Artificial Intelligence in Schizophrenia

Howard Schneider

Contents

1 Introduction 2
2 Artificial Intelligence Applied to the Research, Diagnosis, and Treatment of Schizophrenia and Related Disorders: Pre-2000 3
3 Artificial Intelligence Applied to the Research, Diagnosis, and Treatment of Schizophrenia and Related Disorders: 2000–2012 4
4 Artificial Intelligence Applied to the Research, Diagnosis, and Treatment of Schizophrenia and Related Disorders: 2012–2018 5
5 Artificial Intelligence Applied to the Research, Diagnosis, and Treatment of Schizophrenia and Related Disorders: 2019–Present 7
6 Current and Future Clinical Use of AI Techniques in the Diagnosis and Treatment of Schizophrenia and Related Disorders 10
7 Cross-References 11
References 11

Abstract

Principles and methods in artificial intelligence applied to the research, diagnosis, and treatment of schizophrenia and related disorders are reviewed from the 1980s to 2020. Support vector machines (SVMs), neural networks, expert systems, deep learning neural networks, autoencoders, deep belief networks, random forests, ensemble methods, and cognitive architectures are some of the AI techniques reviewed as applied to schizophrenia and related disorders. Connectionist models are used to better explain the development of schizophrenia. SVMs and deep learning neural networks are used to help interpret neuroimaging data in patients with schizophrenia. Deep learning networks are used to predict various outcomes for patients with schizophrenia. Deep learning neural networks and SVMs are used in the schizophrenia drug discovery process. AI-powered avatar therapy and socially

Supplementary Information: The online version of this chapter (https://doi.org/10.1007/978-3-030-58080-3_214-1) contains supplementary material, which is available to authorized users.

H. Schneider (✉)
Sheppard Clinic North, Toronto, ON, Canada
e-mail: hschneidermd@alum.mit.edu

N. Lidströmer, H. Ashrafian (eds.), *Artificial Intelligence in Medicine*,
https://doi.org/10.1007/978-3-030-58080-3_214-1

interactive robots are used in the therapy of patients with schizophrenia. At the time of this writing, use of AI techniques is starting to switch from the research setting to the clinical setting to help diagnose and treat patients with schizophrenia or schizophrenia-related disorders. For example, a multimodal machine model combined with human evaluations can fairly accurately predict the transition to psychosis for high-risk young individuals.

Keywords

Schizophrenia · Psychosis · Artificial intelligence · Machine learning · Precision psychiatry · Precision medicine · Personalized medicine · Subsymbolic · Symbolic · Avatar therapy

1 Introduction

Artificial intelligence (AI) is defined by Russell and Norvig [1] in terms of inclusion as a member in one of four broad categories – thinking rationally, acting rationally, thinking humanly, or acting humanly. In the "thinking rationally" class, an AI system applies logical reasoning to facts in order to solve a problem. In the "acting rationally" class, the AI system acts somewhat autonomously to obtain the best possible outcome of some goal given the existing constraints. In the "thinking humanly" class, the AI system should think like a human, thus there must essentially be cognitive modeling on the part of the AI system in this category of the definition. In the "acting humanly" class, an AI system successfully approaching the popular Turing Test (i.e., the AI system functions so well that a human asking written questions in a different room, could not tell whether the responses are from another human or from an AI system) is required. Here the AI system needs to have the following abilities – natural language processing (to communicate with the questioner), knowledge representation, automated reasoning, and machine learning (to improve knowledge representation as well as to recognize patterns). Applications of artificial intelligence to areas of schizophrenia fall in all these areas, as well as in areas that are more statistical in nature and less in keeping with the categories above (Video 1).

The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), classifies schizophrenia within the chapter on "Schizophrenia Spectrum and Other Psychotic Disorders" [2]. Schizophrenia diagnostic criteria require that there must be, for much of the time, at least one month of delusions, hallucinations, or incoherent or derailed speech, resulting in a reduced level of functioning. As well there must be at least two of the following: delusions, hallucinations, disorganized speech, catatonic or very disorganized behavior, and/or negative symptoms such as reduced emotions. While as noted above the active symptoms must be present for at least a month, there must also be active or residual symptoms for 6 months. The diagnosis requires exclusion of affective disorders with psychotic features, autism spectrum disorder (although comorbid diagnoses are possible), and physiological or medical causes of symptoms.

In the chapter of the DSM-5 on "Schizophrenia Spectrum and Other Psychotic Disorders," in addition to schizophrenia, there are other related disorders listed [2]. These disorders include delusional disorder, brief psychotic disorder, schizophreniform disorder, schizoaffective disorder, substance/medication-induced psychotic disorder, psychotic disorder due to another medical condition, catatonia associated with another mental disorder, and schizotypal personality disorder, although in the latter details are found in the DSM-5 chapter on "Personality Disorders." While below the focus is principally on applications of AI in the etiology, diagnosis, and treatments in schizophrenia, there will be consideration, where relevant, of AI applications toward any of these DSM-5 schizophrenia-related disorders.

In the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10), in the chapter on "Mental and Behavioural Disorders" there is a block on "Schizophrenia, Schizotypal and Delusional Disorders" [3]. This group includes: schizophrenia, schizophreniform disorder/psychosis, schizophrenia unspecified, schizotypal disorder, persistent delusional disorders, acute and transient psychotic disorders, induced delusional disorder, schizoaffective disorders, other nonorganic psychotic disorders, and unspecified nonorganic psychosis. Although the focus below is mainly on the application of AI for schizophrenia, applications of AI for the study, diagnosis, or treatment of any of these ICD-10-described schizophrenia-related disorders will be included where relevant.

The field of artificial intelligence is often arbitrarily divided into what are termed “Symbolic AI” and “Subsymbolic AI” approaches. Symbolic AI uses symbolic formulations of problems and symbolic logical solutions, i.e., there is manipulation of discrete symbols. Symbolic AI is sometimes referred to as “good old-fashioned AI (GOFAI)” due to the more current predominance of subsymbolic AI approaches. In subsymbolic AI there is not a formulation of the problem or its solution with a particularly human-obvious symbolic-like representation. For example, in artificial neural networks (ANNs), typically referred to as “neural networks,” there is not an obvious symbolic representation of a problem, but instead there is a massive collection of nodes (or “artificial neurons”) with connections (or “synapses”) to each other in a variety of wiring arrangements. Below both symbolic and subsymbolic approaches to AI applied to schizophrenia and related disorders will be included.

