Article



# Machine Learning in Detecting Schizophrenia: An Overview

Gurparsad Singh Suri<sup>1</sup>, Gurleen Kaur<sup>1</sup> and Sara Moein<sup>2,\*</sup>

<sup>1</sup>College of Behavioral and Social Sciences, California Baptist University, Riverside, 92504, USA

<sup>2</sup>Center for Innovation in Brain Science, University of Arizona, Tucson, 85721, USA

\*Corresponding Author: Sara Moein. Email: saramoein@arizona.edu

Received: 04 November 2020; Accepted: 09 December 2020

**Abstract:** Schizophrenia (SZ) is a mental heterogeneous psychiatric disorder with unknown cause. Neuroscientists postulate that it is related to brain networks. Recently, scientists applied machine learning (ML) and artificial intelligence for the detection, monitoring, and prognosis of a range of diseases, including SZ, because these techniques show a high performance in discovering an association between disease symptoms and disease. Regions of the brain have significant connections to the symptoms of SZ. ML has the power to detect these associations. ML interests researchers because of its ability to reduce the number of input features when the data are high dimensional. In this paper, an overview of ML models for detecting SZ disorder is provided. Studies are presented that applied magnetic resonance imaging data and physiological signals as input data. ML is utilized to extract significant features for predicting and monitoring SZ. Reviewing a large number of studies shows that a support vector machine, deep neural network, and random forest predict SZ with a high accuracy of 70%–90%. Finally, the collected results show that ML methods provide reliable answers for clinicians when making decisions about SZ patients.

**Keywords:** Support vector machine (SVM); deep neural network (DNN); magnetic resonance imaging (MRI); accuracy; classification; feature

#### 1 Introduction

Schizophrenia (SZ), a debilitating mental disease, affects the thinking and feeling capacities in patients. Currently, there is no cure for SZ; however, methods like machine learning (ML) may help in its early detection, predict behaviors, and slow the decline of brain functioning. There were an estimated 20 million SZ cases across the globe in 2019 [1]. Researchers are challenged to predict SZ from subtle signs. Neuroimaging data is a promising resource in the application of pattern-recognition approaches, supporting clinicians in their decision-making processes. Magnetic resonance imaging (MRI) is another ML resource used to detect SZ [2]. During the onset of SZ, there are multiple abnormalities in cognition and physiological signals, including electroencephalogram (EEG) signals and MRI images. SZ is often diagnosed through clinical examination by psychiatrists. However, it can take up to two years for an accurate diagnosis. ML algorithms may help diagnose SZ in earlier stages [3].



In comparison with traditional methods, ML tools work with high-dimensional data to extract significant features. ML methods detect SZ by finding complex relationships between features, distinguishing between nonlinear associations. Traditional methods are unable to discover these associations. The output change in nonlinear systems is proportional to the change of features. Another advantage of ML models, their learning ability, uses current data (training data) to predict future data output.

There is a growing interest in the application of AI and ML in the field of biological psychiatry [4–7]. Researchers in ML and AI apply mathematical models to extract attributes or features from signals and images to determine associations between the features and the brain state to define if the brain is in a normal state [8]. As a powerful tool to unravel patterns in SZ datasets, ML interests scientists because some ML algorithms can discover nonlinear relationships among features. These, in turn, can predict diseases like SZ and monitor a disease's nonlinear nature. Examples of highly accurate ML methods include the support vector machine (SVM), random forest (RF), Naïve Bayes (NB), artificial neural network (ANN), logistic regression (LR), and deep neural network (DNN) methods.

