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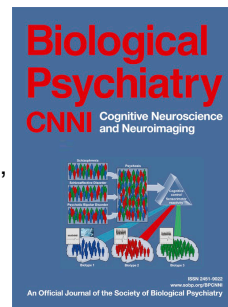
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Artificial Intelligence for Mental Healthcare:

Clinical Applications, Barriers, Facilitators, and Artificial Wisdom

Short title: AI for Mental Healthcare

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Abstract (unstructured)

Artificial intelligence (AI) is increasingly employed in healthcare fields such as oncology, radiology, and dermatology. However, the use of AI in mental healthcare and neurobiological research has been modest. Given the high morbidity and mortality in people with psychiatric disorders, coupled with a worsening shortage of mental healthcare providers, there is an urgent need for AI to help identify high-risk individuals and provide interventions to prevent and treat mental illnesses. While published research on AI in neuropsychiatry is rather limited, there is a growing number of successful examples of AI's use with electronic health records, brain imaging, sensor-based monitoring systems, and social media platforms to predict, classify, or subgroup mental illnesses as well as problems like suicidality. This article is the product of a Study Group held at the American College of Neuropsychopharmacology conference in 2019. It provides an overview of AI approaches in mental healthcare, seeking to help with clinical diagnosis, prognosis, and treatment, as well as clinical and technological challenges, focusing on multiple illustrative publications. While AI could help re-define mental illnesses more objectively, identify them at a prodromal stage, personalize treatments, and empower patients in their own care, it must address issues of bias, privacy, transparency, and other ethical concerns. These aspirations reflect human wisdom, which is more strongly associated than intelligence with individual and societal well-being. Thus, the future AI or Artificial Wisdom (AW) could provide technology that enables more compassionate and ethically sound care to diverse groups of people.

The global burden of mental illnesses accounts for 32% of years lived with disability, making mental illnesses the first in global burden of disease (1). Moreover, mental health challenges have increased in recent decades with a rise in suicides, substance use, and loneliness (2), worsened by the Covid-19 pandemic (3). Mental healthcare is compounded by a shortage of nearly 4.5 million mental healthcare providers, including well over 100,000 psychiatrists in the US (4). Artificial Intelligence (AI) presents a potential solution to address this shortage, and is increasingly employed in healthcare fields like oncology, radiology, and dermatology (5–7). The global AI in healthcare market is expected to grow from $5 billion in 2020 to $45 billion by 2026 (8). Also, there are increasing numbers of large-scale databases like Electronic Health Records (EHRs) in various countries (9).

The use of AI in mental healthcare is, however, limited. The computational power harnessed by AI systems could be leveraged to reveal the complex pathophysiology of psychiatric disorders and thus better inform therapeutic applications (10). Mental healthcare relies on strong clinician-patient relationships that are often hindered by the limited interaction time allotted for clinical care. AI technologies offer a way to streamline tasks that do not require a "human touch" and thus provide complementary support that enables clinicians to focus on delivering more empathic care, thus "humanizing" medical practice (11). A recent survey of psychiatrists highlighted documenting/updating medical records and synthesizing information as two time-consuming tasks where AI could replace a human clinician (12). AI may further complement clinical intuition by enhancing diagnostic accuracy by supporting the clinical reasoning process (13) and advancing the mechanistic understanding of mental illnesses (14,15).

This article is the product of a Study Group held at the American College of Neuropsychopharmacology that included academic, clinical, and industry experts in mental health and AI in 2019. While there have been several excellent reviews of AI in psychiatric disorders, they have focused on specific conditions like autism (16) or bipolar disorder (17), or a specific goal such as genetic prediction (18). This article provides an overview of AI approaches in mental healthcare, to help with clinical diagnosis, prognosis, and treatment as well as clinical and technological challenges, and the future of AI (- i.e., Artificial Wisdom or AW), focusing on multiple illustrative examples.

