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AI for Precision Medicine—Review

## A Brief Review of Artificial Intelligence Applications and Algorithms for Psychiatric Disorders

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### ABSTRACT

A number of brain research projects have recently been carried out to study the etiology and mechanisms of psychiatric disorders. Although psychiatric disorders are part of the brain sciences, psychiatrists still diagnose them based on subjective experience rather than by gaining insights into the pathophysiology of the diseases. Therefore, it is urgent to have a clear understanding of the etiology and pathogenesis of major psychiatric diseases, which can help in the development of effective treatments and interventions. Artificial intelligence (AI)-based applications are being quickly developed for psychiatric research and diagnosis, but there is no systematic review that summarizes their applications. For this reason, this study briefly reviews three main brain observation techniques used to study psychiatric disorders—namely, magnetic resonance imaging (MRI), electroencephalography (EEG), and kinesics-based diagnoses—along with related AI applications and algorithms. Finally, we discuss the challenges, opportunities, and future study directions of AI-based applications.

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### 1. Introduction

According to the Global Burden of Disease Study in 1990 and 2010 [1], the main causes of the fourth largest disease burden measured in disability-adjusted life years (DALYs) are mental and substance-use disorders [2,3], which are jointly considered to be the leading cause of lived-with disability worldwide.

A number of brain research projects have recently been carried out to study the etiology and mechanisms of psychiatric disorders [4], which could help improve brain interventional and clinical treatment capabilities [5]. For example, the United States proposed the Brain Research through Advancing Innovative Neuroethology initiative [4] in 2013, the European Union initiated the Human Brain Project (HBP) [4] in 2013, and Japan started the Japan Brain Bank Network project in 2014 [5]. China launched the Chinese

Brain Project in 2016, which covers both basic research for the neural mechanisms of brain disease and clinical research on brain disease [6].

Although psychiatric disorders are a research area in brain science, most psychiatrists still diagnose them based on subjective experience rather than by gaining insights into the pathophysiology of the diseases [7,8]. As a result, psychiatrists may misdiagnose diseases and incorrectly delineate distinct paths of treatment. Therefore, it is urgent to develop a clear understanding of the etiology and pathogenesis of major psychiatric diseases in order to develop effective treatments and interventions for major brain diseases.

In recent years, artificial intelligence (AI)-based applications have rapidly been developed for psychiatric research and diagnosis [9–15]. For example, Jan et al. [16] proposed an AI system to monitor depression that can predict Beck Depression Inventory II (BDI-II) scores from vocal and visual expressions. In addition, Wen et al. [17] extracted multi-type gray–white matter features based on multimodal neuroimaging and used a multicore learning classifier to assign weights to the kernel functions of each feature.

However, to the best of our knowledge, there is no systematic review that illustrates the use of these AI-based applications for

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psychiatric research and diagnosis. Thus, we will briefly review commonly used AI-based applications for psychiatric disorders and illustrate how to apply AI technology to explore biomarkers for psychiatric disorders.

## 2. Major AI-related techniques for psychiatric disorder diagnosis

AI techniques [18,19] are being progressively introduced for psychiatric disorders. Brain structure and function are the most important biological phenotypes and key diagnostic biomarkers for psychiatric disorders [20]. Therefore, AI-related techniques that can obtain detailed information to characterize different psychiatric disorders should be used for the diagnosis of these diseases [16].

Fig. 1 describes three major techniques for brain observation in the study of psychiatric disorders: magnetic resonance imaging (MRI), electroencephalography (EEG), and kinesics diagnosis [21]. We will subsequently discuss their related AI-based applications.

### 2.1. Magnetic resonance imaging

MRI is the predominant technique for behavioral and cognitive neuroscience since it can explore obvious psychiatric abnormalities that cannot be detected by computed tomography (CT) [22–25]. At present, commonly used AI technologies for brain imaging include multitask/multimodal learning, classification, kernel, and deep learning methods [26], which can help in effectively analyzing existing disease data for key biomarkers exploration and increasing the capacity for clinical brain disease treatment [24,25].

