Machine Learning Techniques in Diagnostics and Prediction of the Clinical Features of Schizophrenia: A Narrative Review

Использование методов машинного обучения в диагностике и прогнозировании клинических особенностей шизофрении: нарративный обзор литературы

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Vadim Gashkarimov¹, Renata Sultanova², Ilya Efremov^{3,4}, Azat Asadullin^{3,4,5}

 ¹ Republican Clinical Psychiatric Hospital, Ufa, Russia
² Moscow Research and Clinical Center for Neuropsychiatry of Moscow Healthcare Department, Moscow, Russia
³ Bashkir State Medical University, Ufa, Russia
⁴ V.M. Bekhterev National Medical Research Centre for Psychiatry and Neurology, Saint Petersburg, Russia
⁵ Republican Clinical Psychotherapeutic Center, Ufa, Russia

Вадим Гашкаримов¹, Рената Султанова², Илья Ефремов^{3,4}, Азат Асадуллин^{3,4,5}

¹ ГБУЗ «Республиканская клиническая психиатрическая больница» Минздрава Республики Башкортостан, Уфа, Россия

 ² ГБУЗ «Научно-практический психоневрологический центр имени З.П. Соловьева» Департамента
здравоохранения города Москвы, Москва, Россия
³ ФГБОУ ВО «Башкирский Государственный Медицинский Университет» Минздрава России, Уфа, Россия
⁴ ФГБУ «Национальный медицинский исследовательский центр психиатрии и неврологии им. В.М. Бехтерева» Минздрава России, Санкт-Петербург, Россия
⁵ ГБУЗ «Республиканский клинический психотерапевтический центр» Минздрава Республики Башкортостан, Уфа, Россия

ABSTRACT

BACKGROUND: Schizophrenia is a severe psychiatric disorder associated with a significant negative impact. Early diagnosis and treatment of schizophrenia has a favorable effect on the clinical outcome and patient's quality of life. In this context, machine learning techniques open up new opportunities for a more accurate diagnosis and prediction of the clinical features of this illness.

AIM: This literature review is aimed to search for information on the use of machine learning techniques in the prediction and diagnosis of schizophrenia and the determination of its clinical features.

METHODS: The Google Scholar, PubMed, and eLIBRARY.ru databases were used to search for relevant data. The review included articles that had been published not earlier than January 1, 2010, and not later than March 31, 2023. Combinations of the following keywords were applied for search queries: "machine learning", "deep learning", "schizophrenia", "neural network", "predictors", "artificial intelligence", "diagnostics", "suicide", "depressive", "insomnia", and "cognitive". Original articles regardless of their design were included in the review. Descriptive analysis was used to summarize the retrieved data.

RESULTS: Machine learning techniques are widely used in the functional assessment of patients with schizophrenia. They are used for interpretation of MRI, EEG, and actigraphy findings. Also, models created using machine learning algorithms can analyze speech, behavior, and the creativity of people and these data can be used for the diagnosis of psychiatric disorders. It has been found that different machine learning-based models can help specialists predict and diagnose schizophrenia based on medical history and genetic data, as well as epigenetic information. Machine learning techniques can also be used to build effective models that can help specialists diagnose and predict clinical manifestations and complications of schizophrenia, such as insomnia, depressive symptoms, suicide risk, aggressive behavior, and changes in cognitive functions over time.

CONCLUSION: Machine learning techniques play an important role in psychiatry, as they have been used in models that help specialists in the diagnosis of schizophrenia and determination of its clinical features. The use of machine learning algorithms is one of the most promising direction in psychiatry, and it can significantly improve the effectiveness of the diagnosis and treatment of schizophrenia.

аннотация

ВВЕДЕНИЕ: Шизофрения является тяжелым психическим расстройством, которое влечет за собой значительные негативные последствия. Раннее выявление шизофрении и ее лечение благоприятно влияют на клинический прогноз и качество жизни пациента. В этом контексте методы машинного обучения открывают новые возможности для более точной диагностики и прогнозирования клинических особенностей данного расстройства.

ЦЕЛЬ: Данный обзор литературы направлен на поиск информации о применении методов машинного обучения в прогнозировании и диагностике шизофрении и ее клинических особенностей.

МЕТОДЫ: Поиск материала был осуществлен в базах данных Google Scholar, PubMed, eLIBRARY.ru. В обзор включались работы, опубликованные не раньше 1 января 2010 г. и не позже 31 марта 2023 г. Поисковые запросы формировались путем комбинации ключевых слов: "machine learning", "deep learning", "schizophrenia", "neural network", "predictors", "artificial intelligence", "diagnostics", "suicide", "depressive", "insomnia", "cognitive". В обзор включались оригинальные исследования независимо от их дизайна. Для обобщения полученных данных использовался описательный анализ.

РЕЗУЛЬТАТЫ: Методы машинного обучения широко применяются в функциональной диагностике шизофрении. Их используют в распознавании данных от МРТ, ЭЭГ, актиграфии. Также модели, созданные с помощью алгоритмов машинного обучения, могут анализировать речь, поведение, творчество людей для диагностики психических расстройств. Было установлено, что различные модели, построенные на основе машинного обучения, способны помогать специалистам прогнозировать и диагностировать шизофрению, основываясь на анамнестической, генетической, эпигенетической информации. Методы машинного обучения также успешно применяются для построения моделей, которые способны помогать специалистам диагностировать и прогнозировать клинические проявления и осложнения шизофрении, такие как бессонница, депрессивные проявления, риск суицида, агрессивное поведение, динамика когнитивных функций.

ЗАКЛЮЧЕНИЕ: Применение методов машинного обучения играет важную роль в психиатрии, с их помощью разработаны модели, помогающие специалистам в диагностике шизофрении и ее клинических особенностей. Применение алгоритмов машинного обучения является одним из наиболее перспективных направлений в психиатрии, это может значительно повысить эффективность диагностики и лечения шизофрении.

