



AI-DRIVEN PRECISION MEDICINE IN NEUROPHARMACOLOGY: REVOLUTIONIZING TREATMENT AND GUIDANCE FOR NEUROLOGICAL DISORDERS

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ABSTRACT

Background: Neurological disorders represent one of the most pressing and complex challenges in modern medicine, affecting hundreds of millions of individuals globally and imposing an enormous burden on healthcare systems. Traditional pharmacological approaches, while effective for some patients, are often limited by inter-individual variability in drug response, adverse effects, and the intricate pathophysiology underlying conditions such as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, and major depressive disorders. The emergence of artificial intelligence (AI) and machine learning (ML) as transformative tools in biomedical research has opened unprecedented avenues for precision medicines in neuropharmacology. This paper reviews the current landscape of AI-driven approaches for identifying neurological drug targets, predicting therapeutic outcomes, optimizing treatment regimens, and discovering novel neuroactive compounds. We further discuss the integration of multi-omics data, neuroimaging biomarkers, and electronic health records (EHRs) within AI frameworks, highlighting both the promising advances and the formidable challenges- including data privacy, algorithmic bias, and regulatory considerations- that must be addressed to realize the full clinical potential of AI-driven precision neuropharmacology. **Objectives:** This comprehensive review systematically examines the current landscape, principal methodologies, clinical applications, and translational challenges of AI-driven precision medicine in neuropharmacology, with a focus on Alzheimer's disease (AD), Parkinson's disease (PD), epilepsy, multiple sclerosis (MS), stroke, psychiatric disorders, and rare neurological conditions. **Results and conclusions:** AI methodologies- including supervised and unsupervised learning, deep learning architectures, graph neural networks, generative models, reinforcement learning, natural language processing, and federated learning- are delivering transformative advances across drug target identification, de novo molecular design, virtual screening, drug repurposing, neuroimaging biomarker analysis, and pharmacogenomics.

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INTRODUCTION

The pharmacological management of neurological disorders has historically been constrained by a basic disparity between the biological complexity of CNS disease and the capacity of conventional drug development and therapeutic frameworks to address it. The central nervous system presents unique obstacles for drug development: the blood-brain barrier (BBB) obstructs the entry of most pharmacological agents into the CNS; variability in drug metabolism, target expression, and disease mechanisms among individual patients' management; and the absence of validated, accessible biomarkers has impeded early diagnosis and the evaluation of pharmacological treatment effects [1]. The clinical drug attrition rate for CNS diseases exceeds 90%, significantly surpassing the failure rates observed in oncology and cardiovascular medicines [2]. This indicates that numerous people with neurological disorders are still not receiving appropriate therapy, despite the availability of several medications.

Neurological disorders constitute a significant cause of mortality and disability globally. The Global Burden of Disease study indicates that dementia, stroke, epilepsy, Parkinson's disease, and multiple sclerosis account for almost 276 million disability-adjusted life years (DALYs) annually [3]. Despite extensive research and clinical efforts in recent decades, developing effective pharmacological interventions remains challenging because of the central nervous system's (CNS) complexity, the diverse manifestations of these diseases, and the blood-brain barrier, which hinders therapeutic agents from reaching their targets. Precision medicine, which tailors treatment to each patient's needs, is a promising approach to addressing these issues [4]. Precision medicine aims to identify the suitable drug, dose, patients, and timing by applying genomic, proteomic, metabolomic, and clinical data. In this regard, artificial intelligence and machine learning technologies are highly significant. Artificial intelligence is an invaluable asset for accelerating drug discovery, improving diagnostic precision, and customizing pharmacological treatment strategies in neurology, as deep learning algorithms can identify intricate, high-dimensional patterns within extensive and varied datasets.

This paper examines how AI-driven precision medicines can enhance neuropharmacology. We begin by contextualizing AI within the intricate landscape of neurological disorders. We then examine AI applications in drug development, clinical decision support, and patient stratification. We also discuss the ethical,

legal, and practical challenges that must be addressed to transition AI advancements from the laboratory to patient care. This review provides a comprehensive, critical examination of AI-driven precision medicine in neuropharmacology. (Section 2) examines the primary AI and ML methodologies (Section 3), discusses their use in drug development and target identification (Section 4), addresses precision diagnostics and patient stratification (Section 5), and discusses clinical decision support and pharmacological optimization. (Section 6) It provides further information on applications for particular disorders. (Section 7) addresses the challenges, ethical dilemmas, and regulations that must be adhered to, while (Section 8) delineating the critical domains for future inquiry. (Section 9) concludes by examining the profession's current state and its potential for transformation.

USING AI AND MACHINE LEARNING IN NEUROPHARMACOLOGY

AI methods differ substantially in the neuropharmacology problems they solve best, how much data they require, and how close they are to clinical translation. In general, classical supervised models remain the most practical choice for small to medium-sized tabular datasets. At the same time, deep learning is more powerful for raw imaging, time-series, and sequence data. Unsupervised and self-supervised approaches are especially valuable when labels are scarce, whereas GNNs, generative models, RL, NLP, and federated learning address more specialized but increasingly important translational tasks. Taken together, the field is moving from isolated predictive models toward multi-modal, privacy-aware, and clinically deployable systems.

