Applicable Artificial Intelligence for Brain Disease: A Survey

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Abstract

Brain diseases threaten hundreds of thousands of people over the world. Medical imaging techniques such as MRI and CT are employed for various brain disease studies. As artificial intelligence succeeded in image analysis, scientists employed artificial intelligence, especially deep learning technologies, to assist brain disease studies. The AI applications for brain disease studies can be divided into two categories. The first category is preprocessing, including denoising, registration, skull-stripping, intensity normalization, and data augmentation. The second category is the clinical application that contains lesion segmentation, disease detection, grade classification, and outcome prediction. In this survey, we reviewed over one hundred representative papers on how to apply AI to brain disease studies. We first introduced AI-based preprocessing for brain disease studies. Second, we reviewed the influential works of AI-based brain disease studies. At last, we also discussed three development trends in the future. We hope this survey will inspire both expert-level researchers and entry-level beginners.

Keywords

Artificial intelligence, Brain disease, Deep learning, Stroke, Convolutional neural network

1. Introduction

Brain diseases are humans' most commonly seen and dangerous illnesses [1]. According to the World Health Statistics 2020 published by WHO, over ten million people have died of brain diseases yearly since 2016. Brain diseases have become one of the biggest threats to people worldwide. Various brain diseases include cerebral vascular accidents (CVAs), brain tumors, sleep disorders, multiple sclerosis, and dementia. These brain diseases are caused for different reasons and occur in different brain structures. For example, CVA, also known as stroke, is caused by vessel blockage or rupture inside the brain. When a hemorrhage stroke occurs within the brain, it is called intracranial hemorrhage. It is called a subarachnoid hemorrhage when it occurs between the inner and outer layers of the tissue covering the brain. In this circumstance, when a brain disease attacks, we want to know where it occurs, which brain disease it belongs to, how bad it is, and even what outcome it will be. In order to figure out these questions, scientists have presented numerous methods for lesion segmentation, detection-based diagnosis, grade or subtypes classification, and outcome prediction. These are the mainstreams of applying computer-aided technologies to brain disease studies.

Due to brain structure being complex and easily misguided, doctors and scientists usually adopt medical imaging techniques to examine the brain condition. Magnetic resonance imaging (MRI), computed tomography (CT), magnetic resonance angiography (MRA), and computed tomography angiography (CTA) are the four most commonly applied medical imaging techniques. These medical imaging modalities can be utilized to illustrate the inner structure of brains and delineate the three-dimensional model for clinical and research purposes [2]. However, we cannot ignore that these imaging techniques usually come with noise, unbalanced sample distribution, irrelative tissue background, and non-standardized intensity distribution. These factors will interfere with further brain image analysis, such as segmentation, detection, and classification [3]. Thus, quantities of preprocessing methods are put forward to relieve these negative factors. For example, denoising preprocessing methods aim to reduce the noise from original medical images. In this way, these denoising preprocessing methods enhance the image quality. Skull-stripping preprocessing methods are used to remove non-brain tissue from brain MRI images. It would enable the subsequent analysis tasks like segmentation to acquire a higher segmentation accuracy. Nowadays, brain image preprocessing has become an essential field in the studies of brain diseases.

Artificial intelligence [4-7] has been broadly applied in many fields, including face recognition, translation, transportation, and medical image analysis. Scientists have proposed many approaches [8-11] for lesion segmentation, illness detection, and survival prediction based on medical imaging techniques such as MRI, CT, and X-rays using artificial intelligence, especially the deep learning model. One of the most applicable deep learning models is the convolutional neural network (CNN). A CNN includes convolution layers that equip the CNN with a strong ability to extract deep features from input images [12]. A fully convolutional network (FCN) is another typical deep learning model [13]. It differs from a CNN in that an FCN contains upsampling layer, which makes it suitable for three-dimensional extraction and segmentation. A generative adversarial network (GAN) is also a representative deep learning model applied widely in various fields [14]. U-Net has become one of the most popular methods for medical image segmentation due to its unique architecture [15].

Further, the 3D U-Net was proposed to enhance the original U-Net's capacity for three-dimensional structure segmentation, such as cerebral vessels and brain tumors [16]. As new advanced deep learning models sprang out, scientists became more interested in developing AI methods for brain disease studies. We adopted artificial intelligence and brain disease as keywords and counted each year how many papers were published according to search results at Google Scholar. As shown in **Figure 1**, the trend of published papers for AI-based brain disease studies has risen during the past ten years. This trend can be considered as side evidence of the superiority of artificial intelligence over traditional methods in the field of brain disease study. In general, deep learning-based methods often have higher accuracy and better results than traditional methods [17-20]. For brain disease research, it means that deep learning-based methods can help physicians to determine conditions and cut lesions more accurately and efficiently. Another major advantage of AI is its potential for data exploitation. As more and more training data becomes available, researchers can continually improve the performance of deep learning-based models, even surpassing the ability of humans to accomplish the same tasks. This is a huge advantage that traditional methods do not offer and is where the significance of AI-based methods for brain disease study is built on.

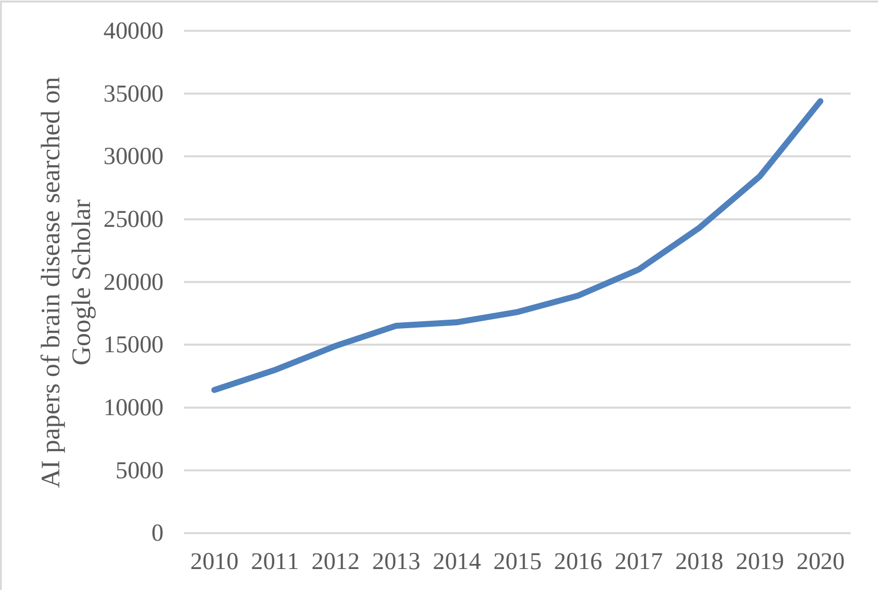

Figure 1 The trend of AI studies for brain disease

Artificial intelligence is applied to the studies of brain diseases generally in two directions [21-26]. The first one is preprocessing [27-29]. Preprocessing is an indispensable part of constructing an approach to analyzing brain images [30-32]. Moreover, artificial intelligence itself is a commonly-used method for developing state-of-the-art preprocessing approaches [33-35]. Scientists have adopted advanced deep learning models to propose more effective preprocessing technologies [36]. Thus, in this article, we will first review artificial intelligence applications of brain image preprocessing. The other direction is designing novel methods of brain image analysis to assist with the clinical diagnosis, treatment, and assessment. These methods vary from lesion segmentation to outcome prediction [37-39]. Therefore, after introducing applicable artificial intelligence in preprocessing, we will investigate several commonly-seen brain diseases and survey their intelligence-based methods. In order to make it more clear, we offered **Figure 2** to show how AI can be applied to brain disease studies in these two directions. Finally, we will discuss AI's future in brain disease studies.

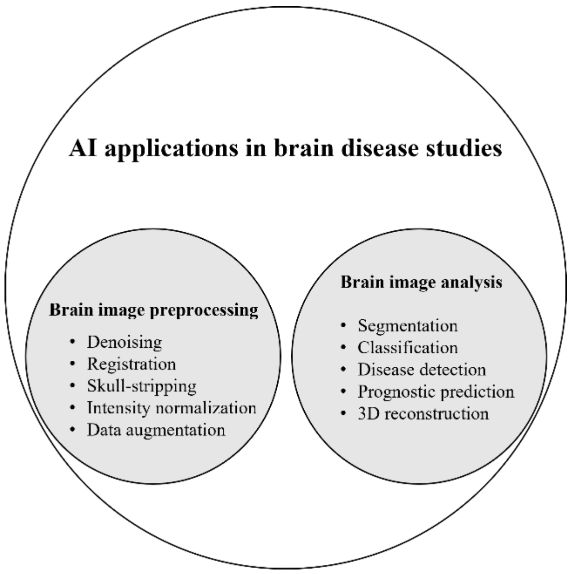

Figure 2 How AI can be applied in brain disease studies

Overall, we categorized the reviewed papers into two main aspects, preprocessing and analysis of brain images. In the aspect of brain image preprocessing, we surveyed over thirty articles covering the topics of denoising, registration, skull-stripping, intensity normalization, and data augmentation. In the aspect of brain image analysis, we reviewed over one hundred papers containing the most commonly seen brain diseases, including ischemic strokes, transient ischemic attack, intracranial hemorrhage, intracranial aneurysm, subarachnoid hemorrhage, arteriovenous malformation, moyamoya disease, Alzheimer's disease, and multiple sclerosis. In addition to investigating a large number of recent and comprehensive papers in the field of deep learning-assisted diagnosis of brain diseases, our contribution is to sort out the general process and framework for the application of deep learning in brain diseases. We provided detailed descriptions, including formulas and images, and summarised the state of development for a number of fundamental and key domain technical models. We also presented an outlook on potentially promising deep learning technologies and discussed scenarios for their use in the field of brain diseases. We hope that this survey paper will benefit both scientists and clinicians.

