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REVIEW

Artificial intelligence in neurology: opportunities, challenges, and policy implications

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Abstract

Neurological conditions are the leading cause of disability and mortality combined, demanding innovative, scalable, and sustainable solutions. Brain health has become a global priority with adoption of the World Health Organization's Intersectoral Global Action Plan in 2022. Simultaneously, rapid advancements in artificial intelligence (AI) are revolutionizing neurological research and practice. This scoping review of 66 original articles explores the value of AI in neurology and brain health, systematizing the landscape for emergent clinical opportunities and future trends across the care trajectory: prevention, risk stratification, early detection, diagnosis, management, and rehabilitation. AI's potential to advance personalized precision neurology and global brain health directives hinges on resolving core challenges across four pillars—models, data, feasibility/equity, and regulation/innovation—through concerted pursuit of targeted recommendations. Paramount actions include swift, ethical, equity-focused integration of novel technologies into clinical workflows, mitigating data-related issues, counteracting digital inequity gaps, and establishing robust governance frameworks balancing safety and innovation.

Keywords Artificial intelligence · Machine learning · Digital health · Neurology · Brain health · Policy · Future trends

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Background

Despite remarkable advancements in biomedical research and technology, the prevention, diagnosis, management, and rehabilitation of neurological conditions remain a critical unmet need. Over the last three decades, neurological conditions have become the primary cause of disability and mortality combined [1], with 276 million disability-adjusted life years (DALYs), 9 million deaths in 2016 [2], and a 50% projected global increase in DALYs until 2040 [2]. This escalating burden is propelled by demographic change, lifestyle shifts, pollution, climate change, and post-COVID conditions [3]. Low- and middle-income countries (LMICs) are disproportionately affected [4]. The socioeconomic sequelae attributed to neurological disability are enormous.

Encouragingly, the year 2022 marked an inflection point for the global neurology community: recent milestones in clinical neuroscience—cutting across science, medicine, and the policy arena—are generating what was termed a 'neurology revolution' [5]. Emerging neurotechnologies and breakthrough discoveries have enabled recording, decoding, and modulating neural activity at unprecedented spatiotemporal resolution [6, 7], the introduction of biocompatible brain–computer interfaces (BCIs) for motor, somatosensory, and cognitive neuroprosthetics [8], and the decoding of large tumor-synaptic networks [9] with emergence of cancer neuroscience, [10] among others.

From a global health policy perspective, the World Health Organization (WHO)'s Intersectoral Global Action Plan on Epilepsy and other Neurological Disorders 2022–31 (IGAP) [4] and WHO Brain Health Initiative have anchored neurological conditions as a top priority on the global policy agenda, calling for synergistic intersectoral collaboration to tackle the global neurological burden. The neurology community is increasingly uniting around the brain health [11] paradigm and its value for human advancement [12], including economic prosperity, societal cohesion, thriving political institutions, and environmental sustainability [13, 14].

Concurrently, artificial intelligence (AI), i.e., 'intelligence demonstrated by machines' [15], and its prominent subdiscipline machine learning (ML), i.e., optimizing mathematical models to predict variables of interest from data, are evolving at an unprecedented pace. Recently, medical AI has been moving away from task-specific models trained on 'conventional' clinical data [16] to utilizing omic, wearable, or neural activity data, often equipped with data-specific inductive biases [17], or generalist Foundation Models (FMs) [18] (cf. Glossary) that represent distributions over vast, diverse, multimodal datasets. FMs such as MedPaLM [19] and MedPaLM multimodal [20] are the first generalist biomedical models of their kind, achieving state-of-the-art performance and zero-shot generalization capabilities across a wide range of medical tasks (cf. Panel I) [19, 20]. These developments are paired with an ever-growing supply of diverse medical data modalities [21] (molecular, imaging, biosensors, electronic health records, neural activity, etc.). Additionally, cross-fertilization between the neurosciences and AI, including the novel discipline of NeuroAI, [22] is rapidly advancing both neuroscientific and AI innovation (cf. Panel II) [22, 23].

AI is poised to revolutionize healthcare [24] and will advance the global IGAP and brain health agendas. However, despite its vast transformative potential for biomedicine, widespread use of AI in medical research and clinical practice is still lagging. Several important technical, structural, societal, and ethical challenges must be resolved to catalyze uptake of these novel techniques among neurology stakeholders [16, 25, 26].

This review explores the value of AI in neurology and brain health, systematizing the landscape, focusing on trends and transformative future directions. Emerging AI applications for improved prevention and risk stratification, early detection and diagnosis, and management and rehabilitation of neurological conditions are contextualized with key opportunities, critical challenges, and policy implications to ensure ethical, safe, and sustainable embedding of AI technology into the global neurology infrastructure.

Panel I. A brief technical overview of artificial intelligence and machine learning

Artificial intelligence (AI) can be defined as 'intelligence demonstrated by machines' [15]. Machine learning is a proper subfield of AI (although they are often used quasi-synonymously) and deep learning is a proper subfield of machine learning.

Formally, every machine learning problem is an optimization problem, where a model is optimized according to a predefined performance metric (the 'loss function' or 'cost function') that measures how well the model solves a given task. The machine learning model itself is a mathematical object, in most cases a function with parameters, that maps given data to a desired output variable. The procedure of optimizing the given function is referred to as 'training' or 'learning'. The distinction between 'supervised learning' and 'unsupervised learning' (and variants thereof, e.g., 'semi-supervised learning') refers to the presence or absence of labels in the data, respectively. 'Reinforcement learning' is the process of optimizing a model to emulate decision-making

by means of reward and punishment (similar to operant learning in animal models). Reinforcement learning is specifically apt to solve sophisticated planning problems, such as chess.

In medical AI, there is a small array of a dozen or so model types that are used in the overwhelming majority of studies (to which we refer to as the 'quasi-canonical' suite of model architectures in the main text), some of which are logistic regression, Decision Tree, naïve Bayes, Support Vector Machine, Random Forest, XGBoost, and artificial neural networks (ANNs). 'Deep learning' simply means optimizing ANNs with one or more hidden layers.

