



Deep learning frameworks for MRI-based diagnosis of neurological disorders: a systematic review and meta-analysis

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Abstract

The automatic diagnosis of neurological disorders using Magnetic Resonance Imaging (MRI) is a widely researched problem. MRI is a non-invasive and highly informative imaging modality, which is one of the most widely accepted and used neuroimaging modalities for visualizing the human brain. The advent of tremendous processing capabilities, multi-modal data, and deep-learning techniques has enabled researchers to develop intelligent, sufficiently accurate classification methods. A comprehensive literature review has revealed extensive research on the automatic diagnosis of neurological disorders. However, despite numerous studies, a systematically developed framework is lacking, that relies on a sufficiently robust dataset or ensures reliable accuracy. To date, no consolidated framework has been established to classify multiple diseases and their subtypes effectively based on various types and their planes of orientation in structural and functional MR images. This systematic review provides a detailed and comprehensive analysis of research reported from 2000 to 2023. Systems developed in prior art have been categorized according to their disease diagnosis capabilities. The datasets employed and the tools developed are also summarized to assist researchers to conduct further studies in this crucial domain. The contributions of this research include facilitating the design of a unified framework for multiple neurological disease diagnoses, resulting in the development of a generic assistive tool for hospitals and neurologists to diagnose disorders precisely and swiftly thus potentially saving lives, in addition to increasing the quality of life of patients suffering from neurodegenerative disorders.

Keywords Brain MRI · Classification · Computer aided diagnosis · Deep learning · Neurological diseases

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1 Introduction

Neurological disorders are among the most common causes of death worldwide. Even in developed countries with adequate medical facilities, disorders such as Alzheimer's disease (AD) and stroke are among the top three biggest killers (WHO 2020). With timely diagnoses, neurological disorders can be cured or contained (Minz and Mahobiya 2017; Yagis et al. 2021), thereby saving lives and the quality of life could be improved for patients with non-curable neurodegenerative disorders (Nandpuru et al. 2014; Minz and Mahobiya 2017; Mikolas et al. 2018; Majib et al. 2021; Ocasio and Duong 2021; Zhang 2022; Alhassan et al. 2022; Garcia-Gutierrez et al. 2022; Wood et al. 2022). Diagnosing neurological disorders based solely on clinical findings is difficult (Nandpuru et al. 2014), because hallmark symptoms may not always be present, especially in the early phase of a disease (Nemoto et al. 2021). Conventional computer vision (CV) algorithms are generally not capable to process vast datasets and assimilate classification features from them. Artificial Intelligence (AI) proved to be a game changer in this direction, with the capabilities to analyze massive data and tune millions of learnable parameters adaptively in real-time. This resulted in an exponential increase in classification accuracies, though at the cost of computational intensiveness. This issue was resolved by the marvels the graphics processing unit (GPU) technology has achieved over the past decade in terms of computational speed (Boeken et al. 2023). The recent massive data storage and processing capabilities of machines paved the way for AI to be an integral part of our lives in the world today. AI in healthcare (Miotto et al. 2018) and medical imaging (Greenspan et al. 2016) has played a pivotal role in the past decade, resulting in the development of fast, accurate, and automatic systems for assisting in the diagnosis, treatment, and monitoring of patients. Neurological disorders are no exception (Ahmed et al. 2018). A tremendous amount of research has used multi-modal brain signals to assist doctors and patients in the diagnosis, prognosis, and management of neurological disorders (Yang et al. 2018). Among the numerous available biomedical imaging modalities, Magnetic Resonance Imaging (MRI) is often considered the most versatile and non-invasive imaging tool for examining the human body. MRI offers high spatial resolution, high soft tissue contrast, tomographic imaging, multidirectional scans, and the integration of anatomical, physiological, metabolic, and functional imaging features. These have assisted neurologists in diagnosing a vast number of disorders Tian et al. (2021). MRI measurements vary widely depending on the technology used, brain scan orientation, and magnetic strength. In addition to planar data that deal with 2D brain images (slices), 3D volumetric MRI data of the entire brain are available for expert and machine examination. Brain MRI images possess similar features, especially in the case of neurodegenerative disorders that contain subtle and intricate changes (Tomson 2006; Avants et al. 2008; Mikolas et al. 2018; Yagis et al. 2019) rendering the diagnostic process very challenging (Noor et al. 2019). Manual inspection of such images by experts produces diagnoses based on personal expertise (Kanmani and Mariikkannu 2018; Majib et al. 2021), with a probability of misdiagnosis owing to subtle changes in such images depending on the disease stage and overlapping features (Mathkunti and Rangaswamy 2020; Talai et al. 2021), among other factors (Raghavaiah and Varadarajan 2022). In the case of experts being unavailable in remote areas, accurate and timely diagnosis can be a problem. From the perspective of Computer Aided Diagnosis (CAD), due to the similarity of features in MRI data, Deep Learning (DL) has outperformed traditional Machine Learning (ML) in classifying neurological disorders

Jo et al. (2019); Zhu et al. (2019); Rashid et al. (2020); Salehi et al. (2020); Zhang et al. (2020); Zhao and Zhao (2021); Abrol et al. (2021). With the help of DL, the structural (Mateos-Pérez et al. 2018; Bhatele and Bhadauria 2020; Falkai et al. 2022) and functional Rashid et al. (2020) states of the brain MRI can very well be examined and analyzed (Kumar and Karnan 2014; Liu et al. 2014; Somasundaram and Genish 2015; Miranda et al. 2016; Arora and Dhir 2017; Valliani et al. 2019; Mazurowski et al. 2019; Francis and Babu 2019; Tyagi 2019; DS 2019; Yao et al. 2020; Zhang et al. 2020; Wang et al. 2021; Zhao and Zhao 2021; Lima et al. 2022; Behrad and Abadeh 2022; Wang et al. 2022), assisting neurologists to reach an optimal diagnosis (Arbabshirani et al. 2017; Calhoun and Sui 2016). Substantial research has already been done toward the development of CAD systems to assist neurologists in reaching precise diagnoses (Mårtensson et al. 2020). Most proposed systems can diagnose a single disease but very few comprehensive frameworks have been proposed with the ability to diagnose multiple diseases. However, the models have been trained with very limited data and hence confidence in their accuracy is lacking.

Many studies have been conducted in this area; however, almost 64% of the work deals with the diagnosis of a single disease or with the binary normal/abnormal MRI classification, and only 36% of the research has presented or developed systems capable of handling the diagnosis of two or more diseases. In a thorough literature survey of more than 1200 research articles, postgraduate theses, and patents from 2000 to December 10, 2023, as presented in Fig. 1, only approximately 1% effectively diagnosed five or more neurological disorders using a single framework, but they too, with extremely limited training datasets achieved questionable performance accuracy (Khani et al. 2013; Aggarwal et al. 2021; Maleki et al. 2022; Castiglioni et al. 2021).

Along with the traditional treatment regimens for neurological disorders, many non-invasive intervention techniques also exist, including Transcranial Magnetic Stimulation (TMS) and transcranial Direct Current Stimulation (tDCS) (Wang et al. 2023; Camacho-Conde et al. 2023). Employing such techniques, very precise and well-controlled stimulation of cortical and subcortical brain areas can result in improvements in symptoms of major depression, AD, Parkinson's Disease (PD), Attention Deficit Hyperactivity Disorder (ADHD), and other neurological disorders Camacho-Conde et al. (2022). But in order to choose an appropriate intervention method or treatment course, the first and foremost step is the accurate diagnosis. The intervention techniques are beyond the purview of this work as this paper focuses primarily on the CAD systems.

This review provides the prior art selection criteria in Sect. 2. Sect. 2.5 describes the details pertaining to MRI-based neurological disorder diagnosis systems designed since 2000, ranging from two- to multiple-disease diagnosis frameworks. This section describes the capabilities and deficits of these diagnoses, assists in research, and builds on the motivation for developing a unified framework capable of assisting neurologists in accurately diagnosing multiple neurological diseases. The following two sections succinctly provide information on certain publicly available datasets and developed tools. This will be followed by challenges and future research in this area.