2 Artificial Intelligence Applied to the Research, Diagnosis, and Treatment of Schizophrenia and Related Disorders: Pre-2000

Artificial intelligence techniques started to become more consistently applied to the field of schizophrenia in the mid-1980s. Work by Hoffman used specialized Hopfield neural networks to simulate models of psychosis induction [4]. However, during this era, in general in the field of AI, expert systems were the most predominantly used paradigm for AI systems, and started to find applications in psychiatry. An expert system is a symbolic approach to AI, utilizing a large collection of if–then rules obtained from a human expert, and software that applies these if–then rules to the properties of a problem that is to be solved. Work by Maurer and colleagues in the late 1980s compared an expert system that diagnosed schizophrenia from patient data with diagnoses obtained via the more traditional classification systems, with the expert system giving similar results [5].

By the 1990s expert systems in many different areas of AI had not performed as well as had been hoped for, and the entire AI field received less funding and attention, often referred to as the “AI Winter.” Artificial neural networks (or “neural networks”), essentially related to the modern deep learning artificial neural networks that would later be developed, were at this time unfortunately not thought to hold much promise. However, work did slowly continue on artificial neural networks. Cohen and Schreiber in 1992 described a neural network model which explored attention and language deficits in schizophrenia [6], and Hoffman and McGlashan in 1993 used artificial neural networks to model a breakdown in corticocortical communication [7].

Symbolic reasoning algorithms had long been part of the AI field, and during this time, indeed continued to be used in applications related to schizophrenia. For example, work by Garfield and Rapp in 1994 applied semantic networks with node and pathway-based reasoning rules to psychotic speech [8]. A semantic network is essentially a diagram representing knowledge, with lines between the nodes representing concepts, i.e., a symbolic approach to AI. In Garfield and Rapp’s work, reasoning rules operated on the nodes of and the lines in the semantic network diagram, and could recognize what they termed “crazy talk” from the violations of the reasoning rules.

As noted by Seeman, work on artificial neural network models of schizophrenia started to increase modestly by the mid-1990s, with the hope that these models could provide better explanations for the pathophysiology in schizophrenia [9]. Work by Lowell and Davis used artificial neural networks (ANNs) for the more practical purpose of predicting the length of hospital stay based on schizophrenic and other psychiatric patient data the ANNs were trained on [10]. Work by Hoffman and McGlashan in 1998 used ANNs to show that decreased cortical connectivity modeled the development of auditory hallucinations [11]. Work by Corson and colleagues in 1999 used an ANN to identify and measure the caudate nucleus in neuroimages of first-episode psychosis patients and control subjects [12].

3 Artificial Intelligence Applied to the Research, Diagnosis, and Treatment of Schizophrenia and Related Disorders: 2000–2012

During this era there was work on both symbolic and subsymbolic artificial intelligence approaches to schizophrenia and related disorders. For example, Razzouk and colleagues in 2006 described using decision support systems, which are essentially expert systems, to help the practicing physician in the clinical diagnosis of schizophrenia [13].

As neural network theory and technology slowly improved over this decade, there was the obvious application of using machine learning to extract indicators of schizophrenia and related disorders from neuroimaging. For example, Jafri and Calhoun used ANNs to attempt to detect the presence of schizophrenia from brain fMRIs [14]. Bose and colleagues in 2008 describe using an ANN model to distinguish schizophrenic patients from controls in PET imaging with an 89% sensitivity and 94% specificity [15].

Support vector machines (SVMs) started to be more widely used during this time period to classify features in a variety of datasets obtained from research on patients with schizophrenia. Support vector machines are not actually machines but a type of supervised machine learning model, useful for classifying data into a particular category as well as finding relationships between variables. As shown below in Fig. 1, the SVM model attempts to find the best hyperplane between different classes of datapoints. Similar to a neural network, there is a training phase where annotated training examples (i.e., annotated with the correct category an example belongs to) allows the SVM to build a model of the data. The SVM can then be used to classify data it has not seen before. Modifications of the SVM algorithm allow it to also function in an unsupervised fashion and find clustering of similar items in a large collection of data. Struyf and colleagues in 2008 used a variety of classification algorithms including SVMs, nearest shrunken centroids, decision trees, naïve Bayes, and nearest neighbor classification to classify patient genomics, demographics, and clinical data as bipolar disorder versus schizophrenia [16]. SVMs classified significantly better than the other algorithms used. Ozyurt and Brown in 2009 described a variety of AI techniques including SVMs and probabilistic reasoning, for retrieving knowledge from the scientific literature including schizophrenia abstracts [17].

The nodes or "neurons" in an ANN, while originally inspired by biological neurons, are artificial constructs quite different and much simplified compared to a natural neuron, as is their organization or wiring. There is an interest in the computational neuroscience community for more biologically realistic neural networks. Unlike in ANNs, biological neurons are much more sparsely and recurrently connected to each other [18]. Given that a variety of hippocampal

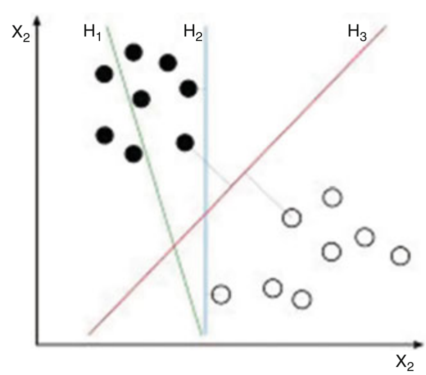

Fig. 1 SVM model creates a "hyperplane" that allows classification of data points. In this simple low-dimension example note that H3 separates the classes with a better margin than H1 or H2. (Creative Commons License BY-SA. Credit to Zack Weinberg)

abnormalities are found in schizophrenia, more realistic hippocampal computer simulations, for example, were thought to help better understand its etiology [19]. ANNs continued to be used to model aspects of the pathology of schizophrenia. For example, Karolidis and colleagues in 2010 used ANNs to model a number of cloned molecules which could bind to human dopamine D1 and D2 receptors [20].

4 Artificial Intelligence Applied to the Research, Diagnosis, and Treatment of Schizophrenia and Related Disorders: 2012–2018

The theory and technology behind various machine learning approaches, including ANNs with multiple hidden layers and termed “deep learning,” had started to greatly improve in the mid-2000s. In 2012 work by Krizhevsky, Sutskever, and Hinton using deep learning won a computer vision competition by a large margin over older methods [21]. This achievement is regarded as an approximate start of what is called the “deep learning revolution” and propelled the utilization of deep learning into many domains, including the research and clinical aspects of the field of schizophrenia. In the ImageNet contest a computer-based system needed to classify as accurately as possible large numbers of different images into some thousand different classes. Krizhevsky and colleagues used a deep convolutional neural network. In such a neural network there are multiple layers of nodes (or “neurons”) connected with layers where the nodes act as convolutional layers where such layers extract features from the previous layers preserving the spatial relationships but essentially mapping into a small-size receptive field and extracting features as such. Krizhevsky and colleagues used 650,000 neurons arranged in a number of layers including five convolutional layers. Within a few years deep learning neural networks improved (and grew in size and processing power) to the point where they could classify the ImageNet images more accurately than human competitors.

