

Deep learning for neuroimaging-based diagnosis and rehabilitation of Autism Spectrum Disorder: A review

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ABSTRACT

Accurate diagnosis of Autism Spectrum Disorder (ASD) followed by effective rehabilitation is essential for the management of this disorder. Artificial intelligence (AI) techniques can aid physicians to apply automatic diagnosis and rehabilitation procedures. AI techniques comprise traditional machine learning (ML) approaches and deep learning (DL) techniques. Conventional ML methods employ various feature extraction and classification techniques, but in DL, the process of feature extraction and classification is accomplished intelligently and integrally. DL methods for diagnosis of ASD have been focused on neuroimaging-based approaches. Neuroimaging techniques are non-invasive disease markers potentially useful for ASD diagnosis. Structural and functional neuroimaging techniques provide physicians substantial information about the structure (anatomy and structural connectivity) and function (activity and functional connectivity) of the brain. Due to the intricate structure and function of the brain, proposing optimum procedures for ASD diagnosis with neuroimaging data without exploiting powerful AI techniques like DL may be challenging. In this paper, studies conducted with the aid of DL networks to distinguish ASD are investigated. Rehabilitation tools provided for supporting ASD patients utilizing DL networks are also assessed. Finally, we will present important challenges in the automated detection and rehabilitation of ASD and propose some future works.

1. Introduction

ASD is a disorder of the nervous system that affects the brain and

results in difficulties in speech, social interaction and communication deficits, repetitive behaviors, and delays in motor abilities [1]. This disease can generally be distinguished with extant diagnostic protocols

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from the age of three years onwards. ASD influences many parts of the brain. This disorder also involves a genetic influence via the gene interactions or polymorphisms [2,3]. One in 70 children worldwide is affected by ASD. In 2018, the prevalence of ASD was estimated to occur in 168 out of 10,000 children in the United States, one of the highest prevalence rates worldwide. ASD is significantly more common in boys than in girls. In the United States, about 3.63% of boys aged 3–17 years have ASD, compared with approximately 1.25% of girls [4–6].

In the past, ASD was divided into five groups: Asperger's syndrome (AS) [7], Rett syndrome (RS) [8], childhood disintegrative disorder (CDD) [9], autistic disorder (classic autism) [10], and pervasive developmental disorder – not otherwise specified (PDD-NOS) [11]. Diagnostic and statistical manual of mental disorders, 5th Edition (DSM-5) is a book published by the American psychiatric association (APA) for the classification of mental disorders using common language and standard criteria [12]. The book was approved by the APA board of trustees on December 1, 2012 and published on May 18, 2013. Significant changes to the DSM-5 has been made to autism to include the removal of subtypes of autism, namely Asperger's syndrome, classic autism, RS, PDD-NOS, and their placement under an umbrella called ASD [13]. The severity level of ASD is determined on a spectrum that includes 3 levels of severity: level 1: needs support, level 2: needs substantial support, and level 3: needs very substantial support [13]. [Figure \(1\)](#) shows the distribution map of ASD throughout the world [14]. [Figure \(2\)](#) shows the visualization of different levels of ASD [15].

No certain treatment has been presented for ASD, but various intervention techniques have been studied and developed to decrease the symptoms, improve the cognitive ability, improve daily life skills, and increase the capabilities of ASD patients. Various intervention approaches are used for the patients suffering from ASD, where most of them are based on behavioral approaches, and some of them are based on evolutionary/cognitive approaches [16].

In recent years, noninvasive brain stimulation (NIBS) methods [17], including transcranial direct current stimulation (tDCS) [18] and transcranial magnetic stimulation (TMS) [19], have been examined as new treatment alternatives for modifying pathological neuroplasticity in ASD disorders [17]. tDCS is a non-invasive brain stimulation method

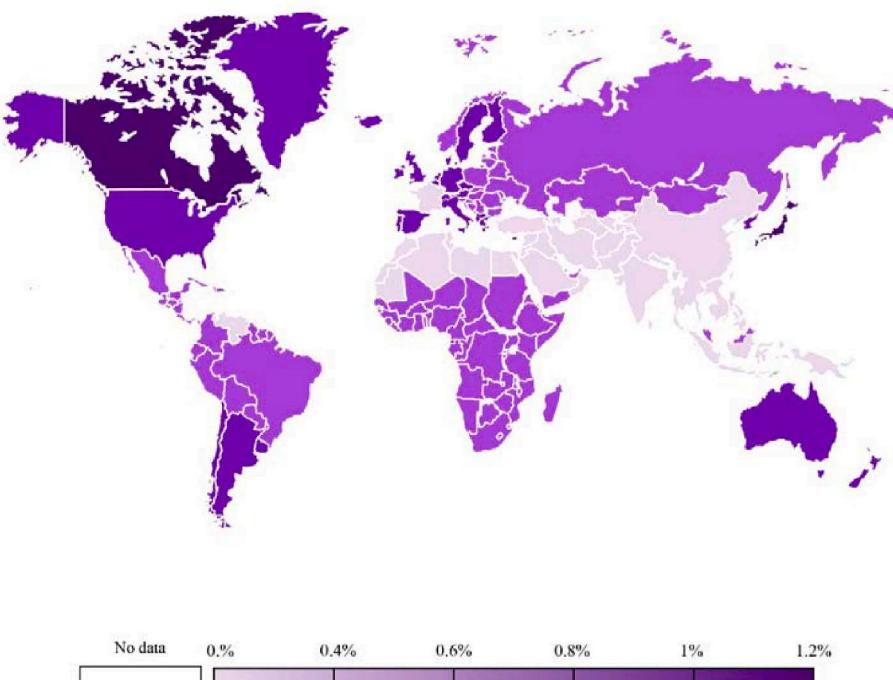
that employs direct electric currents to stimulate certain parts of the brain [18]. Also, TMS is a non-invasive brain stimulation method based on electromagnetic induction that concentrates on the brain areas that play an essential role in adjusting the behavior of ASD patients [19].

[ASD diagnosis methods](#) include various tools used by psychologists, specialists, and facilitators [20]. The tests are autism diagnostic observation schedule 2nd edition (ADOS-2) [21], autism diagnostic interview-revised (ADI-R) [22], childhood autism rating scale (CARS) [23], diagnostic interview for social and communication disorder (DISCO) [24], Gilliam autism rating scale (GARS) [25], developmental, dimensional, and diagnostic interview (3di) [26] and modified checklist for autism in toddlers (M-CHAT) [27]. These methods are mainly interview-based, with the advantage that interviews can be easily done for all ages [28]. The interview-based methods have [few disadvantages](#) [29]. The major shortcoming of these methods is that they are subjective. The [diagnosis of the disease](#) depends on the physician's expertise, skill, and schedule. Another [disadvantage](#) of the interview-based methods is that the child's family members may not be honest in filling the questionnaire or answering the questions, which may result in an incorrect diagnosis [30].

[Neuroimaging techniques](#) are another class of ASD diagnosis methods that are preferred by specialists. In the recent decade, various investigations for the diagnosis of ASD have been conducted on neuroimaging data (structural and functional). Analyzing anatomy and structural connections of brain areas with structural neuroimaging is an essential tool for studying structural disorders of the brain in ASD. The principal tools for structural brain imaging are magnetic resonance imaging (MRI) techniques [31–33].

Cerebral anatomy is investigated by structural MRI (sMRI) images and anatomical connections are assessed by diffusion tensor imaging MRI (DTI-MRI) [34]. Investigating the activity and functional connections of brain areas using functional neuroimaging can also be used for studying ASD. Brain functional diagnostic tools are more primary approaches than structural methods for studying ASD.

The most basic modality of functional neuroimaging is electroencephalography (EEG), which records the electrical activity of the brain from the scalp with a high temporal resolution (in milliseconds order)



[Fig. 1.](#) Distribution map of ASD throughout the world [14].

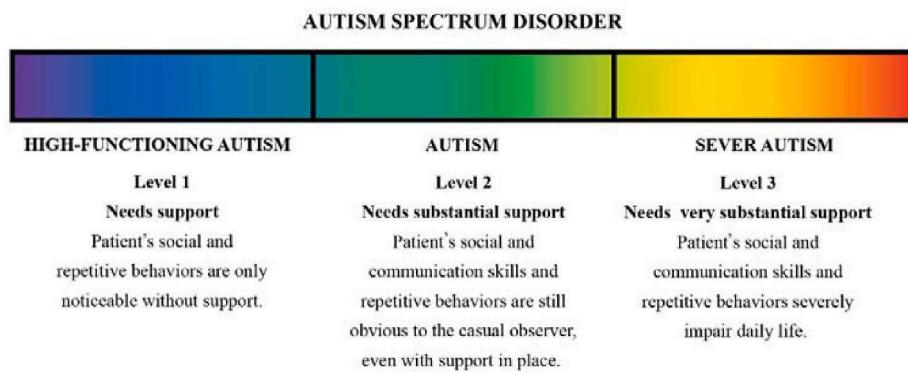


Fig. 2. Visualization of different levels of ASD [15].

[35]. Studies have shown that employing EEG signals to diagnose ASD have been useful [36–38]. Functional MRI (fMRI) is one of the most promising imaging modalities in functional brain disorders, used as task-based (T-fMRI) or resting-state (rs-fMRI) [39,40]. fMRI-based techniques have a high spatial resolution (in the order of millimeters) but a low temporal resolution due to slow response of the hemodynamic system of the brain as well as fMRI imaging time constraints and is not ideal for recording the fast dynamics of brain activities. In addition, these techniques have a high sensitivity to motion artifacts. It should be stressed that in consonance with studies, three less prevalent modalities of electrocorticography (ECOG) [41], functional near-infrared spectroscopy (fNIRS) [42], and Magnetoencephalography (MEG) [43] can also attain reasonable performance in ASD diagnosis.

An appropriate approach is to utilize machine-learning techniques alongside functional and structural data to collaborate with physicians in the process of accurately assessing ASD. In the field of ASD, applying machine learning methods generally entail two categories of traditional methods [44] and DL methods [45]. As opposed to traditional methods, much less work has been done on DL methods to explore ASD or design rehabilitation tools.

In this review, IEEE Xplore, ScienceDirect, SpringerLink, ACM, as well as other conferences or journals were used to acquire papers on ASD diagnosis and rehabilitation using DL methods. Further, the keywords "ASD", "Autism Spectrum Disorder" and "Deep Learning" were used to select the papers. The papers are analyzed until November 08th, 2020 by the authors. Figure (3) depicts the number of considered papers using DL methods for the automated detection and rehabilitation of ASD each year.

This study reviews assessment and rehabilitation of ASD patients with DL networks. The outline of this paper is as follows. Section 2 presents the DL networks employed for automated detection of ASD. In section 3, various available public datasets and brief description of various DL models used for ASD are presented. In section 4, DL-based rehabilitation tools for supporting ASD patients are introduced.

Section 5 reveals the challenges of ASD diagnosis and rehabilitation using DL techniques. The state-of-the-techniques proposed to detect ASD accurately are discussed in section 6. The future works are described in section 7 and finally paper concludes in section 8.

2. Deep learning techniques for ASD diagnosis and rehabilitation

Nowadays, DL algorithms are used in many areas of medicine, including structural and functional neuroimaging. The application of DL in neural imaging ranges from brain MR image segmentation [46], to the detection of brain lesions such as tumors [47], diagnosis of the brain functional disorders such as ASD [48], and production of artificial structural or functional brain images [49]. Machine learning techniques, based on the type of feedback they need for training, are categorized into three fundamental categories of learning: supervised learning [50], unsupervised learning [51], and reinforcement learning (RL) [52]. DL methods have been applied for nearly all of these categories; so far, most studies applied to identify ASD using DL have been based on supervised or unsupervised approaches. Figure (4) illustrates generally employed types of DL networks, organized by their underlying structure, to study ASD.