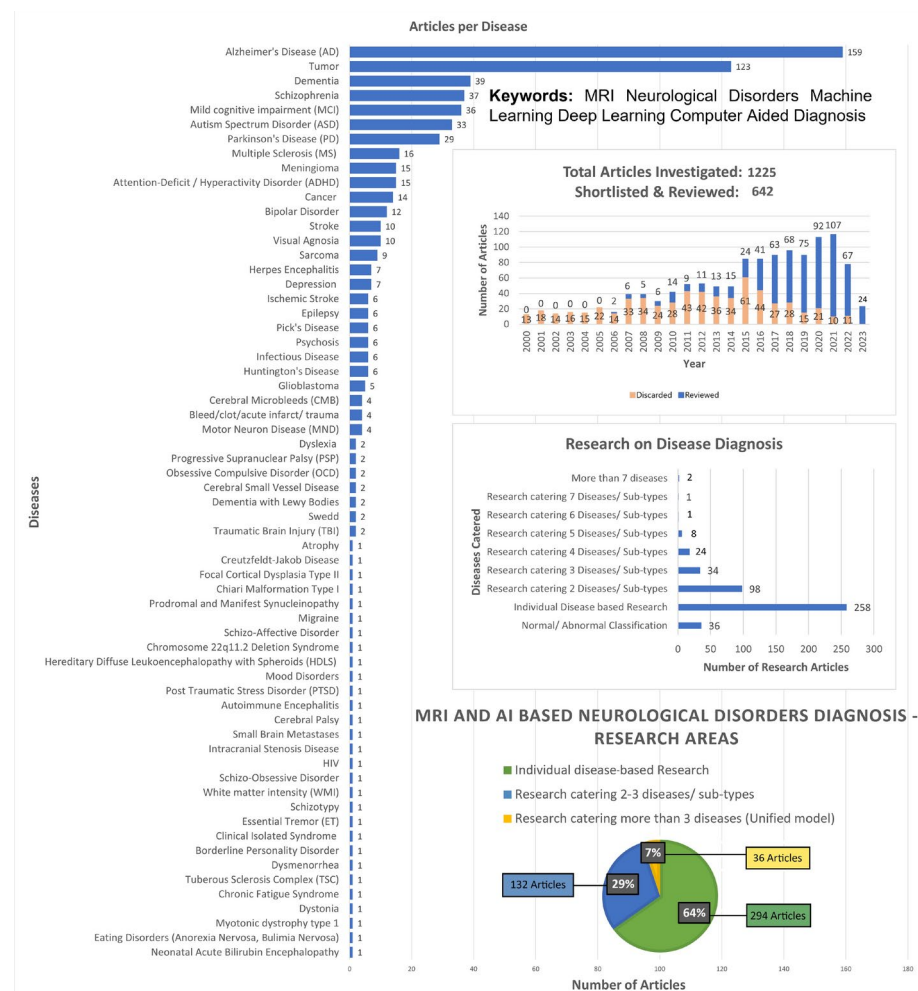


Fig. 1 Statistics—Diseases studied for CAD using brain MRI (Left), total articles investigated, shortlisted and reviewed (Top), number of diseases catered per article (Center), individual to multiple disease CAD research (Bottom)

2 Materials and methods

2.1 Study selection

The host databases Scopus, Web of Science, and Google Scholar underwent keyword searches for articles published until 10 December 2023. The search phrases included “MRI and neurological disorder diagnosis using deep learning.” The filters were set for each year from 2000 to 2023. The search returns per year were individually scanned, and the titles of articles included in the first 10 pages were examined. Only the most relevant articles with full-text access were downloaded. After removing the duplicates, these articles were later screened for abstracts, and only approximately half of the original number was retained.

This was followed by a thorough examination of the full texts, and the details of further disqualifications of articles are provided in subsequent sections and Fig. 2. We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

2.2 Inclusion criteria

Research related to the CAD of neurological disorders using ML with MRI as the sole data modality was included in this review. The CAD of neurodegenerative disorders was also included, along with congenital malformations, trauma, stroke and vascular malformations, neoplasms, infectious or inflammatory diseases, and demyelinating diseases. Models that handle multiple types of MRI data, including structural and functional MRI data, were also considered in this review.

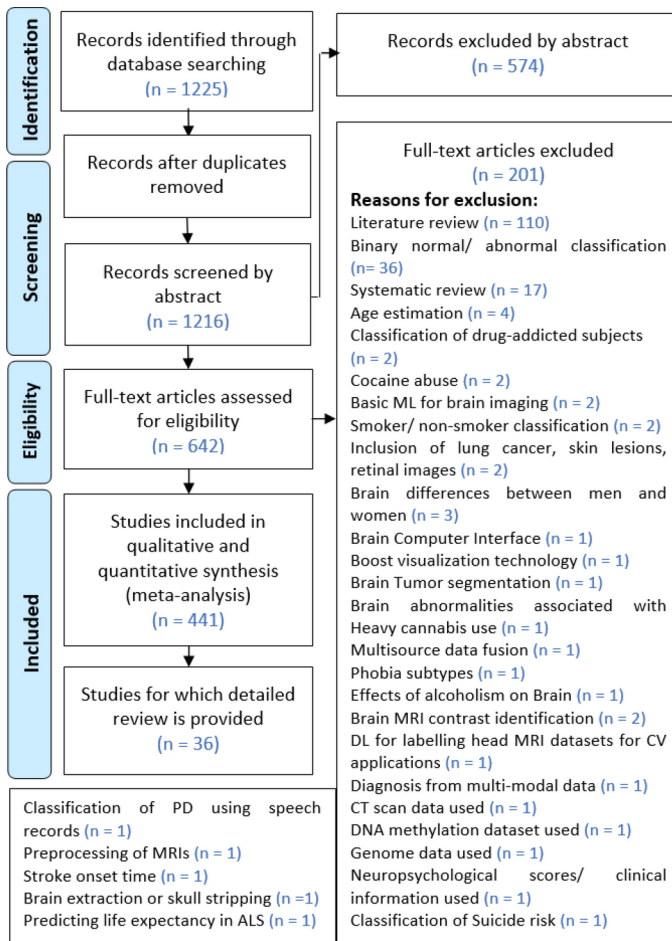


Fig. 2 PRISMA study selection diagram—of the 1225 articles identified, 441 were included in the qualitative and quantitative analysis. Details of the articles excluded are briefly stated

2.3 Exclusion criteria

Various articles were excluded from this review based on certain criteria, they are enumerated here.

1. **Normal/abnormal brain classification** Studies dealing with normal/abnormal brain classifications without a diagnosis of a specific disease were excluded, since such systems do not have the capability to serve as CAD tools.
2. **One to three disease diagnosis** Single-, two-, and three-disease diagnosis systems were studied and included in the meta-analysis; however, their details were excluded for brevity. This was done due to the overwhelming number of research articles (390).
3. **Literature Reviews** Systematic and Literature reviews have also been excluded from this review.
4. **Age/Gender Prediction** Research to infer age and sex information from MRI images was also excluded. Although such age inference can be useful in obtaining maximum information about the patient and reaching a concrete diagnosis if a patient's history is unavailable.
5. **Drug, alcohol abuse/addiction classification** Studies identifying drug abuse from brain MRIs have also been excluded but could be considered if a generic unified framework must be designed for the complete assessment of a patient using a single modality, that is a brain MRI. Patients with smoking status, alcoholism, cocaine abuse, and brain abnormalities associated with heavy cannabis use were excluded from this category.
6. **Phobia identification** Classification of Phobia types was excluded, although this category could also be included in a robust CAD system.
7. **Multi-modal Data** Cases of CAD using modalities other than brain MRI were also excluded. Such modalities include Computed Tomography (CT), speech, Deoxyribonucleic acid (DNA), genome information, data acquired from other sensors, questionnaires, neuropsychological scores, and other clinical information. The reason for this was to keep the CAD system as simple and economical as possible and to identify the potential of MRI data alone for accurate diagnosis.
8. **Brain MRI contrast identification, Brain extraction, Skull stripping** Research falling under this section could also be useful in developing an omnipotent CAD tool but has been excluded here for brevity.
9. **Life expectancy prediction, inference of onset times** Yet another important aspect which a powerful CAD tool must have, excluded here.
10. **Miscellaneous** Studies on brain segmentation, basic ML for brain imaging, and preprocessing of MRIs, among others, were excluded to limit the scope of this review. The main reasons are given in Fig. 2.

2.4 Highlights and information extracted

The following information was extracted and summarized from the articles reviewed in this study.

1. Year of study.
2. Diseases researched.

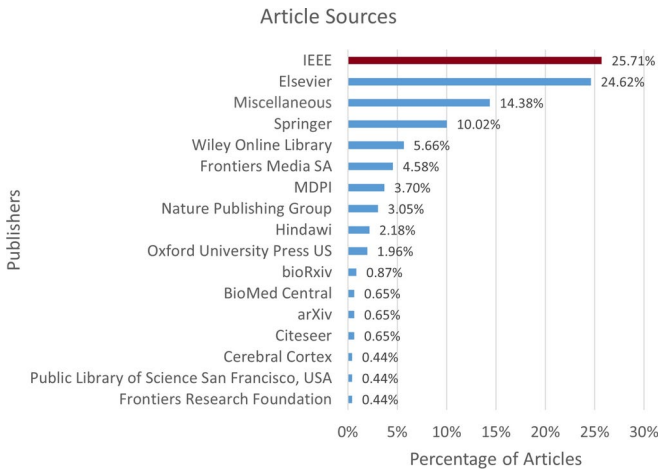
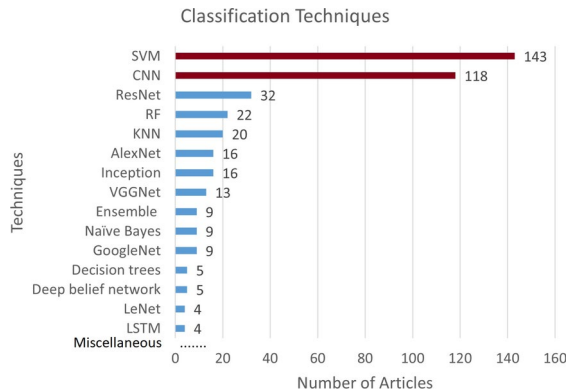


Fig. 3 Article sources—percentages computed from a total of 441 articles. IEEE dominant

Fig. 4 Classification methods used in articles—numbers computed from a total of 441 articles. Support Vector Machine (SVM) and Convolutional Neural Networks (CNN) dominant



3. Classification techniques used.
4. Accuracy of developed techniques.
5. Datasets used.
6. MRI types and orientations used.
7. Number of MRI images used for training.