A review by Veronese and colleagues in 2013 gives an overview of machine learning approaches in schizophrenia but describes little of deep learning [22]. However, within a few years deep learning was being used in the field. In 2016 Kim and colleagues note that deep neural networks (DNNs) with multiple hidden layers were performing much better in classification tasks compared to SVMs and earlier AI models. They used a DNN to obtain functional connectivity patterns from resting-state functional magnetic resonance imaging [23]. A review by Arbabshirani and colleagues in 2017 considers the application of machine learning techniques including the emergence of deep learning to the prediction of brain disorders from patient neuroimaging data [24].

From 2016 onwards there was increasing application in the research and clinical aspects of schizophrenia of not only deep learning but also a variety of artificial intelligence techniques. For example, innovative work by Miotto and colleagues used a deep learning network incorporating autoencoders on a hospital-wide patient database to extract in an unsupervised fashion actionable features on individual patients such as personalized prescription, disease prediction, and clinical trial recruitment with better predictions for patients with schizophrenia than many other disorders [25]. Miotto and colleagues used a stack of particular denoising autoencoder layers. An autoencoder is a neural network that has an encoder layer of neurons that as its name suggests encodes an input signal. The encoded signal, usually reduced in dimensionality, i.e., there is a reduction in size of the input via nonlinear modifications, is then reconstructed by the decoder layer of neurons to give an output that maps in some way to the input signal. Thus, the output is not an exact copy of the input but a transformation of the input signal and, depending on how the autoencoder is constructed as well as combined with multiple layers of other autoencoders, can allow unsupervised learning to produce an efficient coding of the input signal which can extract or classify features of the input data (Fig. 2).

An interesting area of robotics in the 2010s was the development of "socially interactive robots" which are engineered to improve human-robot interactions by displaying nonverbal cues including facial emotions. Since nonverbal social interactions are known to be poorer in patients with schizophrenia, Raffard and colleagues in 2016 considered the use of a humanoid iCub robot, shown in Fig. 3 albeit without emotions activated in this photograph, in patients with schizophrenia [26]. It was found that both patients and controls recognized better the emotional facial expressions of humans than robots. Thus, the authors conclude that while humanoid robots have a theoretical potential in the role of increasing social functioning in patients, this study should only be considered exploratory.

Work by Arnon and colleagues in 2016 approached the theoretical realm of what is possible using modern electronics and AI technologies. Arnon and colleagues described the potential use of thought-controlled nanoscale robots which are activated by a magnetic field which is produced when an external sensor detected a particular EEG pattern, and can do a particular function such as make available bioactive molecules that could treat schizophrenia [27].

Use of SVM methods continued in the 2010s. For example, work by Mikolas and colleagues in 2016 used SVM analysis on the resting-state fMRI images of patients with a first-episode schizophrenia spectrum disorder and healthy controls, and was able to distinguish the anterior

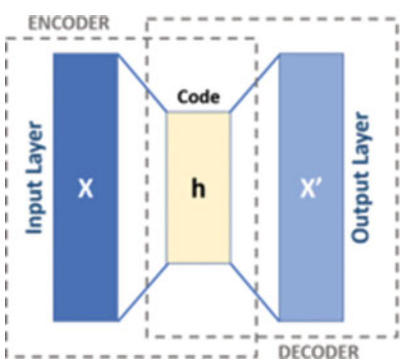

Fig. 2 Overview of an autoencoder. (Creative Commons License BY-SA. Credit to Michaela Massi)

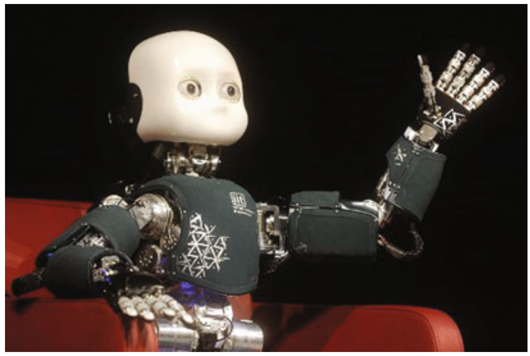

Fig. 3 iCub socially interactive robot, neutral emotions. (Creative Commons License BY-SA. Credit to Niccolò Caranti)

insula connectivity of patients from controls with an accuracy of 73.0% [28]. Work by Zarogianni and colleagues used SVM analysis in predicting schizophrenia based on a self-completed measure of schizotypy, a declarative memory test and a structural MRI brain scan [29].

A deep belief network is a type of deep neural network with a stack of layers of simpler often unsupervised learning neural models. Each layer in the deep belief network extracts a higher level of features of the input signal. Deep belief networks had been used for extracting information from and recognizing images, for example. Work by Pinaya and colleagues trained a deep belief network on features from MRI brain morphometry to distinguish between patients with schizophrenia and healthy controls with an accuracy of 73.6% [30].

A technique known as random forest creates many different decision trees during training and later will use the class decided by, for example, the most decision trees. Work by Pergola and colleagues in 2017 used random forests methodology to classify grey matter volume in the thalamus of MRIs from patients with schizophrenia, non-affected siblings, and controls, and found a familial relation associated with reduced thalamic grey matter volume in patients with schizophrenia [31].

Just as older AI techniques in the 1980s were used to model possible mechanisms in the development of psychosis, this continued in the 2010s with the now popular deep learning neural networks. For example, Keshavan and Sudarshan discuss how deep learning algorithms can possibly overemphasize objects the network believes are recognized leading to outputs that are detached from reality, and thus may possibly model some mechanisms involved in psychosis [32].

As in other fields of medicine, mobile apps incorporating AI features began to emerge with increasing frequency, especially from 2016 onwards. Work by Bain and colleagues in 2017 describe a mobile app to assess medication adherence by visual confirmation for patients with schizophrenia [33]. Work by Birnbaum and colleagues in 2017 used machine learning of Twitter (American blogging service) feeds from users self-diagnosed with schizophrenia in an attempt to classify users of this blogging service with schizophrenia from users who were considered healthy controls [34].

Machine learning started to become commonplace in imaging. For example, Dluhoš and colleagues describe creating a meta-model by combining SVM classifiers trained on local datasets and combining data from multiple centers [35]. Honnorat and colleagues used a clustering machine learning method that indicated a distinction between schizophrenia patients and controls in the temporal-thalamic-peri-Sylvian regions, frontal regions, and thalamus [36].