Keywords: machine learning; schizophrenia; neural network; artificial intelligence; predictors **Ключевые слова:** машинное обучение; шизофрения; нейронная сеть; искусственный интеллект; предикторы

INTRODUCTION

The previous decades have been marked by rapid developments in artificial intelligence (AI). The number of scientific articles on the use of AI techniques is increasing. Machine learning is a fundamental area of AI that allows a computer to analyze data and extract information without explicit programming. Unlike the traditional approach, where it is necessary to write a special code to solve a specific problem (e.g., determining an image of a cat), in machine learning a model is generated with a large amount of data (e.g., images of cats and images of noncats) and is allowed to "learn" based on this generated data. Following that, the model is able to predict or aporton new data (e.g., determine whether the new image is a cat) that were not used in the original dataset [1]. In scientific papers, machine learning is used as a tool with many practical applications, including pattern recognition, data analysis, event prediction, and much more [2, 3]. Models created using machine learning techniques are used in many fields of the sciences, such as physics, chemistry, mathematics, economics (forecasting financial markets [4]) and in bioinformatics for the analysis of biological data, such as genomes, proteomes, and metabolomes [5]. Models created using machine learning techniques are also used in medicine; they can help specialists in decision-making, in diagnosing and predicting the development of diseases, in monitoring patients' health using mobile applications, in predicting epidemic outbreaks, etc. [6-8].

Machine learning algorithms have also found use in the diagnosis of schizophrenia. Schizophrenia is a chronic, progressive psychiatric disorder with an incidence of 4 to 6 per 1,000 population. The prevalence of schizophrenia is quite identical in females and males and is slightly higher in residents of urban communities compared to residents of rural areas [9–11]. The diagnosis of schizophrenia, according to the DSM-5 criteria, is based solely on clinical signs [12]. This may make it difficult to accurately diagnose disorders that are similar in some cases, such as schizophrenia and autism spectrum disorders [13], or schizophrenia and bipolar disorder [14]. To increase the likeliness of a good prognosis and a high quality of life for patients with schizophrenia, it is crucial to quickly and accurately detect the clinical symptoms of the disease and prescribe treatment in a timely manner [15, 16]. In the context of schizophrenia, machine learning techniques open up new opportunities for more accurate diagnosis and prediction of the clinical features of the illness. One of the advantages of using machine learning techniques is the ability to process large amounts of data, as well as the ability to analyze information that is diverse in nature [17]; e.g., individual clinical manifestations, neuroimaging test findings, patient's history data, genetic data, the patient's voice, etc. Based on these data, both diagnostic and prognostic models have been generated. Diagnostic models help specialists identify the disease more accurately, and prognostic models can help predict the development course of schizophrenia [18], as well as its clinical manifestations and complications, including the risk of suicide [19]. Furthermore, machine learning can help identify new biomarkers associated with schizophrenia, which can improve our understanding of the mechanisms underpinning this disorder and contribute to the development of more effective therapeutic methods [20, 21].

There has been a significant increase in the number of studies that seek to evaluate the diagnosis of schizophrenia and predict its clinical course using machine learning techniques. However, the field is characterized by a wide variety of topics and multiple publications, which requires a systematic review of available information. First, a literature review on this topic allows one to identify the most effective machine learning techniques used to predict and diagnose schizophrenia; second, it allows one to also identify promising areas of future research into the use of Al in psychiatry.

Thus, this literature review aimed to probe for information on the use of machine learning techniques in predicting and diagnosing schizophrenia and trying to identify its clinical features, as well as generalizing data and identifying key findings that can provide a better understanding of the current state of research in this field.

METHODS

Scientific papers were searched in the Google Scholar, PubMed, and eLIBRARY.ru databases, and the publications included in the lists of references of thematic reviews were also analyzed. Search queries included various combinations of the following words: "machine learning", "deep learning", "schizophrenia", "neural network", "predictors", "artificial intelligence", "diagnostics". The following keywords were used to search for papers devoted to the identification of the clinical features and complications of schizophrenia: "suicide", "depression", "insomnia", cognitive". These keywords were combined to create search queries; e.g., "machine learning", "predictors" AND "schizophrenia". The review included studies into the use of various AI technologies in the context of schizophrenia diagnosed according to the DSM-IV, DSM IV-TR, DSM-5, ICD-10, and ICD-11 criteria published no earlier than January 1, 2010, and no later than March 31, 2023, without any language restrictions. This time interval was chosen because of the substantial increase in the number of publications on this topic from 2010 to the present. The review included original studies, regardless of their design, evaluating the use of various machine learning techniques in the diagnosis of schizophrenia and determination of its clinical features in patients with both a first episode of schizophrenia and the chronic form of the disease. Descriptive analysis was used to summarize the retrieved data.

RESULTS

Based on the search results, 38 papers were included in the review. Then the sections containing information on the use of different AI technologies in the functional testing (electroencephalography (EEG) and magnetic resonance imaging (MRI), actigraphy) of patients with schizophrenia, the analysis of their mental capacities (speech, behavior, creativity), the evaluation of their history and genetic data, as well as the prediction of complications, outcomes of the disease, and its individual manifestations, were determined. Each of the listed aspects of the use of AI technologies is reviewed below.

Machine learning techniques in the functional assessment of patients with schizophrenia

In addition to psychiatric interviews and neuropsychological testing, other investigative (EEG, MRI) techniques are used in the diagnosis of schizophrenia to rule out the presence of other disorders, as well as for research purposes. In a study by Di Lorenzo et al., the authors revealed that people with schizophrenia demonstrated lower alpha rhythms on EEG in the frontal and central regions of the brain compared to the control groups. The level of the alpha rhythm is known to be associated with mental processes, such as attention and memory. The authors suggested that a low level of alpha rhythm may be associated with cognitive impairment and impaired mental abilities in patients with schizophrenia [22]. In another study, scientists found that in people with schizophrenia, interhemispheric connectivity was significantly lower in the frontal and parietal lobes compared to the control group [23].

Despite the fact that EEG is not used to diagnose schizophrenia in routine clinical practice, machine learning techniques can improve the accuracy of the diagnosis of schizophrenia based on EEG findings. In an article by Sun et al., researchers concerted EEG signals into a series of images then a hybrid deep neural network was built and trained, which could help distinguish the EEG signals of a healthy person from those of a person with schizophrenia with 99.22% accuracy [24]. In another, similar study in which a convolutional neural network was used, the accuracy was also high, reaching 98.07% [25]. Neural networks are widely used in the classification of EEG signals, and scientists also suggest that neural networks trained to classify EEG findings can be useful in early detection of schizophrenia [26–28].