Most articles were selected from IEEE, followed by Elsevier publications (Fig. 3). The top two classification techniques applied were Support Vector Machines (SVMs) and Convolutional Neural Networks (CNNs), followed by transfer learning (Fig. 4). The Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset was the most commonly used (Fig. 5), with T1-weighted (T1W) structural MRI employed for diagnosis in the majority of studies (Fig. 6). Most researchers prefer the axial MRI planes (Fig. 7). Figure 8 shows the relationship between number of images used for training and the corresponding accuracy of the model developed for single-disease diagnosis, where as Fig. 9 shows the same for multiple

Fig. 5 Publicly available Dataset Statistics—numbers computed from a total of 441 articles. Alzheimer’s Disease Neuroimaging Initiative (ADNI) dominant since AD is the most widely researched disease in CAD systems

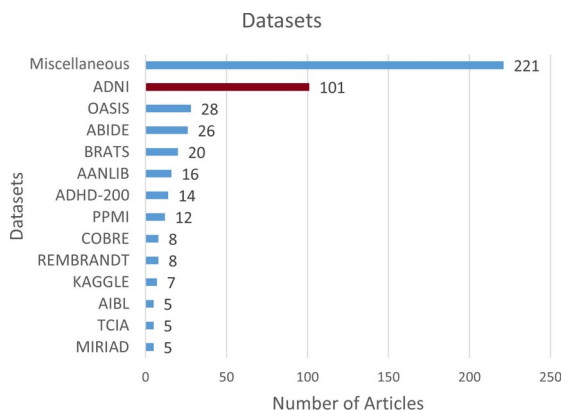


Fig. 6 Brain MRI types, usage-percentages computed from a total of 441 articles. T1-weighted MRI dominant

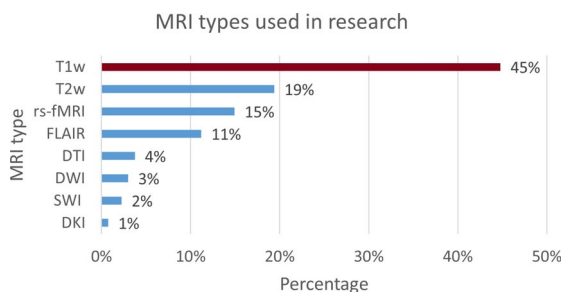


Fig. 7 Brain MRI planes usage—percentages computed from a total of 441 articles. Axial orientation dominant

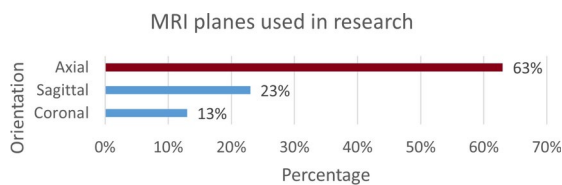


Fig. 8 Training dataset vs. accuracy for single disease diagnosis—The blue dots represent individual studies, and the red line represents the trend

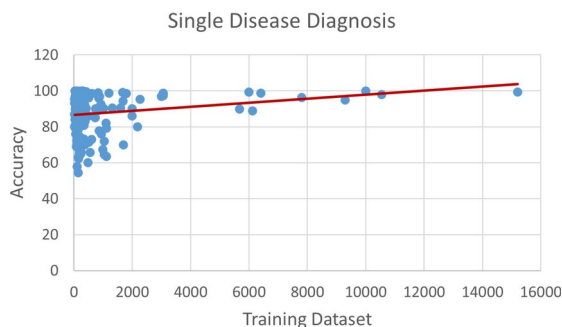
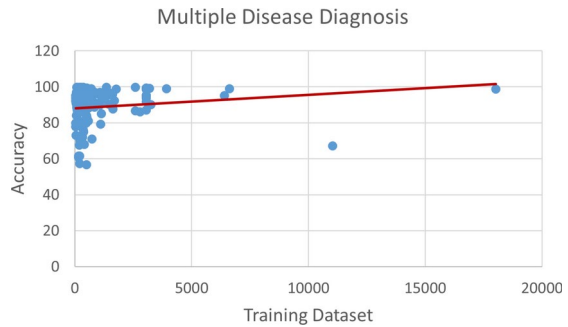


Fig. 9 Training dataset vs. accuracy for multiple disease diagnosis—The blue dots represent individual studies, and the red line represents the trend



disease classification systems. This confirms that the larger the dataset, the better the system's accuracy.

2.5 The evolution of AI-based CAD approaches for neurological disorders

Research on computer-aided neurological disorder diagnosis using MRI started using ML approximately two decades ago Arimura et al. (2009), with algorithms such as the SVM dominating the classification aspect and support from techniques such as Principal Component Analysis (PCA) for dimensionality reduction and computational efficiency. This was followed by the advent of DL (Quaak et al. 2021) which has proven to be a faster, more accurate, and efficient approach (Qiu et al. 2018) because the feature extraction part, which was conducted separately in ML, is integrated, making it easier for scientists and researchers to extract latent features quickly and train, test, analyze, compare, tune, optimize, and deploy their models in real-time applications (Zegers et al. 2021). Aggressive research in the domain of DL has enabled such models to be deployed on machines with high computational capabilities and storage space (using TensorFlow (TF) as an example), on mobile devices (TFLite), and later, on low-power chips using TinyML. Research on CAD for neurological disorders has gradually grown to multiclass (multiple diseases) diagnosis from the simple binary (normal/abnormal) classification or identification of a single disease. A thorough literature survey was conducted, which consisted of more than 1200 articles (from conference/journal papers, theses, and patents). It was observed that a great deal of research has been conducted on single disease diagnosis as well as normal/abnormal classification, but only a very small fraction capable of handling the diagnosis of multiple diseases was found. Figure 1 shows the statistics of the literature survey along with the search keywords. Among more than 63 neurological disorders researched since 2000, most have been on the diagnosis of AD and its types. AD is a neurodegenerative disorder that starts with Mild Cognitive Impairment (MCI) and memory loss and may later progress into severe degradation in socializing traits. Extensive research has been conducted to diagnose AD Ahmed et al. (2018); Pellegrini et al. (2018); Yamanakkanavar et al. (2020); Altinkaya et al. (2020); Lazli et al. (2020); Al-Shoukry et al. (2020); Ebrahimighahnavieh et al. (2020); Ansart et al. (2021); Arafa et al. (2022); Frizzell et al. (2022); Loddó et al. (2022) with the majority focusing on SVMs and CNNs (Bernal et al. 2019) for classification. Systems that distinguish patients with AD from MCI and normal controls have also been studied and proposed in large numbers. The second most researched disease is brain tumors Kamboj et al. (2018); Somasundaram and Gobinath (2019); Shaver et al. (2019); Tandel et al. (2019); Gore and

Deshpande (2020) Nadeem et al. (2020); Abbood et al. (2021); Al-Galal et al. (2021); van Kempen et al. (2021); Nazir et al. (2021); Arabahmadi et al. (2022); Neromyliotis et al. (2022). Brain or central nervous system cancer is the twelfth leading cause of death in both men and women (Ilic and Ilic 2023; Tandel et al. 2020). Most studies deal with the classification of MRI scans with or without tumors. Others have classified tumors as benign or malignant, whereas a small fraction has worked to identify multiple types of tumors in a multi-class paradigm. Substantial research has been conducted on tumor segmentation. CAD systems using ML/DL and MRI for other neurological disorders predominantly Autism Spectrum Disorder (ASD) Khodatars et al. (2007); Yulianto et al. (2018); Parlett-Pelleriti et al. (2022), PD Noor et al. (2020), Multiple Sclerosis (MS) (Kontopodis et al. 2021; Shoeibi et al. 2021), ADHD Eslami et al. (2021), Stroke, Schizophrenia Guney et al. (2021); Quaak et al. (2021), among others, have also been presented, but in relatively lower numbers. Additionally, research on inferring sex Xin et al. (2019); Yeung et al. (2022), age (Herent et al. 2018; Yeung et al. 2022) and smoking (Ding et al. 2015)/drug abuse has also been conducted, and the inferences of these models can be used in neurological disorder diagnosis models to make the best possible diagnosis from MRI. In some disorders, information pertaining to age, sex (Jang et al. 2022) and drug abuse (Yücel et al. 2008) can be useful in diagnosing the disease based on the features presented on MRI. In addition to the research mentioned above, a multitude of sensors (Krokidis et al. 2022) available in Android devices Krichen (2021) have been used for gathering information such as patient speech, facial expressions (Gola et al. 2017; Yolcu et al. 2017) and gait Chen et al. (2021), among others. Analysis of these supplementary data using various computer vision/image processing techniques, Natural Language Processing (NLP), statistical analysis algorithms, and thresholding have also been used in CAD. In addition, various standard questionnaires Prisie et al. (2018) have been used to assist patients with CAD Lahmiri and Shmuel (2019). However, incorporating such methodologies in addition to MRI data may result in a computational time overhead for processing supplementary data. To simplify the framework and utilize the capabilities of DL to identify features and classify very similar MRIs with minor differences owing to disorders, supplementary sensor data were not incorporated in this research, aiming to infer multiple neurological disorders using only one modality as an input to the framework with adequate accuracy.