AI Approaches: Machine Learning and Natural Language Processing

No FDA-approved or FDA-cleared AI applications currently exist in psychiatry (19). However, such applications have long been envisioned – e.g., the potential of expert systems and computerized therapy (20). Reasons for the delayed adoption of AI into routine psychiatric practice include the sensitive nature of data generated by mental health patient-clinician interactions (e.g., written clinical notes, conversations with patients) and multi-faceted diagnostic criteria in the DSM-5 (21,22). These types of data and clinical decision-making in psychiatry are far more complex than specific and objective tasks (e.g., tumor identification from an image) that are well-supported by current AI methods (23). AI technologies are also notoriously "data-hungry," and the field of mental healthcare has been limited in its access to large, high-quality datasets.

Machine Learning (ML): This is the most commonly used subset of AI in healthcare. It employs data-driven algorithms to learn from data, estimating or predicting

outcomes for new data and/or future events (13,24). ML differs from more traditional statistical approaches in several key ways: being more hypothesis-generating than hypothesis-driven; having minimal model assumptions rather than the strict assumptions required for statistical inference; and being focused more on predictions and pattern recognition than estimating parameters of interest (for details see (10,25)). Recommendations for using ML with mental health data are available. The International Society for Bipolar Disorders Big Data Task Force (17) has outlined the essential steps from acquiring patient data from multiple sources and biological levels to translating the knowledge to generate risk calculators. Similarly, Park, et al. (26) described clinical research strategies to systematically evaluate AI model performance in healthcare. Liu et al. (27) provided a guide on how to interpret ML-based publications and assess the appropriateness of the ML model for the size and type of input data.

AI is well-suited to handle "big data," granular, or digitized data (28). The potential of a subset of ML, deep learning (DL), in psychiatry is just beginning to be realized [see (29)]. DL has been used to support diagnostics, in particular for dementia, using the largest possible publicly available datasets (e.g., Alzheimer's Disease Neuroimaging Initiative, or ADNI) (30). EHRs, digital phenotyping data from mobile phones, and social media platforms represent additional sources of high-dimensional data that could provide the necessary inputs to fully harness the power of DL for mental health applications. Medical data sharing has become increasingly more important, as models trained on high-dimensional data with small samples (e.g., more features than participants) lead to poor generalizability (31).

One potential solution to address small samples is transfer learning, which enables use of pretrained AI algorithms, designed for different purposes, as a starting point for analysis of new data (32). For example, Wang et al. (33) used a pre-existing algorithm (with fine tuning) called AlexNet that was originally trained on the large visual database ImageNet to classify alcoholism vs. non-alcoholism. Another example is that of Banerjee et al. (34) who used knowledge from a large speech-recognition database called TIMIT to detect post-traumatic stress disorder (PTSD). These approaches work because of similarities in the structure of the different datasets. Transfer learning is an economical and efficient solution, avoiding the development of a new model from scratch and requiring less training data. Given the relative dearth of large psychiatric datasets, transfer learning could prove useful for AI in mental healthcare.

Natural Language Processing (NLP): This includes techniques like speech recognition, sentiment, lexical, and semantic analysis, and optical character recognition to transfer text from unstructured to structured formats in order to enable subsequent analyses (35). NLP techniques are relevant for psychiatry because language and speech are the primary sources of information used to diagnose and treat mental disorders. Unstructured psychiatric evaluation records are readily available, inexpensive, and rich in information to help identify phenotypes and comorbidities (36,37). Relevant examples in mental health include applying NLP within the Clinical Record Interactive Search (CRIS) platform (38), and predicting the risk of suicide (39) and early psychiatric readmission (40), from hospital discharge notes within the EHR. NLP can also be applied more broadly to EHR or insurance claims data for automating

chart reviews, clustering patients into particular phenotypes, and predicting patient-specific outcomes (41,42).