... → more need

3. CADS-based deep learning techniques for ASD diagnosis by MRI modalities

A traditional AI-based CADS encompasses several stages of data acquisition, data pre-processing, feature extraction, and classification [53–56]. In [57–59] existing traditional algorithms for diagnosing ASD have been reviewed. In contrast to traditional methods, in DL-based CADS, feature extraction, and classification are performed intelligently within the model. Also, due to the structure of DL networks, using large dataset to train DL networks and recognize intricate patterns in datasets is incumbent. The components of DL based CADS for ASD detection are

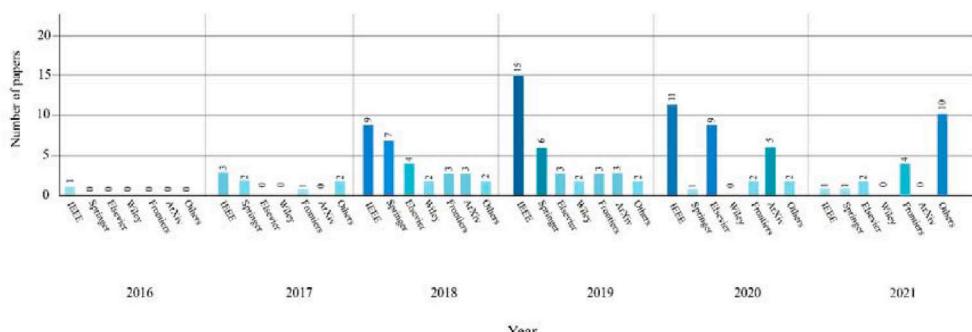


Fig. 3. Number of papers published every year for ASD diagnosis and rehabilitation.

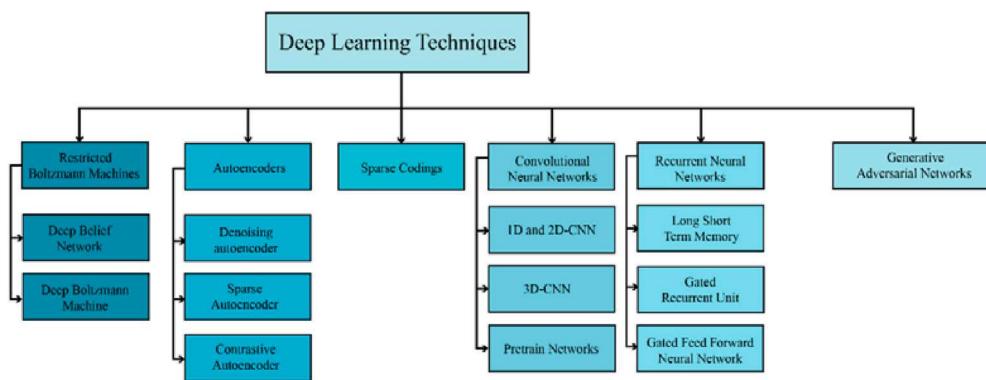


Fig. 4. Illustration of various types of DL methods.

shown in Figure (5). It can be noted from the figure that, large and free databases are first introduced to diagnose ASD. In the second step, various types of pre-processing techniques are used on functional and structural data to be scrutinized. Finally, the DL networks are applied to the preprocessed data.

3.1. Neuroimaging ASD datasets

3.1.1. ABIDE dataset

Datasets are the heart of any CADS development, and the capability of CADS depends primarily on the affluence of the input data. To diagnose ASD, several brain functional and structural datasets are available. The most complete free dataset available is ABIDE [60] dataset with two subsets: ABIDE-I and ABIDE-II, which encompasses sMRI, rs-fMRI, and phenotypic data. ABIDE-I involves data from 17 international sites, yielding a total of 1112 datasets, including 539 individuals with ASD and 573 healthy individuals (ages 6–47). In accordance with HIPAA guidelines and 1000 FCP/INDI protocols, these data are anonymized. In contrast, ABIDEII contains data from 19 international sites, with a total of 1114 datasets from 521 individuals with ASD and 593 healthy individuals (ages 5–64). Also, preprocessed images of the ABIDE-I series called PCP [61] can be freely downloaded by the researchers. The second recently released ASD diagnostic database is called NDAR, which comprises various modalities, and more information is provided in [62].

3.1.2. EEG available dataset

This EEG dataset has been presented by King Abdulaziz University (KAU) Brain Computer Interface (BCI) Group, Jeddah, Saudi Arabia which includes a total of 18 files, where 8 files are associated with the disorders group and 10 files belong to the normal group. The disorder group comprises of 8 boys (10–16 years), and the normal group consists of 10 boys (9–16 years). The EEG records were taken in the resting state without artifacts. EEG with a sampling rate of 256 Hz was obtained using active electrodes, active digital EEG amplifier, and BCI2000 recording system. The recording system contained g.tec EEGcap, 16 Ag/AgCl electrodes, g.tec GAMMAbox, g.tec USBamp and BCI2000. While recording, data was filtered using a band-pass filter with the frequency band of 0.1–60 Hz and sampled with a frequency of 256 Hz. The notch filter was also applied to remove power-line noise [63,64].

3.2. Preprocessing techniques

Neuroimaging data (especially functional ones) is of relatively complicated structure, and if not pre-processed properly, it may affect the final diagnosis. Preprocessing of this data typically entails multiple common steps performed by different software as standard. Indeed, occasionally prepared pipelines are applied to the dataset to yield pre-processed data for future researches. In the following section, preprocessing steps are briefly explained for fMRI data.

3.2.1. Standard (low-level) fMRI preprocessing steps

Low-level pre-processing of fMRI images normally has fixed number of steps applied to the data, and prepared toolboxes are usually used to reduce execution time and yield better accuracy. Some of these reputable toolboxes are FMRIB software libraries (FSL) [65], BET [66], FreeSurfer [67], and SPM [68]. Also, important and vital fMRI pre-processing incorporates brain extraction, spatial smoothing, temporal filtering, motion correction, slice timing correction, intensity normalization, and registration to the standard atlas, which are summarized as follows:

(1). Brain extraction

Brain extraction is the process of removing non-brain tissues like eyes, ears, and skull from the MRI data to obtain a clear image of the brain [69–71]. It is an essential step in the structural analysis that require brain segmentation and functional analyses of brain activity, in which a clear and accurate image of the brain would be obtained. It is implemented in processing toolboxes such as FSL and FreeSurfer [69–71].

(2). Spatial smoothing

Involves averaging the adjacent voxels signal. This process is persuasive on account of neighboring brain voxels being usually closely related in function and blood supply [69–71].

(3). Temporal filtering

The aim is to eliminate unwanted components from the time series of

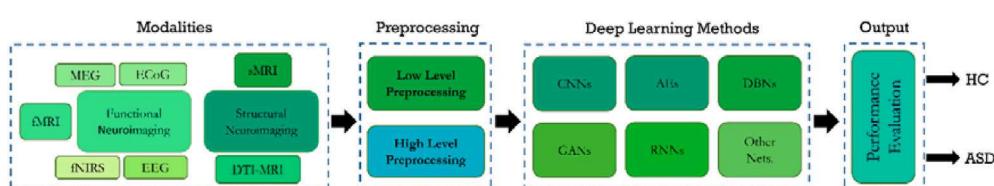


Fig. 5. Block diagram of CAD system using DL architecture for ASD detection.

voxels without impairing the signal of interest [69–71].

(4). Realignment (Motion Correction)

During the fMRI test, people often move their heads. The objective of motion correction is to align all images to a reference image so that the coordinates and orientation of the voxels be identical in all fMRI volumetric images [69–71].

(5). Slice time correction

The purpose of modifying the slice time is to adjust the time series of the voxels so that all the voxels in each fMRI volume image have a common reference time. Usually, the corresponding time of the first slice recorded in each fMRI volume image is selected as the reference time [69–71].

(6). Intensity normalization

In this step, the average intensity of fMRI signals are rescaled to compensate for global deviations within and between the recording sessions [69–71].

(7). Registration to a standard atlas

The human brain entails hundreds of cortical and subcortical areas with various structures and functions, each of which is very time consuming and complex to study. To overcome the problem, brain atlases are employed to partition brain images into a confined number of ROIs, following which the meantime series of each ROI can be extracted [72]. ABIDE datasets use a manifold of atlases, including Automated Anatomical Labeling (AAL) [73], Eickhoff-Zilles (EZ) [74], Harvard-Oxford (HO) [75], Talaraich and Tournoux (TT) [76], Dosnenbach 160 [77], Craddock 200 (CC200) [78] and Craddock 400 (CC400) [79] and more information is provided in [80]. Table 1 provides complete information on preprocessing tools, atlases, and some other preprocessing information.

(8). Pipeline methods

Pipelines present preprocessed images of ABIDE databases. They embrace generic preprocessing procedures. Employing pipelines, distinct methods can be compared with each other. In ABIDE datasets, preprocessing is performed by four pipeline techniques: neuroimaging analysis kit (NIAK) [161], data processing assistant for rs-fMRI (DPARSF) [162], the configurable pipeline for the analysis of connectomes (CPAC) [163], or connectome computation system (CCS) [164]. The preprocessing steps carried out by the various pipelines are comparatively analogous. The chief differences are in the particular algorithms for each step, the software simulations, and the parameters applied. Details of each pipeline technique are provided in [80]. Table 1 demonstrates the pipeline techniques used in ASD detection exploiting DL.

3.2.2. Standard (low-level) sMRI preprocessing steps

Similar to fMRI preprocessing, structural MR images are also usually preprocessed before feeding to a neural network. Brain extraction and registration to a standard atlas are common steps in both fMRI and sMRI preprocessing. The rest of the steps are described as follows:

(1). Denoising

Diagnosis of ASD using sMRI images may confront serious challenges due to the noise resulted from the recording image process. To reduce these noises, there is a wide range of filtering approaches such as low-pass filters, wavelet-based filters, NLM filters, etc. [165].

(2). Inhomogeneity correction

The static magnetic field must be homogeneous when recording sMRI data, but in reality, this homogeneity is diminished due to the presence of brain tissues and creates artifact on images. Therefore, Inhomogeneity Correction must be carried out before sMRI image processing. More information is available in [165].

(3). Intensity standardization

Generally, sMRI images with contrasts like T1-Weighted, acquired by different scanners have not the same intensity. Intensity standardization techniques in sMRI endeavor to remove these scanner-dependent intensity variations [165]. Most simple approaches to standardize the intensity of sMRI images rely on histogram matching techniques [165].

(4). De-oblique

During the sMRI data acquisition, the scan angle occasionally deviates from the horizon to cover the whole brain. This scan is called an oblique scan. Oblique scanning allows data to be acquired with less noise but can make registration between two different images more demanding. To address this problem, the de-oblique preprocessing step is fulfilled [166].

(5). Re-orientation

The orientation of sMRI images depends on the settings of the image recording process. In order to process images accurately, all of them must have the same orientation. The orientation of sMRI images encompasses right or left, anterior or posterior, and finally superior or inferior [166].

(6). Segmentation:

Sometimes it is imperative to segment sMRI images before applying high-level processing. In sMRI modalities, segmentation of brain images usually aims to isolate three types of brain tissues: white matter (WM), gray matter (GM), and cerebrospinal fluid (CSF) [167].

3.2.3. High-level preprocessing steps

High-level techniques for pre-processing brain data are important, and using them accompanying preliminary pre-processing methods can enhance the accuracy of ASD recognition. These methods are applied after the standard pre-processing of functional and structural brain data. These include sliding window (SW) [48], data augmentation (DA) [83], functional connectivity matrix (FCM) estimation [107,108] and applying fast Fourier transformation (FFT) [93]. Furthermore, some of the researches utilized feature extraction [121] techniques and some also use feature selection methods. Precise information on reviewed studies is indicated in detail in Table 1.

