



Artificial Intelligence in Neuroinformatics: Applications, Methodological Challenges, and Clinical Considerations

Utkarsh Raj^{1,*}, Rahul Semwal², and Mohini Vats^{1,3}

¹Department of Biotechnology and Bioinformatics, NIIT University, Neemrana, Rajasthan, India.

²Department of Computer Science and Engineering, IIIT Nagpur, Nagpur, Maharashtra, India.

³Department of Biotechnology, Sharda University, Greater Noida, Uttar Pradesh, India.

Correspondence: Utkarsh Raj, utkarsh.iiita@gmail.com

Abstract

Neuroinformatics brings together neuroscience, computational approaches, and large-scale multimodal data to study brain structure, function, connectivity, and disease-related alterations. Advances in artificial intelligence (AI), including deep learning, foundation models, federated learning, and explainable AI, have expanded the analysis of neuroimaging, electrophysiological, genetic, behavioural, and clinical data. This narrative review examines representative literature on current applications of AI in brain mapping, neuroimaging analysis, electroencephalography (EEG) classification, biomarker discovery, neuroinformatics data resources, brain ageing research, and brain-computer interfaces. Representative studies were considered according to their relevance to these application areas and, where appropriate, their study population, data modality, validation design, and reported findings. The review also examines methodological and ethical issues affecting the interpretation of these studies, including data heterogeneity, population representation, validation, database governance, model explainability, and clinical translation. The available evidence shows that technical model performance and clinical usefulness should be considered separately, particularly when studies differ in population, validation design, and data source.

Keywords: artificial intelligence; neuroinformatics; machine learning; neuroimaging; EEG; biomarkers; brain-computer interface; explainable artificial intelligence

Abbreviations: AI, artificial intelligence; BCI, brain-computer interface; EEG, electroencephalography; fMRI, functional magnetic resonance imaging; MRI, magnetic resonance imaging.

Received: 14 September 2026. **Accepted:** 29 September 2026. **Published:** 16 October 2026 (version 1).

1. Introduction

Neuroinformatics brings together neuroscience, information technology, and computational analysis to support the organization, integration, and interpretation of large-scale brain data. As artificial intelligence (AI) continues to develop, neuroinformatics has become an important approach for detecting patterns across neuroimaging, electrophysiological, behavioural, genetic, and clinical datasets. In this way, the field connects data-driven neuroscience with computational methods used to study brain structure, function, connectivity, and disease-related changes (1, 2). Neuroinformatics is a rapidly growing, highly interdisciplinary field in which AI and neuroscience research converge. Worldwide initiatives in neuroscience and neuroinformatics require substantial investment in data infrastructure, computational tools, and interdisciplinary collaboration. Neuroinformatics has strengthened the

capacity to organize, integrate, and analyse complex brain data, contributing to a more detailed understanding of brain structure, function, connectivity, and disease-associated patterns. Nevertheless, a complete mechanistic account of how the brain works remains an unresolved scientific challenge. Neuroinformatics-derived neuromarkers may help identify disease-associated patterns in conditions such as autism, schizophrenia, obsessive-compulsive disorder, and depression through the analysis of functional magnetic resonance imaging (fMRI), electroencephalography (EEG), and magnetoencephalography (MEG) data. These neuromarkers, however, should be interpreted cautiously. At present, AI-based neuroimaging and EEG/MEG models are best understood as tools for detecting disease-associated patterns, risk profiles, or clinically relevant features, rather than as universal diagnostic systems (3). Recent studies have broadened the scope of neuroinformatics by using foundation models, generative AI, and self-supervised

learning to analyse large-scale brain data. These methods are being investigated for tasks such as representation learning, data augmentation, multimodal modelling, brain-computer interfaces, and more generalizable neuroimaging analysis. For instance, work on brain magnetic resonance imaging (MRI) foundation models has highlighted the value of reusable representations learned from large imaging datasets, while recent reviews of generative AI in neuroscience have discussed its potential for handling complex and heterogeneous brain data. At the same time, this literature cautions that strong predictive performance does not, by itself, demonstrate mechanistic understanding or clinical validity. These models should therefore be regarded primarily as tools for hypothesis generation, feature learning, and clinician-supported decision-making until they are validated in independent, multicentre, and demographically diverse cohorts (4, 5).

Neuroinformatics may be useful for improving the creation of systems that simulate human brain functioning in storing and retrieving information. Understanding the biological structure and working processes in the human brain requires computational methods, mathematical modeling, as well as organizing and using neuroscience information. Three key domains in which neuroinformatics is applied are:

- Developing software for handling neuroscience data at different stages of analysis. (Figure 1).
- Improving tools for modelling and interpreting neuroscientific information.
- Creating computational models to study nervous-system function.

These domains affect the processing and interpretation of experimental data, which are increasingly large, complex, and fine-structured. Neuroinformatics researchers contribute to the development of interoperable databases that allow clinicians and scientists to access, share, and analyse neuroscience data. Thus, information sharing is very important. The Human Brain Project, initiated in the 1990s, catalyzed the development of neuroinformatics. A primary goal of both the project and the field of neuroinformatics is to develop novel database architectures, search engines, and data-sharing protocols. This will enable researchers to generate models of the brain as well as simulations of how it functions. In this review, the term simulation is used to refer to computational brain-modelling approaches described in the existing literature. No original simulation experiment or simulation-based validation was conducted as part of this manuscript.

Despite these developments, several challenges still hinder the use of AI-based neuroinformatics in robust research and clinical settings. Many AI models are trained on datasets that are heterogeneous, small, or demographically restricted, which may limit their generalizability across populations, imaging systems, institutions, and stages of disease. In addition, external validation, data provenance, harmonization methods, and clear reporting of model

limitations are not consistently addressed across studies. Although explainable AI approaches can indicate which features contribute to a model's prediction, they cannot, on their own, confirm biomarker validity, biological causality, or clinical reliability. Similarly, federated learning can limit the need to centralize patient-level data. However, it does not address demographic or biological bias if the participating datasets are homogeneous, insufficiently characterized, or unevenly represented (6–10). Existing literature has examined specific areas, including foundation and generative models in neuroscience (4), EEG-based brain-computer interfaces (11), and disease-specific deep learning applications in Parkinson's and Alzheimer's disease (12, 13). The present review brings these areas together within the broader context of neuroinformatics and examines them at three linked levels: the application of AI to different types of neuroscience data, the validation of the reported findings, and the limitations affecting their biological or clinical interpretation. Accordingly, brain mapping, neuroimaging, electrophysiological analysis, biomarker discovery, neuroinformatics databases, brain ageing, and brain-computer interfaces are discussed together with issues related to data provenance, demographic representation, external validation, explainability, federated learning, and clinical validity. This framework allows technical model performance to be considered separately from evidence of generalizability and clinical usefulness. Because this article is a review, it does not propose a new algorithm, model architecture, or experimental pipeline. Accordingly, the limitations discussed in the manuscript concern the AI-based neuroinformatics methods reported in the existing literature, rather than any method newly introduced in this work.

Demographic validity is a key concern in AI-based neuroinformatics, as model performance is shaped not only by algorithmic design but also by the populations represented in the data used for training, testing, and external validation. Neuroimaging datasets may inadequately represent groups defined by age, sex or gender, race, ethnicity, geography, socioeconomic status, disease stage, or clinical comorbidities. If these imbalances are not clearly reported and assessed, AI models may learn patterns associated with a dominant subgroup, scanner site, or recruitment setting, rather than features that generalize across populations. For this reason, studies should report demographic composition, data provenance, and subgroup-level performance whenever feasible. AI-derived neuromarkers should therefore be regarded as population and dataset dependent findings until they are validated in independent, multicentre, and demographically diverse cohorts (7, 8, 10).

In addition to demographic validity, it is important to account for neurobiological heterogeneity within diagnostic categories. Clinical labels such as Alzheimer's disease, Parkinson's disease, autism, schizophrenia, depression, multiple sclerosis, and long COVID-related fatigue often encompass patients who differ in underlying mechanisms, disease stage, comorbid conditions, and biomarker pro-

files. Comparable symptom severity therefore does not necessarily indicate a shared neural or metabolic basis. For example, FDG-PET studies of fatigue-related conditions suggest that clinically similar fatigue may be associated with distinct frontal–striatal metabolic patterns depending on the disease context. Accordingly, when developing or interpreting AI-based neuroinformatics models, diagnostic categories should be viewed as clinically useful grouping variables rather than biologically uniform classes (14–16).

2. Application of AI and Neuroinformatics

Neuroinformatics integrates neuroscience, information technology, and analytical methods to support the study of brain structure, function, and disease-related processes. Data sets, some of which are provided in Table 1, are analyzed and integrated using neuroinformatics methods including the use of advanced computational methods. AI is widely used in brain mapping, assisting in both analysis and visualization of brain maps. Following are examples of neuroinformatics and AI applications:

2.1 Mapping the brain with AI

A detailed understanding of brain function requires mapping large-scale neuronal connections and relating these connectivity patterns to neural activity. Brain mapping research aims to elucidate cerebral function by leveraging statistical frameworks, computational models, and advanced neuroimaging.