2.6 Review of multi-class CAD systems

The following section covers the crux of the survey with reference to a subset of the literature reviewed for brevity. The literature surveyed was categorized according to the number of diseases diagnosed. For brevity, four or more diseases/classes (Table 1) classification research is presented here. In the subsequent section, research catering to the MRI-based diagnosis of four or more diseases/classes (Table 1) is later discussed in detail, stating strengths and weaknesses, to build on the premise for future research directions.

Table 1 ML- or DL-based research catering to CAD of four or more diseases/classes

No	Paper	Disease	Technology	Accuracy	Dataset
1	Luts et al. (2007)	Normal tissue, Cerebrospinal Fluid (CSF), grade II diffuse astrocytomas, grade II oligoastrocytomas, grade II oligodendrogliomas, grade III astrocytomas, grade III oligoastrocytomas, grade III oligodendrogliomas, meningiomas, and grade IV gliomas	LS-SVMs, Linear Discriminant Analysis (LDA)	92.05%—99.9%	MRI and Magnetic Resonance Spectroscopic Imaging (MRSI) data from the INTERPRET project database. 25 patients with a brain tumor and 4 volunteers
2	Khani et al. (2013)	AD, Alzheimer plus visual agnosia, Glioma, Huntington's Disease (HD), Meningioma, Pick, and Sarcoma	2D Discrete Wavelet Transform (DWT), GARCH, PCA, LDA, SVM	Up to 100%	Harvard Medical School website—80 images, 10 images per category—T2-weighted (T2W)
3	Saritha et al. (2013)	Stroke, infectious disease, degenerative disease, brain tumor	Probabilistic neural network	Normal 100%, Stroke 91.3%, Degenerative disease 100%, Infectious disease 91.3%, Brain tumor 95.7%	Harvard Medical School website—T2W axial. 75 images, 15 in each category
4	Hemanth et al. (2014)	4 Metastase, glioma, meningioma, and astrocytoma	Modified Counter Propagation Neural Network (MCPN), Modified Kohonen Neural Network (MKNN)	Up to 98%	540 images—collected from radiologists
5	Sabuncu and Koglu (2015)	AD, Schizophrenia (SZ), ASD, ADHD; age, cerebrospinal fluid derived amyloid- β levels and mini-mental state exam score	Multivariate Pattern Analysis (MVPA)	Up to 86 %	2,800 subjects, from Harvard, ADNI, OASIS, ABIDE, ADHD-200 Consortium, COBRE, MCIC—T1W
6	Sooriya (2017)	Astrocytoma, Glioblastoma Multiforme, Oligodendroglioma, Healthy tissue, Unidentified tumor	CNN	99.68%	REMBRANDT—Images of Normal Subjects (BRAINS) ImageBank repository of University of Edinburgh and from MIRIAD—axial, coronal and sagittal

Table 1 (continued)

No	Paper	Disease	Technology	Accuracy	Dataset
7	Ion-Märgin et al. (2017)	MS—Clinically Isolated Syndrome (CIS), Relapse Remitting (RR), Primary Progressive (PP), and Secondary Progressive (SP)	LDA, SVM, Random Forest (RF)	F1-score up to 87%	87 MS patients (12 CIS, 30 RR, 17 PP, and 28 SP) and 18 Healthy Controls (HCs). Longitudinal data available for each MS patient included clinical (e.g., age, disease duration, Expanded Disability Status Scale), conventional MRI, T1W and spectroscopic imaging
8	Rachma et al. (2017)	White Matter Hyperintensity (WMH), Very Small (VS), Small (S), Medium (M), Large (L), Very Large (VL)	Deep Boltzmann Machine (DBM), Convolutional Encoder Network (CEN), patch-wise CNN (patch-CNN), SVM, RF	Dice Similarity Coefficient (DSC) up to 0.6489	ADNI—60 MRI data from 20 subjects
9	Usman and Rajpoot (2017)	Brain tumor—background, necrosis, edema, enhancing tumor, and non-enhancing tumor	RF	90% ± 3.88% Dice overlap for the complete tumor region, 75% for the core tumor region and 95% for enhancing tumor region	MICCAI BraTS 2013—T1, T2, Gadolinium-Contrast-enhanced T1 (T1C) and Fluid-Attenuated Inversion Recovery (FLAIR)
10	Hemanth et al. (2018)	Metastasis, Meningioma, Glioma, and Astrocytoma	CNN	Up to 97.1%	Brain tumor images collected from M/s. Devaki Scan Centre. Total 220—T1, T2 and T2 FLAIR images
11	Kazemi and Hough (2018)	AD Stages—Normal Control (NC), significant memory concern (SMC), Early Mild Cognitive Impairment (EMCI), Late Mild Cognitive Impairment (LMCI), AD	AlexNet	94.97% for AD, 95.64% for EMCI, 95.89% for LMCI, 98.34% for NC, and 94.55% for SMC	ADNI—Resting state-functional MRI (rs-fMRI) scans of 197 subjects

Table 1 (continued)

No	Paper	Disease	Technology	Accuracy	Dataset
12	Islam and Zhang (2018)	AD—Non-demented, very mild dementia, mild dementia, moderate dementia	Inception-v4, ResNet	99% for non-demented stage, 75% for very mild stage, 62% for mild stage, and 33% for moderate stage	OASIS
13	Talo et al. (2019)	Normal, cerebrovascular, neoplastic, degenerative, and inflammatory diseases classes	Five pre-trained models including ResNet	95.23% \pm 0.6	Harvard Medical School database—42 subjects used in five categories
14	Abrol et al. (2019)	Cognitively normal (CN) aging adults, MCI, AD, BD probands (BDP), schizoaffective disorder probands (SADP), and SZ probands (SZP)	ResNet	CN vs. AD 91%, sMCI vs. AD (86%), CN vs. pMCI (86%) and sMCI vs. pMCI (77%), CN vs. sMCI 65% and pMCI vs. AD 66%	ADNI and BSNIP—828 ADNI baseline scans, 1013 subjects from BSNIP
15	Khagi et al. (2019)	AD—non-demented for Clinical Dementia Rating (CDR) 0, very mild dementia for CDR 0.5, mild dementia for CDR 1 and moderate dementia for CDR 2	CNN, Mutinffs, ReliefF, Laplacian and UDFS, SVM, k-nearest neighbors (kNN), Subspace ensemble	99%	OASIS—sagittal view—18 subjects for CDR level 0, 16 subjects for CDR 0.5, 12 subjects for CDR 1 and 4 subjects for CDR 2, altogether 50 subjects with 5220 images
16	Nayak et al. (2020)	Degenerative disease, stroke, tumor, infectious disease, and normal	CNN	97.50–100%	MD-1, 75 brain MRIs. MD-2, 200 brain MRIs. Harvard Medical School dataset—T2W axial
17	Rudie et al. (2020)	35 Diseases	3D-CNN	—	Multimodal brain MRI scans from 212 patients
18	Mehmod et al. (2020)	AD—CDR-0 (No Dementia), CDR-0.5 (Very Mild Dementia), CDR-1 (Mild-Dementia), and CDR-2 (Moderate AD)	Siamese CNN (SCNN)	99.05%	OASIS—382 images. 167 CDR-0 (No Dementia), 87 CDR-0.5 (Very Mild Dementia), 105 CDR-1 (Mild-Dementia), and 23 CDR-2 (Moderate AD)
19	Ramzan et al. (2020)	AD Stages—CN, SMC, EMCI, MCI, LMCI, and AD	ResNet-18	97.92%	ADNI—A longitudinal cohort of resting-state fMRI of 138 subjects (25 CN, 25 SMC, 25 EMCI, 25 LMCI, 13 MCI, and 25 AD)

Table 1 (continued)