Work by Winterburn and colleagues compared logistic regression, SVMs, and linear discriminant analysis on cortical thickness and tissue density estimates, in patients with schizophrenia and healthy controls, with most accuracies between 55% and 70% [37]. Zeng and colleagues in 2018 used a deep discriminant autoencoder network to learn and distinguish fMRI functional connectivity features from patients with schizophrenia from healthy controls [38]. Bae and colleagues used SVM analysis to show from a public fMRI dataset that there were significant differences in patients with schizophrenia from healthy controls, especially in the anterior right cingulate cortex, the superior right temporal region, and the inferior left parietal region [39]. Work by Mikolas and colleagues used SVM to distinguish diffusion tensor MRI data from patients with first-episode schizophrenia spectrum disorder and healthy controls with an accuracy of 62.3% [40].

5 Artificial Intelligence Applied to the Research, Diagnosis, and Treatment of Schizophrenia and Related Disorders: 2019–Present

Toward the end of the 2010s a variety of AI techniques, including DNNs and SVMs, started to be applied to more relevant challenges in schizophrenia research, diagnosis, and treatment. AI methods allowed better interpretation of neuroimaging of patients with schizophrenia. Machine learning was being used in schizophrenia drug discovery research. AI techniques were being used in clinical schizophrenia diagnosis and care.

Zhao and So used DNNs and SVMs to predict the repositioning of schizophrenia drugs based on their drug expression profiles as candidates for other diseases [41]. Work by Lin and colleagues used three different machine learning algorithms (logistic regression, naïve Bayes classifier, and C4.5 decision tree) to examine two G72 SNP genotypes and G72 (D-amino-acid oxidase activator, DAOA) protein levels (previously associated with schizophrenia patients) to try to classify schizophrenia patients from healthy controls. The G72 protein levels alone gave most of the effect, with the naïve Bayes giving the best specificity of 0.95 and the logistic regression technique yielding the most sensitivity of 0.88 [42].

Fond and colleagues used machine learning via decision trees of data from patients with controlled schizophrenia to predict relapse at two years. High anger, high physical aggressiveness, high lifetime psychiatric hospitalizations, low education level, and high positive symptoms at baseline were the strongest predictors of relapse [43].

Work by Kalmady and colleagues examined resting-state fMRI data from patients with schizophrenia who had not been treated with antipsychotic medications and healthy controls. They used an ensemble machine learning classifier that was able to classify a resting fMRI into the correct schizophrenia/healthy control class with an accuracy of 87% versus 53% accuracy expected by chance alone [44]. An ensemble method uses multiple machine learning algorithms to obtain better accuracy than any one of the individual machine learning algorithms that it is based on. Kalmady and colleagues called their ensemble model "EMPaSchiz" which stood for "Ensemble algorithm with Multiple Parcellations for Schizophrenia prediction."

Work by Brodey and colleagues in 2019 trained SVMs from the responses of patients to the Early Psychosis Screener for Internet (EPSI) and predicted if the patient would be diagnosed with a psychotic disorder in 12 months [45]. Barrera and colleagues used digitally assisted nursing observations (i.e., obtained via computer vision and signal processing) in an acute mental health input ward with patients with schizophrenia, and found that patients' safety was not compromised [46]. Wu and colleagues trained an ensemble machine learning method on the records of 70% patients with first-episode schizophrenia to predict a successful antipsychotic medication selection. Success was defined as not switching medications and not being hospitalized in the next 12 months. The remaining 30% patients' data was not used for training, but kept for testing the machine learning model. If the individualized treatment which the machine learning method suggested was used, then the treatment success was 51.7% versus the actually observed 44.5% success [47].

Parola and colleagues used Bayesian classifier networks and found that pragmatic linguistic (language as well as other expressive means) impairment was the most important factor in classifying patients with schizophrenia versus healthy controls [48]. Using electroencephalographic patient data, Tikka and colleagues used SVM to classify patients with schizophrenia from healthy controls, and to classify patients with schizophrenia with positive symptoms from patients with schizophrenia with negative symptoms [49]. Particular eye movements are associated with schizophrenia and other disorders. However, it can be difficult to experimentally obtain eye movement features and associate the movement pattern with a disease. Mao and colleagues in an exploratory study classified eye movements with a random forest of decision trees [50].

Work by Kim and colleagues published in 2020 trained a convolutional neural network to analyze social media users' posts in a particular social media channel associated with a particular mental illness including schizophrenia, and thus create a deep learning model with natural language processing that could identify social media posts as belonging to various mental disorders including schizophrenia [51]. Work by Adler and colleagues published in 2020 used an app which collected schizophrenia patients' passive cellphone data which included location, acceleration, app use, screen activity, text messages, and as well prompted users every 2–3 days to self-report positive and negative symptoms. A fully connected neural network autoencoder and recurrent unit sequence-to-sequence model learned input time series data from the patients, and was able to predict certain behavioral changes which occurred before there was a clinical relapse [52].

Yang and colleagues reviewed concepts in artificial intelligence that could help with the drug discovery process, although there is little discussion of potential medications which could be used with schizophrenia-related disorders [53]. Zilocchi and colleagues showed an interesting association of 245 mitochondrial proteins to bipolar disorder, schizophrenia, and mood disorders. The authors looked at mitochondrial proteins listed in a number of public databases and then deduced the proteins associated with bipolar disorder, schizophrenia, and mood disorders by comparisons with gene disease listings in the DisGeNET database which already compiles data from many repositories. The authors then examined pharmaceutical repositories for mood stabilizers and obtained a small number of active ingredients, which they then examined in a drug-gene interactions database, and found that seven of the active ingredients actually targeted a number of these 245 mitochondrial proteins. The authors suggested that future use of machine learning methods could allow a virtual synthesis process that explored more of the chemical reactivity space and gave more possible potential drugs [54].

Work by Schneider took biological concepts from schizophrenia and applied them as constraints *back* to the field of artificial intelligence [55]. While neural networks, e.g., deep learning, have emerged as a very important technology in the field of artificial intelligence over the last decade, and while they can recognize patterns beyond human abilities, compared to a young child they are poor in logically and causally making sense of a problem they are solving. Deep learning networks have been getting better at performing their tasks by using ever faster computing hardware and training on ever larger sets of data, in a fashion that is not sustainable. As well, their amazing pattern recognition abilities do not give them many abilities we take for granted from human intelligence, e.g., the ability to usually explain why we made this or that decision.