Investigating brain structure and function relies heavily on neuroimaging modalities such as magnetic resonance imaging (MRI), positron emission tomography (PET), and functional MRI (fMRI). PET and fMRI can provide indirect measures of brain activity through metabolic or haemodynamic changes, whereas MRI provides high-resolution structural information.

Creating computer models that mimic how the brain functions is an essential part of brain mapping. These models test concepts on basic principles of brain activity and can be used to anticipate specific stimuli or treatments (17). Because of machine learning (ML) technology, images taken by machines of the brain can reveal much useful data, starting from the recognition of features and ending with the classification of brain areas. Scientists are able to analyze brain circuits and pathways along with connection strengths between various brain regions, using complex AI technologies such as network analysis and graph theory. Computational models used for reproducing brains through AI research are the result of more advanced research done in the field of brain simulation through artificial intelligence. With the help of artificial intelligence, researchers can build detailed three-dimensional (3D) representations of brain and neuronal structures (18–20). Artificial intelligence allows us to incorporate data from different brain imaging

methods along with other data sources. Brain mapping also includes the development of statistical methods that will allow for the examination of large sets of data. Such an approach can be useful in finding correlations and patterns among various brain regions and exploring the relationship between brain networks. Using image, computation, and statistical processing technologies, scientists are able to develop detailed brain maps and acquire new information about its function. The obtained data might help develop new treatment options for certain neurological and mental disorders.

In neurocognitive studies, the development of brain templates and the subsequent investigation of their anatomy is essential. Normally, a brain template that is created using MRI images from a batch of subjects will represent a reliable reference space to study their structure and function. Taking into account recent achievements in AI approaches, it makes sense to explore AI tools for age-related brain pattern analysis at different ages. According to a recent study, an AI-based age-specific template construction (ASTC) framework may support longitudinal structural brain analysis in neuroimaging studies (21). Whole Brain Connectomic Architecture (WBCA) is a software architecture consisting of empirical information on neural circuits from the entire brain. This architecture is created with the objective of designing an AI that will be able to engage in various cognitive activities in the computer context. WBCA has the capability to accelerate the engineering process of intelligent gadgets through the design of nervous systems of humans (22). Recent neuroinformatics research increasingly uses predictive modelling and pattern recognition to connect computational neuroscience with clinical neurology. In this context, AI methods are moving beyond single-task classification toward more reusable representation-learning frameworks. Foundation and generative models may contribute to data augmentation, transfer learning, multimodal integration, and brain imaging analysis, and self-supervised foundation models for brain MRI could reduce reliance on large, labelled datasets for certain downstream applications. However, these developments do not lessen the need for external validation, transparent reporting of training populations, and careful evaluation of differences related to scanners, imaging protocols, demographics, and disease stage. Likewise, federated learning offers a way to support privacy-preserving model training across institutions, but it should not be viewed as a complete solution to bias or limited generalizability, especially when the participating datasets remain demographically or clinically homogeneous (4–6).

2.2 Machine learning

Machine learning methods are used in neuroinformatics to analyse neuroimaging, electrophysiological, behavioural, genetic, and clinical data and to identify patterns associated with brain function, disease, or treatment response (Figure 2). Applications include classification, prediction, functional-connectivity analysis, and multimodal data inte-

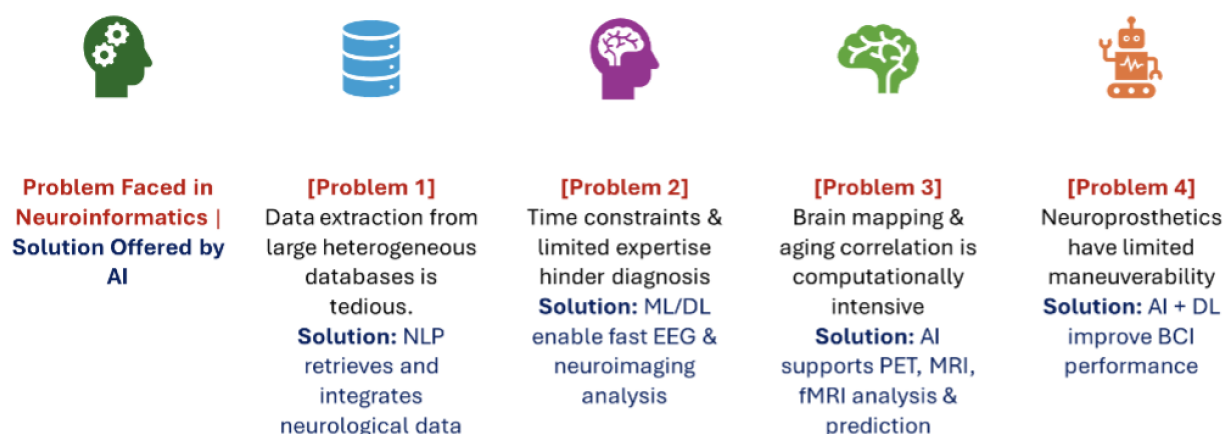


Figure 1: Common challenges in the domain of neuroinformatics and solutions presented through integration with AI.

gration. More recent approaches include federated learning for distributed model development, explainable AI for interpretation of model predictions, and reinforcement learning for adaptive neurotechnology (6, 9, 23–25). The methodological limitations of these approaches, including generalizability, bias, interpretability, and validation, are discussed in the critical-appraisal section.

2.3 Neuroimaging

Neuroimaging is an important technique in neuroinformatics that helps to visualize the brain structure, function, and connectivity. MRI, PET, and fMRI are examples of neuroimaging methods used in neuroinformatics. MRI is an effective non-invasive imaging technique that produces highly detailed images of the brain's anatomy utilizing radio waves and powerful magnetic fields. MRI is used for examining the brain's anatomical structure and identifying changes in its structure caused by neurological diseases. PET is a molecular imaging technique that can be used to assess brain metabolism, receptor binding, and regional blood-flow changes in neurological disorders (26). AI methods have been applied to neuroimaging for image reconstruction, segmentation, feature extraction, and image-based classification. In brain MRI, deep learning methods have been evaluated for the segmentation of brain structures and lesions, including brain tumours (27), while other studies have examined the use of deep learning for neuroimaging analysis more generally (28, 29). These methods may assist quantitative image analysis, but their performance should be interpreted according to the dataset, imaging protocol, and validation setting used in the original study.

2.4 Neuroinformatics data resources and governance

Neuroinformatics resources include research projects, atlases, data repositories, resource registries, and computational platforms, which differ in their purpose, population coverage, data modalities, access conditions, and gover-

nance. These resources support different applications of AI in neuroinformatics, including brain mapping, neuroimaging analysis, biomarker exploration, and the integration and analysis of large-scale neuroscience data (Figure 2). These distinctions are important when such resources are used for the development or validation of AI models. For example, some resources provide openly accessible imaging or molecular data, whereas others contain controlled-access participant-level information that is governed by data-use agreements. Table 1, therefore distinguishes the major resources according to their resource type, population scope, available modalities, access and governance conditions, demographic metadata, and limitations.

The suitability of a neuroinformatics resource for AI development should not be assessed only according to its size. Population composition, completeness of demographic and clinical metadata, acquisition protocols, and restrictions on sensitive information also affect the interpretation and generalizability of model performance. Some resources contain detailed demographic variables but restrict potentially identifying information, whereas others were developed primarily as anatomical or molecular reference atlases and were not designed to represent population-level demographic variability. These characteristics should be considered when data from different neuroinformatics resources are used for model training, comparison, or external validation.

2.5 Applications and impact of AI in neuroinformatics

AI approaches in neuroinformatics differ considerably in the type of data analysed, study population, validation design, and intended application. Therefore, reported model performance should not be compared only on the basis of accuracy or other individual performance measures. Results obtained from internal cross-validation, public benchmark datasets, independent external cohorts, and small experimental studies provide different levels of evidence.

Table 1: Major neuroinformatics resources, their access conditions, governance, and limitations.