2. Brain image preprocessing

Medical imaging technologies are the most effective way to examine a patient's condition. Clinicians usually rely on medical imaging technologies to assist in diagnosing various brain diseases. The most commonly applied medical imaging technologies in brain disease diagnosis include magnetic resonance imaging (MRI), computed tomography (CT), magnetic resonance angiography (MRA), computed tomography angiography (CTA), and digital subtraction angiography (DSA). These imaging modalities have their own characteristics and the type of brain disease for which they are suitable. CT, which uses precisely collimated X-ray beams, gamma rays, and ultrasound to scan around the body one section after another, has a fast rate of scanning and provides clear images. MRI is another commonly used tomographic imaging technique that uses the phenomenon of magnetic resonance to obtain electromagnetic signals from the body and to reconstruct information about body parts. CTA is a non-invasive vascular imaging technique that uses multi-layer spiral CT to scan the target vessel in rapid succession at multiple levels during peak contrast filling after intravenous injection of contrast material.

CTA is a safe, convenient, rapid, qualitative, and localized method for the diagnosis of cerebrovascular lesions, such as cerebral aneurysms and cerebrovascular malformations. MRA is based on saturation, inflow enhancement, and flow dephasing effects and can detect areas of stenosis and occlusion, as well as vascular disease (aneurysms, arteriovenous malformations, etc.) MRA includes direct MRA and enhanced MRA (CE-MRA), both of which have their advantages. Direct MRA is a simple, non-invasive, and low-cost method that has become an indispensable clinical test as it does not use contrast, and CE-MRA is more reliable than direct MRA in showing the lumen of the blood vessels, with significantly fewer artefacts and a more realistic reflection of the degree of stenosis. DSA is an angiographic method of imaging assisted by an electronic computer, which is accomplished by applying a computer programme for two imaging sessions. The first image is taken before the contrast is injected, and the computer converts the image into a digital signal for storage. After the contrast medium is injected, the image is imaged again and converted to a digital signal. The two digital times are subtracted to eliminate the same signal, and a contrast-only image of the blood vessels is obtained. This image is clearer and more visual than the conventional cerebral angiography used in the past, and some of the finer vascular structures can be visualized.

In most cases, scientists need to employ preprocessing technologies to brain medical images due to two reasons. The first reason is to improve image quality. The second reason is that preprocessing technologies enable researchers to apply medical images more easily and conveniently in subsequent studies, such as lesion segmentation, disease detection and classification, and outcome prediction [40]. Therefore, brain image preprocessing technologies can be divided into two categories. The first category is individual image preprocessing, like denoising. The second category is processing progress upon a group of images, which aims at mitigating the negative influence on later image analysis, consisting of registration, skull-stripping, intensity normalization, and data augmentation. In general, the first category is applied to enhance the quality of an individual image, while the second category is deployed to improve the quality of an entire image dataset. As we can see in **Figure 3**, brain image preprocessing is very important to imaging-based brain disease studies. Moreover, brain image preprocessing itself is an essential field of artificial intelligence application. Thus, in this chapter, we presented a brief review of state-of-the-art brain image preprocessing approaches as follows. We hoped the content would enable readers to understand how to actually perform brain disease studies.

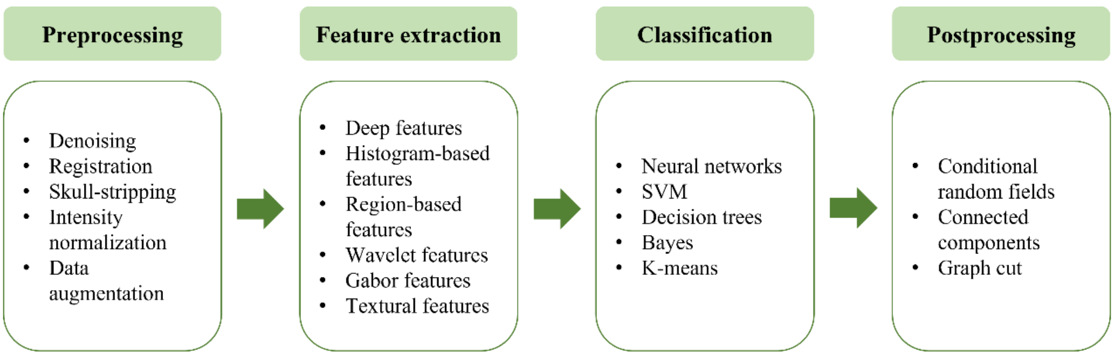

Figure 3 The pipeline of AI-based brain image classification

2.1. Denoising

Image denoising is a technology of a long history. Although massive traditional methods were already put forward [41-44], in recent years, scientists have tended to apply artificial intelligence to develop denoising methods. In 2017, Benou, *et al.* [45] presented an integrated approach for contrast-enhanced brain MRI denoising. They adopted autoencoders (AEs) to extract the noise features and imitate the curve prototypes. They also raised an automated model to generate realistic training sets due to lacking ground-truth data. Their approach was efficient on a stroke dataset and a brain tumor dataset, which indicated that deep neural networks had the potential to build denoising approaches for brain MRI images. In 2018, Jiang, *et al.* [46] introduced the famous DnCNN model into the field of MRI image denoising. They applied residual learning and batch normalization in their approach to accelerate the training and improve performance (shown in **Figure 4**). Their deep learning-based denoising model adopted a noisy observation as the input, which could be written as

$$y = x + r\,. \tag{1}$$

In this formula, x indicates the clean image. The denoising model was to train a residual mapping

$$R(y) \approx r\,. \tag{2}$$

Therefore, the latent clean image could be obtained by

$$x = y - R(y)\,, \tag{3}$$

and the loss function in this training process was defined as

$$loss(\theta) = \frac{1}{2N}\sum_{i=1}^{N}\|R(y_i;\theta) - (y_i - x_i)\|^2\,. \tag{4}$$

The experimental results showed that their approach outperformed other state-of-the-art denoising methods. In 2019, Chauhan, *et al.* [47] proposed a deep learning-based method for brin MRI denoising. They developed the approach by combining the convolutional autoencoders with several fuzzy logic filters. It was demonstrated that their approach acquired state-of-the-art performance in the comparison experiments. At the same time, we could not ignore that researchers were still digging into the potential of traditional denoising methods. Mzoughi, *et al.* [48] proposed a human MRI denoising method using bilateral filters combined with automatic contrast stretching. They claimed that this method was superior to state-of-the-art methods. Rai, *et al.* [49] proposed an integrated method for MRI image denoising. They applied the wavelet transform combined with independent component analysis to obtain better experimental results than classic denoising methods. Back to deep learning-based denoising development, Hong, *et al.* [50] proposed an attention mechanism-based convolutional neural network for MRI denoising. They also applied the feature fusion technique by combining the local features with the global ones to boost the network's capacity. It was demonstrated through the experiment results that their deep learning-based method attained an outstanding performance. Tripathi, *et al.* [51] proposed a CNN-based approach for MRI image denoising. The encoder-decoder architecture was adopted in their approach to preserve the prominent features. By employing the residual learning strategy, their approach achieved promising results in the experiments. Finally, we provided **Table 1** to summarize this section.

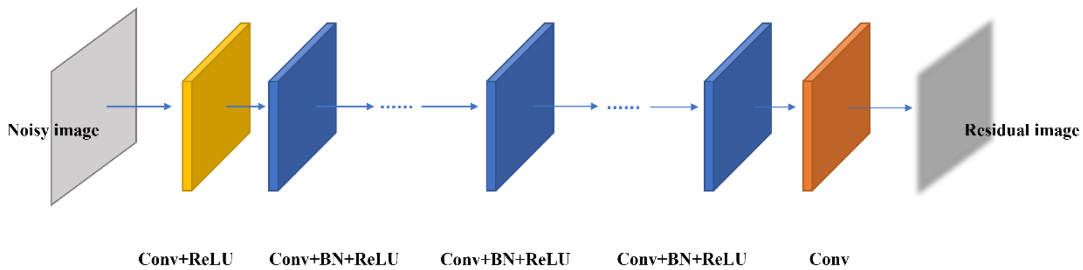

Figure 4 The network structure of DnCNN

Table 1 Methods for denoising

Authors	Year	Modality	Method	Characteristics
Weickert [41]	1998	MRI	Anisotropic diffusion	Representing classic traditional methods
Diaz, *et al.* [42]	2011	MRI	The non-local means algorithm	Outperforming than other conventional methods
Agarwal, *et al.* [43]	2017	MRI	Wavelet transform	Convincing performance
Benou, *et al.* [45]	2017	MRI	Autoencoders	Automatically generating realistic training sets
Saladi, *et al.* [44]	2017	MRI	The spatial adaptive non-local means algorithm	Outstanding performance
Jiang, *et al.* [46]	2018	MRI	DnCNN	Residual learning and batch normalization
Chauhan, *et al.* [47]	2019	MRI	Autoencoders	Combined with fuzzy logic filters
Mzoughi, *et al.* [48]	2019	MRI	Bilateral filters	Combined with contrast-enhancement technique
Rai, *et al.* [49]	2019	MRI	Wavelet transform	Combined with independent component analysis
Hong, *et al.* [50]	2020	MRI	An attention-based CNN	Combined with the feature fusion technique
Tripathi, *et al.* [51]	2020	MRI	The encoder-decoder networks	Residual learning

