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Deep Learning-Based OCT for Epilepsy: A Review

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ABSTRACT

Automating screening and diagnosis in the medical field saves time and decreases the likelihood of misdiagnosis whilst saving physicians cost and labor time. Deep learning methods development and their feasibility have enabled machines to interpret complex features in medical data, leading to rapid advances in automation. This research discusses how deep learning has been applied to Optical Coherence Tomography in epileptic patients to improve clinical diagnostic categorization, treatment outcome prediction, and comprehension of cognitive comorbidities. It covers the present deep learning research's strengths and weaknesses, as well as the necessity for further studies employing constrained datasets to evaluate the repeatability and generalizability of existing findings, as well as studies to test the clinical utility of deep learning methodologies.

Key words: Optical Coherence Tomography, Epilepsy, Deep learning

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INTRODUCTION

Epilepsy is a chronic neurological condition characterized by abnormally high central nervous system activity. It affects approximately 50 million individuals globally, with symptoms ranging from repeated seizures and their physical consequences to numerous psychosocial and mental comorbidities [1]. Appropriate seizure control and medicines for various elements of epilepsy are critical for properly treating people with epilepsy. However, epilepsy exhibits some heterogeneity, which can make it difficult to determine the optimal course of action for every patient. In terms of optimizing clinical diagnostics, prediction, and customized treatment, machine learning algorithms have the potential to surpass traditional approaches.

As the retina is connected to the brain, it has been discovered that changes that occur in the brain in relation to small blood vessels and nerves can be seen in the retina, which is more accessible to image. My research has looked at how the retina changes with epilepsy to investigate what some of these changes are and whether they occur in an earlier stage of the disease. If we know how the retina changes in epilepsy, in the future, an early warning could potentially be flagged at a routine optometrist appointment. Most people with epilepsy have normal MRI scans [2]. It is critical that new technologies are developed to better understand epileptogenesis and to facilitate diagnostic confirmation.

Over the past two decades, Optical coherence tomography (OCT) has gained popularity across a number of medical specialties, notably in ophthalmology and neurology. It offers histologic data on brain tissue in vivo and is a noncontact, no radiation, quick, effective, safe, and repeatable diagnostic imaging method. OCT images and a variety of machine learning methods have been developed to identify abnormalities of the central nervous system (CNS).

Neurology and epileptology are two areas of medicine where deep learning (DL) is a developing trend. Accurate, automated, and quick pattern learning, which may be utilized to design and/or refine therapeutically applicable algorithms for clinical treatment and fundamental research, are three benefits of DL above conventional approaches. Furthermore, DL models incorporating neural networks can handle data increase better than typical ML models. Many image recognition models have been constructed using DL approaches. In contrast to natural RGB visuals, OCT comprises 2D grayscale images and 3D volumes. Furthermore, OCT pictures frequently contain quantitative information that may be used to improve the performance of neural networks. The precise intensity of a pixel, the size of abnormalities, and their position in a scan can all be important clues. Thus, when using DL in OCT pictures, altering the network topologies designed for natural images and accounting for discrepancies might considerably enhance outcomes and push towards clinically viable solutions [3]. Modern OCT image processing techniques, including as retinal layers and avascular region segmentation, disease diagnosis and prognosis prediction, and image quality evaluation, have been greatly enhanced by advances in DL. Different types of traditional OCT input, such as 2D en face pictures, 2D B scans, and 3D volumetric scans, may be used to train DL-based models (Figure 1).

This paper attempts to give a high-level overview of various modalities by concentrating mostly on the current applications of ML for OCT and other modalities that have been employed in epilepsy. It also highlights potential difficulties with clinical application of DL models and potential future research directions.

Domain knowledge

Epilepsy

Epilepsy is a temporary occurrence of signs and/or symptoms associated with abnormally excessive or synchronized brain neuronal activity [4]. People may develop epilepsy due to genetic factors, inflammation, infections, changes of normal brain anatomy or factors not yet completely understood [2]. Epilepsy can be broadly divided into focal and generalized, lobe of onset or clinical presentation and underlying neurological disorder [5]. This distinction is helpful as the correct identification of phenotype has implications in diagnosis, investigations, treatment, and, most importantly, prognosis.