Resource	Resource type	Population scope and modalities	Access and governance	Demographic metadata	Principal limitations	Primary citation
Human Connectome Project-Young Adult (HCP-YA) / ConnectomeDB	Research project and associated data repository	Approximately 1,200 healthy young adults, primarily 22–35 years of age. Data include structural MRI, resting-state and task fMRI, diffusion MRI, behavioural and phenotypic measurements, with 7T MRI and MEG available for subsets.	Imaging data and most non-sensitive behavioural data are available after registration and acceptance of HCP data-use terms. Potentially identifying or sensitive variables are controlled through restricted-access procedures.	Banded age and gender are available in open-access data; exact age, race/ethnicity, family structure and some other participant characteristics are restricted.	The original HCP-YA cohort consists primarily of healthy young adults and therefore does not by itself represent neurological patient populations or the complete age range. Some demographic variables required for subgroup analysis have restricted access.	Van Essen et al. (30)
Allen Human Brain Atlas	Anatomical and transcriptomic atlas/data resource	Adult post-mortem human brain tissue with anatomical mapping and genome-wide gene-expression information. The downloadable microarray resource contains data from six brains, while RNA-sequencing data are available for a subset.	Data can be downloaded from the Allen Institute resources and are governed by the Allen Institute Terms of Use and Citation Policy.	Donor- and sample-associated information is available with the resource, but the small post-mortem donor set is not designed to represent demographic variation at the population level.	Small number of post-mortem donors and limited demographic representation restrict population-level inference. The resource is primarily an anatomical and molecular reference atlas rather than a clinical cohort.	Hawrylycz et al. (31)
Neuroimaging Tools & Resources Collaboratory (NITRC)	Resource registry, image repository, and computational environment	Hosts or links neuroimaging software, datasets and computational resources across MRI, PET/SPECT, CT, EEG/MEG, optical imaging, computational neuroscience and imaging genomics. Population scope depends on the individual hosted dataset.	General platform use is available through NITRC; access to individual datasets may be open or may require registration or approval from the original data provider. Dataset-specific governance therefore applies.	Demographic variables and their completeness depend on the individual dataset or contributing project rather than on NITRC as a whole.	NITRC is not a single harmonized cohort. Data acquisition, participant characteristics, metadata completeness, access procedures and governance can differ considerably among hosted resources.	Kennedy et al. (32)
NIMH Data Archive (NDA; incorporates the former National Database for Autism Research,NDAR)	Controlled-access research data repository	Human-subject research data across mental-health and related domains, including clinical, behavioural/phenotypic, imaging, genomic and other data. The current NDA extends beyond the original autism-focused NDAR.	Summary information and data dictionaries are publicly searchable, whereas participant-level shared data are generally controlled through permission groups, Data Use Certification and applicable consent-based data-use limitations.	NDA data structures support standardized demographic variables such as age, sex, race/ethnicity and socioeconomic measures, although availability and completeness depend on the contributing study or collection.	Data originate from heterogeneous studies with different populations, protocols, consent conditions and levels of metadata completeness. Access restrictions and data-use limitations may also differ among collections.	Hall et al. (33) and current NIMH/NDA documentation

The following sections describe the major applications of AI in neuroinformatics, while Table 2 provides a comparative assessment of representative studies according to their population, validation strategy, external validation, demographic reporting, calibration, and principal limitations.

The strength of evidence differs across these applications. Technical benchmarking is comparatively well established for tasks such as brain tumour segmentation, where standardized datasets and predefined evaluation measures allow different algorithms to be compared under similar conditions. This technical maturity, however, should not be interpreted as evidence of clinical maturity. Evidence for disease classification from neuroimaging is more mixed. For example, reproducible evaluation of Alzheimer's disease classification has shown that strong within-dataset performance does not always transfer to cohorts with different inclusion criteria or demographic characteristics, and deep learning models do not consistently outperform conventional machine learning approaches (12). EEG-based seizure prediction has also been evaluated across multiple datasets, but much of the evidence remains retrospective and patient-specific (34). In BCI research, controlled experimental studies demonstrate that AI-based systems can de-

code neural activity and provide closed-loop feedback, but studies based on small healthy-participant cohorts provide preliminary evidence for clinical rehabilitation applications (35). Across these areas, external validation, demographic subgroup analysis, model calibration, and prospective clinical evaluation remain less consistently reported than conventional measures of technical performance.

2.6 Impact of deep learning on neuroinformatics

Deep learning has been applied to automated brain tumour segmentation in MRI data. Havaei et al. developed a convolutional neural network-based segmentation method using the BRATS 2013 dataset, which included 30 labelled training cases and separate test and leaderboard datasets (27). The study demonstrated technical performance for segmentation of low- and high-grade gliomas, but it did not evaluate clinical diagnosis or treatment planning. Deep learning has also been investigated for imaging-based classification of Alzheimer's disease, although the reported performance varies across datasets and validation settings (12). Using brain activity data, such as EEG signals, deep learning has

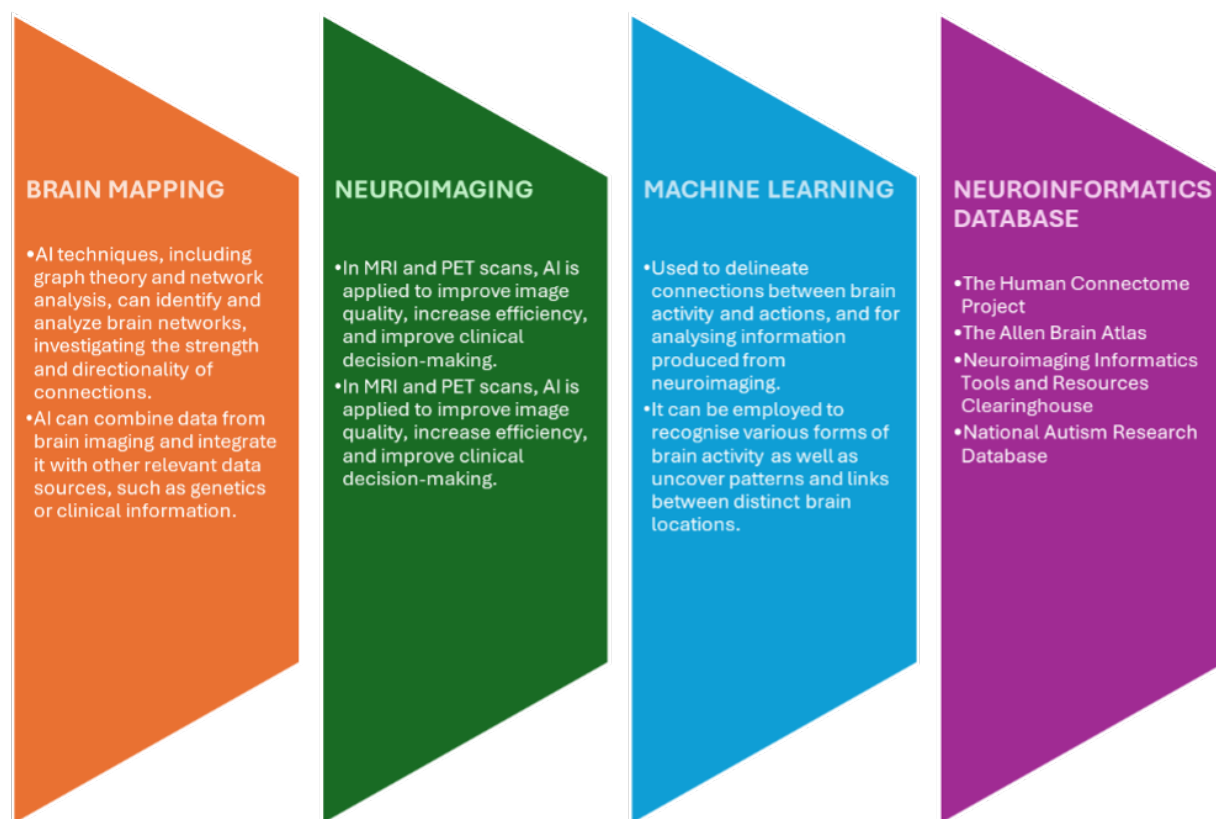


Figure 2: Major roles of AI in neuroinformatics, including brain mapping, neuroimaging analysis, biomarker exploration, and management of large-scale neuroinformatics data resources.

also been applied to classification and prediction tasks related to cognitive and neurological states (Figure 3).

Recurrent neural networks (RNNs) and other models are used to assess the temporal dynamics of EEG in order to forecast brain conditions and states (36). Deep learning has also been used to examine fMRI data, where blood-flow-related signals are analysed to identify brain regions associated with cognitive functions, emotional processing, or disease-related patterns (28). AI-based image-analysis approaches have been applied to computed tomography (CT) and MRI data to support the detection of stroke-related imaging features (29).

Diagnostic claims based on AI models should therefore be interpreted cautiously. In most neuroinformatics studies, reported performance reflects experimental classification, pattern recognition, risk prediction, or decision-support capacity rather than fully validated clinical diagnosis. AI-based neuroimaging and electrophysiological models may help identify disease-associated patterns, support risk stratification, and inform clinical decision-making. However, they require rigorous external validation in independent, multicentre, and demographically diverse cohorts before they can be considered reliable diagnostic tools.

2.7 Machine learning techniques for EEG signal categorisation

Traditional machine learning methods were among the first approaches used for EEG signal classification in neuroinformatics, allowing researchers to identify brain states and activities automatically from labeled EEG data (Figure 3). Common algorithms, including k-nearest neighbours (KNN), random forest (RF), and support vector machines (SVMs), have been widely used after extracting informative features such as wavelet coefficients, statistical measures, and spectral power density. However, the reported performance of these approaches cannot be compared directly when the studies use different EEG tasks, participant groups, pre-processing procedures, datasets, and validation strategies. Therefore, differences in reported accuracy should be interpreted together with the experimental design rather than as evidence that one class of algorithm is generally superior. KNN has been applied in motor imagery classification, emotion recognition, and sleep-stage classification (37). RF is well suited to multidimensional EEG data and has been used for emotion identification, cognitive-state classification, and epileptic-event recognition (38). SVM-based methods have also been used in EEG analysis for motor imagery classification, epileptic seizure detection, and the study of

cognitive processes (39).