Assistance with Clinical Diagnosis, Prognosis, and Treatment

Clinical Diagnosis: Today's AI systems can help with differential diagnostic challenges in several key ways. First, AI approaches can bolster the ability to differentiate between diagnoses with similar initial clinical presentations but divergent treatment approaches (43) – e.g., identifying bipolar versus unipolar depression based on brain imaging features (44), or differentiating between types of dementia using structural MRI scans (45). Secondly, data-driven AI methods can help identify novel disease subtypes based on heterogeneity of presentations, demographic features, and environmental factors (43). Examples include neurocognitive profiles in bipolar disorder (46), genetic profiles in schizophrenia (47), biomarker profiles in psychoses (48), and neuroimaging subtypes in depression (49). Thirdly, AI approaches can build models from unusual/novel data sources and reconcile data from multiple heterogeneous data-streams, e.g., EHR, behavioral data from digital phenotyping and wearable sensors, speech, social media feeds, neurophysiology, imaging, and genetics (50), to coalesce explanatory and mechanistic models of mental illness across self-report to molecular assessments. Illustrations include Instagram photographs to predict risk of developing depression (51), speech data to predict psychosis onset in high-risk youth (52), and identifying individuals with PTSD (53). AI methodology can also incorporate both genetic and environmental risks (54), accounting for complex environment-gene interactions and psych-bio-social factors, particularly relevant in PTSD (55).

Furthermore, AI methodologies are well-suited for deciphering patterns from longitudinal data (56), critical for honing the accuracy of diagnoses based on evolving psychiatric symptoms. Lastly, AI methods may have a growing role in gathering sensitive and accurate data from patients. One study found that individuals were more forthcoming disclosing sensitive information with a computer system than with a person (57).

Use of Non-Clinical Data: The digital health movement is closely aligned with AI methods using data outside of typical physician-patients interactions (58). Day-to-day and longitudinal monitoring of sensors (59) and social media can enable early detection of symptoms or relapse, and shed light on helpful versus harmful behaviors (60,61). Multimodal-sensing including smartphones, wearable devices, physiological sensors (e.g., heart rate, electrodermal activity), and ambient sensors (e.g., motion, temperature, light) enables collection of real-world, continuous data concerning symptoms, treatment response, and behaviors, thoughts, and emotions (62,63). Platforms designed to enable multimodal data collection, like mindLAMP (64), AWARE (65), and CrossCheck (66) aid in continuous remote monitoring and identification of subjective and objective indicators of psychotic relapse. ML techniques can derive meaningful or novel features from inherently noisy signals generated by sensors (62). Behaviors like social withdrawal may be detected using smartphones and Fitbit data (67).

Social media platforms represent a new form of social communication, reflecting day-to-day functioning of many individuals (68), thus providing an unprecedented, unobtrusive "lens" into longitudinal behaviors and moods (69,70), especially for adolescents and young adults who are both the highest internet users and at the

greatest risk for the emergence of mental disorders (71,72). Examining the content, language, and consumption patterns of social media provide novel insights into relationships and communication, as well as create new opportunities for seeking help (73,74). Web-based influences impact people's knowledge of, and attitudes toward, healthcare practices like vaccination, at population and individual levels (75). Mental illnesses may be observable in online contexts, and social media data have been leveraged to predict diagnoses and relapses (51,72,76,77), with accuracies comparable to clinician assessments and screening surveys (78).

However, sensor data do not yet have clear usability in clinical mental health settings (79) due to lacking clinical validity and implementation challenges. Likewise, analyses of social media data need AI-based innovations, e.g., shared infrastructures for data collection and data donation. Furthermore, important privacy and ethical issues regarding social media data (80,81) as well as public distrust of data usage for sensitive purposes may hinder research and creation of large-scale data sets necessary for AI algorithms (82).

Prognosis: AI methodologies applied to longitudinal data can bolster accurate prognoses for psychiatric patients (43). Studies have harnessed neuroimaging, EHR, genetic, and speech data to model trajectories of depression (83), suicide risk (84), future substance abuse (85), and functional outcomes (86). AI algorithms can also use data-driven approaches to build new clinical risk prediction models (87) without relying primarily on current theories of psychopathology. However, internal and external validation of an AI algorithm is essential for its clinical utility. Cross validation or split-sample validation are important steps for preliminary internal validation; though these

steps do not ensure generalizability of the results. Temporal validation (newly recruited participants) and geographical validation (data from a different site) are more rigorous strategies to ensure clinical utility (see (87,88)).