3.3. Deep neural networks

DL in various medical applications, including the diagnosis of ASD has become extremely popular in recent years. In this section of the paper, the types of DL networks used in ASD detection are examined, which include CNN, RNN, AE, DBN, CNN-RNN, and CNN-AE models. Notably, CNN is the most common structure in reviewed research; this is arguably due to their structure being suitable for finding patterns in ASD datasets; more straightforward implementation, and more accessible transfer learning compared to other methods. Details of each ASD diagnosis study using neuroimaging modalities and DL models are shown in Table 1. It can be noted from this table that, the neuroimaging modalities used in the diagnosis of ASD include sMRI, DTI, rs-fMRI, T-fMRI, fNIRS, and EEG with their data in 1D, 2D, and 3D format. It can be observed that CNN models are used in most of the

Table 1

Summary of articles published using DL methods for neuroimaging-based ASD detection.

Work	Datasets	Neuroimaging Modalities	Number of Cases	Pipeline and Atlas	High level Preprocessing	DNN Toolbox	DNN	Performance Criteria (%)
[48]	Clinical	T-fMRI Residual fMRI	82 ASD 48 HC	MNI152	SW	–	2CC3D + MV	F1-Score = 89
[81]	Clinical	T-fMRI	82 ASD 48 HC	AAL	SVE, C-SVE, H-SVE, Monte Carlo Approximation	–	2CC3D + Sigmoid	Acc = 97.32
[82]	HCP Dataset in the HAFNI Project	T-fMRI rs-fMRI	68 Subjects with 7 Tasks and 1 rs-fMRI Data	–	Dictionary Learning and Sparse Coding	–	3D-CNN + Softmax	Acc = 94.61
[83]	Clinical	T-fMRI	21 ASD 19 HC	AAL	DA	Keras	LSTM + Sigmoid	Acc = 69.8
[84]	Different Datasets	T-fMRI rs-fMRI Phenotypic Info	1711 ASD 15903 HC	AAL	DWT and Different Techniques	Keras	2D-CNN + Softmax	AUC = 0.92 Acc = 85.19
[85]	Clinical	T-fMRI	82 ASD 48 HC	AAL	SW Corrupting Strategy	–	2CC3D + Sigmoid	Acc = 87.1
[85]	ABIDE-I	rs-fMRI	41 ASD 54 HC	AAL	Prediction Distribution Analysis	–	2CC3D + Sigmoid	Acc = 85.3
[86]	ABIDE-I	rs-fMRI	379 ASD, 395 HC	CPAC + All ABIDE Atlases	FCM	–	3D-CNN + Sigmoid	Acc = 73.3
	ABIDE II		163 ASD, 230 HC					
[87]	ABIDE-I	rs-fMRI	505 ASD 530 HC	CPAC + CC-200 CPAC + AAL CPAC + Dosenbach160	FCM, DA	PyTorch	AE + SLP	Acc = 70.1 Sen = 67.8 Spec = 72.8
[88]	ABIDE-I	rs-fMRI	872 Subjects	CPAC + HO	–	–	G-CNNs + Softmax	Acc = 70.86
[89]	ABIDE-I	rs-fMRI	474 ASD 539 HC	CCS + AAL	FCM	–	BrainNetCNN + Softmax	Acc = 68.7 Sen = 69.2 Spe = 68.3
[90]	ABIDE-I	rs-fMRI	13 ASD 22 HC	AAL	Qcut, NMI Statistic Matrix	–	DAE	Acc = 54.49
[91]	ABIDE	rs-fMRI	11 ASD 16 HC	–	Convert NII Files to PNG Images	Caffe	LeNet-5	Acc = 100 Sen = 99.99 Spec = 100
[92]	ABIDE-I	rs-fMRI	55 ASD 55 HC	NIAK + AAL	FCM, Feature Selection	–	Multiple SAEs + Softmax	Acc = 86.36
[93]	ABIDE-I	rs-fMRI	54 ASD 62 HC	–	FFT	Keras	MCNNes + SR	Acc = 72.73 Sen = 71.2 Spec = 73.48
	ABIDE-II ABIDE-I + II		156 ASD 187 HC		Dimension Reduction	Theano		
[94]	ABIDE	rs-fMRI	542 ASD 625 HC	CPAC + All Atlases	Creating Stochastic Parcellations by Poisson Disk Sampling	–	3D-CNN + VM	Acc = 72
[95]	ABIDE-I	rs-fMRI	465 ASD 507 HC	DPARSF + AAL	FCM	Keras	VAE	–
[96]	ABIDE-I	rs-fMRI	539 ASD 573 HC	CCS + Craddock 200	DA	Keras	LSTM + Sigmoid	Acc = 68.5
[97]	ABIDE	rs-fMRI Phenotypic Info	505 ASD 530 HC	CC200	Slice timing, Spatial Standardization, Smoothing, Filtering, Removing Covariates, FCM, AE-MKFC	–	SAE + Clustering	Acc = 61 F1-Score = 60.2
[98]	ABIDE	rs-fMRI	42 ASD 42 HC	–	Independent Components	–	SAE + Softmax	Acc = 87.21 Sen = 89.49 Spec = 83.73
[99]	ABIDE-I	rs-fMRI	NY site UM site US site UC site	CCS + AAL	DA	Keras	LSTM + Sigmoid	Acc = 74.8
[100]	ABIDE-I	rs-fMRI	408 ASD 401 HC	CPAC + HO CPAC + AAL CPAC + CC200	–	Keras	DANN + Sigmoid	Acc = 73.2 Sen = 74.5 Spec = 71.7
[101]	ABIDE	rs-fMRI	At Least 60 Subjects	CCS + AAL	DTL-NN Framework: Offline Learning, Transfer Learning FCM	–	SSAE + Softmax	Avg Acc = 67.1 Avg Sen = 65.7 Avg spec = 68.3
[102]	ABIDE I + II	rs-fMRI	993 ASD 1092 HC	AAL Schaefer-100 HO Schaefer-400	–	–	1D-CNN + Softmax	Acc = 68
[103]	ABIDE-I	rs-fMRI		All Pipelines	Single Volume Image Generator	Keras		

(continued on next page)

Table 1 (continued)

Work	Datasets	Neuroimaging Modalities	Number of Cases	Pipeline and Atlas	High level Preprocessing	DNN Toolbox	DNN	Performance Criteria (%)
			529 ASD 573 HC				4 Deep Ensemble Learning + Sigmoid	Acc = 87 F1-score = 86 Recall = 85.2 Pre = 86.8
[104]	ABIDE-II	rs-fMRI	303 ASD 390 HC	–	–	–	1D-CAE	Acc = 65.3
[105]	ABIDE	rs-fMRI	40 ASD 40 HC	CCS	Thresholding Based Segmentation	–	AlexNet + Softmax	Acc = 82.61
[106]	ABIDE	rs-fMRI	Whole Dataset	All Pipelines	DA Using SMOTE and Graph Network Motifs, FCM	–	ASDDiagNet + SLP	Acc = 82 Sen = 79.1 Spec = 83.3
[107]	ABIDE-I	rs-fMRI	12 ASD 14 HC	CPAC + SCSC	Time Series Extraction from Different Regions, Connectivity Matrix, SMOTE Algorithm	PyTorch	Auto-ASDNetwork + SVM	Acc = 80 Sen = 73 Spec = 83
[108]	ABIDE-I	rs-fMRI	505 ASD 530 HC	CPAC + CC400	FCM	–	2D-CNN + MLP	Acc = 70.20 Sen = 77.00 Spec = 61.00
[109]	ABIDE	rs-fMRI	505 ASD 530 HC	–	FCM	–	1D CNN-AE + Softmax	Acc = 70 Sen = 74 Spec = 63
[110]	ABIDE-I	rs-fMRI	539 ASD 573 HC	–	–	Theano	3D-FCNN + Softmax	Mean DSC = 91.56
[111]	ABIDE-I	rs-fMRI	501 ASD 553 HC	DPARSF + AAL	FCM, Converting to 1D-Vector	–	SSAE + Softmax	Acc = 93.59 Sen = 92.52 Spec = 94.56
[112]	ABIDE-I	rs-fMRI	100 ASD 100 HC	–	Online Dictionary Learning and Sparse Representation Techniques, Generating Spatial Overlap Patterns	Theano	3D-CNN	Avg Acc = 70.5 Avg Sen = 74 Avg Spec = 67
[113]	ABIDE-I	rs-fMRI Phenotypic Info	529 ASD 571 HC	CPAC + HO	Population Graph Construction, Feature Selection Strategies (RFE, PCA, AE)	Scikit-learn	GCN + Softmax	Acc = 80.0
[114]	ABIDE-I	rs-fMRI Phenotypic Info	403 ASD 468 HC	CCS + CC200	DA	Keras	LSTM + Sigmoid	Acc = 70.1
[115]	ABIDE-I	rs-fMRI s-MRI Phenotypic Info	505 ASD 530 HC	CPAC + CC200	FCM	–	Two SDAE + MLP	Acc = 70 Sen = 74 Spec = 63
[116]	Clinical	rs-fMRI Fetal BOLD fMRI	75 Qualified Subjects	–	Extraction of Fetal Brain fMRI Data, SW	PyTorch	3D-CNN + Sigmoid	F1-score = 84 AUC = 91
[117]	ABIDE-I ABIDE-II	rs-fMRI s-MRI	116 ASD 69 HC	AAL	Segmentation, Average Mean Time Series of Each ROI	Theano	DBN + LR	Acc = 65.56 Sen = 84 Spec = 32.96
[118]	IMPAC	rs-fMRI s-MRI	418 ASD 497 HC	All Atlases	FCM, Features Extraction from sMRI	Keras TensorFlow Caffe	Different Networks + VM	AUC = 80
[119]	ABIDE-I	rs-fMRI s-MRI	368 ASD 449 HC	CPAC + AAL CPAC + CC200 CPAC + Destrieux	FCM, Fisher Score	–	Ensemble of 5 Stacked AEs and MLP	Acc = 85.06 Sen = 81 Spec = 89
[120]	NDAR	rs-fMRI s-MRI	61 ASD 215 HC	–	Data-Driven Landmark Discovery Algorithm, Patch Extraction	–	Multi-Channel CNN + Softmax	Acc = 76.24
[121]	NDAR	All Modalities	78 ASD 124 HC	Proposed Atlas	Probabilistic Independent Component Analysis (PICA), Extraction of PSD	–	SAEs + PSVM	Acc = 88.5 Sen = 85.1 Spec = 90.4
[122]	NDAR	s-MRI	60 ASD 211 HC	–	3D Patches Extraction	–	DDUNET	–
[123]	ABIDE-I	s-MRI	21 ASD 21 HC	–	Segmentation, Shape Feature Extraction	–	SNCAE + Softmax	Acc = 96.88
	NDAR/Pitt		16 ASD 16 HC					
	NDAR/IBIS		10 ASD 10 HC					
[124]	ABIDE-I	s-MRI	78 ASD 104 HC	Destrieux	Construction of Individual Network, F-score	–	SAE + Softmax	Acc = 90.39 Sen = 84.37 Spec = 95.88
[125]	HCP ABIDE-I	s-MRI	1113 HC 83 ASD 105 HC	Desikan–Killia	Normalization, Apply One-Hot Coding	TensorFlow Keras	DEA	AUC = 63.9
[126]	ABIDE CombiRx	s-MRI	1112 Subjects	–	–	Keras	DCNN + Sigmoid	Acc = 84 Sen = 77 Spec = 85
[127]	ABIDE-II	s-MRI	–	DKT	Segmentation	PyTorch	FastSurfer CNN + Softmax	–
[128]	ABIDE-I	s-MRI	500 ASD 500 HC		GABM Method, New Chromosome Encoding Scheme	–	3D-CNN + Softmax	Acc = 70