2.2. Registration

As we know, in most cases, scientists need to communicate brain imaging results regarding anatomical regions. The brain images require registration to construct the corresponding structure-based relationship among different brains before subsequent analysis [52-54]. In this circumstance, scientists developed various registration methods. Apart from classic traditional registration methods [55-57], deep learning-based methods were put forward in these years as well. In 2018, Fan, *et al.* [54] presented a study on using adversarial similarity networks for MRI image registration. Their model consisted of a registration network and a discrimination network. The feedback of the discrimination network trained the registration network. This adversarial training approach was claimed to outperform state-of-the-art methods. In 2019, Xu, *et al.* [58] proposed a semi-supervised learning approach for MRI segmentation and registration. Their approach jointly learns segmentation and registration. In this way, both segmentation and registration were enhanced owing to each other's assistance. The experimental results suggested their approach's efficiency. In 2020, Zhu, *et al.* [59] proposed a three-dimensional end-to-end cascaded network structure for brain MRI registration. The architecture contained one subnetwork for acquiring affine alignment and the other subnetwork for deformable non-rigid registration. Their approach was demonstrated to be effective through the experimental results. In 2021, Liu*, et al.* [60] proposed a multi-step context-aware inpainting framework for brain MRI registration. They also applied a feature-level patch-match refinement module. The framework was proved effective through the experiments. In the end, we provided **Table 2** as the summary of this section.

Table 2 Methods for registration

Authors	Year	Modality	Method	Characteristics
Mang*, et al.* [55]	2008	MRI	Parametric registration	Less time-consuming
Klein*, et al.* [56]	2009	MRI	Non-linear registration	Performance nearly not affected by subject selection
Dadar*, et al.* [57]	2018	MRI	The revised BestLinReg registration	State-of-the-art performance
Fan*, et al.* [54]	2018	MRI	Adversarial similarity networks	No need for ground-truth deformations and specific similarity metrics
Xu*, et al.* [58]	2019	MRI	The DeepAtlas model	Deep CNN architecture with joint learning for segmentation and registration
Zhu*, et al.* [59]	2020	MRI	The cascaded FCN	No need for independent rigid alignment
Liu*, et al.* [60]	2021	MRI	A multi-step context-aware inpainting framework	Usage of a feature-level patch-match refinement module

2.3. Skull-stripping

The brain is considered the most complex anatomical structure in the human body. Skull-stripping enables researchers to precisely extract the brain tissue and delineate its region from medical images. In this way, nonbrain tissue, such as skulls, muscles, fats, and eyes, could be removed, which is beneficial to performing subsequent analysis, including segmentation, detection, and prediction [61-63]. Therefore, scientists regard skull-stripping as one of the most important preprocessing steps for brain image analysis. In 2006, Fennema - Notestine*, et al.* [64] presented a study comparing four popular traditional skull-stripping methods, including the brain extraction tool (BET), the 3dIntracranial, a hybrid watershed algorithm (HWA), and the brain surface extractor (BSE). They suggested that each method had its strength and defect through sufficient experiments, so researchers should choose the proper skull-stripping method based on the actual situation. In 2011, Speier*, et al.* [65] proposed a modified ROBEX method for brain MRI skull-stripping and reported obtaining better results than popular methods such as BET, BSE, and HWA. In 2016, Kleesiek*, et al.* [66] proposed a deep learning-based method for brain

MRI skull-stripping using a three-dimensional convolutional neural network architecture. The experimental results showed that their method achieved competitive performance among state-of-the-art methods. In 2019, Hwang, *et al.* [67] applied the 3D-UNet to establish an approach for MRI brain extraction and claimed to achieve better performance than mainstream methods. Finally, we summarized this section by giving **Table 3**.

Table 3 Methods for skull-stripping

Authors	Year	Modality	Method	Characteristics
Fennema - Notestine, *et al.* [64]	2006	MRI	BET, 3dIntracranial, HWA, BSE	Comparison study
Speier, *et al.* [65]	2011	MRI	A modified ROBEX method	Outperforming popular methods
Kleesiek, *et al.* [66]	2016	MRI	FCN	3D convolutional neural network structure
Hwang, *et al.* [67]	2019	MRI	3D-UNet	Outstanding performance

2.4. Intensity normalization

Due to most brain image analysis methods like segmentation and detection assuming that the image intensity was distributed in a standardized range, scientists usually employ intensity normalization before performing the subsequent medical analysis. The process of intensity normalization plays a significant role in brain MRI image analysis as other methods like histogram matching can not ensure the same correspondence between intensity and brain tissue. Take Z-score intensity normalization as an example. We utilized $I(x)$ to represent a brain MRI image and B to describe the corresponding brain mask. Then we achieve the mean μ_{ZS} and standard deviation σ_{ZS} of brain mask intensity. And the Z-score normalized image could be recorded as

$$I_{z-score}(x) = \frac{I(x) - \mu_{ZS}}{\sigma_{ZS}}. \quad (5).$$

If we skip intensity normalization in the study, it will affect the results of segmentation or detection and prevent them from acquiring the best performance. Thus, intensity normalization is recognized as one of the most vital preprocessing steps. Back in 1999, Nyúl, *et al.* [68] proposed a two-stage method for intensity normalization. Their study revealed that similar intensity might indicate similar tissue when sharing the same MR protocol and body region. Shah, *et al.* [69] tested Nyúl's method via numerous experiments and demonstrated its effectiveness in the clinic. In 2010, Tustison, *et al.* [70] proposed the famous N4ITK method, which has been considered a baseline in later studies. In 2015, Sun, *et al.* [71] proposed a histogram-based method for intensity normalization on brain MRI images and claimed to achieve satisfying performance. In 2019, Simkó, *et al.* [72] proposed artificial neural network architecture for MRI intensity normalization and reported better performance than N4ITK. In the end, we provided **Table 4** to summarize this section.

Table 4 Methods for intensity normalization

Authors	Year	Modality	Method	Characteristics
Nyúl, *et al.* [68]	1999	MRI	A two-stage method	Correspondence of

				intensity and body tissue
Shah, *et al.* [69]	2011	MRI	A two-stage method	Convincing performance
Tustison, *et al.* [70]	2010	MRI	N4ITK	State-of-the-art performance
Sun, *et al.* [71]	2015	MRI	A histogram-based method	Outstanding performance
Simkó, *et al.* [72]	2019	MRI	ANN	Promising performance

2.5. Data augmentation

Since deep learning was widely applied in studies of brain image analysis, lacking training data has been a general problem bothering researchers. If training data is insufficient, the deep learning-based model cannot reach its best ability, including segmentation, classification, detection, and prediction. Data augmentation applies approaches like affine transformation to multiply more training samples based on the given dataset. Through data augmentation, the quantity of image samples is enlarged, and overfitting is suppressed. In this circumstance, data augmentation became one of the essential preprocessing technologies. It attracted scientists' interest in developing more powerful data augmentation methods recently. In 2018, Shin, *et al.* [73] proposed a deep learning-based data augmentation method applying the generative adversarial network (GAN). They employed the GAN for brain image synthesis and used synthetic images to supplement the training data. Their method achieved promising performance according to the experimental results. In 2019, Afzal, *et al.* [74] presented a data augmentation framework based on transfer learning and successfully applied this framework to Alzheimer's disease detection. Mok, *et al.* [75] proposed another GAN-based data augmentation method and reached state-of-the-art performance. Sajjad, *et al.* [76] also proposed a deep learning-based data augmentation method for brain tumor grading and obtained satisfying experimental results. Zhao, *et al.* [77] proposed a data augmentation method based on learned transformations. In 2020, Han, *et al.* [78] proposed a novel data augmentation method using the progressive growth of generative adversarial network (PGGAN) and obtained better experimental results than conventional GAN-based methods. Li, *et al.* [79] put forward a new framework for brain-tumor-image data augmentation called TumorGAN. They employed a regional perceptual loss and a regional L1 to improve the framework's performance. Furthermore, this framework was efficient according to their experimental results. Safdar, *et al.* [80] presented a research of comparing several popular data augmentation techniques. According to their study results, rotation attained the best performance improvement. At last, we provided **Table 5** to summarize this section.

