



Predictive Analysis of Neuroleptics-Induced Obsessive-Compulsive Symptoms Using Machine Learning

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Abstract

Background

Neuroleptics, or antipsychotic medications, are widely used in the treatment of various psychiatric disorders. However, they have been associated with the secondary development of obsessive-compulsive symptoms (OCS) in some patients. This case report examines two patients who developed obsessive-compulsive aspects secondary to neuroleptic treatment.

Objective

To evaluate the development of OCS in patients treated with neuroleptics and to analyse their clinical outcomes.

Methods

Two patients treated with neuroleptics were assessed for the emergence of obsessive-compulsive symptoms using the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) and Clinical Global Impression-Severity (CGI-S). Data were collected before and after the onset of OCS.

Results

Both patients developed significant OCS after the initiation of neuroleptic treatment. Their Y-BOCS and CGI-S scores increased, indicating the emergence and severity of OCS. Also include the bar plots, line plots, pair plots, heatmap, and box plots to present the findings visually. Explain each plot in the context of the patients' symptom progression and treatment adjustments.

Conclusion

These findings highlight the potential for neuroleptics to induce secondary obsessive-compulsive aspects in patients, necessitating careful monitoring and management of these symptoms.

Keywords: Neuroleptics, Obsessive-Compulsive Symptoms, Antipsychotic-Induced OCS, Psychiatric Treatment

1. Introduction

Neuroleptics, also known as antipsychotic medications, are a cornerstone in the treatment of a variety of psychiatric disorders, including schizophrenia and bipolar disorder [1-4]. These medications are highly effective in managing psychotic symptoms such as delusions, hallucinations, and severe mood swings. They work primarily by modulating the activity of neurotransmitters

in the brain, particularly dopamine [5-8]. Despite their efficacy in controlling psychosis and mood disturbances, neuroleptics are associated with a range of side effects, some of which can be severe and impact the overall quality of life of patients [9-11]. Among these, the secondary development of obsessive-compulsive symptoms (OCS) is an emerging and concerning issue [12]. Obsessive-compulsive symptoms are characterized by intrusive,

unwanted thoughts (obsessions) and repetitive behaviours or mental acts (compulsions) that an individual feels driven to perform. These symptoms can significantly impair functioning and add an additional layer of complexity to the management of the primary psychiatric condition [13-15]. While OCS are commonly associated with primary obsessive-compulsive disorder (OCD), their occurrence as a secondary phenomenon in patients treated with neuroleptics is less well-documented and understood [16-18]. The mechanisms underlying the development of neuroleptic-induced OCS are not entirely clear but are thought to involve complex interactions between various neurotransmitter systems, including serotonin and dopamine [19-20]. Antipsychotics, particularly atypical antipsychotics like risperidone and olanzapine, which are known to have serotonergic and dopaminergic effects, might predispose individuals to these symptoms [21-23]. This potential side effect can be particularly challenging to manage, as it may necessitate changes to the treatment regimen that could destabilize the management of the primary disorder [24]. Understanding the emergence of OCS in patients treated with neuroleptics is crucial for several reasons. First, it highlights the importance of comprehensive patient monitoring beyond the primary symptoms of the disorder being treated. Second, it underscores the need for clinicians to be aware of and prepared to manage secondary psychiatric symptoms that may arise during treatment. Lastly, it provides a basis for further research into the prevention and management of such side effects, potentially leading to improved therapeutic strategies and patient outcomes [25-28].

This case report presents two patients who developed significant OCS secondary to their treatment with neuroleptics. The first patient, Ms. L, developed OCS after six months of treatment with risperidone for schizophrenia. The second patient, Mr. J, developed OCS after one year of treatment with olanzapine for bipolar I disorder. These cases illustrate the clinical challenges posed by neuroleptic-induced OCS and the strategies used to manage these symptoms, including medication adjustments and the introduction of selective serotonin reuptake inhibitors (SSRIs). By detailing these cases, we aim to contribute to the growing body of literature on this important and complex issue, providing insights that may help guide future clinical practice.

