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Artificial Intelligence Techniques for Automated Diagnosis of Neurological Disorders

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Keywords
Neurological disorder · Computer-aided diagnosis · Machine learning · Classification algorithm

Abstract
Background: Authors have been advocating the research ideology that a computer-aided diagnosis (CAD) system trained using lots of patient data and physiological signals and images based on adroit integration of advanced signal processing and artificial intelligence (AI)/machine learning techniques in an automated fashion can assist neurologists, neurosurgeons, radiologists, and other medical providers to make better clinical decisions. ***Summary:*** This paper presents a state-of-the-art review of research on automated diagnosis of 5 neurological disorders in the past 2 decades using AI techniques: epilepsy, Parkinson's disease, Alzheimer's disease, multiple sclerosis, and ischemic brain stroke using physiological signals and images. Recent research articles on different feature extraction methods, dimensionality reduction techniques, feature selection, and classification techniques are reviewed. ***Key Message:*** CAD systems using AI and advanced signal processing techniques can assist clinicians in analyzing and interpreting physiological signals and images more effectively.

Introduction

Neurological disorders are the diseases connected with peripheral and central nervous systems. The common symptoms include muscle weakness, paralysis, seizures, pain, poor coordination, and loss of consciousness [1]. There are >600 diseases related to the nervous system such as brain tumor, Parkinson's disease (PD), Alzheimer's disease (AD), multiple sclerosis (MS), epilepsy, dementia, headache disorders, neuroinfections, stroke, and traumatic brain injuries among others. Various viral infections (i.e., HIV, Zika, West Nile Virus, Enteroviruses), bacterial infections (such as *Neisseria meningitides* and *Mycobacterium tuberculosis*), fungal-related infections (such as *Aspergillus* and *Cryptococcus*), and parasitic infections (such as Chagas and malaria) can affect the entire

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nervous system [1–6]. The aforementioned neurological symptoms possibly occur due to immune response or infection itself. Hundreds of millions of people worldwide are affected by neurological disorders [7–10]. More than 6 million people die because of stroke each year; majority of these deaths take place in low- and middle-income countries [1, 11, 12]. It is reported that around 50 million people will have epilepsy [1], and 47.5 million people will suffer from dementia [1, 13–17].

The abnormal or the anomalous neurological conditions are commonly identified by a neuropathological examination. Anomalous neurological conditions are found in majority of the population and are not always associated with a neurological disorder [18].

Dementia is usually progressive in nature. The dementia syndromes disturb multiple cortical functions, that is, memory, orientation, thinking, calculation, language, comprehension, judgment, and learning capacity. AD is found to be the most common cause of dementia, which is characterized by neurofibrillary and cortical amyloids accounting for 3 quarters of the cases [16, 19, 20]. Dementia affects mainly older people, above 65 years, but also 2% of the people under 65 years old. The prevalence of dementia doubles with age every 5 years. A genetic polymorphism increases the risk for 25% of entire population [21, 22].

Epilepsy, a chronic neurological disorder, is defined as, "*disorder of brain characterized by enduring predisposition to generate the epileptic seizures*." [23–25]. The epilepsy definition requires at least occurrence of one epileptic seizure [26, 27]. It affects both male and female sexes and people of all ages. The diagnosis for epileptic seizures is performed by first determining the event of epilepsy and later differentiating between the conditions called provoked or chronic epileptic seizures [28, 29]. The overall incidence of epilepsy is found to be 23–190 per 100,000 of population [30]. The prevalence is lower in early ages and gradually increases with aging [31–34]. Since the pioneering work of Adeli et al. [35], wavelet transform (WT) has been used extensively for electroencephalogram (EEG) analysis, seizure detection, and epilepsy diagnosis [36, 37]. Kugiumtzis et al. [27] investigate the dynamics of epileptiform discharges induced by transcranial magnetic stimulation in epilepsy. Yuan et al. [38] present a method for epileptic seizure prediction using diffusion distance and Bayesian linear discriminate analysis [39] in intracranial EEG.

MS, a disorder caused by a condition called inflammatory demyelinating of the nervous system, is the most common among all neurological disorders. MS causes disabilities in young adults and affects nearly 2.5 million people worldwide. The diagnosis of MS is generally performed by magnetic resonance imaging (MRI). There are no treatments available for this disease [40, 41].

PD is a chronic neurodegenerative disorder often characterized by the presence of predominantly motor symptomatology [42, 43], but it can have nonmotor hyposmia, paresthesia, depression, and pain [44]. PD is a universal disorder with incidence rate of 4.5–19 per 100,000 of population per year [45–47] for both females and males of all ages. The therapy depends on severity, mental status, and age of the patient. Gálvez et al. [48] investigate the short-term effects of Binaural Beats on EEG power, functional connectivity, cognition, gait, and anxiety in PD patients.

Stroke is a clinical syndrome of cerebral deficit that lasts for >24 h with no apparent cause except the vascular one [49]. In the modern developed countries, 75–80% of the strokes are attributed to brain ischemia, and 10–15% are attributed to intracerebral hemorrhage. Stroke diagnosis is made accurately completely based on clinical grounds by a specialist alone.

Traumatic brain injury is one of the foremost causes of disability and death in young adults and children worldwide. More than five million people suffer from the traumatic brain injury disability in the United States alone [50–52].

Authors have been advocating the research ideology that a computer-aided diagnosis (CAD) system trained using lots of patient data and physiological signals and images based on adroit integration of advanced signal processing and artificial intelligence (AI)/machine learning (ML) techniques in an automated fashion can assist neurologists, neurosurgeons, radiologists, and other medical providers to make better clinical decisions. Research in this area has been growing at an accelerating rate in the past decade. In this paper, authors explore and review recent articles on the applications of AI-based CAD systems for the diagnosis of 5 major neurological disorders: epilepsy, AD, PD, MS, and ischemic brain stroke.

Figure 1 shows the functional block diagram of a typical ML-based CAD system consisting of 5 stages: (1) signal transformation, (2) feature extraction, (3) feature dimensionality reduction, (4) optimal feature selection/ranking, and (5) classification.