No	Paper	Disease	Technology	Accuracy	Dataset
20	Bashyam et al. (2020)	Brain age and AD, MCI, SZ, and major depression	Inception-Resnet-v2	Up to 86%	T1W brain MRI scans from NCs (n= 11,729). ADNI 1 and 2 (n= 1699, NC = 513, MCI = 833, AD = 353), SZ consortium (n= 835, NC = 448, schizophrenia = 387) and matched NC and major depression subjects from UK Biobank (n= 408, NC = 204, major depression = 204)
21	Deepa et al. (2021)	High-grade tumor, low-grade tumor, acute stroke, sub-acute stroke	Hybridized support vector-based RF classifier	88.3% for brain tumor and 99.2% for stroke	BRATS 2013 and ISLES—1100 image, 600 tumor affected and 500 stroke affected images
22	Chagué et al. (2021)	Dementia—early-onset AD (EOAD), late-onset AD (LOAD), Frontotemporal Dementia (FTD), depression	SVM	Up to 82%	3D T1 MRI—34 patients with EOAD, 49 with LOAD, 39 with FTD and 24 with depression from the pre-existing cohort CLIN-AD. Department of Neuroradiology at Pitie-Salpetriere Hospital
23	Mozhdeh et al. (2021)	PD stages—Control, Prodromal, as well as stages 1, 2 and 3	CNN	94%	PPMI—100 images, 20 subjects for each stage of PD and 20 NC
24	Poyraz et al. (2022)	Atrophy, normal, white matter intensity WMI, and ischemia	MobilNetV2, Iterative Neighborhood Component Analysis (INCA), SVM	99.10%	444 MR images. 100, 150, 92, and 102 brain MR images for atrophy, normal, white matter intensity WMI, and ischemia categories
25	Zhu et al. (2022)	Chronic SZ (ChSZ) from HCs, First-Episode Psychosis (FEP), ultra-high risk for psychosis (UHR), ASD	PCA, SVM	Up to 76%	Total 359 T1W MRI scans, 154 with SZ spectrum (UHR, n = 37; FEP, n = 24; and ChSZ, n = 93), 64 with ASD, and 141 HCs
26	Marwa et al. (2023)	AD, Non-Demented (ND), Moderately Demented (MoD), Mild Demented (MD), and Very Mild Demented (VMD)	CNN	99.68%	OASIS—3200, 64, 896, and 2240 images for ND, MoD, MD, and VMD respectively
27	Yousaf et al. (2023)	Normal tissue, necrosis, edema, non-enhancing tumor, and enhancing tumor, acute and sub-acute stroke	Encoder-decoder architecture based UNET	99.56%	BRATS 2015 and ISLES 2015
28	Thangavel et al. (2023)	ND, VMD, MD, MoD	ResNet	98%	374 records from Github and Kaggle
29	Srinivasan et al. (2023)	Glioma, meningioma, no tumor, and pituitary tumor	RCNN	98.17%	REMBRANDT dataset—620 MR images for testing, 2480 for training from 235 patients

Table 1 (continued)

No	Paper	Disease	Technology	Accuracy	Dataset
30	El-Latif et al. (2023)	ND, VMD, MD, MoD	CNN	95.93%	Alzheimer's 4 class Dataset—Kaggle 6400 images
31	Mujahid et al. (2023)	ND, VMD, MD, MoD	EfficientNet-B2 and VGG-16	97.35%	Kaggle—3200, 64, 896, and 2240 images for ND, MoD, MD, and VMD respectively
32	Yao et al. (2023)	ND, VMD, MD, MoD	Fuzzy-VGG	Up to 97%	9109 2D MRI samples from Kaggle Alzheimer's classification dataset (KACD) and 749 3D MRI samples from the Recognition of Alzheimer's Disease dataset (ROAD)
33	Apostolopoulos et al. (2023)	Glioma, meningioma, and pituitary tumor. AD, PD, and HC. ND, VMD, MD, MoD	Attention Feature Fusion VGG19 (AFF-VGG19)	93.53% for three brain tumor classes, 95.65% for AD and PD, and 94.97% in grading cases of dementia	Kaggle—Brain Tumors Dataset (26,249), Brain Disorders Dataset (7756), Dementia Grading Dataset (6400 images)
34	Al-lada et al. (2023)	AD, EMCI, LMCI, MCI, HC	VGG-19	91.05%	1326 images in 5 classes from ADNI
35	Saeedi et al. (2023)	Glioma, meningioma, pituitary tumor, and HC	2D-CNN, auto-encoder, kNN, RF, SVM, Logistic Regression (LR), Stochastic Gradient Descent (SGD), Multi-Layer Perceptron (MLP)	96.47% for 2D-CNN, 95.63% for auto-encoder and 86% for kNN	Kaggle—3264 T1w contrast-enhanced MRI. glioma (926), meningioma (937), pituitary gland tumor (901), and healthy brain (500 images)
36	Ullah and Jamjoom (2023)	ND, VMD, MD, MoD	CNN	99.38%	Kaggle—3200, 64, 896, and 2240 images for ND, MoD, MD, and VMD respectively

The table provides the diagnosable diseases, DL/ML architecture used, accuracy of inference, and dataset (and number of subject scans) used to train the system

3 Discussion

Luts et al. (2007) studied pattern recognition methods using MRI to assist medical experts in the CAD of brain tumors. Although a multiclass classification system, it only considers different types of tumors and no other diseases. Two modalities are used instead of one, rendering the data computationally intensive. In addition, the dataset used was very limited, rendering the accuracy of 99.9% questionable. Sabuncu et al. (2012) conducted an empirical benchmark MVPA study using structural neuroimaging. Although the datasets used in this study are reasonable, the disease set was limited. In addition, deep learning, which presents

a window for enhancing accuracy, has not been applied. The method proposed by Khani et al. (2013) classifies an MRI as normal or one of seven different diseases. The system was trained using a very limited dataset with only ten images per category, as well as from a single patient's volumetric MRI. This raises serious concerns regarding its performance. A similar limited dataset problem persists in studies by Ramzan et al. (2020), Chagué et al. (2021), Mozhdeh et al. (2021) and Hemanth et al. (2014). Saritha et al. (2013) combined wavelet-entropy-based spiderweb plots, probabilistic neural networks, and disease diagnosis using brain MRI. These diseases include stroke, degenerative diseases, infectious diseases, and brain tumors. They employed wavelet-entropy-based spiderweb plots for feature reduction, followed by a probabilistic neural network for classification. As expected, the sensitivity for detecting brain tumors was moderately good. However, degenerative and infectious diseases encompass a wide range of disorders and hence their system does not provide a pinpoint diagnosis. Sabuncu and Koglu (2015) used three classes of MVPA algorithms and structural measurements from brain MRIs to predict with varying degrees of accuracy, multiple parameters, including AD, Schizophrenia, Autism, as well as ADHD, age, cerebrospinal fluid-derived amyloid levels, and the Mini-Mental State Examination score. They claimed that although the choice of features has a considerable impact on prediction accuracy, clinical examination, and evaluation remain the gold standard determinants of diagnosis accuracy. Saritha et al. (2013) used only 15 images per class for a five-class classification system, catering for four diseases and a normal category. In addition, infectious and degenerative diseases were used as generalized categories, resulting in a system that lacks the capability for specific disease diagnosis. The accuracy of this study is questionable from the perspective of reliable diagnosis because of the small training dataset used. Sooriya (2017) proposed a CNN model to classify brain tumors into five classes using brain MRI. The model achieved an average F1-score of 99.46%. In addition, the proposed model's accuracy was 99.68%. Axial, coronal, and sagittal planes were used for training and testing. A limitation of this study was that it could only diagnose a single disease. Ion-Mărgin et al. (2017) presented the results for nine binary classification problems using clinical data, lesion loads, and metabolic features for MS. Their results indicated that metabolic features were better at differentiating between relapsing-remitting and primary progressive forms, whereas lesion loads were better at differentiating between relapsing-remitting and secondary progressive forms. They concluded that combining clinical data with magnetic resonance lesion loads and metabolic features could improve the discrimination between the relapsing-remitting and progressive forms. A modified DCNN was employed by Hemanth et al. (2018) to classify brain tumors into four classes using brain MRI. Only 20 images per category were used for training in this study, classifying brain tumors only. The accuracy was questionable because of the small dataset used for training. Kazemi and Hough (2018) applied the CNN-architecture AlexNet to fMRI datasets to classify five stages of AD. They successfully classified normal healthy controls, SMC, EMCI, LMCI, and AD however, the system is capable of handling only a single disease and its subtypes. Islam and Zhang (2018) proposed computer-aided early diagnosis of AD using brain MRI. Their study suggested that the non-demented stage can be predicted with very high accuracy, although the accuracy drastically decreases for very mild, mild, and moderate stages. Therefore, although the model has acceptable performance for non-demented patient classification, scope remains for improving the diagnosis of dementia. Training the proposed model with a dataset containing more samples from patients with dementia could help overcome this