Although many AI-related applications have been developed to assist MRI [26–28], this section only focuses on convolutional neural networks (CNNs) [29] and deep neural networks (DNNs) [30–32], which are employed in neuroimaging studies to elucidate the neural correlates of psychiatric disorders [30,33–36]. For example, Hosseini-Asl et al. [37] proposed a new depth-supervised adaptive three-dimensional (3D) CNN that can automatically extract and recognize Alzheimer's disease features, capture changes caused by Alzheimer's disease, and use these networks to analyze and recognize MRI images. In addition, Koyamada et al. [38] built up a subject-transfer decoder using a DNN. It is trained by a functional MRI (fMRI) dataset in the Human Connectome Project (HCP), the decoder of which has been assessed as having higher decoding accuracy than other methods.

Although MRI is currently an important tool for diagnosis in general, it still has several major shortcomings. First, it requires extensive computer configurations. Second, big data is needed to optimize the key parameters of the model. Third, the imaging process takes a long time. Thus, the question of how to improve the current AI-based applications to solve these problems for MRI is an important future research direction.

### 2.2. Electroencephalography

Diagnosis and treatment of human brain and nervous system diseases can be performed by detecting and recording human EEG signals. EEG signals are critical for both understanding how the human brain processes information and diagnosing psychiatric disorders [39]. In comparison with CT and MRI, EEG has a higher temporal resolution [40]. Therefore, despite the limited spatial resolution of EEG, it is still a valuable tool for research and diagnostics, especially when specified studies require time resolution in the millisecond range, such as studies on anxiety, psychosis, and depression [41].

Here, we focus on describing the application of the classical machine learning algorithm for EEGs. Since EEG data is represented by a graph, it is always analyzed by AI-based models [42–45]. For example, Field and Diego [46] employed linear discriminant analysis to process EEG data and obtained 67% accuracy when classifying normal patients and patients with depression. In addition, Iosifescu et al. [47] employed a support vector machine (SVM) to process resting-state EEG data for 88 subjects at the midpoint of the eight-lead connection at the forehead and achieved a 70% classification accuracy. Moreover, Bisch et al. [48] used logistic regression (LR) to classify a nine-lead EEG for depression with an 83.3% classification accuracy.

Although EEGs can simplify the data acquisition process, they encounter information loss. More importantly, too many undetermined factors in EEG data result in a large amount of noise in the classification decision. Therefore, developing a machine learning model that is more suitable for EEG data is a future research direction.

### 2.3. Kinesics

Kinesics data (including behavioral [49], facial [50], and other data [48]) is becoming very important for the study of the pathogenesis, development transition, and diagnosis assistance of

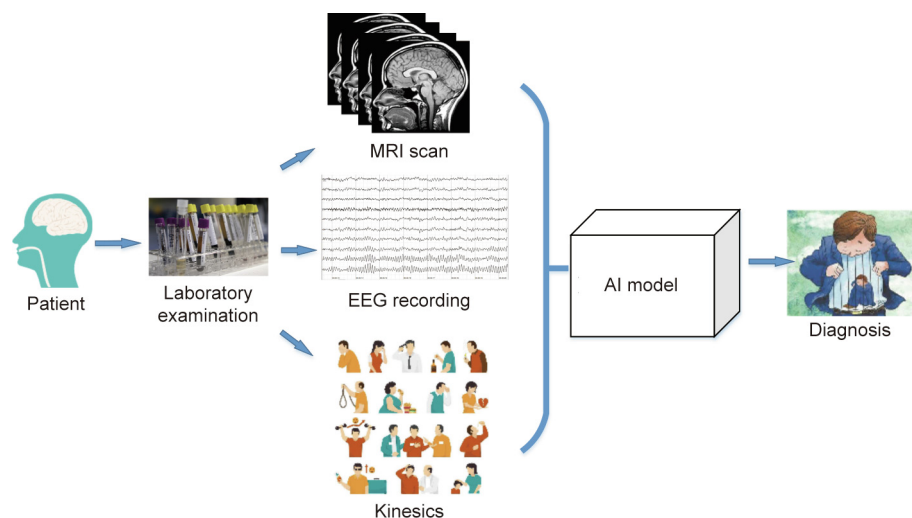


Fig. 1. Major observation techniques for psychiatric disorders.

psychiatric disorders. AI-based technologies are widely employed to analyze such data to help diagnose and predict psychiatric disorders.