ML-Based CAD

Input Data Description

Input data for a CAD system are normally signals and/or images. For PD, many CAD systems use speech and

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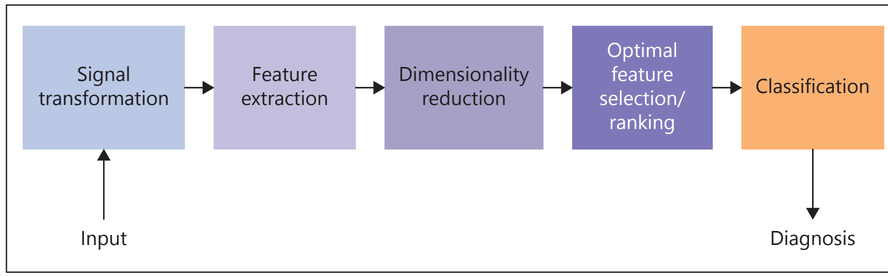

Fig. 1. General block diagram of a typical ML-based CAD system.

EEG for the diagnosis. Image-based approaches normally use MRI and single-photon emission computed tomography scan. For epilepsy, most authors have used Bonn University EEG data set [53]. In MS, T1 and T2 weighted MRI images are commonly used for the diagnosis, where T1 and T2 refer to the time taken between magnetic pulses and the image is taken. Most of the AD systems have used T2-weighted MRI images from Alzheimer Disease Neuro Imaging [54] and Open Access Series of Imaging Studies [55] databases.

Image Transformation

In general, image transformation is performed first where the redundant information is removed and then features are extracted from the transformed images. This step helps in gathering significant information that can be used for feature extraction.

Feature Extraction

Signal-Based Approach

Discrete wavelet transform (DWT) is often used to convert the signal to low- and high-frequency components [56–58]. The curvelet transform that is a higher dimensional DWT represents the images in multiple angles and scales [59]. The higher-order spectra (HOS) features are also used for feature representation and extraction [60, 61]. The extracted features must represent the hidden clues present in the input data.

Image-Based Approach

In image preprocessing methods, intensity normalization, adaptive histogram equalization [62], and background subtractions are performed prior to level set segmentation to detect the region of interest [63]. The gray level co-occurrence matrix features are most commonly used for the images [64]. The entropy and energy features are also used in many articles [65–70]. The wavelet-based energy and entropy features are also employed [71–74]. Various statistical measures such as Hu's moments [75], Zernike moments [76], central moments [77], and statistical moments [77] are used as features both in signal- and image- based approaches for developing CAD systems for neurological disorder.

Dimensionality Reduction

Feature extraction techniques often yield a large number of features that may be redundant and result in excessive computational requirements which in turn may make their real-time application impractical or unnecessarily difficult. Hence, various feature dimensionality reduction techniques are commonly used. The most commonly used methods are principal component analysis (PCA) [78], linear discriminant analysis [78], and independent component analysis [79]. Extended versions of PCA such as kernel PCA have also been employed in the literature [80].

Optimal Feature Selection and Ranking

Majority of features exhibit redundant information, which need to be removed to obtain optimum classification performance. The analysis of variance [81] is the most commonly used method when 3 or more classes are involved. Other commonly used optimal feature selection techniques are Student *t* test [82], entropy [83, 84], Wilcoxon rank tests [85–88], Bhattacharyya distance [89], receiver operating characteristic [90], genetic algorithm [91], particle swarm optimization [92, 93], and ant colony optimization [94]. A number of researchers have combined different selection methods in order to obtain the most significant features [95]. The fuzzy logic-based min-redundancy and max-relevance feature selection have been used for diagnosis of PD [96].

Feature Classification

Classification techniques generally have 2 phases: (i) training and (ii) testing. They need to be trained using previously collected data. Once trained, they can be used for classification of new cases. The most commonly used

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Table 1. Summary of CAD systems for diagnosis of epilepsy (modality: EEG)

Authors, years	Methodology/features	Classifier	Accuracy, %
Acharya et al. [149], 2009	CD, Hurst exponent (H), ApEn	GMM + SVM	$_{EPacc}$ = 100
Acharya et al. [150], 2011	WPD and HOS	Fuzzy	$_{EPacc}$ = 98.5
Acharya et al. [151], 2011	RQA features	SVM	$_{EPacc}$ = 95.6
Acharya et al. [152], 2012	Entropies + HOS + higuchi FD + hurst/nonlinear features	Fuzzy	$_{EPacc}$ = 99.7
Acharya et al. [153], 2012	Entropy parameters	Fuzzy	$_{EPacc}$ = 98.1
Acharya et al. [154], 2012	Eigen values + WPD coefficients + PCA	GMM	$_{EPacc}$ = 99
Acharya et al. [155], 2013	DWT + ICA	SVM	$_{EPacc}$ = 96
Aslan et al. [156], 2008	–	RBFNN + MLPNN	$_{EPacc}$ = 95.2
Chua et al. [157], 2011	HOS-based features	GMM	$_{EPacc}$ = 93.1
Faust et al. [158], 2010	Frequency parameters + Burg's method	SVM	$_{EPacc}$ = 93.3
Ghosh-Dastidar et al. [159], 2007	Mixed-band feature space	LMBPNN	$_{EPacc}$ = 96.7
Ghosh-Dastidar et al. [160], 2008	Mixed-band feature space + PCA	RBFNN	$_{EPacc}$ = 96.6
Ghosh-Dastidar et al. [161], 2009	Mixed-band feature space	MuSpiNN	$_{EPacc}$ = 94.8
Guler et al. [162], 2005	Lyapunov exponents	RNN	$_{EPacc}$ = 96.79
Guo et al. [163], 2009	Relative wavelet energy	ANN	$_{EPacc}$ = 95.2
Guo et al. [164], 2010	ApEn + wavelet transform	ANN	$_{EPacc}$ = 99.85
Guo et al. [165], 2010	Line length features + wavelet transform	ANN	$_{EPacc}$ = 99.6
Guo et al. [166], 2011	Genetic programming	KNN	$_{EPacc}$ = 99.2
Iscan et al. [167], 2011	Cross correlation and power spectral density	SVM	$_{EPacc}$ = 100
Kannathal et al. [168], 2005	Entropy measures	ANFIS	$_{EPacc}$ = 90
Lima et al. [169], 2010	DWT	SVM	$_{EPacc}$ = 100
Martis et al. [170], 2012	EMD	C4.5	$_{EPacc}$ = 95.33
Nigam and Graupe [171], 2004	Nonlinear filter	LAMSTAR ANN	$_{EPacc}$ = 97.2
Orhan et al. [172], 2011	DWT and K-means clustering	MLPNN	$_{EPacc}$ = 100
Polat and Gunes [173], 2007	FFT	DT	$_{EPacc}$ = 98.72
Polat and Gunes [174], 2008	FFT + PCA	AIRS	$_{EPacc}$ = 100
Polat and Gunes [175], 2008	AR	C4.5	$_{EPacc}$ = 99.32
Sadati et al. [176], 2006	DWT	ANFN	$_{EPacc}$ = 85.9
Srinivasan et al. [177], 2005	Time and frequency domain features	EN	$_{EPacc}$ = 99.6
Srinivasan et al. [178], 2007	ApEn	PNN, EN	$_{EPacc}$ = 100
Subasi [179], 2007	DWT + statistical measures	ME	$_{EPacc}$ = 94.5
Subasi and Gursoy [180], 2010	DWT + PCA	SVM	$_{EPacc}$ = 100
Tzallas et al. [181], 2007	Time–frequency methods	ANN	$_{EPacc}$ = 99.28