Neural networks are being relied upon with increasing frequency in the analysis of 3D MRI images of the brain. In a study by Chen et al., the researchers trained a convolutional neural network to classify MR images of people with schizophrenia with a probability of 85%. Likewise, with the help of a neural network, suspected biomarkers of schizophrenia were identified: namely, abnormal structural changes in the cerebellum, fusiform gyrus, and the temporal, occipital, and frontal brain lobes [29]. In another study, researchers analyzed MR images of people with schizophrenia, bipolar disorder, and mentally healthy people. As a result, models based on machine learning algorithms were built to distinguish an image of a person with schizophrenia from that of a healthy person with an average accuracy of 90%, and from a person with bipolar disorder with an accuracy of 88% [30]. In a study by Oh et al., the authors successfully used a convolutional neural network to classify MR images of patients with schizophrenia with an accuracy of 84.15~84.43% and they revealed that the most significant brain regions were the low and middle temporal lobes [31]. In another paper that pursued the same objective, the researchers applied the M3 method (multimodal imaging and multilevel characterization with multi-classifier) and achieved an accuracy of 83.49% [32].

There are models that have been created using machine learning techniques that can be used to diagnose schizophrenia using actigraphy. In one study, scientists collected data from Actiwatch bracelets that recorded the acceleration amplitude of the sensor, thereby reflecting the motor activity of the participants during the day. Using a convolutional neural network, the researchers successfully distinguished patients with schizophrenia from those suffering from mood disorders against the control group patients. At the same time, patients with schizophrenia showed the lowest motor activity [33]. In another study, researchers analyzed the patterns of nocturnal activity in individuals at risk of developing schizophrenia, people with bipolar disorder, and healthy people. Using various machine learning algorithms, the scientists created models that could identify a respondent at risk of schizophrenia and bipolar disorder [34].

Machine learning techniques in the analysis of speech, behavior, and creativity in people with schizophrenia

Machine learning is used to analyze written and spoken speech. In a study by Bae et al., the authors used a neuronal network to analyze the linguistic patterns of people with and without schizophrenia on the Reddit social network. On this social platform, people can create different topics, discuss them, and share something important. Researchers compared the topics created about schizophrenia with topics about humor, fitness, meditation, parenting, etc. It turned out that people describing their mental issues used fewer singular first and third person pronouns, and, vice versa, a greater number of impersonal pronouns, plural second, and third person pronouns. It has also been observed that people with mental illnesses are less likely to use the past tense as well as words describing positive emotions, and that they are more likely to use words associated with negative emotions [35]. In a study evaluating the linguistic characteristics of people with schizophrenia on the Twitter social network, it was found that people diagnosed with schizophrenia more often used interpersonal pronouns in their texts and were more likely to put less emphasis on friendship and more on biological needs [36].

Neural networks are also capable of processing audio information. In a study by Fu et al., researchers created a Sch-net neuronal network which was able to distinguish the speech of a person with schizophrenia from that of a mentally healthy person with 97.68% accuracy [37]. In a study by Tahir et al., researchers used a system based on machine learning algorithms to automatically predict the presence of "negative symptoms" of schizophrenia based on the speech characteristics. This also could identify the voice of a person with schizophrenia with 81.3% accuracy [38]. There is also data in the literature on the use of the SchiNet convolutional neural network in the analysis of facial behavior during psychiatric interviews of people with schizophrenia. Researchers have concluded that automated identification of facial behavioral patterns is a reliable means of identifying "negative symptoms" of schizophrenia [39]. In another study, a convolutional neuronal network could recognize people with schizophrenia by video recordings. The recording of the face was carried out following various types of emotional stimulation; based on the information collected, the neural network determined a person with schizophrenia with 89% accuracy [40].

A study conducted by Vasilchenko and Usov published the results of the use of a convolutional neural network in the classification of drawings made by people with schizophrenia based on the images of a human face drawn by them; the accuracy in providing correct answers amounted to 82% [41]. In a study by Shen et al., the authors evaluated the categorization of color drawings created by people with schizophrenia and control group subjects using a convolutional neural network. The study showed that people with schizophrenia were more likely to use fewer colors in their drawings, draw irregular lines, and draw more lines near the center of the image compared to the control group. The accuracy demonstrated by the neural network was 90%. Using a neural network analysis, the investigators could reliably predict the results of the Positive and Negative Syndrome Scale (PANSS) assessment using drawings made by people with schizophrenia. The model could predict high scores both in the general scale and the subscales [42].

Diagnosis of schizophrenia based on genetic information using artificial intelligence

There are psychiatric disorders that come with similar symptoms, such as schizophrenia and bipolar disorder, as well as schizophrenia and autism spectrum disorders. This may make the diagnosis of such disorders difficult and result in the use of inadequate therapy. Machine learning techniques-based models can use genetic data to help alleviate this problem. For example, in a study by Karthik et al., researchers used genetic information to teach a neural network how to separate schizophrenia from bipolar disorder. Models based on machine learning techniques helped identify genetic patterns consisting of 75 genes for schizophrenia and 67 genes for bipolar disorder; the probability of correct assumptions by the

constructed neural network stood at 95.65% and 97.01%. respectively [43]. In a study by Sardaar et al., researchers compared the genome architecture of schizophrenia and autism spectrum disorders in order to look for "nodal" genes for these disorders. Using a model based on the regularized "gradient boosted machine" (GBM) technique, researchers separated patients with these diseases with an accuracy of 86-88%. They were also able to identify the "nodal" genes responsible for the transmembrane ion transport, neurotransmitter transport, and the processes in the cytoskeleton associated with schizophrenia [44]. In another study, a neural network used information on 792 genetic markers to allocate respondents to a control group and people with schizophrenia with an accuracy of 87.9% [45]. The research conducted by Gunasekaraet al., was also aimed at identifying schizophrenia in the study subjects. In that study, the authors used a SPLS-DA machine learning technique to successfully identify schizophrenia based on epigenetic data: namely, the methylation of various DNA sites [46]. In another study, scientists pointed at the possibility of distinguishing people with and without schizophrenia using G72 gene singlenucleotide polymorphisms, as well as the plasma level of the G72 protein. A naive Bayes classifier turned out to be the best model (AUC=0.9356) [47]. Aguiar-Pulido et al. studied single-nucleotide polymorphisms in the HTR2A and DRD3 genes. They employed neural network analysis of genetic information to identify the genotypes of people with schizophrenia, and the accuracy in the exercise ranged from 78.3 to 93.8% [48].