Table 5 Methods for data augmentation

Authors	Year	Modality	Method	Characteristics
Shin, *et al.* [73]	2018	MRI	GAN	Using synthetic images to expand training data
Afzal, *et al.* [74]	2019	MRI	Transfer learning	Relieving the unbalanced data distribution
Mok, *et al.* [75]	2019	MRI	GAN	Using a coarse-to-fine

				generator
Sajjad, *et al.* [76]	2019	MRI	GAN	Convincing performance
Zhao, *et al.* [77]	2019	MRI	Transformation-based method	State-of-the-art performance
Han, *et al.* [78]	2020	MRI	PGGAN	Outstanding performance
Li, *et al.* [79]	2020	MRI	TumorGAN	Adopting a regional perceptual loss
Safdar, *et al.* [80]	2020	MRI	Rotation-based method	Outstanding performance

3. Brain diseases

There are many kinds of brain diseases, among which cerebrovascular disease is a very common category. Cerebrovascular diseases usually referred to as cerebral vascular accidents (CVA), are also called strokes in many cases. As one of the most dangerous diseases, stroke kills thousands of lives every year, threatening people's health worldwide. A stroke attack occurs when the cerebral artery encounters blockage or rupture, leading to brain tissue death due to a lack of blood supply. Generally, strokes can be divided into two types: ischemic stroke and hemorrhagic stroke. Most strokes are ischemic strokes because of brain artery blockage, while some hemorrhagic strokes still exist due to brain artery rupture. Transient ischemic attacks (TIAs) belong to one type of ischemic stroke. Hemorrhagic strokes consist of intracranial hemorrhage, intracranial aneurysm, subarachnoid hemorrhage (SAH), arteriovenous malformation (AVM), and moyamoya disease. In addition to cerebrovascular disease, Alzheimer's disease and multiple sclerosis are common brain diseases of great research value.

Artificial intelligence has been broadly utilized in various studies of cerebral vascular accidents in recent years. Scientists have been applying deep learning technologies for segmentation from kinds of medical imaging methods, including magnetic resonance imaging (MRI), magnetic resonance angiography (MRA), computerized tomography (CT), and computerized tomography angiography (CTA). Compared to traditional methods, deep learning-based methods usually attain higher accuracy and achieve better performance in varieties of brain disease studies. For example, deep neural networks are adopted to segment the brain vessel structure on MRA images and the stroke lesion on CTA images. Scientists utilize convolutional neural networks to detect strokes based on MRI images and classify strokes into ischemic strokes and hemorrhagic strokes. In addition to segmentation, detection, and classification tasks, researchers also employ artificial intelligence to predict lesion progress and prognosis, which is beneficial to treatment planning and outcome management. Except for analyzing medical images, artificial intelligence can also predict the stroke onset using the text data such as case reports, medical service data, and health behavior data. This chapter will survey the artificial intelligence-based studies for several most commonly seen cerebrovascular diseases, including ischemic stroke, TIA, intracranial hemorrhage, intracranial aneurysm, SAH, AVM, and moyamoya disease.

3.1. Brain vessel segmentation

As we know, doctors and scientists must segment brain vessels accurately in the head of further research, such as detecting and predicting cerebrovascular diseases. Brain vessel segmentation is the cornerstone of imaging-based cerebrovascular disease research. Thus, we cannot skip the brain vessel segmentation technologies when introducing cerebrovascular disease research. This section will review the methods and applications of cerebrovascular segmentation. Some of them are traditional methods, while most advanced approaches nowadays are based on deep learning. At the end of this section, we gave a summary by providing **Table 6**.

In 2006, Hassouna, *et al.* [81] proposed a cerebrovascular segmentation approach based on stochastic methods. Their approach adopted a time-of-light magnetic resonance angiography (TOF-MRA) dataset using a Markov random field (MRF) model and the maximum pseudo-likelihood estimator (MPLE) algorithm to extract blood-vessel voxels from background noise ones. The experimental results showed that their approach could segment cerebral vessels down to 3 voxel diameters. In 2013, Babin, *et al.* [82] put forward a method for cerebrovascular segmentation based on line-shaped profiles. It was demonstrated that their method could segment large blood vessel tree structures and delineate fine structures of cerebral vessel networks. In 2015, Wang, *et al.* [83] raised a threshold segmentation method for automatically segmenting brain vessels on brain magnetic resonance angiography (MRA) images. The experimental results proved its capacity to segment brain vessels accurately. These three methods above are representative of traditional methods for cerebrovascular segmentation. In recent years, scientists tended to develop deep learning-based methods for brain vessel segmentation. Compared with traditional methods, deep learning-based methods usually could achieve a better precision and robustness of segmentation. In 2017, Phellan, *et al.* [84] applied deep convolutional neural networks to segment cerebral vessels on TOF-MRA images. The experimental result showed their method acquired an average Dice coefficient ranging from 0.764 to 0.786, which indicated that deep learning-based methods could obtain high performance in cerebrovascular segmentation as well.

In 2018, Zhao, *et al.* [85] proposed a semi-supervised learning method for cerebrovascular segmentation based on a hierarchical convolutional neural network architecture. They applied the centerlines and estimated radii to produce the tube-level labels of brain vessels from MRA images. The experimental results showed that this method achieved a sensitivity of 94.69% and an accuracy of 97.85%. In 2019, Livne, *et al.* [86] applied the U-Net architecture (shown in **Figure 5**) to develop a deep learning-based segmentation method for brain vessels and reported to assure a Dice value of 0.88, which is better than traditional graph-cuts methods. Sanchesa, *et al.* [87] proposed a novel approach for cerebrovascular segmentation on MRA images. They combined the advantages of the three-dimensional U-Net structure with the Inception modules to develop their segmentation model. The experimental results proved that this model could attain state-of-the-art performance. In 2020, Fan, *et al.* [88] developed a hybrid deep learning-based approach for cerebral vessel segmentation on TOF-MRA images. Their training dataset was labelled by a hidden Markov random field (HMRF) model rather than hand-crafted annotations. Their hybrid approach achieved a Dice value of 0.79 due to it united the strengths of deep convolutional neural networks and HHRF. Hilbert, *et al.* [89] proposed the BRAVE-NET for cerebrovascular segmentation based on a three-dimensional U-Net architecture. They applied the three-dimensional U-Net as the backbone and integrated the multiscaling context path into it. Their multiscale three-dimensional convolutional neural network model obtained a Dice coefficient of 0.931, more accurate than the comparison groups. Meng, *et al.* [90] proposed a novel multiscale model for brain vessel segmentation on MRA images. They developed an encoder-decoder structure based on U-Net. They also designed a multiscale module for brain vessels with different diameters and improved the skip connections and the dense blocks to enhance high-level feature extraction. Their model obtained an F1 score of 0.8813, an accuracy of 0.9784, a sensitivity of 0.8775, and a specificity of 0.9886, which was superior to the state-of-the-art methods. Ni*, et al.* [91] proposed an attention mechanism-based convolutional neural network architecture for brain vessel segmentation. They applied a multi-channel attention mechanism to aggregate the low-level features and the high-level ones. And they also adopted the Atrous Spatial Pyramid Pooling (ASPP) to boost multiscale feature extraction. The experimental results suggested that this approach reached a Dice coefficient of 0.965, which is more outstanding than other state-of-the-art methods. Tatsat*, et al.* [92] proposed a new CNN-based architecture called DeepMedic (shown in **Figure 6**) for cerebrovascular segmentation. They employed the multi-resolution inputs to expand the perception field, improving the segmentation precision of tiny vessels. Their model achieved a Dice value of 0.94 and a Connectivity-Area-Length (CAL) of 0.84, outperforming the baseline methods like U-Net. Tetteh*, et al.* [93] proposed their deep learning-based model called DeepVesselNet for brain vessel segmentation. Compared to ordinary deep learning-based methods, they presented three innovations. First, they developed two-dimensional orthogonal cross-hair filters with three-dimensional context information in order to relieve computing pressure. Second, they employed a false-positive rate correction embedded cross-entropy loss function for class balancing. Third, they applied a computational angiogenesis model which could imitate vascular tree growth to construct a synthetic dataset. Then they utilized this synthetic dataset for transfer learning to improve the performance. The experimental results showed that their model acquired promising performance, especially in the segmentation of voxel-sized vessel structures.

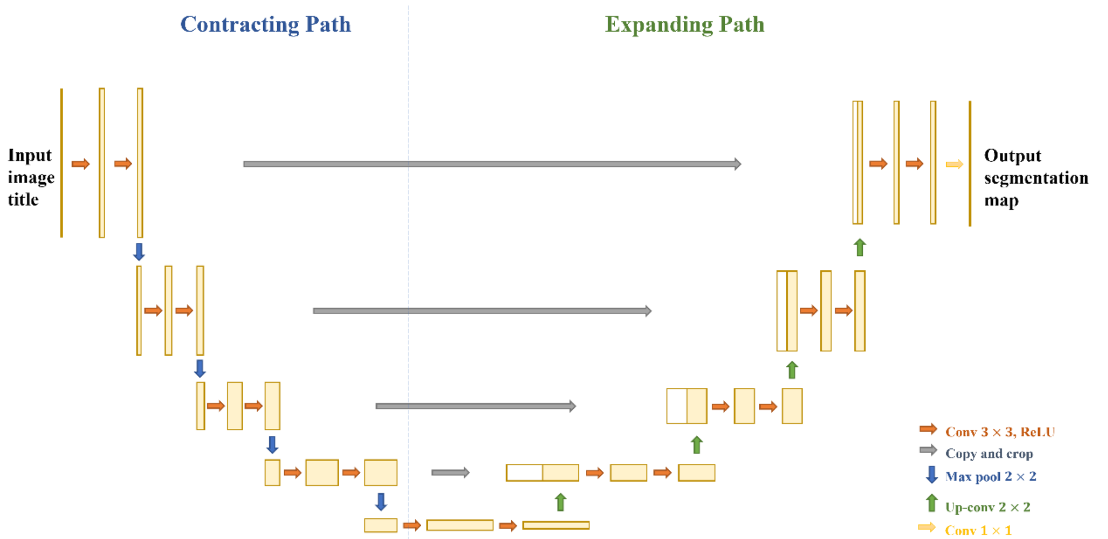

Figure 5 The illustration of U-Net architecture [15]