Models that parametrize (conditional) probability distributions over a data space are called 'generative models', as they allow sampling novel data points from the distribution. For instance, an ANN with many parameters (on the order of billions or more) that parametrizes a conditional probability distribution over embeddings of word pieces, called 'tokens', conditioned on previous tokens, is called a Large Language Model (LLM). These models typically require lots of training data.

If the data domain is highly structured (e.g., representing physical processes governed by differential equations) incorporating prior assumptions about the domain structure, so-called 'inductive biases', into the model architecture can benefit training efficiency and performance. Foundation Models (FMs) are large-scale generative models, trained in an unsupervised manner on large datasets, and consecutively fine-tuned on downstream tasks. FMs often demonstrate superior performance across a range of tasks compared to specialist models, and can routinely adapt to unseen tasks without further fine-tuning. Their capabilities, and novel techniques to adapt them to certain tasks, such as in-context learning, are actively researched.

Panel II. Moonshot perspective: potential future developments for AI in neurology

Here, we highlight seminal "moonshot" ideas that current developments in medical AI might develop into or that have been proposed, but have not yet seen the light of day.

Generalist 'neurologist in the pocket'. Moor et al. have hypothesized future emergence of 'generalist medical AI' (GMAI) [26]—models developed on large, extremely diverse datasets (e.g., text, medical images, health records, omics, protein graphs, EEGs), able to execute a wide range of tasks without additional fine-tuning on labeled data. A conceivable extension to this idea would be generalist neurology-specific AI (GNAI), trained on general health- and neurology-specific data, including relevant molecular pathways, neural activity data, and specific pathologies. 'Embodied' GNAI models are conceivable as the next step to this scheme, where generalist agents are trained on task planning and execution for optimal control and flexible interaction with the outside world [22]. Conceivable applications include direct interaction with patients, healthcare providers, and software/instruments in a hospital environment, and seamless interfacing between the 'patient brain' and external devices, e.g., neuroprosthetics.

Biophysical brain modeling. AI has proven valuable for basic scientific discovery, including data collection and analysis, representation learning from biophysical priors, learning solutions to differential equations or functionals between solution spaces, scientific hypothesis generation in differentiable hypothesis spaces, and optimizing simulations, among others [17]. With the advent of spatial multi-omics, [28] whole-brain recordings in freely behaving animals, and advanced techniques for neural population-level readout and control, a wealth of novel, yet largely unused data could be leveraged to explore novel AI-generated hypotheses. These may enable discovery of novel biomolecular pathways underpinning neural signaling, plasticity, and disease pathogenesis, as well as spatiotemporal computation of large-scale biological neural networks. Such advances could ultimately lead to a high-fidelity, individualized 'virtual patient brain' [66] augmenting neurology at every step of the care trajectory.

NeuroAI. The AI-neurosciences nexus has long history of cross-pollination, [23] resulting e.g., in the development of artificial neural networks, foundational principles behind reinforcement learning (inspired by operant learning in animals), and artificial attention. Some researchers have posited that achieving human-like AI critically hinges on "matching the perceptual and motor abilities of animals" [22] used in embodied interaction with the natural world. Zador et al. [22] hence proposed the 'embodied Turing test', an extension to the original Turing test. To this end, overcoming critical weak points of current AI (e.g., sensorimotor capabilities, dealing with uncertainty and extremely limited information) needs natural intelligence as a template. Indeed, biological neural networks have a myriad of properties currently missing in their artificial counterparts: discrete, sparse neural codes; non-linear dendritic computation; local, sparse synaptic learning rules; hierarchical, controlled input and output orchestration; massively parallel processing and multiplexing; various memory types across different timescales, to name just a few. Critically, natural neural networks operate on the basis of finely orchestrated, persistent internal states. In contrast, the most performant models to-date are not

stateful, mainly because stateful ANNs cannot perform effective temporal credit assignment, that is, roughly, the ability to attribute outcomes to specific past events effectively [22]. Understanding and emulating computational principles behind these computations may advance AI far beyond its capabilities today, and incur robustness to perturbations, novel situations, uncertainty, energy efficiency, and free sensorimotor interaction with the world. This, in turn, can cross-fertilize biophysical modeling and neurology-specific FMs, endowing them with human-like capabilities for flexible, natural interaction.

Search strategy and selection criteria

Search strategy

Following the PRISMA extension for Scoping Reviews (PRISMA-ScR) guidelines, we mapped the current body of literature on AI applications in neurology and brain health (Sect. 3). After defining MeSH terms (cf. Supplementary Material), a systematic search for studies published between January 1, 2021, and December 1, 2023, was conducted across PubMed/MEDLINE, Embase, and Google Scholar. We built a PubMed API wrapper for automated title, abstract, publication year, authors, journal, and DOI retrieval. Embase and Google Scholar were searched manually, along with targeted manual searches of published and gray literature (cf. Supplementary Material).

Selection criteria

Publications were screened for and selected based on, methodological rigor, journal impact, study quality, and utilization of recent AI technologies with transformative potential in neurology.

Data extraction and collation

We developed a Python-based search tool and a wrapper around the OpenAI API to remove duplicates, structure retrieved literature, and extract motivation, data, machine learning technique, and results from paper titles and abstracts. Results were tabulated for publication selection and content accuracy was corroborated via manual checks, resulting in a total of 66 original articles to be included for in-depth review. The underlying code for this study is available at https://github.com/sebvoigtlaender/search_and_structure.

Value of AI in clinical neurology and brain health

Machine learning applications permeate biomedical/neuroscientific research and retrospective clinical studies [16], yet clinical validation and bench-to-bedside translation remain limited [25]. Still, early AI-assisted tools and devices with clinical use cases across several neurological disciplines are emerging (cf. Table 1). Simultaneously, the computational integration of high-dimensional molecular, neurophysiological, neural activity, and clinical data has led to an increasingly systemic understanding of disease heterogeneity and pathogenesis at molecular, cellular, and tissue levels [27, 28], specifically in brain cancers [29] and neurodegenerative diseases [30].