ML methods have successfully used neuroimaging data to classify cases as healthy controls and SZ, as well as predict an outcome [9,10]. Recently, studies have integrated data to generate rich input data, which has improved the classification of SZ patients from healthy controls [10]. In one study [11], researchers used structural MRI and resting-state functional MRI data from 295 patients with SZ and 45 healthy control samples from five research centers. The following features were extracted from the data: (a) matter volume, (b) white-matter volume, (c) amplitude of low-frequency fluctuation, and (d) regional homogeneity. In addition, the features included two connectome-wide metrics: functional connectivity (FC) matrices and structural covariance matrices. The SVM method was used to classify the data into SZ and healthy control groups. It applied 10-fold cross validation to confirm the results. Better performance is achieved using functional data with an accuracy of 82%. The use of all data (structural and functional) generated the best results, with an accuracy of 90%. This high performance of ML methods versus human decisions is based on mathematical functions in generating connections between features. Therefore, both clinical and non-clinical professionals are interested in applying ML to improve the quality of healthcare in the diagnosis, monitoring, and prognosis of SZ.

In one study [12], authors reported that the treatment of psychopathological patients was predicted with high accuracy by incorporating the ML method through cognitive and electrophysiological data. The study pooled data from comparable cohorts of antipsychotic-naïve in first-episode SZ patients. ML techniques have varying power in predicting the outcome. In ML, the "no free lunch" theorem states there is no algorithm that provides the highest performance for solving all problems. Therefore, researchers must test different ML models to obtain the performance and select the best version after a comparison of accuracy.

There are multiple definitions on ML and related tools. In the following sections, ML tools and review studies are discussed that prove the high performance of ML methods in the prediction, diagnosis, and prognosis of SZ. Finally, studies that have applied ML methods on significant regions of the brain for SZ diagnosis are explored.

## 2 Subgroups of AI

AI has multiple subgroups, including ML, natural language processing (NLP), and computer vision. These subgroups make decisions regarding SZ disorder.

#### 2.1 ML

ML tools are a set of methods based on mathematical functions. These functions use input data to train a model, making it usable for calculating answers to future questions. The trained model predicts the future, generating results for the diagnosis and prognosis of SZ. In other words, there is no explicit rule when

using ML tools to predict answers based on the training process. Training is the process of mathematical calculations to obtain a numerical value (or weight) to make connections between input and output features. Based on the ML model calculation, clinicians can detect the SZ state among other states of the brain.

Supervised learning and unsupervised algorithms are two categories of ML algorithms. In supervised algorithms, an output is associated with each of the input training data. Unsupervised algorithms do not have an output label related to the input data. ML algorithms include Bayesian networks, SVMs, linear regression, RFs, DNNs, and ANNs. The SVM kernel function utilizes nonlinear mapping to separate the data, which makes SVM an accurate method for prediction purposes. A DNN, a kind of ANN, provides high accuracy due to hidden layers within its structure. Therefore, most current studies apply these tools for detecting SZ and other diseases. Research centers have applied ML to detect SZ and predict its symptoms. Indicators of SZ include delusions, hallucinations, and disorganized thinking [13].

#### 2.1.1 Evaluating ML Models

Researchers used multiple evaluation measures to evaluate their proposed intelligent method, including ML algorithms (as listed below). The objective of an AI-based method is to increase the accuracy, precision, recall, and R<sup>2</sup> coefficient and decrease the mean square error (MSE):

$$Accuracy = \frac{correct\ predictions}{all\ predictions},\tag{a}$$

$$Precisions = \frac{true \ positives}{true \ positives \ + \ false \ positives},$$
 (b)

$$Sensitivity = \frac{true \ positives}{true \ positives + false \ negatives},$$
 (c)

$$MSE = \frac{1}{N_{samples}} \sum (Y_{true} - Y_{pred})^2,$$
 (d)

where  $Y_{true}$  is the actual output, and  $Y_{pred}$  the predicted output, and

 $N_{samples}$  is the number of samples,

$$R^{2} = 1 - \sum \frac{\left(Y_{true} - Y_{pred}\right)^{2}}{\left(Y_{true} - \bar{Y}\right)^{2}} \bar{Y} = Average Y_{true}.$$
 (e)

Other evaluation measures of ML models are the receiver operating characteristic (ROC) and area under the curve (AUC). An ROC curve is a graphical tool for evaluating the performance of the ML algorithm when the data are classified into two classes or binary classifications (for example, the exploration of a patient's SZ diagnosis). An ROC curve is obtained based on a false positive and true positive rate, changing the threshold of classification from 0 to 1. AUC is the area under the ROC curve. A larger area signifies a more accurate ML model. When AUC is 0.5, the ML model cannot classify the data and has low performance. When AUC is 1, the classifier has a high accuracy in detecting the classes.