(continued on next page)

Table 1 (continued)

Work	Datasets	Neuroimaging Modalities	Number of Cases	Pipeline and Atlas	High level Preprocessing	DNN Toolbox	DNN	Performance Criteria (%)
[129]	Clinical	s-MRI	48 HC	–	HO Cortical & Subcortical Structural Atlas	Sparse Annotations, DA	Caffe	3D-CNN + Softmax Acc = 91.6 AUC = 94.1
[130]	ABIDE-I	rs-fMRI	270 ASD 305 HC	CPAC + Brain-Netome Atlas (BNA)	Filtering, Calculating Mean Time Series for ROIs Using BrainNetome Atlas (BNA), Normalization	–	CNN-GRU + Sigmoid	Acc = 74.54 Sen = 63.46 Spec = 84.33
[131]	Clinical	fnIRS	25 ASD 22 HC	–	Transformation of the Time Series to Three Variants	Keras	1D CNN-LSTM + Bagging	Acc = 95.7 Sen = 97.1 Spec = 94.3
[132]	Clinical	fnIRS	25 ASD 22 HC	–	SW Converted into the 3D Tensor	–	CGRNN	Acc = 92.2 Sen = 85.0 Spec = 99.4
[133]	Different Datasets	s-MRI	–	Various Methods	Geometric DA	Theano	ConvNet	–
[134]	ABIDE I + II	rs-fMRI	620 ASD 2085 HC	CPAC + HO	Performed an Automatic Quality Control, Visually Inspection, Feature Extraction, Occlusion of Brain Regions	–	3D-CNN + MV	Acc = 64 F1-Score = 66
[135]	ABIDE-I	rs-fMRI Phenotypic Info	184 ASD 110 HC	CPAC	Down Sampling	–	3D-CNN -LSTM + Softmax	Acc = 77 F1-score = 78
[136]	ABIDE-I	rs-fMRI s-MRI	403 ASD 468 HC	264 ROIs Based Parcellation Scheme	FCM, Different Features	–	AE + DNN	Acc = 79.2 AUC = 82.4
[137]	ABIDE-I	rs-fMRI	505 ASD 530 HC	CPAC + CC200	FCM	PyTorch	CapsNet + K-Means	Acc = 71 Sen = 73 Spec = 66
[138]	ABIDE	rs-fMRI	184 ASD	CCS	Motion Realignment, Rigid Registration, Spatially Downsampled	–	convGRU-CNN3D	Acc = 67 F1-score = 71
[139]	ABIDE	rs-fMRI	252 ASD 252 HC	CPAC + CC200	FCM, Multistage SAAK Transform, Feature Selection	–	1D-CNN + Softmax	Acc = 74.55
[140]	ABIDE	rs-fMRI	419 ASD 530 HC	CPAC + CC200 CPAC + AAL CPAC + Dosenbach	Multiple Functional Connectivity Based On 3 Atlases Using PCC	–	SDA + different methods	Acc = 74.52 Sen = 80.69 Spe = 66.71 AUC = 80.26
[141]	ABIDE-I	rs-fMRI	505 ASD 530 HC	CPAC + AAL	ROI Extraction	PyTorch	Parallel 3D & ResNet-18	Acc = 74 Recall = 95 F1 score = 80.5
[142]	ABIDE	MRI	946 ASD 1046 HC	–	Spatial Transformation	–	Combination of DNNs	Different Results
[143]	ABIDE	rs-fMRI	79 ASD 105 HC	DPARSF	Low-Frequency Drifts, Nuisance Signal Removal	–	RBM + SVM	Acc = 83 Pre = 81 Recall = 81 F1-Score = 80.50
[144]	ABIDE I ABIDE II	rs-fMRI	300 ASD 300 HC	GCA HO DCA	Whole Brain Mask Preparation and ROIs Extraction, Partial and Full Correlation Methods Such As GLASSO, MDMC, PCCE, CRF Feature Reduction	TensorFlow	1D-CNN + Softmax	Acc = 70.31 Sen = 67.66 Spe = 73 Pre = 71.55 AUC = 73
[145]	IMPAC	sMRI	537 ASD 590 HC	MSDL Functional Atlas	sMRI Measures of Cortical Thickness, Surface Area & Volume	–	CNN + Softmax	Acc = 69 Sen = 79 Spe = 68.9 AUC = 73.3
		rs-fMRI			fMRI Connectomes, Dictionary Pair Learning			
[146]	ABIDE I	MRI	500 ASD 500 HC	HO SSA	GABM	–	3D-CNN + Softmax	Acc = 73
[147]	ABIDE	rs-fMRI	525 ASD 532 HC	CCS + Craddock 200	ROIs Extraction, Functional Connectivity Matrix, Graph Construction (k-NN Graph)	Keras, TensorFlow	cGCN	Acc = 70.7
[148]	ABIDE I	sMRI	518 ASD 567 HC	SRI24	Individual-Level Morphological Covariance Brain Networks	–	2D-CNN (ResNet)	Acc = 71.8 Sen = 81.25 Spec = 68.75 F1-Score = 68.7
[149]	ABIDE I	rs-fMRI	505 ASD 530 HC	CPAC + CC200	Functional Connectivity	PyTorch	ASD-SAENet	Acc = 70.8 Sen = 62.2 Spec = 79.1
[150]	ABIDE I	rs-fMRI	40 Subjects	MSDL	Masking	Keras, TensorFlow	1D-CNN	Acc = 92 AUC = 97
[151]	ABIDE I	rs-fMRI			MSTEPS	–		

(continued on next page)

Table 1 (continued)

Work	Datasets	Neuroimaging Modalities	Number of Cases	Pipeline and Atlas	High level Preprocessing	DNN Toolbox	DNN	Performance Criteria (%)
			403 ASD 468 HC	Bootstrap Analysis of Stable Clusters (BASC) CCS			Different CNN And RNN Networks Inception-ResNetV2 VGG-16, ResNet-50	Acc = 74.74 Sen = 72.95 Spec = 76.28 Acc = 57.6
[152]	ABIDE I	rs-fMRI	74 ASD 98 HC	—	2D Neuroimages Acquisition Stages 3D to the 2D Conversion	—	TensorFlow	Acc = 87
[153]	ABIDE I	rs-fMRI	539 ASD 573 HC	—				
	ABIDE II		521 ASD 573 HC					
[154]	ABIDE I	rs-fMRI	402 ASD 464 HC	CPAC, BASC, Power, CC200, AAL	ROIs Extraction, Functional Connectivity	Keras, TensorFlow	DNN	Acc = 88 Sen = 90 F1-score = 87 AUC = 96
[155]	NDAR	rs-fMRI, ADOS	78 ASD 78 HC	Different	rs-fMRI Analysis and ROIs Extraction, PSD	—	AE	Acc = 93 Sen = 91 Spec = 94
[156]	6 Different Databases	sMRI and fMRI in Task and Rest Conditions	14178 Subjects	AAL	Functional Connectivity, GM Volume and Single-Participant Structural Similarity Matrices	—	2D-CNN + Softmax	Acc = 69.7062 AUROC = 72.98
[157]	King Abdulaziz University (KAU) Dataset	EEG	9 ASD 10 HC	—	Windowing, Filtering Process, RNN-GRU, FastICA	Keras, TensorFlow	2D-CNN + Softmax	Acc = 99.5 Sen = 52.13 Spec = 96.21
[158]	King Abdulaziz University (KAU) Dataset	EEG	12 ASD 4 HC	—	Re-Referencing, Filtering, Normalization, STFT	—	2D-CNN + Softmax	Acc = 99.15 Sen = 99.19 Spec = 99.04
[159]	Clinical	EEG	8 ASD 12 Epilepsy 18 HC	—	Filtering, ICA, Segmentation, PSDED	TensorFlow	DCNN + Softmax	Acc = 80
[160]	Clinical	rs-EEG	86 ASD 89 HC	—	Segmentation, Filtering, DFT	—	CNN with Q-Learning + Sigmoid	Acc = 92.63

studies on automated autism detection using neuroimaging modalities. The high performance is achieved by the supervised learning tasks due to their well-known structures such as VGG and ResNet. Also, their intrinsic matching with the neuroimaging modalities format and interpretability make it easier for researchers to apply and debug them. These papers have contributed significantly in resolving difficulties due to CNNs and obtain higher performances of the various DL techniques used for ASD diagnosis are presented in the following sections.

3.3.1. Convolutional neural networks (CNNs)

In this section, the types of popular convolutional networks used in ASD diagnosis are surveyed. These networks involve 1D-CNN, 2DCNN, 3D-CNN models, and a variety of pre-trained networks such as VGG. In CNN models, feature extraction is unsupervised, which is an advantage. Also, increasing the convolutional layers help to extract high-level features. Besides the advantages of CNN models, they have many training parameters resulting in high computational load and the need for powerful computers to implement [168–171].

(1). 1D AND 2D-CNN

There are many spatial dependencies present in the data and it is difficult to extract these hidden signatures from the data. Convolution network uses a structure alike to convolution filters to extract these features properly and contribute to the knowledge that features should be processed taking into account spatial dependencies; so the number of network parameters are significantly reduced. The principal application of these networks is in image processing and due to the two-dimensional (2D) image inputs, convolution layers form 2D structures, which is why these networks are called 2D convolutional neural network (2D-CNN). By using another type of data, one-dimensional signals, the convolution layers' structure also resembles the data structure [172,173]. In convolution networks, assuming that various data sections do not

require learning different filters, the number of parameters are markedly lessened and make it feasible to train these networks with smaller databases [45]. Figure (6) shows the block diagram of 2D-CNN used for ASD detection.

(2). 3D-CNN

By transforming the data into three dimensions, the convolution network will also be altered to a three-dimensional format (Fig. 7). It should be noted that the manipulation of three-dimensional CNN (3D-CNN) networks are less beneficial than 1D-CNN and 2D-CNN networks for diverse reasons. First, the data required to train these networks must be much larger which conventionally such datasets are not utilizable and methods such as pre-training, which are extensively exploited in 2D networks, cannot be used here. Another reason is that with the more complicated structure of networks, it becomes much tougher to fix the number of layers, and network structure. The 3D activation map generated during the convolution of a 3D CNN is essential for analyzing data where volumetric or temporal context is crucial. This ability to analyze a series of frames or images in context has led to the use of 3D CNNs as tools for action detection and evaluation of medical imaging [174].

3.3.2. Deep belief networks (DBNs)

DBNs are not popular today as they used to be, and have been substituted by new models to perform various applications (e.g., autoencoders for unsupervised learning, generative adversarial networks (GAN) for generative modes [175], variational autoencoders (VAE) [176]). However, disregarding the restricted use of these networks in this era, their influence on the advancement of neural networks cannot be overlooked. The use of these networks in this paper is related to the feature extraction without a supervisor or pre-training of networks. These networks serve as unsupervised, consisting of several

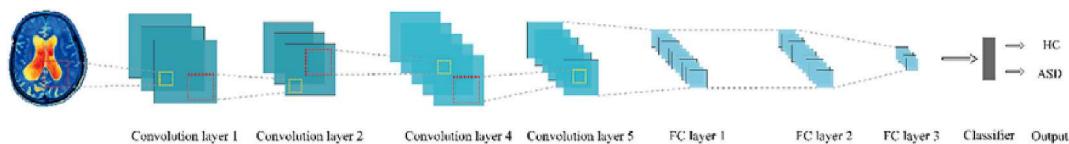


Fig. 6. Overall block diagram of a 2D-CNN used for ASD detection.