With the growth of deep learning, EEG classification has gradually shifted from manually designed features to models that can learn useful representations directly from raw or minimally processed signals. Convolutional neural networks (CNNs) are especially valuable because they can learn spatially relevant patterns through convolutional filters, reducing the need for predefined feature-selection methods. For this reason, CNNs have been used in applications such as epileptic episode detection, resting-state classification, and emotion recognition based on EEG data (40). More generally, artificial intelligence has become an important tool in EEG classification because it supports the automated analysis of labeled data and helps identify brain-activity patterns related to cognitive tasks, mental-health conditions, sleep stages, and neurological disorders (11, 41).

In cases where the temporal structure of EEG signals is important, recurrent neural networks (RNNs) offer additional advantages. RNN-based models, including long short-term memory (LSTM) and gated recurrent unit (GRU) networks, are designed to model sequential dependencies in time-series data. This makes them useful for classifying EEG signals based on changes over time. While CNNs are effective for identifying spatial patterns associated with specific brain conditions, RNNs are better suited to capturing temporal patterns across EEG sequences (34).

Machine learning and deep learning models have been applied to EEG recordings for tasks such as automated seizure detection and seizure prediction in epilepsy (34, 42). These studies demonstrate the ability of computational models to identify or predict EEG patterns under specific experimental and retrospective validation settings. Such performance should not, by itself, be interpreted as evidence that AI-based EEG analysis provides early diagnosis or improves the clinical management of neurological disorders.

2.8 Artificial intelligence techniques for discovering biomarkers of neurological illnesses

The analysis of medical imaging for candidate biomarker discovery includes machine learning and deep learning approaches. Wen et al. evaluated CNN-based Alzheimer's disease classification using T1-weighted MRI from ADNI, AIBL, and OASIS and showed that performance depended on dataset characteristics and validation design (12). Model-derived imaging features should therefore be described as candidate or exploratory biomarkers unless their biological validity and reproducibility have been established independently. Several machine learning approaches used for candidate biomarker analysis across neurological diseases are summarized in Table 3. The distinction between technical classification performance, biomarker validity, and clinical utility is discussed in the critical-appraisal section.

A further limitation is the biological heterogeneity within

diagnostic categories. AI-based biomarker studies often treat diagnostic labels as training targets, yet these labels can group together patients with distinct pathophysiological mechanisms. Consequently, a classifier may learn patterns that reflect a dominant biological subtype, disease stage, sex or gender subgroup, medication profile, or comorbidity pattern rather than features that characterize the diagnosis as a whole. Such patterns may appear predictive in the original dataset but may not generalize to other patient groups with the same clinical diagnosis. For this reason, biomarker studies should be cautious about presenting a single model-derived feature as a universal disease marker unless it has been evaluated across relevant clinical and biological strata. Where possible, studies should report subgroup analyses, disease-stage information, comorbidities, medication status, and sensitivity analyses assessing whether the identified biomarker remains stable across heterogeneous patient groups (14–16).

2.9 Brain-computer interfaces and the role of AI in controlling them

Brain-Computer Interfaces (BCIs) are instruments that facilitate the exchange of information between the brain and external technologies such as computers or prosthetic instruments. This technology has potential applications in assistive technologies, neuro rehabilitation, prosthetics, and clinical research. For a proper interface and manipulation to take place, AI is used to analyze brain activity. The use of artificial intelligence to operate on BCI is prevalent in motor neuroprosthetics. Motor neuroprosthetics are devices that help regain movement abilities of paralyzed people by utilizing brain-computer interfaces to analyze brain activity and control robotic limbs. DL provides one of the best solutions for automatic extraction of unique features.

Many conventional AI models are developed using fixed datasets, whereas BCI applications often require the analysis of dynamic brain activity in near real time. Deep learning can be useful in BCI systems because it can learn complex spatial and temporal patterns from continuously changing neural signals. Two relevant benefits associated with deep learning include: First, learning of unique information by implementing back propagation on brain signals without any preprocessing and feature engineering required. Second, deep learning is capable of detecting latent relationships along with representative high-level features (28).

In an EEG cognitive-load classification study, Saha et al. compared deep-learning models based on stacked denoising autoencoders and LSTM with conventional classifiers including SVM, KNN, and LDA and reported better performance for the deep-learning models within that dataset (48). This finding represents a task- and dataset-specific comparison and should not be generalized as evidence that deep learning outperforms conventional classifiers across BCI applications. CNNs, RNNs, and other deep-learning architectures may be useful when the spatial or temporal

Table 2: Comparative synthesis of representative AI applications in neuroinformatics

Study	Task	Modality	Population/sample size	Validation design	Main performance measure	External validation / dataset shift	Demographic reporting	Calibration / uncertainty	Principal limitation
Havaei et al. (27)	Brain tumour segmentation	Multimodal brain MRI (T1, T1c, T2, FLAIR)	BRATS 2013; 30 training cases (20 high-grade and 10 low-grade glioma), with separate test and leaderboard cases	Training on the BRATS training cohort and evaluation using the challenge test/leaderboard datasets	Dice-based segmentation measures and related segmentation performance	Separate benchmark test data were used, but no independent clinical cohort outside the BRATS setting	Demographic subgroup performance was not a focus of the study	Predictive calibration was not evaluated	Strong technical benchmark performance, but evidence concerns segmentation performance rather than prospective clinical utility
Plis et al. (28)	Neuroimaging representation learning and schizophrenia classification	Structural MRI; additional functional/structural imaging analyses	198 participants with schizophrenia and 191 matched healthy controls from four sites for the classification analysis	10-fold cross-validation within the combined multisite cohort	Precision, recall and F-score	Multisite data were included, but no fully independent external cohort was used for the schizophrenia classification experiment	Clinical groups were described, but demographic subgroup performance was not evaluated	Calibration was not reported	Multisite internal validation supports technical feasibility, but external generalization and subgroup robustness remain uncertain
Wen et al. (12)	Alzheimer's disease and MCI classification	T1-weighted MRI	ADNI: 1,455 participants; AIBL: 598 participants; OASIS: 193 participants	Subject-level train/validation/test separation with model selection restricted to training/validation data; 5-fold validation	Balanced accuracy	Yes. Models trained using ADNI were evaluated on ADNI test data and independent AIBL and OASIS datasets	Age and sex/gender distributions and clinical measures were reported	Calibration was not a primary analysis	Performance generalized relatively well to similar populations but decreased substantially when inclusion criteria and demographic characteristics differed
Truong et al. (34)	Epileptic seizure prediction	Intracranial and scalp EEG	Multiple epilepsy datasets, including 13 usable Freiburg patients and 23 paediatric CHB-MIT patients, together with the American Epilepsy Society challenge dataset	Patient-specific retrospective analysis with cross-validation across seizures and evaluation on multiple datasets	Sensitivity and false prediction rate per hour	Evaluated across three EEG datasets, but the analysis remained retrospective and patient-specific	Dataset and patient characteristics were described, but demographic subgroup performance was not evaluated	Calibration was not reported	Performance across multiple datasets supports technical robustness, but prospective clinical validation was not performed
Ramos-Murguialday et al. (35)	EEG-based BCI control with proprioceptive feedback	128-channel EEG with robotic hand orthosis	Small experimental cohort of healthy volunteers; approximately two dozen participants divided among feedback conditions	Controlled experimental comparison of contingent-positive, contingent-negative and sham feedback conditions	Sensorimotor-rhythm modulation and BCI-control measures	No independent clinical cohort; study performed in healthy volunteers	Participant characteristics were reported, but demographic subgroup analysis was not the purpose of the experiment	Predictive calibration was not applicable/reported	Demonstrates experimental feasibility of closed-loop proprioceptive BCI, but does not establish effectiveness for neurological rehabilitation patients

structure of the neural signals is relevant to the classification task.

Proof-of-concept brain-machine interface studies have demonstrated that motor-cortex activity can be decoded to control external devices. In a non-human-primate study, Velliste et al. used motor-cortical activity to control a multi-jointed prosthetic arm and gripper during a self-feeding task (49). This experiment demonstrated embodied prosthetic control in monkeys and should not be interpreted as evidence of clinical effectiveness in human patients.

Human studies have also examined neuroadaptive and proprioceptive BCI paradigms. Zander et al. used real-time EEG responses associated with expectation violations to adapt cursor behaviour in a human-computer interaction experiment (50); the study did not involve a

working-memory task. Ramos-Murguialday et al. evaluated a 128-channel EEG BCI coupled to a robotic hand orthosis in healthy participants and found that contingent proprioceptive feedback improved BCI-related sensorimotor-rhythm measures (35). Because this study was conducted in healthy volunteers, it provides experimental proof-of-concept and does not establish rehabilitation effectiveness in patients with stroke or spinal-cord injury.

3. Ethical and legal issues with the use of AI in neuroinformatics

Ethical and legal issues in neuroinformatics include privacy protection, data ownership, informed consent, intellectual

Table 3: AI algorithms and their application in identifying and analyzing biomarkers for neurological diseases.