Studies have used AUC to measure performance. The model accuracy is increased when the ML algorithm correctly predicts all the output labels (for example, in the classification of SZ patients and the healthy control group, detecting correct labels for SZ patients and healthy individuals). Precision increases when, among all SZ-predicted patients with class 1, more patients belong to class 1.

Recall or sensitivity increases when a greater number of SZ patients are predicted correctly. For example, 300 patients are predicted by the ML algorithm. One-hundred and fifty are SZ patients and

150 are normal. If the model predicted that 100 SZ patients from 300 and 70 are correctly SZ-predicted, the precision would be 70/100 = 0.7. The recall would be  $70/150 \sim 0.46$ .

## 2.1.2 K-fold Cross Validation

K-fold cross validation is a validation technique used to avoid overfitting or underfitting the model. In this method, the data are split into K non-overlapping subcategories. (K-1) categories are used for training the model; one remaining subcategory is used for validation. This process is repeated K times. The final performance of the model is based on averaging the performance from each validation set.

ML algorithms use K-fold cross validation to generalize their performance. In one study [14], researchers trained several classification models using 5-fold cross validation for the generalization of an error. Researchers separated the data into 80% training and 20% validation. Next, the precision, recall, accuracy, and F1 score on the validation set are calculated. The following subsection introduces powerful ML methods applied in SZ diagnosis and monitoring.

#### 2.1.3 LR

LR is a popular algorithm for the classification of binary problems. The binary classification aims to predict if a patient has SZ. LR uses the sigmoid function to obtain the probability of an occurrence per event (for example, obtaining the probability of a patient having SZ). LR has been used for the diagnosis of SZ in multiple studies. In one study [15], researchers used LR to select significant factors in the recovery stages of SZ patients among 75 Hong Kong adults. Data were collected on socio-demographic factors, recovery stages, and elements associated with recovery. LR could detect stage 3 recovery, "living with disability," with an accuracy of 75.45%, and stage 4, "living beyond disability," with a classification accuracy of 75.50%. LR could detect that age plays a meaningful role in distinguishing recovery stages.

#### 2.1.4 NB

NB is a supervised classifier that works based on Bayes theory. The basic assumption of NB is the independence of features. An NB classifier is a classic ML model; however, it provides significant performance in classification problems. In one study [16], data for 48 SZ patients and 24 healthy controls were collected and classified by NB. The dataset's features included age, sex, full-scale intelligence quotient, positive and negative syndrome scale, and Wisconsin Card Sorting Test. The NB model could detect SZ with an accuracy of 67%.

## 2.1.5 SVM

A SVM is a popular algorithm for nonlinear transformation of input data based on kernel functions. There are several types of kernel functions, e.g., Gaussian radial basis, linear kernel, and polynomial functions. A SVM was used in many studies for detecting SZ. In one study [17], authors used MRI data collected from structural MRI scans. This was based on whole-brain gray-matter densities estimated using voxel-based morphometry of 212 individuals in SZ and healthy control categories. The cross validation technique was used to validate the results. The obtained accuracy for trained data was 86% for 127 individuals and 83% for the validation set with 85 individuals. The high accuracy of a SVM for classification of MRI data to distinguish SZ patients from normal individuals shows high performance of ML methods for detecting nonlinear associations between input and output data. This showcases that it can effectively handle high-dimensional data as well avoid overfitting.

### 2.1.6 RF

RF, an ensemble ML model, is composed of multiple weak decision trees. Each decision tree works with two-thirds of the input data and includes a subset of features. The final prediction result from RF is based on averaging the results from all the trees. RF is a powerful ML algorithm that handles missing or duplicate data, as well as avoiding underfitting or overfitting. In addition, RF can obtain importance scores for each feature

in the features set. Multiple studies have applied RF in detecting significant features in the detection and prediction of SZ.