Increased personalization of prevention, diagnosis, and intervention along the neurological care trajectory paves the way toward personalized precision neurology. This entails discovery of predictive, diagnostic, and prognostic biomarkers, patient subtyping for risk stratification and targeted interventions, translational utilization of routine clinical data, and advanced understanding of pathomechanisms underpinning disease states. Herein, we delineate use cases of medical AI along the neurological care trajectory, focusing on recent developments that bear transformative potential (cf. Fig. 1).

Prevention and risk stratification

Identification, optimization, and scaling of effective prevention and brain health promotion strategies are essential to tackle the growing neurological disease burden [52]. Timely initiation of preventive measures is markedly enhanced by AI-based individualized risk prediction, involving monitoring and risk stratification via predictive biomarkers.

Monitoring

Stroke accounts for the majority of neurological DALYs, but is largely preventable, if at-risk individuals are identified and preventive behaviors are enacted [53]. Miniaturized biosensors embedded in wearable devices, like wristbands, smartphones, or rings, enable noninvasive collection of clinical parameters for preventative purposes. Examples include heart rate/rhythm monitoring, accelerometry, and photoplethysmography (e.g., for arrhythmia or hypertension detection) [54]. Such AI-based monitoring may yield personalizable recommendations for preventative health behaviors [55]. This opportunity for cost-effective individualized prevention may substantially support scalable brain health promotion strategies (cf. IGAP strategic objective 3) [4]. In addition, wearable-derived health insights may enable decentralized

Table 1 The neurologist's 'AI Armamentarium'

Discipline	Device and description
Neurovascular	Rapid ASPECTS, iSchemaView, Inc.: Brain tissue abnormality detection in CT image data [31]; Albers et al. utilized Rapid ASPECTS for early detection of brain ischemia in patients with stroke and large hemispheric infarcts [32] StrokeSENS LVO, Circle Neurovascular Imaging, Inc.: Binary classifier for large vessel occlusion detection in head CTA images for diagnostic assistance [33] FastStroke, CT Perfusion 4D, GE Medical Systems SCS: Computer-aided visualization of head and neck vasculature from CT images across different scans; CNN-based CT perfusion image analysis to calculate perfusion-related parameters (e.g., regional blood flow) [34]
Neurodegenerative & movement disorders	NeuroRPM, New Touch Digital, Inc.: Quantification of movement disorder symptoms (tremor, bradykinesia, and dyskinesia) during wake periods in adult patients with PD Neurophet AQUA, NEUROPHET, Inc.: MRI segmentation, labeling, automated morphometric report generation [35] Cognixion ONE Axon, Cognixion, Inc.: Wearable AI-powered assistant for home automation control and assistive communication; usable without eye-tracking via BCI for patients with locked-in syndrome and/or ALS [36] (not FDA-cleared, but received breakthrough device designation [37])
Neuroimmunology	iQ-solutions, Sydney Neuroimaging Analysis Centre: ANN-based analysis of brain MRI for multiple sclerosis monitoring in terms of lesion activity and quantitative brain volumetric measures; case-level sensitivity 0.93 compared to 0.58 in standard radiology reports [38] (not FDA-cleared)
Neuro-oncology	VBrain, Vysioneer, Inc.: Radiation therapy treatment planning assistance via segmentation of diagnosed brain tumors from axial T1 contrast-enhanced MRI using deep ANNs: gross tumor volume estimation [39]; Wang et al. [40] assessed the performance of the algorithm for detection of brain metastases (sensitivity 0.96 for metastases 5 mm or greater)
Epilepsy	Persyst 15 EEG Review and Analysis Software, Persyst Development Corporation: EEG recording analysis and monitoring seizure detection in adults and infants, visualization (MRI-EEG overlay), detection of wake-sleep states, quantitative EEG artifact reduction [41]; Ganguly et al. [42] assessed the algorithms' accuracy in a critical care setting, demonstrating a modest added value (sensitivity 0.50 at the individual seizure level) Ceribell Status Epilepticus Monitor, Ceribell, Inc.: Electrographic Status Epilepticus diagnosis from EEG waveforms [43]
Neurotraumatology	Brainscope TBI, Brainscope Company, Inc.: Diagnostic support in patients with closed head injury via Concussion Index based on EEG, neurocognitive measures, and clinical symptoms (Estimating likelihood of structural brain injury visible on head CT, EEG-based measure of brain function) [44] EyeBOX (Model EBX-4), Oculogica, Inc.: Diagnosis of mild traumatic brain injury within one week of head injury via automated analysis of eye movements [45]
Neurosurgical navigation	7D Surgical System Cranial Biopsy and Ventricular Catheter Placement Application, 7D Surgical, Inc.: Stereotaxic image guidance system for spatial positioning and orientation of neurosurgical instruments during cranial surgery [46]
Neuropsychology	EarliPoint System, EarliTec Diagnostics, Inc.: ASD diagnosis based on eye-tracking data [47] Cognoa ASD Diagnosis Aid, Cognoa, Inc.: Diagnostic aid for ASD in infants and children [48]
Omics	Squidpy [49]: Python framework for integrative multi-omics data analysis, e.g., graph-based pattern identification in spatial transcriptomics data, ANN-based image analysis, etc. (not FDA-cleared)
Conversational medical AI	AMIE (Articulate Medical Intelligence Explorer) [50]: LLM-based history-taking, diagnosis, management reasoning, and communication (not FDA-cleared)
Medical documentation	Dragon Ambient eXperience (DAX™) Copilot, Nuance Communications, Inc.: LLM-based software for assisted medical documentation via speech recognition, specifically in the EHR; company claims to reduce medical documentation burden by up to 50% [51] (not FDA-cleared)

Selected FDA-cleared and potentially impactful, non-FDA-cleared AI-powered medical devices, stratified by neurological subdisciplines. *AD* Alzheimer's disease; *AI* artificial intelligence; *ALS* amyotrophic lateral sclerosis; *ANN* artificial neural network; *ASD* autism spectrum disorder; *BCI* brain–computer interface; *CNN* convolutional neural network; *CT* computed tomography; *CTA* computed tomography angiography; *FDA* US Food and Drug Administration; *EEG* electroencephalogram; *EHR* electronic health record; *LLM* large language model; *MRI* magnetic resonance imaging; *PD* Parkinson's disease

*Disclaimer: This list is non-exhaustive and does not constitute device or company endorsement by the authors

patient monitoring (at home or in 'site-less' clinical trials) [25, 27], ensuring easier health surveillance of groups in rural/remote areas lacking crucial health infrastructure.