Sr. No.	AI Technique	Description	Reference
1.	Multi-Modal Data Fusion	AI approaches have been used to combine information from several modalities, such as imaging data, genetic data, and clinical data, in order to discover biomarkers of neurological disorders. ML algorithms, for example, have been used to predict biomarkers of schizophrenia with an amalgam of neuroimaging and genetic data	(43)
2.	Graph-Based Approaches	To discover biomarkers of neurological illnesses, brain connection data was evaluated using graph-based methodologies such as graph theory and network analysis. Graph theory metrics like nodal degree, clustering coefficient, and betweenness centrality, for instance, have been used to identify Alzheimer's disease biomarkers using fMRI data	(44)
3.	Feature Selection using ML	Machine learning algorithms have been used to select key traits from large-scale datasets such as neuroimaging data in order to discover biomarkers of neurological disorders. Recursive feature elimination (RFE) and L1 regularisation, for example, have been used to choose discriminative features from brain MRI data to identify biomarkers of multiple sclerosis	(45)
4.	Data Fusion from Imaging and Omics	AI approaches have been used to link imaging data with omics data, including genetic data, to discover biomarkers of neurological disorders. Combining brain imaging data, such as MRI or PET scans, with genetic data, for example, has been used to uncover biomarkers of disorders including Parkinson's and Alzheimer's disease	(46)
5.	Transfer Learning	It is an approach that involves extracting information from one domain and applying them to another, has been used to uncover biomarkers of neurological illnesses. DL models, such as VGGNet and ResNet, have been fine-tuned using neuroimaging data to uncover biomarkers of epilepsy and schizophrenia	(47)

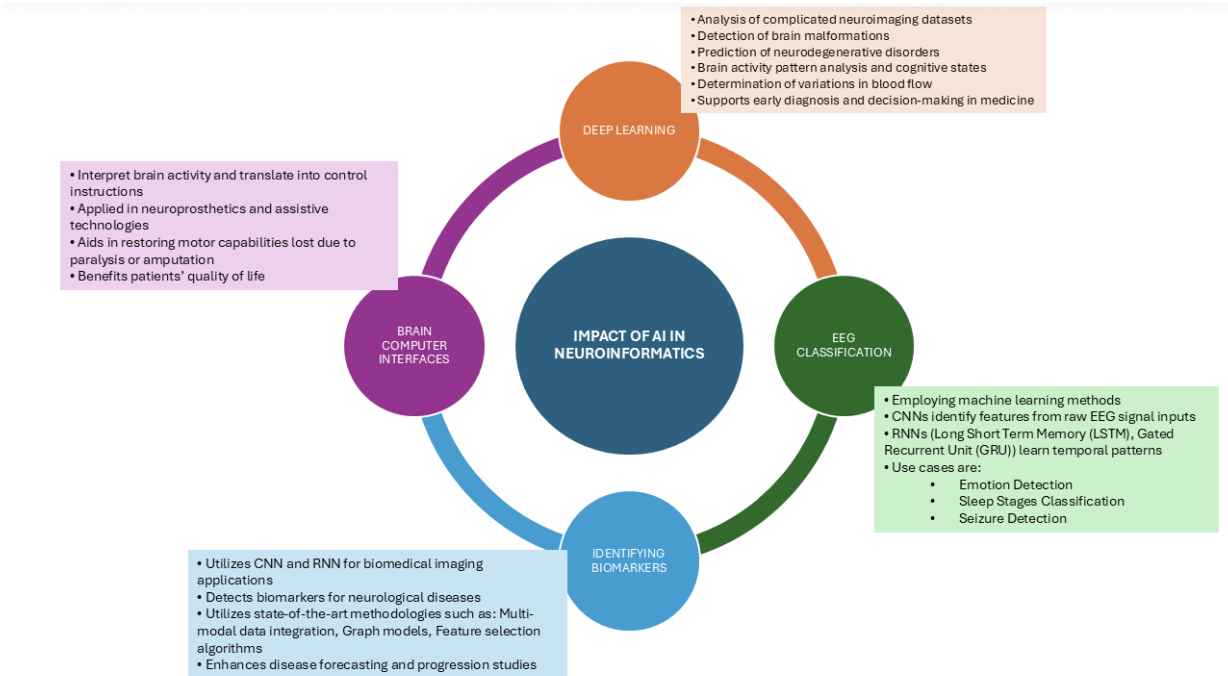


Figure 3: Examples of AI applications in neuroinformatics, including EEG classification, candidate biomarker analysis, BCI signal decoding, and model-based analysis of disease-associated patterns.

property, and responsible data sharing (51, 52). These issues are especially important because neuroinformatics databases may contain sensitive neuroimaging, genetic, behavioural, and clinical information. Researchers and data users should understand the provenance of shared data, the conditions under which data were collected, and the governance mechanisms that regulate access and reuse.

It is essential that privacy is maintained when collecting data, processing the data, integrating the findings within a conceptual framework, and finally writing up an academic paper. Ethical concerns about protecting confidential information and establishing standards or norms within both organizational and legal arenas should not be neglected.

Norms must be established to promote good discussion and collaboration with regards to neuroscience testing. For ensuring protection of individual privacy from the unauthorized sharing of information, tougher and more rigorous mechanisms must be enforced. Conversely, the control of database content, database access, and database utilization is a recent problem arising from international cooperation and the need to comply with Institutional Ethical Review Board (IERB) standards. Researchers should apply appropriate safeguards to maintain confidentiality during data collection, processing, modelling, analysis, and publication.

4. Application of AI in analysing and studying brain ageing

Brain age estimation has become an important topic in computational neuroscience because estimated brain age may provide information about ageing-related brain changes and disease-associated patterns. Various machine learning and deep-learning models have been developed for age estimation using brain imaging data. Deep learning can model complex imaging patterns, but it should not be assumed to be more accurate or less biased than conventional machine learning without a task-specific comparison and appropriate validation. Interpretability also remains an important consideration because predictive performance alone does not explain the biological processes underlying a brain-age estimate.

Recently, explainable artificial intelligence (XAI) methods have been proposed in order to produce explanations about the outputs of machine learning and deep learning algorithms. Previous work has suggested that SHAP-based approaches may help identify personalized imaging features associated with brain-age prediction (53). Through the creation of a relationship between age and biological information obtained through brain imaging, for example, AI and machine learning techniques could lead to insights into the process of aging. Such relationships can be exploited to create an algorithm capable of estimating a subject's age, which would subsequently be considered as biological age or a "physiological clock" that is either equal or different from the person's chronological age. The discrepancy between biological age and chronological age can serve as a biomarker for age-related diseases represented by the biological data used in the algorithm. This discrepancy is known as "brain age gap" when the biological data concerns the brain.

Lee et al. (54) developed deep-learning brain-age models using structural MRI and FDG-PET data from 2,349 participants with 4,127 scans, aged 26–98 years. The models were trained using cognitively unimpaired participants, evaluated using cross-validation, and further assessed using an independent ADNI cohort. Higher brain-age gaps were observed in groups with mild cognitive impairment, Alzheimer's disease, frontotemporal dementia, and dementia with Lewy bodies, and associations were examined with cognitive measures and imaging biomarkers. These findings support the brain-age gap as an investigational imaging marker, but they do not establish it as a standalone diagnostic test for neurodegenerative disease.

The capabilities of AI in tracking and assessing an individual's performance could be exploited to determine disease states at an early stage in relation to neurological conditions characterized by aging. One of the biggest issues involved in diagnosing preclinical states of diseases like dementia involves the substantial variability in how aging impacts cognitive functioning from one individual to another. Rather than making comparison based on demographic data, AI

could be used to track and assess changes in an individual's performance and functionality over time (55). An overview of AI applications in brain imaging and neuroinformatics is presented in Table 4.

5. Critical appraisal of AI in neuroinformatics: validation, generalizability, and clinical considerations

The evidence summarized in this review shows that the performance of AI models in neuroinformatics is influenced by the quality, size, composition, and origin of the data used for training and evaluation. Models developed using small, single-centre, or demographically restricted datasets may capture population-, scanner-, or site-specific patterns that do not transfer to independent cohorts. External validation is therefore different from repeated internal cross-validation, particularly when the external population differs in demographics, disease stage, acquisition protocol, or clinical setting. The comparative evidence summarized in Table 2 illustrates this distinction, as some applications have been evaluated on independent datasets whereas others remain based mainly on retrospective or internally validated studies.

Explainable AI and federated learning address different problems but should not be interpreted as evidence of clinical validity. Explainable AI methods such as SHAP, LIME, and attention-based approaches can indicate which features contribute to model predictions, but feature importance does not establish biological causality or biomarker validity (23, 24, 53, 56, 57). Federated learning can support model development across institutions without requiring centralization of participant-level data, but the resulting model can still retain demographic, clinical, or acquisition-related biases present across the participating sites (6, 9). Therefore, explainability and privacy-preserving learning should be considered together with external validation, subgroup assessment, calibration, uncertainty estimation, and biological evaluation.