In one study [18], researchers applied EEG signals to generate datasets and predict SZ and health controls with RF. The EEG signals were obtained from an online resource [19]. The dataset contained 32 health controls and 49 SZ patients. The dataset contained event-related potentials (ERPs) from basic sensory tasks. The data were collected from 64 EEG channels; however, only ERP averages from nine electrodes (Fz, FCz, Cz, FC3, FC4, C3, C4, CP3, and CP4) were used in the dataset for training the RF.

An EEG time series may contain four components:

- a) Level: Baseline for a signal (when it is a straight line)
- b) Trend: May linearly increase or decrease over time
- c) Seasonality: Repeating pattern of a series over time
- d) Irregularity: Variations in the series due to an unpredictable parameter and a pattern that does not repeat

Based on these components, the dataset is generated. Gender, age, and education are added to the feature set, and the RF is trained. The predicted outcome's accuracy is 74%.

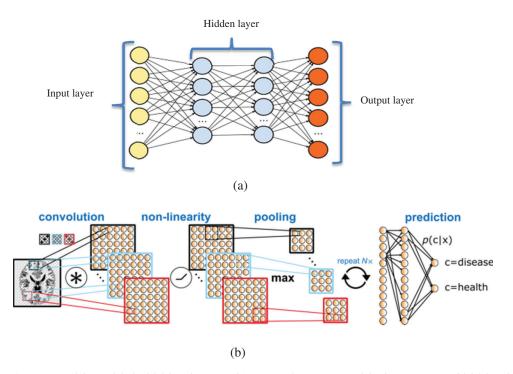
#### 2.1.7 DNN

An ANN is a powerful ML method for solving problems, especially in SZ. An ANN is an analogy of the human brain with multiple connections between computation nodes. Each ANN has three layers: (a) input, (b) hidden, and (c) output. An artificial neuron, a mathematical unit for a nonlinear transformation, takes the weighted summation of nodes in the input layer and feeds the summation to the activation function [sigmoid, rectified linear unit (ReLU), and hyperbolic tangent]. The simplest ANN is a feedforward neural network.

A DNN is a complicated ANN with more than one hidden layer. These layers are responsible for discovering nonlinear relationships between input and output data. Researchers have used DNNs in various image processing tasks, including MRI analysis and the prediction of mental disease based on MRI images. A convolutional neural network (CNN), a kind of DNN, has been widely used for detecting mental health disorders [4–7]. The general shapes of DNNs and CNNs are introduced in Fig. 1, which are extracted from [20].

Some articles proposed a CNN as a useful tool for the analysis of mental conditions based on EEG signals. Acharya et al. [21] applied a CNN for feature extraction from EEG signals, finding that EEG signals collected from the right hemisphere of the human brain are distinctive for detecting depression. A CNN is suitable for a diagnosis based on EEG signals. The raw signals are corrupted with environmental noises, which makes them unsuitable for prediction purposes. Therefore, pre-processing steps like data-transformation and -interpolation techniques are required to remove noise. In a CNN, the convolutional layers are responsible for the noise-removal process. This attribute makes it an interesting technique for researchers to use to detect diseases, including SZ.

Multiple studies show the superior performance of DNNs for detecting SZ based on MRI data with acceptable accuracy (68.1%–85.0%) [21–24]. In one study [22], higher accuracy was achieved using a deep belief network compared with traditional ML algorithms. Using a DNN, SZ was identified in the study through five multicenter datasets of structural MRI. The results showed the brain region that contributed to the decisional process of DNN. A deep-learning algorithm was trained to identify SZ based on five multicenter datasets of structural MRI results. Researchers validated their results using the single-center clinical validation set. Their classification results show that the right-hand region of the brain provides higher accuracy for predicting SZ. The DNN could predict SZ with AUCs of 70%–90% for validation datasets. Tab. 1 shows studies that applied ML algorithms to the detection of SZ disorders.