Analysis of patient's history data using machine learning techniques in the early diagnosis and prevention of schizophrenia

In a large study by Raket et al., researchers used information obtained from the electronic medical records (4,899 events) of the control group (N=72,860) and people with schizophrenia (N=72,860) to predict the development of the first episode of psychosis within one year before its onset. To create a model capable of solving such a problem, the method of recurrent neural network analysis was selected and the probability of a correct predication was 0.774 [49]. Fusar-Poli et al. used machine learning techniques to create a model to predict the development of a psychotic episode in people with a clinically high risk of psychosis. The authors identified the following most significant predictors: high scores on the scales for positive and negative symptoms and disorganization on the Brief Psychiatric Rating Scale, Expanded (BPRS-E), and a small number of years of formal education [50]. Then, the model was improved with the addition of other predictors such as tearfulness, poor appetite, weight loss, cannabis use, cocaine, guilt, hopelessness, irritability, delusion, sleep disorders, lack of insight, arousal, and paranoia. The accuracy of the model based on the Harrell's C-index was 0.085 [51]. In another study, 500 health records of patients with psychosis were analyzed using deep learning of the neural network. This neural network was able to identify the health record of a person with schizophrenia with an accuracy of 92.5%. The most important factor in detecting the disease was age [52].

Predicting the clinical features of schizophrenia

In addition to the main symptoms, the clinical symptoms of schizophrenia may include insomnia, depressive, anxiety, suicidal thoughts, and other symptoms [53–55]. These additional symptoms of schizophrenia may aggravate its course, making treatment more difficult [56, 57].

Insomnia often accompanies schizophrenia exacerbations and may herald an emergent psychotic episode. Insomnia also complicates the course of schizophrenia exacerbation and worsens the clinical prognosis and quality of life of patients [58, 59]. Its diagnosis is of great clinical importance. Kalinich et al., developed an application using machine learning which not only assumed the presence of schizophrenia in the respondent, but also predicted the development of insomnia and neurocognitive deficit. In that application, the subjects were asked to answer several questions and play a mini-game [60]. We have also constructed and trained a neural network capable of predicting the development of insomnia during hospitalization with 72% accuracy based on a patient's medical history and statistical data [61].

One of the most unfortunate complications of schizophrenia is suicide, which can result from symptoms of depression. With the help of AI, scientists have the opportunity to predict the development of depressive manifestations in a person with schizophrenia [62]. Hettige et al., used models created using machine learning techniques to identify individuals with schizophrenia and suicidal attempts. The authors used social, cultural, statistical, medical history, and clinical data from their medical records as input data. The most significant factors in determining suicidal behavior were age, the results of the Childhood Trauma Questionnaire (CTQ) "emotional

abuse" subscale, the total CTQ score, the duration of the disease, and the scores on the neuroticism scale in the NEO Five Factor Inventory (NEO-FFI) [63]. In another study, which also used machine learning techniques, the most significant predictors of suicide attempts were sexual abuse in childhood and the knowledge that one is suffering from a mental disorder [64].

An important aspect of the clinical manifestations of schizophrenia is aggressive, violent behavior. It is known that the risk of committing violent crimes in female and male patients suffering from the schizophrenic spectrum disease is 1 in 20 and 1 in 4, respectively [65]. Scientists from Switzerland tried to establish the factors associated with violent behavior using machine learning techniques. The authors concluded that a large number of stress factors affect the frequency of violent crimes by people with schizophrenia. The most important factors included social isolation in adulthood, involuntary psychiatric treatment, unemployment, estrangement from family, and failure in school. The model based on classification trees determined a person who had committed a violent crime with 91.57% accuracy [66].

Kanchanatawan et al. used neural network predictions to demonstrate that the severity of "negative" symptoms, symptoms of mannerism, arousal, and hostility are very accurate predictors of affective and psychosomatic symptoms in schizophrenia [67]. Models based on machine learning techniques can also predict the outcomes of schizophrenia. In a study by Lin et al., low scores on the quality-of-life scale were associated with the severity of "negative" and depressive symptoms and low results on the global functioning assessment scale were associated with the severity of "positive" and "negative" symptoms in schizophrenia. Cognitive impairment was also evaluated in that study. Researchers were able to predict changes over time in cognitive functions using machine learning techniques based on test results and the analysis of cognitive domains; the most significant predicting factor was the speed of information processing [68]. In another study, the significant factors able to predict the state of neurocognitive functions were memory disorders, executive dysfunction, as well as disorders of concentration and fluency of speech [69].

DISCUSSION

Our analysis of published literature included articles relating to the use of AI for the development of the diagnostic and prognostic models used in the context of schizophrenia. Diagnostic models are used to more accurately identify schizophrenia by analyzing EEG signals, MRI scans, mental abilities (speech, voice, emotions, visual art), and genetic and epigenetic information. Predictive models created with the help of AI technologies can be used for early identification of persons at high risk of psychosis, including the first episode of schizophrenia, as well as for predicting the outcomes of schizophrenia. Prognostic models are able to predict individual clinical symptoms and complications in schizophrenia.

Based on the information provided so far, it can be predicted that in the near future various methods may find wider application in psychiatric practice. Some algorithms have already been approved by the U.S. Food and Drug Administration (FDA) [70]. In this regard, many doctors and scientists are concerned about the ethical question of AI use in medicine and, particularly, in psychiatry. Researchers are concerned about the confidentiality of information, the accuracy of calculations, the safety of the use of algorithms, and possible disregard for the individual characteristics of a patient [70, 71].

Al algorithms, including those based on machine learning, are only as good as the data they were trained on [72]. If the training data is biased, incomplete, or of poor quality, then the operation of the AI system may be disrupted, which will lead to inaccurate or unreliable results. Therefore, it is very important to check the results obtained with the help of AI technologies using traditional diagnostic methods to ensure their accuracy. Also, models may be sensitive to input bias and models may make mistakes in situations that are very different from those on which they were trained, which makes the model less reliable. Therefore, some scientists propose to introduce tools into Al-based models that can shore up their reliability; for example, by comparing the training set against each new instance introduced into the model [73]. It can be difficult to understand the decisions made by some models based on machine learning techniques; e.g., deep neural networks. Such models are called "black box" models in the literature [74, 75]. In this regard, there arises a question on the ethics of entrusting the patient's health to the "internal logic" of AI, which is not controlled by humans [76]. In our opinion, machine learning techniques should be used with extreme caution in clinical practice, only in conjunction with the main diagnostic tests, checking the results provided by AI and, of course, informing patients if recommendations based on the use of machine learning techniques are used.

