cao L, Li H, Hu X, Liu J, Gao Y, Liang K, Zhang L, Hu X, Bu X, Lu L, *et al*: Distinct alterations of amygdala subregional functional connectivity in early- and late-onset obsessive-compulsive disorder. J Affect Disord 298: 421-430, 2022.
95. Park I, Ha M, Kim T, Lho SK, Moon SY, Kim M and Kwon JS: Cortical gyrification differences between early- and late-onset obsessive-compulsive disorder: Neurobiological evidence for neurodevelopmentally distinct subtypes. Psychol Med 53: 5976-5985, 2023.
96. Bloch MH and Storch EA: Assessment and management of treatment-refractory obsessive-compulsive disorder in children. J Am Acad Child Adolesc Psychiatry 54: 251-262, 2015.
97. Nazeer A, Latif F, Mondal A, Azeem MW and Greydanus DE: Obsessive-compulsive disorder in children and adolescents: epidemiology, diagnosis and management. Transl Pediatr 9 (Suppl 1): S76-S93, 2020.
98. Girone N, Benatti B, Bucca C, Cassina N, Vismara M and Dell'Osso B: Early-onset obsessive-compulsive disorder: Sociodemographic and clinical characterization of a large outpatient cohort. J Psychiatr Res 172: 1-8, 2024.
99. Wungvivatchareon N and Anuroj K: Disillusionment mediates the associations between perceived stressors and affective symptoms in Thai medical students: A cross-sectional survey. East Asian Arch Psychiatry 35: 83-90, 2025.
100. Anuroj K and Wannaiampikul S: Factor structure and convergent validity of perceived psychosocial stressor questionnaire: A thai measure of subjective adversities. East Asian Arch Psychiatry 35: 146-152, 2025.
101. Nisu S, Anuroj K, Wannaiampikul S, Pangsorn A, Chiencharoenthanakij R and Chongbanyatcharoen S: Moderation effects of positive core belief and social-emotional responsiveness on the relationship between cyberbullying victimization and affective Symptoms. Psychol Res Behav Manag 16: 2545-2551, 2023.
102. Anuroj K: Effects of cyberbullying and coping strategies on depression. J Med Assoc Thai 105 (Suppl 1): S58-S67, 2022.
103. Musthafa FF and Baitina A: Coping Strategies to Improve the Quality of Life among Thai Students. In: Proceedings of the 4th ASEAN Conference on Psychology, Counselling, and Humanities (ACPCH 2018). Atlantis Press, Surat Thani, 2019.
104. Tschirhart N, Straiton M, Ottersen T and Winkler AS: 'Living like I am in Thailand': Stress and coping strategies among Thai migrant masseuses in Oslo, Norway. BMC Women's Health 19: 139, 2019.
105. Murata A, Moser JS and Kitayama S: Culture shapes electrocortical responses during emotion suppression. Soc Cogn Affect Neurosci 8: 595-601, 2013.
106. Rapp AM, Bergman RL, Piacentini J and McGuire JF: Evidence-based assessment of obsessive-compulsive disorder. J Cent Nerv Syst Dis 8: 13-29, 2016.