Predictive biomarkers

Various neurological conditions exhibit significant polygenicity [56], potentially precluding statistical analyses, given high data dimensionality and nonlinear gene–gene

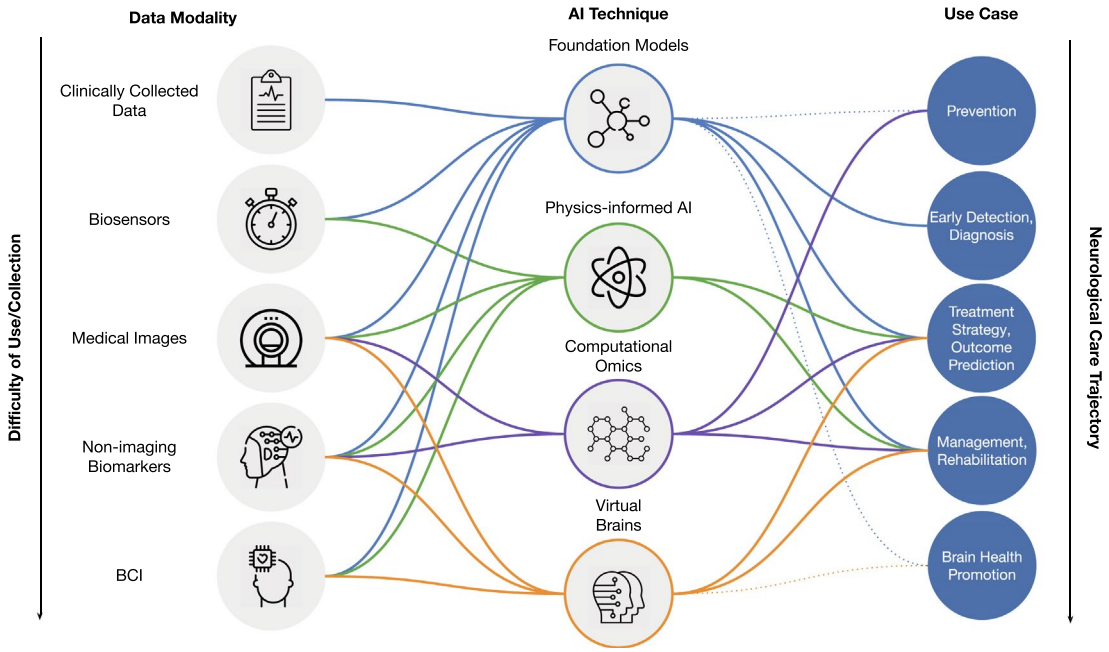

Fig. 1 Relational graph between main data modalities (left icons), types of AI (middle icons), and clinical applications (right icons). Arrows signal the main connections. Normal arrows signify a strong connection, while dotted arrows signify a weak or hypothesized connection. More details on AI use cases in neurology and brain health can be found in Tables 1 and 2. *AI* artificial intelligence; *BCI* brain–computer interface

interactions [57]. Polygenic risk score (PRS) prediction by deep neural networks, trained on genomic, imaging, and clinical data, constitutes a viable alternative to conventional PRSs, e.g., for Alzheimer's disease (AD) [57] and stroke [58]. For instance, a convolutional neural network (CNN) was trained on retinal fundus images to predict retinal age, showing that predicted retinal age gap (predicted retinal age–chronological age) is associated with a 4% stroke risk increase, performing comparably to established risk factor-based models (AUC 0.68 vs. AUC 0.66) [58]. Additionally, model features can be analyzed to uncover single-nucleotide polymorphism–endophenotype associations, allowing insight into disease etiology [57].

Early detection and diagnosis

Early detection and diagnosis of neurological conditions remains challenging and resource-intensive due to subtle, heterogeneous early clinical manifestations, high rates of misdiagnosis, and therapeutic delays, exacerbated by limited access to care and neurological workforce paucity in low-resource settings [59]. Several of these challenges are potentially addressable with advances in neuroimaging/radiomics and other diagnostic biomarkers, multi-omics, and generative AI.

Neuroimaging and radiomics

Deep learning has demonstrated expert-level performance on various medical image classification and segmentation tasks [16]. This includes predicting the presence/severity of a neurological condition or localizing regions of interest, e.g., as demonstrated in stroke diagnostics for lesion detection in diffusion-weighted MR imaging [60] or vessel occlusion detection in CT-angiography [61]. Radiomics—the extraction of high-dimensional quantitative medical image descriptors [62]—has seen a surge of interest in neuroradiology: radiomic features are used for noninvasive identification of prognostic biomarkers, automated response assessment, differentiation between treatment-related changes and tumor progression [62] (e.g., pseudoprogression detection in glioblastoma) [63], temporal lobe epilepsy onset/duration prediction (using cortical atrophy in MRI-based brain morphology data) [64], and identification of incident cardiovascular events (atrial fibrillation, heart failure, myocardial infarction, stroke) [65]. Specifically, in neuro-oncology, radiomic features are used translationally to infer genetic [66], epigenetic [67], or transcriptomic biomarkers [68], advancing molecular characterization of pathologies from images alone, e.g., for glioma subtyping, using a CNN to predict isocitrate dehydrogenase (IDH) mutation status (a key diagnostic marker in gliomas) from preoperative MR images (AUC 0.88) [67]. However, for effective clinical use,

radiomics signatures require further tissue-based pathological validation [69].

Biomarkers beyond neuroimaging

Non-imaging data modalities are potentially more readily available and can offer complementary insight in specific clinical scenarios. Acoustic signals, such as nocturnal breathing signals, can enable remote detection and severity assessment of Parkinson's disease (PD) [70], and motion capture suit data are utilized to predict Friedreich's ataxia progression, a rare neurological condition, demonstrating superior predictive accuracy compared to standard clinical assessments [71]. Monitoring longitudinal data via wearables has proved especially valuable in time-critical applications, e.g., seizure detection in epilepsy [72] or disease onset prediction (e.g., in PD using wearable-recorded accelerometry data) [73], at times surpassing models trained on genomic, blood biochemistry, or lifestyle factor data [73].