Treatment: AI technologies have great potential to support clinical treatments in psychiatry in several ways. First, AI can be used to predict treatment response, potentially bypassing ineffective medication trials, invasive and expensive brain stimulation therapies, or time-consuming psychotherapies (43). Studies have predicted response to antidepressant medications using clinical questionnaire items (89) and EEG signals (90), response to antipsychotics based on EEG (91), response to electroconvulsive therapy (ECT) based on brain structure (44), response to CBT for anxiety based on brain fMRI (92), and response to brain stimulation based on MRI (93). Such studies can identify the target populations for various treatments (94), though not all studies are positive (95,96). Secondly, AI approaches can help predict serious side effects of treatments (97). One study used EHR data to predict development of renal insufficiency among patients treated with lithium (98). Thirdly, AI approaches can aid in building new theoretical models of disease pathophysiology. One study reported progressive divergence of neuroimaging abnormalities in bipolar patients (from non-psychiatric controls), supporting the hypothesis of bipolar disorder as a neuroprogressive disease (99). Similarly, characterizing the timing and course of brain changes during the conversion from psychosis prodrome to schizophrenia (100) can contribute to understanding risk and resilience factors during the prodromal phase. These approaches may also uncover novel opportunities for early intervention, through identifying the most heavily weighted risk factors for transitions to illnesses. Fourthly,

ML approaches can help identify gene expression patterns characteristic of different psychiatric disorders (101). One study described a model that could accurately predict which individuals would develop PTSD based on pre-deployment blood transcriptome data (102), highlighting immune-related gene dysregulation as a risk factor for, and not just a consequence of, PTSD. Lastly, AI can aid directly in the discovery of new treatments (103). AI methods can aid in predicting the clinical action of drugs through simulation or data-driven approaches, thus discovering novel compounds with therapeutic potential (94) – e.g., pharmacodynamics of ketamine infusion through BOLD fMRI response to ketamine and other drugs (104).

Clinical Challenges

There are unique challenges to use of ML in psychiatry. Performance of supervised algorithms depends on the quality of the diagnostic labels used to train a model. Given the heterogeneity characteristic of mental illnesses, labels of disease states may not be specific enough to yield AI algorithms with high sensitivity and specificity. One possibility is to use ML algorithms to predict specific symptoms or functional consequences rather than diagnoses. Another opportunity lies in leveraging the strength of deep neural networks that can operate without human oversight to identify novel biomarkers for detecting specific diseases (29). However, a barrier to using ML algorithms is so-called "stealth science" which protects trade secrets though transparency and reproducible methods are necessary. Big data (e.g., EHR, clinical notes, sensor data, social media data) are inherently messy and require considerable transformation before they are usable (105). When the results of ML algorithms are

published, they must include information regarding the quality of the data used to train the model as well as any potential biases in it, which is rarely done at present.

The major advantage of AI tools is their superior ability to handle large quantities of data quickly to guide clinical decision-making. However, there are still relatively few examples of adoption of ML into clinical psychiatry practice and little evidence of clinical or economic impact. Sendak et al. (105) have proposed four phases of translation necessary to bridge this gap: design and development of ML products that can support clinical decision-making and are actionable; evaluation and validation; diffusion and scaling across settings such that the tools are more widely applicable; and continued monitoring and maintenance to remain current with clinical practice needs. An exemplar is the ML product IDx-DR used to automatically diagnose diabetic retinopathy.

Healthcare systems face key challenges in adopting AI systems (106,107). One case study at Yale University involved implementation of AI-based decision support for improving selection of antidepressant treatments (108–110). The cost-benefit assessment conducted by the healthcare system considered both clinical benefits for patients and financial benefits to the healthcare system. The upfront cost of building a specialized IT infrastructure, skepticism of its utility, and concern for unintended consequences were key hurdles. In addition, enabling a larger pool of primary care physicians to treat poorly reimbursed psychiatric disorders might increase the burden on these physicians and reduce their overall productivity, thus affecting the hospital's revenues. Both clinicians and patients expressed concern about the eventual regular utilization of these clinical tools. Thus, for AI-based clinical tools to become fixtures of

hospital-based clinical practice, they must be incorporated into the culture of the healthcare setting.