Table 1. (continued)

Authors, years	Methodology/features	Classifier	Accuracy, %
Jaiswal and Banka [182], 2017	SpPCA and SubXPCA	SVM	$_{EPacc}$ = 94.60
Ubeyli [183], 2010	AR	LS-SVM	$_{EPacc}$ = 99.56
Wang et al. [184], 2011	Wavelet + entropy	KNN + HKB	$_{EPacc}$ = 100
Swami et al. [185], 2016	DTCWT	GRNN	–
Peker et al. [186], 2016	DTCWT	CVNN	$_{EPacc}$ = 100
Sharma and Pachori [187], 2017	TQWT	LS-SVM + FD	$_{EPacc}$ = 100
Patidar et al. [188], 2017	TQWT and kraskov entropy	LS-SVM	$_{EPacc}$ = 97.75
Gandhi et al. [189], 2011	DWT, energy, SD, entropy	PNN	$_{EPacc}$ = 99.9
Chen [190], 2014	DTCWT, fourier features	NN	$_{EPacc}$ = 100
Swami et al. [191], 2014	Energy, SD, entropy features	SVM	$_{EPacc}$ = 99.53
Pachori and Patidar [192], 2014	EMD and SODP	ANN	$_{EPacc}$ = 100
Sharma and Pachori [193], 2015	EMD and PSR of IMF	LS-SVM	$_{EPacc}$ = 98.67
Bhattacharyya et al. [194], 2017	TQWT and KNN entropies	SVM	$_{EPacc}$ = 100
Bhattacharyya et al. [195], 2016	Empirical wavelet transform	LS-SVM	$_{EPacc}$ = 90
Bhati et al. [196], 2017	Time–frequency localized three-band biorthogonal linear phase wavelet filter bank	MLPNN	$_{EPacc}$ = 99.33
Sharma et al. [197], 2017	Orthogonal wavelet filter banks	LS-SVM	$_{EPacc}$ = 94.25
Kaya et al. [198], 2014	1D – LBP	FT	$_{EPacc}$ = 99.5
Zhu et al. [199], 2014	FWHVA	KNN	$_{EPacc}$ = 100
Samiee et al. [200], 2015	DSTFT	MLPNN	$_{EPacc}$ = 99.8
Riaz et al. [201], 2016	EMD	SVM	$_{EPacc}$ = 96.2
Diykh et al. [202], 2017	Weighted complex network combined with time domain features	LS-SVM	$_{EPacc}$ = 98
Li et al. [203], 2017	MODWT and LND	RFC	$_{EPacc}$ = 100
Acharya et al. [7]	–	CNN	$_{Eac}$ = 88.7
Ghayab et al. [205], 2016	SRS and SFS	LS-SVM	$_{EPacc}$ = 99.9
Sharma et al. [206], 2018	MMSFL-OWFB based KE	SVM	$_{EPacc}$ = 100
Tiwari et al. [207], 2017	Pyramid scheme for key-point localisation and LBP	SVM	$_{EPacc}$ = 99.89
Bajaj and Pachori [208], 2012	EMD based intrinsic mode functions and hilbert transform	LS-SVM	$_{EPacc}$ = 100
Nicolaou and Georgiou [209], 2012	Permutation entropy	SVM	$_{EPacc}$ = 93.55
Xie and Krishnan [210], 2013	Wavelet-based sparse functional linear model	KNN (1NN)	$_{EPacc}$ = 100
Mursalin et al. [211], 2017	ICFS	RFC	$_{EPacc}$ = 100
Upadhyay et al. [212], 2016	DWT based features	LS-SVM	$_{EPacc}$ = 100

Table 1. (continued)