Many AI-related applications have recently been developed for kinesics-based diagnoses [50–52]. For example, Wang et al. [53] proposed a computational approach to develop probabilistic facial expression profiles for video data, which can automatically quantify the difference in emotional expression between patients with psychiatric disorders (e.g., schizophrenia) and healthy controls [16]. Zhu et al. [54] implemented automatic diagnosis of depression by means of a deep learning algorithm, which significantly improved the depression prediction performance by reducing the mean absolute error by 30.3%. In addition, Kaletsch et al. [55] examined differences in emotional expression by body movements between patients with major depressive disorder (MDD) and their healthy counterparts, and demonstrated that patients with MDD are more negative than their healthy counterparts.

In addition, Dhamecha et al. [56] proposed an algorithm to investigate human and machine performance for recognizing/verifying disguised faces [57]. The method can identify disguised face patches and account for this information to obtain improved matching accuracy by automatically localized feature descriptors. The experiments showed that the proposed algorithm can not only outperform popular commercial systems, but also evaluate the disguised face images when they are matched.

In general, with the development of AI and precision medicine, collecting and analyzing kinesics data will become easier, cheaper, and more convenient. Moreover, kinesics data could help to improve models' predictive accuracy, reduce the misdiagnosis rate, and assist psychiatrists in diagnosing and treating psychiatric disorders.

### 3. Artificial intelligence algorithms

#### 3.1. Bayesian model

In AI, the naïve Bayes classifier [58–60] is a general term for a classification algorithm. The naïve Bayesian method is a classification method based on Bayes' theorem and characteristic condition-independent hypothesis.

Recent studies have often employed Bayesian models to diagnose psychiatric disorders. For example, the Strüngmann Forum on Computational Psychiatry [61–63] proposes using Bayesian inference to connect underlying causes (genetics and sociological phenomena [15,64]), latent hypothesized theoretical constructs, and symptoms [65]. Furthermore, Grove et al. [66] used a Bayesian model comparison approach to explore the relationship between visual integration and general cognition. The results showed that a Bayesian model can draw a comparison of the disease categorization systems and have common psychopathological information from diagnostic groups.

#### 3.2. Logistic regression

In statistics, logistic models [67,68] (or logit models) are widely used statistical models, and LR is an important AI algorithm [68,69]. Recent studies often employ LR models to diagnose psychiatric disorders. For example, Hagen et al. [70] evaluated the associations between psychological distress and two cognitive screening tools by means of a LR method. The results demonstrated that performance-based assessment could reduce the impact of psychological distress on cognitive screening.

In addition, Barker et al. [71] employed models of multivariable LR to predict 30-day psychiatric readmission. Their findings are

considered to be crucial predictors for psychiatric readmission, and have provided a better way of readmission prediction.

Shen et al. [72] generated a risk stratification model to obtain the odds ratio (OR) of psychiatric comorbidities by a classification and regression tree method. Using the LR method, the OR of psychiatric comorbidities was calculated between subjects with and without borderline personality disorder.

In general, the accuracy of LR models is so high that they are commonly applied in clinical practice.

#### 3.3. Decision tree

A decision tree [73] is a flowchart-like diagram that shows the various outcomes from a series of decisions, including chance event outcomes and utility. Decision trees are one of the most widely and broadly used algorithms for supervised classification learning. In AI, a decision tree is a predictive model that represents a mapping between object properties and object values. Most modern decision tree learning algorithms adopt a purity-based heuristic [74]. Information gain,  $\text{gain}(D, X)$ , is defined by Eq. (1) [75,76].

$$\text{gain}(D, X) = \text{info}(D) - \sum_x \frac{|D_x|}{|D|} \text{info}(D_x) \quad (1)$$

where  $D$  is a set of training instances,  $X$  is an attribute,  $x$  is its value,  $D_x$  is a subset of  $D$  consisting of the instances with  $X = x$ , and  $\text{info}(D)$  is defined as shown in Eq. (2).

$$\text{info}(D) = - \sum_{i=1}^m p_i \log_2(p_i) \quad (2)$$

where  $p_i$  is estimated by the percentage of instances and  $m$  is the number of classes.