Machine Learning with supervision

Supervised methods such as logistic regression, random forests, SVMs, and gradient boosting remain the most mature and immediately useful tools for many neuropharmacology tasks. Their main advantage is that they perform well on structured clinical and pharmacogenomic data and often provide some interpretability, which matters when sample sizes are limited and clinical trust is essential. Among them, tree-based ensembles and gradient boosting usually outperform simpler linear models when relationships are non-linear. However, they still depend heavily on feature engineering and may not capture complex spatiotemporal patterns [11]. Therefore, supervised learning is best viewed as the most clinically practical starting point for tabular prediction problems, not as a universal solution. These

methods are especially useful in neurological applications with small- to medium-sized training datasets, where understanding the findings is crucial, and the risk of overfitting is considerable. Random forest ensembles perform effectively with high-dimensional genomic and clinical characteristics, providing

estimates of feature relevance that facilitate biological interpretation. Gradient boosting algorithms are most effective on organized tabular clinical data and have demonstrated superior accuracy in predicting pharmacogenomic reactions [12].

Table 1: Method-to-use-case mapping in neuropharmacology

AI method	Best use-case in neuropharmacology	Typical input data	Typical output	Common validation metrics	Typical failure modes	Ref
Supervised learning (logistic regression, SVM, random forest, XGBoost)	Drug response prediction, adverse drug reaction risk, pharmacogenomic stratification	Tabular clinical variables, genotypes, biomarkers, treatment history	Class label, risk score, probability of response	AUC, accuracy, F1-score, sensitivity, specificity, calibration	Overfitting, feature leakage, poor external generalizability	[5]
CNNs	Neuroimaging diagnosis, lesion detection, segmentation	MRI, PET, CT, histology images	Diagnosis, segmentation mask, lesion probability	AUC, Dice coefficient, precision, recall	High data requirement, domain shift, low interpretability	[6]
RNNs/LSTMs	Longitudinal disease progression, dose response trajectory modelling.	Time-series clinical data, repeated biomarker measures, wearable sensor data	Future state, progression risk, next-step prediction	AUROC, MAE, RMSE	Vanishing gradients, instability with long sequences	[7]
Transformers	Clinical text mining, literature synthesis, multi-modal integration	EHR text, clinical notes, reports, sequences, mixed-modal data	Entities, labels, summaries, predictions	F1-score, exact match, AUROC	Hallucination, bias, large data requirement, poor transparency	[8]
Unsupervised learning (k-means, PCA, autoencoders)	Disease subtyping, phenotype discovery, exploratory biomarker analysis	Omics profiles, imaging embeddings, clinical variables	Clusters, latent representations	Silhouette score, cluster stability, downstream utility	Unstable clusters, weak clinical interpretability	[9]
GNNs	Target discovery, drug-target interaction prediction, connectome analysis	Biological networks, PPI graphs, pathway graphs, brain connectomes	Ranked targets, interaction probabilities	AUC, average precision, hit rate	Sparse labels, over-smoothing, limited interpretability	[10]

Deep learning extends supervised learning by reducing manual feature engineering and learning rich representations from images, waveforms, and biological sequences. CNNs are especially strong in neuroimaging, where local spatial patterns matter, while RNNs and LSTMs suit longitudinal trajectories and temporal biomarker data. Transformers have become the leading architecture for next- and multi-modal integration because they model long-range dependencies and scale well across diverse inputs. However, these models generally require larger datasets, are harder to interpret, and are more vulnerable to dataset shift; thus, their clinical value is strongest when data are abundant and external validation is available [13]. Convolutional neural networks (CNNs) use trained convolutional filters across many layers of hierarchical

abstraction to leverage local spatial correlations in image input. They perform tasks such as neuroimaging analysis and medical image classification and segmentation. Recurrent neural networks (RNNs), particularly long short-term memory (LSTM) architectures, effectively model sequential and temporal dependencies in time-series data [14]. Researchers have used them to examine longitudinal patient trajectories, serial biomarker assessments, and pharmacokinetics time series in neuropharmacology [15]. Transformer architectures use self-attention mechanisms to identify long-range dependencies in sequential data and have become the predominant framework for natural language processing (NLP), and are increasingly used to integrate clinical and biological data from diverse sources. BioBERT, PubMed Bert, ClinicalBERT, and BioGPT are all

extensive language models (LLMs) founded on the transformer architecture [16]. They have shown strong potential for biomedical text mining, forecasting drug-drug interactions, extracting adverse events from clinical documentation, and autonomously synthesizing evidence from pharmacological literature [17].

Unsupervised learning and Self-supervised learning

Unsupervised learning is most useful when the goal is discovery rather than prediction. Clustering, PCA, and autoencoders can reveal latent disease subtypes and endophenotypes, especially in disorders such as Alzheimer's disease, Parkinson's disease, epilepsy, and multiple sclerosis, where clinical labels are often incomplete or biologically coarse. The main strength of these methods is hypothesis generation, but the clusters they produce may be unstable, difficult to interpret, and not always clinically actionable. In other words, unsupervised learning is valuable for finding structure in heterogeneous neurological data, but it rarely provides a ready-to-use therapeutic decision rule on its own [18]. Dimensionality reduction techniques, such as t-SNE and UMAP, help visualize and compress high-dimensional neurological data. This facilitates exploratory analysis and feature selection for subsequent supervised tasks [19]. Self-supervised learning addresses a key bottleneck in neuropharmacology: the shortage of well-annotated datasets. By pretraining on large unlabelled corpora, it can improve downstream performance in imaging, EHR, and omics tasks, often with fewer labels than traditional supervised learning requires. Its main limitation is that performance gains depend on whether the pretraining task is biologically meaningful and whether the learned representation transfers across institutions and patient populations. This makes self-supervision highly promising, but still methodologically dependent on careful validation [20]. Self-supervised pretraining on extensive neuroimaging and electronic health record datasets has yielded transferable feature representations that significantly enhance performance on labeled neurological datasets, particularly in clinical environments with constrained data availability. This facilitates exploratory analysis and feature selection for subsequent supervised tasks [21].