Authors, years	Methodology/features	Classifier	Accuracy, %
Kabir et al. [213], 2016	Optimum allocation technique	LMT	$_{EPacc}$ = 95.33
Murugavel and Ramakrishnan [214], 2016	Wavelet transform based features	H-MSVM with ELM	$_{EPacc}$ = 93.63
Pippa et al. [215], 2016	Time domain and frequency domain features	Bayesian net	$_{EPacc}$ = 95
Kumar et al. [216], 2014	LBP	kNN (1-NN)	$_{EPacc}$ = 98.33
Naser et al. [217], 2019	DWT and approximation and abe entropies	SVM	$_{EPacc}$ = 98.75
Tzimourta et al. [218], 2018	Wavelet transform based features	Random forest classifier	$_{EPacc}$ = 95
Lamhiri and Shmuel [219], 2019	Hurst exponent	k-NN	$_{EPacc}$ = 100
Raghu et al. [220], 2019	Sigmoid entropy	SVM	$_{EPsen}$ = 100
Wang et al. [221], 2019	Symlet wavelet processing, and grid search optimizer	Gradient boosting machine	$_{EPacc}$ = 96.5
Bose et al. [222], 2019	Multifractal detrended fluctuation analysis	SVM	$_{EPacc}$ = 100
Dalal et al. [223], 2019	FAWT and FD	RELS-TSVM	$_{EPacc}$ = 90.2
Sriam et al. [224], 2018	Teager energy feature	Supervised back propagation neural net-work	$_{EPsen}$ = 96.66
Shaikh et al. [225], 2017	EMD	ANN	$_{EPacc}$ = 96.1
Osman and Alzahrani [226], 2019	SOM	RBFNN	$_{EPacc}$ = 97.47
Sudalaimani et al. [227], 2018	Sub-frequency band features	GRNN	$_{EPacc}$ = 91.6
Raghu and Sriram [228], 2018	NCA	SVM	$_{EPacc}$ = 98.8
Li et al. [37], 2018	GMM and GLCM features, RFE-SVM	SVM	$_{EPacc}$ = 100
Cooman et al. [229], 2018	HRI features	SVM + Adaptive Heuristic classifier	$_{EPsen}$ = 83.3
Li et al. [230], 2018	WPT and KDE	LS-SVM	$_{EPacc}$ = 99.6
Cruz et al. [231], 2018	ACC and EMG	SVM on cloud computing platform	$_{EPsen}$ = 83.3
Kocadagli and Langari [232], 2017	DWT and fuzzy relations	ANN	$_{EPacc}$ = 99.9
Zhang et al. [233], 2018	WPD, fDistIn	kNN	$_{EPsen}$ = 98.33
Feng et al. [234], 2018	WPD	SVM	$_{EPacc}$ = 98.67
Tanveer et al. [235], 2018	FAWT and entropy-based features	RELS-TSVM	$_{EPacc}$ = 100
Choudhury et al. [236], 2018	XHST	kNN	$_{EPacc}$ = 100
Torse et al. [237], 2017	EMD	CSM-SVM	$_{EPacc}$ = 96.4
Tomanik et al. [238], 2019	Complex networks	–	$_{EPacc}$ = 98.2
Wani et al. [239], 2018	DWT	ANN	$_{EPacc}$ = 95

Table 1. (continued)

Authors, years	Methodology/features	Classifier	Accuracy, %
Deep learning based techniques			
Yuan et al. [136], 2017	STFT-Mssda	Softmax	$_{\text{EPacc}}$ = 93.82
Ullah et al. [137], 2018	P-1D-CNN		$_{\text{EPacc}}$ = 99.9
Johansen et al. [135], 2016	CNN		$_{\text{AUC}}$ = 94.7
Antoniades et al. [134], 2016	CNN		$_{\text{EPacc}}$ = 87.51
Qi et al. [240], 2014	MCC-based R-SAE model	SVM	$_{\text{EPsen}}$ = 100
Lin et al. [241], 2016	SSAE	Softmax	$_{\text{EPacc}}$ = 96
Gogna et al. [242], 2017	Semi-supervised stacked autoencoder		$_{\text{EPacc}}$ = 96.9
Acharya et al. [9], 2018	CNN		$_{\text{EPacc}}$ = 88.67
Tjepkema-Cloostermans et al. [139], 2018	Convolutions (1D and 2D) and/or LSTMs		$_{\text{EPspe}}$ = 99.9
Hussein et al. [243], 2019	LSTM + FC		$_{\text{EPspe}}$ = 100
Thodoroff et al. [244], 2016	CNN + RNN		$_{\text{EPsen}}$ = 85
Emami et al. [245], 2019	CNN		$_{\text{Detection rate}}$ = 100
Van Putten et al. [139], 2018	CNN + RNN		$_{\text{EPspe}}$ = 100
Jang and Cho [246], 2019	Dual deep neural network	–	$_{\text{EPsen}}$ = 100
Zuo et al. [247], 2019	CNN	–	$_{\text{EPsen}}$ = 83.23
Wei et al. [248], 2016	Multichannel CNN	–	$_{\text{EPacc}}$ = 92.40
Achilles et al. [249], 2016	CNN	–	$_{\text{AUC}}$ = 78.33
Yuvaraj et al. [250], 2018	CNN	–	$_{\text{EPsen}}$ = 86.29
Maria Hugle et al. [251], 2018	CNN	–	$_{\text{EPsen}}$ = 96
Thomas et al. [252], 2018	CNN	SVM	$_{\text{EPacc}}$ = 83.86

CAD, computer aided diagnosis; CD, correlation dimension; EEG, electroencephalogram; ApEn, approximate entropy; SVM, support vector machine; RQA, recurrence quantification analysis; HOS, higher order spectra; PCA, principal component analysis; KNN, k-nearest neighbour; DWT, discrete wavelet transform; ICA, independent component analysis; GMM, gaussian mixer model; PNN, probabilistic neural network; SRS, simple random Sampling; SFS, sequential feature selection; HRI, heart rate increases; XHST, cross hyperbolic S-transform; CNN, convolutional neural network.

classifiers for diagnosis of the neurological disorder are probabilistic neural network classifier [97], support vector machine (SVM) with different kernel functions such as polynomial (Poly) of orders 1, 2, and 3 [58, 98], Naive Bayes [99, 100], k-nearest neighbor [101], linear discriminant analysis, quadratic discriminant analysis [102], decision tree [101], random forest, and Gaussian mixer model [103, 104]. Among these, SVM classifier is one of the most commonly used. More recently, enhanced probabilistic neural network has been used for accurate diagnosis of PD [105].

The consolidated lists of various machine ML-based CAD systems for the diagnosis of neurological disorders are presented in Tables 1–7 for epilepsy, PD, AD, ischemic brain stroke, and MS.