Next, we detail two commonly used decision tree applications for psychiatric disorders.

Carpenter et al. [77] used the decision tree algorithm to test whether individual Preschool Age Psychiatric Assessment (PAPA) items can predict whether a child is likely to have generalized anxiety disorder (GAD) or separation anxiety disorder (SAD). They used a decision tree to identify children who were on the brink of experiencing anxiety disorder, and their results showed that the decision tree can achieve accurate prediction up to 96% for both GAD and SAD.

With a decision tree, Scattler et al. [78] analyzed data from the Spence Children's Anxiety Scale (SCAS) and SCAS-P obsessive-compulsive disorder subscales, and worked out two screening algorithms to diagnose obsessive-compulsive disorder from a combined clinical and community sample of children and families. The results showed that the algorithms that reduced the number of SCAS-P items needed to make a diagnosis of obsessive-compulsive disorder diagnoses up to 67%–83% without sacrificing the nature relative to the full subscales.

#### 3.4. Support vector machines

The SVM is a current supervised learning method, the decision boundary of which is the maximum margin hyperplane for solving learning samples [79]. It can be described as follows: Start from a training dataset of  $n$  points of the form  $(\vec{x}_1, y_1), \dots, (\vec{x}_n, y_n)$ , where  $y_i \in \{-1, 1\}$  is used to denote the class labels. Each  $\vec{x}_i$  is a  $p$ -dimensional real vector. The goal is to find the maximum margin hyperplane that divides the group of points  $\vec{x}_i$  for which  $y_i = 1$  from the group of points for which  $y_i = -1$ .

SVM models have been commonly used for diagnosing psychiatric disorders. For example, in order to describe users' situations, Peng et al. [80] employed a multi-kernel SVM-based model to locate potential users who might suffer from depression by

extracting three social methods (user microblog text, user profile, and user behaviors). Based on a multiclass SVM, Al-Shargie et al. [81] put forward a discriminant analysis method. The results showed that the method could discriminate between different stress levels for EEG with a 94.79% average classification accuracy.

### 3.5. Deep learning

Classic machine learning methods, such as the Bayesian model and SVM, have been widely employed in psychiatry and neuroscience [64–66] studies for a long time. At present, deep learning [82–84], which is a hot machine learning research direction, outperforms the aforementioned AI models by a considerable margin [85–87].

Deep learning refers to a set of algorithms on a multi-layer neural network that uses various machine learning algorithms to solve various problems such as images and text. Combined with low-level features, deep learning can develop more abstract high-level attribute categories or features that can discover distributed feature representations of data. Weight updating can be solved by the stochastic gradient descent method using the following formula:

$$\Delta w(t+1) = \Delta w(t) + \eta \frac{\partial C}{\partial w} \quad (3)$$

where  $\Delta w(t)$  is the weight of time  $t$ ,  $\eta$  is the learning rate, and  $C$  is the cost function. The choice of this function is related to the type of learning (such as supervised learning, unsupervised learning, and enhanced learning) and the activation function.

Here, we detail two commonly used deep learning applications for psychiatric disorder diagnosis.

By leveraging a DNNs on the TensorFlow framework, Khan et al. [88] proposed a computational tool (integrated mental-disorder GEnome score, or iMEGES) to analyze the whole genome/exome sequencing data on personal genomes. Based on the deep learning framework, this tool creates prioritized gene scores for psychiatric disorders [89]. The findings revealed that the property of this tool are better than that of competing approaches when a large training dataset is available.

In addition, Heinsfeld et al. [39] applied deep learning algorithms on a large brain imaging dataset in order to identify patients with autism spectrum disorder based solely on the patients' brain activation patterns. The findings revealed that 70% accuracy was achieved in the dataset, and that deep learning methods can classify large datasets better than other methods. Furthermore, the results showed the promise of deep learning for clinical datasets and illustrated the future application of AI in the identification of mental disorders.

