

# A Survey on Deep Learning Methodologies for Neurological Disorders- Alzheimer's, Autism, Epilepsy

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Received: 21 April 2022    Revised: 19 August 2022    Accepted: 1 September 2022

Published: 10 September 2022

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## Abstract

Deep learning has frequently been utilized for detection of neurological disorders. Generally, two types of data, i.e., Neurophysiological signals such as Electroencephalogram (EEG), Electrocorticography (ECoG) and Neuroimages, such as Positron Emission Tomography (PET), structural Magnetic Resonance Imaging (MRI) and functional MRI are taken into consideration for diagnosis of neurological diseases. Deep learning has achieved substantial performance developments over handcrafted feature extraction followed by machine learning techniques in computer-aided diagnosis (CAD) of neurological ailments. This study presents a broad assessment of the deep learning methodologies for neurophysiological and neuroimaging-based neurological disorders, i.e., epilepsy, Alzheimer's, and autism.

**Keywords:** Alzheimer's disease, autism disorder, deep learning, EEG, epilepsy, MRI

## Introduction

Medical data (signals and images) encompasses a variety of technologies that offer visual illustrations of the internal part of the human body to help clinicians discover, diagnose, and treat diseases more quickly and effectively<sup>1</sup>. Medical imaging, which includes computed tomography (CT), mammography, RI, PET, X-ray, and ultrasound, has fast become a

dominating and effective technology over the last few decades<sup>2</sup>. Neurophysiological signals which include EEG is widely used for the detection of epilepsy. For diagnosis and research, the data gathered by these technologies provides numerous information about the various human organs. Human professionals, such as radiologists and doctors, must undertake detailed interpretations of medical data in taking decisions. However, due to the large amount of medical data, elucidation is time-consuming and simply affected by human specialist's prejudices and exhaustion. As a result, clinicians have been using CAD systems to understand neural signals and brain images to increase their effectiveness.

Handcrafted feature extraction followed by classical machine learning techniques is capable of extracting informative features that explain the immanent patterns from data in CAD systems, and it renders an important part in medical data analysis. The structures of medical data, on the other hand, are extremely complicated, and feature selection is still done by humans using their domain knowledge. This makes machine learning approaches in medical image and signal analysis and difficult for non-experts to use.

As a result, handmade feature selection isn't appropriate for medical signals and images. Although the efficacy of sparse learning and dictionary learning for impetuously identifying inequitable features from training samples has been shown, these algorithms' shallow designs limit their representational power.

Deep learning, in contrast to typical handcrafted feature extraction techniques, automatically extracts useful information without the need for domain experts' knowledge, allowing non-experts to effectively apply deep learning approaches. As a result, deep learning has quickly become the preferred procedure for medical data analysis in recent times. Deep learning has perceived unparalleled accomplishment in numerous artificial intelligence applications, such as speech recognition, autonomous vehicles, and computer vision, thanks to increased computation facilities and, the availability of enormous data. The use of deep learning in medical data analysis was driven by the simultaneous progress and successes of computer vision.

Deep learning is currently driving significant progress in medical image analysis. Classification, detection/localization, registration, and segmentation are the four major categories of medical image analysis tasks<sup>3</sup>. The initial job in which deep learning makes a significant involvement to medical image processing is categorization. The goal of this job is to divide medical images into two or more categories. To identify Alzheimer's disease or

moderate cognitive impairment, the stacked auto-encoder model was utilized by merging medical imaging and biological<sup>4</sup>. The detection/localization challenge entails locating and identifying features or lesions in a whole medical image. Deep convolutional neural networks, for example, were utilized to locate lymph nodes in CT scans. The objective of segmentation is to divide a medical image into distinct segments, such as tissue classes, organs, diseases, etc. The U-net, is the widely utilized deep learning architecture for segmentation is composed of convolutional network. Medical image registration technique corrects the alignment of images. In an unsupervised approach<sup>5</sup>used convolutional layers to extract characteristics from input patches. The acquired feature vectors were then employed in the HAMMER registration process to substitute the handcrafted features. Other important tasks in medical image analysis include content-based picture retrieval and image synthesis and augmentation in conjunction with image data and reports.