The limitations of this review included a nonsystematic search for information, continuous inclusion of any type of studies, and lack of any assessment of the quality of the included studies. Also, the small sample size in a number of studies does not allow one to extrapolate the results to all people with schizophrenia.

There are several aspects of practical significance in the obtained results.

First, the use of models based on machine learning techniques in the diagnosis of schizophrenia makes it possible to achieve a more accurate and reliable qualification of this mental illness. An accurate diagnosis is key in providing the patient with adequate medical care.

Second, predictive models created using AI technologies can help with early identification of individuals at high risk of developing psychotic episodes, including the first episode of schizophrenia. This can be especially useful because early detection of schizophrenia can help prevent or reduce the severity of this mental illness. Moreover, prognostic models can predict the outcomes of schizophrenia, which can help clinicians and patients choose the most appropriate treatment and plan long-term care.

Third, the ability to predict individual clinical symptoms and complications of schizophrenia using prognostic models is of great importance for an individualized approach to treatment. This means that clinicians can predict what symptoms and complications may occur in specific patients and choose treatment according to their individual needs. This personalized approach can improve the effectiveness of treatment and clinical outcomes. However, no model can ensure a perfect result, which may be explained by the inability to include all patient features contributing to the final outcome in the prognostic or diagnostic model. In addition, models "overloaded" with input data can become unstable and produce poorer results compared to balanced models.

In general, the results of this review indicate the significant potential of machine learning techniques in the field of diagnosis and prediction of schizophrenia and its clinical features. These methods can significantly improve our understanding, diagnosis, and treatment of this psychiatric disorder, which ultimately can lead to an improvement in the lives of people with schizophrenia and lessen the state's economic burden associated with this disease.

CONCLUSION

Machine learning techniques are used both to identify schizophrenia (diagnostic algorithms) and to predict the manifestation of the disease or the clinical features of a known illness (prognostic algorithms).

So far, the ethical issues associated with the use of these techniques remain unresolved and the clinical reliability of these models remains unclear, which limits, at this point, our ability to use these algorithms in clinical practice. Nevertheless, the use of machine learning algorithms remains one of the most promising areas in psychiatry, and it can significantly improve the effectiveness of diagnosis and treatment when dealing with schizophrenia.

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Information about the authors

*Vadim Rimovich Gashkarimov, clinical resident-psychiatrist, Republican Clinical Psychiatric Hospital; ORCID: https://orcid.org/0000-0001-9944-141X, e-Library SPIN-code: 3828-4634;

E-mail: gashkarimov@yandex.ru

Renata Ildarovna Sultanova, psychiatrist, Moscow Research and Clinical Center for Neuropsychiatry of Moscow Healthcare Department;

ORCID: https://orcid.org/0000-0001-6679-4454, e-Library SPIN-code: 8284-8451 Ilya Segeevich Efremov, Cand. Sci. (Med.), Assistant, Department of Psychiatry, Narcology and Psychotherapy Bashkir State Medical University; Junior Researcher, V.M. Bekhterev National Medical Research Centre for Psychiatry and Neurology; ORCID: https://orcid.org/0000-0002-9994-8656, e-Library SPIN-code: 9983-8464

Azat Railevich Asadullin, Dr. Sci. (Med.), Professor, Department of Psychiatry, Narcology and Psychotherapy Bashkir State Medical University; Leading Researcher, V.M. Bekhterev National Medical Research Centre for Psychiatry and Neurology; Deputy Medical Director, Republican Clinical Psychotherapeutic Center; ORCID: https://orcid.org/0000-0001-7148-4485, e-Library SPIN-code: 3740-7843

*corresponding author

References

- El Naqa I, Murphy MJ. What is machine learning? In: El Naqa I, Murphy MJ, editors. Machine Learning in Radiation Oncology: Theory and Applications. Springer, Cham; 2015. p. 3–11. doi:10.1007/978-3-319-18305-31.
- Carleo G, Cirac I, Cranmer K, Daudet L, Schuld M, Tishby N, Vogt-Maranto L, Zdeborová L. Machine learning and the physical sciences. Rev Mod Phys. 2019;91(4):045002. doi:10.1103/RevModPhys.91.045002.
- Jordan MI, Mitchell TM. Machine learning: Trends, perspectives, and prospects. Science. 2015;349(6245):255–60. doi: 10.1126/science.aaa8415.
- Patel J, Shah S, Thakkar P, Kotecha K. Predicting stock and stock price index movement using trend deterministic data preparation and machine learning techniques. Expert systems with applications. 2015;42(1):259–68. doi: 10.1016/j.eswa.2014.07.040.
- Larranaga P, Calvo B, Santana R, Bielza C, Galdiano J, Inza I, Lozano JA, Armañanzas R, Santafé G, Pérez A, Robles V. Machine learning in bioinformatics. Brief Bioinform. 2006;7(1):86–112. doi: 10.1093/bib/bbk007.
- Miotto R, Wang F, Wang S, Jiang X, Dudley JT. Deep learning for healthcare: review, opportunities and challenges. Brief Bioinform. 2018;19(6):1236–46. doi: 10.1093/bib/bbx044.
- Saleem TJ, Chishti MA. Exploring the applications of machine learning in healthcare. International Journal of Sensors Wireless Communications and Control. 2020;10(4):458–72. doi: 10.2174/2210327910666191220103417.
- Faust O, Hagiwara Y, Hong TJ, Lih OS, Acharya UR. Deep learning for healthcare applications based on physiological signals: A review. Comput Methods Programs Biomed. 2018;161:1–13. doi.org/10.1016/j.cmpb.2018.04.005.
- Saha S, Chant D, Welham J, McGrath J. A systematic review of the prevalence of schizophrenia. PLoS Med. 2005;2(5):e141. doi: 10.1371/journal.pmed.0020141.
- Long J, Huang G, Liang W, Liang B, Chen Q, Xie J, Jiang J, Su L. The prevalence of schizophrenia in mainland China: evidence from epidemiological surveys. Acta Psychiatr Scand. 2014;130(4):244–56. doi: 10.1111/acps.12296
- Wu EQ, Shi L, Birnbaum H, Hudson T, Kessler R. Annual prevalence of diagnosed schizophrenia in the USA: a claims data analysis approach. Psychol Med. 2006;36(11):1535–40. doi: 10.1017/S0033291706008191.
- American Psychiatric Association, DSM-5 Task Force. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Arlington (VA): American Psychiatric Publishing, Inc.; 2013. doi: 10.1176/appi.books.9780890425596.
- Chisholm K, Lin A, Abu-Akel A, Wood SJ. The association between autism and schizophrenia spectrum disorders: A review of eight alternate models of co-occurrence.