**Figure 1:** (a): DNN with multiple hidden layers; (b): CNN is a DNN with three types of hidden layers: (1) convolution layer for generating the feature map from MRI images; (2) nonlinearity layer for generating the sum of input weights from each feature is passed to a nonlinear function (such as ReLU); and (3) pooling layer for reducing the dimensionality (number of input features) for prediction. Input features will be used for prediction and detection of SZ or other disorders

Table 1: Studies using ML methods to detect SZ patients

Article	Number of samples	ML method	Validation method	Accuracy
Borgwardt et al. (2013) [25]	22 HC, 23 FEP	SVM (nonlinear)	Nested cross validation	86.7%
Davatzikos et al. (2005) [26]	79 HC, 69 SZ	SVM (nonlinear)	LOOCV	81.1%
Fan et al. (2007) [27]	Female sample: 38 HC, 23 SZ	SVM (nonlinear)	LOOCV	91.8%
[27]	Male sample: 41 HC, 46 SZ			90.8%
Nieuwenhuis et al. (2012) [28]	Training sample: 111 HC, 128 SZ	SVM (linear)	LOOCV	71.4%
, ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	Validation sample: 122 HC, 155 SZ		Independent sample	70.4%
Yushkevich et al. (2005) [29]	46 HC, 46 SZ	SVM	LOOCV	70.7%
Zanetti et al. (2013) [30]	62 HC, 62 FE	SVM (nonlinear)	LOOCV	73.4%

Table 1 (continued).						
Article	Number of samples	ML method	Validation method	Accuracy		
Sun et al. (2009) [31]	36 HC, 36 ROS	Sparse multinomial logistic regression	LOOCV	86.1%		
Greenstein et al. (2012) [32]	99 HC, 98 SZ	Random forests	Out-of-bag (33% left out at each tree)	73.6%		
Karageorgiou et al. (2011) [33]	47 HC, 28 ROS	LDA	LOOCV	64.3% sensitivity, 76.6% specificity		
Kasparek et al. (2011) [34]	39 HC, 39 FEP	LDA	Jackknife (LOOCV)	71.8%		
Kawasaki et al. (2007) [35]	Training sample: 30 HC, 30 SZ	LDA	LOOCV	76.7%		
	Held-out group: 16 HC, 16 SZ		Held-out group	84.4%		
Nakamura et al. (2004) [36]	Female sample: 22 HC, 27 SZ	LDA	Unknown	81.6%		
	Male sample: 25 HC, 30 SZ			80.0%		

FEP: First-Episode Psychosis; HC: Healthy Control; LDA: Linear Discriminant Analysis, LOOCV: Leave-One-Out Cross-Validation

## 2.2 NLP

NLP is the automatic method of extracting information from text data and training the intelligent method to detect the output or SZ disorder. NLP applies the linguistic context around the word, searching keywords and interesting phrases in the text. For example, it uses patients' statements to distinguish stated symptoms of their SZ experiences. A keyword cannot classify patients. Therefore, it is necessary to extract the semantics using techniques to distinguish between these patients. Recently, ML algorithms have been used in NLP techniques to generate efficient results by combining learning processes with NLP methods. There are different resources of text data for detecting SZ. For example, Facebook and Twitter are rich resources for data using the NLP method for disease diagnosis [37].

The study reported in Rezaii et al. [3] used a skip-gram version of Word2vec from the Genism modules in Python [38]. This method identified a window of five words before and after the target word. The DNN had 200 hidden nodes; the text (42,833,581 sentences) was created by the Linguistic Data Consortium [39]. The proposed method could predict psychosis states in people with an accuracy of 93% in the training set and 90% in the validation set. The results show that the main signals of converting to psychosis are low semantic density and talking about voices.

Another study [38] used NLP for predicting psychosis based on 40 interview transcripts with the first episode of psychosis. The DNN discriminated speech of patients from the healthy control group with an accuracy of 99%. This study demonstrates the power of ML to extract knowledge from speech based on NLP techniques.

Twitter is a text resource for NLP methods and the detection of SZ patients. To detect patients, a set of features must be extracted from Twitter texts, including extracted words related to SZ and words describing emotions. For this purpose, a Natural Language Toolkit from Python was used to run the tokenization and lemmatization. Then, NumPy was used to extract numerical features [40].

