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RESEARCH ARTICLE

Predicting Antidepressant Use in Patients with Bipolar Disorder

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Abstract

Background: Bipolar disorder (B.D.) defines mood disorders that lead to an imbalance in emotional mood and substantially impact the well-being of patients with B.D. Antidepressants are commonly prescribed in patients with B.D. to improve the severity of depressive symptoms. However, several symptoms are associated with long-term antidepressant use, such as metabolic, psychological, cardiological, and sexual problems. Thus, it is essential to manage the use of antidepressants in patients with B.D.

Goal of Study: The study aimed to predict antidepressant use status in patients with B.D. with parameters related to childhood trauma (C.T.) and the severity of B.D. symptoms.

Methods: We utilized publicly available open data from an fMRI database to examine individuals with B.D. These individuals provided signed consent forms for the sharing of their anonymized data. The study included twenty patients with B.D., with fifteen of them being prescribed antidepressants and the remaining five not receiving such medication.

Results: Our primary findings indicated that the RF machine learning model accurately predicted antidepressant status at a rate of 67%. Additionally, the NN machine learning model achieved a prediction accuracy of 50%.

Conclusion: The study's conclusion highlighted that the RF machine learning model could predict antidepressant usage status in patients with B.D. above the chance level (60%). In contrast, the NN model did not achieve predictions above chance level.

Abbreviations

B.D., bipolar disorder; ML, Machine learning; AUC, area under curve; CTQ, childhood trauma questionnaire; DSM, diagnostic statistical manual; C.T., childhood trauma; KNN, K-Nearest Neighborhood; ZAN-BPD, Zanzarini Rating Scale for Borderline Personality Disorder.

1. Introduction

Bipolar disorder (B.D.) is a common psychiatric disease that impacts many individuals' well-being and psychological balance. Antidepressants were commonly prescribed to control depressive symptoms associated with B.D. However, not all patients with B.D. respond to antidepressants, and some may experience adverse side effects. Despite the less side effect likelihood of the antidepressants compared with other psychiatric drugs (e.g., antipsychotics), there are several metabolic^[1], psychological^[2], and sexual side effects^[3] associated with regular use of antidepressants. Furthermore, functional impairment has received little attention in patients with B.D.^[4] In the literature, the impact of antidepressants is controversial as compared with mood stabilizers, antidepressants were not associated with a risk of affective change^[5]. Therefore, it is necessary to investigate the association among symptom severity concerning trauma symptoms and B.D. symptoms and antidepressant use. It is suggested that patients diagnosed with B.D. should be evaluated concerning childhood trauma (C.T.) history to prevent aggressive behavior^[6]. Furthermore, it is vital to understand the severity of C.T. symptoms and B.D. symptoms can be used to predict antidepressant use status.

Considering the previous literature showing the relationship between antidepressant use and severity of symptoms (e.g., trauma and B.D.), our study aimed to predict antidepressant use in patients with B.D. By identifying predictors of treatment response, we hope to improve the accuracy and effectiveness of antidepressant treatment for patients with bipolar disorder, ultimately leading to improved outcomes and quality of life.

2. Methods

2.1. Participants

In this study, most patients were on antidepressants (n=15). In addition, most patients with bipolar disorder (B.D.) were females (n=17). Patients were diagnosed according to the diagnostic statistical manual (DSM) version 4.

In addition, most of the patients were on antipsychotics (n=12) which is one of the major confounding factors of our study. A few patients were on antiepileptics. Their mean age was "35.75". Most of the participants use their right hands (n=19). The data from a previous study was used^[7]. As mentioned in the previous study, ethical approval was obtained from the Lothian National Health Service Research Ethics Committee (09/S1101/49), and all participants provided written informed consent before taking part^[7].

2.2. Statistical Analysis

In this study, Python (3.8.8.) was used to create various prediction algorithms to predict antidepressant status in patients with B.D. Scikit-learn model was used to develop prediction models of Random Forest (R.F.) and Neural Networks (N.N.)^[8]. There was no missing value.

2.3. Machine Learning Models

2.3.1. Random Forest Model

R.F. model was used to predict antidepressant status. Many researchers commonly use R.F. model to create prediction models related to psychiatry^[9]. On the other hand, it may not be a great selection for problems where interpretability is crucial.

2.3.2. Neural Networks Model

The NN ML model was used to predict antidepressant status. NN ML model was used in the fields of psychology^[10], psychiatry^[10], and neurology^[11].