### **Alzheimer's Disease Analysis using Deep Learning Techniques**

Alzheimer's disease (AD) is the supreme prevalent basis of dementia and is a neurological, irreversible, growing brain illness. Although the causes of Alzheimer's disease are unknown at this time, correct diagnosis of the disease is critical in-patient management, particularly in the early stages. The Alzheimer's Disease Neuroimaging Initiative (ADNI), a research study is targeted to progress clinical studies for the precaution and therapeutics of AD, has the prominent public neuroimaging dataset for AD diagnosis. The ADNI study began in 2004 and is currently in its third phase. The ADNI dataset currently covers over 1,000 patients and includes ADNI-1, ADNI-GO, ADNI-2, and ADNI-3. These individuals were in three phases of disease which are normal control (NC), mild cognitive impairment (MCI), and Alzheimer's disease (AD).

A slew of articles on deep learning algorithms for Alzheimer's diagnosis have just been released. These methods can be loosely separated into two types based on various architectures: DGM-based and Convolutional Neural Network based methods. The Deep Belief Networks (DBN), Stacked Auto-Encoders (SAE), and Auto-Encoders (AE) variants were included in the DGM-based approaches. Authors in<sup>6</sup>built a sturdy deep learning structure by stacking multiple restricted Boltzmann machines (RBMs) and using the reliability selection and multi-task learning technique. In<sup>7</sup>, authors suggested a number of deep learning approaches, including the Deep Boltzmann Machine (DBM) and SAE<sup>4-8</sup>. To merge longitudinal and cross-sectional characteristics calculated from MR brain images, Authors used multi-modality stacked

denoising sparse AE (SDAE)<sup>9</sup>. Multiscale patch-wise metabolic attributes as input on multiscale deep learning network is also used<sup>10</sup>. Authors employed a deep convolution AE (DCAE) model to extract features that have strong relationships with clinical variables including cognitive exams, age, and tau protein deposits<sup>11</sup>. Authors in<sup>12</sup> efficiently fuse and learn feature representation using a multimode-stacked deep polynomial network (DPN) from a short multimodal neuroimaging dataset due to tiny labelled samples in neuroimaging dataset. Authors in<sup>13</sup> used a sparse AE on random patches of natural images to pre-train a 2D-CNN based on sMRI data. The use of cross-domain characteristics to show MRI data was an important strategy. On ImageNet, Liu and Shen utilized an analogous method and trained a pre-trained deep CNN<sup>14</sup>. The fMRI data was originally used in deep learning applications by authors in<sup>15</sup>. In the preprocessing step, the 4D resting state-fMRI and 3D MRI data were fragmented into 2D format images, which were then fed into the CNN-based architecture's input layer.

Billones et al. adapted VGGNet structure and proposed a DemNet model where the coronal image slices were chosen for classification task<sup>16</sup>. By reducing 3D PET scans into 2D slices, introduced a unique classification methodology which learns characteristics from a succession of 2D slices<sup>17</sup>. The intra-slice features were captured using hierarchical 2D-CNN, while the inter-slice features were extracted using GRU.

The 3D brain images must be split into 2D slices in the preprocessing step, resulting in 2D-CNN approaches removing the spatial information. As a result, many 3D-CNN algorithms have been presented, all of which can straightforwardly input 3D brain images. A sparse AE to train a 3D-CNN on tiny 3D patches from sMRI data was proposed<sup>18</sup>. To encapsulate anatomical structure fluctuations in sMRI data, Authors suggested a deep 3D-CNN based on a 3D CAE (Convolutional AE)<sup>19</sup>. Extracted features from PET and MRI images-using several deep 3D-CNN on various local image patches<sup>20</sup>. The learnt local features were then ensembled and latent multi-modal features for AD classification were identified using a set of higher high-level CNN. To increase performance, authors in<sup>21</sup> presented a 39-layer 3D-CNN architecture which works on a residual learning network (ResNet).