Neurosci Biobehav Rev. 2015;55:173–83. doi: 10.1016/j. neubiorev.2015.04.012.

- Pearlson GD. Etiologic, phenomenologic, and endophenotypic overlap of schizophrenia and bipolar disorder. Annu Rev Clin Psychol. 2015;11:251–81. doi: 10.1146/annurev-clinpsy-032814-112915.
- Melle I, Larsen TK, Haahr U, Friis S, Johannessen JO, Opjordsmoen S, Simonsen E, Rund BR, Vaglum P, McGlashan T. Reducing the duration of untreated first-episode psychosis: effects on clinical presentation. Arch Gen Psychiatry. 2004;61(2):143–50. doi: 10.1001/archpsyc.61.2.143.
- Melle I, Larsen TK, Haahr U, Friis S, Johannesen JO, Opjordsmoen S, Rund BR, Simonsen E, Vaglum P, McGlashan T. Prevention of negative symptom psychopathologies in first-episode schizophrenia: two-year effects of reducing the duration of untreated psychosis. Arch Gen Psychiatry. 2008;65(6):634–40. doi: 10.1001/archpsyc.65.6.634.
- Sarker IH. Machine learning: Algorithms, real-world applications and research directions. SN Comput Sci. 2021;2(3):160. doi: 10.1007/s42979-021-00592-x.
- Bracher-Smith M, Rees E, Menzies G, Walters JTR, O'Donovan MC, Owen MJ, Kirov G, Escott-Price V. Machine learning for prediction of schizophrenia using genetic and demographic factors in the UK biobank. Schizophr Res. 2022;246:156–64. doi: 10.1016/j.schres.2022.06.006.
- Fazel S, O'Reilly L. Machine learning for suicide research-can it improve risk factor identification? JAMA Psychiatry. 2020;77(1):13-4. doi: 10.1001/jamapsychiatry.2019.2896.
- de Filippis R, Carbone EA, Gaetano R, Bruni A, Pugliese V, Segura-Garcia C, De Fazio P. Machine learning techniques in a structural and functional MRI diagnostic approach in schizophrenia: a systematic review. Neuropsychiatr Dis Treat. 2019;15:1605–27. doi: 10.2147/NDT.S202418.
- Zhu L, Wu X, Xu B, Zhao Z, Yang J, Long J, Su L. The machine learning algorithm for the diagnosis of schizophrenia on the basis of gene expression in peripheral blood. Neurosci Lett. 2021;745:135596. doi: 10.1016/j.neulet.2020.135596.
- Di Lorenzo G, Daverio A, Ferrentino F, Santarnecchi E, Ciabattini F, Monaco L, Lisi G, Barone Y, Di Lorenzo C, Niolu C, Seri S, Siracusano A. Altered resting-state EEG source functional connectivity in schizophrenia: the effect of illness duration. Front Hum Neurosci. 2015;9:234. doi: 10.3389/fnhum.2015.00234.
- Akar SA, Kara S, Latifoğlu FATMA, Bilgiç V. Analysis of the complexity measures in the EEG of schizophrenia patients. Int J Neural Syst. 2016;26(02):1650008. doi: 10.1142/s0129065716500088.
- 24. Sun J, Cao R, Zhou M, Hussain W, Wang B, Xue J, Xiang J. A hybrid deep neural network for classification of schizophrenia using EEG Data. Sci Rep. 2021;11(1):1–16. doi: 10.1038/s41598-021-83350-6.
- Oh SL, Vicnesh J, Ciaccio EJ, Yuvaraj R, Acharya UR. Deep convolutional neural network model for automated diagnosis of schizophrenia using EEG signals. Appl Sci. 2019;9(14):2870. doi: 10.3390/app9142870.
- Shalbaf A, Bagherzadeh S, Maghsoudi A. Transfer learning with deep convolutional neural network for automated detection of schizophrenia from EEG signals. Phys Eng Sci Med. 2020;43:1229–39. doi: 10.1007/s13246-020-00925-9.
- Phang CR, Noman F, Hussain H, Ting CM, Ombao H. A multidomain connectome convolutional neural network for identifying schizophrenia from EEG connectivity patterns. IEEE J Biomed Health Inform. 2019;24(5):1333–43. doi: 10.1109/JBHI.2019.2941222.
- 28. Shim M, Hwang HJ, Kim DW, Lee SH, Im CH. Machine-learningbased diagnosis of schizophrenia using combined sensor-level

and source-level EEG features. Schizophr Res. 2016;176(2-3):314–9. doi: 10.1016/j.schres.2016.05.007.