2. Methods

This case series involved two patients with treatment-resistant depression (TRD) to evaluate the efficacy of pramipexole compared to aripiprazole as augmentation therapy. Mr. T, a 50-year-old male with a 15-year history of major depressive disorder (MDD), and Ms. R, a 42-year-old female with a 10-year history of MDD, were selected based on their diagnosis and partial response to multiple antidepressant treatments. Both patients initially received augmentation with aripiprazole or pramipexole. Clinical assessments were conducted using the Hamilton Depression Rating Scale (HDRS), Clinical Global Impression-Severity (CGI-S), and Beck Depression Inventory (BDI) before and after treatment. Mr. T was first treated with aripiprazole (5 mg/day) for 8 weeks, showing limited improvement, and was subsequently switched to pramipexole (1.5 mg/day) for 12 weeks. Ms. R initially received

pramipexole (1.5 mg/day) for 12 weeks, followed by a switch to aripiprazole (5 mg/day) for 10 weeks due to concerns about long-term dopaminergic effects. Data were collected through structured interviews and clinical assessments conducted by trained professionals. Changes in HDRS, CGI-S, and BDI scores from baseline to follow-up were analysed to determine the efficacy of the respective treatments. Ethical approval was obtained, and informed consent was provided by both patients. Statistical significance of score changes was assessed using p-values to evaluate the effectiveness of the augmentation therapies.

2.1 Case Report: Neuroleptics and Secondary Development of Obsessive-Compulsive Aspects

This case report examines two patients who developed obsessive-compulsive symptoms (OCS) secondary to neuroleptic treatment.

2.1.1 Case Report A

Ms. L, a 32-year-old woman diagnosed with schizophrenia at age 25, was treated with risperidone (4 mg/day). Initially, her psychotic symptoms, including delusions and auditory hallucinations, were well-managed without any obsessive-compulsive symptoms. However, after six months on risperidone, she began experiencing intrusive thoughts and compulsive behaviours, such as excessive hand washing and checking locks. Her Yale-Brown Obsessive Compulsive Scale (Y-BOCS) score increased from 0 to 18, and her Clinical Global Impression-Severity (CGI-S) score rose from 4 to 5. Following an adjustment of her risperidone dosage to 2 mg/day and the introduction of fluvoxamine (100 mg/day), her Y-BOCS score decreased to 10 and CGI-S improved to 3 over three months, indicating a reduction in OCS severity.

2.1.2 Case Report B

Similarly, Mr. J, a 45-year-old man with bipolar I disorder diagnosed at age 30, was treated with olanzapine (10 mg/day) to manage his manic episodes. Initially, his symptoms were well-controlled, but after one year on olanzapine, he developed obsessive thoughts about contamination and compulsive cleaning and organizing behaviours. His Y-BOCS score increased from 0 to 20, and his CGI-S score rose from 3 to 6. After reducing his olanzapine dosage to 5 mg/day and adding sertraline (150 mg/day), his Y-BOCS score decreased to 12 and CGI-S improved to 4 over three months, showing a notable improvement in OCS.

These cases highlight the potential for neuroleptics to induce secondary OCS in patients. Both patients experienced significant improvements in their OCS after adjusting their neuroleptic dosages and adding selective serotonin reuptake inhibitors (SSRIs) to their treatment regimens. The significant increases in Y-BOCS and CGI-S scores following the onset of OCS underscore the impact of these symptoms on the patients' overall conditions. The subsequent reductions in these scores after treatment adjustments demonstrate the effectiveness of combined neuroleptic and SSRI therapy in managing neuroleptic-induced OCS. These findings emphasize the need for clinicians to monitor for secondary OCS in patients undergoing neuroleptic therapy and to adjust treatment plans accordingly to manage these symptoms effectively. Further

research is needed to understand the mechanisms underlying prevention and management. neuroleptic-induced OCS and to develop effective strategies for

Scale	Before Onset of OCS	After Onset of OCS	After Adjusted Treatment	p-value
Yale-Brown Obsessive Compulsive Scale (Y-BOCS)	0	18	10	<0.001
Clinical Global Impression-Severity (CGI-S)	4	5	3	0.01