Retinal structure

The human eye is an organ that uses light-sensitive tissue to absorb focused light to gather visual information. The retina is the eye's light-sensitive layer. The eye is an organ that uses light-sensitive tissues to absorb focused light to gather visual information. The information sensed by the photoreceptors, which respond to certain spectrum areas of light, is transformed into electrical impulses and sent to the visual cortex of the brain through nerve fibres. The signals are then interpreted as visual images in the brain. There are significant biological markers in the eye. The photoreceptors are heavily concentrated for optimal resolving power in the macula, the centre of the imaging area. The fovea, which is at the macular region's core, is in charge of high-definition central vision. The circular region on the ocular fundus known as the optic disc, also known as the optic nerve head (ONH), is where the nerve fibres that go to the visual cortex converge. The retinal vasculature spreads out from the optic disc to the retinal layers. The retinal layers are classified into seven levels based on the cell kinds [6]. The retinal veins can be classified according to their positions. The retinal veins are categorized based on their location. The nerve fibre layer and the sidewalls of the inner nuclear layers include the superficial, intermediate, and deep retinal arteries. The choroid arteries are found underneath the RPE and Bruch's membrane. The photoreceptors are supplied with nutrients and oxygen via these veins [7].

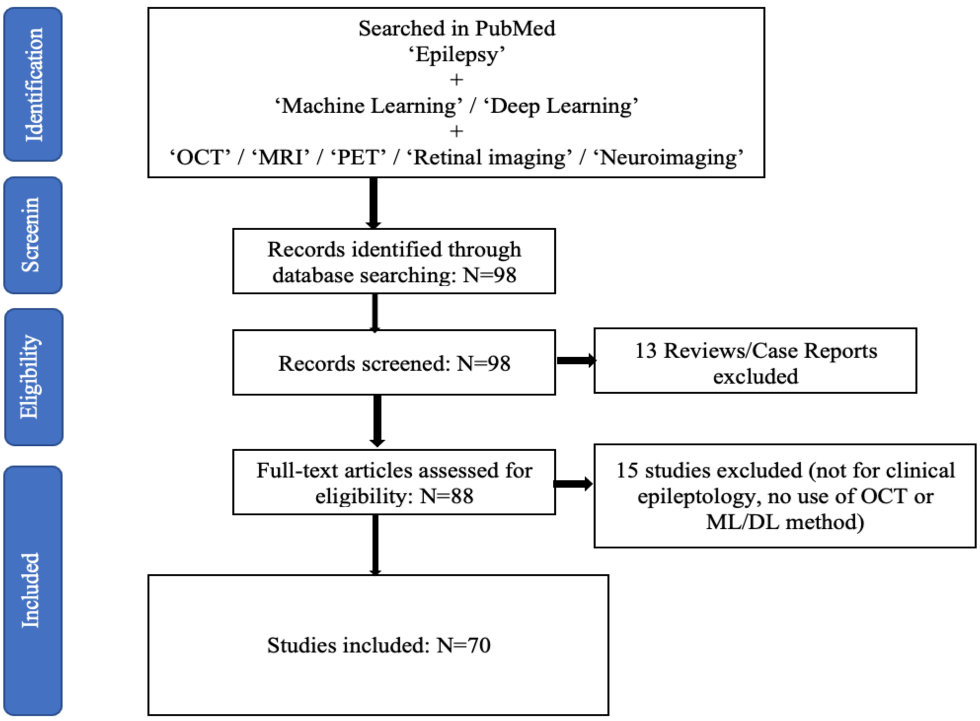

Figure 1: The search and inclusion of research papers in this review.

Optical coherence tomography (OCT)

The optical coherence tomography technique, which uses interferometry to obtain high-resolution cross-sectional pictures of the retina, allows for in-vivo viewing of tissue microstructure. OCT, as a medical imaging modality, is most comparable to ultrasound in that it uses light waves instead of sonic waves. OCT allows for the identification of the retina's cellular layers and the measurement of the thickness of these layers or the retina as a whole, which aids in the early detection and diagnosis of retinal illnesses and disorders. OCT technology has advanced in recent years, allowing it to be applied to a greater number of medical specializations [8]. OCT has been used to perform real-time imaging at a rate of many frames per second. Recent OCT imaging studies have examined developmental biology samples at the cellular level. The interior body may be imaged with OCT using catheters, endoscopes, and laparoscopes. OCT's capacity to give cross-sectional retinal imaging and see the tiny structures in the eye is one of the technology's many medical benefits [9].