Lately, Wang*, et al.* [94] proposed a novel approach called the JointVesselNet for brain vessel segmentation. The JointVesselNet embedded the maximum intensity projection (MIP) image composition into MRA images, improving the morphology extraction capacity of slender vessels. Their approach, combined with two-dimensional projection, showed convincing performance compared with the state-of-the-art methods. Zhang*, et al.* [95] presented a data-driven deep learning-based approach for brain vessel segmentation on TOF-MRA images. They put forward a semi-supervised mixture probability model to produce a large number of labelled points from the sparse annotations, simulating the intensity distribution of brain vessels. Then they applied a Clean-Mechanism model to correct the mislabeled points. Finally, a dilated dense convolutional neural network (DD-CNN) was employed based on the corrected labelled points and reported to achieve high segmentation performance in the completeness and sensitivity for thin vessels, obtaining an average Dice coefficient of 93.20%. Zhang*, et al.* [96] proposed a scheme for brain vessel segmentation based on a reverse edge attention network. Before segmentation, their scheme adopted a Retinex model for noise modelling and enhanced the vessel regions by noise reduction. The experimental results proved the efficiency of their proposed scheme. Guo*, et al.* [97] improved the ordinary U-Net model with focal loss function, presenting a new approach for cerebrovascular segmentation. They divided normalized MRA images into three groups: the axial-direction slices, the coronal-direction slices, and the sagittal-direction slices. Then they applied three single U-Net models to be trained on these three groups respectively. Moreover, they introduced the focal loss function to relieve the unbalancing distribution of positive and negative samples. At last, they applied the voting feature fusion and the connected domain analysis to combine the output probabilities of three single U-Nets. The experimental results showed that their approach outperformed than a single U-Net, which indicated their approach could effectively elevate the cerebrovascular segmentation performance of the U-Net architecture. Kossen*, et al.* [98] proposed a novel method for cerebrovascular segmentation with the anonymization potential based on a generative adversarial network (GAN) architecture. They applied the GAN to generate anonymous labels on MRA patches and then utilized a U-Net for cerebral vessel segmentation with the labels produced by the GAN. The experimental results showed that among three different GANs, the Wasserstein-Gan with gradient penalty and spectral normalization (WGAN-GP-SN) acquired the best segmentation performance on the real testing data. Their study also suggested that the synthetic patches generated by GANs and real data could be applied in transfer learning, which would be beneficial to the circumstances of data scarcity and anonymization analysis.

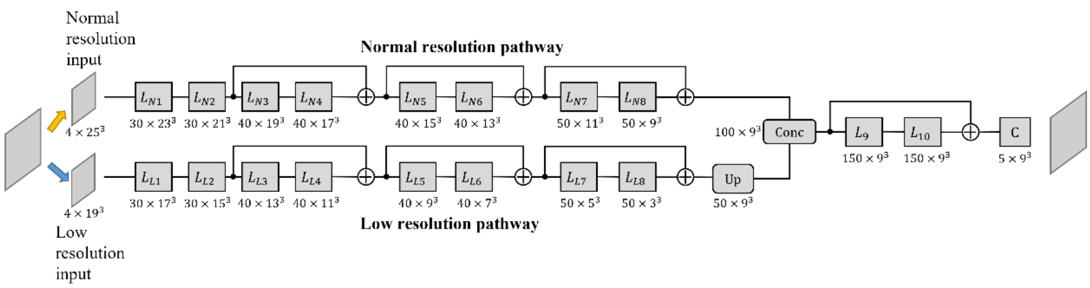

Figure 6 The architecture of DeepMedic

Table 6 Methods for brain vessel segmentation

Authors	Year	Modality	Method	Characteristics
Hassouna, *et al.* [81]	2006	TOF-MRA	MRF	Applying the maximum pseudo-likelihood estimator algorithm
Babin, *et al.* [82]	2013	TOF-MRA	The line-shaped algorithm	Outstanding performance
Wang, *et al.* [83]	2015	TOF-MRA	The threshold segmentation algorithm	High accuracy
Phellan, *et al.* [84]	2017	TOF-MRA	CNN	Promising performance
Zhao, *et al.* [85]	2018	TOF-MRA	A hierarchy CNN	High sensitivity
Livne, *et al.* [86]	2019	TOF-MRA	U-Net	Higher performance

				than traditional methods
Sanchesa, *et al.* [87]	2019	TOF-MRA	U-Net	Combined with the Inception modules
Fan, *et al.* [88]	2020	TOF-MRA	CNN	Applying a hidden MRF model for labelling
Hilbert, *et al.* [89]	2020	TOF-MRA	BRAVE-NET	Combined with the multiscaling context path
Meng, *et al.* [90]	2020	TOF-MRA	Encoder-decoder	U-Net architecture
Ni, *et al.* [91]	2020	TOF-MRA	CNN	Multi-channel attention mechanism
Tatsat, *et al.* [92]	2020	TOF-MRA	DeepMedic	Better than U-Net
Tetteh, *et al.* [93]	2020	TOF-MRA	DeepVesselNet	Applying the 2D orthogonal cross-hair filters
Wang, *et al.* [94]	2020	TOF-MRA	JointVesselNet	Combined with the maximum intensity projection image composition
Zhang, *et al.* [95]	2020	TOF-MRA	A dilated dense CNN	Applying a Clean-Mechanism model for label correction
Zhang, *et al.* [96]	2020	TOF-MRA	A reverse edge attention network	Applying a Retinex model for denoising
Guo, *et al.* [97]	2021	TOF-MRA	U-Net	Combined with a focal loss function
Kossen, *et al.* [98]	2021	TOF-MRA	WGAN-GP-SN	Applying the GAN architecture

3.2. Ischemic stroke

An ischemic stroke refers to the death of brain tissue due to reduced blood flow to the brain or insufficient oxygen supply to the brain. Ischemic strokes are usually caused by blood clots that block the arteries in the brain due to atherosclerosis. The stroke symptoms can occur suddenly and may include: muscle weakness on one side of the body, paralysis, paresthesia or numbness, language difficulty, confusion, vision abnormality, dizziness, and loss of balance or coordination. Artificial intelligence has been widely applied in ischemic stroke studies of stroke detection, lesion segmentation, and outcome prediction. In 2017, Chin, *et al.* [99] presented an automatic system for ischemic early detection using convolutional neural networks. They applied data augmentation technologies on brain CT images and obtained an identification accuracy higher than 90%. In 2018, Nielsen, *et al.* [100] proposed a deep convolutional neural network architecture to predict the final stroke lesion volume based on acute MRI images. The experimental results showed that their study attained better performance than traditional methods. In 2019, Clèrigues, *et al.* [101] proposed a deep learning-based approach for stroke lesion segmentation on CT perfusion images using the regularized training procedure, symmetric modality, and uncertainty filtering. The experimental results proved its efficiency, which meant that doctors could apply this approach to assess the lesion size and location without MRI in the clinic. Dourado Jr*, et al.* [102] proposed a transfer learning-based method for stroke classification based on brain CT images. They applied convolutional neural networks as the feature extractor and employed various machine learning-based classifiers, including the Bayesian classifier, multilayer perception, k-nearest neighbor, random forest, and support vector machines. Their method achieved 100% accuracy, F1-score, recall, and precision on testing data, which demonstrated its effectiveness. Hilbert*, et al.* [103] proposed a method to predict stroke outcome using the ResNet architecture on reperfusion CT images. They applied the structured receptive fields and auto-encoders to initialize neural network weights. The experimental results suggested that their method acquired promising prediction performance and was capable of assisting treatment planning. Ho*, et al.* [104] developed a deep learning-based method to classify the time since stroke (TSS) based on the MR perfusion-weighted images. The experimental results supported that their method could help doctors to determine the stroke treatment timing like thrombolysis. Kim*, et al.* [105] proposed a deep learning-based method for cerebral infarction segmentation based on diffusion-weighted imaging (DWI). They applied the U-Net architecture to be trained on the DWI and apparent diffusion coefficient (ADC) data. Their method has been proved effective through the experimental results. In 2020, Bacchi*, et al.* [106] presented an approach for stroke outcome prediction combining convolutional neural networks with artificial neural networks on non-contrast CT images. Kumar*, et al.* [107] proposed a novel model named as CSNet for ischemic stroke lesion segmentation on the acute perfusion CT data. They introduced the self-similar fractal networks into the U-Net architecture, replacing the residual connections with the repetitive generation of self-similar fractals. The experimental results indicated that their segmentation model was superior to other state-of-the-art methods. Yu*, et al.* [108] successfully applied the U-Net architecture to predict the infarct lesion on the baseline perfusion CT images without further reperfusion data, which made a significant meaning for ischemic stroke patients. In the end, we provide **Table 7** to summarize this section.