Graphs Neural Network

Graph neural networks extend deep learning to data organized in graph structures. This enables us to model biological systems in which relational structure, rather than node-level characteristics alone, is crucial for biological function. Graph neural networks

(GNNs) have become integral to neuropharmacology for modeling protein-protein interaction networks, gene regulatory networks, drug-target interaction graphs, metabolic networks, and brain connectomes. Graph neural network (GNN) models excel at forecasting drug-target interactions, drug-drug interactions (DDIs), novel molecular characteristics, and prioritizing disease-related genes via network propagation [22]. Using Graph Neural Networks (GNNs) to investigate the brain's functional and structural connectomes has shown that conditions such as Alzheimer's, epilepsy, major depressive disorder, and schizophrenia alter network topology, which may serve as imaging biomarkers and indicate network-level pharmacological targets [23].

AI models in Pharmacology

Generative AI models, including variational autoencoders (VAEs), generative adversarial networks (GANs), normalizing flows, and diffusion models, estimate the probability distribution of molecular or biological data and generate new instances by sampling from it. Generative models trained on extensive chemical databases can provide SMILES or graph representations of molecular structures that are syntactically accurate and possess specific activity profiles, physical properties, and ADMET characteristics. VAE-based molecular generators enable gradient-based optimization within a continuous latent chemical space, helping scientists identify novel lead compounds with strong affinity for the central nervous system that can traverse the blood-brain barrier.

Zhavoronkov et al. (2019) provided a seminal demonstration of AI-designed DDR1 kinase inhibitors, achieving proof of concept for AI-accelerated drug discovery within 46 days and subsequently attracting significant investment in generative molecular AI [24]. Diffusion models, designed to reverse a stochastic noise-corruption process applied to training data, have recently achieved unprecedented success in predicting protein structures and generating three-dimensional molecules [25]. The AlphaFold2 protein structure prediction system uses an attention-based deep learning architecture to accurately predict protein three-dimensional structure from amino acid sequences, achieving near-experimental precision [26]. It has transformed structure-based drug design by providing precise structural models for the majority of the human proteome, including numerous CNS therapeutic targets that were previously intractable for structural analysis.

Reinforcement Learning

Reinforcement learning (RL) optimizes decision-making under uncertainty about future outcomes. This renders it highly beneficial for the complex, temporal pharmacological decision-making challenges central to clinical neuropharmacology. Reinforcement learning algorithms determine optimal treatment plans by analyzing the relationship between actions and rewards in real or simulated patient scenarios [27]. They do so by identifying therapeutic sequences that provide patients with the greatest long-term benefit. Reinforcement learning has shown it can identify superior adaptive treatment techniques compared with static clinical protocols in managing epilepsy, optimizing deep brain stimulation parameters for Parkinson's disease, and dynamically dosing antidepressants [28]. Incorporating deep reinforcement learning into molecular optimization-utilizing molecular property scores as reward signals to guide iterative molecular generation and modification-represents a significant advancement in the integration of reinforcement learning with generative molecular design [29].

Table 2: Disease-specific comparison of AI applications

Disease	Main data source	AI method(s) most relevant	Therapeutic decision point	Clinical impact claimed	Ref.
Alzheimer's Disease Heterogeneity	MRI, PET, CSF/plasma biomarkers, genomics, transcriptomics	CNNs, multi-modal deep learning, supervised ML, autoencoders, GNNs	Early diagnosis, subtype stratification, biomarker staging, target discovery	Earlier detection, improved subtype classification, biomarker-based stratification	[36]
Parkinson's Disease Heterogeneity	MRI, gait/voice sensors, genomics, transcriptomics, connectomes	Supervised ML, deep learning, GNNs, digital biomarker models	Phenotyping, therapy selection, DBS optimization, progression monitoring	Remote monitoring, subtype-specific insights, adaptive management	[37]
Epilepsy Heterogeneity	EG, MRI, gene panels, clinical phenotypes	CNNs, supervised ML, NLP, GNNs	Syndrome classification, lesion detection, AED selection	Better detection of focal lesions, improved syndrome stratification	[38]
Multiple Sclerosis Heterogeneity	MRI, NfL/GFAP, clinical disability data	CNNs, supervised ML, trajectory models, federated learning	Risk stratification, treatment escalation, progression prediction	Lesion segmentation, disability forecasting, PML risk support	[39]

AI APPLICATION IN NEUROLOGICAL DISORDERS

Different Types of Pathophysiology

Neurological disorders are not isolated phenomena; they represent a clinically and physiologically varied spectrum of problems arising from complex interactions among genetic, epigenetic, environmental, and behavioral influences [33]. Alzheimer's disease (AD) has many molecular subtypes characterized by distinct amyloid and tau pathologies, neuroinflammatory profiles, and synaptic dysfunction patterns. Parkinson's disease (PD) manifests in various ways, including early-onset familial variants resulting from mutations in

Federated Learning

Federated learning (FL) enables organizations with data to collaborate to train collective AI models without consolidating raw patient data in a single location. This lets institutions learn from interconnected neurological datasets that no single institution could compile independently [30]. This is crucial for neurological AI research because patient data is highly sensitive, data-sharing is tightly regulated, and the diversity and volume of training data strongly influence an AI model's efficacy and applicability across contexts [31].

FL-trained neuroimaging models that classify Alzheimer's disease, segment gliomas, and quantify multiple sclerosis lesions have shown performance comparable to centrally trained models while requiring significantly less training to avoid memorizing individual patients' records. These systems offer formal mathematical privacy assurances that work well with federated learning methodologies [32].