Although the retina contains very little optical backscattering, OCT imaging may be quite sensitive, making it possible to observe details with very little backscattering, such as the vitreo-retinal interface. RPE and choroid, on the other hand, stand out in OCT images due to their bright (hyper reflective) appearance. When seen with OCT, the layer of retinal nerve fibres appears as a hyper reflective structure that is thickest at the optic disc and goes thinner as it approaches the fovea. OCT has been utilized to examine retinal laser injuries in addition to studying the retina's dynamic reactions. Intelligent algorithms may be used to quantitatively analyse OCT images, such as determining the thickness of the retinal nerve tissue or the thickness of the retinal nerve fibre layer. The use of OCT, which can offer quantitative data regarding the prognostic assessment used for the diagnosis and monitoring of retinal damage caused by conditions like glaucoma or diabetic macular edoema, is on the rise. Due to its ability to identify and diagnose diseases in their earliest stages before any outward signs or symptoms appear, OCT has been used to prevent irreparable loss of vision [10].

Machine learning methods

The term "machine learning" describes a class of algorithms that may be used in systems designed to tackle issues in a variety of industries. Depending on how the target information must be learnt, it may be divided into two primary categories [11]. The learning process is referred to as supervised learning when there is explicit information or direct human involvement. In the absence of human assistance, learning is referred to as unsupervised or semi-supervised learning, depending on how autonomously the corresponding system interprets the target-related pattern. Unsupervised learning includes k-means clustering, fuzzy c-means (FCM), the Gaussian mixture model (GMM), and reinforcement learning. Supervised learning includes all deep learning techniques that use labels for training, such as k nearest neighbor (kNN), a support vector machine (SVM), fuzzy techniques, and random forest (RF). The existence of parameters in the developed models, or the lack thereof, is another criterion for classifying the kind of learning. The model may be built up with a fixed number of parameters if the data are taken to have a particular distribution. The model has the benefit of being a reasonably simple model because of past information. However, there is less room for improvement when adding new data that does not fit the existing distribution. Bayesian networks, artificial neural networks, logistic regressions, and linear regressions are examples of this type of model. However, the flexibility and somewhat slow processing speed of a non-parametric model created by utilizing the characteristics of data distribution are advantages. These models include the k-nearest neighbor (KNN) classifier, decision trees, and RF [12]. Building neural networks for deep learning is now seen to be an effective way to turn the input data into a condensed representation with end-to-end learning. Depending on the fundamental elements of the architecture and how the nodes are connected, there are several formats for building neural networks. Nodes in the same layer are often not linked to one another since layers are collections of a particular number of nodes. Regarding the fundamental building blocks of a neural network, a fully connected network are one in which every node in one layer is linked to every node in the next layer (FCN). A network is referred to be a convolutional neural network (CNN) if a layer propagates the input by partly connecting to the nodes of the following layer at regular intervals and with the same weights [13]. Furthermore, the network is known as a recurrent neural network (RNN) and is often built to handle sequential data if the inference processes progress by repeatedly feeding the previous outcomes as inputs. Given that deep learning is an advanced technique that is known to outperform traditional machine learning, deep learning models are the main emphasis of the approaches covered in this study. However, if traditional methods can assess the required patterns and produce results that are as excellent as deep learning approaches, they are also covered for some jobs (Figure 2 and Table 1) [14].

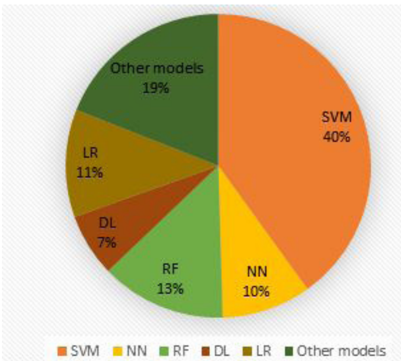

Figure 2: The ML models used in epilepsy studies. DL, deep learning; LR, logistic regression; NN, neural network; RF, random forest; SVM, support vector machine. Other models: XGBoost, Light GBM, CatBoost, decision tree, quadratic discriminant analysis.

There are also various ML applications for more direct associations with clinical outcomes than lesion/focus detection. A major trend is the prediction of postsurgical seizure [13,19–23], in light of the clinical importance. Most of the studies reported 70–90% accuracy for the prediction of seizure outcomes after resection surgery. Other studies presented approximately 85% accuracy for the identification of responders to vagus nerve stimulation (VNS) [24,25]. In terms of surgery, ML methods were also applied and generated good predictive values for postsurgical functional deficit [26], lateralization of the language hemisphere and optimal planning for laser surgery [27] Cognitive dysfunctions in epilepsy were also shown to be predicted by ML methods [5,28,29]. Functional neuroimaging and/or network measurement are often used for this prediction. Other ML applications included predicting drug responsiveness [30], acquiring epileptogenicity [31], and the differentiation of types of autoantibodies.

