Immunological Responses and Drug-Ligand Interactions in Predicting Binding Affinity of the Drug for ADHD Treatment Using Big Data-Driven Modified Extreme Gradient Boosting Model

Ramakrishnan Varadharajan[1*], P. Anbalagan[2], M.S.Saravanan[3]

[1]Research Scholar, Department of Computer Science and Engineering, Annamalai University, Chidambaram, Tamil Nadu. India. Pincode: 608002, Email: vramki2007@gmail.com
[2]Assistant Professor, Department of Computer Science and Engineering, Annamalai University, Chidambaram, Tamil Nadu. India. Pincode: 608002.
[3]Professor, Department of Computer Science and Engineering, Saveetha School of Engineering, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai, Tamilnadu, India.
*Corresponding Author

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ABSTRACT
Attention Deficit Hyperactivity Disorder (ADHD) affects both adults and children. It is a neuro-developmental illness that requires drug treatment to assess the degree of immune reactions and drug-ligand interactions with human body cells to treat ADHD in both adult and child populations. We suggest Modified Extreme Gradient Boosting (M-XGBoost) to determine the degree of drug ligand interactions with human body cells and immunological reactions to treat the ADHD brain condition. M-XGBoost, a powerful and popular gradient-boosting technique, has the capacity to estimate binding affinities. We start by compiling an extensive dataset of pharmacological molecules and how they interact with cells in the human body. To ensure consistency and dependability, this dataset undergoes thorough preparation, which includes procedures for data cleaning and normalization. M-XGBoost is used to produce binding affinity scores, which are used to predict immunological responses. These ratings work as a quantifiable indicator of how a therapeutic molecule interacts with its intended target cells, offering insightful information about the potential effectiveness of various substances for the treatment of ADHD. The selected medication candidates' immunological reactions can be predicted using the suggested M-XGBoost machine learning model. Using this prediction model, we could find medications that interact with the target cells and result in a positive immunological reaction in the patient's body.

Keywords: Attention Deficit Hyperactivity Disorder (ADHD), immunological responses, scoring and ranking, binding affinity, Modified Extreme Gradient Boosting (M- XGBoost).

1. INTRODUCTION

Attention Deficit Hyperactivity Disorder (ADHD) is a common neurodevelopment condition [1] illustrated by chronic patterns of hyperactivity, inattention, and impulsivity that impair both daily functioning and quality of life [2]. Although it is connected to childhood, it can last throughout adolescence and maturity, posing a lifetime problem. Considering that ADHD can affect anybody, regardless of gender, color, or socioeconomic class, a thorough understanding of its causes, clinical effects, and available treatments is vital. ADHD has a complex etiology that includes complex interactions between genetic [3], environmental, and neurobiological variables [4]. There is a significant neurological foundation for the disease, according to genetic studies that have highlighted the possible involvement of numerous genes linked to the control of the dopamine and norepinephrine pathways [5]. A higher chance of developing ADHD has been related to prenatal and perinatal risk factors, including mother smoking, alcohol use and exposure to environmental pollutants. The prefrontal cortex, striatum and cerebellum, in particular, have shown structural and functional abnormalities in neuroan atomical and neuro imaging investigations, highlighting the complex neurological basis of ADHD [6].

ADHD manifests clinically as a variety of symptoms that fall into three basic categories: inattentive, hyperactive-impulsive and mixed. People who tend to be hyperactive-impulsive suffer from excessive motor activity, restlessness and impulsivity, whereas people who tend to be predominantly inattentive have difficulty sustaining attention, focusing, or organizing work [7]. The mixed subtype manifests with a

mix of inattentive and hyperactive-impulsive symptoms, leading to a variety of problematic behavioral manifestations that impede scholastic, social, and vocational activities. Amphetamines and methylphenidate are two common psycho-stimulant drugs used to treat ADHD [7], [8]. These drugs work by altering the levels of neurotransmitters in the brain. Despite their success in treating the symptoms of ADHD, these drugs have several side effects and dangers, such as changes in immunological function and interactions with other endogenous ligands and exogenous chemicals [9]. To maximize the effectiveness and safety of ADHD medication, it is essential to comprehend the complex processes behind immune reactions and drug-ligand interactions [9], [10]. M-XGBoost is a potential computational method presented in this article for assessing the complex drug-ligand interactions with human body cells and their immune responses in the context of treating ADHD. The foundations of M-XGBoost are built by this sophisticated machine learning method, which includes adjustments made to handle the intricacies of immune system dynamics and neuropharmacological interactions.