Deep Learning-Based Techniques

To solve the limitations of ML-based techniques, deep learning techniques have recently been advanced. An example of deep learning is the convolutional neural network

Table 2. Summary of CAD systems for diagnosis of PD using measurable indicators (modality: EEG)

Authors, years	Methodology/features	Classifier	Accuracy, %
Yuvaraj et al. [253], 2014	HOS (6 basic emotional states)	KNN, SVM	PDacc: 93.42 (happiness)
Yuvaraj et al. [254], 2014	BNoA (bispectrum feature), ICA	SVM, RBF	PDacc: 76.90±1.08
Yuvaraj et al. [255], 2016	Bispectral functional connectivity index	SVM	PDacc: 51.66±1.02
Nilashi et al. [256], 2017	Data mining technology	CART	–
Tucker et al. [257], 2015 (modality: sensors)	Data mining driven technology	Naïve Bayes	PDacc: 78.00
Prashantha et al. [258], 2018	Machine learning techniques	Logistic regression, random forests, boosted trees, SVM	Acc: >95
Deep learning based techniques			
Ali et al. [259], 2016	DBF (handwriting analysis)	–	Acc: 94.00
Caliskan et al. [260], 2017	Deep neural network (speech dataset)	Softmax classifier	Acc: 86.09, sensitivity: 58.27, specificity: 95.38
Grover et al. [261], 2018	Deep neural network (voice data)	UPDRS	Total UPDRS accuracy: 62.73

CAD, computer-aided diagnosis; PD, Parkinson's disease; EEG, electroencephalogram; HOS, higher-order spectra; ICA, independent component analysis; DBF, deep belief network; SVM, support vector machine.

Table 3. Summary of CAD systems for the detection of PD using brain images (modality: MRI)

Authors, year	Methodology/features	Classifiers	Accuracy, %
Oliveira et al. [262], 2015	Voxel features	SVM	PDacc: 97.86, PDsen: 97.75, PDspe: 98.09
Hirschauer et al. [105], 2015	–	EPNN	PDacc: 92.50
Banerjee et al. [263], 2016	CDT + FA	PGA	PDacc: 98.53, PDsen: 98, PDspe: 100
Cigdem et al. [264], 2018	GM + WM + PCA	SVM	PDacc: 93.75, PDsen: 95, PDspe: 92.50
Segovia et al. [265], 2015 (modality: PET CT)	NB	SVM	PDacc: 78.16
Ahmadlou et al. [266], 2010 (modality: SPECT)	Gaussian Kernel	–	PDacc: 92.5
Deep learning-based techniques			
Choi et al. [267], 2017 (modality: SPECT)	Deep neural network	Softmax classifier	Acc: 98.8, sensitivity: 98.6, Specificity: 100
Sivaranjini et al. [268], 2019	CNN	Alexnet	Acc: 88.90, sensitivity: 84.40, specificity: 884.40

CAD, computer-aided diagnosis; PD, Parkinson's disease; MRI, magnetic resonance imaging; PCA, principal component analysis; NB, Naive Bayes; CNN, convolutional neural network; SVM, support vector machine; PGA, principal geodesic analysis.

Table 4. Summary of CAD systems for the detection of PD using physiological signals (modality: EEG)

Authors, year	Methodology/features	Classifiers	Accuracy, %
Han et al. [269], 2013	WPE	AR Burg	–
Yuvaraj et al. [270], 2016	HOS, PD diagnosis index	SVM	PDacc: 99.62, PDsen: 100, PDspe: 99.25
Hariharan et al. [271], 2014	Dysphonia + GMM + PCA + LDA + SFS	SVM	PDacc: 100
Zhang et al. [272], 2017	Dysphonia + stacked autoencoders	KNN	PDacc: 94–98
Hlavnicka et al. [273], 2017	Zero-crossing rate + VAC function	GMM	PDacc: 71.30, PDsen: 56.70, PDspe: 80
Joshi et al. [274], 2017	DWT	SVM	PDacc: 90.32
Ornelas-Vences et al. [275], 2017	Turn analysis + biomechanical features	Fuzzy model	–
Sama et al. [276], 2017	Butterworth filter	SVM	PDacc: <90
Oung et al. [277], 2018	EWPT, wavelet energy, entropy	ELM	PDacc: 95.93
Little et al. [278], 2019	Preselection filter, exhaustive Search	SVM	PDacc: 91.4
Shahbaba and Neal [279], 2009	Dirichlet process mixtures	Decision tress, SVM	PDacc: 87.70
Das [280], 2010	Back-propagation learning algorithm	ANN	PDacc: 92.9
Sakar and Kursun [281], 2010	Mutual information-based feature selection	SVM	PDacc: 92.75
Psorakis et al. [282], 2010	Improved mRVMs	SVM	PDacc: 89.47
Guo et al. [283], 2010	Genetic programming and the expectation maximization algorithm	GP-EM	PDacc: 93.10
Ozcift and Gulten [284], 2011	CFS	RF	PDacc: 87.10
Li et al. [285], 2011	Fuzzy-based nonlinear transformation	SVM	PDacc: 93.47
Luukka [286], 2011	Fuzzy entropy measures	Similarity classifier	PDacc: 85.03
Spadoto et al. [287], 2011	PSO, harmony search, gravitational search	Optimum path forest classifier	PDacc: 73.53
Astrom and Koker [288], 2011	Nine layer neural networks	PNN	PDacc: 91.20
Ozcift [289], 2012	RF ensemble of IBk (a KNN variant) algorithm	SVM	PDacc: 97.00
Polat [290], 2012	FCMFW	KNN	PDacc: 97.93
Tsanas et al. [291], 2012	Feature selection: LASSO, mRMR, RELIF, LLBFS	SVM	PDacc: ~90.00
Daliri [292], 2013	STFT, FDR	SVM	PDacc : 91.20
Chen et al. [293], 2013	PCA	FKNN	PDacc: 96.07
Zuo et al. [294], 2013	PSO	FKNN	PDacc: 97.47
Ma et al. [295], 2014	SCFW	KELM	PDacc: 99.49
Drotár et al. [296], 2016	Entropy and energy	SVM, RBF	PDacc: 81.30
Connolly et al. [297], 2015 (modality: sensors)	Feature reduction	SVM	–
Wahid et al. [298], 2015	Neural networks	SVM	PDacc: 86.00

Table 4. (continued)

Authors, year	Methodology/features	Classifiers	Accuracy, %
Smith et al. [299], 2015 (modality: sensors)	Evolutionary algorithms	ROC	PDacc: 78.00
Hirschauer et al. [105], 2015	Neural networks	EPNN	PDacc: 92.5
Shamir et al. [300], 2015	Clinical decision support systems	SVM	PDacc: 71.00
Procházka et al. [301], 2015 (modality: sensors)	Bayesian	Bayesian probability classifiers	PDacc: 94.1
Nilashi et al. [302], 2018	Partial least squares, self organizing map	SVM	UPDRS acc: 46.56
Deep learning based techniques			
Tagaris et al. [140], 2017	Deep neural network	CNN-RNN	Acc: 74
Kim et al. [303], 2018	Neural networks	CNN	PDacc: 85
Oh [304], 2018	CNN	–	Acc: 88.25, sensitivity: 84.71, specificity: 91.77

CAD, computer aided diagnosis; ICA, independent component analysis; EEG, electroencephalogram; HOS, higher order spectra; PD, Parkinson's disease; WPE, wavelet packet entropy; SVM, support vector machine; GMM, gaussian mixture model; KNN, k-nearest neighbour; DWT, discrete wavelet transform; CNN, convolutional neural network; PSO, particle swarm optimization; PNN, probabilistic neural network; PCA, principal component analysis.