2.4. Psychological Tests to Predict Antidepressant Status

2.4.1. Childhood Trauma Questionnaire

This study used the Childhood Trauma Questionnaire (CTQ) to determine childhood trauma (C.T.) symptoms. Subscales of CTQ were determined according to emotional abuse, physical abuse, sexual abuse, and emotional neglect.

2.4.2. Zanarini Bipolar Disorder Scale (ZAN-BPD)

This study aimed to assess the several properties of the Zanarini Rating Scale for Borderline Personality Disorder (ZAN-BPD), the clinician-administered scale for measuring the change in DSM-IV borderline pathology^[12]. The B.D. The scale was used to diagnose patients with B.D. ZAN-BPD is a scale for assessing change in borderline pathology^[12].

The scale may also be useful in research, where it can be used to identify subgroups of individuals with B.D. who may benefit from interventions. In this study, patients were diagnosed according to the ZAN-BPD scale.

3. Results

3.1. Machine Learning Models Used in this Study

In this study, machine learning (ML) models of Random Forest (R.F.) and Neural Networks (N.N.) were used to predict antidepressant status. Table 3 and Table 4 include accuracy, precision, recall, and F1 score.

3.1.1. Random Forest Machine Learning Prediction Model

As shown in the confusion matrix (Table 1) R.F. model predicted antidepressant status with an accuracy of 67%.

3.1.2 Neural Networks Machine Learning Prediction Model

As shown in the confusion matrix (Table 2), NN ML model predicted antidepressant status with an accuracy of 50%.

3.2. Descriptive Statistics

In this study, the mean age of all participants was "35.75". Among the patients on antidepressants, the mean age was "35.2". Among the patients who are not on antidepressants, the mean age was "37.4".

4. Discussion

Overall, we have found several main findings, (1) antidepressant status can be predicted in patients with bipolar disorder (B.D.) with parameters related to the severity of childhood trauma (C.T.) symptoms and severity of B.D. symptoms. (2) In detail, Random Forest (R.F.) machine learning (ML) model predicted antidepressant status with an accuracy of 67% (Area Under Curve (AUC):100%) (3) The most critical parameters that predict antidepressant status were Childhood Trauma Questionnaire (CTQ) sexual abuse, CTQ physical abuse, CTQ emotional neglect, and CTQ emotional abuse respectively according to R.F. model. Furthermore, the Neural networks (N.N.) ML model predicted antidepressant status with an accuracy of 50% (AUC:50%). Also, according to the NN ML model, the most predictive factors were CTQ sexual abuse, Zanzarini subscale 3, CTQ emotional neglect, Zanzarini subscale 1, and Zanzarini subscale 5, respectively.

Overall, trauma-related symptoms were more predictive than the severity of B.D. symptoms. Especially sexual trauma was the most predictive factor according to both N.N. and R.F. models. To our best knowledge, no previous study predicts antidepressant prescription status in patients with B.D. using novel ML methods such as N.N. and R.F. Besides, the main confounding factors in this study were age and gender. Moreover, the antidepressant type was one of the confounding factors as, according to the literature, serotonin reuptake inhibitors may have lower rates of manic switch than tricyclic antidepressants^[13].

4.1. The relationship between Bipolar Disorder and Trauma

C.T.s are associated with higher attachment-related anxiety^[14]. A study mentioned the impact of environmental determinants on the B.D. such as prenatal and early lifespan-related factors^[15]. Therefore, the findings supported the role of trauma history as a risk factor for poor course in B.D.^[16].

The findings of another study suggest a relationship between psychosocial adversity at an earlier age and depressive mood in B.D.^[17]. Despite these findings, the relationship between B.D. and trauma is complex and not fully understood. It is likely that there are multiple factors, including genetic, environmental, and psychological factors, that contribute to the development and course of B.D.

4.2. Side Effects of Antidepressants Use

Several side effects of antidepressants related to metabolic, sexual, cardiological, and psychological were mentioned in the literature. Side effects of antidepressants include addiction, while some antidepressants may have a clinical liability to cause dependence^[18]. Furthermore, they have limited short-term efficacy in some depressive disorders, such as acute B.D.^[19]. A different study found that 14% of these individuals taking A.D.s experience AD-associated mania within a few weeks of treatment^[20].

Another study suggests that antidepressant use in combining it with mood stabilizers may not be adequate in preventing switches^[21]. Besides, antioxidant venlafaxine is associated with weight gain^[22], cardiac^[23], and gastrointestinal side effects^[24]. In summary, antidepressants can be a useful tool in treating mental health, it is crucial to measure the potential benefits of medication use.