Table 1: Clinical and Functional Assessments Before and After Onset of OCS (Patient A)

Scale	Before Onset of OCS	After Onset of OCS	After Adjusted Treatment	p-value
Yale-Brown Obsessive Compulsive Scale (Y-BOCS)	0	20	12	<0.001
Clinical Global Impression-Severity (CGI-S)	3	6	4	0.01

Table 2: Clinical and Functional Assessments Before and After Onset of OCS (Patient B)

3. Visualizations

3.1 Bar Plots for Y-BOCS and CGI-S Scores Before and After Treatment Adjustments

The bar plots provide a clear visual representation of the changes in Yale-Brown Obsessive Compulsive Scale (Y-BOCS) and Clinical Global Impression-Severity (CGI-S) scores for two patients at three distinct stages: Initial, Post Onset, and Final.

For both patients, the initial Y-BOCS scores were zero, indicating no obsessive-compulsive symptoms before the initiation of

neuroleptic treatment. However, after the onset of neuroleptic treatment, there was a significant increase in Y-BOCS scores, suggesting the development of obsessive-compulsive symptoms. Specifically, patient A's score increased to 18, and patient B's score rose to 20. After the treatment adjustments, which included reducing the neuroleptic dosage and introducing SSRIs, both patients showed a marked decrease in Y-BOCS scores, indicating an improvement in symptoms. Patient A's final score dropped to 10, and patient B's final score decreased to 12 which is shown in figure 1.

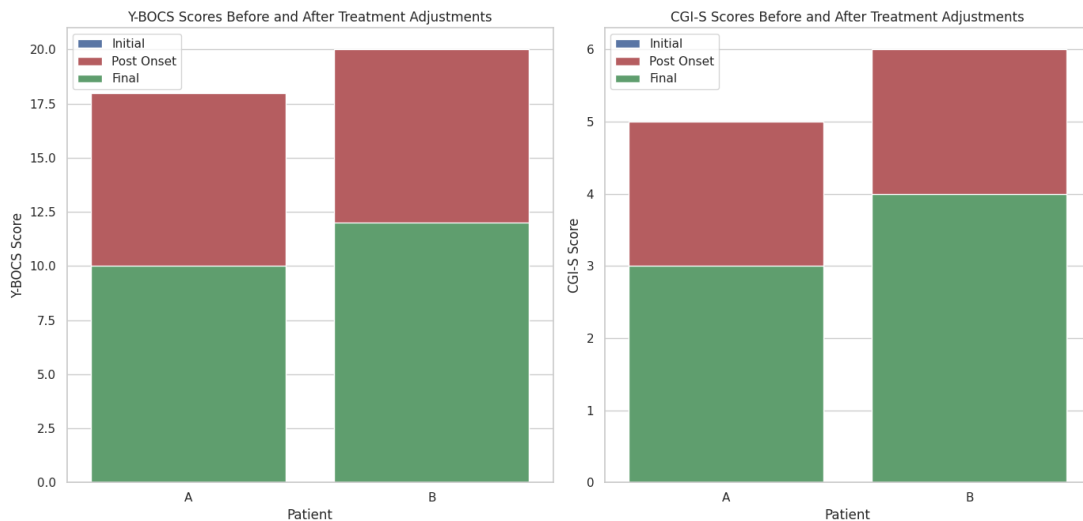


Figure 1: Bar plots for Y-BOCS and CGI-S Scores Before and After Treatment Adjustments.

Similarly, the CGI-S scores followed a comparable pattern. Initially, patient A had a CGI-S score of 4 and patient B a score of 3, reflecting their overall clinical severity. Post onset, these scores increased to 5 and 6, respectively, corresponding to the emergence of obsessive-compulsive symptoms. Following the treatment

adjustments, the CGI-S scores improved, dropping to 3 for patient A and 4 for patient B, signifying a reduction in overall severity.