LRRK2, SNCA, or PINK1, as well as sporadic late-onset cases characterized by a complex polygenic architecture [34]. This variability has historically impeded the development of universally effective medicines, as interventions advantageous for one patient subgroup may be ineffective or harmful for another [35].

Problems with Traditional Drug Therapy

Numerous neurological disorders have shown minimal advancements with conventional pharmacological treatments that are universally effective. Over 90% of CNS drug research

studies are unsuccessful, significantly exceeding failure rates in other medical disciplines [40]. Reasons include improper patient grouping, clinical objectives that fail to reflect early pathophysiological changes, inadequate translation of animal models to human disease, and the absence of validated

biomarkers to assist physicians in therapeutic decision-making. Polypharmacy, prevalent among elderly neurological patients, complicates drug-drug interactions, rendering them more difficult to predict and manage using conventional methods [41].

Table 3: Evidence hierarchy for AI in neuropharmacology. AI applications differ substantially across neurological diseases in terms of data source, clinical decision point, and translational maturity, so disease-specific synthesis is necessary to avoid overgeneralization.

Evidence level	Definition	Typical study type	Examples of AI use	Ref.
Preclinical / proof of concept	Demonstrates technical feasibility or biological plausibility, usually before patient-level validation	In silico screening, model development, benchmark datasets, simulation studies	Generative molecule design, target prioritization by GNNs, RL-based optimization, early NLP pipelines	[44]
Retrospective cohort / case-control	Tests the model on existing patient data, often from one or more centers	Single-site or multi-site retrospective validation	MRI-based diagnosis, EEG classification, pharmacogenomic risk prediction, ADR prediction from EHR	[45]
External validation	Evaluates performance on independent datasets from different institutions or populations	Independent test cohorts, temporal or geographic validation	Cross-site neuroimaging models, multi-center biomarker classifiers	[46]
Prospective validation	Tests the AI system in a forward-looking clinical setting	Prospective observational study, silent trial, prospective diagnostic study	CDSS for treatment selection, digital biomarker monitoring, real-time risk prediction	[47]
Implementation / clinical deployment	Measures impact on workflow, decision-making, or patient outcomes in routine care	Pragmatic trials, implementation studies, health system rollout	AI-assisted imaging triage, pharmacogenomic decision support, integrated CDSS	[48]

The Potential of Multi-Omics Integration

The advent of high-throughput technology has generated extensive biological data-genomic sequences, transcriptome profiles, proteome landscapes, and metabolomic fingerprints—that are crucial for understanding disease mechanisms at a systemic level [42]. Nonetheless, integrating and interpreting this multi-omics information presents a formidable analytical challenge that conventional statistical methods cannot adequately address. Artificial intelligence, particularly machine learning algorithms that can process high-dimensional, non-linear data, is crucial in this context [43]

AI TECHNIQUES IN NEUROPHARMACOLOGY

Uses of Machine Learning

Supervised Learning

Multiple studies have employed supervised learning algorithms such as random forests, support vector machines (SVMs), and gradient boosting techniques like XGBoost to predict the efficacy of CNS drugs [49]. These algorithms can analyze labeled datasets comprising patient genomic profiles, clinical factors, and treatment outcomes to identify which patients are

most likely to respond to a certain treatment. For instance, support vector machines (SVMs) trained on cerebrospinal fluid (CSF) biomarker panels have demonstrated significant efficacy in predicting the onset of Alzheimer's (AD) in individuals with mild cognitive impairment (MCI). This enables earlier, more targeted initiation of pharmacological treatment [50].

Unsupervised learning

Unsupervised learning techniques, such as clustering algorithms, principal component analysis (PCA), and autoencoders, can help identify novel patient types and disease endophenotypes without relying on pre-existing labels. K-means and hierarchical clustering of RNA-sequencing data from post-mortem brain tissue have identified molecularly distinct subgroups of Alzheimer's disease, distinguished by inflammatory and synaptic gene expression profiles, suggesting potential avenues for targeted therapeutic development [51].

Deep Learning and Neural Networks

Deep learning architectures, such as convolutional neural networks (CNNs) and recurrent neural networks (RNNs), have

fundamentally changed how we interpret neuroimaging data and longitudinal clinical records [52]. When convolutional neural networks (CNNs) are applied to MRI and PET neuroimaging datasets, they can reliably diagnose conditions such as Alzheimer's disease, Parkinson's disease, and brain tumors, potentially matching or surpassing the proficiency of

experienced radiologists [53]. Long short-term memory (LSTM) networks exemplify a recurrent architecture that models temporal dynamics in longitudinal patient data. This facilitates predicting disease progression and the optimal initiation of pharmacotherapy [54].