Deep learning techniques

Deep neural networks are structures with more hidden layers than conventional neural networks, or so-called shallow networks. The number of network parameters increases significantly as networks get bigger, necessitating adequate learning strategies as well as precautions against over fitting the taught network. Convolutional networks drastically reduce the number of trainable parameters by using filters convolved with input patterns rather than multiplying a weight vector (matrix).

Other approaches are also proposed [32] to enable the network in learning. The input pattern size for the subsequent convolutional layer is decreased by pooling layers. Techniques such as batch normalization, dropout, early halting, unsupervised or semi-unsupervised learning, and regularization work to boost learning capacity and speed while preventing the learnt network from over fitting. To prevent over fitting for small amounts of labelled data, the AE and DBN are first used for unsupervised learning and then fine-tuned. RNNs that are able to disclose the long-term time dependencies of data samples include long short-term memory (LSTM) and gated recurrent units (GRU).

Deep learning applications for epilepsy

While deep learning algorithms and tools may not be able to replace visual examination of MRIs by imaging professionals in all circumstances, they may offer crucial support tools and may become very important when such knowledge is not accessible. Some deep learning technologies have already been incorporated into clinical treatment for epilepsy, but for newer ML and DL approaches to be adapted for clinical usage, it will still be crucial for physicians and AI scientists to maintain close communication.

Numerous machine learning techniques have been put forth to automatically classify and identify abnormalities in OCTs [33,34]. These methods often focus on the segmentation of the retinal layer or the categorization of images with similar properties [35]. These techniques provide low-cost, high-performance analytical assistance.

Deep learning–based image quality assessment of OCT

For a more thorough and accurate disease evaluation using OCT images, image quality management is crucial. A DL-based image quality assessment model was created by Ran et al [36] to distinguish between gradable and upgradable OCT optic disc volumetric scans. It performed well in both the two external testing datasets and the internal validation datasets, and it could be used in epilepsy detection models for OCT analysis based on DL. To analyse the quality of OCT scans, Kauer, et al. [37] suggested an automated quality evaluation network based on CNN. The model successfully classified images as good, poor, higher, or lower quality with an accuracy of 99.5%. A multilayer deep CNN was created by

Table 1: Machine learning applications used to predict clinical outcomes in epilepsy.

References	Subjects	Imaging modality	classifiers	Main outcome
Akeret et al.[14]	923 brain tumors	T1, FLAIR	DT, GLM, RF, GBM, NN, SVM, GAM	AUC = 0.79, ACC = 0.72 to predict seizure occurrence when combined with clinical info
Lee et al. [15]	89 FE (P)	DTI	CNN	ACC = 0.92 to predict functional deficit after surgery
Wang et al.[16]	205 LGG-related EPI	T2WI	Novel radiomic nomogram	AUC = 0.863 to predict epilepsy type
Sinha et al.[17]	51 TLE, 29 HC	T1, DTI	SVM	AUC = 0.84 to predict seizure outcome after surgery
Kini et al.[18]	89 TLE	FDG-PET	RF	ACC = 0.71 to predict seizure outcome after surgery

ACC: Accuracy; AUC: Area under the ROC curve; DT: Decision tree; DTI: Diffusion tensor imaging; EPI: Epilepsy; FE: Focal epilepsy; GBM: Gradient boosting algorithm; GLM: Generalized linear model; HC: Healthy controls; NN: Neural network; RF: Random forest; SVM: Support vector machine; TLE: Temporal Lobe Epilepsy.

Table 2: Machine learning applications used to the differentiation of individuals with epilepsy and healthy subjects.

References	Subjects	Imaging modality	classifiers	Main outcome
Del Gaizo et al. [40]		DKI	SVM	ACC = 0.82 for TLE vs. HC by MK
Bharath et al. [41]	42 TLE-HS (18 R, 19 L, 5 B)	rs-fMRI	SVM	ACC = 0.975 for TLE vs. HC. Correlation of network with clinical variables
Si et al. [42]	15 JME, 15 HC	HARDI, NODDI	CNN	ACC = 0.752, AUC = 0.839 for JME vs. HC
Nguyen et al. [43]	63 DRE (P), 259 HC	rs-fMRI	CNN	ACC = 0.74, AUC = 0.86 for DRE vs. HC

ACC: Accuracy; AUC: Area under the curve; DKI: Diffusion kurtosis imaging; DT: Decision tree; DTI: Diffusion tensor imaging; EPI: Epilepsy; FE: Focal epilepsy; GBM: Gradient boosting algorithm; GLM: Generalized linear model; HC: Healthy controls; HARDI: High-angular-resolution diffusion imaging; NN: Neural network; RF: Random forest; RS: Resting-state; SVM: Support vector machine; TLE: Temporal lobe epilepsy.