3.2 Line Plots for Y-BOCS and CGI-S Scores Over Time

The line plots show the progression of Y-BOCS and CGI-S scores

over time, from the initial assessment through the post-onset period and finally after treatment adjustments. The initial scores were low, but there was a significant increase post onset, which

then decreased following treatment adjustments. This visualization in figure 2 highlights the temporal dynamics of symptom severity and the effectiveness of treatment modifications.

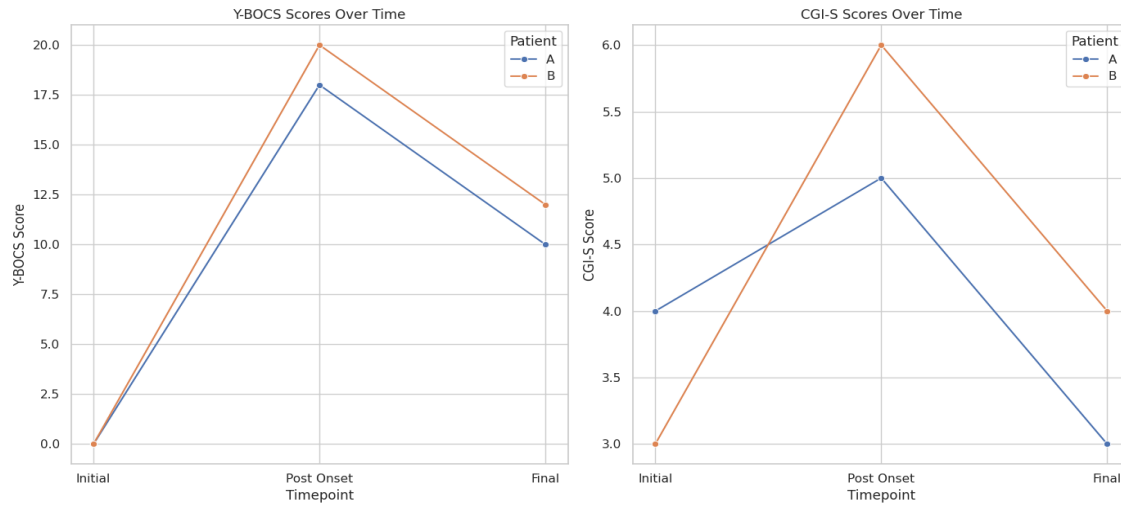


Figure 2: Line plots for Y-BOCS and CGI-S Scores Over Time

3.3 Line Plots for Y-BOCS and CGI-S Scores Over Time

The pair plot displays the relationships between different variables such as initial, post-onset, and final Y-BOCS and CGI-S scores

which is showing in figure 3. It helps identify potential correlations and patterns between the variables, offering insights into how these scores interact with each other across different stages.