Mammalian brains are characterized by cortex organized in repeating minicolumns. Schneider's Causal Cognitive Architecture 1 (CCA1) [56] preprocesses input sensory vectors through a hierarchy of Hopfield-like neural networks, but then feeds them to a navigation module. Unlike a deep neural network or unlike a symbolic artificial intelligence system, everything is processed and stored as navigation maps, which are inspired by the biological cortical minicolumns. Maps are stored, and retrieval can be triggered by other maps as well as operations on the maps. The architecture is not a tabula rasa but starts off with basic procedures termed "Instinctive Primitives" and learns procedures during its lifetime termed "Learned Primitives." The primitives are triggered by input sensory vectors and by maps in the navigation module. As well there are a number of other modules such as a "Goal/Emotion Module." This architecture is capable of performing pattern recognition much like artificial neural networks, but emerging almost automatically from the CCA1 architecture is a map-based precausal behavior to simple problems.

Just as feedback pathways abound in the human brain, they similarly exist in the CCA1 and downstream circuits can affect what inputs upstream circuits are to expect. The topic of whether any animal, other than humans and possibly some primates, possesses true causal behavior is controversial, but no nonhuman possesses robust causal behavior, chimpanzees included. Of interest, psychosis seems to readily emerge in humans, e.g., even though only small percentage of the population will suffer from schizophrenia, more than 10% of the population will actually experience psychotic-like symptoms [57]. In Schneider's CCA1 architecture if the navigation module feeds back intermediate results to the input circuits, then they can be processed again, and over and over again, with each of the input-processing output cycles the architecture follows. Full causality readily emerges from the architecture when this occurs, as opposed to precausal behavior otherwise [56]. As well, the navigation maps do not need to be used for physical navigation but automatically allow navigation of complex concepts. As well, explainability emerges (which really is just sequential retrieval of maps executed), and the ability to use and create analogies almost automatically emerges from the architecture. However, in this fuller architecture, any small flaw of many possible such small flaws causes a cognitive dysfunction as well as misinterpretation of intermediate results as sensory input signals (i.e., delusion-like and hallucination-like).

Rezaii and colleagues used neural networks to show that during the prodromal phase, low semantic density, i.e., essentially what is clinically referred to as poverty of content, increased the likelihood of conversion to psychosis [58]. McFarlane and Illes discuss the work of Rezaii and other researchers who have developed techniques of identifying psychosis by machine learning methods of analyzing speech and use of social media, and write of the ethical concerns in making such early predictions of psychosis, some of which will be flawed [59].

Craig and colleagues, including Julian Leff, the inventor of the therapy, discuss patients with persecutory auditory hallucinations interacting with a digital avatar representing the hallucinated persecutor, such that the avatar becomes less hostile and the patient feels more in control. In a 12-week study of 75 patients receiving AVATAR therapy versus controls receiving supportive therapy, there was a significant reduction in the severity of the auditory hallucinations in the AVATAR therapy group compared to the control group [60].

Work by Oh and colleagues, published in 2020, took ordinary structural MRI (1.5 and 3 T) brain images and trained a deep learning convolutional neural network to infer whether or not an image had cortical features of a patient with schizophrenia compared to normal subjects [61]. In the training data the neural network was able to correctly classify 840 out of 866 images, i.e., an accuracy of 97%. When the network was then tested on new images from different patients, the accuracy dropped, as is to be expected when a neural network starts classifying images it has not seen before in its training data, but it still was able to classify images reasonably well. It should be noted that human clinical specialists (five psychiatrists and two radiologists) had difficulty in discerning schizophrenia patients from the normal subjects in a random selection of the structural MRI images above.

6 Current and Future Clinical Use of AI Techniques in the Diagnosis and Treatment of Schizophrenia and Related Disorders

Fernandes and colleagues in 2017 write about what they consider the "new field of precision psychiatry" [62]. Just as "precision medicine" takes the individual features, i.e., the differences of each patient into account in crafting a prevention and treatment strategy [63], so does precision psychiatry. Bzdok and Meyer-Lindenberg write about the need for machine learning in precision psychiatry [64]. However, at the time of this writing, December 2020, the direct utilization of artificial intelligence techniques is not considered a standard of care (i.e., a legal term describing the expectations that health-care providers are to deliver in the care of their patients) in the diagnosis and treatment of patients with schizophrenia and schizophrenia-related disorders, in Canada where this chapter is being written, and it would seem worldwide as well. As well, in research studies related to schizophrenia it could be argued that many studies incorporating artificial intelligence techniques could be rewritten to instead incorporate advanced conventional statistical techniques, including some of the references described above. However, all this is starting to change.

For example, consider the work by Koutsouleris and colleagues, with preliminary publication online in December 2020 [65]. In young people who meet the clinical high-risk (CHR) criteria for psychosis development, only about a fifth will have a transition to psychosis over a three-year timespan. As well, psychotic disorders do develop in individuals who would not have been classified in the CHR group. Koutsouleris and colleagues fed patient information including MRI imaging, clinical data, and neurocognitive data into a multimodal machine learning model, to predict the transition to a psychotic disorder in 167 patients meeting the criteria for CHR, 167 patients with a recent-onset depression, and 334 healthy matched controls. The mean age was 25.1 years old. The machine learning model was combined with clinicians' risk estimates (where clinicians' predictions had relatively high specificity but lower sensitivity versus the model's relatively high sensitivity but lower specificity) and was able to predict the transition to psychosis with an accuracy of 85.9% (sensitivity 84.6%, specificity 87.3%). As a result, the authors recommend that this work be clinically implemented: "…. . . augmentation of human prognostic abilities with algorithmic pattern recognition improves prognostic accuracy to margins that likely justify the clinical implementation of cybernetic decision-support tools."

At the time of this writing, there is much controversy about the need for functional neuroimaging in clinical as opposed to research psychiatry. However, in 2020 Henderson and colleagues [66] write about the field clinically using functional neuroimaging to "guide the ordering diagnostician to a better and more efficient evaluation and treatment of the neurobiological processes that underlie a particular patient's symptoms." As noted in many of the references above with regard to neuroimaging of patients with possible schizophrenia, incorporation of AI techniques was a part of obtaining higher accuracies in the functional, as well as structural, imaging. For example, as noted above, Kalmady and colleagues [44] using AI techniques were able to differentiate healthy control subjects from patients with schizophrenia on fMRI with an accuracy of 87%. For example, as noted above, Oh and colleagues [61] using AI techniques were able to distinguish cortical features on ordinary structural MRIs between patients with schizophrenia and healthy controls. Indeed, Topol writes about the convergence of human decision-making with artificial intelligence in treating patients, particularly in the interpretation of imaging [67].