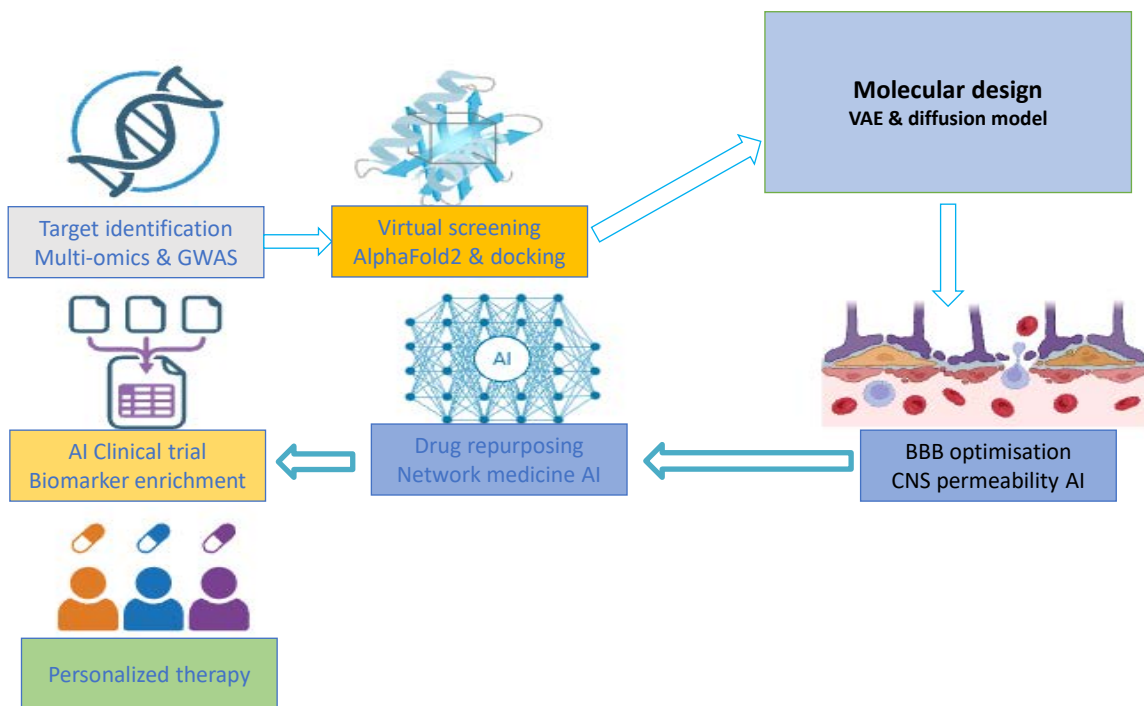


Figure 1: AI-Driven Drug Discovery pipeline in Neuropharmacology

Natural Language Processing in Clinical Neurology

Natural language processing (NLP) facilitates extracting organized, pertinent information from unstructured text in electronic health records (EHRs), clinical trial reports, and biological literature [55]. Neuropharmacology has employed natural language processing to analyze adverse drug event reports, identify drug-drug interactions, gather phenotypic data for pharmacogenomic research, and synthesize material from numerous scientific publications to facilitate drug repurposing initiatives [56]. Large language models (LLMs), particularly transformer-based models, are being enhanced with clinical and biological datasets to support neurologists' decision-making.

Finding the Best Treatment with Reinforcement Learning

Reinforcement learning (RL) is an effective method for enhancing dynamic, multi-step therapeutic protocols for neurological disorders. These are situations in which a clinician must make a sequence of treatment decisions over time amid uncertainty [57]. Reinforcement learning algorithms determine

optimal treatment plans by simulating a series of therapeutic decisions and their impact on the patient over time, consistently seeking the most favorable long-term outcome. Reinforcement learning (RL) can improve antiepileptic drug (AED) dosing regimens by adjusting them based on patient responses [58]. This diminishes the likelihood of seizures and mitigates adverse side effects.

USING AI TO FIND NOVEL MEDICATIONS AND TARGETS

Finding and Identifying Targets

One of the foremost challenges in neuropharmacology is identifying molecular targets amenable to pharmacological intervention. AI-driven network medicine methodologies use gene co-expression data, protein-protein interaction networks, and genome-wide association study (GWAS) findings to identify molecular hubs and disease-associated pathways. Graph neural networks (GNNs) effectively model biological networks and identify hub proteins that may serve as promising

therapeutic targets [59]. AI analysis of GWAS data has identified novel targets in neuroinflammatory pathways associated with Alzheimer's disease (AD) and Parkinson's disease (PD), including TREM2, BIN1, and the complement system. This has redirected pharmacological development initiatives towards previously overlooked biological processes [60].

Drug discovery and Virtual Screening

Generative AI models, such as variational autoencoders (VAEs) and generative adversarial networks (GANs), are transforming drug design by producing innovative molecular structures with predicted activity at designated targets and advantageous ADMET (absorption, distribution, metabolism, excretion, toxicity) profiles [61]. These models learn the chemical syntax of bioactive compounds from extensive compound libraries and can generate novel candidates that explore previously unexplored chemical domains [62]. AI generative models have been used to improve blood-brain barrier permeability in CNS drug discovery, given the rigorous physicochemical constraints imposed by the blood-brain barrier. This has significantly reduced early-stage attrition.

Drug repurposing

Drug repurposing refers to identifying novel medical applications for previously approved or under-evaluation drugs. This is a rapid, cost-effective method for identifying novel neurological therapies [63]. AI-driven repurposing solutions integrate gene expression profiles to identify potential repurposing candidates [64]. One notable example uses AI to identify sildenafil as a potential treatment for Alzheimer's disease because it interacts with gene networks essential to the condition. Another example involves using anti-inflammatory drugs to protect neurons in Parkinson's disease. These approaches are particularly effective because extensive safety data for licensed medications reduce the likelihood of unforeseen toxicity [65].