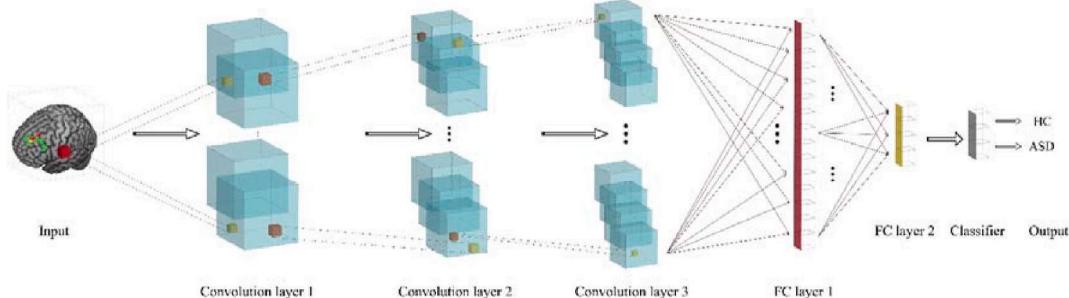


Fig. 7. Overall block diagram of a 3D-CNN used for ASD detection.

layers after the input layer, which are shown in [Figure \(8\)](#). The training of these networks is done greedily and from bottom to top, in other words, each separate layer is trained and then the next layer is appended. After training, these networks are used as a feature extractor, or the network weights are used as initial weights of a network for classification [45]. Training the DBN models is simpler than other DL models with improper performance and small number of data. One disadvantage of DBN models is that they do not consider the 2D structure of the input image. Thus, using them for machine vision applications is challenging [168–171].

3.3.3. Autoencoders (AEs)

Autoencoders (AEs) are more than 30 years old, and have undergone dramatic changes over the years to enhance their performance. But the overall structure of these networks has remained the same [45]. These networks consist of two parts: coder and decoder so that the first part of the input leads to coding in the latent space and the decoder part endeavors to convert the code into preliminary data ([Fig. 9](#)). Autoencoders are a special type of feedforward neural networks where the input is the same as the output. They compress the input into a lower-dimensional code and then reconstruct the output from this representation. The code is a compact “summary” or “compression” of the input, also called the latent-space representation. Various methods have been proposed to block the data memorization by the network, including sparse AE (SpAE) and denoising AE (DAE) [45]. Trained properly, the coder part of an Autoencoder can be used to extract features; creating an unsupervised feature extractor. The AE models are based on unsupervised training, which is an advantage. Also, these models suffer from disappearing gradients, which is a disadvantage [168–171].

3.3.4. Recurrent neural networks (RNNs)

In convolution networks, a kind of spatial dependencies in the data is addressed. But interdependencies between data are not confined to this model. For example, in time-series, dependencies may be highly distant from each other, on the other hand, the long-term and variable length of these sequences results in that the ordinary networks do not perform well enough to process these data. To overcome these problems, RNNs can be used. Long short-term memory (LSTM) structures are proposed to extract long term and short-term dependencies in the data ([Fig. 10](#)). Another well-known structure called gated recurrent unit (GRU) is developed after LSTM, and since then, most efforts have been made to enhance these two structures and make them resistant to challenges (e.g., GRU-D [177] is used to find the lost data). The RNN models have memory, and they can be used for disease prediction applications, which is an important advantage. The RNN models also suffer from disappearing gradients. It takes time to train these models due to their recurrent nature [168–171].

3.3.5. CNN-RNN

The initial idea in these networks is to utilize convolution layers to amend the performance of RNNs so that the advantages of both networks can be used; CNN-RNN, on the one hand, can find temporal dependencies with the aid of RNN, and on the other hand, it can discover spatial dependencies in data with the help of convolution layers [178]. These networks are highly beneficial for analyzing time series with more than one dimension (such as video) [179] but further to the simpler matter, these networks also yield the analysis of three-dimensional data so that instead of a more complex design of a 3D-CNN, a 2D-CNN with an RNN is occasionally used. The superiority of this model is due to the feasibility of employing pre-trained models. [Figure \(11\)](#) demonstrates

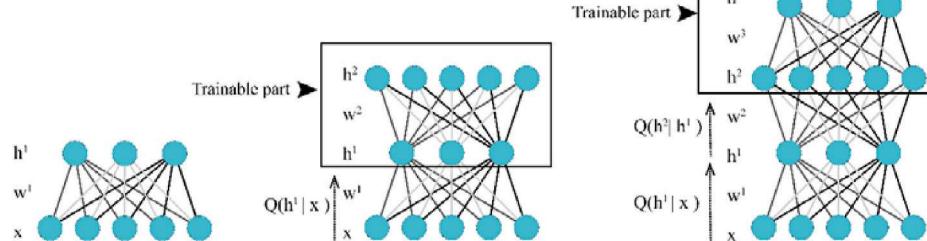


Fig. 8. Overall block diagram of a DBN used for ASD detection.

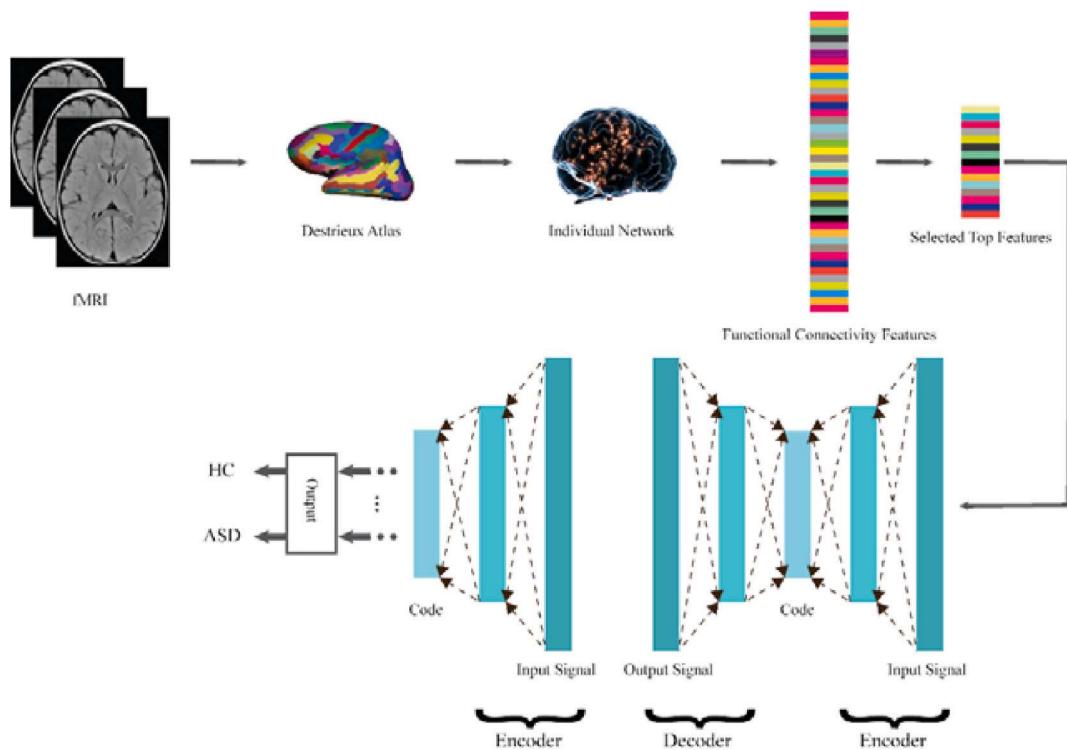


Fig. 9. Overall block diagram of an AE used for ASD detection.

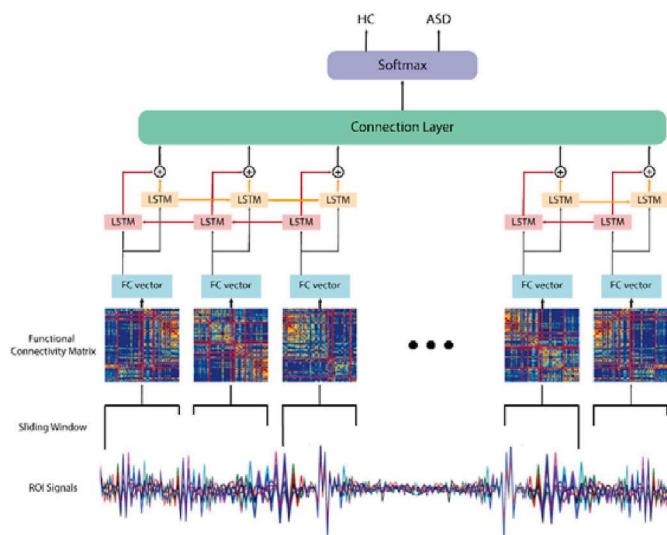


Fig. 10. Overall block diagram of an LSTM used for ASD detection.

the CNN-RNN model. These models employ the advantages of CNN and RNN models in extracting features from medical data with high performance. Also, complicated training is the disadvantage of CNN-RNN models [168–171].

3.3.6. CNN-AE

In the construction of these networks, the principal aim and prerequisite have been to decrease the number of parameters. As shown before, changing merely the network layers to convolution markedly lessens the number of parameters; combining AE with convolution structures also makes a significant contribution. This helps to exploit higher dimensional data and extracts more information from the data without changing the size of the database. Similar structures, with or

without some modifications, are widely deployed for image segmentation [180], and likewise the unsupervised network can be applied for network pre-training or feature extraction. Figure (12) depicts the CNN-AE network used for ASD detection. The CNN-AE models perform well in extracting features from medical data due to convolution-based feature extraction using AE layers. Complicated training is the disadvantage of CNN-AE model [168–171,181].

Tables (1) and (2), provide the summary of papers published on detection and rehabilitation of ASD patients using DL, respectively.

4. Deep learning techniques for ASD rehabilitation

Rehabilitation tools are employed in multiple fields of medicine and their main purpose is to help the patients to recover after the treatment. Various and multiple rehabilitation tools using DL algorithms have been presented. Rehabilitation tools are used to help ASD patients using mobile, computer applications, robotic devices, cloud systems, and eye tracking, which will be discussed below. Also, the summary of papers published on rehabilitation of ASD patients using DL algorithms are shown in Table 2.

4.1. Mobile and software applications

Facial expressions are a key mode of non-verbal communication in children with ASD and play a pivotal role in social interactions. The use of brain computer interface (BCI) systems provides insight into the user's inner-emotional state. Valles et al. [185] conducted research focused on mobile software design to assist children with ASD. They aimed to design a smart iOS app based on facial images according to Figure (13). In this way, people's faces at different angles and brightness are first photographed and are turned into various emoji so that the autistic child can express his/her feelings and emotions. In this group's investigation [185], Kaggle's (The Facial Expression Recognition 2013) and KDEF (Kaggle's FER2013 and Karolinska Directed Emotional Faces) databases were used to train the VGG-16. In addition, the LEAP system was adapted to train the model at the University of Texas. The research

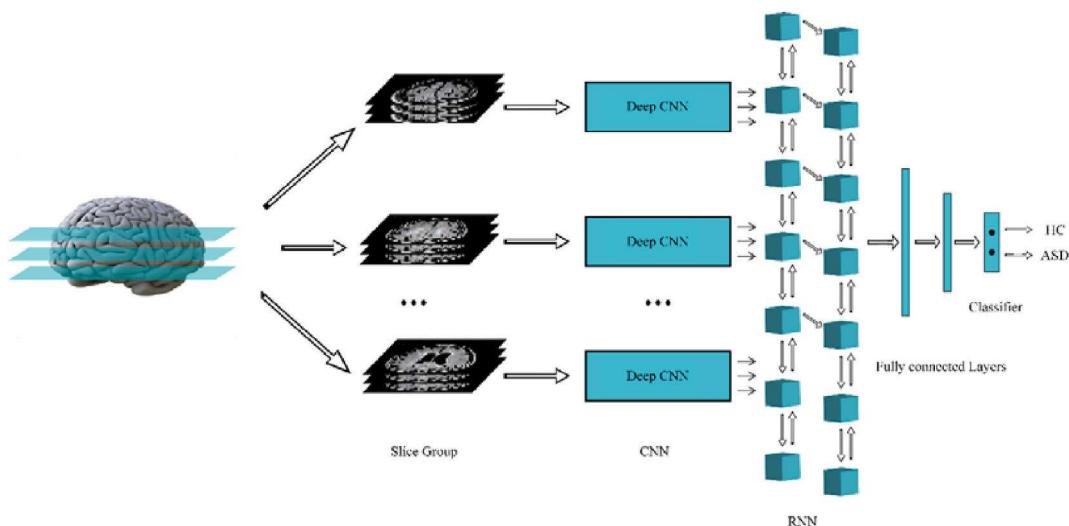


Fig. 11. Overall block diagram of a CNN-RNN used for ASD detection.