Starke and colleagues, writing in 2020, note that while machine learning is not routine in the clinical practice of psychiatry, in particular in schizophrenia, this is starting to occur, and thus there is a need to consider the ethical issues [68]. For example, machine learning algorithms, which could potentially be used in the future to diagnose and treat patients with schizophrenia, often do not explain well how they came up with their decisions.

The use of artificial intelligence in the clinical diagnosis and care of patients with schizophrenia is at the time of this writing in its infancy but starting to accelerate quickly. It is expected that in the 2020s not only will the capabilities of AI in the care of patients with schizophrenia keep improving, but the details of clinical implementations will start to become better managed.

7 Cross-References

▶ AIM and Medical Innovation
▶ AIM and the Emergence of Deep Medicine
▶ AIM in Anxiety and Depression
▶ Applying Principles from Medicine back to Artificial Intelligence
▶ Basic Concepts of AI
▶ Basic Concepts of AIM
▶ Introduction to AIM and "Lessons for All Doctors"

References

1. Russell S, Norvig P. What is AI? In: Artificial intelligence: a modern approach. 3rd ed. Upper Saddle River: Prentice Hall; 2010. p. 1–5.
2. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed. Arlington: American Psychiatric Association; 2013.
3. World Health Organization. The international statistical classification of diseases and related health problems, 10th revision (ICD-10). Geneva: World Health Organization; 2019. https://icd.who.int/browse10/2019/en
4. Hoffman RE. Computer simulations of neural information processing and the schizophrenia-mania dichotomy. Arch Gen Psychiatry. 1987;44:178–88.
5. Maurer K, Biehl K, Kühner C, Löffler W. On the way to expert systems. Comparing DSM-III computer diagnoses with CATEGO (ICD) diagnoses in depressive and schizophrenic patients. Eur Arch Psychiatry Neurol Sci. 1989;239(2):127–32. https://doi.org/10.1007/BF01759586.
6. Cohen JD, Servan-Schreiber D. Context, cortex, and dopamine: a connectionist approach to behavior and biology in schizophrenia. Psychol Rev. 1992;99(1):45–77. https://doi.org/10.1037/0033-295x.99.1.45.
7. Hoffman RE, McGlashan TH. Parallel distributed processing and the emergence of schizophrenic symptoms. Schizophr Bull. 1993;19(1):119–40. https://doi.org/10.1093/schbul/19.1.119.
8. Garfield DA, Rapp C. Application of artifical intelligence principles to the analysis of "crazy" speech. J Nerv Ment Dis. 1994;182(4):205–11. https://doi.org/10.1097/00005053-199404000-00002.
9. Seeman MV. Neural networks and schizophrenia. Can J Psychiatr. 1994;39(8):353–4. https://doi.org/10.1177/070674379403900801.
10. Lowell WE, Davis GE. Predicting length of stay for psychiatric diagnosis-related groups using neural networks. J Am Med Inform Assoc. 1994;1(6):459–66. https://doi.org/10.1136/jamia.1994.95153435.
11. Hoffman RE, McGlashan TH. Reduced corticocortical connectivity can induce speech perception pathology and hallucinated 'voices'. Schizophr Res. 1998;30(2):137–41. https://doi.org/10.1016/s0920-9964(97)00142-4.
12. Corson PW, Nopoulos P, Andreasen NC, Heckel D, Arndt S. Caudate size in first-episode neuroleptic-naive schizophrenic patients measured using an artificial neural network. Biol Psychiatry. 1999;46(5):712–20. https://doi.org/10.1016/s0006-3223(99)00079-7.
13. Razzouk D, Mari JJ, Shirakawa I, Wainer J, Sigulem D. Decision support system for the diagnosis of schizophrenia disorders. Braz J Med Biol Res. 2006;39(1):119–28. https://doi.org/10.1590/s0100-879x2006000100014.
14. Jafri MJ, Calhoun VD. Functional classification of schizophrenia using feed forward neural networks. Conf Proc IEEE Eng Med Biol Soc. 2006;