AI-POWERED PRECISE DIAGNOSTICS AND PATIENT CLASSIFICATION

Neuroimaging Biomarkers

Neuroimaging has historically been a crucial component of neurological diagnosis and research. AI-driven image processing is significantly enhancing efficiency in clinical settings. Deep CNN models trained on structural MRI datasets have attained diagnostic accuracy that has shown performance

comparable to expert readers in selected retrospective studies of experienced neurologists in classifying Alzheimer's disease (AD), mild cognitive impairment (MCI), Parkinson's disease (PD), multiple sclerosis (MS), epilepsy, and brain tumors. Multi-modal deep learning architectures that concurrently assess structural MRI, amyloid PET, tau PET, and FDG-PET show greater diagnostic and prognostic efficacy than single-modality models, enabling automated application of the biological AT(N) staging framework for Alzheimer's disease diagnosis, regardless of clinical manifestations [66]. Automated volumetric examination of hippocampal atrophy and cortical thickness, powered by AI, exhibits a sensitivity for detecting early structural changes associated with Alzheimer's disease that far surpasses that of visual radiological assessment. Furthermore, prospective studies have shown that AI-generated MRI signals can predict the transition from a cognitively normal state to moderate cognitive impairment (MCI) and from MCI to Alzheimer's disease (AD) three to five years before clinical diagnosis [67]. Quantitative susceptibility mapping (QSM) and free-water imaging of the substantia nigra, evaluated through deep learning algorithms, serve as non-invasive biomarkers of nigral neurodegeneration, exhibiting diagnostic precision adequate to distinguish Parkinson's Disease (PD) from essential tremor and atypical parkinsonian syndromes, and reduce reliance on some established methods in research settings for dopamine transporter SPECT imaging [68]. In multiple sclerosis, AI-driven automated segmentation and longitudinal tracking of T2 white matter lesion burden and T1 gadolinium-enhancing lesions exhibit reproducibility that markedly surpasses inter-rater agreement among human evaluators [69]. This improves the precise detection of treatment effects in clinical trials and facilitates evidence-based escalation decisions in clinical practice. Deep learning analysis of structural MRI in epilepsy has shown the ability to detect focal cortical dysplasia (FCD) lesions, a common cause of drug-resistant focal epilepsy. This technique shows greater sensitivity than expert radiological review, even in cases deemed MRI-negative on routine evaluation [70]. This directly affects surgical eligibility and reduces the need for extended empirical treatment.

Classification of Genomics and Pharmacogenomics

Pharmacogenomics is an essential component of precision neuropharmacology. It examines how genetic variations affect drug efficacy and adverse effects. Genetic variations in CYP450 enzymes (CYP2D6, CYP2C19, CYP3A4, CYP2C9), drug

transporters (ABCB1, SLC6A4), and pharmacodynamic targets significantly contribute to the heterogeneity in central nervous system medication responses and toxicity among individuals. AI-driven pharmacogenomic decision support tools integrate CYP enzyme genotypes, co-medication profiles, and target gene variants within machine learning frameworks to produce patient-specific dosing recommendations and adverse effect risk evaluations for neurological and psychiatric medications, such as lamotrigine, carbamazepine, clozapine, lithium, and levodopa/carbidopa [71]. AI models utilizing extensive pharmacogenomic datasets, such as the UK Biobank ($n > 500,000$) and the Clinical Pharmacogenomics Implementation Consortium (CPIC) evidence base, are now capable of generating polygenic pharmacogenomic scores (PGx scores) that amalgamate the effects of multiple variants to more accurately forecast an individual's response to antidepressants, their tolerance to AEDs, and the probability of experiencing side effects from antipsychotics, surpassing single-gene models. Combining PGx scores with clinical phenotyping, neuroimaging, and digital biomarker data within multi-omics AI frameworks signals imminent advances in precision pharmaceutical decision-making in neurology and psychiatry [72].

Digital Biomarkers and Technology You Can Wear

The widespread adoption of smartphones, smartwatches, and wearable inertial sensors has enabled continuous collection of behavioral and physiological data that AI algorithms can use as digital biomarkers to assess disease progression and treatment effectiveness [73]. Accelerometry-based gait analysis in Parkinson's disease (PD), using wrist-worn devices and smartphone sensors, has produced quantified digital biomarkers for bradykinesia, gait freezing, tremor severity, and medication on/off states. These indicators show a robust correlation with UPDRS motor scores and greater sensitivity to levodopa administration, enabling remote, frequent monitoring of pharmacological effects beyond clinical settings [74].

Deep learning algorithms applied to voice recordings have identified vocal biomarkers linked to Parkinson's disease, such as dysphonia, diminished pitch variability, hypophonia, and imprecise articulation. These biomarkers possess adequate sensitivity and specificity for distant illness surveillance and early identification [75]. In Alzheimer's disease and mild cognitive impairment (MCI), digital cognitive phenotyping utilizing passive smartphone sensing-evaluating typing speed,

navigating complexity, search query content, and social communication patterns-has identified early cognitive decline months before clinical diagnosis, providing a scalable and accessible approach for early detection appropriate for large-scale population screening [76]. Wearable EEG headbands and multi-channel ambulatory EEG systems, assessed by deep learning seizure detection algorithms, facilitate continuous seizure monitoring and evaluation of antiepileptic drug efficacy in a home setting, yielding ecologically valid pharmacodynamic data for accurate AED management.

AI-POWERED CLINICAL DECISIONS IN NEUROLOGY Systems for recommending treatments

AI-driven clinical decision support systems (CDSS) that integrate patient-specific multi-modal data to generate individualized pharmacological therapy recommendations represent the most direct translational application of AI precision medicine in clinical neurology. The design of sophisticated AI-CDSS for neuropharmacology integrates various data layers—genomic and pharmacogenomic profiles, neuroimaging biomarkers, fluid biomarker panels, clinical and neuropsychological assessment data, medication history, and real-world outcome data—within machine learning or deep learning prediction frameworks, yielding probabilistic treatment recommendations and outcome predictions at the individual patient level [77]. In epilepsy, AI-CDSS integrating genetic testing data (such as epilepsy gene panel reports), EEG syndrome classification, seizure semiology, imaging findings, and clinical phenotype have been developed and evaluated to select AEDs [78]. They show superior predicted pharmacological outcomes compared with conventional empirical prescribing algorithms and expert panel consensus in many cohort studies. A clinical decision support system (CDSS) for multiple sclerosis (MS) integrates MRI lesion activity, disability progression, prognostic risk stratification, and individualized adverse effect risk profiles for each disease-modifying therapy, facilitating evidence-based treatment initiation and escalation decisions. Preliminary evidence suggests improved long-term disability outcomes in real-world implementation studies [79]. In psychiatry, AI-CDSS using pharmacological data, dimensional symptom profiles, historical treatment responses, and comorbidity information show superior efficacy in selecting appropriate antidepressants and antipsychotics compared with conventional clinical care in prospective studies [80].