Article remains are grouped as follows: Our relevant research is summarized in section two. The third part gives extensive instructions for data collection, preprocessing and the proposed model. Part four examines the findings and efficiency of the proposed approach. The report finishes with a summary and research suggestions.

2. LITERATURE REVIEW

The study used an algorithm with deep learning to estimate missing data in ADHD rating scales and evaluated the imputed dataset's (i.e., the data generated by the imputation process, which replaced the original missing values) ability to distinguish between adolescent patients and healthy controls [9], [10], [11]. The purpose of the research was to create a machine learning model that could distinguish between people with ADHD and healthy controls based on their Event-Related Potentials (ERPs), which were extracted from their electroencephalograms (EEGs) while they performed an auditory oddball task [12]. The research examined the relationship between neural flexibility and the severity of attention deficit hyperactivity disorder in children [12]. To identify children with ADHD from those with TDC and to evaluate the severity of their symptoms, we used machine learning techniques for neural flexibility estimations [9]. They postulated that it would discriminate groups and predict symptom severity, with children with ADHD showing less neural flexibility than that of TDC.

The study was to inform doctors on the pharmacology and mechanisms of action differences between amphetamine and methylphenidate to better treat ADHD patients who can have co-occurring mental issues [13]. The study examined the neurobiology of ADHD utilizing imaging genetics techniques, concentrating on functional and structural alterations in the ADHD brain and their relationships to complex chromosomal variations [14]. They discuss the genetic variations thought to be connected to the emergence of ADHD and how these can impact the functioning of the brain power circuits and associated performance. The review paper provided an overview of PET investigations performed on adult ADHD patients [15], [16], [17] . Although dopamine, serotonin and norepinephrine function abnormalities have been linked to ADHD, our research revealed that PET investigations of ADHD individuals have not revealed any distinctive results. Prior PET research on the ligands associated with central dopaminergic transmission in ADHD patients revealed altered basal ganglia binding of dopamine markers.[14], [18]

The study used the ADHD 2000 dataset to examine methods for diagnosing ADHD using a number of well-established machine learning techniques, such as SVM and neural network models, as well as the neurology of the disorder [19]. An SVM model is used in this study to conduct multiclass classification on phenotypic data [20]. The paper provides a deep-learning model with a classifier and a feature extraction for spatiotemporal data. Using the nested residual convolutional denoising autoencoder (NRCDAE), three-dimensional spatial features are extracted while reducing the spatial dimension of rs-fMRI [7]. After that, the 3D convolutional Gated Recurrent Unit (GRU) is used to extract spatial and temporal data simultaneously.

3. METHODOLOGY

We begin by assembling a large collection of pharmacological compounds and their interactions with human body cells. This dataset receives careful preparation, which includes steps for data cleansing and normalization to guarantee consistency and reliability. Binding affinity evaluations from M-XGBoost are used to predict immunological responses.

3.1 Data preparation

The methodology involves creating a synthetic dataset for ADHD medications Adderall XR and Concerta. It defines age groups, genders and drug attributes that generate 2000 simulated patient entries. A set of dosage rules is established for each drug, specifying recommended dosages based on age groups. This

approach enables the creation of a dataset with patient characteristics and corresponding drug dosage rules, facilitating research into the relationship between patient attributes and medication dosages in the context of ADHD treatment. Figure 1 illustrates the flow of our suggested approach.