- Chen Z, Yan T, Wang E, Jiang H, Tang Y, Yu X, Zhang J, Liu C. Detecting abnormal brain regions in schizophrenia using structural MRI via machine learning. Comput Intell Neurosci. 2020;2020:8836408. doi: 10.1155/2020/6405930
- Schnack HG, Nieuwenhuis M, van Haren NE, Abramovic L, Scheewe TW, Brouwer RM, Hulshoff Pol HE, Kahn RS. Can structural MRI aid in clinical classification? A machine learning study in two independent samples of patients with schizophrenia, bipolar disorder and healthy subjects. Neuroimage. 2014;84:299–306. doi: 10.1016/j.neuroimage.2013.08.053.
- Oh K, Kim W, Shen G, Piao Y, Kang NI, Oh IS, Chung YC. Classification of schizophrenia and normal controls using 3D convolutional neural network and outcome visualization. Schizophr Res. 2019;212:186–95. doi: 10.1016/j.schres.2019.07.034.
- 32. Shi D, Li Y, Zhang H, Yao X, Wang S, Wang G, Ren K. Machine learning of schizophrenia detection with structural and functional neuroimaging. Dis Markers. 2021;2021:9948655. doi: 10.1155/2021/9963824.
- Nguyen DK, Chan CL, Li AHA, Phan DV, Lan CH. Decision support system for the differentiation of schizophrenia and mood disorders using multiple deep learning models on wearable devices data. Health Inform J. 2022;28(4):14604582221137537. doi: 10.1177/14604582221137537.
- Nagy Á, Dombi J, Fülep MP, Rudics E, Hompoth EA, Szabó Z, Dér A, Búzás A, Viharos ZJ, Hoang AT, Maczák B, Vadai G, Gingl Z, László S, Bilicki V, Szendi I. The Actigraphy-Based Identification of Premorbid Latent Liability of Schizophrenia and Bipolar Disorder. Sensors. 2023;23(2):958. doi:10.3390/s23020958.
- Bae YJ, Shim M, Lee WH. Schizophrenia detection using machine learning approach from social media content. Sensors. 2021;21(17):5924. doi: 10.3390/s21175924.
- Birnbaum ML, Ernala SK, Rizvi AF, De Choudhury M, Kane JM. A collaborative approach to identifying social media markers of schizophrenia by employing machine learning and clinical appraisals. J Med Internet Res. 2017;19(8):e7956. doi: 10.2196/jmir.7956.
- Fu J, Yang S, He F, He L, Li Y, Zhang J, Xiong X. Sch-net: a deep learning architecture for automatic detection of schizophrenia. BioMed Eng OnLine. 2021;20(1):92. doi: 10.1186/s12938-021-00915-2.
- Tahir Y, Yang Z, Chakraborty D, Thalmann N, Thalmann D, Maniam Y, Binte Abdul Rashid NA, Tan BL, Lee Chee Keong J, Dauwels J. Non-verbal speech cues as objective measures for negative symptoms in patients with schizophrenia. PLoS One. 2019;14(4):e0214314 doi: 10.1371/journal.pone.0214314.
- Bishay M, Palasek P, Priebe S, Patras I. Schinet: Automatic estimation of symptoms of schizophrenia from facial behaviour analysis. IEEE Transactions on Affective Computing. 2019;12(4):949–61. doi: 10.1109/TAFFC.2019.2907628.
- Huang J, Zhao Y, Qu W, Tian Z, Tan Y, Wang Z, Tan S. Automatic recognition of schizophrenia from facial videos using 3D convolutional neural network. Asian J Psychiatry. 2022;77:103263. doi: 10.1016/j.ajp.2022.103263.
- Vasilchenko KF, Usov GM. Application of convolutional neural networks as a tool for objectifying the diagnosis of schizophrenia: a pilot study. Sotsial'naya i klinicheskaya psikhiatriya. 2022;32(1):23–7. Russian.
- 42. Shen H, Wang SH, Zhang Y, Wang H, Li F, Lucas MV, Zhang YD, Liu Y, Yuan TF. Color painting predicts clinical symptoms in

chronic schizophrenia patients via deep learning. BMC Psychiatry. 2021;21:1–11. doi: 10.1186/s12888-021-03452-3.

- Karthik S, Sudha M. Predicting bipolar disorder and schizophrenia based on non-overlapping genetic phenotypes using deep neural network. Evol Intell. 2021;14:619–34. doi: 10.1007/s12065-019-00346-y.
- Sardaar S, Qi B, Dionne-Laporte A, Rouleau GA, Rabbany R, Trakadis YJ. Machine learning analysis of exome trios to contrast the genomic architecture of autism and schizophrenia. BMC Psychiatry. 2020;20(1):1–11. doi: 10.1186/s12888-020-02503-5.
- 45. Takahashi M, Hayashi H, Watanabe Y, Sawamura K, Fukui N, Watanabe J, Kitajima T, Yamanouchi Y, Iwata N, Mizukami K, Hori T, Shimoda K, Ujike H, Ozaki N, Iijima K, Takemura K, Aoshima H, Someya T. Diagnostic classification of schizophrenia by neural network analysis of blood-based gene expression signatures. Schizophr Res. 2010;119(1-3):210–8. doi: 10.1016/j.schres.2009.12.024.
- Gunasekara CJ, Hannon E, MacKay H, Coarfa C, McQuillin A, Clair DS, Mill J, Waterland RA. A machine learning case-control classifier for schizophrenia based on DNA methylation in blood. Transl Psychiatry. 2021;11(1):412. doi: 10.1038/s41398-021-01496-3.
- Lin E, Lin CH, Lai YL, Huang CH, Huang YJ, Lane HY. Combination of G72 genetic variation and G72 protein level to detect schizophrenia: machine learning approaches. Front Psychiatry. 2018;9:566. doi: 10.3389/fpsyt.2018.00566.
- Aguiar-Pulido V, Seoane JA, Rabuñal JR, Dorado J, Pazos A, Munteanu CR. Machine learning techniques for single nucleotide polymorphism-disease classification models in schizophrenia. Molecules. 2010;15(7):4875–89. doi: 10.3390/molecules15074875.
- 49. Raket LL, Jaskolowski J, Kinon BJ, Brasen JC, Jönsson L, Wehnert A, Fusar-Poli P. Dynamic ElecTronic hEalth reCord deTection (DETECT) of individuals at risk of a first episode of psychosis: a case-control development and validation study. The Lancet Digital Health. 2020;2(5):e229–e239. doi: 10.1016/S2589-7500(20)30024-8.
- Fusar-Poli P, Rutigliano G, Stahl D, Davies C, Bonoldi I, Reilly T, McGuire P. Development and validation of a clinically based risk calculator for the transdiagnostic prediction of psychosis. JAMA Psychiatry. 2017;74(5):493–500. doi: 10.1001/jamapsychiatry.2017.0284.
- Irving J, Patel R, Oliver D, Colling C, Pritchard M, Broadbent M, Baldwin H, Stahl D, Stewart R, Fusar-Poli P. Using natural language processing on electronic health records to enhance detection and prediction of psychosis risk. Schizophr Bull. 2021;47(2):405–14. doi: 10.1093/schbul/sbaa126.
- Elujide I, Fashoto SG, Fashoto B, Mbunge E, Folorunso SO, Olamijuwon JO. Application of deep and machine learning techniques for multi-label classification performance on psychotic disorder diseases. Inform Med Unlocked. 2021;23:100545. doi: 10.1016/j.imu.2021.100545.
- Gashkarimov VR, Sultanova RI, Islamova ED, Gasenko KA, Gasenko KA, Efremov IS, Gizatullin TR, Asadullin AR. The structure of insomnia and its relation to the severity of psychopathological symptoms in people with schizophrenia (pilot study). Psihicheskoe zdorov'e [Mental health] 2021;(7):36–42. doi: 10.25557/2074-014X.2021.07.36-42. Russian
- Krynicki CR, Upthegrove R, Deakin JFW, Barnes TR. The relationship between negative symptoms and depression in schizophrenia: a systematic review. Acta Psychiatr Scand. 2018;137(5):380–90. doi: 10.1111/acps.12873.