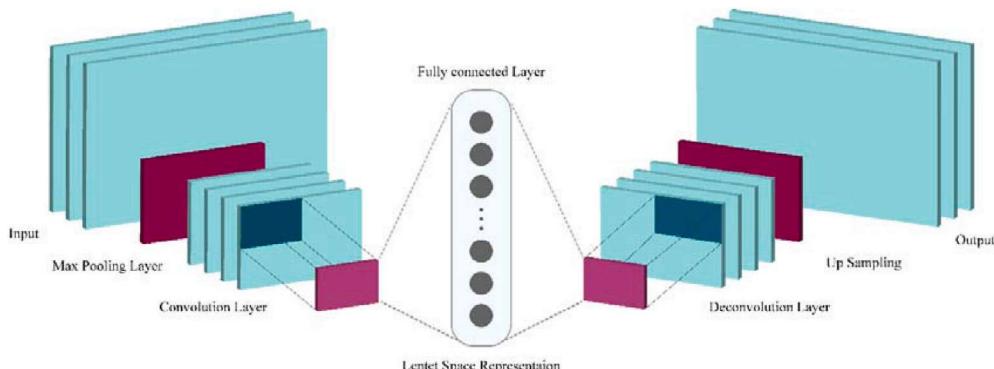


Fig. 12. Overall block diagram of a CNN-AE used for ASD detection.

provided the highest rate accuracy of 86.44%. In another similar study, they achieved an accuracy of 78.32% [183].

4.2. Cloud systems

Mohammadian et al. [211] proposed a new application of DL to facilitate automatic stereotypical motor movement (SMM) identification by applying multi-axis inertial measurement units (IMUs). They applied CNN to transform multi-sensor time series into feature space. An LSTM network was then combined with CNN to obtain the temporal patterns for SMM identification. Finally, they employed the classifier selection voting approach to combine an ensemble of the best base learners. After various experiments, the superiority of their proposed procedure over other base methods was proven. Figure (14) shows the real-time SMM detection system. First, IMUs, which are wearable sensors, are used for data collection; the data can then be analyzed locally or remotely (using Wi-Fi to transfer data to tablets, cell phones, medical center servers, etc.) to identify SMMs. If abnormal movements are detected, an alarm will be sent to a therapist or parents.

4.3. Eye tracking

Wu et al. [195] proposed a model of DL saliency prediction for autistic children. They used deep convolutional network (DCN) in their proposed paradigm, with a saliency map (SM) output. The fixation density map (FDM) was then processed by the single-side clipping (SSC) to optimize the proposed loss function as a true label along with the SM

saliency map. Finally, they exploited an ASD eye-tracking dataset to test the model. Their proposed model outperformed other base methods. Elbattah et al. [197] aimed to combine unsupervised clustering algorithms with DL to help ASD rehabilitation. The first step involved the visualization of the eye tracking path and the images captured from this step were fed to an AE to learn the features. Using AE features, clustering models are developed using the K-Means algorithm. Their method performed better than other state-of the art techniques.

5. Challenges

In this section, the most important challenges of ASD diagnosis are introduced using neuroimaging modalities, including neuroimaging datasets, tDCS and TMS challenges. Finally, the software and hardware challenges are discussed. These challenges are briefly presented in the following subsections.

5.1. Neuroimaging datasets

The most important challenges of neuroimaging datasets are the inaccessibility of MRI modalities and other huge neuroimaging datasets, datasets with hybrid modalities, and datasets of various ASD disorders. In the following, these challenges are studied.

5.1.1. Unavailability of MRI neuroimaging modalities datasets

In the ABIDE dataset, the diffusion tensor imaging (DTI) modality has not been presented for large number of subjects. Thus, limited

Table 2

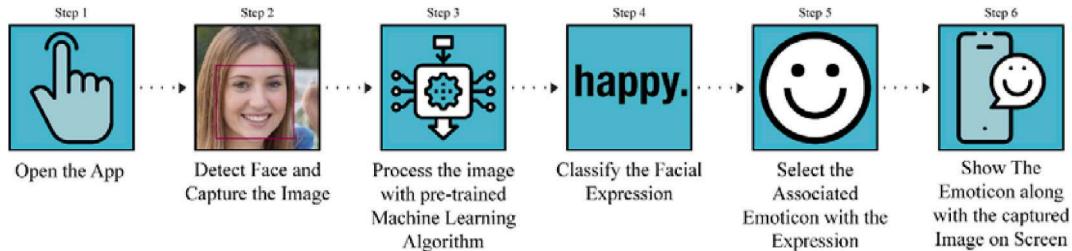
Summary of papers published on rehabilitation of ASD patients using DL algorithms.

Work	Datasets	Type of Applications	Number of Cases	Preprocessing	DNN Toolbox	DNNs	Performance Criteria (%)
[182]	OSIE	–	20 ASD 19 HC	HFM Construction, Filtering Normalizing, DA	Caffe TensorFlow	VGGNet + Softmax	Acc = 85 Sen = 80
[183]	KDEF	Facial Expression Recognition	70 Individuals	DA	Keras	DCNN + Softmax	Acc = 78.32
[184]	Clinical	Detecting Audio Regimes That Directly Estimate ASD Severity Social Affect scores	33 ASD	MFCC Spectrograms	NA	Noisemes Network + RF DiarTK Diarization Network	Acc = 84.7
[185]	Kaggle's FER2013	Facial Expression Recognition	–	–	Keras, TensorFlow	DCNN + Softmax	Acc = 86.44
[186]	SALICON	ASD Classification	14 ASD 14 HC	SalGAN Model, Feature Extraction	–	SP-ASDNet	Acc = 57.90 Rec = 59.21 Pre = 56.26
[187]	BigFaceX	Facial Expression Recognition	196 Subjects	SW, Merge in the Channel Dimension, DA	Keras	TimeConvNet + Softmax	Acc = 97.9
[188]	Different Datasets	Suitable Courseware for Children with ASD	–	Interactive and Intelligent Chat bot, NLP, Visual Aid	–	Different Nets	–
[189]	Camera Images	Estimating Visual Attention in Robot-Assisted Therapy	6 ASD and ID	Resizing, Frame Extraction, Visual Inspection Face Detection (Viola-Jones)	–	R-CNN + KNN MTCNN + Nave	Acc = 88.2 Pre = 83.3 Sen = 83.0
[190]	Sensor Data	Automatic SMM detection	6 ASD 5 HC	Resampling, Filtering, SW	Keras	CNN-LSTM + MV	–
[191]	KOMAA	Facial Expression Recognition	55 subjects	Segmentation, Different Features, Z Score	–	CNN + SVM	Acc = 96
[192]	Story-Telling Narrative Corpora	ASD Classification	31 ASD 36 HC	DA, ChineseWord2Vec	–	LSTM	Acc = 92
[193]	Ext-Dataset (video dataset)	ASD Classification using Eye Tracking	136 ASD 136 HC	TLD Method, Accumulative Histogram Computation	Keras	LSTM	Acc = 92.6 Sen = 91.9 Spec = 93.4
[194]	MIT1003	Predicting Visual Attention of Children with ASD	300 Images	–	–	DCN	SIM = 67.8 CC = 76.9 AUC-J = 83.4
[195]	Scan Path Data, Including Location and Duration	ASD Classification	14 ASD 14 HC	DA Methods	Pytorch	ResNet18 + Softmax	Acc = 55.13 Sen = 63.5 Spec = 47.1
[196]	UCI ML Repository	ASD Classification	704	Different Methods	–	CNN	Acc = 99.53 Sens = 99.39
[197]	Eye Tracking Scanpath	ASD Classification	29 ASD 30 HC	Visualization of Eye-Tracking Scanpaths Scaling Down, PCA	Keras, Sk-learn	AE + K-Means	Silhouette score = 60
[198]	Video Data	Engagement Estimation of Children with ASD During a Robot-Assisted Autism Therapy	30 children	–	Keras, TensorFlow	CultureNet + Softmax	ICC = 43.35 CCC = 43.18 PC = 45.17
[199]	YouTube ASD Dataset	Modeling Typical and Atypical Behaviors in ASD Children	68 video Clips	Different Methods	openCV, Caffe	DCNN + DT	Avg Pre = 73 Avg Recall = 75 Avg Acc = 71
[200]	Video Dataset	Behavioral Data Extracted from Video Analysis of Child-Robot Interactions.	5 ASD 7 HC	Segmentation, Upper Body tracking, Laban Movement Analysis to Drive Weight, Different features	–	CNN + Softmax	Acc = 88.46 Pre = 89.12 Recall = 88.53
[201]	Video Data	Developing Automatic SMM Detection System	6 ASD	Resampling, Filtering, SW, Data Balancing, Normalizing	Deepy Library	CNN + SVM	F1-score = 95
[202]	ASD Screening	Autism Screening	513 ASD 189 HC	Cleaning Missing Values and Outliers, Visualization, Identity Mapping	–	DENN + Sigmoid	Acc = 100 Sen = 100 F1-score = 99
[203]	ASD Screening Datasets	Classification of Adults with ASD	–	Handling of Missing Values, Variable Reduction, Normalization, and Label Encoding	Keras	DNN + Sigmoid	Acc = 99.40 Sen = 97.89 Spec = 100
[204]	GazeFollow4ASD Dataset	Gaze-Following	8 ASD 10 HC	Saliency Map Generation (SMG)	–	DNN + Softmax	Acc = 79.94
[205]	ADOS-2	Child-Adult Speaker Classification	86 ASD 79 Others	MFCC Feature Extraction	–	GAN	F1-Score = 78.27
[206]	Videos Dataset	Gaze Direction Prediction	8 ASD 23 HC	Gray-scaling, Face Detection By a Cascade Classifier With LBP Features, Eye Detection By Cascade Classifier With Haar Features, DA	Caffe	2D-CNN + Softmax	Acc = 97.38
[207]	Image Dataset	Face Image Classification	20 ASD 19 HC	–	–	ResNet-50 + Softmax	Acc = 89.2
[208]	72 ADOS Sessions	Estimate ADOS Scores	56 ASD 10 Other 6 HC	Segmentation, Feature Extraction, Sequential Forward Feature Selection (SFS)	–	1D-CNN	RMSE = 4.65 Correlation = 0.72
[209]	Clinical EEG	–	–	Filtering, Windowing	Keras	LSTM	Acc = 93.27

(continued on next page)

Table 2 (continued)

Work	Datasets	Type of Applications	Number of Cases	Preprocessing	DNN Toolbox	DNNs	Performance Criteria (%)
[210]	Clinical EEG	Anxiety Classification from EEG in Adolescents with Autism EEG-Based Mental Stress Classification in Adolescents with Autism for Breathing Entrainment BCI	8 ASD 5 HC 8 ASD 5 HC	Filtering, Windowing	Keras	LSTM	Acc = 93.27

**Fig. 13.** Block diagram of iOS application for ASD rehabilitation.**Fig. 14.** Cloud system design for ASD rehabilitation.

studies have been done to diagnose ASD from DTI modalities and DL models. Another challenge is that neuroimaging modalities like diffusion weighted imaging (DWI) and perfusion-weighted imaging (PWI) have not been presented.