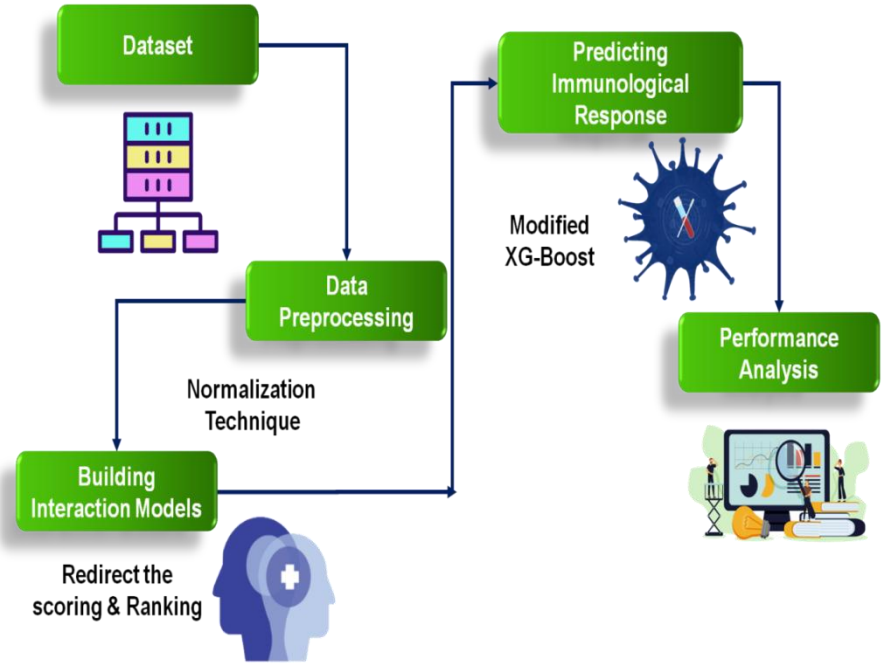

Figure 1: Architecture of our suggested approach

3.2 Preprocessing using normalization

In this investigation, we make use of categorical data that is transformed into numerical form during the data preparation step known as label encoding. Data that depicts traits or categorizes them is referred to as categorical data and it is provided in non-numeric form. Each distinct category in the data is given a special numerical value using label encoding. Since many machine learning algorithms are built to cope with numerical data, this method enables them to comprehend the data. The following equation can be used to illustrate label encoding: Assume that we have a categorical variable X with N distinct categories, denoted as $x1, x2, \dots, xn$. Following label encoding, a distinct integer value is given to each category, resulting in:

$$X: \{x_1, x_2, \dots, x_n\} \rightarrow \{0,1, \dots, n-1\} \quad (1)$$

The equation states that each distinct category x_i is mapped to an associated integer value $i-1$. This enables the numerical representation of the categorical data, which is appropriate for analysis by machine learning algorithms. But it's crucial to remember that label encoding acts as an algorithmic representation for the categories. It does not provide the categories any intrinsic meaning or order. Instead, the assigned number values are arbitrary.

3.3 M-XGBoost Analysis of Drug-Ligand Interactions and Immunological Responses in ADHD Treatment

The fast extraction of intricate characteristics from intricate datasets is made possible by M-XGBoost, enabling a thorough comprehension of the precise molecular and cellular mechanisms behind drug interactions with human body cells. M-XGBoost facilitates the discovery of crucial molecular fingerprints that affect treatment results by identifying subtle differences in receptor-ligand binding patterns and immune cell responses. When treating ADHD, M-XGBoost is used to examine the complex interactions between drugs and ligands in human body cells and their immune reactions. It has been demonstrated that Friedman's M-XGBoost model is efficient. Tree boosting is a very powerful and commonly used machine learning technique and one of the most well-known gradient boosting methods. In this research, a scalable end-to-end tree-boosting method called M-XGBoost has been used to treat and discover the Drug-Ligand Interactions and Immunological Responses. Data scientists utilize M-XGBoost to solve challenging machine learning problems at the cutting edge. Figure 2 shows the architecture of M-XGBoost.