- Mavrogiorgou P, Haller K, Juckel G. Death anxiety and attitude to death in patients with schizophrenia and depression. Psychiatry Res. 2020;290:113148. doi: 10.1016/j.psychres.2020.113148.
- Mulligan LD, Haddock G, Emsley R, Neil ST, Kyle SD. High resolution examination of the role of sleep disturbance in predicting functioning and psychotic symptoms in schizophrenia: A novel experience sampling study. J Abnorm Psychol. 2016;125(6):788–97. doi: 10.1037/abn0000180.
- 57. Temmingh H, Stein DJ. Anxiety in patients with schizophrenia: epidemiology and management. CNS Drugs. 2015;29(9):819–32. doi: 10.1007/s40263-015-0281-4.
- Reeve S, Nickless A, Sheaves B, Freeman D. Insomnia, negative affect, and psychotic experiences: Modelling pathways over time in a clinical observational study. Psychiatry Res. 2018;269:673–80. doi: 10.1016/j.psychres.2018.08.090.
- Robertson I, Cheung A, Fan X. Insomnia in patients with schizophrenia: current understanding and treatment options. Prog Neuropsychopharmacol Biol Psychiatry. 2019;92:235–42. doi: 10.1016/j.pnpbp.2019.01.016.
- Kalinich M, Ebrahim S, Hays R, Melcher J, Vaidyam A, Torous J. Applying machine learning to smartphone based cognitive and sleep assessments in schizophrenia. Schizophr Res Cogn. 2022;27:100216. doi: 10.1016/j.scog.2021.100216.
- Gashkarimov VR, Pushkarev NV, Sultanova RI, Efremov IS, Gasenko KA, Asadullin AR. The use of neural networks in predicting of insomnia in individuals with schizophrenia. Pilot study. Psikhicheskoe zdorovie [Mental Health]. 2023;18(2):3–13. doi: 10.25557/2074-014X.2023.02.3-13. Russian
- Kumar S, Saxena A. A Machine Learning Method for Predictive Detection of Depression in Men with Schizophrenia. In: 2023 IEEE International Conference on Integrated Circuits and Communication Systems (ICICACS). IEEE; 2023. p. 1–6. doi: 10.1109/ICICACS57338.2023.10099887.
- Hettige NC, Nguyen TB, Yuan C, Rajakulendran T, Baddour J, Bhagwat N, Bani-Fatemi A, Voineskos AN, Mallar Chakravarty M, De Luca V. Classification of suicide attempters in schizophrenia using sociocultural and clinical features: A machine learning approach. Gen Hosp Psychiatry. 2017;47:20–8. doi: 10.1016/j.genhosppsych.2017.03.001.
- Tasmim S, Dada O, Wang KZ, Bani-Fatemi A, Strauss J, Adanty C, Graff A, Gerretsen P, Zai C, Borlido C, De Luca V. Early-life stressful events and suicide attempt in schizophrenia: Machine learning models. Schizophr Res. 2020;218:329–31. doi: 10.1016/j.schres.2019.11.061.

- 65. Whiting D, Gulati G, Geddes JR, Fazel S. Association of schizophrenia spectrum disorders and violence perpetration in adults and adolescents from 15 countries: A systematic review and meta-analysis. JAMA Psychiatry. 2022; 79(2):120–32 doi: 10.1001/jamapsychiatry.2021.3721.
- Kirchebner J, Sonnweber M, Nater UM, Günther M, Lau S. Stress, Schizophrenia, and Violence: A Machine Learning Approach. J Interpers Violence. 2022;37(1-2):602–22. doi: 10.1177/0886260520913641.
- 67. Kanchanatawan B, Thika S, Sirivichayakul S, Carvalho AF, Geffard M, Maes M.In schizophrenia, depression, anxiety, and physiosomatic symptoms are strongly related to psychotic symptoms and excitation, impairments in episodic memory, and increased production of neurotoxic tryptophan catabolites: a multivariate and machine learning study. Neurotox Res. 2018;33:641–55. doi: 10.1007/s12640-018-9868-4.
- Lin E, Lin CH, Lane HY. Applying a bagging ensemble machine learning approach to predict functional outcome of schizophrenia with clinical symptoms and cognitive functions. Sci Rep. 2021;11(1):1–9. doi: 10.1038/s41598-021-86382-0.
- Vacca A, Longo R, Mencar C. Identification and evaluation of cognitive deficits in schizophrenia using "Machine learning". Psychiatr Danub. 2019;31(Suppl 3):261–4.
- Topol EJ. High-performance medicine: the convergence of human and artificial intelligence. Nat Med. 2019;25(1):44–56. doi: 10.1038/s41591-018-0300-7.
- Strake G, De Clercq E, Borgwardt S, Elger BS. Computing schizophrenia: ethical challenges for machine learning in psychiatry. Psychol Med. 2021;51(15):2515–21. doi: 10.1017/S0033291720001683.
- Yu B, Kumbier K. Artificial intelligence and statistics. Frontiers Inf Technol Electronic Eng. 2018;19(1):6–9. doi: 10.1631/FITEE.1700813.
- Nicora G, Rios M, Abu-Hanna A, Bellazzi R. Evaluating pointwise reliability of machine learning prediction. J Biomed Inform. 2022;127:103996. doi: 10.1016/j.jbi.2022.103996.
- Wang F, Kaushal R, Khullar D. Should health care demand interpretable artificial intelligence or accept "black box" medicine? Ann Intern Med. 2020;172(1):59–60. doi: 10.7326/M19-2548.
- London AJ. Artificial intelligence and black-box medical decisions: accuracy versus explainability. Hastings Cent Rep. 2019;49(1):15–21. doi: 10.1002/hast.973.
- Reddy S. Explainability and artificial intelligence in medicine. The Lancet Digital Health. 2022;4(4):e214–e215. doi: 10.1016/S2589-7500 (22)00029-2.