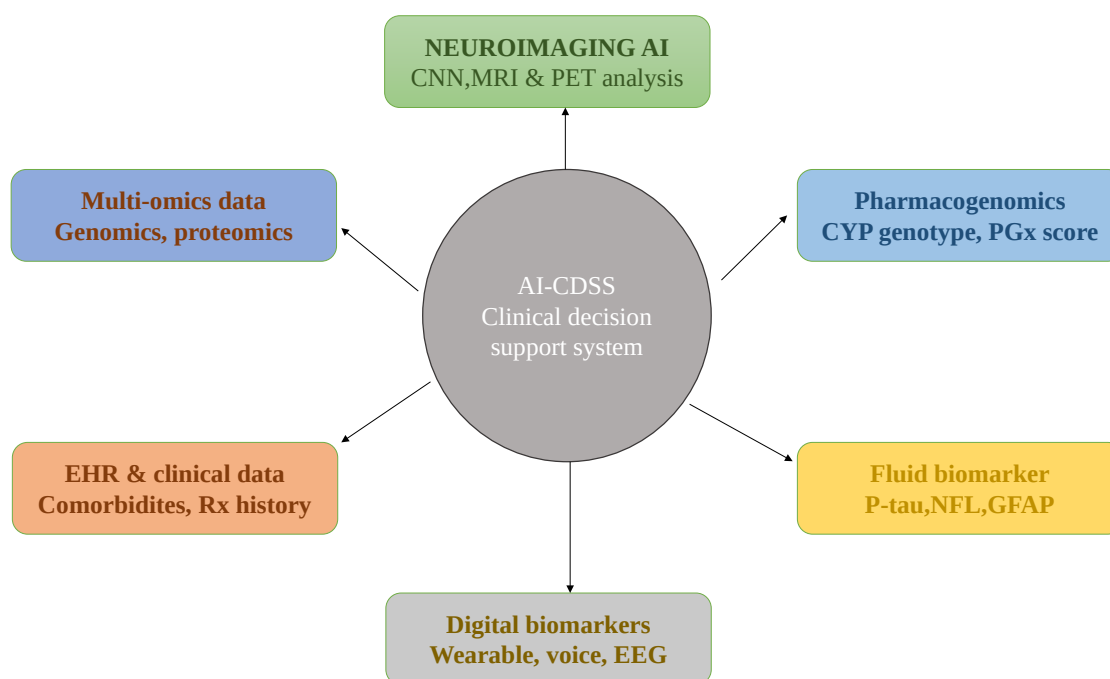


Figure 2: The precision medicine wheel showing the patient S-shaped flow

Predicting Adverse drug response

Adverse drug responses (ADRs) in neuropharmacology are a substantial source of patient harm, resulting in treatment cessation, emergency hospital admissions, enduring disability, and avoidable mortality. The formulary for neurological and psychiatric medications contains numerous drugs with clinically significant adverse drug reaction (ADR) risks, including antiepileptic drugs (AEDs) characterized by narrow therapeutic windows and idiosyncratic toxicities (such as Stevens-Johnson syndrome, aplastic anaemia, and drug reaction with eosinophilia and systemic symptoms [DRESS]), clozapine-related agranulocytosis, lithium toxicity, drug-induced parkinsonism, neuroleptic malignant syndrome, and serotonin syndrome resulting from antidepressant combinations [81]. AI-driven ADR prediction algorithms that use EHR data, genetic information, and pharmaceutical databases are markedly improving the accuracy and patient specificity of ADR risk evaluation relative to population-level package insert recommendations.

Deep learning models evaluating longitudinal electronic health record (EHR) data have exhibited significant predictive accuracy for drug-induced liver injury (DILI) in patients administered valproate and carbamazepine, for clozapine-induced agranulocytosis (by identifying high-risk patients via early hematological monitoring trajectories), and for predicting

lithium nephrotoxicity in the treatment of bipolar disorder [82]. NLP-driven pharmacovigilance systems use ML-based disproportionality analysis and semantic mining to identify novel ADR signals in near real time by analyzing spontaneous ADR reporting databases (FAERS, Eudravigilance, Yellow Card), EHR free text, and social media platforms. These tools can identify safety issues months before formal regulatory evaluation [83].

Genomically informed adverse drug reaction prediction models using HLA allele data, particularly HLA-B*15:02 and HLA-A*31:01 for severe cutaneous adverse reactions associated with carbamazepine, are used in pre-treatment screening algorithms to prevent potentially fatal idiosyncratic reactions in genetically predisposed patients through dosing optimization and therapeutic drug monitoring [84].

Modeling of pharmacokinetics and pharmacodynamics

AI-driven pharmacokinetic/pharmacodynamic (PK/PD) modeling enables more precise, individualized dosing of neuropharmacological medicines. Dosing CNS medicines is challenging because the blood-brain barrier creates a pharmacokinetic compartment that cannot be sampled non-invasively [85]. Many neurological medications have narrow therapeutic windows, and CYP polymorphisms cause significant variability in clearance among people [86].