Furthermore, ML methods can detect relevant patterns not amenable to human detection in clinically collected data, e.g., questionnaires or retinal photographs. For example, an ensemble-based discriminative model predicted PD diagnosis several years into the future, using only questionnaires and noninvasive clinical tests (3 years AUC 0.82; 5 years AUC 0.77) [74]. Another study demonstrated AI-based retinal photograph interpretation alone as sufficient for accurate AD detection (AUC 0.73–0.91) [75]. These examples highlight the potential of AI-based utilization of clinically or wearable-collected data to ameliorate critical constraints in low-resource settings, including LMICs, where collection/utilization of such data might present a cost-effective alternative to diagnostic procedures heavily reliant on specialist equipment/personnel.

Translational omics and modeling disease mechanisms

Computational integration of multimodal omics can offer meaningful insights into neurological disease mechanisms, enabling identification of common omic signatures for genetically distinct disease subtypes (e.g., in amyotrophic lateral sclerosis) [76]. Neuron-type-specific molecular profiles can be integrated with genomic data, e.g., using probabilistic models: a recent study showed that AI-based genetic characterization of vulnerable neuron subtypes in AD can lead to re-ranking of known genome-wide association study (cf. Glossary) loci, ranking microtubule-associated protein tau first [30].

While molecular-genetic risk factors are implicated in pathogenesis of many neurological conditions, detailed molecular data are rarely collected without prior indication; their clinical utility not only depends on predictive value, but also on cost and effort required to obtain them. MLs' 'data type agnosticism' is conducive to utilization of diverse data types for diagnostic biomarker discovery and data gap mitigation via cross-modal inference. For example, a CNN trained on stimulated Raman histology (cf. Glossary) could distinguish molecular subtypes in diffuse gliomas (AUC 0.93) by predicting key molecular markers (IDH mutation, 1p19q co-deletion, ATRX mutation) [77]. Similarly, a random forest (cf. Glossary) trained on DNA methylation data accurately predicted somatic alterations in gliomas (AUC 0.99–1.0), enabling direct phenotype inference from epigenetic signatures, bypassing the need for multiple, separate genomic assays [29].

Foundation models

With most medical AI studies focused on narrow tasks utilizing only few data types, recent work has highlighted the need for multimodal, task-flexible approaches [18, 26, 27]. Alongside fully generalist models like MedPaLM [19, 20], smaller FMs for specific applications are emerging: MedSAM [78] can segment medical images (e.g., brain MRI), and RETFound [79] was pretrained on 1.6 million unlabeled retinal images and fine-tuned for 3-year incidence prediction of ischemic stroke (AUC 0.75) and PD (AUC 0.67), among others. Another FM trained on electronic health record data could generate artificial clinical text data indistinguishable from real clinical text [80]. These examples underscore FMs' utility for domain- or data-specific applications or administrative use cases, e.g., reducing medical documentation burden [81]. To our knowledge, no exclusively neurology-specific FM to-date exists.

Treatment, management, and rehabilitation

The past decades have seen significant therapeutic advancements in neurology, including entirely new treatment avenues (e.g., biologicals, immunotherapies), approval of effective therapeutic and disease-modifying agents, tailored to specific clinical and molecular-genetic patient characteristics, and comprehensive, data-driven mechanistic models of the brain in health and disease [82]. AI can markedly accelerate personalized precision neurology, especially prognostication, treatment planning and efficacy prediction, and neurorehabilitation.

Personalized treatment planning and guidance

ML-driven integrative omics can catalyze a 'pathway to personalization' by revealing potential therapeutic targets. For instance, a semi-supervised Support Vector Machine (cf. Glossary) was used to uncover glioblastoma-associated

master kinases PKCδ and DNA-PKcs as key therapeutic targets in functionally distinct tumor subtypes [83]. Similarly, combined XGBoost regression (cf. Glossary) and gene set enrichment analyses could delineate intratumoral glioblastoma heterogeneity, revealing distinct proteomic programs associated with differential drug sensitivities [84]. High failure rates and lengthy processes in CNS drug discovery, stemming from complex pathoetiology, blood–brain-barrier constraints, and pharmacoresistance, identify a strong future role for AI in streamlining all stages from target validation to clinical trials, addressing neurology-specific drug development challenges [85].

Data-driven computational models acting as virtual replicas of patients, so-called 'digital twins' [86], can be used to simulate dynamics of neurological conditions or system–intervention responses. Recent work has highlighted digital twins to support clinical decision-making in neurological conditions, like epilepsy [87]. Jirsa et al. elucidated the future role of virtual brains—simulations constructed from functional and structural brain imaging data tuned to individual patients—in estimating the extent and organization of the epileptogenic zone for surgical treatment planning in drug-resistant focal epilepsy [87]. The virtual brain paradigm can be extrapolated to other neurological conditions, as large-scale neural dynamics and abilities to simulate and interpret specific activity patterns evolve.

Response, progression, and outcome prediction

Alongside guiding treatment planning, AI-based methods can offer personalized prognostication or post hoc treatment efficacy estimation. For example, a deep learning model was trained to predict spatially resolved transcriptional glioblastoma subtypes from histology images, linking predicted tumor architecture to prognosis [88]. Another translational study trained an ensemble of artificial neural networks (ANNs) on clinical and MR images to estimate the conditional average treatment effect (cf. Glossary) of anti-CD20 antibodies and the immunomodulator laquinimod in multiple sclerosis treatment for time-to-confirmed-disability progression [89].

AI-guided personalized outcome prediction also has manifold applications in the neurological intensive care unit (ICU) setting, e.g., in patients with acute cervical spinal cord injury (SCI) [90], acute brain injury (related to cardiac arrest, traumatic brain injury (TBI), or hemorrhage) [91], or stroke (acute, subacute, and chronic) [92]. For example, AI-based electroencephalography (EEG) analysis could detect spoken command-induced brain activation patterns in clinically unresponsive patients with TBI, and correlate responses to functional outcomes at 12 months [91].

