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Review

Can deep learning revolutionize clinical understanding and diagnosis of optic neuropathy?

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ABSTRACT

Artificial intelligence (AI) based on deep learning (DL) has sparked tremendous global interest in recent years. Deep Learning has been widely adopted in speech and image recognition, natural language processing which has an impact on healthcare. In the recent decade, the application of DL has exponentially grown in the field of Ophthalmology. The fundoscopy, slit lamp photography, optical coherence tomography (OCT), and magnetic resonance imaging (MRI) were employed for clinical examination of various ocular conditions. These data served as a perfect platform for the development of DL models in Ophthalmology. Currently, the application of DL in ocular disorders is majorly studied in Diabetic retinopathy (DR), age-related macular degeneration (AMD), macular oedema, retinopathy of prematurity (ROP), glaucoma, and cataract. In Ophthalmology, DL models are gradually expanding their scope in optic neuropathies. Glaucoma and optic neuritis are optic nerve disorders, where DL models are currently studied for clinical applications. For further expansion of DL application in inherited optic neuropathies, we discussed the recent observational studies revealing the pathophysiological changes at the optic nerve in Leber's hereditary optic neuropathy (LHON). LHON is an inherited optic neuropathy leading to bilateral loss of vision in early age groups. Hence for early management, further footsteps in the application of DL in LHON will benefit both ophthalmologists and patients. In this review, we discuss the recent advancements of AI in the Ophthalmology and prospective of applying DL models in LHON for clinical precision and timely diagnosis.

Introduction

Artificial intelligence (AI) has taken over healthcare by playing a major part in revolutionizing diagnosis in the present era. Any complexity in healthcare precision, the AI model finds its application. In diagnosis, AI aced in mimicking human behaviour through machine learning (ML) technology to increase efficiency. AI comprehend machine learning provides techniques or algorithms that empowers computers to make effective predictions or judgement using available input data. It requires a large number of training data to build an exact model [1]. Deep learning (DL) is a subgroup of ML which has significant accuracy in many domains including natural language processing, recommender systems, sound recognition, and image recognition. It can also recognize complex, unstructured, and interconnected data with fair accuracy [2].

Gulshan et al. [3] first introduced the algorithm of DL in diabetic retinopathy (DR). Soon after the development of DL in DR, researchers were interested to work on different algorithms and successfully developed DL models, that could detect and moderate ocular conditions like Age-related macular degeneration (AMD), glaucoma, retinopathy of prematurity (ROP), and cataract [4]. To date, two complete algorithms have been successfully approved by the FDA. Amongst them, IDx-DR is a digital diagnosis system for DR. The other one is Viz.AI, which analyses images indicating a stroke. These devices are termed "Locked algorithms" [5]. These algorithms for ML have the potential to evolve continuously and are highly adaptive in the application of other fields.

Artificial Intelligence in neuro-ophthalmology is an emerging field and AI algorithms have shown high accuracy in detecting neuro-ophthalmic diseases in papilledema and glaucoma. Algorithms in AI are developed for detecting neuro-ophthalmic diseases through monitoring retinal nerve fibre layer (RNFL) thickness and optic disc alterations using fundus and OCT images [6]. This emerging technology in neuro Ophthalmology further signifies insight to expand its application in inherited optic neuropathy especially LHON. This review discusses the current application and recent innovations of AI in Ophthalmology, and the possible role of AI-based models in inherited optic neuropathy.

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Potential of AI in healthcare

The major reason for the exponential growth of AI worldwide is due to demand in big data processing and to enhance human work in healthcare diagnostics [7]. At present, tremendous growth in diagnostics and imaging is benefiting radiologists, ophthalmologists, and other treatment managing sectors (Fig. 4). Therefore, AI models in the field of Ophthalmology are rapidly increasing [8]. Deep Learning is employed in several medical imaging of disease conditions like tuberculosis from chest X-rays [9], malignant melanoma on skin photography [10], lymph node metastases to breast cancer from tissue sections [11], lung cancer using chest images [12], cardiovascular risk using computer CT [13], Pulmonary embolism using CT angiography [14], polyps using virtual colonoscopy [15], glioma using MRI [16], Alzheimer's disease detection using functional MRI [17].

Ophthalmology involves the latest electrical, acoustic, mechanical, and optical imaging techniques. Therefore, the application of AI in Ophthalmology is widely implemented and accepted. Using advanced DL models, AI classifies images based on pattern recognition [8]. In collaboration with the optic system, different models of DL algorithms like neural networking are successfully applied in various disease diagnoses and it's progression [18]. In DR, continuous monitoring is required to observe the disease progression. However, the introduction of AI has made it possible to image the fundus of patients with early DR efficiently. In the future, requirements for continuous monitoring of DR patients may be compromised, as AI can demonstrate the development and progression of the disease [19].