limitation. Talo et al. (2019) compared the neurological disorder classification performances of different pretrained models. From among the five pre-trained models, they obtained the best classification accuracy of $95.23\% \pm 0.6$ with the ResNet-50 model. The shortcomings of this study include the use of a limited dataset. In addition, very few neurological disorders were identified because the vaguely defined categories for Neoplastic, Cerebrovascular, Inflammatory and Degenerative diseases, encompass many disorders. Abrol et al. (2019) tested the diagnostic classification performance of the ResNet architecture. The diagnostic groups included cognitively normal aging adults, aging adults with MCI and neurodegenerative AD, and psychotic diagnostic groups such as bipolar disorder probands, schizoaffective disorder probands, and schizophrenia probands, which were studied in pairs; hence, several binary classification tasks were performed. The CN vs. AD classification task revealed the highest cross-validated accuracy of 91%, whereas the other tasks produced considerably lower accuracies. Khagi et al. (2019) utilized deep-layer features from a deep neural network architecture and trained ML architectures, such as SVM, kNN, and Sub-space Ensemble, under different testing conditions for AD classification using those features. Nayak et al. (2020) employed a deep CNN-based approach to diagnose multi-class brain abnormalities. The proposed CNN model comprised five layers with learnable parameters: four convolutional layers and one fully connected layer. The limitations of this system include the limited dataset and few disease diagnoses. Multiple diseases are included in the generally defined categories of infectious and degenerative diseases, making diagnosis non-specific. Only 165 images were used for training in the five categories, rendering the accuracy of up to 100% questionable. Rudie et al. (2020) used multimodal brain MRI scans of 212 patients with 35 neurological diseases. 3D CNN and atlas-based image processing were used to extract 11 imaging features. Expert-derived Bayesian networks incorporating domain knowledge were used for differential diagnosis. The system's performance was assessed by comparing its diagnostic accuracy with that of radiologists. A limited dataset was used in this study, with some categories being trained without images. Despite the significance of the disease pool, the system cannot serve as an assistive CAD tool for neurologists. Mehmod et al. (2020) developed a Siamese CNN model inspired by VGG-16 (also named OxfordNet) to classify dementia stages using augmentation to handle data imbalances. Although their system claimed acceptable accuracy, the disease pool for this CAD system was limited. Deepa et al. (2021) proposed a method for classifying tumors and strokes in MRI images using a hybrid ML algorithm. Texture-, intensity-, and shape-based features were used for classification. A maximum a priori (MAP)-based firefly algorithm was proposed for feature selection, and a hybridized support vector-based RF classifier was used for classification. This study used a reasonably sized dataset for training, but the diseases for which it caters are very few for it to act as a generic diagnostic assistance tool. The study deals only with tumors and stroke, with room for improving its 88.3% accuracy in classifying tumors. Poyraz et al. (2022) proposed an exemplar-based automated brain disease detection model using a computer vision technique with MobilNetV2 as the feature extractor and an SVM classifier. This study only dealt with three diseases. The training set was also limited, employing only 444 images in four categories, which resulted in questionable accuracy. Zhu et al. (2022) evaluated whether a model differentiating patients with chronic schizophrenia from healthy controls could be applied to earlier clinical stages, such as first-episode psychosis, ultra-high risk psychosis and ASD. A very limited number of diseases (ASD and types of SZ only) for diagnosis, only using 359 images in four categories

for training, and its low accuracy are the major weaknesses of this system. A similar trend was observed in the most recent research pertaining to CAD of multiple neurological disorders. Most of the multi-class research presented in 2024 was aimed at classifying brain tumors into gliomas, meningiomas, and pituitary gland tumors Zhou et al. (2024); Akter et al. (2024); Rastogi et al. (2024); Simo et al. (2024); Liu and Wang (2024); Haque et al. (2024); Agrawal and Maan (2024); Saboor et al. (2024), and different stages of AD Ayus and Gupta (2024); Li et al. (2024); Heidari and Ghazikhani (2024); El-Assy et al. (2024). These two diseases hold the most widely researched spot from CAD point of view. Although the accuracy claims in the proposed systems reach up to 99%, similar limitations including poor generalizability still persist, with capabilities to diagnose only a single disease and its subtypes or stages. Most research conducted in this domain lacks datasets of sufficient scale and deals with the diagnosis of a few diseases, mostly a single disease and its subtypes. This reflects the research gap that has attracted the attention of medical experts and data scientists.

3.1 Datasets

DL requires a substantial amount of training data to achieve optimal performance. Table 2 contains the details of the multiple datasets identified during the literature survey, including MRI data for various diseases. MRI data are available in Joint Photographic Experts Group (JPEG), Digital Imaging and Communications in Medicine (DICOM), or Neuroimaging Informatics Technology Initiative (NIfTI) data formats (Clayden et al. 2011). Most DICOM files involve a single slice for acquisition. Conversely, NIfTI files store volumetric data comprising multiple MRI slices that constitute the whole brain. In addition, axial, coronal, and sagittal views of the slices are available, which can serve as useful additional information sources for better diagnosis by analyzing multiple brain perspectives. After adequate pre-processing, these MRI signals can be used to train smart DL models using 2D slices and even 3D volumes, which produce the best results with minimum computational overhead.

3.2 Tools

Very few CAD tools have been developed to assist neurologists in differential diagnosis. Of the 441 articles analyzed, only four embedded their trained networks into publicly accessible tools. The tool developed by Deepa et al. (2021) classifies tumors and stroke only, dealing with two types of each, using the MATLAB Graphical User Interface (GUI). Helaly et al. (2021) developed a web-based application to diagnose AD and its types. Collective information on these tools and a few other tools is presented in Table 3.

3.3 Key findings

Binary normal/abnormal brain classification systems have very little impact on differential diagnosis and, therefore, cannot serve as CAD tools in medical practice. Most CAD research has revolved around single-disease diagnosis, with a few extensions to cater to their subtypes. Very few CAD systems have been proposed that are capable of handling multiple disorders. The major shortcoming of such systems is the inadequacy of the training data, rendering them unreliable. Some systems trained with substantial datasets have low

Table 2 Publicly available datasets containing brain MR scans with different pathologies

No	Dataset	Details
1	OpenNeuro https://openneuro.org/search/modality/mri	538 Public Datasets
2	fastMRI (Zbontar et al. 2018) https://fastmri.med.nyu.edu/	6,970 fully sampled brain MRIs
3	The MICCAI 2008 MS Lesion Segmentation Challenge Dataset https://www.nitrc.org/projects/msseg	MS
4	The MICCAI 2016 MS Lesion Segmentation Challenge Dataset (Commowick et al. 2021) https://shanoir.irisa.fr/shanoir-ng/challenge-request	MS
5	ISBI 2015 Longitudinal MS Lesion Segmentation Challenge Dataset (Carass et al. 2017) https://smart-stats-tools.org/lesion-challenge	MS
6	eHealth Lab http://www.medinfo.cs.ucy.ac.cy/index.php/facilities/32-software/218-datasets	MS
7	UK Biobank and Human Connectome Project (Alfaro-Almagro et al. 2017)	-
8	Alzheimer's Disease Neuroimaging Initiative (ADNI) (Jack Jr et al. 2008) https://adni.loni.usc.edu/methods/mri-tool/standardized-mri-data-sets/	AD
9	The Open Access Series of Imaging Studies (OASIS) database (Marcus et al. 2007) https://www.oasis-brains.org/	AD
10	Parkinson's Progression Markers Initiative (PPMI) (Marek et al. 2011) https://www.ppmi-info.org/access-data-specimens/download-data	PD
11	Center for Biomedical Research Excellence (COBRE) https://tinyurl.com/fcon1000-cobre	Schizophrenia
12	The Minimal Interval Resonance Imaging in Alzheimer's Disease (MIRIAD) dataset (Malone et al. 2013) https://www.ucl.ac.uk/drc/research/research-methods/minimal-interval-resonance-imaging-alzheimers-disease-miriad	AD
13	National Alliance for Medical Image Computing (NAMIC) https://www.na-mic.org/wiki/Downloads	Schizophrenia, Autism, Lupus
14	The Federal Interagency Traumatic Brain Injury Research (FITBIR) informatics system datasets https://fitbir.nih.gov/	Traumatic Brain Injury
15	Function Biomedical Informatics Research Network (FBIRN) Keator et al. (2016) http://www.schizconnect.org/ https://www.nitrc.org/projects/hid	Schizophrenia
16	1000 Functional Connectomes Project (FCP) Mennes et al. (2013) http://fcon_1000.projects.nitrc.org/	1200+ resting state functional MRI (R-fMRI) datasets
17	Human Connectome Project (HCP) http://www.humanconnectomeproject.org/data/inventory/	
18	Medical School of Harvard University www.med.harvard.edu/aanlib/home.html	Normal Aging, Stroke, Tumors, Degenerative Diseases, Inflammatory or Infectious Diseases
19	The Multimodal Brain Tumor Image Segmentation Datasets BRATS 2014, 2015, 2016, 2017, 2018 https://paperswithcode.com/dataset/brats-2015-1 , https://paperswithcode.com/dataset/brats-2018-1	Brain Tumor
20	ISLES (Ischemic Stroke Lesion Segmentation) 2015 (Maier et al. 2017), 2016, 2017, 2018, 2022 https://www.isles-challenge.org/	Stroke
21	Department of Radiology, Firat University Hospital Poyraz et al. (2022) https://www.kaggle.com/turkertuncer/brain-disorders-four-categories/	Atrophy, Ischemia, WMI
22	ADHD-200 (Sasabe et al. 2014) http://fcon_1000.projects.nitrc.org/indi/adhd200/index.html	ADHD

Table 2 (continued)