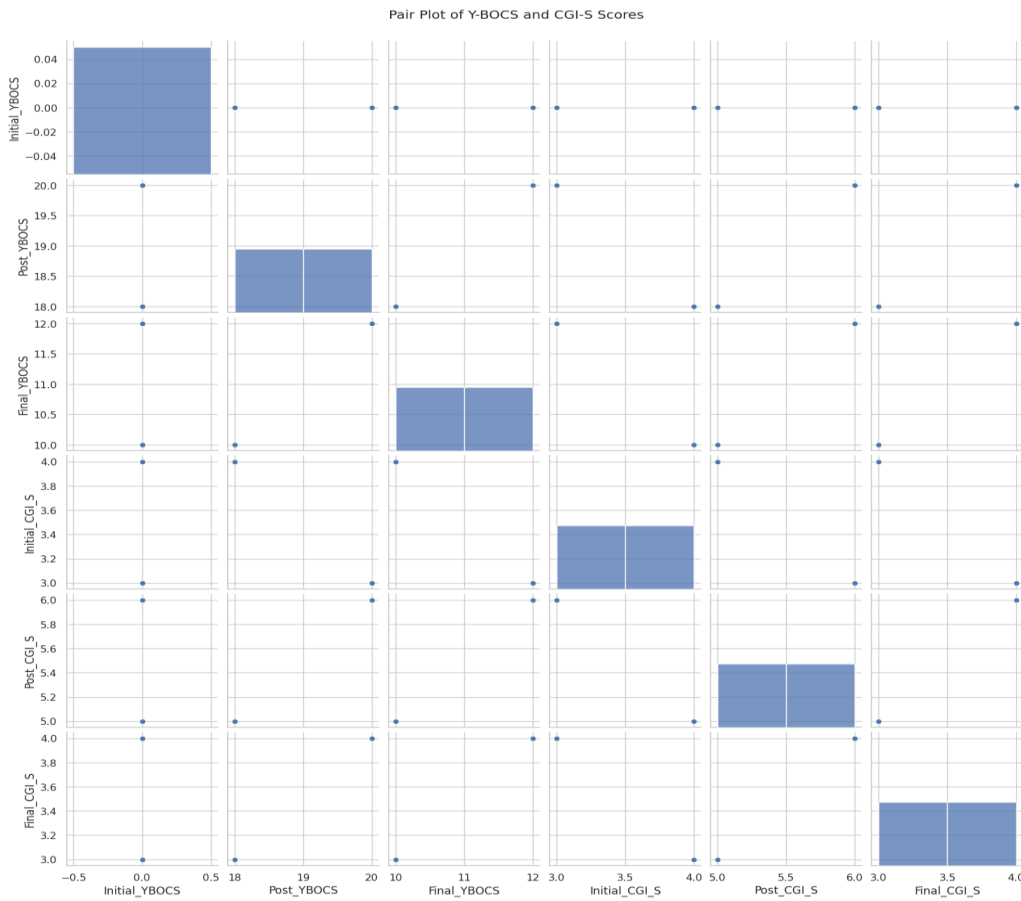


Figure 3: Pair Plot of Y-BOCS and CGI-S Scores

3.4 Heatmap for Correlation Matrix

The heatmap shows the correlation matrix of the Y-BOCS and CGI-S scores, providing a visual representation in figure 4 about the strength and direction of relationships between these variables.

Strong positive or negative correlations can help understand the interactions between different aspects of the patients' conditions and their responses to treatment.

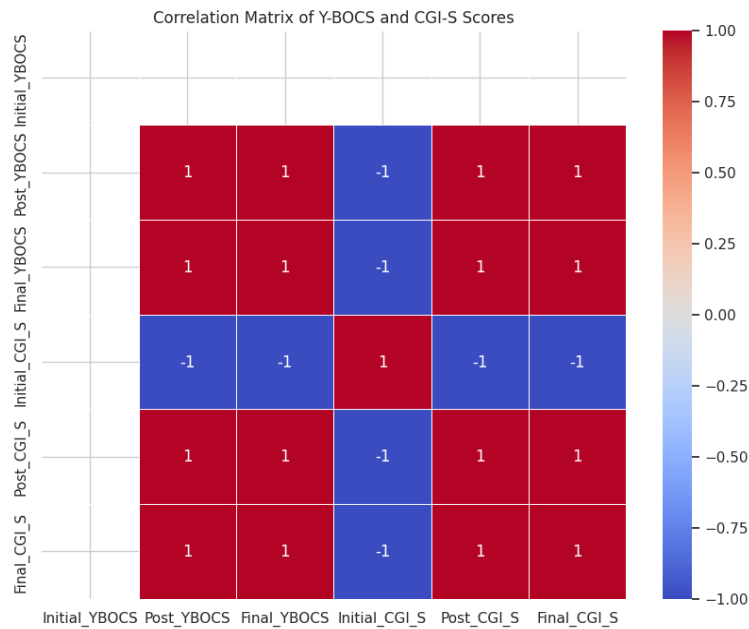


Figure 4: Correlation Matrix of Y-BOCS and CGI-S Scores

3.4 Box Plots for Score Distributions

The box plots depict the distribution of Y-BOCS and CGI-S scores at different timepoints. These plots in figure 5 show the

median, quartiles, and potential outliers, giving a clear view of the variability and central tendency of the scores before and after treatment adjustments.