Ensuring optimal patient management involves mitigating treatment-related adverse effects (AEs) as much as optimizing treatment strategies [93]: ML-based detection of functional connectivity abnormalities can facilitate therapeutic target selection for repetitive transcranial magnetic stimulation in the treatment of neurocognitive dysfunction post-craniotomy, leading to significantly improved quality of life, functional status, and symptoms [94]. Other research investigated glioblastoma treatment response, demonstrating effective AI-based differentiation between true progression and treatment-related AEs, i.e., pseudoprogression, using response assessment in neuro-oncology (RANO) criteria along with a combination of clinical, radiomic, and epigenomic data (AUC 0.80) [95]. The application of ML to AE mitigation remains infrequent.

Function restoration and neurorehabilitation

Neurodegenerative diseases, stroke, and injuries (SCI, TBI) can cause significant motor, somatosensory, and/or cognitive deficits. Restoration of motor function (e.g., speech synthesis) [96, 97], somatosensory function, and, to some extent, cognitive function, has been enabled by remarkable advances in neurotechnologies, including neuroprosthetics and BCIs [8]. Techniques to record and decode high-dimensional neural population activity [6] have yielded (intracortical) BCIs: a recurrent neural network enabled attempted handwriting movement-to-text translation in SCI-paralyzed patients [98]; similarly, representations of perceived speech were decodable from noninvasive brain recordings (e.g., using a model trained with contrastive learning (cf. Glossary) on EEG/MEG [7] or a FM on fMRI [99]).

Concurrently, the ability to manipulate neural activity may catalyze next-generation neuroprostheses, potentially enabling restoration/alteration of higher-order cognitive functions mediated by distributed, large-scale neural networks [8]. Scaling such technology may significantly contribute to optimization of brain health across the life course: early and effective neurorehabilitation is critical to restore personal agency and autonomy, social connection, and societal participation. However, controlling neural activity is prone to malicious manipulation requiring ethical guardrails to secure rights to mental privacy and cognitive liberty (cf. Glossary) [100].

Opportunities, challenges, and future directions

AI could usher in a new era of personalized precision neurology, a field grappling with a public health crisis marked by a massive growing burden of neurological conditions worldwide. Unlocking this potential requires effectively leveraging

Table 2 Mapping the field

Clinical/global neurology challenge	Recommended techniques/policy implications
High disease burden of preventable neurological diseases [53] Lack of healthy behaviors and health literacy	Prevention by personalized risk stratification/wearable-based monitoring [54] Site-less/remote multicentered clinical trials [25] Predictive biomarker discovery, AI-based PRS [57] and SNP-phenotype association
Subtle or ambiguous early clinical manifestation of many neurological conditions [59] Imprecise, non-personalized diagnostics	Prognostic and diagnostic biomarker discovery Tissue-based validation of radiomic/radio-genomic/modeling-based image analysis [62] Translational AI-based medical image interpretation [66, 67] Computational multi-omics [27], biophysical/neurophysiological models [87]
Neurological workforce paucity in rural areas/LMICs Precise, personalized diagnosis unaffordable or unavailable	Affordable prognosis/diagnosis using imaging, clinically collected [74, 79] or attainable biosensor data [72] AI-based diagnostic assistants to reduce specialist need; locally deployed FMs
'Broadband' therapeutic strategies not tailored to individual patient needs No causal treatment available for most neurological conditions	Discovery of therapeutic targets [83], mechanistic disease modeling [82] AI-based treatment planning [87] Treatment response prediction, causal modeling (e.g., CATE) [89] Mitigate treatment-related AEs [95, 101] AI-powered drug discovery, clinical trials [25]
High disease burden in terms of DALYs [1]; rehabilitation and restoration of neurological function difficult or impossible	Outcome prediction, resource triaging BCI-based neurorehabilitation [96–98] Effective prevention and rehabilitation, leading to greater societal participation
Lack of comprehensive, unbiased, accessible datasets for neurological AI research	Broad collection of centralized (semi-)open-source neurological data Inclusiveness, civic agency, and cognitive liberty [100] as leading data-safeguarding principles
Lack of guidelines for deployment/validation of AI-based medical products	Feasibility studies, rapid 'sandbox' testing AI-human collaboration studies [102] Stakeholder involvement across six Ps [12] Adhere to/extend existing validation frameworks [103]
Adoption difficulties and inaccessibility of novel techniques due to digital divide (infrastructure, access, quality, literacy)	Equity-focused, patient-centric data collection, development, and rollout Multi-level awareness campaigns focused on digital health literacy Infrastructure updates, 'small medical FMs', high-structure-low-data techniques [104, 105], clinically collected data-focused development
Bench-to-bedside translation gap [25] due to 'expertise siloing' and unbalanced regulation of medical AI	Needs-driven, value-based regulatory frameworks, balancing risk-based quality assurance [106], ethically responsible data handling and innovation [107], and rapid testing/deployment

This table details the clinical or global health core challenges and associated opportunities in terms of applicable AI-based techniques, existing frameworks, or recommendations. *AI* artificial intelligence; *BCI* brain–computer interface; *CATE* conditional average treatment effect; *FDA* food and drug administration; *FM* foundation model; *LMIC* low- and middle-income country; *PRS* polygenic risk score; *SNP* single-nucleotide polymorphism

AI's strengths while resolving critical challenges across four pillars: models (technical challenges, FMs, biophysical modeling), data (quality, collection, use), feasibility and equity (trust, AI–user interaction, digital health equity), as well as regulation and innovation (stakeholder alignment, co-creation, policy). While these pillars pertain to medical AI per se, [16, 18, 25–27] neurology-specific considerations and future directions can be delineated. This includes AI interventions (and policies) directed at overcoming core issues persisting in clinical and global neurology (cf. Table 2).