Table 7 Studies of ischemic stroke

Authors	Year	Modality	Method	Characteristics
Chin*, et al.* [99]	2017	CT	CNN	Applying data augmentation
Nielsen*, et al.* [100]	2018	MRI	CNN	Higher performance than traditional methods
Clèrigues*, et al.* [101]	2019	CT	CNN	Applying the regularized training procedure
Dourado Jr*, et al.* [102]	2019	CT	CNN	Transfer learning
Hilbert*, et al.* [103]	2019	CT	ResNet	Applying the structured receptive fields for weight initialization
Ho*, et al.* [104]	2019	MRI	CNN	Convincing experimental results
Kim*, et al.* [105]	2019	DWI	U-Net	Multimodality
Bacchi*, et al.* [106]	2020	CT	CNN	Promising results
Kumar*, et al.* [107]	2020	CT	CSNet	Combined with the self-similar fractal networks
Yu*, et al.* [108]	2020	CT	U-Net	No need for reperfusion CT

3.3. Transient ischemic attack

A transient ischemic attack (TIA) is a brain disorder that usually lasts less than an hour and is caused by a temporary blockage of blood supply to the brain. The aetiology and symptoms of TIA are similar to those of ischemic stroke. TIA differs from ischemic stroke in that symptoms usually resolve within an hour without permanent brain damage. A TIA can be a red flag for an impending ischemic stroke. People who have had TIAs are more likely to have ischemic strokes than those who have not had TIAs. The risk of ischemic stroke is highest in the first 24 to 48 hours after a TIA. Detection of TIA and identification of its cause will be beneficial in preventing ischemic strokes. However, TIA symptoms disappear shortly and completely, leading to few or no brain cells death—at least not enough to cause any changes that can be detected by brain imaging or a neurologic examination. Thus, scientists tend to apply artificial intelligence to combine medical imaging data with medical records, wearable device data, or weather reports, presenting integrated data-driven TIA detection and prediction methods. In 2017, Chantamit-o-pas, *et al.* [109] proposed a deep learning-based method to predict TIA in heart disease patients. They built their prediction model based on the atrial fibrillation symptoms from heart disease datasets. Their method's efficiency was proved through the experimental results. In 2018, Haridas, *et al.* [110] proposed an artificial intelligence approach for TIA prediction based on the medical institute records. They applied principle component analysis to abandon the unrelated data dimensions, accelerating the modelling. The experimental results showed that their approach obtained convincing performance. In 2019, Bacchi, *et al.* [111] presented an intelligent method to predict a transient ischemic attack based on a public TIA dataset. They extracted useful information, including the symptom description, past medical history, the medication list, CT or MRI reports, and the ABCD2 score, to establish the prediction model using recurrent neural networks (RNNs) and convolutional neural networks (CNNs). The experimental results suggested that their study was potential. In 2020, Zhang, *et al.* [112] proposed a contactless approach to detect TIA in the indoor environment. They employed a microwave sensing platform to collect monitoring data and then performed the support vector machine (SVM) and the random forest (RF) to build the recognition model. The RF-based model attained an accuracy of 98.7%, which showed better performance than the SVM-based model. In 2021, Katsuki, *et al.* [113] presented a study to demonstrate that a TIA could be predicted through meteorological and calendar factors using deep neural networks. Okuno, *et al.* [114] proposed a method for TIA prediction using autoencoder neural networks based on a combination of the clinical and imaging data. We provide a summary at the end of this section, as shown in **Table 8**.

Table 8 Studies of transient ischemic attack

Authors	Year	Modality	Method	Characteristics
Chantamit-o-pas, *et al.* [109]	2017	The heart disease datasets	CNN	Based on records of the atrial fibrillation symptoms
Haridas, *et al.* [110]	2018	The medical institute records	CNN	Applying PCA to abandon the unrelated data dimensions
Bacchi, *et al.* [111]	2019	A TIA dataset	RNN and CNN	Abundant data dimensions
Zhang, *et al.* [112]	2020	The microwave sensing data	Random forest	Applying contactless microwave sensing data
Katsuki, *et al.*	2021	The meteorological and	DNN	Adopting the meteorological

[113]		calendar data		and calendar factors
Okuno, *et al.* [114]	2021	The clinical and imaging data	Auto-encoder	Combination of the clinical and imaging data

3.4. Intracranial hemorrhage

An intracranial hemorrhage refers to the bleeding inside the brain. Chronic hypertension is a common cause of intracranial hemorrhage. The intracranial hemorrhage accounts for about 10% of all strokes, but the mortality rate of the intracranial hemorrhage is much higher than that of ischemic stroke. Intracranial hemorrhage diagnosis mainly relies on medical imaging examinations. Since artificial intelligence has been widely applied in medical image analysis, many deep learning-based methods for intracranial hemorrhage studies have been proposed in recent years. The deep learning-based methods for examing intracranial hemorrhage are close to those for ischemic stroke. Both apply a deep neural network's capacity to detect and segment the lesion area in brain images. In 2018, Arbabshirani*, et al.* [115] proposed an automated method for intracranial hemorrhage identification using a 7-layer convolutional neural network with brain CT scans. The experimental results showed that their method could recognize the intracranial hemorrhage effectively, even for subtle intracerebral bleeding. Kamal*, et al.* [116] adopted a three-dimensional convolutional neural network to extract features from the cross-sectional brain CT images, proposing an automatic approach for intracranial hemorrhage identification. Kuo*, et al.* [117] proposed an active learning-based method for intracranial hemorrhage detection and segmentation on brain CT images using a cost-sensitive system. Their method was reported to achieve state-of-the-art performance. Further, they improved this method to an expert level based on fully convolutional neural networks next year [118]. Majumdar*, et al.* [119] proposed an automatic deep learning-based method for intracranial hemorrhage detection without burdensome hand-tuned processes. In 2019, Cho*, et al.* [120] proposed a cascaded deep learning-based approach for intracranial hemorrhage identification and segmentation. They applied a cascade model that consisted of 2 CNNs and 2 FCNs and claimed to achieve high performance in both sensitivity and specificity. Lee*, et al.* [121] proposed an interpretable deep learning-based method for intracranial hemorrhage detection and subtypes classification. They applied an attention map and retrieved a prediction basis from training data to provide the model's interpretability. The experimental results showed that their method acquired satisfying performance. Ye*, et al.* [122] presented a method for intracranial hemorrhage detection using non-contrast brain CT images. They developed a three-dimensional joint convolutional and recurrent neural network which was demonstrated to obtain promising experimental results. In 2020, Anupama*, et al.* [123] proposed an approach to detect intracranial hemorrhage using a GrabCut-based segmentation synergic deep learning model (GC-SDL). Hssayeni*, et al.* [124] presented their study in intracranial hemorrhage segmentation using the U-Net architecture on CT images. Mansour*, et al.* [125] proposed an integrated scheme for intracranial hemorrhage diagnosis on brain CT images. They applied Kapur's thresholding with an elephant heard optimization algorithm (KT-EHO) to segment the intracranial hemorrhage region. Then they employed an Inception neural network to extract features and a multilayer perception for classification. Their research was suggested to obtain promising performance. At the end of this section, we provide **Table 9** to summarize the AI studies of intracranial hemorrhage.

Table 9 Studies of intracranial hemorrhage

Authors	Year	Modality	Method	Characteristics

Arbabshirani, *et al.* [115]	2018	CT	7-layer CNN	Effective for subtle intracranial hemorrhage
Kamal, *et al.* [116]	2018	CT	3D-CNN	Promising performance, AUC of 0.87
Kuo, *et al.* [117]	2018	CT	Cost-sensitive active learning	State-of-the-art performance
Majumdar, *et al.* [119]	2018	CT	CNN	End-to-end method, the high specificity of 98%
Kuo, *et al.* [118]	2019	CT	FCN	Expert-level performance
Cho, *et al.* [120]	2019	CT	Cascaded deep learning model	The cascade model consisted of 2 CNNs and 2 FCNs
Lee, *et al.* [121]	2019	CT	FCN	Interpretability due to an attention map and the prediction basis
Ye, *et al.* [122]	2019	CT	A 3D joint CNN-RNN	Precise diagnosis of intracranial hemorrhage subtypes
Anupama, *et al.* [123]	2020	CT	A GC-SDL model	GrabCut-based segmentation
Hssayeni, *et al.* [124]	2020	CT	U-Net	Efficient segmentation performance
Mansour, *et al.* [125]	2021	CT	Inception	Outstanding performance

3.5. Intracranial aneurysm

An intracranial aneurysm refers to a dilation that occurs in the artery of the brain. Clinicians usually apply computed tomography angiography (CTA) or magnetic resonance angiography (MRA) to examine the intracranial aneurysm. Lately, scientists have presented a lot of artificial intelligence approaches to analyze medical images of the intracranial aneurysm. In 2018, Ueda, *et al.* [126] reported that their deep learning-based method could improve the detection sensitivity of early intracranial aneurysms on TOF-MRA images. In 2019, Duan, *et al.* [127] proposed a two-stage convolutional neural network architecture for automated detection of intracranial aneurysms. The experimental results demonstrated that the CNN architecture could detect intracranial aneurysms effectively on the two-dimensional digital subtraction angiography (2D-DSA) images. Park, *et al.* [128] proposed a deep learning-based approach called the HeadXNet model to detect intracranial aneurysms on CTA images. They employed the three-dimensional convolutional neural network architecture and achieved outstanding experimental results. Sichtermann, *et al.* [129] presented a retrospective study in which they put forward a CNN-based method for intracranial aneurysm detection and obtained competitive experimental results. In 2020, Faron, *et al.* [130] proposed a similar approach for intracranial aneurysm detection on the three-dimensional TOF-MRA images. Jin, *et al.* [131] proposed an automatic method for intracranial aneurysm segmentation and detection using the U-Net architecture on the two-dimensional DSA images. Joo, *et al.* [132] proposed an automated method for recognizing intracranial aneurysms based on the three-dimensional ResNet architecture from the extracted TOF-MRA images. Podgorsak, *et al.* [133] presented a CNN-based method for intracranial aneurysm automatic detection in a retrospective study. Shi, *et al.* [134] presented their study of applying a U-Net architecture to detect intracranial aneurysms with several improvements. They replaced the convolution blocks in the original U-Net with the residual blocks. They adopted the dilated convolutions in the top of encoders and inserted a dual attention module between the encoder and the decoder. The experimental results demonstrated that these architecture improvements were efficient and satisfying performance. Yang*, et al.* [135] demonstrated that deep learning-based methods could apply CTA images to build an automatic intracranial aneurysm detection system. Yang*, et al.* [136] built a public three-dimensional intracranial aneurysm dataset for testing various intracranial aneurysm detection and segmentation methods. Zeng*, et al.* [137] proposed a deep learning-based method to detect intracranial aneurysms automatically on DSA images. They introduced a spatial information fusion (SIF) algorithm to transform the processed data into two-dimensional image sequences from the three-dimensional vessel model. Their method proved its effectiveness through the experimental results and was superior to other intracranial aneurysm detection methods for it costed fewer computation than those did. To summarize this section, we provide **Table 10** as follows.