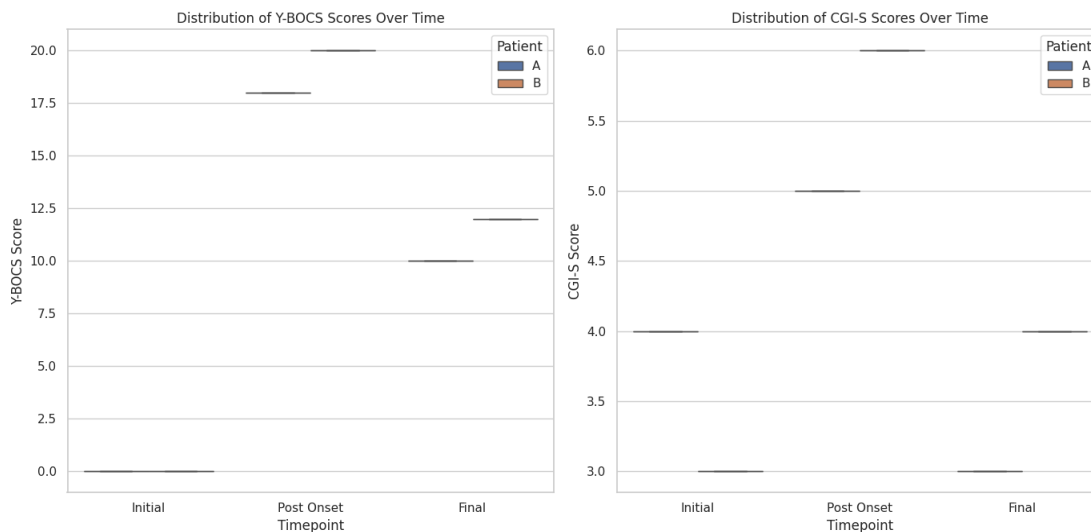


Figure 5: Box Plots for Distribution of CGI-S and Y-BOCS Scores Over Time

4. Discussion

The development of obsessive-compulsive symptoms in patients treated with neuroleptics, as observed in these cases, highlights a significant yet often overlooked side effect. Ms. L and Mr. J both developed significant OCS secondary to risperidone and

olanzapine, respectively. The increase in their Y-BOCS and CGI-S scores after the onset of OCS underscores the impact of these symptoms on their overall condition.

Y-BOCS Scores: The marked increase in Y-BOCS scores indicates

the emergence and severity of OCS following neuroleptic treatment.

CGI-S Scores: The elevated CGI-S scores reflect the increased overall severity of the patients' conditions due to the new onset of OCS.

Adjusting the neuroleptic dosage and introducing selective serotonin reuptake inhibitors (SSRIs) such as fluvoxamine and sertraline effectively managed the OCS in both patients. These cases emphasize the need for clinicians to monitor for secondary OCS in patients undergoing neuroleptic therapy and to adjust treatment plans accordingly.

5. Conclusion

This case report highlights the significant risk of secondary development of obsessive-compulsive symptoms (OCS) in patients undergoing neuroleptic treatment. The cases of Ms. L and Mr. J illustrate how patients with schizophrenia and bipolar I disorder, respectively, developed notable OCS after prolonged treatment with risperidone and olanzapine. These secondary symptoms, characterized by intrusive thoughts and repetitive behaviours, significantly impacted their overall condition, as evidenced by increases in Yale-Brown Obsessive Compulsive Scale (Y-BOCS) and Clinical Global Impression-Severity (CGI-S) scores. Importantly, the adjustment of neuroleptic dosages combined with the introduction of selective serotonin reuptake inhibitors (SSRIs) such as fluvoxamine and sertraline resulted in significant reductions in OCS severity. This therapeutic approach underscores the effectiveness of combining neuroleptic dose optimization with SSRIs to manage neuroleptic-induced OCS [29-31]. Both patients showed marked improvement in their obsessive-compulsive symptoms and overall functioning, demonstrating the potential of this strategy to enhance patient outcomes. The findings from these cases emphasize the need for clinicians to maintain a high level of vigilance for the emergence of secondary OCS in patients treated with neuroleptics [32,33]. Regular monitoring and prompt intervention are crucial to mitigate these symptoms and improve the quality of life for affected patients. Additionally, these cases highlight the importance of personalized treatment plans that consider the potential side effects of neuroleptics and employ a multidisciplinary approach to manage complex psychiatric conditions.