Models: opportunities and technical limitations

ML models suffer from prediction error, uncertainty, and a proclivity to underperform on 'out-of-distribution' data. Lack of generalizability can hinder clinical validation, e.g., as demonstrated for AI-derived meningioma classification systems [108]. To ensure robust performance, end-to-end deployment studies must therefore include calibration, uncertainty estimation, and generalizability evaluation; guidelines for end-to-end co-creation have been detailed by Tomašev et al. [101] Furthermore, model performance critically depends on data quality, as models trained on biased

datasets might perpetuate stigma surrounding neurological conditions [12], exacerbating health inequities in disfavor of identifiable groups [109].

Despite promising applications, there is a certain 'hesitance' for adopting the latest ML techniques, given widespread use of 'quasi-canonical' methods, high-quality data scarcity, inadequate interactivity/explainability of most complex models, associated regulatory and ethical hurdles, and insufficient cross-disciplinary communication.

Foundation models

FMs may signal a paradigm shift for augmenting specialist care, outperforming various 'narrow' models, eventually evolving toward highly capable, 'generalist medical AI' (cf. Panel II) that needs little data to acquire novel tasks and return expressive outputs [26].

Beyond their conceivable role as 'pocket neurology assistants', their future use may include neuro-rehabilitative applications, acting as generalist interfaces for patient communication/interaction with the outside world. Reciprocally, external signal transduction into neural activity could restore active societal participation.

FMs have yet to permeate medical space due to recency, suboptimal alignment with human intent/values, unquantifiable extrapolation capabilities, and prohibitive resource requirements. How to improve alignment and validate medical FMs (e.g., to prevent reproducing personally identifiable information) remain open questions [26], currently precluding their approval as medical devices [110]. Moreover, FMs' infrastructure requirements may risk 'undemocratic' use, potentially aggravating global neurological care disparities and excluding LMICs from equal participation in utilizing FMs at scale.

Biophysical computational disease models

Current FM architectures possess weak inductive biases (cf. Glossary), which may benefit performance when data have little inherent structure. However, much of the complexity of biomedical/neural data lies in physical, functional, and semantic interdependencies between biomedical entities. Spatiotemporal neural activity can be described by systems of differential equations and simulated to varying degrees of fidelity, given prior knowledge about neuroanatomy and connectivity. Furthermore, neural population codes often possess intrinsic low-dimensional geometry, i.e., they can be represented by low-dimensional variables without significant loss of information [111]. This structural information can be leveraged by physics-informed neural networks (PINNs) [104] and geometric deep learning [105], incorporating physical, geometric, or relational domain structure as inductive biases. This enables learning even when very little training data are available and confers robustness to data distribution shifts (i.e., significant differences between the training and, potentially external, real-world, validation/test datasets) [17], improving biophysical simulations, decoding, and interpretation of large-scale neural data, e.g., for interactive BCI and virtual brain development. Furthermore, computational microstructure modeling and MR fingerprinting (cf. Glossary) [112] of brain neoplasms might obviate the need for invasive diagnostic procedures (e.g., tissue biopsy) altogether [113].

We recommend:

(i) Promotion of ethics-by-design AI, [114] e.g., enforcing ethical principles during training; continual validation to ensure fair, equitable AI. Follow end-to-end medical AI development guidelines [101].
(ii) Data- and structure-aware use of techniques, e.g., pretrained FMs or canonical models in low-data, low-structure regimes, PINNs in high-structure regimes, e.g., virtual brains or brain microstructure modeling.
(iii) Deliberate mitigation of infrastructure burden for medical FM utilization and local deployment, e.g., via cloud services, model distillation, open-sourcing 'small' FMs (cf. Glossary), or financial support for targeted infrastructure updates. Alleviate resource burden by utilizing 'simple' clinical data, like retinal photographs, or biosensors for 'site-less' multicenter clinical trials.

Data: quality, collection, use

Neurological data are often partially incomplete, unstructured and unlabeled, multimodal, longitudinal, and recorded non-continuously. Detailed molecular/neural activity data remain unavailable for most neurological conditions [56]. Most clinical data are not readily accessible to the research and broader neurology communities because of anonymization, digitization, centralization, and harmonization constraints, regulatory hurdles, and privacy concerns. These are especially pronounced in neurology, given inherent deidentification challenges surrounding head MRIs, and ethical concerns with deciphering/manipulating neural activity.

To counteract data-related issues, globally concerted data collection and curation efforts are paramount, paired with ethical regulatory frameworks for data compliance. Although partially mitigable with decentralized, privacy-preserving techniques such as federated learning (cf. Glossary) [115], poor accessibility limits development of complex models.

We recommend:

(i) Establish standards for centralization, anonymization, and curation of existing high-quality population-level data (e.g., the European Health Data Space) [116]; ensure inclusiveness and civic agency over data use.
(ii) Establish benchmarks and structures for improved data collection in neurology; facilitate responsible and transparent data sharing, access, and usage (e.g., Medical Open Network for Artificial Intelligence (MONAI)), preventing commercial data exploitation; promote ethical, culturally appropriate handling to prevent misuse and harm, protecting patient rights to cognitive liberty [100].

Feasibility and equity

To enable widespread AI use in clinical neurology, models must be thoroughly validated, trustworthy, and seamlessly integrated into clinical workflows. The demand for trustworthiness often presupposes explainability. Explainability and interactivity risk user over-trust, potentially facilitating human error [117]. For high-stakes clinical settings, it has been proposed to dispense with black box models in favor of inherently explainable models [117]. A diametrically opposed view constitutes accepting a model's internal reasoning opaqueness, but establishing rigorous validation procedures [118].

However, even accurate models may not improve expert performance, as experts may undervalue AIs' predictions, illustrating a critical need for greater digital literacy among healthcare providers [102]. Global disparities in digital literacy further exacerbate adoption challenges, particularly in LMICs. The existing 'digital divide' (e.g., access, quality, literacy, and outcome disparities) [119] must be closed by identifying antecedents and consequences of digital heath inequities, leading to equity-focused, person-centered AI development.