Lauermann, et al. [38] for automatic evaluation of the quality of OCT images of the superficial capillary plexus (sufficient vs. insufficient). The DL model's sensitivity, specificity, and accuracy were all over 90.0 percent. Other research used DL to rebuild or denoise OCTA pictures, which significantly improved the image quality and may increase the number of adequate photos, shorten the time it takes to analyse the images, and improve the ability to identify retinal diseases.

The identification of a particular artefact is useful in addition to generic image quality assessment. To identify the capillary NPA from signal reduction artefacts in 6x6mm2 OCTA, Guo, et al. [39] created a CNN-based DL model. A vital quantitative biomarker used in the OCTA assessment of DR is the capillary NPA. For NPA identification, the suggested DL model performed well across a wide range of DR severity and scan quality. It may be able to solve the issue of signal reduction artefacts while measuring capillary dropout in the retina using OCTA.

The differentiation of individuals with epilepsy from healthy controls

The distinguishing of epileptic retinas from healthy retinas is a typical use of machine learning for retina imaging in epilepsy. As shown in Table 2, multiple ML classifiers have achieved above 70% accuracy in distinguishing between persons with epilepsy and healthy controls.

In recent years, ML algorithms using multimodal MRI have been shown to lateralize hippocampal pathology in patients with temporal lobe epilepsy (TLE) and hippocampal sclerosis (HS). A recent ENIGMA-Epilepsy study investigated the performance of ML and DL algorithms using structural MRI and diffusion MRI (dMRI) to classify controls vs patients with TLE with HS andMRI-negative TLE. This study revealed that structural MRI and dMRI-based models had similar accuracy and that models for TLE-HS were more accurate than for MRI negative TLE. While the ability of automatic quantification methods may not currently exceed visual inspection of MRIs by imaging experts in all situations, AI algorithms and tools provide important support tools and may become of great importance when such expertise is not available. Some AI tools have already been integrated into clinical care for epilepsy, but it will remain important for clinicians and AI-experts to remain in close dialog for newer ML and DL approaches to be adapted for clinical use. Focal cortical dysplasia (FCD) is one of the most common causes of pharma coresistant focal epilepsy [14]. However, FCDs are often undetected on conventional MRI and the pre-surgical diagnosis depends heavily on the expertise of the examiner. Several MRI post-processing techniques have been used to improve the detection of subtle FCDs. A recent Multicentre validated study [4] showed that DL using multimodal MRI data could reliably identify previous MRI-negative FCD lesions, suggesting that DL shows promise for assisting non-expert clinicians in this challenging diagnosis. AI methods can also combine imaging and clinical data to build models for predicting clinical outcomes in patients with epilepsy. For example, automated volumetric MRI measurements incorporated into statistical models help to predict postoperative seizure outcomes in TLE and frontal lobe epilepsy (FLE), revealing that subtle cortical atrophy beyond the surgical resection influences seizure outcome. DL applied to whole brain connectives can also help to predict postoperative seizure control in patients with TLE. Another application of AI has been implemented by the MELD project—a retrospective multicenter cohort of 580 patients with FCD. Here, AI was not used for lesion detection. Rather, the MELD team trained logistic regression models to test for associations between clinical data and the location of FCD lesions that were delineated on T1-weighted MRI scans by imaging experts. Their data-driven atlas validated smaller independent studies which showed a non-uniform distribution of FCDs with higher concentrations in the superior frontal sulcus, frontal pole, temporal pole, and superior temporal gyrus. Lesions in primary sensory areas were associated with earlier age of epilepsy onset whereas lesions in association cortices were associated with a later epilepsy onset. The likelihood of seizure freedom decreased with a longer duration of epilepsy [19]. Finally, AI, including ML and DL, has been applied to neuroimaging data for predicting clinical diagnosis, that is, clinical phenotyping from imaging, and predicting response to antiseizure medications. For example, dMRI measures and connectome profiles may identify patients with juvenile myoclonic epilepsy and distinguish patients with focal epilepsy vs healthy controls. However, these studies are few in number and larger studies that are validated in external datasets are needed to determine.