Another example of the promise and challenges of AI implementation in psychiatric population health is the REACH VET program at the US Veterans Affairs (111,112). The VA has leveraged its immense and harmonized EHR system to investigate a new ML-based program that identifies high suicide risk individuals. Qualitative research indicated that Veterans were less concerned about the predictive origin of the outreach than the tone and clinical skill of the clinician providing outreach. The ongoing Yale and VA projects are experiments in how large clinical datasets can potentially lead to predictive interventions and integrated into patient-centered care systems.

Technological Challenges

A major challenge for AI in mental health is that the underlying biological processes of psychiatric disorders are still poorly understood (113). Therefore, AI models have to be bootstrapped from observations, rather than be derived from first principles. However, a major problem for data-based derivations of models is the statistical bias-variance trade-off (114). A complex model may overfit – i.e., fit the observed data well (minimizing statistical bias) but is unstable and highly dependent on the specific data used to fit it (maximizing variance). Conversely, a simple model may underfit the observed data and miss relevant structures. Good ML approaches seek to optimize the statistical bias-variance trade-off by finding the "sweet spot" for prediction.

Predictive models evaluate how accurately a built model can forecast future outcomes and need well-defined metrics of individual-level model performance (115); explanatory disease models identify robust effects on understandable variables (116). Despite the clear trade-off between accuracy and explainability, explainable models are needed to ensure safety of the patients and establish trust in the AI models. Recent developments in AI include recurrent neural network (RNN) variant models that can control data inputs at various stages and self-evaluate which timepoints and data inputs are most predictive of the outcome, visualizing techniques, association rule mining (using biologically-based relationships between data elements), and functional validation of the results (117,119). In instances where the biological associations are not well-understood, e.g., in analyses of complex imaging and language data, the AI models may not be as clearly interpretable. However, future AI models must strive to improve transparency in order to establish their clinical utility.

Regulatory oversight of AI technologies is essential for reducing another type of bias – evaluative bias, i.e., particularly for continually evolving AI models (118). Ungoverned AI might perpetuate such bias through furthering social inequities or demonstrating prejudices by arriving at different conclusions for individuals (e.g., based on race or gender) without any rational basis [see (120)]. Non-diverse unrepresentative training data or data that reflects human biases (e.g., due to systemic racism that leads to unequal treatment of racial minorities) can lead to evaluative bias in healthcare applications. Training ML models on human biases may lead to pernicious propagation of inequity. EHR data (generated by humans) can be less in-depth for some segments of the population than others, leading to erroneous conclusions (121). If a feature is rare

in a training set, then a model will be less prepared to detect similar occurrences. Undetected evaluative bias is obviously difficult to eliminate, however, there are tools to help detect and mitigate bias in AI models. For example, the Google What-If tool enables visualization of AI algorithm results and manual manipulation of datapoints to view effects of changing certain parameters. The IBM AI Fairness 360 is an open-source tool available on Git Hub to test for algorithmic bias. Beyond rigorously assessing algorithms for bias, ML offers an opportunity to advance health equity through ensuring equality in patient outcomes, performance, and resource allocation (122).

It is important to highlight a distinction between pragmatic and explanatory approaches (29,123). Pragmatic approaches using automated ML (124) aim to develop tools that can lead to robust and accurate predictions that are clinically useful; however, these optimization procedures are computationally expensive, and are limited by interpretability of how the various workflows' features contribute to the predictions – the black box. The explanatory models seek to establish relationships between variables that provide meaningful insights into how the system works. We need ML tools that provide pragmatic guidance and are explainable. More in-depth understanding of how to develop AI systems like DL to capture the complexity of patients is needed.