We recommend:

(i) Conduct targeted feasibility and AI-human collaboration studies, protecting human autonomy/agency while safeguarding patient–provider interaction [24]. Ensure stakeholder accountability, including resolution of medico-legal aspects and regulatory compliance [109].
(ii) Promote digital health literacy by awareness/educational interventions and technology co-creation.
(iii) Utilize/develop digital health equity frameworks to guide AI policy development/implementation.

Regulation and innovation

Successful adoption of AI in neurology requires deliberate cross-disciplinary collaboration and communication of domain-specific challenges to overcome existing 'bench-to-bedside' translation gaps [25]. This necessitates striking the right balance between regulation and innovation, implicating adherence to ethical and quality assurance principles (e.g., risk-based practices for healthcare technology governance, evaluation, monitoring, and safety surveillance) [106] without hindering progress. For instance, regulators could establish progress-friendly regulatory and administrative infrastructures, enabling 'sandbox environments' for rapid medical AI testing and fast-tracked medical device approval (for a selection of FDA-cleared AI tools/devices in neurology, see Table 1).

We recommend:

(i) Ensure balanced approaches to AI regulation; ensure ethically responsible innovation, using the OECD Responsible Innovation in Neurotechnology principles [107], UNESCO Recommendation on the Ethics of AI [120], WHO guidance on ethics and governance of artificial intelligence for health using large multimodal models [121], and the 'Dignity Neuroscience' framework [122] as reference points.
(ii) Adhere to validation guidelines, covering safety, reproducibility, explainability, harmlessness, fairness, robustness, and alignment, accounting for continually learning and generalist models [19].
(iii) Enhance collaboration across the six Ps [12]—patients, healthcare providers, policymakers, payors, implementation partners, general public—to facilitate effective co-creation, stakeholder alignment, and integration into existing workflows, while mitigating potential skill decline of health professionals, and preventing the spread of misinformation. Promote early and meaningful patient and public involvement to augment needs-driven, value-based AI development.

Conclusions

The integration of AI into clinical neurology presents unprecedented opportunities but is fraught with substantial challenges. The confluence of enhanced computational power, large-scale datasets, and advanced machine learning algorithms may revolutionize neurology along the care trajectory and foster brain health optimization across the life course. This encompasses predictive, diagnostic, and prognostic biomarker discovery, biophysical disease modeling—accelerating discovery of novel therapeutic targets, 'virtual brain' development, and neurorehabilitation—and the advent of large-scale, generalist foundation models.

To achieve this paradigm shift, we call on the global neurology community to engage in ethical-by-design, data- and structure-aware, and equity-centered co-creation across the six Ps, fostering positive AI–human interaction while safeguarding autonomy and accountability. Efficient, comprehensive, and inclusive data collection/utilization, preserving civic agency, as well as balanced approaches to AI regulation are paramount to foster innovation, firmly anchored in regulatory frameworks to ensure rapid yet ethically responsible progress.

Glossary

AUC A measure of a model's performance, often utilized in binary classification problems. AUC quantifies the total area under the receiver operating characteristic (ROC) curve, with a value of 1 indicating perfect prediction and a value of 0.5 indicating random chance.

Brain Health The state of brain functioning across cognitive, sensory, social-emotional, behavioral and motor domains, allowing a person to realize their full potential over the life course, irrespective of the presence or absence of disorders (WHO definition).

Cognitive liberty A right to access and change one's brain, making advances in brain health crucial to securing cognitive liberty to individuals, and a right from interference with mental privacy and freedom of thought. The concept provides an important framework to ensure ethical innovation of advances to improve brain health.

Conditional average treatment effect The difference between the expected response under control and the response under treatment.

Contrastive learning A learning framework that trains models to distinguish between similar (positive) and dissimilar (negative) pairs of data samples, enhancing the capability of models to learn robust and discriminative features.

Epigenome The ensemble of modifications to DNA and DNA-associated proteins that signal and regulate gene expression and other DNA-related processes.

European health data space A health specific ecosystem comprised of rules, common standards and practices, infrastructures and a governance framework.

Federated learning A privacy-preserving machine learning approach where a model is trained across multiple decentralized devices or servers, using local data samples without sharing them.

Foundation model Large-scale artificial neural networks trained on vast, diverse, multimodal datasets that have shown the capability to excel at a variety of tasks by additional fine-tuning, or to flexibly adapt to novel tasks via text instructions or examples ('in-context learning') without additional training, enabling fine-grained control over model outputs. 'Small FMs' are FMs with fewer parameters than state-of-the-art large FMs.

Genome-wide association studies An observational study of a genome-wide set of genetic variants in different individuals to see if any variant is associated with a trait. GWASs typically focus on associations between single-nucleotide polymorphisms (SNPs) and traits like major human diseases.

Inductive bias The set of assumptions or a priori information that a machine learning model or algorithm uses for prediction, e.g., physical, geometric, or causal.

MR fingerprinting The recording of multiple MR sequences with pseudorandomized acquisition parameters, combined with computational matching of resulting "fingerprints" to a predefined dictionary of predicted signal evolutions

Random forest	A machine learning technique that constructs multiple decision trees during training and outputs the mode of their predictions for classification or the mean for regression, enhancing prediction accuracy and reducing overfitting.
Stimulated Raman histology	Non-invasive, label-free histological imaging, based on stimulated Raman spectroscopy.
Support vector machine	A supervised learning model that identifies the optimal hyperplane in a high-dimensional space to segregate different classes, maximizing the margin between data points of different categories.
XGBoost	An optimized distributed gradient boosting library that enhances the efficiency, accuracy, and scalability of machine learning models, particularly in tree boosting methods.

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Data availability The code, MeSH terms, and prompts used to generate the data tables are available at [URL blinded for review]. Tables are available upon reasonable request from any qualified investigator.

Declarations

Conflict of interest S.V. is an employee of QuantCo Inc., M.G. is an employee of NVIDIA. V.N. is an employee of Alphabet. All other authors declare no competing interests.

Declaration of generative AI and AI-assisted technologies in the writing process During the preparation of this work the authors used a custom-made wrapper around the OpenAI API, accessing GPT-4 in order to automatically structure and extract information from the paper title and abstracts retrieved during search. After using this tool/service, the authors reviewed and edited the search content as needed and take full responsibility for the content of the publication.

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