The scientists initially identified parametric anatomical landmarks from MR images using a data-driven approach, and then developed a 3D-CNN to learn patch-based features. This technique avoids the high-dimensional voxel-level difficulty and manual ROI-level definition. Following that, A deep multi-instance CNN methodology is presented, in which several image

patches were employed as a bag of illustrations to characterize individual subject, with the whole-image-level class label determining the label of each bag<sup>22</sup>. In<sup>23</sup>, authors predicted missing PET images from sMRI using a 3D-CNN and authors has achieved classification accuracy similar to the genuine PET images. In<sup>24</sup> authors proposed Cycle-GAN to study sMRI and PET mapping in order to create missing PET scans created on their associated sMRI scans. Authors in <sup>25</sup>presented a CNN architecture based on T1-weighted MRI.

MCI had a transformation frequency of 10–15 percent per year in 5 years as an early stage of AD, but it was also the ideal time for treatment. As a result, developing an accurate prediction model for early MCI diagnosis has become an important subject. MCI prediction has recently been the subject of some Graph Convolutional Networks (GCN) based studies. In <sup>26</sup>and <sup>27</sup>, combines neuroimaging data with the demographic relationship on GCN for MCI prediction. In<sup>28</sup>, authors used a multi-class GCN classifier to divide people on the Alzheimer's spectrum into four groups. PETNET, a model based on the GCN, was proposed by authors in <sup>29</sup>to analyze PET signals.

### **Autism Spectrum Disorder (ASD) Analysis using Deep Learning Techniques**

ASD is a prevalent neurodevelopmental disease that impacts approximately 62.2 million people worldwide. The Autism Imaging Data Exchange (ABIDE) project gathered fMRI brain scans from laboratories all over the world. Two large-scale collections were released as part of the ABIDE initiative: ABIDE I and ABIDE II. The ABIDE I study encompassed 17 international sites and included 1,112 people, 539 of whom were autistic sufferers and 573 of whom were not. The ABIDE II compilation, which included 19 worldwide sites and 1,114 subjects from 521 people with ASD and 593 people without ASD, aimed to increase the number of specimens with enhanced depicted genotypes.

Many approaches using deep learning techniques for Autism detection have been proposed. To minimize data dimension and discover highly inequitable representations, AE-based approaches exploited several AE variations or layered numerous AE. The basic SAE was developed by Hazlett et al., who primarily extracted surface area information from brain MRI to diagnose autism in children in <sup>30</sup>. In <sup>31</sup>employed a stacked multiple sparse AE (SSAE) to develop whole-brain functional connectivity patterns, whereas in <sup>32</sup>only used the top 3,000 F-score ordered connectivity features from SSAE in descending order.

In<sup>33</sup>, authors employed 34 sparse AE for 34 spatial activation zones to create an automated autism diagnosis method. Each sparse AE lowered the dimensionality of feature vectors. In

<sup>34</sup>employed VAE to extract two-dimensional features from functional connection networks. One feature was discovered through a high level of discriminating between ASD and NC, and it was found to be narrowly linked to ASD-related brain regions. In<sup>35</sup> authors employed DAE to increase generalization and lessen the effect of multi-site heterogeneous data. In<sup>36</sup>, authors used transfer learning to build a deep neural network architecture for ASD classification due to a lack of training samples. First, an SSAE was used to train this framework to discover functional connectivity patterns. After then, it was moved to a new categorization with fewer target subjects.

In<sup>37</sup>, authors devised a technique which augment the data to generate artificial datasets for the ASD-DiagNet model's training. To enhance the condition of retrieved attributes, this model included a single-layer perceptron and an AE. The aforementioned techniques ignored the spatial shape of the brain networks since the resting state-fMRI data were flattened into a feature vector. Authors in <sup>38</sup>presented a CNN architecture on ABIDE dataset to classify ASD patients and control subjects. In <sup>39</sup>used pretrained models VGG-19 and NASNETMobile to detect ASD on facial dataset publicly available on kaggle.

### **Epileptic Seizure Detection using Deep Learning Techniques**

Around 65 million people are suffering from epileptic seizures worldwide out of which mostly are developing countries. To detect seizures EEG reports are used by neurologists which is captured by 10-20 system. Various publicly datasets are available for researchers to implement their CAD system. One of the most widely used EEG dataset is developed by University of Bonn, Germany. Temple University and CHB-MIT EEG datasets are also publicly available used by various researchers. First CAD system to detect seizures using deep learning model was done by authors<sup>40</sup>. They proposed a 13-layer 1D-CNN architecture. Authors proposed a pyramidal 1D-CNN model which has less training parameters and gives good accuracy<sup>41</sup>. In<sup>42</sup>, authors proposed a 1D-CNN model to extract features followed by machine learning classifiers. In <sup>43</sup>proposed a CNN model which classifies the seizures only in 20 epochs. Authors in <sup>44</sup>presented a 2D- deep convolution autoencoder followed by Bi-LSTM model to detect seizures in children.