Four levels of evidence should be distinguished when interpreting AI studies in neuroinformatics. Technical performance refers to how well a model performs the defined computational task on internal or external test data. Clinical utility requires evidence that use of the model provides a meaningful benefit in the intended clinical setting. Biological validity concerns whether a model-derived feature or candidate biomarker reflects a reproducible biological process rather than a dataset-specific association. Regulatory readiness represents a separate level and requires evidence and documentation appropriate to the intended use, including performance characterization, risk management, and lifecycle considerations. High classification or segmentation performance in a retrospective dataset therefore es-

Table 4: A summary of application of AI in Brain imaging and Neuroinformatics

S.No	Neuroinformatics Data	AI Application	Purpose in Brain Aging
1	MRI Data	Deep learning image analysis	Detect brain volume loss
2	fMRI Data	Pattern recognition	Identify functional connectivity changes
3	EEG Signals	Neural network classification	Detect cognitive decline patterns
4	Genomic Data	Machine learning prediction	Identify aging-related genes
5	Proteomic Data	Biomarker discovery	Detect neurodegenerative markers
6	Cognitive Test Data	Predictive modeling	Assess memory decline
7	Brain Connectivity Data	Graph-based AI models	Study neural network degeneration
8	Multimodal Data	Data integration using AI	Estimate biological brain age

establishes technical performance under the conditions of that study, but does not by itself establish clinical utility, biological validity, or regulatory readiness.

Simulation-based and computational modelling studies in neuroinformatics are built on several important assumptions. These studies often assume that the input datasets adequately represent the target population, that preprocessing and harmonization methods can reduce scanner- or site-related variability, that simplified computational models can capture relevant aspects of neural processes, and that connectivity or activity patterns identified in one dataset will generalize to other cohorts. Although these assumptions are necessary for modelling complex brain systems, they also place limits on how the findings should be interpreted. For example, when training data are demographically limited, clinically heterogeneous, or influenced by site-specific acquisition factors, models may reflect dataset-specific patterns rather than underlying biological signals. Likewise, simplified models of neural circuits can be useful for generating hypotheses, but they should not be viewed as complete mechanistic accounts of brain function. For these reasons, findings from simulation-based studies should generally be considered exploratory and supportive unless they are validated using independent, multicentre, and demographically diverse datasets (22, 28, 58, 59).

More broadly, the AI-based neuroinformatics approaches reviewed in this manuscript are subject to several methodological and practical limitations. Model performance is strongly influenced by the quality, size, and representativeness of the training data. As a result, findings from small, single-centre, or demographically narrow datasets may not generalize reliably to other populations or clinical settings. In addition, variation in scanner protocols, preprocessing methods, feature-selection procedures, and labelling criteria can introduce site- or task-specific biases. Although explainable AI methods can help identify the features that contribute to a model’s prediction, they do not establish whether these features are biologically causal, clinically meaningful, or sufficiently reliable as biomarkers. Other challenges, including privacy protection, database governance, computational cost, and integration into routine clinical workflows, also remain important barriers to implementation. Therefore, the reviewed methods should be regarded as supportive tools for research, risk stratification, and clinician-assisted decision-making, rather than

as standalone diagnostic systems, unless they are externally validated using independent and population-diverse datasets (4–6, 52, 60, 61). A model may achieve high classification accuracy, even with explanations from SHAP, LIME, or attention-based methods, but its predictions can still be driven by dominant subgroup patterns, scanner-related effects, or correlations specific to a particular dataset rather than by a biomarker that generalizes across all patients in the diagnostic category. For this reason, explanation maps and feature-importance scores should be interpreted together with subgroup validation, calibration, uncertainty estimation, and checks for biological plausibility.

Also, multidisciplinary collaboration is necessary in order to make progress in the application of AI within neuroinformatics. In order to develop efficient AI models, analyze their findings, and integrate them into the clinical process, researchers from neuroscience, computational sciences, and medicine should cooperate. The collaboration would allow sharing of the specialized knowledge, incorporation of ethical considerations, and resolution of the specific problems that different sciences are encountering. Neuroinformatics is emerging as a source of assistance to people suffering from injuries of the brain or people who have been having severe and consistent problems associated with the brain. Neuroimaging is a ray of hope for such people. Nevertheless, it would require better clinical information in addition to the expensive machinery and trained professionals leading to many challenges from the point of view of finance. Integrating knowledge across different levels of brain organization remains a significant challenge. Currently, information on brain regions, disease groups, imaging modalities, and molecular datasets is often stored in separate databases, limiting the ability to connect findings across domains. Future neuroinformatics efforts should therefore prioritize interoperable database architectures that support links across biological scales, data modalities, institutions, and clinical contexts.

AI offers opportunities for analysing multimodal data from neuroimaging, electrophysiology, molecular studies, and clinical records and for investigating patterns associated with disease risk or treatment response (58, 59). At present, such applications should be described as research or decision-support approaches unless prospective studies demonstrate clinical benefit in the intended population. Model output should not be equated with a personalized

treatment recommendation solely because the model integrates genetic, imaging, or clinical variables.

AI-based BCIs also allow neural signals to be decoded and adapted in real time under experimental conditions. However, technical improvement in signal decoding or device control should be distinguished from evidence of functional benefit in patients and from readiness for routine clinical use.

AI-based analysis may also support research on disease-associated patterns across genetic, environmental, imaging, and clinical variables (62–64). Such models may contribute to risk-stratification research, but claims concerning early prevention, diagnosis, or treatment require prospective validation and clinically relevant outcome assessment. Ethical concerns, data security, and appropriate governance should also be considered when these approaches are applied to neuroscience data.

6. Conclusion

AI is increasingly being applied across neuroinformatics for brain mapping, neuroimaging analysis, EEG classification, biomarker discovery, brain ageing research, data integration, and Brain-Computer Interfaces. The studies reviewed here show substantial technical progress, but the strength of evidence differs across applications according to the population, data source, validation strategy, and intended clinical task. Future work should place greater emphasis on independent validation, transparent reporting of data and population characteristics, reproducible comparison across datasets, and appropriate governance of neuroscience data. Progress in these areas will require continued collaboration among neuroscientists, clinicians, computational scientists, and researchers working on the ethical and responsible use of AI.

Declarations

Acknowledgements

None

Authors' contributions

Mohini Vats drafted the manuscript, created figures, and Rahul Semwal reviewed & contributed to manuscript editing. Utkarsh Raj designed the study, supervised, and edited the manuscript. All authors reviewed the revised manuscript, verified the final content, and approved the submitted version.

Funding

No financial support was provided relevant to this article.

Competing interests

Authors declare no conflict of interest between them.

Data availability

No original datasets were generated or analysed as part of this narrative review. The information discussed in this article is derived from the published literature cited in the manuscript.

Ethics approval and consent to participate

Not applicable. This article is a narrative review of previously published literature and did not involve the recruitment of human participants, collection of patient data, or animal experiments by the authors.

Consent for publication

Not applicable. The manuscript does not contain identifiable information from individual participants.

Review protocol and registration

This narrative review was not registered, and no predefined review protocol was prepared.

Author responsibility

All authors have reviewed the revised manuscript and accept responsibility for the accuracy of the cited literature, citation verification, interpretation of the published evidence, and the final content of the manuscript.

Use of artificial intelligence tools

Generative artificial intelligence tools were used during manuscript revision for assistance with language editing and organization of text. The authors independently reviewed and verified the scientific content, references, interpretations, and all revisions and take full responsibility for the final manuscript.

References

- Amunts K, Ebell C, Muller J, Telefont M, Knoll A, Lippert T. The Human Brain Project: Creating a European Research Infrastructure to Decode the Human Brain. *Neuron*. 2016 Nov 2;92(3):574–81. doi:10.1016/j.neuron.2016.10.046
- Oprisan SA. Interdisciplinary curriculum for computational neuroscience at primarily undergraduate institutions. *Journal of Computational Science*. 2022 May 1;61:101642. doi:10.1016/j.jocs.2022.101642
- Jaiswal AK, Jamal SB, Gabriel Rodrigues Gomes L, Profeta R, Sales-Campos H, Oliveira CJF, et al. Neuroinformatics Insights towards Multiple Neurosyphilis Complications. *Venereology*. 2022 Jun;1(1):135–60. doi:10.3390/venereology1010010
- Wang R, Chen ZS. Large-scale foundation models and generative AI for BigData neu-