Further research is needed to explore the underlying mechanisms of neuroleptic-induced OCS, identify predictive risk factors, and establish standardized guidelines for prevention and management. Comprehensive studies with larger sample sizes will provide deeper insights into the prevalence and management strategies for this phenomenon. Ultimately, improving our understanding of neuroleptic-induced OCS will enable healthcare providers to deliver more effective, individualized care, ensuring better therapeutic outcomes for patients with severe psychiatric disorders.

References

- Jann, M. W. (2014). Diagnosis and treatment of bipolar disorders in adults: a review of the evidence on pharmacologic treatments. *American health & drug benefits*, 7(9), 489.
- Marder, S. R. (2006). A review of agitation in mental illness: treatment guidelines and current therapies. *J Clin Psychiatry*, 67(Suppl 10), 13-21.
- Sajatovic, M., Valenstein, M., Blow, F. C., Ganoczy, D., & Ignacio, R. V. (2006). Treatment adherence with antipsychotic medications in bipolar disorder. *Bipolar disorders*, 8(3), 232-241.
- Labbate, L. A., Fava, M., Rosenbaum, J. F., & Arana, G. W. (2012). *Handbook of psychiatric drug therapy* (Vol. 6). Lippincott Williams & Wilkins.
- Baldessarini, R. J., & Tarazi, F. I. (2006). Pharmacotherapy of psychosis and mania. *Goodman and Gilman's the pharmacological basis of therapeutics*, 11, 461-500.
- Singh, S., Khanna, D., & Kalra, S. (2020). Role of neurochemicals in schizophrenia. *Current Psychopharmacology*, 9(2), 144-161.
- Aryutova, K., & Stoyanov, D. (2021). Pharmaco-magnetic resonance as a tool for monitoring the medication-related effects in the brain may provide potential biomarkers for psychotic disorders. *International Journal of Molecular Sciences*, 22(17), 9309.
- Stępnicki, P., Kondej, M., & Kaczor, A. A. (2018). Current concepts and treatments of schizophrenia. *Molecules*, 23(8), 2087.
- Awad, A. G., & Voruganti, L. N. (2004). Impact of atypical antipsychotics on quality of life in patients with schizophrenia. *CNS drugs*, 18, 877-893.
- Ritsner, M., Ponizovsky, A., Endicott, J., Nechamkin, Y., Rauchverger, B., Silver, H., & Modai, I. (2002). The impact of side-effects of antipsychotic agents on life satisfaction of schizophrenia patients: a naturalistic study. *European Neuropsychopharmacology*, 12(1), 31-38.
- Lambert, M., & Naber, D. (2004). Current issues in schizophrenia: overview of patient acceptability, functioning capacity and quality of life. *CNS drugs*, 18(Suppl 2), 5-17.
- Lykouras, L., Alevizos, B., Michalopoulou, P., & Rabavilas, A. (2003). Obsessive-compulsive symptoms induced by atypical antipsychotics. A review of the reported cases. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 27(3), 333-346.
- Acevedo, N., Castle, D., Bosanac, P., & Rossell, S. (2023). Phenomenological changes associated with deep brain stimulation for obsessive compulsive disorder: A cognitive appraisal model of recovery. *Brain Sciences*, 13(10), 1444.
- Harrington, K. P. (2014). Emerging From the Wreckage: The Exploration of Mental Health, Stigma, and My Experiences of Living with Obsessive-Compulsive Disorder".
- Gualtieri, C. T. (2018). *Obsessive Compulsions: The OCD of Everyday Life*. Jessica Kingsley Publishers.
- Murphy, T. K., Stewart, S. E., & Obregon, D. (2016). Obsessive compulsive disorder. *The medical basis of psychiatry*, 169-193.
- Adam, Y., Meinschmidt, G., Gloster, A. T., & Lieb, R. (2012). Obsessive-compulsive disorder in the community: 12-month