Table 10 Studies of intracranial aneurysm

Authors	Year	Modality	Method	Characteristics
Ueda*, et al.* [126]	2018	TOF-MRA	ResNet-18	The high sensitivity of detection
Duan*, et al.* [127]	2019	2D-DSA	CNN	A two-stage cascaded approach
Park*, et al.* [128]	2019	CTA	The HeadXNet model	FCN-based method
Sichtermann*, et al.* [129]	2019	TOF-MRA	The DeepMedic model	An 11-layer CNN architecture
Faron*, et al.* [130]	2020	TOF-MRA	The DeepMedic model	Convincing performance
Jin*, et al.* [131]	2020	2D-DSA	U-Net	Promising results
Joo*, et al.* [132]	2020	TOF-MRA	A deep leaning-based method	3D ResNet architecture
Podgorsak*, et al.* [133]	2020	2D-DSA	CNN	Outstanding performance
Shi*, et al.* [134]	2020	CTA	DAResUNet	Improvements for U-Net
Yang*, et al.* [135]	2020	CTA	CNN	The performance is potential
Yang*, et al.* [136]	2020	TOF-MRA	Deep learning-based methods	Establishing an open-access dataset
Zeng*, et al.* [137]	2020	2D-DSA	A 2D-CNN method	Little computational cost

3.6. Subarachnoid hemorrhage

A subarachnoid hemorrhage (SAH) refers to the bleeding in the space between the inner and middle layers of the brain covering tissues. A ruptured intracranial aneurysm is the most commonly seen cause of a subarachnoid hemorrhage. A subarachnoid hemorrhage is a hazardous disease. Patients would suffer from a sudden severe headache, usually followed by unconsciousness or even death. Lately, scientists have attempted to develop methods to detect subarachnoid hemorrhage and predict the outcome using artificial intelligence technologies. In 2019, Sales Barros*, et al.* [138] proposed a CNN-based method to segment subarachnoid hemorrhage on brain CT images. The experimental results showed that the convolutional neural network architecture could effectively be employed for SAH segmentation and detection. Ramos*, et al.* [139] demonstrated that artificial intelligence could use the SAH CT images to predict delayed cerebral ischemia. They applied an auto-encoder to extract features from CT images and adopted logistic regression as the predictor. In 2020, Shahzad*, et al.* [140] proposed a deep learning-based method for SAH segmentation and detection using a three-dimensional convolutional neural network architecture called the DeepMedic. They performed the experiments on brain CT images and attained satisfying results. In 2021, Dengler*, et al.* [141] proposed an approach to predict the SAH outcome based on CT images and the clinical records using machine learning methods, including a support vector machine (SVM), the CatBoost tree boosting algorithm, a Naïve Bayes classifier, and the multilayer perceptions (MLPs). Their approach was reported to achieve promising performance through the experimental results. Pennig*, et al.* [142] proposed an approach for SAH diagnosis on CTA images using ensemble learning technology via three separate DeepMedic models. Nishi*, et al.* [143] proposed a deep learning-based method for the SAH diagnosis that could enable non-specialists to recognize the SAH accurately. At the end of this section, **Table 11** was given as a summary.

Table 11 Studies of subarachnoid hemorrhage

Authors	Year	Modality	Method	Characteristics
Sales Barros, *et al.* [138]	2019	CT	CNN	Promising experimental results
Ramos*, et al.* [139]	2019	CT and clinical records	An integrated AI model	Applying an auto-encoder as the feature extractor and a logistic regression model as the predictor
Shahzad*, et al.* [140]	2020	CT	The DeepMedic model	A 3D-CNN architecture
Dengler*, et al.* [141]	2021	CT and clinical records	Machine learning-based methods	Promising experimental results
Pennig*, et al.* [142]	2021	CTA	The DeepMedic model	Ensemble learning
Nishi*, et al.* [143]	2021	CT	Deep learning	Outstanding performance

3.7. Arteriovenous malformation

An arteriovenous malformation (AVM) is a mass of dilated blood vessels directly connected to an artery and vein, bypassing the capillaries that ought to connect an artery and vein under normal circumstances. AVM could lead to seizures or headaches as a rare cerebrovascular disease, especially in young adult patients. AVM may not cause an intracerebral hemorrhage. Clinicians usually adopt medical imaging methods such as CT, MRI, CTA, and MRA to assist the AVM diagnosis. In recent years, artificial intelligence technologies have been introduced into AVM diagnosis. Scientists put forward several applicable deep learning-based approaches for automatic segmentation or detection of an arteriovenous malformation. In 2019, Wang*, et al.* [144] proposed a three-dimensional supervised method to segment the AVM on CT simulation images automatically. They applied a 3D V-Net architecture with a compound loss function, including logistic and Dice losses. The experimental results suggested that their approach could automatically segment the AVM volume and obtain a satisfying delineating accuracy. In 2020, Yabo, *et al.* [145] presented an automatic segmentation model for the AVM. They first proposed a fast region proposal network to build the bounding box for the AVM lesion. Then they employed the V-Net architecture to predict the final labels. It was demonstrated that their approach could delineate the automatic contours very close to the ground truth contours. In 2021, Shi, *et al.* [146] proposed a deep learning-based approach to first extract vascular features from DSA videos and second apply these features in the AVM detection. They adopted the Fast-RCNN architecture and claimed that their approach showed a competitive performance in the experiments. In the end, we provide **Table 12** as the summary of this section.

Table 12 Methods of arteriovenous malformation

Authors	Year	Modality	Method	Characteristics
Wang, *et al.* [144]	2019	CT	A 3D V-Net model	3D supervision mechanism
Yabo, *et al.* [145]	2020	CT	A 3D V-Net model	The bounding box trained by a fast region proposal network
Shi, *et al.* [146]	2021	DSA	Faster-RCNN	Two-stage scheme

3.8. Moyamoya Disease

As a rare and progressive cerebrovascular disease, the moyamoya disease was caused by the blockage of cerebral arteries located at the base of the brain, also named the basal ganglia. The moyamoya disease mainly occurs in children. Patients of moyamoya disease will first suffer a stroke or a transient ischemic attack, followed by muscular weakness or paralysis influencing one side of the body. Researchers have tended to apply artificial intelligence to develop detection methods for the moyamoya disease. In 2019, Kim, *et al.* [147] proposed a deep learning-based approach for moyamoya disease detection in plain skull radiography. They adopted an 8-layer convolutional neural network to recognize moyamoya disease and claimed to achieve promising experimental results. In 2020, Akiyama, *et al.* [148] proposed a method for moyamoya disease diagnosis on MRI images. They employed the VGG-16 with fine-tuning to differentiate the patients with moyamoya disease from the patients with atherosclerotic disease and healthy people. The experimental results proved deep learning's efficiency in MRI-based moyamoya disease detection. In 2021, Hu, *et al.* [149] proposed a spatiotemporal feature-based approach to detect moyamoya disease using the DSA data. They first applied a three-dimensional convolutional neural network to extract spatial features from each frame of DSA. Then they obtained the long-term spatiotemporal features from DSA sequences using the BiConvGRU. Finally, they performed feature fusion for further classification. According to the experimental results, their approach acquired state-of-the-art performance among several advanced moyamoya disease detection methods. Lei, *et al.* [150] also proposed a deep learning method for moyamoya disease detection and hemorrhagic risk prediction using the DSA data. They employed ResNet-152 as the backbone and reported to attain outstanding performance. To end this section, **Table 13** was given as a summary.