4.3. Antidepressant Use Status and Childhood Trauma Questionnaire

C.T.s and stressful childhood experiences may have a role in various psychological problems, including schizophrenia^[25], B.D.^[26], depression^[27], and anxiety^[28].

Epigenetics may provide insight into the pathology of major depression^[29].

Antidepressants can cause side effects on the central nervous system^[30].

Another study aimed to develop models to identify individuals at high risk for transition from a diagnosis of depressive disorder to B.D.^[31]. According to one study, C.T. can predict the severity of depression, while the effect of C.T. on depression status was mediated by dysfunctional attitude^[32]. Furthermore, another study found that genetic factors have failed to predict phenotype, and polymorphisms have been shown to moderate the impact of environmental adversity on depression^[33]. Considering the previous literature, C.T. may impact BD-related symptoms and thus affect the decision to prescribe antidepressants in patients with B.D. It is crucial for healthcare providers to know the potential impact of childhood trauma on psychology.

4.4. Suggestions for Further Studies

Further studies should investigate antidepressant status in a larger sample. Moreover, it is crucial to measure stress and trauma-related symptoms in childhood using more advanced methods such as brain imaging. It is important to validate predictive models in diverse populations to ensure that they are generalizable across different patient populations.

4.5. Limitations

Polypharmacy was one of the major limitations, as most patients were also on antipsychotics. Besides, their age and gender were heterogeneous. Thereby, this sample cannot represent general patients with B.D. In addition, the small sample size was one of the study's significant limitations. In addition, prediction models may be impacted by selection bias or measurement bias.

Tables and Figures

Table

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Table 3. Accuracy, Precision, Recall, and F1 score (Neural Networks)

	Precision	Recall	F1-score
0	50	33	40
1	50	67	57
Macro avg	50	50	49
Weighted average	50	50	49

Table 4. Accuracy, Precision, Recall, and F1 score (Random Forest)