- rosience. *Neuroscience Research*. 2025 Jun 1;Does BigData change Neuroscience?215:3–14. doi:10.1016/j.neures.2024.06.003
5. Tak D, Garomsa BA, Zapaishchikova A, Chaunzwa TL, Climent Pardo JC, Ye Z, et al. A generalizable foundation model for analysis of human brain MRI. *Nat Neurosci*. 2026 Apr;29(4):945–56. doi:10.1038/s41593-026-02202-6
6. Koutsoubis N, Waqas A, Yilmaz Y, Ramachandran RP, MB S, Rasool G. Privacy-preserving federated learning and uncertainty quantification in medical imaging. *Radiology: Artificial Intelligence*. 2025;7:240637. doi:10.1148/ryai.240637.
7. Sterling E, Pearl H, Liu Z, Allen JW, Fleischer CC. Demographic reporting across a decade of neuroimaging: a systematic review. *Brain Imaging and Behavior*. 2022;16:2785–2796. doi:10.1007/s11682-022-00724-8.
8. Lock C, Tan NSM, Long IJ and Keong NC: Neuroimaging data repositories and AI-driven healthcare—Global aspirations vs. ethical considerations in machine learning models of neurological disease. *Frontiers in Artificial Intelligence*. 2024;6:1286266. doi:10.3389/frai.2023.1286266.
9. Topaloglu MY, EM M, Rajendran S. In the pursuit of privacy: The promises and predicaments of federated learning in healthcare. *Frontiers in Artificial Intelligence*. 2021;4:746497. doi:10.3389/frai.2021.746497.
10. Rudroff T. Neurological diversity and generalizability: building on AMPA receptor imaging advances in long COVID. *Brain Commun*. 2026 Feb 1;8(1):fcf499. doi:10.1093/braincomms/fcaf499
11. Cao Z. A review of artificial intelligence for EEG-based brain-computer interfaces and applications. *Brain Science Advances*. 2020;6(3):162–70. doi:10.26599/BSA.2020.9050017
12. Wen J, Thibeau-Sutre E, Diaz-Melo M, Samper-González J, Routier A, Bottani S. Convolutional neural networks for classification of Alzheimer's disease: Overview and reproducible evaluation. *Medical Image Analysis*. 2020;63:101694. doi:10.1016/j.media.2020.101694.
13. Loh HW, Hong W, Ooi CP, Chakraborty S, Barua PD, Deo RC, et al. Application of Deep Learning Models for Automated Identification of Parkinson's Disease: A Review (2011–2021). *Sensors*. 2021 Jan;21(21):7034. doi:10.3390/s21217034
14. Rudroff T. Frontal-striatal glucose metabolism and fatigue in patients with multiple sclerosis, long COVID, and COVID-19 recovered controls. *Experimental Brain Research*. 2024;242:2125–2136. doi:10.1007/s00221-024-06882-z.
15. Feczko E, Miranda-Dominguez O, Marr M, Graham AM, JT N, Fair DA. The heterogeneity problem: approaches to identify psychiatric subtypes. *Trends in Cognitive Sciences*. 2019;23:584–601. doi:10.1016/j.tics.2019.03.009.
16. Parkes L, TD S, Bassett DS. Towards precise resting-state fMRI biomarkers in psychiatry: synthesizing developments in transdiagnostic research, dimensional models of psychopathology, and normative neurodevelopment. *Current Opinion in Neurobiology*. 2020;65:120–128. doi:10.1016/j.conb.2020.10.016.
17. Li AWY, King J. Spatial memory and navigation in ageing: A systematic review of MRI and fMRI studies in healthy participants. *Neurosci Biobehav Rev*. 2019 Aug;103:33–49. doi:10.1016/j.neubiorev.2019.05.005 PubMed PMID: 31129234.
18. Arabi H, AkhavanAllaf A, Sanaat A, Shiri I, Zaidi H. The promise of artificial intelligence and deep learning in PET and SPECT imaging. *Physica Medica*. 2021 Mar 1;83:122–37. doi:10.1016/j.ejmp.2021.03.008
19. Ham H, Wesley J, Hendra H. Computer Vision Based 3D Reconstruction : A Review. *International Journal of Electrical and Computer Engineering (IJECE)*. 2019 Aug 1;9(4):2394–402. doi:10.11591/ijece.v9i4.pp2394-2402
20. Wang H, Song Y, Tang Z, Zhang C, Yu J, Liu D, et al. AI-Enhanced 3D Biomedical Data Analytics for Neuronal Structure Reconstruction. In: Chen F, Zhou J, editors. *Humanity Driven AI: Productivity, Well-being, Sustainability and Partnership* [Internet]. Cham: Springer International Publishing; 2022 [cited 2026 Sep 27]. p. 135–63. Available from: https://doi.org/10.1007/978-3-030-72188-6_7 doi:10.1007/978-3-030-72188-6_7
21. Gu D, Shi F, Hua R, Wei Y, Li Y, Zhu J. An artificial-intelligence-based age-specific template construction framework for brain structural analysis using magnetic resonance images. *Human Brain Mapping*. 2023;44:861–875. doi:10.1002/hbm.26126.
22. Mizutani H, Ueno M, Arakawa N, Yamakawa H. Whole brain connectomic architecture to develop general artificial intelligence. *Procedia Computer Science*. 2018 Jan 1;8th Annual International Conference on Biologically Inspired Cognitive Architectures, BICA 2017 (Eighth Annual Meeting of the BICA Society), held August 1-6, 2017 in Moscow, Russia123:308–13. doi:10.1016/j.procs.2018.01.048
23. Ribeiro MT, S S, Guestrin C. Why should I trust you?" Explaining the predictions of any classifier. In: *Proceedings of the 22nd ACM SIGKDD International Conference on Knowledge Discovery and Data Mining*. 2016. p. 1135–1144. doi:10.1145/2939672.2939778.

24. Ali S, Abuhmed T, El-Sappagh S, Muhammad K, Alonso-Moral JM, Confalonieri R. Explainable artificial intelligence (XAI): What we know and what is left to attain trustworthy artificial intelligence. *Information Fusion*. 2023;99:101805,. doi:10.1016/j.inffus.2023.101805.
25. Lundberg SM, Lee SI. A Unified Approach to Interpreting Model Predictions. In: Guyon I, Luxburg UV, Bengio S, Wallach H, Fergus R, Vishwanathan S, et al., editors. *Advances in Neural Information Processing Systems* [Internet]. Curran Associates, Inc.; 2017. Available from: <https://tinyurl.com/yhf9hs8y>
26. Politis M, Piccini P. Positron emission tomography imaging in neurological disorders. *J Neurol*. 2012 Sep 1;259(9):1769–80. doi:10.1007/s00415-012-6428-3
27. Havaei M, Davy A, Warde-Farley D, Biard A, Courville A, Bengio Y, et al. Brain tumor segmentation with Deep Neural Networks. *Med Image Anal*. 2017 Jan;35:18–31. doi:10.1016/j.media.2016.05.004 PubMed PMID: 27310171.
28. Plis SM, Hjelm DR, Salakhutdinov R, Allen EA, Bockholt HJ, Long JD, et al. Deep learning for neuroimaging: a validation study. *Front Neurosci*. 2014 Aug 20;8. doi:10.3389/fnins.2014.00229
29. Xu B, Chai Y, Galarza CM, Vu CQ, Tamrazi B, Gaonkar B, et al. ORCHESTRAL FULLY CONVOLUTIONAL NETWORKS FOR SMALL LESION SEGMENTATION IN BRAIN MRI. *Proc IEEE Int Symp Biomed Imaging*. 2018 Apr;2018:889–92. doi:10.1109/ISBI.2018.8363714 PubMed PMID: 30344893; PubMed Central PMCID: PMC6192017.
30. Van Essen DC, Smith SM, Barch DM, Behrens TEJ, Yacoub E, Ugurbil K. The WU-Minn Human Connectome Project: An Overview. *Neuroimage*. 2013 Oct 15;80:62–79. doi:10.1016/j.neuroimage.2013.05.041 PubMed PMID: 23684880; PubMed Central PMCID: PMC3724347.
31. Hawrylycz MJ, Lein ES, Guillozet-Bongaarts AL, Shen EH, Ng L, Miller JA, et al. An anatomically comprehensive atlas of the adult human brain transcriptome. *Nature*. 2012 Sep 20;489(7416):391–9. doi:10.1038/nature11405 PubMed PMID: 22996553; PubMed Central PMCID: PMC4243026.
32. Kennedy DN, Haselgrove C, Riehl J, Preuss N, Buccirossi R. The Three NITRCs: A Guide to Neuroimaging Neuroinformatics Resources. *Neuroinformatics*. 2015 Jul;13(3):383–6. doi:10.1007/s12021-015-9263-8 PubMed PMID: 25700675; PubMed Central PMCID: PMC4470758.
33. Hall D, Huerta MF, McAuliffe MJ, Farber GK. Sharing Heterogeneous Data: The National Database for Autism Research. *Neuroinformatics*. 2012 Oct 1;10(4):331–9. doi:10.1007/s12021-012-9151-4
34. Truong ND, Nguyen AD, Kuhlmann L, Bonyadi MR, Yang J, Ippolito S, et al. Convolutional neural networks for seizure prediction using intracranial and scalp electroencephalogram. *Neural Netw*. 2018 Sep;105:104–11. doi:10.1016/j.neunet.2018.04.018 PubMed PMID: 29793128.
35. Ramos-Murguialday A, Schürholz M, Caggiano V, Wildgruber M, Caria A, Hammer EM, et al. Proprioceptive feedback and brain computer interface (BCI) based neuroprostheses. *PLoS One*. 2012;7(10):e47048. doi:10.1371/journal.pone.0047048 PubMed PMID: 23071707; PubMed Central PMCID: PMC3465309.
36. Lawhern V, Solon A, Waytowich N, Gordon S, Hung C, Lance B. EEGNet: a compact convolutional neural network for EEG-based brain–computer interfaces. *Journal of Neural Engineering*. 2018 Jul;15. doi:10.1088/1741-2552/aace8c
37. Tang X, Wang T, Du Y, Dai Y. Motor imagery EEG recognition with KNN-based smooth auto-encoder. *Artif Intell Med*. 2019 Nov;101:101747. doi:10.1016/j.artmed.2019.101747 PubMed PMID: 31813489.
38. Jeevan RK, S.P. VMR, Shiva Kumar P, Srivikas M. EEG-based emotion recognition using LSTM-RNN machine learning algorithm. In: 2019 1st International Conference on Innovations in Information and Communication Technology (ICIICT) [Internet]. 2019 [cited 2026 Sep 27]. p. 1–4. Available from: <https://ieeexplore.ieee.org/document/8741506> doi:10.1109/ICIICT1.2019.8741506
39. Lotte F, Guan C. Regularizing Common Spatial Patterns to Improve BCI Designs: Unified Theory and New Algorithms. *IEEE Transactions on Biomedical Engineering*. 2011 Feb;58(2):355–62. doi:10.1109/TBME.2010.2082539
40. Li C, Lin X, Liu Y, Song R, Cheng J, Chen X. EEG-Based Emotion Recognition via Efficient Convolutional Neural Network and Contrastive Learning. *IEEE Sensors Journal*. 2022 Oct;22(20):19608–19. doi:10.1109/JSEN.2022.3202209
41. Gopinath N. Artificial intelligence and neuroscience: An update on fascinating relationships. *Process Biochemistry*. 2023 Feb 1;125:113–20. doi:10.1016/j.procbio.2022.12.011
42. Abbasi B, Goldenholz DM. Machine learning applications in epilepsy. *Epilepsia*. 2019 Oct 1;60(10):2037–47. doi:10.1111/epi.16333
43. Ardekani BA, Tabesh A, Sevy S, Robinson DG, Bilder RM, Szeszko PR. Diffusion tensor imaging reliably differentiates patients with schizophrenia from healthy