Suppl:6631–4. https://doi.org/10.1109/IEMBS.2006.260906.
15. Bose SK, Turkheimer FE, Howes OD, Mehta MA, Cunliffe R, Stokes PR, Grasby PM. Classification of schizophrenic patients and healthy controls using [18F] fluorodopa PET imaging. Schizophr Res. 2008;106(2–3):148–55. https://doi.org/10.1016/j.schres.2008.09.011.
16. Struyf J, Dobrin S, Page D. Combining gene expression, demographic and clinical data in modeling disease: a case study of bipolar disorder and schizophrenia. BMC Genomics. 2008;9:531. https://doi.org/10.1186/1471-2164-9-531.
17. Ozyurt IB, Brown GG. Knowledge discovery via machine learning for neurodegenerative disease researchers. Methods Mol Biol. 2009;569:173–96. https://doi.org/10.1007/978-1-59745-524-4_9.
18. Eliasmith C, Anderson CH. Neural engineering: representation, computation, and dynamics in neurobiological systems. Cambridge, MA: MIT Press; 2003.
19. Siekmeier PJ. Evidence of multistability in a realistic computer simulation of hippocampus subfield CA1. Behav Brain Res. 2009;200(1):220–31. https://doi.org/10.1016/j.bbr.2009.01.021.
20. Karolidis DA, Agatonovic-Kustrin S, Morton DW. Artificial neural network (ANN) based modelling for D1 like and D2 like dopamine receptor affinity and selectivity. Med Chem. 2010;6(5):259–70. https://doi.org/10.2174/157340610793358891.
21. Krizhevsky A, Sutskever I, Hinton GE. ImageNet classification with deep convolutional neural networks. In: Proceedings of the 25th international conference on neural information processing systems – volume 1 (NIPS'12). Red Hook: Curran Associates; 2012.
22. Veronese E, Castellani U, Peruzzo D, Bellani M, Brambilla P. Machine learning approaches: from theory to application in schizophrenia. Comput Math Methods Med. 2013;2013:867924. https://doi.org/10.1155/2013/867924.
23. Kim J, Calhoun VD, Shim E, Lee JH. Deep neural network with weight sparsity control and pre-training extracts hierarchical features and enhances classification performance: evidence from whole-brain resting-state functional connectivity patterns of schizophrenia. Neuroimage. 2016;124(Pt A):127–46. https://doi.org/10.1016/j.neuroimage.2015.05.018.
24. Arbabshirani MR, Plis S, Sui J, Calhoun VD. Single subject prediction of brain disorders in neuroimaging: promises and pitfalls. Neuroimage. 2017;145(Pt B):137–65. https://doi.org/10.1016/j.neuroimage.2016.02.079.
25. Miotto R, Li L, Kidd BA, Dudley JT. Deep patient: an unsupervised representation to predict the future of patients from the electronic health records. Sci Rep. 2016;6:26094. https://doi.org/10.1038/srep26094.
26. Raffard S, Bortolon C, Khoramshahi M, Salesse RN, Burca M, Marin L, Bardy BG, Billard A, Macioce V, Capdevielle D. Humanoid robots versus humans: how is emotional valence of facial expressions recognized by individuals with schizophrenia? An exploratory study. Schizophr Res. 2016;176(2–3):506–13. https://doi.org/10.1016/j.schres.2016.06.001.
27. Arnon S, Dahan N, Koren A, Radiano O, Ronen M, Yannay T, Giron J, Ben-Ami L, Amir Y, Hel-Or Y, Friedman D, Bachelet I. Thought-controlled nanoscale robots in a living host. PLoS One. 2016;11(8):e0161227. https://doi.org/10.1371/journal.pone.0161227.
28. Mikolas P, Melicher T, Skoch A, Matejka M, Slovakova A, Bakstein E, Hajek T, Spaniel F. Connectivity of the anterior insula differentiates participants with first-episode schizophrenia spectrum disorders from controls: a machine-learning study. Psychol Med. 2016;46(13):2695–704. https://doi.org/10.1017/S0033291716000878.
29. Zarogianni E, Storkey AJ, Johnstone EC, Owens DG, Lawrie SM. Improved individualized prediction of schizophrenia in subjects at familial high risk, based on neuroanatomical data, schizotypal and neurocognitive features. Schizophr Res. 2017;181:6–12. https://doi.org/10.1016/j.schres.2016.08.027.
30. Pinaya WH, Gadelha A, Doyle OM, Noto C, Zugman A, Cordeiro Q, Jackowski AP, Bressan RA, Sato JR. Using deep belief network modelling to characterize differences in brain morphometry in schizophrenia. Sci Rep. 2016;6:38897. https://doi.org/10.1038/srep38897.
31. Pergola G, Trizio S, Di Carlo P, Taurisano P, Mancini M, Amoroso N, Nettis MA, Andriola I, Caforio G, Popolizio T, Rampino A, Di Giorgio A, Bertolino A, Blasi G. Grey matter volume patterns in thalamic nuclei are associated with familial risk for schizophrenia. Schizophr Res. 2017;180:13–20. https://doi.org/10.1016/j.schres.2016.07.005.
32. Keshavan MS, Sudarshan M. Deep dreaming, aberrant salience and psychosis: connecting the dots by artificial neural networks. Schizophr Res. 2017;188:178–81. https://doi.org/10.1016/j.schres.2017.01.020.
33. Bain EE, Shafner L, Walling DP, Othman AA, Chuang-Stein C, Hinkle J, Hanina A. Use of a novel artificial intelligence platform on mobile devices to assess dosing compliance in a phase 2 clinical trial in subjects with schizophrenia. JMIR Mhealth Uhealth. 2017;5(2):e18. https://doi.org/10.2196/mhealth.7030.
34. 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):e289. https://doi.org/10.2196/jmir.7956.
35. Dluhoš P, Schwarz D, Cahn W, van Haren N, Kahn R, Španiel F, Horáček J, Kašpárek T, Schnack H. Multi-center machine learning in imaging psychiatry: a meta-model approach. NeuroImage. 2017;155:10–24. https://doi.org/10.1016/j.neuroimage.2017.03.027.
36. Honnorat N, Dong A, Meisenzahl-Lechner E, Koutsouleris N, Davatzikos C. Neuroanatomical heterogeneity of schizophrenia revealed by semi-supervised machine learning methods. Schizophr Res.