(CNN) with a number of advantages over conventional ML-based CAD systems. First and foremost is that it can handle large data sets using its multilayer architecture. It can also handle imbalanced data samples and execute the results without biasing toward majority class. The CNN architecture generally includes a convolution layer, a pooling layer, and fully connected layers [106]. These layers can be extended with few additional layers based on the requirements. Recently, various CNN-based techniques have shown good results in detecting neurological disorders [107–116]. But, detection of such abnormalities in its early stage may require more deeper architecture. Such deeper architecture can pick distinct features from the signals by convolving with kernels defined in each layers [106].

In the past few years, deep neural network learning techniques have been used to solve intractable problems in a variety of disciplines such as image recognition [117–119], pavement crack detection [120], structural damage detection [121, 122], vehicle-type detection [123], transportation systems [124, 125], concrete strength estimation [126], big data time series forecasting [127], and computer-brain interface [128]. Following that trend, a number of researchers have developed CAD systems using deep learning techniques. These techniques can discover structures or patterns in the biological signals or images. Its effectiveness in signal and image-based CAD systems has been demonstrated recently [117, 127, 129–133].

Deep learning techniques can be broadly classified into 2 types: (1) supervised learning and (2) unsupervised learning. The CNN belongs to the first and auto encoders belong to second type. Antoniades et al. [134] analyze the epileptic intracranial EEG data using deep learning. Johansen et al. [135] use CNN for epileptiform spike detection. Yuan et al. [136] employ a combination of deep learning and short-time Fourier transform for epileptic seizure detection. Ullah et al. [137] report application of deep learning for epilepsy diagnosis. Martinez-Murcia et al. [138] employ the CNN for analysis of neuroimaging in PD.

The most common architecture of CNN includes a bank of convolution, max-pool, fully connected, and softmax layers as shown in Figure 2 [129–131]. The 3D CNN and CNN – Recurrent neural network (RNN) are more recent networks used in the diagnosis of epilepsy [139], PD [140] and AD [141]. Other CNN variants are also experimented on PD and ischemic brain stroke detection. The list of approaches used is presented in Tables 1–7. It

Table 5. Summary of CAD systems for the detection of AD (modality: MRI)

Authors, years	Methodology/features	Classifier	Accuracy, %
Al-nuaimi et al. [305], 2015	Tsallis entropy	K-means clustering	ADacc: 77
Silveira and Marques [306], 2010 (modality: PET CT)	Boosting classification method	Boosting classifier	ADacc: 90.97 MCIacc: 79.63
Mahanand et al. [307], 2011	PCA + VBM + ANN	SRAN	Eff: 91.18
Mahmood and Ghimire [308], 2013	PCA + ANN	Feed forward multilayer neural network	ADacc: 90
Yi Ding et al. [309], 2015	VBM + GLCM + gabor filters	SVM	ADacc: 92.86
Herrera et al. [310], 2013	DWT + PCA	SVM	ADacc: 93.90
Sweety and Jiji [311], 2014	PCA + PSO	SVM + decision tree classifier	ADacc: 91.89
Saraswathi et al. [312], 2013	PSO + VBM	GA-ELM-PSO classifier	ADacc: 94.57
Mahanand et al. [313], 2013	VBM + ICGA + ELM	ELM classifier	ADacc: 91.86
Mahanand et al. [314], 2014	VBM + RFE	PBL-McRBFN classifier	ADacc: 89.81
Mathew et al. [315], 2016	DWT + PCA + FDR	SVM	ADacc: 84
Escudero et al. [316], 2013	Machine learning biomarkers	Locally weighted learning	ADacc: 80
Gunawardena et al. [317], 2016	CNN	SVM	Error: 13.13
Zhang et al. [318], 2017	PCA	SVM	ADacc: 84.40
Escudero et al. [319], 2011	K-means clustering + bioprofile analysis	Semi-supervised classifier	–
Zhang et al. [320], 2016	Landmark-based AD diagnosis system	SVM	ADacc: 83.7
Iftikhar et al. [321], 2016	Cortical thickness-based features + volume based features + F-score method	SVM	ADacc: 83.65
Bates et al. [322], 2011	Point-cloud laplacian + spectral signatures + shape analysis	Linear SVM	ADacc: 77.5
Ye et al. [323], 2011	KNN + RAVENS maps + ISOMAP algorithm	LapSVM	ADacc: 94.1
Rabeh et al. [324], 2017	NLMS	Bayes probability	ADacc: 92
Ullah et al. [325], 2018	CNN	SVM	ADacc: 80.25
Donini et al. [326], 2016	MKL RFE	SVM RFE	ADacc: 96.14±3.55
Deep learning based techniques Sarraf et al. [327], 2016	CNN	LeNet and GoogleNet binary classifier	ADacc: 99.9 (fMRI) AD acc: 98.84 (MRI)
Cheng and Liu [129], 2017 (Modality: PET CT)	3D-CNN	–	ADacc: 92.2 ADsen: 91.4 ADspe: 92.4
Cullen et al. [130], 2018	CNN	–	ADmean: 0.9969 ADSD: 0.0018

Table 5. (continued)