No	Dataset	Details
23	Bipolar and Schizophrenia Network for Intermediate Phenotypes BSNI (Tamminga et al. 2014)	Psychosis, schizophrenia, schizoaffective disorder (SAD), and psychotic bipolar disorder (BDP)
24	Genetic Risk and Outcome of Psychosis (GROUP) (Korver et al. 2012)	Psychosis
25	Autism Brain Imaging Data Exchange (ABIDE I Di Martino et al. (2014) and ABIDE II Alexander et al. (2017) https://fcon_1000.projects.nitrc.org/indi/abide/	Autism
26	FRONTIER (Frontotemporal Dementia Research Group) patient database https://www.sydney.edu.au/brain-mind/our-clinics/frontotemporal-dementia-clinic.html	Dementia
27	National Cancer Institute database (TCIA) Clark et al. (2013) http://cancerimagingarchive.net/	Cancer
28	Machine Learning for Signal Processing (MLSP) 2014 Challenge Competition Silva et al. (2014) https://www.kaggle.com/c/mlsp-2014-mri	Schizophrenia
29	CADDementia Dataset (Bron et al. 2015) https://caddementia.grand-challenge.org/	AD, MCI
30	MRI brain images collected from Brainix—Brain Tumour image collection from Pixmeo (Medical Imaging Software Company), Swiss and National Institutes of Health, USA	Brain Tumor
31	Mind Research Network (MRN) https://www.mrn.org/collaborate/data-community	Autism
32	Australian Schizophrenia Research Bank (ASRB) Loughland et al. (2010) https://www.neura.edu.au/discovery-portal/asrb/	Schizophrenia
33	PREDICT-HD project https://www.ncbi.nlm.nih.gov/projects/gap/cgi-bin/document.cgi?study_id=phs000222.v1.p1&phd=2424	Huntington Disease
34	Data from four separate SZ studies conducted at Johns Hopkins University (JHU), the Maryland Psychiatric Research Center (MPRC), the Institute of Psychiatry, London, UK (IOP), and the Western Psychiatric Institute and Clinic at the University of Pittsburgh (WPIC)	Schizophrenia
35	ADHD dataset for NYU, Neuro and OHSU fMRI data Bellec et al. (2017) http://fcon_1000.projects.nitrc.org/indi/adhd200/	ADHD
36	AddNeuroMed cohort	AD
37	Adolescent Brain-Behavior Research Clinic (ABBR) https://karlsgodtlab.psych.ucla.edu/abbr/#:~:text=Adolescent	-
38	INTERPRET project database http://azizu.uab.es/INTERPRET/	-
39	https://www.fil.ion.ucl.ac.uk/spm/data/ fMRI	
40	https://www.ncbi.nlm.nih.gov/projects/gap/cgi-bin/dataset.cgi?study_id=phs000007.v13.p5&pht=690	Dementia
41	Repository of Molecular Brain Neoplasia Data (REMBRANDT) https://wiki.cancerimagingarchive.net/display/Public/REMBRANDT	Glioma
42	https://www.kaggle.com/datasets/ahmedhamada0/brain-tumor-detection/metadata (Alanazi et al. 2022)	Brain Tumor
43	https://www.kaggle.com/datasets/sartajbhuvaji/brain-tumor-classification-mri (Alanazi et al. 2022)	Glioma tumor, Meningioma tumor, and Pituitary tumor
44	https://figshare.com/articles/dataset/brain_tumor_dataset/1512427 (Alanazi et al. 2022)	Brain Tumor
45	https://nda.nih.gov/ (Hall et al. 2012)	Autism
46	https://www.brainsimagebank.ac.uk/	Normal Brain

Table 2 (continued)

No	Dataset	Details
47	The Australian Imaging, Biomarker and Lifestyle Flagship Work of Ageing (AIBL) database (Ellis et al. 2009) https://aibl.csiro.au/	AD
48	Baltimore Longitudinal Study of Aging (BLSA) https://blsa.nih.gov/	Dementia
49	Multi-Ethnic Study of Atherosclerosis (MESA) (Bild et al. 2002; Olson et al. 2016)	Cerebral microbleeds
50	Dr. Andreia V. Faria (afaria1@jhmi.edu). The STIR data STIR/Vista Investigators—Dr. Marie Luby (lubym@ninds.nih.gov) Liu et al. (2021)	Stroke
51	Anatomical Tracings of Lesions After Stroke (ATLAS) Liew et al. (2018) https://fcon_1000.projects.nitrc.org/indi/retro/atlas.html	Stroke
52	MPI-Leipzig_Mind-Brain-Body https://legacy.openfmri.org/dataset/ds000221/	Resting-state fMRI
53	Brain development website (IXI dataset) http://brain-development.org/ixi-dataset/	Healthy Subjects
54	Kaggle Alzheimer's classification dataset (KACD) www.kaggle.com/tourist55/alzheimers-dataset-4-class-of-images	AD
55	Recognition of Alzheimer's Disease dataset (ROAD) https://www.datafountain.cn/competitions/369	AD

The Universal Resource Locators (URLs) to access them are also provided here, but in some cases permission may be required to access data

Table 3 Publicly available tools for CAD of neurological disorders

No	Tool	Disease
1	Stroke classification, MATLAB GUI Deepa et al. (2021)	Stroke
2	Tumor Classification, MATLAB GUI Deepa et al. (2021)	Tumor
3	AD stage prediction for MRI medical images Helaly et al. (2021)	AD
4	Tumor Ucuza et al. (2019)	Tumor
5	MRI Predict Tool Salvador et al. (2017)	Psychosis

accuracy. Sabuncu et al. (2012) employed data from 2800 subjects from multiple datasets to classify multiple disorders; however, their system failed to surpass 86% accuracy. However, systems developed to classify five to eight disorders and claim to reach an accuracy of 100%, such as those developed by Khani et al. (2013) and Saritha et al. (2013), use 10 to 15 images per class from a single online source. Such systems cannot be generalized and are failure-prone when tested using data from different sources. Publicly available CAD tools in this domain were very scarce. Furthermore, the majority of developed tools work with a single widely researched disease and its subtypes, including AD and tumors. However, open sharing in the neuroscience community has provided access to big MR data. Many publicly available datasets, ranging from structural to functional MRI data, have been identified in various studies for a wide spectrum of neurological disorders. This vast amount of data, such as 2D slices and 3D whole brain volumes is available in multiple sequences and orientations in JPEG, DICOM, NIfTI, and other formats. In addition to the datasets compiled for this study, numerous others are available that can assist the CAD pipeline using brain MRI, including preprocessing operations such as skull stripping or brain extraction Hoopes et al. (2022), brain lesion segmentation (Commowick et al. 2021) and substance abuse identification (Angeles-Valdez et al. 2022) from brain MRI. Despite the huge amount of publicly

available data, drastic uplift in storage and computational resources, and a multitude of complex, fast, and efficient DL architectures, to date, no study has encompassed them collectively to train an omnipotent CAD tool.

The development of DL frameworks for MRI-based diagnosis of neurological disorders has led to significant advancements in research and clinical applications. Here are some key highlights: 1. **Enhanced Access to Care and Empowerment through Technology:** Deep learning models, particularly CNNs, have shown remarkable improvements in detecting and classifying neurological disorders, such as AD, MS, and brain tumors. These models can analyze complex patterns in MRI images that are often imperceptible to the human eye (Shojaei et al. 2023). DL frameworks facilitate the automation of image interpretation, reducing the burden on radiologists and enabling faster diagnosis. This automation is particularly beneficial in settings with a high volume of scans. By improving diagnostic efficiency and accuracy, these technologies can help ensure that patients receive appropriate care quicker, potentially addressing past inadequacies in healthcare systems (Pinto-Coelho 2023). By utilizing advanced DL techniques, healthcare providers are better equipped to serve their patients, leading to improved treatment outcomes and empowering patients with informed choices regarding their health (Alowais et al. 2023). 2. **Reduction of Health Disparities Through Personalized Medicine:** DL enables the identification of specific disease subtypes, which can guide personalized treatment plans. By analyzing large datasets, researchers can uncover correlations between MRI findings and patient outcomes. Improved diagnostic techniques could help identify neurological disorders more effectively, especially in underserved populations, thus contributing to more equitable healthcare outcomes (Krishnan et al. 2023). Furthermore, early and precise diagnoses can provide families with answers and clearer pathways to management and support, helping to mitigate the emotional and psychological burden associated with uncertain diagnoses (Okoye et al. 2023).

3.4 The challenges

Brain imaging can be tremendously fruitful in visualizing structural and functional brain changes resulting from the underlying pathophysiological abnormalities. There are several non-invasive imaging techniques that can assist in the diagnosis and prognosis of neurological disorders. Structural MRI deals with morphometry of cortical structures whereas functional MRI can detect changes in blood flow resulting from brain activities (Garcia Santa Cruz et al. 2023). In clinical practice, medical experts typically fuse these modalities to reach concrete diagnosis (Shoeibi et al. 2023), making it an interesting approach for data scientists and engineers working on AI powered CAD tools to consider as well. This multimodal data fusion for CAD of neurological disorders comes with certain challenges. For optimum performance, DL requires massive, labelled datasets during training (Yang et al. 2022). The unavailability of such multi-modal data for multiple neurological disorders is the major challenge in CAD research in this domain, since the models trained using small datasets result in generalizability issues rendering them unusable in routine clinical practice (Viswan et al. 2024). Another similar challenge is the class imbalance issue Johnson and Khoshgoftaar (2019). The inference of the DL model trained on imbalanced data for different classes is observed to show a bias towards the dominant class Shoeibi et al. (2023). The choice of DL architectures as well as adequate hardware resources capable of handling massive multi-dimensional arrays have also been observed as bottlenecks in CAD research

catering to multi-class and multi-modal medical imaging data (Shoeibi et al. 2023). In addition to the current performance issues of the AI powered CAD regimens, including lack of robustness and generalizability, the major factor responsible for hindering the integration of such CAD tools in routine clinical practice is the lack of explainability (Jahan et al. 2023; Taşcı 2023). In the quest to increase the accuracies of CAD tools, the complexity of the AI system architectures increased exponentially. This resulted in a drastic reduction in interpretability and explainability. The DL architectures grew complex with hundreds of hidden layers and millions of trainable parameters, and despite their near-perfect performance Górriz et al. (2023); Farahani et al. (2022), the operations got wrapped in a “Black Box” Zeineldin et al. (2024); Qian et al. (2023); Borys et al. (2023); Tjoa and Guan (2020). This resulted in a decrease in trust of medical domain experts El-Sappagh et al. (2021), since in diagnostic radiology and clinical practice, precious human lives are on the line and a single error can lead to catastrophic consequences Viswan et al. (2024); Nazir et al. (2023); Jin et al. (2023); Van der Velden et al. (2022). This is one of the foremost reasons that despite the tremendous technological advancements Viswan et al. (2024), AI has not yet been able to secure a permanent placement in mainstream clinical diagnostic regimens. To bridge this gap between AI and medical experts, Explainable AI (XAI), a relatively new subdomain of AI, seems very promising Jin et al. (2022); Herent et al. (2018); Holzinger et al. (2017).