- volunteers. *Hum Brain Mapp.* 2010 Dec 14;32(1):1–9. doi:10.1002/hbm.20995 PubMed PMID: 20205252; PubMed Central PMCID: PMC2896986.
44. Tijms BM, Seriès P, Willshaw DJ, Lawrie SM. Similarity-based extraction of individual networks from gray matter MRI scans. *Cereb Cortex.* 2012 Jul;22(7):1530–41. doi:10.1093/cercor/bhr221 PubMed PMID: 21878484.
 45. Weiss N, Rueckert D, Rao A. Multiple Sclerosis Lesion Segmentation Using Dictionary Learning and Sparse Coding. In: Mori K, Sakuma I, Sato Y, Barillot C, Navab N, editors. *Medical Image Computing and Computer-Assisted Intervention – MICCAI 2013.* Berlin, Heidelberg: Springer Berlin Heidelberg; 2013. p. 735–42.
 46. Balachandar R, John JP, Saini J, Kumar KJ, Joshi H, Sadanand S, et al. A study of structural and functional connectivity in early Alzheimer's disease using rest fMRI and diffusion tensor imaging. *International Journal of Geriatric Psychiatry.* 2015;30(5):497–504. doi:10.1002/gps.4168
 47. Quéllec G, Cazuguel G, Cochener B, Lamard M. Multiple-Instance Learning for Medical Image and Video Analysis. *IEEE Reviews in Biomedical Engineering.* 2017;10:213–34. doi:10.1109/RBME.2017.2651164
 48. Saha A, Minz V, Bonela S, Sreeja SR, Chowdhury R, Samanta D. Classification of EEG Signals for Cognitive Load Estimation Using Deep Learning Architectures. In: Tiwary US, editor. *Intelligent Human Computer Interaction.* Cham: Springer International Publishing; 2018. p. 59–68.
 49. Velliste M, Perel S, Spalding MC, Whitford AS, Schwartz AB. Cortical control of a prosthetic arm for self-feeding. *Nature.* 2008 Jun 19;453(7198):1098–101. doi:10.1038/nature06996 PubMed PMID: 18509337.
 50. Zander TO, Krol LR, Birbaumer NP, Gramann K. Neuroadaptive technology enables implicit cursor control based on medial prefrontal cortex activity. *Proceedings of the National Academy of Sciences.* 2016 Dec 27;113(52):14898–903. doi:10.1073/pnas.1605155114
 51. Alexiou A, Theocharopoulou G, Vlamos P. Ethical Issues in Neuroinformatics. In: Papadopoulos H, Andreou AS, Iliadis L, Maglogiannis I, editors. *Artificial Intelligence Applications and Innovations.* Berlin, Heidelberg: Springer Berlin Heidelberg; 2013. p. 700–5.
 52. Bancroft TD. Ethical Aspects of Computational Neuroscience. *Neuroethics.* 2013 Aug 1;6(2):415–8. doi:10.1007/s12152-012-9163-7
 53. Lombardi A, Diacono D, Amoroso N, Monaco A, Tavares JMRS, Bellotti R, et al. Explainable Deep Learning for Personalized Age Prediction With Brain Morphology. *Front Neurosci.* 2021 May 28;15. doi:10.3389/fnins.2021.674055
 54. Lee J, Burkett BJ, Min HK, Senjem ML, Lundt ES, Botha H, et al. Deep learning-based brain age prediction in normal aging and dementia. *Nat Aging.* 2022 May;2(5):412–24. doi:10.1038/s43587-022-00219-7 PubMed PMID: 37118071; PubMed Central PMCID: PMC10154042.
 55. Summers MJ, Madl T, Vercelli AE, Aumayr G, Bleier DM, Ciferri L. Deep Machine Learning Application to the Detection of Preclinical Neurodegenerative Diseases of Aging. *DigitCult - Scientific Journal on Digital Cultures.* 2017 Dec 11;2(2):9–24. doi:10.4399/97888255088952
 56. Albarracín M, Hipólito I, Tremblay SE, Fox JG, René G, Friston K, et al. Designing Explainable Artificial Intelligence with Active Inference: A Framework for Transparent Introspection and Decision-Making. In: Buckley CL, Cialfi D, Lanillos P, Ramstead M, Sajid N, Shimazaki H, et al., editors. *Active Inference.* Cham: Springer Nature Switzerland; 2024. p. 123–44.
 57. El-Sappagh S, Alonso JM, Islam SMR, Sultan AM, Kwak KS. A multilayer multimodal detection and prediction model based on explainable artificial intelligence for Alzheimer's disease. *Sci Rep.* 2021 Jan 29;11(1):2660. doi:10.1038/s41598-021-82098-3
 58. Doerig A, Sommers RP, Seeliger K, Richards B, Ismael J, Lindsay GW, et al. The neuroconnectionist research programme. *Nat Rev Neurosci.* 2023 Jul;24(7):431–50. doi:10.1038/s41583-023-00705-w PubMed PMID: 37253949.
 59. Gerkin RC, Tripathy SJ, Crook SM, Kotaleski J. Databases and Data Repositories in Computational Neuroscience: Overview. In: Jaeger D, Jung R, editors. *Encyclopedia of Computational Neuroscience [Internet].* New York, NY: Springer New York; 2022. p. 32–5. Available from: https://doi.org/10.1007/978-1-0716-1006-0_780 doi:10.1007/978-1-0716-1006-0_780
 60. Kulynych J. Legal and ethical issues in neuroimaging research: human subjects protection, medical privacy, and the public communication of research results. *Brain Cogn.* 2002 Dec;50(3):345–57. doi:10.1016/s0278-2626(02)00518-3 PubMed PMID: 12480482.
 61. Serre T, Pavlick E. From prediction to understanding: Will AI foundation models transform brain science? *Neuron.* 2025 Nov 5;113(21):3504–8. doi:10.1016/j.neuron.2025.09.039 PubMed PMID: 41130210.
 62. Ghaffar Nia N, Kaplanoglu E, Nasab A. Evaluation of artificial intelligence techniques in disease diagnosis and prediction. *Discov Artif Intell.* 2023 Jan 30;3(1):5. doi:10.1007/s44163-023-00049-5
 63. Hassan M, Awan FM, Naz A, deAndrés-Galiana EJ, Alvarez O, Cernea A, et al. Innovations in Genomics and

Big Data Analytics for Personalized Medicine and Health Care: A Review. *Int J Mol Sci.* 2022 Apr 22;23(9):4645. doi:10.3390/ijms23094645 PubMed PMID: 35563034; PubMed Central PMCID: PMC9104788.

64. Levy J, Lu Y, Montivero M, Ramwala O, McFadden J, Miles C, et al. Artificial Intelligence, Bioinformatics, and Pathology: Emerging Trends Part I—an Introduction to Machine Learning Technologies. *Advances in Molecular Pathology.* 2022 Nov 1; *Advances in Molecular Pathology Volume 5 (Online-only Article)*5(1, Supplement):e1–24. doi:10.1016/j.yamp.2023.01.001