Although extremely advanced performance has been demonstrated in several fields, deep learning has been under close concern for its lack of transparency during the learning and testing processes [90–92]. For example, deep learning has been referred to as a “black box”. In comparison, techniques such as LR are simple and easy to understand.

For this reason, recent endeavors in interpretable DNNs are introduced here. For example, in terms of CNN visualization, Springenberg et al. [93] proposed a deconvolution approach that can be used to acquire features from deep learning. Kindermans et al. [94] proposed a method to visualize the regions in the input image that contribute most to the CNN decision-making process. In a study on interpreting neural networks with traditional machine learning models, Zhang et al. [95] proposed a method to interpret the convolution layer characteristics of pretrained CNNs, and used an explanatory graph to reveal the knowledge level hidden in the CNN. In short, a good AI model should be interpretable,

generalizable, and more adaptive, and should learn from data, rules, and interactions.

## 4. Discussion

Considering the interaction between the environment and multiple susceptibility genes, the process of diagnosing psychiatric disorders is described as follows: first, micromolecular variations [96,97], such as protein expression [98,99], are investigated by EEG; second, changes in brain structure, specific neural circuits, and brain function are examined by MRI; and finally, when patients have clinical phenotype switches, kinesics data is used to identify behavioral changes [100]. In particular, the discovery of these changes at the structural, functional, and behavioral levels can not only help in diagnosing psychiatric disorders at an early stage, but also assist in exploring the key biomarkers for diagnosing psychiatric disorders.

However, the clinical symptoms of psychiatric disorders are complex and diverse. Diagnosing psychiatric disorders is one of the more labor-intensive tasks in medicine, and thus precisely falls within the area of machine learning. The general medical system cannot always accurately and rapidly diagnose patients. The continuous development of clinical examination technology and AI technology can not only greatly reduce costs, but also obtain assistant diagnosis results in real time. AI can help doctors to provide more accurate and efficient diagnoses [101–103], thus improving the level of clinical diagnoses of neuropsychiatric diseases.

The typical application of AI in this context is in diagnosing diseases based on DNNs [104]. DNNs can accurately predict the risk of disease or abnormal lesions through a deep learning model based on the relevant disease data. In the literature, although the analytic performance of deep learning for diagnosing psychiatric disorders is better, there are also some problems, such as: ① higher requirements for computer configurations; ② higher requirements for data quantity (the experimental performance is better only when there is more data); and ③ more time being consumed by experiments. These problems are worthy of further study and discussion in the future.

In short, although AI has made great progress in diagnosing psychiatric disorders, there are still many research areas for the improvement of AI-based applications [105]. First, since current research is based on classic shallow learning algorithms, it is difficult to share and use information among high-dimensional features. Thus, deep learning is a future study direction. Second, it is necessary to employ unsupervised learning to perform automatic annotation for unlabeled psychiatric disorder imaging data. Finally, because the current AI-based model can only process homologous datasets, its generalizability is insufficient. Therefore, migration learning, multi-view learning, and ensemble learning [106] will be used to process big psychiatric disorder data in the distant future.

## 5. Conclusion

At present, MRI, EEG, and kinesics are important methods and references in the diagnosis of psychiatric disorders. With the application of AI technologies in medicine becoming increasingly widespread, traditional artificial diagnostic methods are gradually being eliminated, while the role of MRI, EEG, and kinesics in computer-aided diagnosis methods is becoming increasingly important. Therefore, this study mainly reviewed the application of MRI, EEG, and kinesics by providing the following: ① a brief introduction of the process of psychiatric disorder diagnosis and an analysis of the main data types generated therein; ② an introduction of the important role of AI technology in the diagnosis of psychiatric

disorders, and its application performance; and ③ a summary and analysis of the methods proposed for diagnosing diseases based on the current hot topic of deep learning.

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### Compliance with ethics guidelines

Guang-Di Liu, Yu-Chen Li, Wei Zhang, and Le Zhang declare that they have no conflict of interest or financial conflicts to disclose.

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