Authors, years	Methodology/features	Classifier	Accuracy, %
Islam et al. [131], 2018	DCNN	Softmax classifier	ADacc: 93
Liu et al. [141], 2018	CNN-RNN	Softmax classifier	ADacc: 91.2 ADsen: 91.4 ADspe: 91.0
Liu et al. [328], 2018	Cascaded CNN	Softmax classifier	ADacc: 93.26 ADsen: 92.55 ADspe: 93.94
McCrackin et al. [329], 2018	CNN	–	–
Basaia et al. [330], 2019	CNN	–	ADacc: 99.2 ADsen: 98.9 ADspe: 99.5
Hosseini-Asl et al. [331], 2016	CNN	3D-ACNN	ADacc: 97.60
Awate and Bangare [332], 2018	CNN	Softmax classifier	ADacc: 99
Billones et al. [333], 2016	CNN	DemNet	ADacc: 98.33 ADsen: 98.89 ADspe: 97.78
Gunawardena et al. [334], 2017	CNN	Fully connected layer	ADacc: 96.50 ADsen: 96.00 ADspe: 98.00
Farooq et al. [335], 2017	CNN	GoogLeNet	ADacc: 98.8
Luo et al. [336], 2017	CNN	Fully connected layer	ADsen: 100 ADspe: 93.00
Lin et al. [337], 2018	CNN	–	ADacc: 79.9

CAD, computer-aided diagnosis; MRI, magnetic resonance imaging; DWT, discrete wavelet transform; PSO, particle swarm optimization; ICGA, integer coded genetic algorithm; RFE, recursive feature elimination; FDR, fisher discriminant ratio; CNN, convolutional neural networks; VBM, voxel-based morphometry; NLMS, non local means; MKL, multiple kernel learning.

is observed that, in general, CNN-based techniques outperformed conventional handcrafted techniques with the limitation of requiring more training samples to achieve the optimal performance.

Discussion

Research on automated CAD systems is more prevalent first on epilepsy followed by PD and then AD. For seizure detection and epilepsy diagnosis, they are based on EEG signals. For PD, they are developed using different modalities such as EEG, speech, handwriting, and brain images. The automated systems proposed in last 2 decades are summarized in Tables 1–7. Table 1 summarizes the application of AI techniques used for automated seizure detection and epilepsy diagnosis. It can be seen from Table 1 that WT is the dominant method for multiresolution analysis. The SVM and the back propagation neural network are more commonly used classifiers. Tables 2–4 summarize research on the automated diagnosis of PD using different modalities. WT, HOS coupled with entropy and energy features are found to perform well. SVM is the most commonly used classifier with different kernels for the diagnosis of PD.

For Alzheimer disease, DWT and different dimensionality reduction techniques have been widely used [19, 142–148]. The gray level co-occurrence matrix-based techniques with SVM classifier are the commonly used classifier techniques (Table 5).

Most of the ischemic brain stroke CAD systems are developed using fuzzy clustering and SVM and random forest classifiers (Table 6). It is observed that very little

Table 6. Summary of CAD systems for the detection of ischemic brain stroke (modality: MRI)

Authors, years	Methodology/features	Classifier	Accuracy, %
Li et al. [338], 2004	Manual lesion tracing	MSSC + PVVR	$BS_{similarity}$: 0.97
Filho et al. [339], 2017 (modality: CT)	ABTD extractor used to extract features	MLP, SVM, kNN, OPF, and Bayesian	BS_{acc}: 95
Lutsep et al. [340], 1997	Radiologic techniques	Acute stroke trearment (TOAST) classification scheme	
Wang et al. [341], 2013	Novel framework	LLC	
Alpert et al. [342], 2012	Probabilistic framework	Clustering algorithm	BS_{fscore}: 0.52
Ji et al. [343], 2017	Asymmetric Distribution	Gaussian Mixture Model	BS_{acc}: 5% more
Sridevi et al. [344], 2019	Image segmentation (ACM and SOM)	Supervised model	–
Agrawal et al. [345], 2014	OBPD method	FCM	–
Monteiro et al. [346], 2018	Novel hybrid GA-BFO-CM algorithm	l1 regularized logistic regression; decision tree; SVM; random forest; Xgboost	BS_{auc}: 0.936
MateSin et al. [347], 2001	Rule-based approach	Expert system	–
Ghosh et al. [348], 2011	HRS	Expert system	–
Mitra et al. [349], 2014	Bayesian-MRF	Random forest	$BS_{sensitivity}$: 0.53±0.13 $BS_{meanpositivevalue}$: 0.75±0.18
Maier et al. [350], 2015	FCM approach	Random forest	$BS_{dicecoeff}$: 0.65
Griffs et al. [351], 2016	Probabilistic tissue segmentation	NB classifier	–
Pustina et al. [352], 2016	Manual lesion tracing	Region wise LSM	$BS_{avgcorr}$: 0.77
Pennisi et al. [353], 2016	Skin lesion image segmentation	NB, Adaboost, KNN, and random trees	$BS_{Sensitivity}$: 93.5 $BS_{Specificity}$: 87.1
Chen et al. [354], 2017	Novel framework	Convolutional neural networks	BS_{acc}: 0.67
Muda et al. [355], 2015	FCM algorithm	Expert system	$BS_{Average}$ dice indices 0.73 (acute stroke), 0.68 (tumour) and 0.82 (chronic stroke)
Paul Bentley et al. [356], 2014 (modality: CT)	CT brain machine learning	SVM	BS_{AUC}: 0.744
Lebedev et al. [357], 2018	Artificial intelligence	RetinaNet network detector	–
Subudhi et al. [358], 2018	Delaunay triangulation and fractional order DPSO	Random forest	BS_{sen}: 0.93 BS_{acc}: 0.95
Subudhi et al. [359], 2018	Watershed-based lesion segmentation algorithm	Random forest	BS_{acc}: 0.85 BS_{DSI}: 96
Deep learning based techniques			
Chin et al. [360], 2017	Deep learning	CNN	BS_{acc}: 0.90

CAD, computer aided diagnosis; MRI, magnetic resonance imaging; NB, Naive Bayes; kNN, k-nearest neighbour; FCM, fuzzy C-means; CNN, convolution neural network; LSM, lesion- to- symptom mapping; SVM, support vector machine; LLC, locally linear classification; OBPD, optimum boundary point detection; HRS, hierarchical region splitting; MRF, markov random field.