5.1.2. Unavailability of other neuroimaging modalities datasets

As mentioned in the Introduction section, different functional neuroimaging modalities, including EEG [212], MEG [213], and fNIRS [214] are used for ASD diagnosis. The cost of EEG and fNIRS is lower than MRI modalities, but their efficiency in ASD diagnosis is high. Unfortunately, huge EEG and fNIRS datasets are not available freely for research. Also, to the best of our knowledge, no study has presented the ASD diagnosis using MEG modality and DL models due to the inaccessibility of MEG datasets.

5.1.3. Unavailability of multimodality neuroimaging datasets

In clinical studies, multimodality techniques, including EEG-fNIRS [215], EEG-fMRI [216,217], EEG-MEG [218], and MEG-DTI [219], are being carried out for ASD diagnosis. Clinical studies have shown that using multimodality techniques play an efficient role in increasing the accuracy of ASD diagnosis [220]. Till now, multimodality neuroimaging datasets have not been available to the researchers, which is another challenge. The availability of such datasets can promote many studies in ASD diagnosis using various DL models.

5.1.4. Unavailability of neuroimaging datasets with different types of ASDs

As mentioned before, ASD includes a wide range of disorders with varying levels [221]. But the purpose of most studies is to discriminate

ASD from healthy controls (HC). To the best of our knowledge, there is no study conducted to classify various types of ASD or its different levels due to the unavailability of datasets.

5.2. Unavailability of TMS and tDCS for ASD

The Introduction section discussed brain stimulation using TMS and tDCS techniques. To use these methods, first, the brain is divided into different areas. Then, the brain area of interest is stimulated by a specialist [222,223]. An important challenge in using TMS and tDCS is that brain stimulation should be accurate; otherwise, the patient might encounter some side effects [224]. If the DL models are used along with TMS and tDCS techniques, the brain areas can be segmented with higher accuracy which promotes the brain stimulation with TMS and tDCS.

5.3. Software and hardware challenges for ASD

This section presents the most important software and hardware challenges based on DL for ASD diagnosis. The sMRI modalities are recorded in 3D [225], and they are processed using 3D networks based on DL. Also, standard fMRI data is 4D [226] and requires 4D models based on DL for processing. In practice, using these networks is very challenging; as it requires huge memory, computational load, and hardware cost. Although 2D DL networks have been developed significantly, adding more layers and deepening the network imposes some constraints to the network. Including the number of layers, increasing the network parameters, makes training the network difficult and requires large number of training datasets which is difficult to obtain and

very expensive.

Another problem grappling the researchers is designing the DL-based rehabilitation systems with hardware resources. Nowadays, assistive tools such as Google Colab are available to researchers to improve the processing power. However, the problems still prevail when implementing these systems in real-world scenarios.

6. Discussion

In this study, we proposed a comprehensive overview of the investigations conducted in the scope of DL-based ASD diagnostic CAD systems as well as rehabilitation tools for ASD patients. In the field of ASD diagnosis, numerous papers have been published using functional and structural neuroimaging data as well as rehabilitation tools.

[Tables 1 and 2](#) respectively represent the details of ASD diagnosis and rehabilitation using DL models. In this section, the ML and DL techniques in ASD diagnosis are compared first. Afterwards, the other contents provided in [Table \(1\)](#) and [Table \(2\)](#) namely neuroimaging modalities, DL toolboxes, various DL models, and classification techniques are discussed.

6.1. Comparison of ML with DL methods for ASD diagnosis

Various studies have been proposed to diagnose ASD using ML techniques [227–237]. For example, Hyde et al. have reviewed applications of supervised machine learning methods for the diagnosis of ASD [227]. Song et al. have studied the classification and detection of ASD using ML methods and neuroimaging data [228]. Hosseinzadeh et al. [229] have reviewed ASD methods in the context of IoT devices systematically. Rahman et al. [230] have conducted a review on the analysis of ASD feature selection and classification. Pagnozzi et al. [231] have reviewed the studies on sMRI biomarkers in ASD detection using ML techniques. Xu et al. [232] have presented recent developments in identifying ASD using ML methods.

The preprocessing, feature extraction, feature selection (feature reduction), and classification are employed for ASD detection using ML techniques. Feature extraction is the most important section in ML models for ASD diagnosis. Choosing the appropriate feature extraction algorithms in CADS is very difficult, and, generally, it is done via trial and error, which is one of its important shortcomings [238–242]. Another shortcoming of ML technique is usage of large data that may lead to improper efficiency [243–246].

With the emergence of DL techniques, many scientists have employed these techniques for disease diagnosis [247–249]. The most important difference between ML and DL techniques is in feature extraction [168–171]. In the DL models, feature extraction and feature selection are carried out by deep layers [168–171]. Also, the efficiency of these models does not decrease by increasing the input neuroimaging data. To the best of our knowledge, this study is the first review paper discussing the ASD diagnosis using DL techniques which may help large number of young researchers to use the suitable AI method for the detection of ASD accurately.

6.2. Neuroimaging modalities for ASD diagnosis

[Table \(1\)](#) discuss the studies conducted on ASD diagnosis using neuroimaging modalities and DL models. In [Table \(1\)](#), sMRI, DTI, T-fMRI, rs-fMRI, and fNIRS modalities have been used to diagnose ASD. [Figure \(15\)](#) shows the number of papers published using various neuroimaging modalities for ASD diagnosis with DL technique.

It can be noted from [Figure \(15\)](#) that, rs-fMRI modality is used more than other methods for ASD diagnosis and rehabilitation.

6.3. DL toolboxes for ASD diagnosis and rehabilitation

A variety of DL toolboxes have been proposed for implementing deep

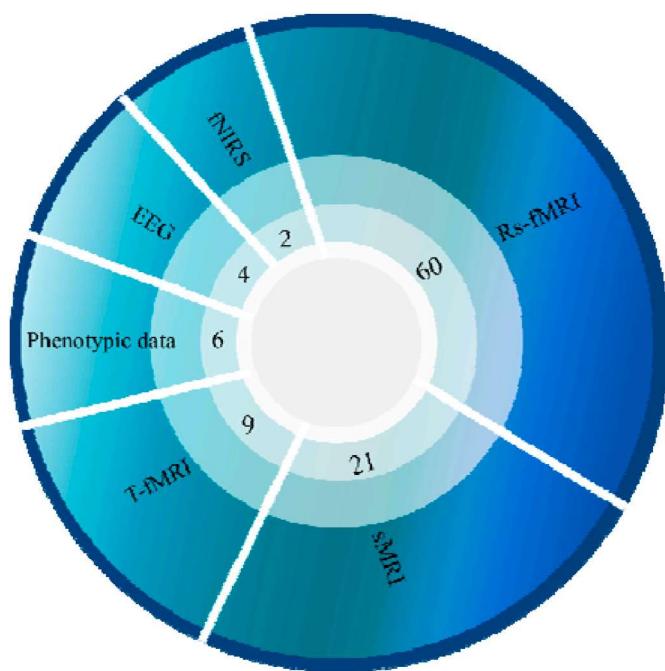


Fig. 15. Number of papers published using various modalities for ASD diagnosis with DL techniques.

networks. In [Tables 1 and 2](#) the types of DL toolboxes utilized for each study are depicted, and the total number of their usage is demonstrated in [Figure \(16\)](#).

The Keras toolbox is used in the majority of the studies due to its simplicity. Keras offers a consistent high-level application programming interface (APIs) to build the models more straightforward, and by using powerful backends such as TensorFlow, its performance is sound. Additionally, due to all pre-trained models and available codes on platforms such as GitHub, Keras is quite popular among researchers.

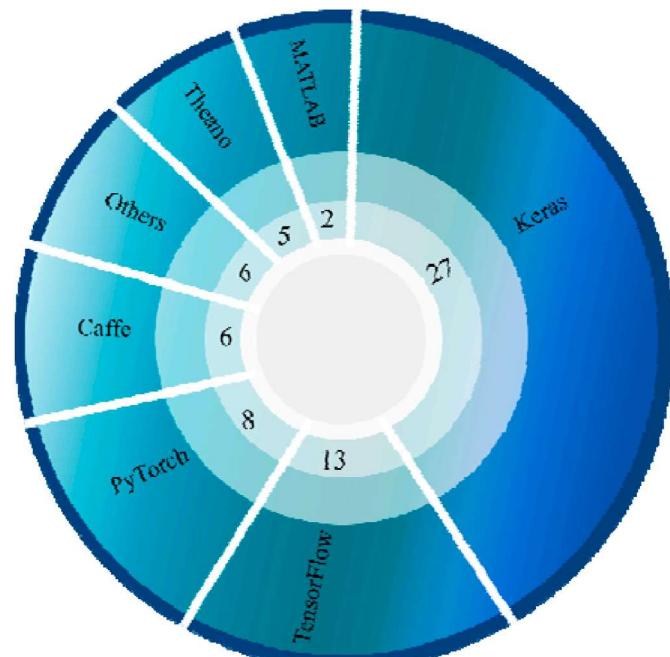


Fig. 16. Number of DL tools used for the diagnosis and rehabilitation of ASD patients in reviewed papers.

6.4. DL methods for ASD diagnosis and rehabilitation

Various DL models have been presented in [Tables \(1\)](#) and [\(2\)](#) for ASD diagnosis and rehabilitation. [Tables \(1\)](#) and [\(2\)](#) show that CNN, RNN, AE, DBN, CNN-RNN, and CNN-AE models have been used for ASD diagnosis and rehabilitation. The number of DL networks used for the ASD detection in the reviewed works is shown in [Figure \(17\)](#).

Among the various DL architectures, CNN is found to be the most popular one as it has achieved more promising results compared to other deep methodologies. The AE, as well as RNN, has yielded favorable results. It can be noted that in recent years, the number of DL-based papers has increased exponentially due to their sound performance and also the availability of vast and thorough datasets.

6.5. Classification methods for ASD diagnosis and rehabilitation

The number of various classification algorithms used in DL networks is shown in [Figure \(18\)](#). One of the best and most widely used is the Softmax algorithm ([Tables \(1\)](#) and [\(2\)](#)). It is most popular since it is differentiable in the entire domain and computationally less expensive.

7. Future works

In this section, future works on ASD diagnosis using neuroimaging modalities and DL models are presented. The future works include developing datasets, DL methods, and rehabilitation systems, which are discussed in the following sections.

7.1. Future works in datasets

In Section 5 (Challenges), the available datasets were discussed. In this section, the future works regarding datasets, including presenting various structural and functional neuroimaging modalities, datasets of different types of ASD, and multimodality datasets are discussed.