DISCUSSION AND FUTURE DIRECTION

As previously stated, the present ML applications for epilepsy imaging are different in terms of epilepsy disorders addressed, imaging modalities, and ML techniques. Multimodal imaging is a recent trend in epilepsy research, and it has the potential to give complete data [44]. As a result, the number of ML research utilizing different imaging modalities has increased, particularly in recent years. However, each study group appears to have certain preferences for imaging modalities, which may have contributed to the diversity of research in this subject. In terms of ML algorithms, more recent research have tended to employ deep-learning approaches such as CNN [45,46]. The fact that there aren't many research employing unsupervised classification—indeed, just two studies did so [47] is another crucial technique issue. In order to learn more about data-driven knowledge, more research employing unsupervised clustering is required. This approach has the ability to detect hidden patterns in unlabeled data.

Open access OCT data: The absence of OCT data from epileptic patients is a major problem in early-stage prediction and analytic studies. Reproducibility of results depends critically on open access sharing of OCT data from epilepsy databases (using Github or similar repositories). Excessive feature extraction will result in increased computation costs and time requirements.

The categorization of disorders, prognosis monitoring, prediction of functional changes, structural segmentation, and image quality assessment on OCT images were all made possible with the use of DL-based models. ResNet, RNN, and Dense Net, the most widely used networks, were utilised. First of all, the training sample size of the DL models for OCT image processing that were already in use was rather tiny. It may result in model over fitting, a loss in generalizability in unexplored OCT datasets, and a reduction in data diversity. It's helpful to increase the training sample size by using various data augmentation techniques including rotation, flipping, shifting, and cropping. Additionally, recent studies in the field of computer science, such as transfer learning, low-shot learning [48], or few-shot learning [49], also hold promise for resolving this problem. Before using these DL models in real-time clinics, the majority of the research were still in the "proof-of-concept" stage and significant problems needed to be resolved.

The "black box" nature of current DL models, which rely on AI to identify items missed by human sight, limits their interpretability and reliability. To create heatmaps and improve the transparency of DL models, occlusion tests, activation maps, and salient maps were frequently employed. Explainable AI (XAI), which offers tools to expose AI judgments, is increasingly known as a means of opening the "black box." For the OCT segmentation problem in monkey eyes, Maloca et al.81 introduced a CNN that was improved with a post hoc XAI method called Traceable Relevance Explain ability (T-REX). After the neural network training process, post hoc XAI may highlight and show areas of the input data that contribute to pertinent prediction judgments. More work must be done in the future to offer clinics with a real-time illustration of the outcomes of DL-based OCT analysis.

Without sufficient external testing, the majority of DL models for OCT image interpretation were often trained and verified on internal datasets. However, there are fewer open source OCT datasets accessible than there are for retinal fundus images [50], and transferring data between institutions is difficult because of concerns about patient privacy and the need for a lot of storage. The "Model-to-Data" technique, which involves packing a digital learning model that is simple to distribute and bringing it to the data, has been shown to be a viable remedy for the problem of data interchange between various organisations. It could make it possible for a reliable DL model to be built centrally and sent to several clinical locations so that distributed training can take place [51]. Federated learning (FL), a paradigm for learning that allows algorithms to be trained jointly without actually exchanging data, has the potential to solve the issues of data governance and privacy. Each participating university conducts local DL model training, and only attributes (such as parameters and gradients) are shared. Without transferring patient data outside the confines of the institutions where they are housed, it allows for the collaborative acquisition of insights, such as in the form of a consensus model [52].

Although some DL models showed good results in internal validation, there are still important problems for real-world application in various settings (i.e., domain shift) because of the variety of devices and imaging protocols, variations in ocular physiological anatomy, and unbalanced data distribution. The robustness of DL models for medical image analysis is now being proposed to be improved by domain adaption strategies such synergistic fusion and batch normalization [53].

CONCLUSION

A number of studies have found promising findings using machine learning, which is an emerging trend in the field of retinal imaging in epilepsy. A further difficulty arises from the variety of targeted epileptic syndromes, imaging modalities, feature extractions, and ML algorithms. Deep learning, multimodal imaging, and regression models are current trends, and unsupervised clustering-based studies should be used in future research. Consistent upgrading procedures and model improvement are required for improved clinical applications to ensure the models' performance is comparable to that of human competence.

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