## 3 SZ Diagnosis Using ML Based on Structural Neuroimaging Data

Researchers have applied structural and functional neuroimaging data to train the ML model, diagnose SZ, and extract knowledge from the data. Salvador et al. [41] compared ML methods like RF, SVM, and Lasso to detect SZ among 128 SZ cases, 128 bipolar cases, and 127 healthy control cases. Input features were gray and white matter voxel-based morphometry (VBM), vertex-based cortical thickness and volume, a set of regions of interest, volumetric measures, and wavelet-based morphometry. VBM is proven to be the most significant feature for distinguishing patients from a healthy control group.

One study [42] showed that SVM is a high-accuracy ML technique for classifying SZ disorder. In addition, pre-frontal and temporal cortices are strongly related to the diagnosis of SZ. SVM was also applied on data from 41 SZ and 42 healthy control cases based on data from gray-matter volume and WM volume of the brain. Abnormalities of the brain were detected by SVM with an accuracy of 88%. The authors concluded that there is a specific neuroimaging profile of the brain for detecting SZ.

A potential biomarker for detecting SZ is the pattern of illness-related gray matter, which identifies the structural brain alterations in SZ cases. In one study [43], researchers used SVM for analyzing the cortical thickness and surface-area measurements of a brain for 163 cases with a first episode of SZ and 163 healthy control cases. The research showed that gray matter is a contributing region in the default mode network (DMN), central executive network, salience network, and visual network (left fusiform, lingual, posterior cingulate, supramarginal, insula and right isthmus cingulate, lateral occipital, and lingual and frontal pole cortex). Their SVM classified the data with an accuracy of approximately 85% for surface area and 81% for cortical thickness. Another study [44] showed the application of SVM in pathologic changes in WM and GM (in bilateral insula, anterior cingulate cortex, thalamus, superior temporal cortex, and parahippocampal gyrus).

## 4 SZ Diagnosis Using ML Based on Functional Neuroimaging

Cabral et al. [45] applied multivariate pattern analysis (MVPA) to structural and functional magnetic-resonance-neuroimaging methods. In the study, the functional magnetic resonance imaging (fMRI) of 21 SZ patients and 74 healthy control cases was applied. The resting state of fMRI (rs-fMRI) and structural MRI (sMRI) generated the same accuracy (70.5% versus 69.7%, respectively) using the ML method. The combination of sMRI and rs-fMRI outperformed the performance of single MRI data with an accuracy of approximately 75%. This method discovered that the main region associated with SZ is subcortical short-range and particularly interhemispheric connections.

Other researchers applied rs\_fMSRI to distinguish 20 SZ patients from 20 major depressive disorder (MDD) and 20 healthy control cases. Their study combined the FC density analysis with MVPA. The local FC density value distinguished MDD patients from SZ patients using data from the orbitofrontal cortex. That is to say, to better explain this result, patients with SZ had significantly lower connections in the pre-frontal cortex compared with MDD patients. Their proposed ML method generated an accuracy of approximately 85%. This study has shown the importance of the ML method in extracting knowledge from MRI data and differentiating between MDD and SZ cases [46].

One study applied neural networks with their designed activation function to classify 19 SZ patients and 15 healthy control cases. The data were based on stimuli responses like faces, scenes, objects, and scrambled images. The neural network analyzed functional MRI using the MVPA method. The study confirmed that the accuracy of their ML model was significantly associated with behavioral measures. It also showed that impairment correlates with decreasing performance for the 1-back matching task and patterns of cortical activity in the pre-frontal, sensory, and visual cortexes, which are reflected in altered behavior [47].

Wang et al. [48] used SVM algorithms for classification of 48 first-episode, drug-naïve adolescent-onset schizophrenia patients and 31 healthy control cases based on data of long- and short-range functional connectivity (IFC)-(sFC) through rs-fMRI. The model could detect abnormalities of lpFC and spFC in the brain. It classified the cases with an accuracy of 92%, sensitivity of 89%, and specificity of 96%. The research shows the power of SVM in finding nonlinear relationships between functional MRI data and the SZ disorder.