### **Future Directions**

It can be observed from this review, research on neurological disorders applying deep learning has been examined across three diseases. Furthermore, in PubMed, the number of papers on

neurological disorders is increasing at an almost exponential rate. Unfortunately, no uniform deep learning architecture exists that could be used for all disease studies. There is no single model which is optimal for all problems. As a result, to detect a specific disease, several deep learning approaches are constructed employing various modalities.

Despite the fact that deep learning models have an unprecedented success in analyzing neurological diseases, there are still certain issues that need to be addressed. The following is a list of probable challenges and possible solutions-

(1) Deep learning methodologies are very dependent on hyper-parameter setting i.e., batch sizes, learning rate, activation function, number of hidden layers etc., which can substantially affect performance. Hyper-parameter optimization approaches such grid search and Bayesian Optimization etc., are proposed to achieve the best configuration. The process for creating the architecture of deep neural networks, is still in the hands of experienced specialists.

(2) Deep neural networks use complex structures to extract features from training data before making predictions for diverse tasks. These technologies have potential to outperform human specialists and give accurate results. However, trusting predictions is tough as we don't have sufficient knowledge of extracted features. As a result, the deep learning algorithms' black-box nature has limited their therapeutic application. Some studies are beginning to explore the explain ability of deep learning architectures in neurological disorders, with the goal of demonstrating the features that have the biggest impact on the predictions.

(3) Deep learning approaches necessitate a high number of samples to train their models, despite the fact that obtaining training samples in various real-world circumstances, particularly for neurological diseases, is sometimes difficult. In neuroimaging analysis, a lack of appropriate training data has been often noted as a barrier to applying deep learning architectures. A data augmentation approach has been presented to overcome this problem, and it is extensively utilized to increase the amount of training samples.

(4) The data having lack of information is unavoidable in multimodal neuroimaging research due to patient withdrawals and substandard data quality, therefore participants may be missing some modalities. Traditionally, data-missing individuals are discarded, resulting in a considerable reduction in the number of training samples and a decrease in diagnosis performance. Most of the data-computing approaches impute the missing hand-crafted feature values set by professionals for describing neuroimages.

## Conclusion

In this study, we focused on three common illnesses and examined the deep learning algorithms presented by several researchers. Alzheimer's is a neurodegenerative disease while ASD is a psychiatric disorder. Using brain images and signals, deep learning models have achieved trailblazing achievement for the three brain illnesses. Finally, we address various research avenues and outline these potential obstacles. CAD systems for disease identification and treatment will become a companion in upcoming days as the etiology of human brain illnesses becomes clearer, deep learning techniques get more advanced, and open-source datasets grow in size.

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## **Glossary:**

**Neuroimages-** these are the images of brain.

**Positron Emission Tomography-**an imaging test that can help reveal the metabolic or biochemical function of your tissues and organs.

**Magnetic Resonance Imaging -** a medical imaging technique that uses a magnetic field and computer-generated radio waves to create detailed images of the organs and tissues in body.

**Autism-**refers to a broad range of conditions characterized by challenges with social skills, repetitive behaviors, speech and nonverbal communication.

**Convolutional Neural Network-** deep Learning algorithm which assign importance (learnable weights and biases) to various objects in the image and be able to differentiate one from the other.

**Auto-Encoders-**an unsupervised artificial neural network that learns how to efficiently compress and encode data then learns how to reconstruct the data back from the reduced encoded representation to a representation that is as close to the original input as possible.

**Deep Boltzmann machine-**a model with more hidden layers with directionless connections between the nodes.

**Long short-term memory-** is an artificial neural network used in the fields of artificial intelligence and deep learning. Unlike standard feedforward neural networks, LSTM has feedback connections.