Federal and Private Funding Support

Driving the field forward will need careful navigation and long-term support from government and industry, such as the National Institute of Mental Health (NIMH) which emphasizes support of explainable AI in mental health. The National Science Foundation (NSF) and other federal agencies are funding AI Research Institutes,

although they do not focus on mental health challenges. Spring Health, an AI-based company to match patients with mental health providers, was born from academic research at Yale University. In the private sector, AI companies have collaborated with mental health startups and universities – e.g., a collaboration between Microsoft and Silvercloud Health, a digital platform for mental healthcare. Microsoft's AI for Accessibility program funds industry-academic partnerships to improve mental healthcare. In one such project, Northwestern University, University of Toronto, and Mental Health America are co-developing a text message-based psychotherapeutic intervention. Amazon is partnering with University of Pittsburgh and Carnegie Mellon University to build sensors for speech and facial expression data and identify changes associated with depression. Georgia Tech University and Befrienders India are co-developing an AI-based system to match crisis-line callers with peer support specialists from similar sociodemographic, cultural, and lived experiences (coauthor MDC is a PI). Another academic-industry partnership example is the UC San Diego and IBM Research's Center on AI for Healthy Living (Investigators include coauthors EEL, CAD, SAG, HCK, DVJ), which is conducting a longitudinal study of older adults residing within a continuing care senior housing community. The researchers assess the participants using wearable sensors, clinical, neuropsychological, and physical functioning measures, and microbiome-based biomarkers, with the ultimate goal of identifying the earliest predictors of cognitive and functional decline (10,36,125).

Future of AI: Artificial Wisdom (AW)

AI is modeled after human intelligence and today's AI can accomplish various concrete tasks far more quickly than a human, through replicating discrete human intelligence skills like processing speed, memory, quantitative reasoning, visuospatial ability, auditory processing, and comprehension-knowledge. AI will continue to improve and develop into super-intelligence. Yet, it does not have the ability to make compassionate, fair, and equitable decisions. AI cannot self-reflect or self-correct or consider diversity among people and perspectives, ethics, and morality. Reframing such future AI for what it really is – i.e., Artificial Wisdom (AW) – highlights the limitations of today's AI and the need for wisdom it should offer in the future.

Human wisdom is a multi-component personality trait that includes pro-social behaviors like empathy and compassion, emotional regulation, self-reflection (with self-correction), acceptance of uncertainty and diversity of perspectives, social decision making, and perhaps spirituality (126). Wisdom, rather than intelligence, is associated with greater individual and societal well-being. In all likelihood, only humans can be truly wise, as uniquely human characteristics including consciousness, autonomy, and will are key to cultivating wisdom. The notion of creating AI that shares our societal values and could be considered to be wise is a relatively new area of exploration (127–129). The future AI will need to have some aspect of emotional intelligence (130), morality (131), and empathy (132). Paiva et al. (133) defined "empathic agents" as "agents that have the capacity to place themselves into the position of a user's or another agent's emotional situation and respond appropriately." It is improbable that human wisdom could be fully programmed into a robot, but partial examples exist in the form of robotic social workers and physical therapists deployed in nursing homes (134,135), social

robots for loneliness, and those providing cognitive assistance to older adults (36).

These tools illustrate the efforts to develop computers that can perform actions which

employ wise principles and result in wise acts.

Ethical and wise AI – i.e., AW, will help promote individual and societal well-being

(136–138). As noted above, freedom from bias is essential for widespread practical use.

Evolution of AW will require active collaboration between computer scientists,

engineers, psychiatrists, psychologists, neuroscientists, and ethicists.

Common concerns about AI today often focus on the "four horsemen of the AI

apocalypse": loss of jobs for humans, unethical decision-making, hostile robot-led

takeovers, and uninterpretable "black box" decision-making (139). These are countered

by the hope for developing behavior-based digital biomarkers; re-defining diagnoses;

facilitating earlier detection of mental illnesses; continuous learning systems that can

assess patients in context; tools to help patients and clinicians better understand an

illness and themselves; personalized approaches to diagnosis and treatment; and built-

in computational models that make mental healthcare safer, more efficient, and

personalized. This dichotomy between fears and aspirations can be reframed by

considering ways to develop AW to support mental healthcare. The path to achieve

sustainability, implementation, and clinician and patient acceptance will require

transparency, trust, and wisdom.

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