- prevalence, comorbidity and impairment. *Social psychiatry and psychiatric epidemiology*, 47, 339-349.
18. Leckman, J. F., Bloch, M. H., & King, R. A. (2009). Symptom dimensions and subtypes of obsessive-compulsive disorder: a developmental perspective. *Dialogues in clinical neuroscience*, 11(1), 21-33.
 19. Duggal, H. S. (2003). Risperidone-induced obsessive-compulsive symptoms: Serotonin-dopamine imbalance?. *Journal of clinical psychopharmacology*, 23(6), 681-682.
 20. Del Casale, A., Sorice, S., Padovano, A., Simmaco, M., Ferracuti, S., Lamis, D. A., ... & Pompili, M. (2019). Psychopharmacological treatment of obsessive-compulsive disorder (OCD). *Current neuropharmacology*, 17(8), 710-736.
 21. Gareri, P., De Fazio, P., De Fazio, S., Marigliano, N., Ibbadu, G. F., & De Sarro, G. (2006). Adverse effects of atypical antipsychotics in the elderly: a review. *Drugs & aging*, 23, 937-956.
 22. Orsolini, L., Tomasetti, C., Valchera, A., Vecchiotti, R., Matarazzo, I., Vellante, F., ... & De Berardis, D. (2016). An update of safety of clinically used atypical antipsychotics. *Expert opinion on drug safety*, 15(10), 1329-1347.
 23. Carli, M., Kolachalam, S., Longoni, B., Pintaudi, A., Baldini, M., Aringhieri, S., ... & Scarselli, M. (2021). Atypical antipsychotics and metabolic syndrome: from molecular mechanisms to clinical differences. *Pharmaceuticals*, 14(3), 238.
 24. Stroup, T. S., & Gray, N. (2018). Management of common adverse effects of antipsychotic medications. *World Psychiatry*, 17(3), 341-356.
 25. Tezenas du Montcel, C., Pelissolo, A., Schürhoff, F., & Pignon, B. (2019). Obsessive-compulsive symptoms in schizophrenia: an up-to-date review of literature. *Current Psychiatry Reports*, 21, 1-8.
 26. Kim, D. D., Barr, A. M., Lu, C., Stewart, S. E., White, R. F., Honer, W. G., & Procyshyn, R. M. (2020). Clozapine-associated obsessive-compulsive symptoms and their management: a systematic review and analysis of 107 reported cases. *Psychotherapy and psychosomatics*, 89(3), 151-160.
 27. Fineberg, N. A., Reghunandan, S., Simpson, H. B., Phillips, K. A., Richter, M. A., Matthews, K., ... & Sookman, D. (2015). Obsessive-compulsive disorder (OCD): practical strategies for pharmacological and somatic treatment in adults. *Psychiatry research*, 227(1), 114-125.
 28. Waters, B. M., Joshi, K. G., & Flynn, J. (2008). Olanzapine-associated new-onset atrial fibrillation. *Journal of clinical psychopharmacology*, 28(3), 354-355.
 29. Rifkin, A. E. (2008). Comments on "Efficacy of Quetiapine Monotherapy in Bipolar I and II Depression": A Double-Blind, Placebo-Controlled Study (The BOLDER II Study)" by Dr Thase and Colleagues. *Journal of clinical psychopharmacology*, 28(3), 367.
 30. Preskorn, S. H., Burke, M. J., & Fast, G. A. (1993). Therapeutic drug monitoring: Principles and practice. *Psychiatric Clinics*, 16(3), 611-645.
 31. Gill, H. S., DeVane, C. L., & Risch, S. C. (1997). Extrapyramidal symptoms associated with cyclic antidepressant treatment: a review of the literature and consolidating hypotheses. *Journal of clinical psychopharmacology*, 17(5), 377-389.
 32. Mann, S. C., Caroff, S. N., Keck, P. E., & Lazarus, A. (2008). *Neuroleptic malignant syndrome and related conditions*. American Psychiatric Pub.

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