Table 7. Summary of CAD systems for the detection of MS (modality: MRI)

Authors, years	Methodology/features	Classifier	Accuracy, %
Elliott et al. [361], 2013	Joint time point bayesian formulation	Bayesian + random-forest	MSsen: 99
Anbeek et al. [362], 2004	MBRASE	KNN	MSsen: 0.791
Ashton et al. [363], 2003	GEORG + DMSS	Bayesian	Coefficient of variation: manual: 8.2, GEORG: 2.4, DMSS: 2.1
Lao et al. [364], 2008	BET	SVM	–
Yamamoto et al. [107], 2010	Rule-based method, level set method	SVM	MSsen: 81.5
Zacharaki et al. [108], 2008	BET	SVM	TVR (% vol increase): 7.58–375, IVR (% vol increase): 11.14–340.32
Deep learning-based techniques			
Zhang et al. [365], 2018	CNN	–	Acc: 98.23
Wang et al. [366], 2018	CNN	–	Acc: 98.77

CAD, computer-aided diagnosis; MRI, magnetic resonance imaging; CNN, convolutional neural network; MS, multiple sclerosis; SVM, support vector machine; kNN, k-nearest neighbour.

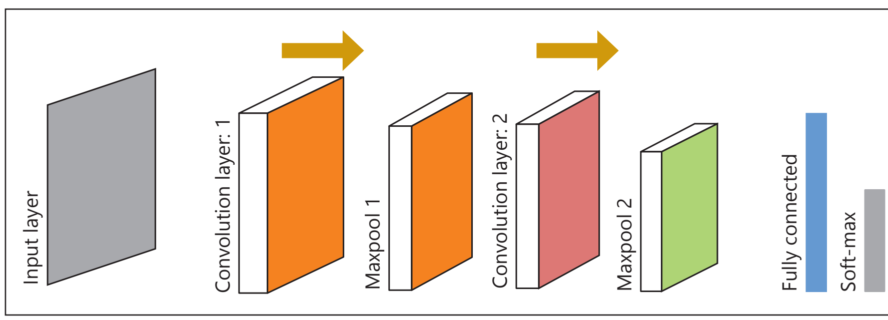

Fig. 2. Conventional architecture of CNN.

research is done on the automated diagnosis of MS. The SVM and k-nearest neighbor classifiers are the most commonly used classifier for the diagnosis of MS.

The transform methods such as DWT and HOS have been widely used with good performances. This can be explained by the fact that after the transformation, these methods can indicate minute changes in the frequency domains. The entropies and energy values of these DWT and HOS coefficients are able to separate the classes.

Conclusion

This study has explored different state-of-the-art AI-based CAD systems developed in last 2 decades for the diagnosis of 5 different neurological disorder. Results are summarized Tables 1–7.

The future research can be in one of 3 directions:

Creation of a Large Public Database for the Validation of All Developed Techniques

As observed in Tables 1–7, the number of subjects used in published research is often small. As such, the conclusions reported should be considered tentative. There is a need to create a large standard public database for all aforementioned neurological disorders.

ML-Based CAD for Early Detection of Neurological Disorders

As more data become available, especially longitudinal data, the research should shift to ML-based CAD systems for early detection of the neurological disorders.

Remote Access by Nonexpert Clinicians

Highly trained and specialized neurologists and associated facilities for diagnosis of neurological disorders may not be available in remote towns and villages. Figure 3

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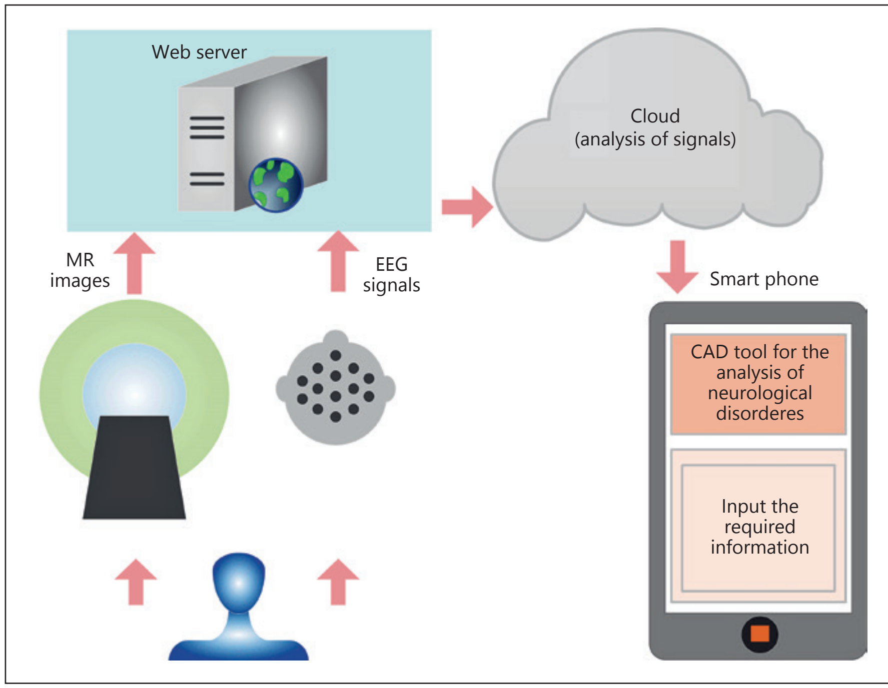

Fig. 3. Prototype of a cloud-based CAD system for diagnosis of neurological disorders using Internet of things. EEG, electroencephalogram; CAD, computer-aided diagnosis.

presents the prototype of a cloud-based CAD system for diagnosis of neurological disorders using Internet of things. The signals or images of patients are transmitted to the cloud where a trained ML-based CAD can provide the diagnosis. The outcome of the model is sent to the cell phone of a nonexpert clinician for a preliminary diagnosis.

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Statement of Ethics

This paper is a review article with no human/animal participants. Hence, no ethical approval was needed.

Disclosure Statement

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Author Contributions

U.R.A. and H.A. conceived the idea. U.R. and U.R.A. designed the paper. H.A. guided the overall direction and improved the design, coherence, and presentation of the paper.

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