Table 13 Studies of moyamoya disease

Authors	Year	Modality	Method	Characteristics
Kim, *et al.* [147]	2019	Radiography	CNN	Promising experimental results

Akiyama, *et al.* [148]	2020	MRI	VGG-16	Effective performance
Hu, *et al.* [149]	2021	DSA	FCN with BiConvGRU	Spatiotemporal feature learned and feature fusion
Lei, *et al.* [150]	2021	DSA	ResNet-152	Outstanding performance

3.9. Alzheimer's disease

As a neurodegenerative disease, Alzheimer's disease mostly occurs in elderly people. It is reported that around 70 percent of cases of dementia were caused by Alzheimer's disease. Patients with Alzheimer's disease are likely to have health problems including cognition disorder, language problems, motivation loss, spatial disorientation, and sleep disorder. In 2014, Liu, *et al.* [151] proposed a deep learning framework for Alzheimer's disease early diagnosis. They adopted auto-encoders and softmax layer to build the network architecture and achieved outstanding performance. In 2018, Aderghal, *et al.* [152] presented a cross-modal transfer learning approach for Alzheimer's disease classification. They pretrained on a structural MRI dataset and transferred the knowledge to mean diffusivity data. The experimental results showed that this approach avoided overfitting effectively and obtained higher performance compared to those approaches using only one imaging modality. In 2019, Ding, *et al.* [153] applied the Inception architecture for early detection of Alzheimer's disease based on PET data and attained improved performance. Martinez-Murcia, *et al.* [154] put forward an approach for Alzheimer's disease diagnosis using deep convolutional auto-encoders. Their model not only obtained a classification accuracy of over 80% for Alzheimer's disease diagnosis but also provided reliable visualization results. In 2020, Mehmood, *et al.* [155] proposed a siamese convolutional neural network based on VGG-16 and applied improved data augmentation technologies for Alzheimer's disease early diagnosis. In 2021, Murugan, *et al.* [156] constructed a convolutional neural network architecture named DEMNET for Alzheimer's disease classification and acquired outstanding performance. Wang, *et al.* [157] designed a novel framework combining attention mechanism and VGG to detect Alzheimer's disease and achieved good results. Zhu, *et al.* [158] proposed a deep learning architecture that applies DenseNet as a feature extractor and Schmidt neural network as a classifier for Alzheimer's disease identification. Finally, these AI methods for Alzheimer's disease study are summarized in **Table 14**.

Table 14 Methods for Alzheimer's disease

Authors	Year	Modality	Method	Characteristics
Liu, *et al.* [151]	2014	MRI	Auto-encoders	Minimal domain prior knowledge
Aderghal, *et al.* [152]	2018	MRI & Diffusion Tensor Imaging	Cross-modal transfer learning	Multimodality
Ding, *et al.* [153]	2019	PET	InceptionV3	Outstanding performance
Martinez-Murcia, *et al.* [154]	2019	MRI	Auto-encoders	Reliable visualization results
Mehmood, *et al.* [155]	2020	MRI	Siamese CNN	Improved data augmentation
Murugan, *et al.* [156]	2021	MRI	DEMNET	Outstanding performance

Wang, *et al.* [157]	2021	MRI	ADVIAN	Attention mechanisms
Zhu, *et al.* [158]	2022		DSNN	Using Schmidt neural network as classifier

3.10. Multiple sclerosis

Multiple sclerosis is a severe degenerative disease of the brain or spinal cord that affects the central nervous system. It is harmful to the immune cells and causes many symptoms such as sensation, movement, balance, and vision degeneration. In 2018, Wang, *et al.* [159] presented a deep convolutional neural network architecture for multiple sclerosis identification. The architecture employed state-of-the-art deep learning technologies, including batch normalization, dropout, and stochastic pooling, and achieved persuasive performance. In 2020, Essa, *et al.* [160] proposed a two-stage deep learning-based approach for multiple sclerosis lesion automatic segmentation. The first stage of this approach is to apply two parallel R-CNNs to segment respectively in T2-w and FLAIR brain MRI images. In the second stage, they adopted an adaptive neuro-fuzzy inference system (ANFIS) to fuse T2-w and FLAIR segmentation results. The experimental results showed that this approach outperformed other advanced competitive models. Narayana, *et al.* [161] put forward a method for multiple sclerosis lesion classification based on VGG-16 and acquired competitive performance. In 2021, Alijamaat, *et al.* [162] proposed an approach to identify multiple sclerosis using convolutional neural networks. Their approach applied the Haar wavelet transform to highlight lesions and ensure more accurate performance. McKinley, *et al.* [163] trained DeepSCAN to segment multiple sclerosis lesions and obtained outstanding experimental results. All these studies were listed in **Table 15**.

Table 15 Studies for multiple sclerosis

Authors	Year	Modality	Method	Characteristics
Wang, *et al.* [159]	2018	MRI	CNN	Stochastic pooling, dropout, and batch normalization
Essa, *et al.* [160]	2020	MRI	Parallel R-CNN	Two-stage approach combined with an adaptive neuro-fuzzy inference system
Narayana, *et al.* [161]	2020	MRI	VGG-16	Competitive performance
Alijamaat, *et al.* [162]	2021	MRI	CNN	Highlight lesions with the Haar wavelet transform
McKinley, *et al.* [163]	2021	MRI	DeepSCAN	Outstanding performance

4. Discussion and Conclusion

Studying brain diseases has a significant meaning for human health. Scientists and clinicians cannot get rid of medical imaging techniques such as MRI, CT, CTA, and MRA to study brain diseases. Deep learning-based methods have become the mainstream of brain image analysis methods recently. In the future, we think that there are three development directions.

The first direction is multimodality. In the past, most approaches for brain disease analysis were based on only one kind of imaging modality. Lately, more and more scientists have attempted to propose brain disease analysis methods based on more than one modality. For example, they applied medical imaging with health records from medical institutions or wearable devices to develop novel approaches for brain disease studies [164]. Adopting multimodality in brain disease studies has three reasons. First, existing methods have nearly made the best use of a single data modality. If we want to improve the performance, we need to break this limitation. Applying multimodality may be a solution for it. Data from different modalities could supplement each other and enhance the expected results. Second, the human body is an integrated living system. Different organs or parts of the body are not independent. They correspond to each other and work together to maintain the body system. It is indicated that different brain diseases share some inner relationship between them. If we apply only one modality to construct our methods, we discard this inner relationship information that may be a key factor, especially for detection and prediction studies. Third, as we always mentioned, deep learning needs large amounts of training data to reach its best capacity. However, training data is insufficient in a brain disease study in most cases. Applying multimodality means introducing new data sources, which will relieve the pressure of data deficiency. Because of these three reasons, we believe that multimodality will be a research hotspot in deep learning-based studies of brain diseases.

The second development direction in the future is interpretability. Although artificial intelligence has succeeded in brain disease studies, most existing methods paid their primary attention to performance rather than interpretability. Explainable artificial intelligence (XAI) has made huge progress in recent years. Many XAI models have been proposed and applied in many AI fields. These XAI models, such as DeConvNet [165], LRP [166], Grad-CAM [167], and the meaningful perturbation [168], have attracted the interest of some researchers. For example, Sagar, *et al.* [169] applied LRP to detect Alzheimer's disease on brain MRI images. Petrov, *et al.* [170] adopted Grad-CAM to visualize three-dimensional brain structure. Sutre, *et al.* [171] proposed a method for brain disease classification based on meaningful perturbation. We believe that more and more brain disease studies based on explainable artificial intelligence will spring out, and researchers will consider model interpretability in the future.

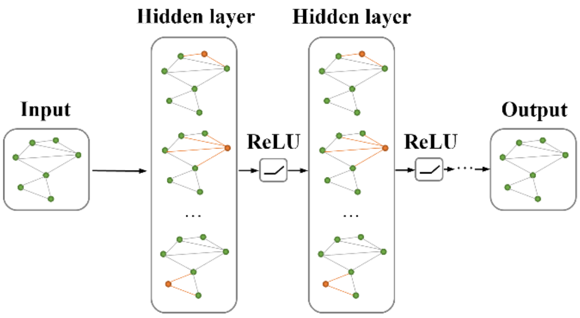

Figure 7 The architecture of GNN

Last but not least, the third direction of brain disease intelligence studies is employing new advanced deep learning models. Graph neural networks (shown in **Figure 7**) [172] and the transformer [173] are two broadly-used advanced deep learning models in recent years. Compared to classic deep learning models such as CNN, FCN, and GAN, these newly proposed models enable scientists to perform better in brain disease studies. Marzullo, *et al.* [174] proposed an approach for multiple sclerosis classification using a graph convolutional neural network. Song, *et al.* [175] presented a method applying a graph convolutional neural network for the classification and staging of Alzheimer's disease. Ma, *et al.* [176] put forward an attention-guided deep graph neural network for the diagnosis of Alzheimer's disease.

They employed an attention-guided random wark (AGRW) module to extract the structural graph features. In 2021, Li, *et al.* [177] raised a graph neural network framework named BrainGNN for the analysis of brain MRI images. Nandakumar, *et al.* [178] applied graph neural networks to localize the eloquent cortex in brain tumor patients automatically. As for applying the transformer architecture in brain disease studies, Barhoumi, *et al.* [179] proposed a hybrid model named n-CNN-ViT that combined CNN and ViT architectures for intracranial hemorrhage classification. Shang, *et al.* [180] adopted a transformer-based architecture to detect intracranial hemorrhage. Wang, *et al.* [181] employed the transformer to propose a brain tumor segmentation method. Li, *et al.* [182] combined the advantages of transformer and CNN and proposed the Trans-ResNet model for Alzheimer's disease classification. In the end, we hope that more and more newborn deep learning models will emerge and contribute to constructing more effective methods for brain disease studies.

Acknowledgement

This study is partially supported by the National Natural Science Foundation of China, China (62002304); the China Fundamental Research Funds for the Central Universities, China (20720210053); Global Challenges Research Fund (GCRF), UK (P202PF11); LIAS Pioneering Partnerships award, UK (P202ED10).

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