The pharmacodynamic correlations between medication concentration and central nervous system effects are complex and vary among patients. Bayesian adaptive dosage methods integrate population pharmacokinetic models with individual patient data obtained from therapeutic drug monitoring [87]. These algorithms continuously revise individual dose recommendations as fresh medication concentration data is received. This significantly enhances the proportion of patients achieving optimal therapeutic medication levels for valproate, phenytoin, lamotrigine, levetiracetam, and clozapine.

CHALLENGES, LIMITATIONS, AND ETHICAL CONSIDERATIONS

Data Quality, Diversity, and Representativeness

The primary constraint on AI efficacy in neuropharmacology is the quality, scale, and representativeness of accessible training data. Notwithstanding the augmentation of neurological data repositories-such as the ADNI, PPMI, UK BIOBANK, ENGIMA consortium, OpenNeuro, and national EHR systems-neurological datasets are still limited in scale compared to the extensive natural image and language datasets that facilitate advancements in general AI, thereby restricting the sophistication of models that can be developed without succumbing to overfitting [88]. The persistent underrepresentation of racially, ethnically, and socioeconomically diverse populations in significant neurological research datasets creates a systematic risk of suboptimal model performance and potentially biased predictions. Crucial datasets for modeling disease progression and therapy response are notably limited due to patient dropout, protocol changes, and the prolonged timelines associated with neurodegenerative disease progression [89].

Model Interpretability and Clinical Trust

Interpretation of AI predictions is a pragmatic and ethical requirement in therapeutic neuropharmacology. High-performing deep learning models are inherently opaque, generating predictions without giving humans understandable explanations of the underlying characteristics and logic [90]. This opacity conflicts with core clinical practice needs: clinicians need to interrogate, critique, and justify treatment decisions; patients have a right to understand the rationale behind recommendations that affect their care; and regulatory bodies require evidence that the model predictions are based on clinically and biologically relevant features rather than spurious correlations in training data [91]. A non-transparent model may

miss important contraindications for patient safety or for patients outside its training distribution, and blindly trusting its predictions could lead to serious injury.

Validation and Regulatory Pathways

A key translation challenge is the gap between AI model performance in internal validation and its deployment in real-world clinical settings. Many published AI-neurology studies report impressive performance metrics based on cross-validation on a single institutional dataset. Independent external validation in different patient populations and clinical settings often reveals a substantial performance drop due to dataset shift, population differences, and variability in imaging or laboratory protocols [92]. The evidence bar for general clinical implementation of AI-based pharmacological decision support tools should be rigorous external prospective validation, ideally randomized controlled trials or well-designed prospective implementation studies, demonstrating measurable patient outcome benefits (not just surrogate accuracy measures) [93]. Although AI methods have shown encouraging performance across several neurological applications, most findings remain at the retrospective or proof-of-concept stage. Claims that AI systems match clinicians or replace established diagnostic methods should be restricted to carefully defined tasks and validated cohorts. At present, the strongest evidence supports AI as a decision-support and prioritization tool rather than a fully autonomous clinical replacement.

CONCLUSION

Artificial intelligence is significantly transforming neuropharmacology, shifting it from population-based pharmacotherapy to authentically personalized precision treatment of neurological and neuropsychiatric disorders. The amalgamation of advanced deep learning architectures capable of processing intricate neuroimaging and biological data, generative AI models that enhance the rationality of molecular design, natural language processing systems that integrate extensive pharmacological knowledge, and privacy-preserving federated learning frameworks facilitating collaborative AI research from decentralized patient data is establishing an unprecedented technological infrastructure for precision neuropharmacology in the annals of CNS medicine.

Artificial intelligence is achieving significant advancements in drug target identification, compound design, biomarker discovery, precision diagnosis, patient stratification,

pharmacological decision support, and adverse effect prevention for various neurological disorders, including Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, stroke, major psychiatric disorders, and rare neurodegenerative diseases. AI-driven target identification, patient selection, and adaptive trial design are facilitating the introduction of disease-modifying therapies into clinical evaluation, which were unattainable through conventional drug development methodologies. AI methods now used in clinical neuroimaging analysis, automated EEG interpretation, and pharmacogenomic prescribing support are improving outcomes for neurological patients in academic and community settings worldwide.

Several complex challenges must be overcome to realize the potential of AI-driven precision neuropharmacology fully. These include the generation of diverse, representative, and high-quality neurological datasets; the enhancement of model interpretability to a level that is acceptable for clinical decision-making; rigorous prospective clinical evaluations of AI tools across diverse healthcare settings; the establishment of regulatory frameworks that are both stringent and flexible; and a strong commitment to health equity in the development and implementation of AI. Solving these problems will require a common purpose for neuroscientists, pharmacologists, clinicians, computer scientists, ethicists, regulators, patient advocates, and lawmakers.

The commitment to change is real and strong. AI-driven precision neuropharmacology can improve the lives of hundreds of millions of people worldwide living with neurological illnesses, and understanding that the traits necessary for excellence in medicine and research include intellectual rigor, ethical commitment, collaborative spirit, and a sustained focus on human health as the ultimate measure of accomplishment.

FINANCIAL ASSISTANCE

NIL

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTION

Shreyansh Saha contributed to the conceptualization, methodology, investigation, data curation, visualization, and writing of the original draft. Monideepa Dey, Garima Kumari, Khyati Mishra, Abhijita Talukder, and Sushmita Ghose

contributed to the investigation, data curation, formal analysis, and critical review and editing of the manuscript. Manoj Kumar Deka contributed to the conceptualization, supervision, project administration, and critical review and editing of the manuscript, and served as the Corresponding Author. All authors contributed to interpreting the results, reviewed and approved the final version of the manuscript, and agreed to be accountable for all aspects of the work.

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