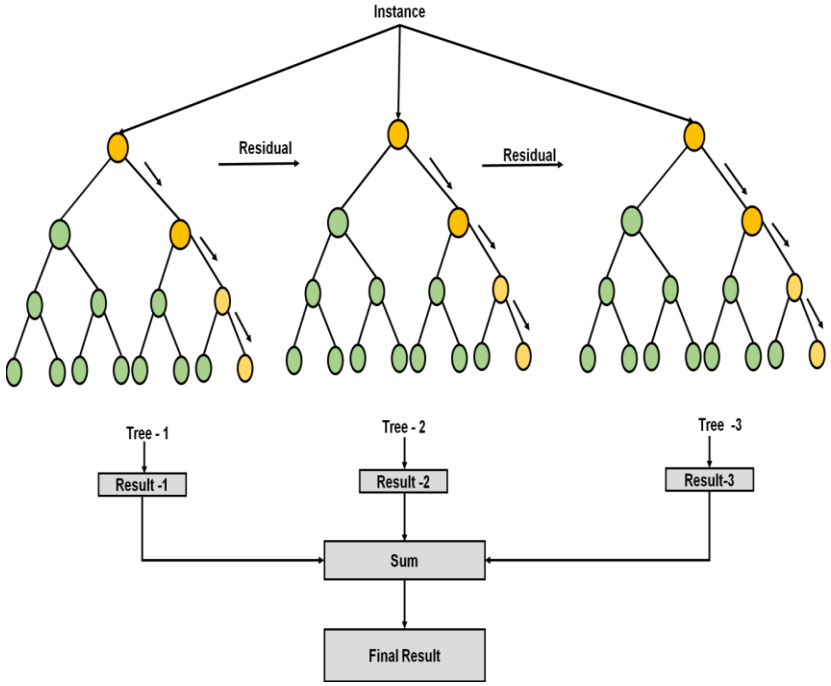

Figure 2: Architecture of M-XGBoost

To predict the outcome of a dataset with M samples and b features, a tree ensemble model applies R additive functions (R trees) features$T = \{(y_j, x_j)\}(|T| = M, y_j \in R^b, x_j \in R)$. Where $L = \{l(y) = \omega_{o(y)}(o: R^b \to D, \omega \in R^D)$ refers to the field of regression trees. Here, o denotes the layout of every tree that translates a case to the relevant leaf index. D is the total amount of leaves in the tree. For any tree that maps a given instance to its corresponding leaf index, o represents the tree's structure. The number of leaves on the tree is denoted by D. Each $l_r$represents a unique tree with a certain o and leaf weights. Each event is assigned a leaf based on the decision criteria in the trees and the final prediction is calculated by summing the weights in the appropriate leaves. By minimizing the subsequent aim in equation (3), we can discover the collection of functions used in the model.

$$\hat{x}_j = \sum_{r=1}^{R} \quad l_r(y_j), l_r \in L \tag{2}$$

$$F(\emptyset) = \sum_{j=1}^{M} \quad loss(x_j, \hat{x}_j) + \sum_{r=1}^{R} \quad \Omega(l_r), \tag{3}$$

Where the distinct convex training loss in equation (3)'s first component represents the distinction between the forecast $\hat{x}_j$ and the goal x_j. The trees' intricacy makes up the second phrase. According to the following equation, the model complexity $\Omega(l_r)$ equals

$$\Omega(l_r) = \gamma^D + \frac{1}{2}\lambda \sum_{i=1}^{D} \quad \|\omega_i\|^2, \tag{4}$$

Where D is the Tree's leaf count, λ stands for the normalization weight, γ is the minimal loss reduction and $\|\omega_i\|$ is the score for the associated leaf. Equation (5) defines the Tree $l_r(y)$,

$$l_r(y) = \omega_o(y), \omega \in R^D, o: R^t \to 1,2, \dots, D. \tag{5}$$

Traditional Euclidean-space optimization techniques are ineffective for the tree ensemble model in equation (3) because it has functioned as parameters. Rather, an additive training approach is used to train the model. Formally, if $\hat{x}_j^{(d)}$ is the forecast of the jth training sample at the dth repetition, we must add l_d to minimize the following objective:

$$F^{(d)} = \sum_{j=1}^{M} \quad loss(x_j, \hat{x}_j^{(d-1)} + l_d(y_j)) + \Omega(l_d) \tag{6}$$

l_dThat contributes the most to better models is included in the framework of the models. Using Taylor's expansion, we can get a better approximation of the regularization term by embedding it in equations (4) and (6).