	Precision	Recall	F1-score
0	0	0	0
1	67	100	80
Macro average	33	50	40
	44	67	53

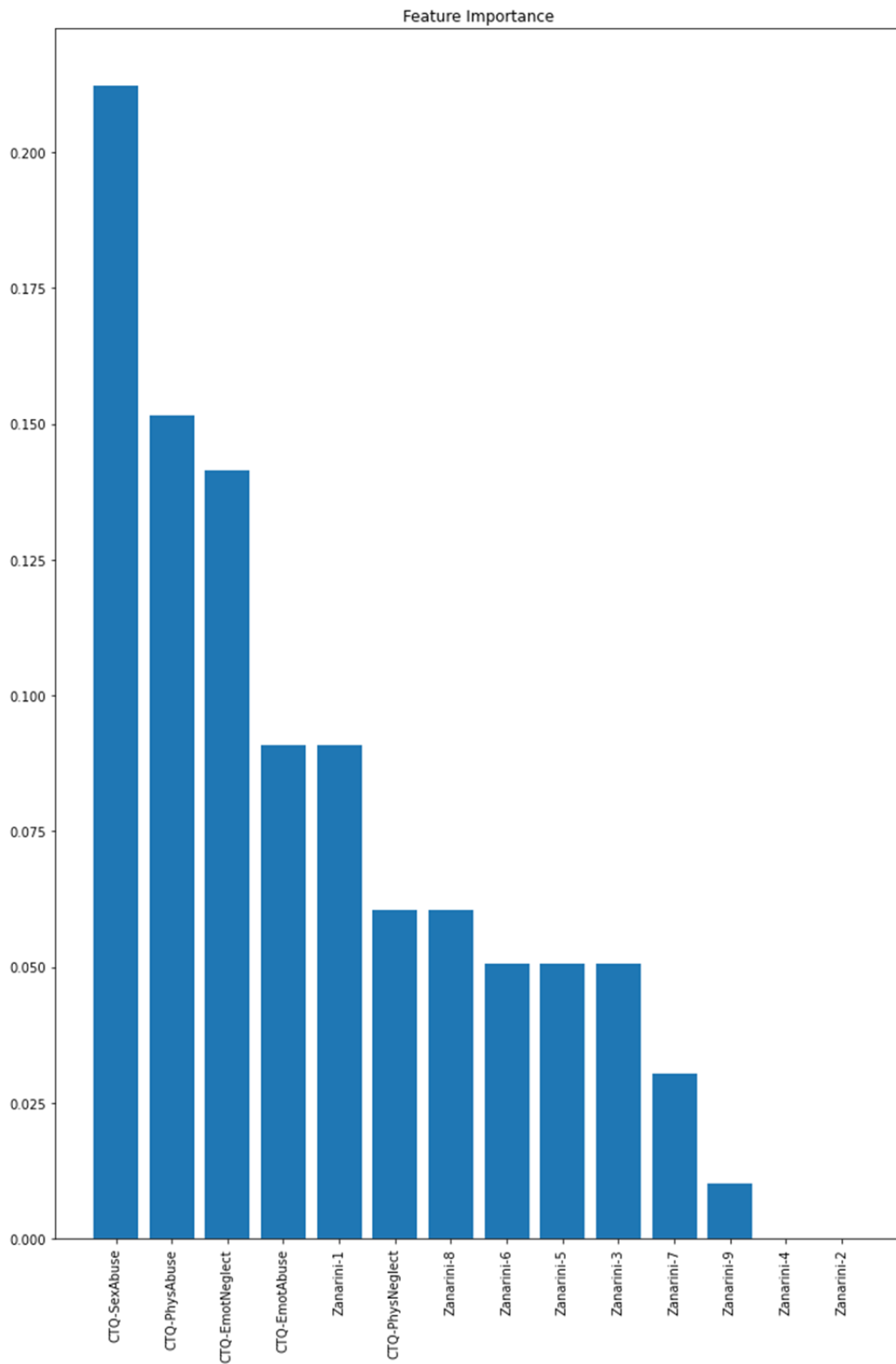


Figure 1. Feature Importances associated with Random Forest

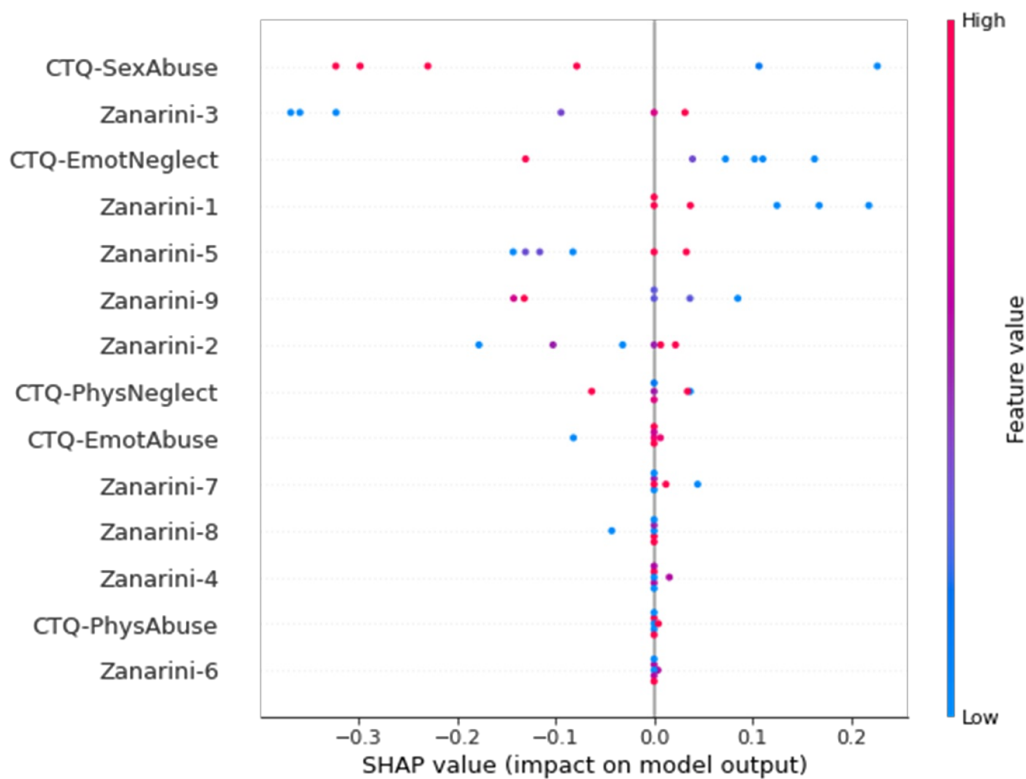


Figure 2. Feature Importances associated with Neural Networks

Statements and Declarations

Ethical Approval

As mentioned in the previous study, ethical approval was obtained from the Lothian National Health Service Research Ethics Committee (09/S1101/49). All participants provided written informed consent before participating^[7].

Conflicts of Interest

In this study, there is no conflict of interest to state.

Authors Contributions

K.U. designed and wrote the manuscript and is the only author of the study.

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There is no funding to report.

Data Availability Statement

This data was obtained from the OpenfMRI database. Its accession number is ds000214. The previous study using this data was supported by a Scottish Senior Clinical Fellowship to Jeremy Hall.

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