2019;214:43–50. https://doi.org/10.1016/j.schres.2017.12.008.
37. Winterburn JL, Voineskos AN, Devenyi GA, Plitman E, de la Fuente-Sandoval C, Bhagwat N, Graff-Guerrero A, Knight J, Chakravarty MM. Can we accurately classify schizophrenia patients from healthy controls using magnetic resonance imaging and machine learning? A multi-method and multi-dataset study. Schizophr Res. 2019;214:3–10. https://doi.org/10.1016/j.schres.2017.11.038.
38. Zeng LL, Wang H, Hu P, Yang B, Pu W, Shen H, Chen X, Liu Z, Yin H, Tan Q, Wang K, Hu D. Multi-site diagnostic classification of schizophrenia using discriminant deep learning with functional connectivity MRI. EBioMedicine. 2018;30:74–85. https://doi.org/10.1016/j.ebiom.2018.03.017.
39. Bae Y, Kumarasamy K, Ali IM, Korfiatis P, Akkus Z, Erickson BJ. Differences between schizophrenic and normal subjects using network properties from fMRI. J Digit Imaging. 2018;31(2):252–61. https://doi.org/10.1007/s10278-017-0020-4.
40. Mikolas P, Hlinka J, Skoch A, Pitra Z, Frodl T, Spaniel F, Hajek T. Machine learning classification of first-episode schizophrenia spectrum disorders and controls using whole brain white matter fractional anisotropy. BMC Psychiatry. 2018;18(1):97. https://doi.org/10.1186/s12888-018-1678-y.
41. Zhao K, So HC. Drug repositioning for schizophrenia and depression/anxiety disorders: a machine learning approach leveraging expression data. IEEE J Biomed Health Inform. 2019;23(3):1304–15. https://doi.org/10.1109/JBHI.2018.2856535.
42. 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 Psych. 2018;9:566. https://doi.org/10.3389/fpsyt.2018.00566.
43. Fond G, Bulzacka E, Boucekine M, Schürhoff F, Berna F, Godin O, Aouizerate B, Capdevielle D, Chereau I, D'Amato T, Dubertret C, Dubreucq J, Faget C, Leignier S, Lançon C, Mallet J, Misdrahi D, Passerieux C, Rey R, Schandrin A, Urbach M, Vidailhet P, Leboyer M, FACE-SZ (FondaMental Academic Centers of Expertise for Schizophrenia) Group, Boyer L, Llorca PM. Machine learning for predicting psychotic relapse at 2 years in schizophrenia in the national FACE-SZ cohort. Prog Neuropsychopharmacol Biol Psychiatry. 2019;92:8–18. https://doi.org/10.1016/j.pnpbp.2018.12.005.
44. Kalmady SV, Greiner R, Agrawal R, Shivakumar V, Narayanaswamy JC, Brown MRG, Greenshaw AJ, Dursun SM, Venkatasubramanian G. Towards artificial intelligence in mental health by improving schizophrenia prediction with multiple brain parcellation ensemble-learning. NPJ Schizophr. 2019;5(1):2. https://doi.org/10.1038/s41537-018-0070-8.
45. Brodey BB, Girgis RR, Favorov OV, Bearden CE, Woods SW, Addington J, Perkins DO, Walker EF, Cornblatt BA, Brucato G, Purcell SE, Brodey IS, Cadenhead KS. The Early Psychosis Screener for Internet (EPSI)-SR: predicting 12 month psychotic conversion using machine learning. Schizophr Res. 2019;208:390–6. https://doi.org/10.1016/j.schres.2019.01.015.
46. Barrera A, Gee C, Wood A, Gibson O, Bayley D, Geddes J. Introducing artificial intelligence in acute psychiatric inpatient care: qualitative study of its use to conduct nursing observations. Evid Based Ment Health. 2020;23(1):34–8. https://doi.org/10.1136/ebmental-2019-300136.
47. Wu CS, Luedtke AR, Sadikova E, Tsai HJ, Liao SC, Liu CC, Gau SS, VanderWeele TJ, Kessler RC. Development and validation of a machine learning individualized treatment rule in first-episode schizophrenia. JAMA Netw Open. 2020;3(2):e1921660. https://doi.org/10.1001/jamanetworkopen.2019.21660.
48. Parola A, Salvini R, Gabbatore I, Colle L, Berardinelli L, Bosco FM. Pragmatics, theory of mind and executive functions in schizophrenia: disentangling the puzzle using machine learning. PLoS One. 2020;15(3):e0229603. https://doi.org/10.1371/journal.pone.0229603.
49. Tikka SK, Singh BK, Nizamie SH, Garg S, Mandal S, Thakur K, Singh LK. Artificial intelligence-based classification of schizophrenia: a high density electroencephalographic and support vector machine study. Indian J Psychiatry. 2020;62(3):273–82. https://doi.org/10.4103/psychiatry.IndianJPsychiatry_91_20.
50. Mao Y, He Y, Liu L, Chen X. Disease classification based on eye movement features with decision tree and random forest. Front Neurosci. 2020;14:798. https://doi.org/10.3389/fnins.2020.00798.
51. Kim J, Lee J, Park E, Han J. A deep learning model for detecting mental illness from user content on social media. Sci Rep. 2020;10(1):11846. https://doi.org/10.1038/s41598-020-68764-y.
52. Adler DA, Ben-Zeev D, Tseng VW, Kane JM, Brian R, Campbell AT, Hauser M, Scherer EA, Choudhury T. Predicting early warning signs of psychotic relapse from passive sensing data: an approach using encoder-decoder neural networks. JMIR Mhealth Uhealth. 2020;8(8):e19962. https://doi.org/10.2196/19962.
53. Yang X, Wang Y, Byrne R, Schneider G, Yang S. Concepts of artificial intelligence for computer-assisted drug discovery. Chem Rev. 2019;119(18):10520–94. https://doi.org/10.1021/acs.chemrev.8b00728.
54. Zilocchi M, Broderick K, Phanse S, Aly KA, Babu M. Mitochondria under the spotlight: on the implications of mitochondrial dysfunction and its connectivity to neuropsychiatric disorders. Comput Struct Biotechnol J. 2020;18:2535–46. https://doi.org/10.1016/j.csbj.2020.09.008.
55. Schneider H. The meaningful-based cognitive architecture model of schizophrenia. Cogn Syst Res. 2020;59:73–90. https://doi.org/10.1016/j.cogsys.2019.09.019.

56. Schneider H. Causal cognitive architecture 1: integration of connectionist elements into a navigation-based framework. Cogn Syst Res. 2021;66:67–81. https://doi.org/10.1016/j.cogsys.2020.10.021.
57. van Os J, Hanssen M, Bijil RV, et al. Prevalence of psychotic disorder and community level psychotic symptoms: an urban-rural comparison. Arch Gen Psychiatry. 2001;58(7):663–8.
58. Rezaii N, Walker E, Wolff P. A machine learning approach to predicting psychosis using semantic density and latent content analysis. npj Schizophr. 2019;5:9. https://doi.org/10.1038/s41537-019-0077-9.
59. McFarlane J, Illes J. Neuroethics at the interface of machine learning and schizophrenia. npj Schizophr. 2020;6:18. https://doi.org/10.1038/s41537-020-0108-6.
60. Craig TKJ, Rus-Calafell M, Ward T, Leff JP, Huckvale M, Howarth E, Emsley R, Garety PA. AVATAR therapy for auditory verbal hallucinations in people with psychosis: a single-blind, randomised controlled trial. Lancet Psychiatry. 2018;5(1):31–40. https://doi.org/10.1016/S2215-0366(17)30427-3.
61. Oh J, Oh B-L, Lee K-U, Chae J-H, Yun K. Identifying schizophrenia using structural MRI with a deep learning algorithm. Front Psych. 2020;11:16. https://doi.org/10.3389/fpsyt.2020.00016.
62. Fernandes BS, Williams LM, Steiner J, Leboyer M, Carvalho AF, Berk M. The new field of 'precision psychiatry'. BMC Med. 2017;15(1):80. https://doi.org/10.1186/s12916-017-0849-x.
63. Collins FS, Varmus H. A new initiative on precision medicine. N Engl J Med. 2015;372(9):793–5. https://doi.org/10.1056/NEJMp1500523.
64. Bzdok D, Meyer-Lindenberg A. Machine learning for precision psychiatry: opportunities and challenges. Biol Psychiatry Cogn Neurosci Neuroimaging. 2018;3(3):223–30. https://doi.org/10.1016/j.bpsc.2017.11.007.
65. Koutsouleris N, Dwyer DB, Degenhardt F, et al. Multimodal machine learning workflows for prediction of psychosis in patients with clinical high-risk syndromes and recent-onset depression. JAMA Psychiatry. Published online December 02, 2020. https://doi.org/10.1001/jamapsychiatry.2020.3604.
66. Henderson TA, van Lierop MJ, McLean M, et al. Functional neuroimaging in psychiatry-aiding in diagnosis and guiding treatment. What the American Psychiatric Association does not know. Front Psych. 2020;11:276. https://doi.org/10.3389/fpsyt.2020.00276.
67. Topol EJ. High-performance medicine: the convergence of human and artificial intelligence. Nat Med. 2019;25:44–56. https://doi.org/10.1038/s41591-018-0300-7.
68. Starke G, De Clercq E, Borgwardt S, Elger BS. Computing schizophrenia: ethical challenges for machine learning in psychiatry. Psychol Med. 2020;15:1–7. https://doi.org/10.1017/S0033291720001683.