$$\tilde{F}^{(d)} \approx \sum_{j=1}^{M} \quad [loss(x_j, \hat{x}_j^{(d-1)}) + s_j l_d(y_j) + \frac{1}{2} z_j l_d^2(y_j)] + \gamma^D + \frac{1}{2}\lambda \sum_{i=1}^{D} \quad \|\omega_i\|^2, \tag{7}$$

Where $s_j = \partial loss(x_j, \hat{x}_j^{(d-1)} \frac{)}{\partial \hat{x}^{(d-1)},} z_j = \partial^2(x_j, \hat{x}_j^{(d-1)} \frac{)}{\partial \hat{x}^{(d-1)},}$ are the first second-order gradient statistics on the loss function. In leaf, i, define $J_i = \{j|o(y_j = i)\}$ as the instance set. The following is a revised version of equation (7).

$$\tilde{F}^{(d)} \approx \sum_{i=1}^{D} \quad \left[\left(\sum_{j \epsilon J_i} \quad s_j\right)\omega_j + \frac{1}{2}\left(\sum_{j \epsilon J_i} \quad z_j + \lambda\right)\omega_i^2\right] + \gamma^D \tag{8}$$

The optimal weight u_i^* of leaf i can be calculated given a fixed decision rule o(y) by setting the initial-order components of $\tilde{F}^{(d)}$ to zero, yielding the following expression:

$$u_i^* = -\frac{S_i}{Z_i+\lambda}, \quad (9)$$

$S_i = \sum_{j\epsilon J_i} s_j$ and $Z_i = \sum_{j\epsilon J_i} z_j$. Respectively. The corresponding ideal value is determined as follows.

$$\tilde{F}^{(d)}(o) = -\frac{1}{2}\sum_{i=1}^{D} \frac{S_i^2}{Z_i+\lambda} + \gamma^D \quad (10)$$

The optimal XGBoost classifier is obtained with the sequential optimization at each scenario. We anticipate gaining a thorough grasp of the complex biochemical pathways and immune regulatory mechanisms at play via the use of M-XGBoost in the exploration of drug-ligand interactions and immunological responses in the treatment of ADHD. This integrated computational method has the power to transform the design of precision-based therapeutic interventions, opening the door to individualized and focused therapies that maximize the effectiveness and security of ADHD medicines.

4. RESULTS

The M-XGBoost networks in Intel need 40 GB of RAM and a Core i7 processor. The suggested model was developed in Python and trained using a graphics processing unit (GPU) from NVIDIA. We conducted a thorough analysis of other approaches to determine the advantages of our strategy compared to traditional and cutting-edge approaches in our study, investigating the degree of drug-ligand interactions and immunological responses in ADHD treatment using Modified Extreme Gradient Boosting (M-XGBoost). Various computational and experimental approaches, such as KNN, SVM, RF, ANN, and DT, were compared using important metrics, including accuracy, sensitivity, specificity, and AUC.

Accuracy is defined as the proportion of accurately categorized classes to the overall population, which is equal to:

$$\text{Accuracy} = \frac{TP+TN}{TP+TN+FP+FN} \times 100 \quad (11)$$

Table 1: Accuracy comparison with existing methods

Methods	Accuracy (%)
D.T [19]	92.1
ANN [19]	90.0
SVM [19]	89.2
M-XGBoost [Proposed]	99.4

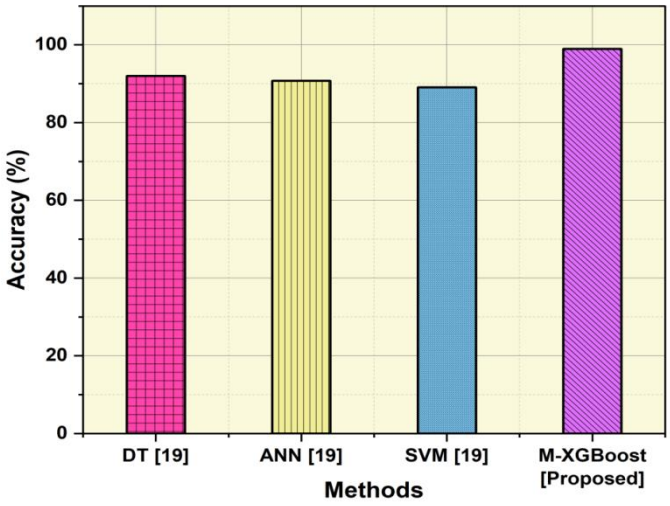

Figure 3: Comparison of accuracy between our proposed and conventional methods

This statistic assesses a model's overall effectiveness in forecasting both positive and negative events. Our evaluation revealed that in terms of accuracy in Table 1. DT achieved 92.1%, ANN attained 90.0% and SVM demonstrated 89.2%. Our novel approach, M-XGBoost, outperformed these conventional methods with a remarkable accuracy of 99.4%, as highlighted in Figure 3.