Guo et al. [49] worked on discovering the role of s-IFCs in fMRI for classification of healthy control cases from SZ patients. The studies used SVM for the classification task, showing that SZ patients with increasing spFC and lpFC in gray matter of DMN decrease both in sensorimotor circuits. One finding combined the spFC values in the right superior parietal lobule and lpFC in the left fusiform cerebellum gyrus, increasing the sensitivity and specificity of distinguishing SZ patients from healthy control cases.

Another study [50] used a hybrid ML model based on combining fMRI and single nucleotide polymorphism (SNP) data (combined SNP-fMRI). It distinguished 20 SZ patients from 20 healthy control cases with an accuracy of 87%. The data contained 150 SNPs; the top 15 SNPs were located in 14 significant genes. Brain regions with more contribution for detecting SZ were the inferior, middle, and medial frontal gyri, cingulate gyrus, superior temporal gyrus, and praecuneus.

Arbabshirani et al. [51] presented a SVM classifier to classify 195 SZ and 175 healthy control cases based on rs-fMRI of two types of features. The first, auto-connectivity, captured the temporal connectivity of the brain network. The second, functional network connectivity, captured the inter-network connectivity pattern. The SVM model could distinguish cases with an accuracy of 88%, 86% sensitivity, and 89% specificity.

#### 5 Discussion

In this review study, ML models are presented for detecting SZ patients among other cases. First, short descriptions of ML models are provided. Next, an application of ML models is presented for detecting significant regions of the brain in association with SZ disorder using MRI data. The important role of MRI data in generating a training dataset of SZ symptoms is discussed. Finally, a description of NLP and examples of extracted features from text resources like Twitter are provided.

The high accuracy obtained by ML models proves their reliability and ability to improve the quality of healthcare for patients. ML models play a significant role in obtaining insight from available data because of the complex nature of disease and data. Discovering nonlinear relationships between data features and outcome is not possible with traditional and statistical methods because of the high dimensionality of the data.

ML tools are complex in methodology, as well as difficult to understand. However, their high performance makes them a desirable tool for the automated prediction of problems. One challenge faced by researchers in the selection of accurate ML tools is the interpretability and simplicity of the model. Basically, high-performance algorithms have a "black box" that hides the mathematical operations, making it non-interpretable for researchers. Regarding problems, an easily interpretable model is useful when relationships between variables are questioned. However, if high accuracy is a major concern, the application of the ML tool with a black box like an ANN, SVM, and DNN is an interesting solution. These models produce high accuracies in prediction; however, they evade interpretation. Therefore, researchers must weigh accuracy and simplicity in the interpretation of the model.

Current studies on the application of ML in the diagnosis and prognosis of SZ show a limited number of papers related to ML models for predicting SZ based on omics data. Examples include significant genes detected by ML based on microarray data or the process to detect genes early in the diagnosis of SZ.

However, there are limited data for detecting SZ. The availability of rich datasets is the best policy to guarantee the prediction accuracy. A large amount of data is required to train the ML model. More research is required to prepare new databases to detect SZ.

Providing new databases would be an effective step in developing an automated decision-support system for improving the quality of healthcare in the field of SZ. In addition, integrating different data (i. e., omics, MRI, and electronic health records) will improve the prediction accuracy. Recent applications of ML models have focused on the use of Big Data for extracting knowledge. This is a valuable path for future studies on effectively predicting SZ.

#### 6 Conclusions

In this paper, it is proved that ML is a powerful tool for predicting SZ disorder. ML's ability to detect the regions of the brain that contribute to SZ symptoms is discussed. Furthermore, studies in which structural and functional neuroimaging data were applied for detecting SZ patients are presented. If ML techniques are included in the diagnosis process of SZ patients, clinicians will be more effective in their detection of patients, even in early stages of the disorder. This will be a significant clinical improvement. Applying Big Data methods to extract knowledge from large databases combined with ML is suggested as future work regarding the detection of SZ disorder.

**Funding Statement**: The authors received no specific funding for this study.

**Conflicts of Interest:** The authors declare that they have no conflicts of interest to report regarding the present study.

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