3.5 The future

AI has revolutionized the world and will continue to do so in the near future, thus enabling new applications that were previously considered science fiction. Simple, robust, and efficient systems can be developed in every field, and medicine is no exception. It would not be over-optimistic to anticipate a single generic framework for the diagnosis of multiple neurological disorders using MRI becoming available to neurologists and radiologists, to assist in quickly reaching concrete diagnoses of intricate neurological disorders. From a broader perspective, a single application capable of diagnosing every medical condition worldwide using a vast variety of human biomarkers, including speech, gait, facial expressions, MRI, X-rays, ultrasound, blood work, and other medical reports as well as patient history, physical interactions, and activities, does not seem far-fetched. Given the huge amount of data and tremendous readily available processing capabilities, such an application could contain a massive network ensemble of multiple modalities used concurrently to achieve a pinpoint diagnosis. The integration of XAI Ker et al. (2017); Miotto et al. (2018); Lundervold and Lundervold (2019) would be the crowning achievement, affording confidence to patients and doctors by providing the reasons for diagnoses, rather than the conventional “Black box” approach Zhang et al. (2021). This omnipotent network would dynamically update its training and disease pool databases with new data, making it the complete physician’s assistant and serving humanity by alleviating diseases.

Recently techniques including Fuzzy logic and Quantum transfer learning have also been observed to gain momentum in CAD research for neurological disorders. Alsharabi et al. (2023) proposed an integration of quantum computing phenomena with deep neural networks for the differential diagnosis of AD and PD using brain MRI. Their AlexNet-quantum transfer learning approach achieved a classification accuracy of 97% and 96% for PD and AD respectively, with high-speed computational power as an added benefit for real time deployment and use. Yao et al. (2023) used Fuzzy theory to reorder and prioritize pixels

based on their most significant local information. This was followed by a VGG architecture for training. The results of their study claim to have an accelerated model convergence along with improvements in classification performance of AD stages using brain MRI. Sharma et al. (2022) also proposed a system to distinguish between AD, MCI and HC. They used a DL model for feature extraction and fuzzy hyperplane based least square twin support vector machine (FLS-TWSVM) for the classification of the extracted features for early diagnosis of AD, with an accuracy of up to 97.29%. Iqbal et al. (2024) addressed the issues of noise and fuzzy boundaries in brain MRI, and interpretability, by proposing a combination of Hybrid Parallel Fuzzy CNN (HP-FCNN) with Adaptive Class Activation Mapping (AD-CAM). Their system claims to outperform classical architectures including ResNet, DenseNet, VGG, and EfficientNet, with an accuracy of 96.81%, along with the valuable addition of explainability which is an indispensable requirement of the hour for such CAD tools to enter routine healthcare regimens.

Data scientists and radiologists have diverse and sometimes contradictory opinions on AI and its potential, particularly in medical applications. During this study, a survey was conducted by radiologists, and expert opinions were requested on whether AI-based tools to examine MR images would be helpful in diagnosing multiple neurological disorders. Their interests and anticipation were found to be overwhelming, with many concerns pertaining to the accuracy of such frameworks, if developed. Skepticism has also been expressed. As an example, the comments from Dr. Shahabuddin Siddiqui, Specialist in Diagnostic Radiology, at the Pakistan Institute of Medical Sciences Hospital, Islamabad, Pakistan, are as follows: *“It is a good idea to develop an app that can read images of the brain and diagnose certain diseases. However, in practice, I do not think it will work for all diseases. Most diseases do not exhibit typical imaging patterns. The signal characteristics and location of the disease process can vary significantly among patients. Therefore, more than one image reader application is required to diagnose a disease accurately. Having background knowledge and experience in clinical neurology and radiology remains the most important factor in patient diagnosis.”* However, radical opposition has emerged and stern comments from data scientists have been noted. Zaharchuk et al. (2018) found that *“DL has the potential to revolutionize all industries, including medical imaging. Given the centrality of neuroimaging in the diagnosis and treatment of neurological diseases, DL is likely to affect neuroradiologists first and most profoundly. One concern is that, if these approaches are successful, some of the work that radiologists have traditionally performed may become obsolete.”* Korfiatis and Erickson (2019) present an even stronger statement: *“There has been a revolution in the world of computer science with new formulations of DL technology achieving performance that exceeds humans in identifying the content in images. This revolution has led some researchers to predict that computers will replace radiologists.”* Others Bakator and Radosav (2018); Zhang and Sejdíć (2019); Chauhan and Choi (2019); Mazurowski et al. (2019); Yao et al. (2020); Lima et al. (2022) believe more in a meet-in-the-middle approach, stating *“Despite the limitations, the advantages of DL far outweigh its shortcomings, and thus, it will become an essential tool for diagnosis and prognosis in the era of precision medicine. Future research teams in medical imaging should integrate DL experts in addition to clinical scientists in their teams to fully harness the potential of DL.”* Kim et al. (2018) and *“With the clearer pathogenesis of human brain disorders, the further development of DL techniques, and larger open source datasets, a human-machine collaboration for medical diagnosis and treatment will ultimately become a symbiosis in the*

future.” Zhang et al. (2020) This undoubtedly presents a wide window of opportunity and invites research into the development of a unified framework capable of classifying multiple neurological disorders with reasonable accuracy to function as a robust and reliable assistive tool for neurologists. To minimize misdiagnoses, the combination of their experience and the machines’ capabilities for analyzing humanly imperceptible pixel-level differences in images would reduce invalid diagnoses for diseases with overlapping MRI abnormalities and features.

4 Conclusion

This review provides an in-depth exploration and synthesis of existing CAD research on neurological disorders, with a particular focus on DL-based frameworks. Our analysis reveals several key insights:

1. **Current State of DL-based CAD Systems:** Most DL-based CAD systems are designed to diagnose a single neurological disease or its subtypes with a reasonable degree of accuracy. However, these systems often fall short when applied to multiple neurological disorders, primarily due to limitations in the datasets used for training and the complexity of the conditions. Statistically, around 64% articles presented systems for single disease diagnosis, whereas a meager 7% experimented with CAD of more than 3 disorders. Out of the 36 multiple disease diagnosis articles discussed in this paper, 26 articles worked with the sub-types or stages of a single disease. Moreover, no publicly available tool capable of diagnosing multiple neurological disorders using brain MRI was found.
2. **Challenges in Multimodal Diagnosis:** We highlight a significant gap in the ability of current CAD systems to handle a wide range of neurological disorders concurrently. Systems capable of diagnosing multiple diseases are either restricted by the number of diseases they can handle or by the limited and often biased datasets used for training, which in turn hampers their effectiveness in clinical settings.
3. **Potential of DL Frameworks:** Despite these challenges, there is promising evidence that a DL-based framework could be developed to function as an assistive tool for neurologists. Such a framework could facilitate the timely and accurate diagnosis of complex neurological conditions from MRI signals, thus improving patient outcomes. We point out that leveraging massive, publicly available datasets across multiple diseases could enable the development of more generic and robust models.
4. **Future Directions:** To address the current limitations, researchers should focus on creating CAD systems that are trained on diverse and extensive datasets, allowing them to be more generalizable across different neurological conditions. Additionally, the implementation of these systems in real-time frameworks could pave the way for their commercial use, making them accessible to a broader range of medical practitioners.
5. **Impact on Clinical Practice:** The deployment of a universally accessible, single imaging modality for the diagnosis of a broad spectrum of neurological disorders could significantly enhance the early detection and treatment of these conditions. This would not only improve the accuracy of diagnoses but also increase the chances of curing or containing the diseases, ultimately leading to a better quality of life for many patients.

In summary, while the current state of DL-based CAD systems shows great potential, there remains a need for further research and development to create more comprehensive and reliable diagnostic tools. The findings from this review, coupled with insights from medical experts, suggest that these advancements are within reach and could revolutionize the way neurological disorders are diagnosed and treated.

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Declarations

Conflict of interest The authors have no conflict of interest to declare.

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