Sensitivity is defined as the fraction of true positives that fall into the correct category out of the total number of true positives and equal to:

$$\text{Sensitivity} = \frac{\text{TP}}{\text{TP}+\text{FN}} \times 100 \quad (12)$$

Table 2: Sensitivity comparison with existing methods

Methods	Sensitivity (%)
D.T [19]	89.0
ANN [19]	90.5
SVM [19]	88.5
M-XGBoost [Proposed]	98.0

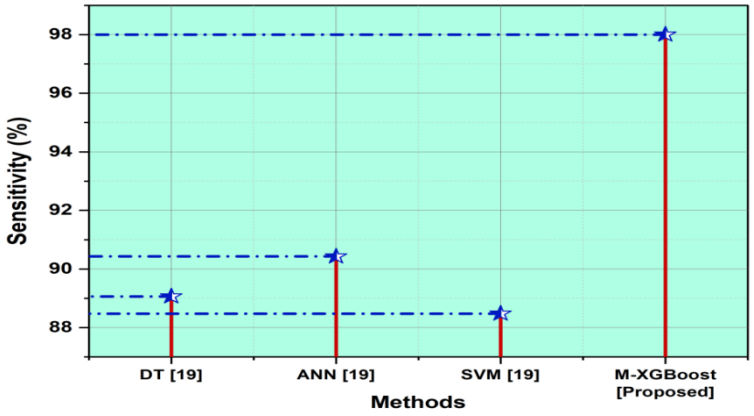

Figure 4: Comparison of Sensitivity between our proposed and conventional methods

Figure 4 shows the percentage of real positive instances detected by the model. Our study found that DT obtained 89.0%, ANN reached 90.5% and SVM achieved 88.5% of sensitivity. Our suggested strategy, as shown in Table 2. The M-XGBoost, surpassed all standard approaches with a stunning sensitivity of 98.0%.

Specificity is the ratio of the overall value of categorized negative classes to the overall value of negative classes and is equal to:

$$\text{Specificity} = \frac{\text{TP}}{\text{TP}+\text{FP}} \times 100 \quad (13)$$

Table 3: Specificity comparison with existing methods

Methods	Sensitivity (%)
D.T [19]	97.4
ANN [19]	96.8
SVM [19]	90.6
M-XGBoost [Proposed]	99.5

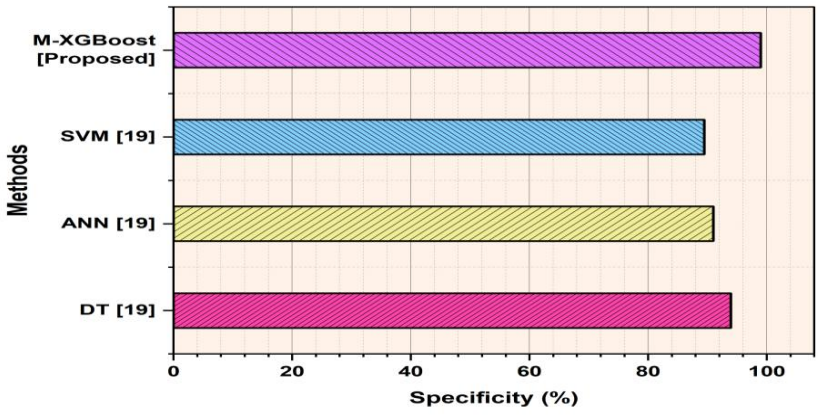

Figure 5: Comparison of specificity between our proposed and conventional methods

In terms of specificity mentioned in Table 3. The DT reached 97.4%, ANN achieved 96.8% and SVM displayed 90.6%. Our proposed approach, M-XGBoost, beat all standard approaches with the highest specificity of 99.5%, as shown in Figure 5. M-XGBoost provides accurate identification of treatment-specific effects while limiting the possibility of false-positive predictions, hence improving analytical accuracy in the context of ADHD medication.