7.1.1. Future works in neuroimaging datasets

As mentioned before, the ABIDE dataset includes different MRI imaging modalities of ASD patients. In section 5, it was discussed that this

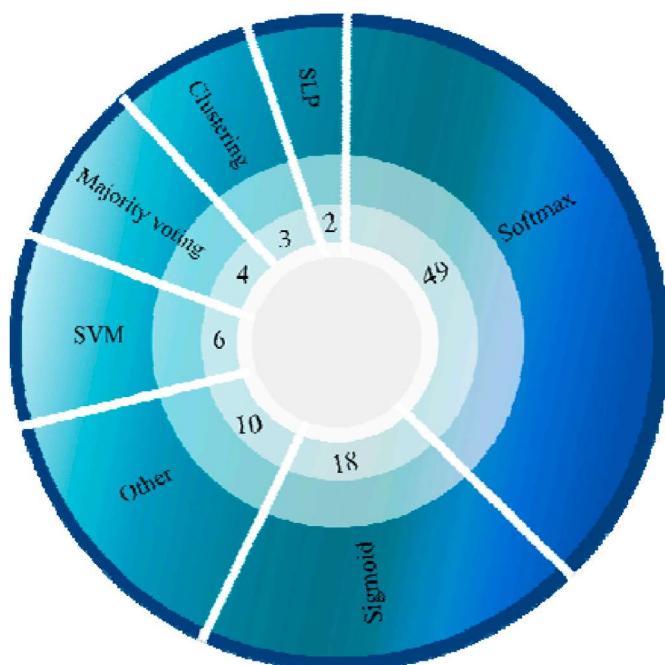


Fig. 18. Number of various classification algorithms used for the detection of ASD and rehabilitation in DL.

dataset consists of images of diffusion tensor imaging (DTI) modalities of few subjects and does not have images of diffusion weighted imaging (DWI) modality. Therefore, providing available datasets of DTI [34] and DWI [250] for ASD diagnosis using DL models in future studies is very important.

Also, a dataset [63,64] was provided for studies that include EEG signals of patients suffering from ASD and healthy controls (HC). This dataset has limited number of subjects. Therefore, DL studies have not focused on it. Also, there is no public dataset available on MEG and fNIRS modalities provided for the researchers. In future works, providing these datasets will help the researcher's to develop novel accurate ASD diagnosis systems using DL methods.

7.1.2. Future works in neuroimaging datasets with different types of ASD

The ASD has various types and intensities [251]. As mentioned in the challenges section, there is no freely available neuroimaging dataset. In future studies, with more freely available datasets on ASD patients of different types and intensities can help to detect ASD accurately using DL models.

7.1.3. Future works in multimodality neuroimaging datasets

In clinical research, EEG-fNIRS, EEG-fMRI, EEG-MEG, and MEG-DTI multi-modalities are used for ASD diagnosis [215–219]. Providing public datasets for these modalities can help the researchers to develop the DL models for ASD diagnosis.

7.2. Future works in deep learning methods for ASD diagnosis

In this paper, various DL methods were studied for ASD diagnosis using neuroimaging modalities. According to [Tables \(1\)](#) and [\(2\)](#), standard DL methods have been used for ASD diagnosis. In the following sections few suggestions are given for using DL methods which include attention techniques [252,253], adversarial techniques [254,255], and transformer techniques [256,257].

7.2.1. Deep attention techniques

In recent years, attention techniques have become one of the most important concepts in DL [252–254,258]. These models are used in

Fig. 17. Number of DL networks used for ASD detection and rehabilitation in the reviewed works.

machine vision [259], speech processing [260], etc. The main idea of attention mechanism is that each time the model predicts the output, the parts of the input in which the most relevant information are concentrated, are processed instead of the whole sequence [261]. Some of these methods include deep attention-based RNNs [262], deep attention auto-encoders [263], deep attention CNN [264], and graph attention CNN [265]. Attention-based models provide a more accurate interpretation and a better description of information than basic models. In future studies, these models can be used for ASD diagnosis using neuroimaging modalities.

7.2.2. Data augmentation techniques

The data shortage is a challenging problem for the scientists in disease diagnosis using DL techniques. Hence, various data augmentation techniques have been proposed [254,255]. GAN models are one of the most popular data augmentation techniques used to resolve the data shortage problems in ASD diagnosis using DL technique. Recently, the simple Copy-Paste methods have been presented for data augmentation [266]. In future studies, this method can also be used for data augmentation for ASD diagnosis using neuroimaging modalities.

7.2.3. Transformer techniques

The transformer techniques are one of the most recent DL methods recently used for medical data classification [256,257]. The first work on transformer models has been introduced in [267]. In this architecture, the self-attention mechanism has been used along with the encoder and decoder [267]. In future studies, this model can be used for ASD diagnosis. Also, new transformer models like graph transformer networks [268] and deep diffeomorphic transformer networks [269] can be used in ASD diagnosis.

7.3. Future works in rehabilitation systems for ASD

Many researchers have proposed various DL-based rehabilitation tools to aid the ASD patients. Designing a reliable, accurate, and wearable low power consumption DL algorithm-based device is the future tool for ASD patients. An achievable rehabilitation tool is to wear smart glasses to help the children with ASD. These glasses with built-in cameras will acquire the images from the different directions of environment. Then the DL algorithm processes these images and produces meaningful images for the ASD children to better communicate with their surroundings.

Nowadays, cloud computing is one of the most important medical technologies, and various studies have been used it for disease diagnosis applications [269]. It helps to store data in the cloud space and implement various DL models [270]. In future studies, cloud computing can be used for ASD diagnosis using neuroimaging modalities and DL techniques.

Also, in future studies, the internet of things (IoT) can be used for ASD diagnosis. Lack of access to specialists in brain centers and hospitals is a challenge to diagnose ASD patients accurately. Hence we feel that,

Appendix A. Statistical Metrics

This section demonstrates the equations for the calculation of each evaluation metric. In these equations, True positive (TP) is the correct classification of the positive class, True negative (TN) is the correct classification of the negative class, False positive (FP) is the incorrect prediction of the positives, False negative (FN) is the incorrect prediction of the negatives [168].

$$\text{Accuracy (Acc)} = \frac{TP + TN}{TP + TN + FP + FN} \quad (1)$$

$$\text{Specificity (Spec)} = \frac{TN}{TN + FP} \quad (2)$$

$$\text{Sensitivity (Sen)} = \frac{TP}{TP + FN} \quad (3)$$

$$\text{Precision (Prec)} = \frac{TP + TN}{TP + TN + FP + FN} \quad (4)$$

$$F1 - Score = 2 * \frac{\text{Prec} * \text{sens}}{\text{TPrec} + \text{Sens}} \quad (5)$$

Receiver Operating Characteristic Curve (ROC CURVE)

The receiver operating characteristic curve (ROC-curve) depicts the performance of the proposed model at all classification thresholds. It is the graph of true positive rate vs. false positive rate (TPR vs. FPR). Equations for calculation of TPR and FPR are presented below [168].

$$TPR = \frac{TP}{TP + TN} \quad (6)$$

$$FPR = \frac{FP}{FP + TN} \quad (7)$$

Area under the ROC Curve (AUC)

AUC presents the area under the ROC-curve from (0, 0) to (1, 1). It provides the aggregate measure of all possible classification thresholds. AUC has a range from 0 to 1. A 100% wrong classification will have AUC value of 0.0, while a 100% correct classified version will have the AUC value of 1.0. It has two folded advantages [168]. One is that it is scale invariant, which implies how well the model is predicted rather than checking the absolute values. The second advantage is that it is classification threshold-invariant as it will verify the performance of the model irrespective of the threshold being selected [168].

Appendix B

Tables (3) and (4) show all the abbreviations presented in this paper and their full forms, sorted alphabetically.

TABLE 3
List of abbreviations, A through O.

A	
AAL	Automated Anatomical Labeling
AEs	Autoencoders
AI	Artificial Intelligence
API	Application Programming Interface
ASD	Autism Spectrum Disorder
AS	Asperger's Syndrome
APA	American Psychiatric Association
ADOS-2	Autism Diagnostic Observation Schedule 2nd Edition
ADI-R	Autism Diagnostic Interview-Revised
B	
BCI	Brain Computer Interface
C	
CADS	Computer-Aided Diagnosis Systems
CC200	Craddock 200
CC400	Craddock 400
CCS	Connectome Computation System
CPAC	Configurable Pipeline for the Analysis of Connectomes
CRF	Conditional Random Forest
CSF	Cerebrospinal Fluid
CDD	Childhood Disintegrative Disorder
CARS	Childhood Autism Rating Scale
D	
DA	Data Augmentation
DAE	Denoising AE
DBNs	Deep Belief Networks
DCA	Diedrichsen Cerebellar Atlas
DCN	Deep Convolutional Network
DL	Deep Learning
DPARSF	Data Processing Assistant for rs-fMRI
DTI-MRI	Diffusion Tensor Imaging MRI
DTI	Diffusion Tensor Imaging
DWI	Diffusion Weighted Imaging
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, 5th Edition
DISCO	Diagnostic Interview for Social and Communication Disorder
3di	Developmental, Dimensional, and Diagnostic Interview
E	

(continued on next page)

TABLE 3 (continued)

A	
ECoG	Electrocorticography
EEG	Electroencephalography
EZ	Eickhoff-Zilles
F	
FCM	Functional Connectivity Matrix
FFS	Forward Feature Selection
FFT	Fast Fourier Transform
fMRI	Functional MRI
fNIRS	Functional Near-Infrared Spectroscopy
FSL	FMRIB software libraries
G	
GABM	Genetic Algorithm Based Brain Masking
GAN	Generative Adversarial Network
GCA	Gordon's Cortical Atlas
GLASSO	Graphical Least Absolute Shrinkage and Selection Operator
GM	Gray Matter
GRU	Gated Recurrent Unit
GARS	Gilliam Autism Rating Scale
GPUs	Graphic Processor Units
H	
HIPAA	Health Insurance Portability and Accountability
HO	Harvard-Oxford
HOG	Histogram of Oriented Gradients
HC	Healthy Control
I	
IMUs	Inertial Measurement Units
IoT	Internet of Things
K	
KLD	Kullback-Leibler Divergence
KAU	King Abdulaziz University
L	
LBP	Local Binary Pattern
LSTM	Long Short-Term Memory
M	
MCNNES	Mixture of CNN Experts
MEG	Magnetoencephalography
MDMC	Max-Det Matrix Completion
MFCC	Mel-Frequency Cepstral Coefficients
MKFC-AE	Multi-kernel Fuzzy Clustering based AE
ML	Machine Learning
MLP	Multilayer Perceptron
MRI	Magnetic Resonance Imaging
M-CHAT	Modified Checklist for Autism in Toddlers
N	
NDAR	National Database for Autism Research
NIAK	Neuroimaging Analysis Kit
NLP	Natural Language Processing
NIBS	Noninvasive Brain Stimulation
O	
1D-CAE	One-Dimensional CNN Autoencoder

TABLE 4
List of abbreviations, P through Z

P	
PCA	Principal Component Analysis
PCC	Pearson Correlation Coefficient
PCP	Preprocess Connectome Projects
PICA	Probabilistic Independent Component Analysis
PSVM	Probabilistic SVM
PDD-NOS	Pervasive Developmental Disorder – Not Otherwise Specified
PWI	Perfusion-Weighted Imaging
R	
RF	Random Forest
RFE	Recursive Feature Elimination
RL	Reinforcement Learning
RNNs	Recurrent Neural Networks
rs-fMRI	Resting-State fMRI
RS	Rett Syndrome
S	
SAE	Stacked AE
SdAE	Stacked Denoising AE

(continued on next page)

TABLE 4 (continued)

P	
SLP	Single Layer Perceptron
SMG	Saliency Map Generation
SMM	Stereotypical Motor Movements
sMRI	Structural MRI
SpAE	Sparse AE
SR	Softmax Regression
SSA	Subcortical Structural Atlas
SVM	Support Vector Machine
SW	Sliding Window
T	
T-fMRI	Task-Based fMRI
3D-CNN	Three Dimensional CNN
2D-CNN	Two Dimensional CNN
tDCS	Transcranial Direct Current Stimulation
TMS	Transcranial Magnetic Stimulation
V	
VAE	Variational Autoencoders
VS	Voting Strategy
W	
WM	White Matter

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