AUC measures a model's overall effectiveness in differentiating between positive and negative classes, with a higher AUC value as given in Table 4. Suggesting stronger discrimination ability. KNN, SVM, and RF have attained 0.86, 0.91, and 0.94 AUC values, respectively. Comparatively, M-XGBoost obtained a higher AUC value [0.99]. Figure 6 shows its enhanced capacity to discriminate between favorable medication effects and possible immunological concerns in treating ADHD.

Table 4: AUC comparison with existing methods

Methods	Sensitivity (%)
KNN [20]	0.86
SVM [20]	0.91
RF [20]	0.94
M-XGBoost [Proposed]	0.99

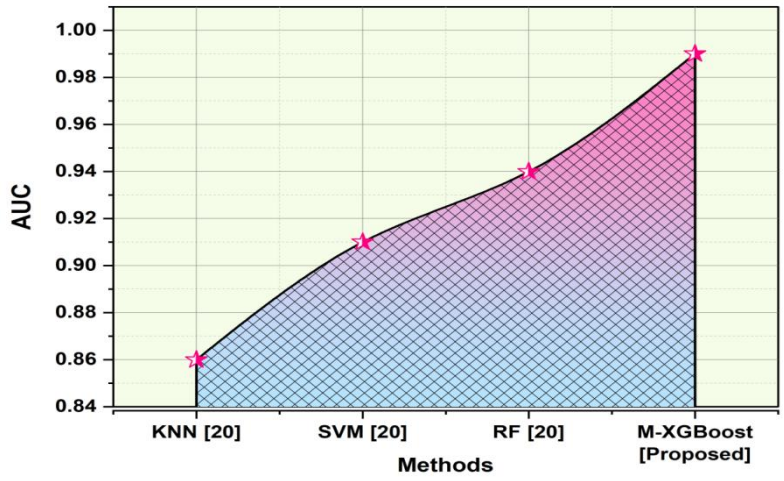

Figure 6: Analysis of AUC

Mean squared Error (MSE)

The MSE provides a statistic that sums together the ratio of the squared variance across the actual results and projected values, a popular statistic for assessing a regression algorithm's effectiveness. It provides a gauge of the actual values that match the model's predictions. The MSE efficiently computes the mean square variance between the actual and expected values. Considering a reduced MSE suggests predictions made by the model have been correlated compared to the actual information, it is indicative of higher accuracy. The MSE must be greatly affected by the presence of significant errors in a small number of data points, as the MSE is vulnerable to outliers in Equation (17).

$$\mathrm{MSE} = \frac{1}{\mathrm{m}}\mathrm{j} = 1\mathrm{m}\left(\mathrm{X_j} - \widehat{\mathrm{X}}_\mathrm{j}\right)^2 \quad (17)$$

M - quantifies the amount of information, X_j - is the value that has been observed for the j-th data point, and $\widehat{X}_j$ - represents the anticipated value for the j-th component of data.

Root Mean Squared Error (RMSE)

As an additional statistic, RMSE is utilized to assess the efficacy of a regression model. It takes the square root to make the metric more understandable and is derived from the MSE. It measures the average magnitude of the errors between expected and actual values in Equation (18).

$$\mathrm{RMSE} = \sqrt{\frac{1}{\mathrm{m}}\mathrm{j} = 1\mathrm{m}\left(\mathrm{X_j} - \widehat{\mathrm{X}}_\mathrm{j}\right)^2} \quad (18)$$

m - Quantifies the amount of information, X_j - is the value that has been observed for the i-th data point, $\widehat{X}_j$ - represents the anticipated value for the ith component of data

To find the most effective model for making accurate predictions, compare their RMSE values or use it as a benchmark. It is critical, though the details of the issue and the data.
MSE and RMSE, two very comparable metrics, shift on considerations like punishing more significant mistakes and the statistic can be understood in the original data units. Both have their place in practice and picking one over the other usually comes down to the needs of the current issue.

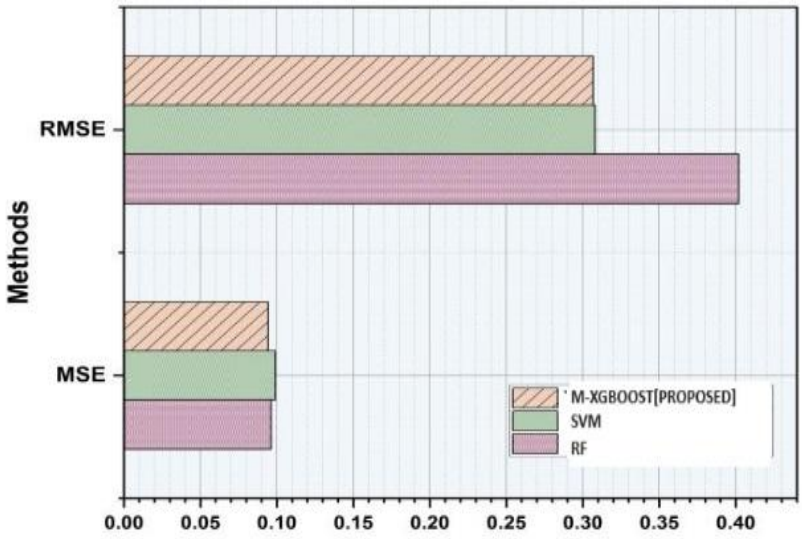

Figure 9: Output for MSE and RMSE

Table 5: MSE and RMSE comparison between existing methods

Methods	RF	SVM	M-XGBOOST [Proposed]
MSE	0.0963	0.099	0.0942
RMSE	0.402	0.308	0.3069

Figure 9 and Table 5 show the output of the existing method with the M-XGBoost method proved MSE and RMSE reached significantly much better than the other one.

5. DISCUSSIONS

The M-XGBoost analysis was successful in illuminating the complex molecular mechanisms underlying the interactions of particular ADHD medications and their corresponding ligands in human brain cells[15] . The model pinpointed crucial structural characteristics and binding preferences that affect how dopaminergic and noradrenergic signaling pathways are modulated, illuminating the precise molecular targets in charge of the therapeutic effects of the drugs . An important development in the field of neuropharmacology is the use of M-XGBoost to assess the interactions between drugs and their ligands as well as immune responses in the context of treating ADHD[15], [16] . The results of our comprehensive study show that M-XGBoost has the potential to be an effective computational framework for deciphering the complex biochemical pathways and immunological dynamics connected to ADHD medication. By combining cutting-edge machine learning algorithms with careful feature creation, M-XGBoost has demonstrated its ability to provide delicate insights into the intricate interplay between medicinal molecules, biological components and immune responses. As a result, it has become simpler to create precision-based therapy approaches that are tailored to the requirements of ADHD patients.

6. CONCLUSIONS

The use of Modified Extreme Gradient Boosting (M-XGBoost) in the evaluation of immune responses and drug-ligand interactions for the treatment of ADHD in adult and pediatric populations marks a significant advancement in the field of neuropharmacology. Our study has shown the potential for accurate and dependable calculation of binding affinities and immunological responses in the context of ADHD treatment by making use of the powerful predictive capabilities of M-XGBoost and utilizing a rich dataset of pharmacological compounds. Our findings show that M-XGBoost has obtained 99 % accuracy, 98 % of

sensitivity, 99% of specificity as well as 0.99 of AUC. The use of M-XGBoost has provided a useful framework for correctly predicting the immunological reactions linked to specific medication candidates, facilitating the discovery of therapeutic molecules that exhibit strong interactions with target cells and elicit favorable immune responses in the body. Practitioners can choose the best pharmacological interventions for people with ADHD by combining clinical assessments and the insights gleaned from M-XGBoost predictions, ensuring a personalized and efficient treatment approach catered to each patient's unique needs. Future studies should include thorough behavioral and cognitive evaluations to examine the overall effects of pharmaceutical therapies on cognitive function, academic performance and social behavior in ADHD patients.

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