AI algorithms for diagnosis

In ophthalmology, ML requires algorithms with huge input data to train for predicting ocular conditions and to standardize its performance. Building a structured algorithm in ML is a crucial step for developing AI models for diagnosis. Fundus images of the optic conditions serve as the major database for building an AI algorithm in Ophthalmology [20]. Other than traditional fundus photography, optical coherence tomography (OCT) scans can also be used for developing algorithms [21]. Combing both the 2-dimensional fundus images and 3-dimensional OCT can improve the sensitivity and specificity of the AI algorithm. These databases are fed into systems with applied logarithms for decision-making through AI [22].

The two forms of AI are supervised learning and unsupervised learning. Supervised learning is the traditional ML method. In traditional ML, expert knowledge is utilized to label the clinical features and prognosis of ophthalmic conditions. The sorted images representing the clinical severity are then used for classification by trained ML models. To build a precise ML model, a larger number of labelled data by experts should be fed to train and validate the algorithm [23]. Some of the popular AI algorithms used for ML in Ophthalmology include decision tree, Bayesian classifiers, random forests, support vector machines, k-means, k-nearest neighbors, discriminate analysis, and neural networks [19]. In unsupervised learning, DL is applied which enables to skip the step involving the supervision of the expert. In DL the authorized input data from clinical diagnosis are extracted from secondary sources like published data, medical records, etc. for self-learning and to classify the ophthalmic conditions based on the diagnosis and severity [22]. The two powerful DL Classification system for identification includes convolutional neural network (CNN) and massive-training artificial neural network (MTANN) [23]. The characteristics of the AI system in Ophthalmology are presented in Fig. 1.

For building AI algorithms for Ophthalmology, the raw image data must be sorted, validated, and pre-processed. These steps involve human intelligence to validate an algorithm and it also reflects on the sensitivity and specificity of the AI system. Pre-processing of the image includes noise reduction, integration, and selection of the most relevant data. This will improve the efficiency of image processing for the outcome. After processing the data, a large number of inputs are fed to achieve maximum test efficiency. The test should be cross-validated before application. For cross-validation, test data should be compared with the training sets involving different variables. K-fold cross-validation is the commonly used method for validation. After validation of algorithms, the sensitivity and specificity of the performance are calculated using the receiver operating characteristic (ROC) curve [19].

Role and application of AI in the ophthalmology

The AI has revolutionized healthcare diagnostics by enabling ML applications to aid physicians with more precision and to reduce turnaround time. The scope of AI is extending exponentially and in the recent decade, ML is practiced in Ophthalmology. Numerous digital imaging data including OCT, MRI, colour fundoscopy, and computerized visual field for manual prediction in the clinical investigation, makes Ophthalmology an ideal field for the application of AI. The errors are common in the manual interpretation of the slit lamp or fundus or OCT images by an ophthalmologist, and it is more subjective. The ML identifies the images as measurable data and enables precision in the recognition. Hence the AI application is well established in Ophthalmology [24,25]. The current research in applying AI in various fields of Ophthalmology is represented in Fig. 2. amongst ocular disorders, DR is the widely studied area in AI serving as a hotspot for ML application. DR is the leading cause of blindness, and all diabetic patients require timely retinal screening for early-stage detection of DR which will help for treatment and management [26]. The progression of DR with pathological changes like cotton-wool spots, microaneurysm, hemorrhages, hard exudates, and neovascularization enable the ideal application of DL for characterization of DR [27]. In DR, the application of DL not only detects the condition but also categorizes them into proliferative DR, non-proliferative DR, and diabetic macular oedema [28]. The recent innovation in neural networks and precision in DL enabled to classify them based on the severity gradings such as mild, moderate, or severe [3]. Wong et al. proposed a three-layer feed-forward neural network based on identifying microaneurysms and hemorrhages [29]. The morphological component analysis (MCA) technique was developed to detect oedema and hemorrhages [30]. Yazid et al. identified hard exudates and optic disc pathologies using inverse surface thresholding and lattice neural network [31]. Another study has detected optic disc changes from fundus images by using keypoint detection, texture analysis, and visual dictionary techniques [32]. The specificity and sensitivity of these studies ranged from 75% to 94.7%. Other than using fundus images, ElTanboly et al. introduced DL based system to detect DR using another imaging modality through 52 OCT images and reported an AUC of 0.98 [33]. The AI in DR is found to be more reliable, and the test sensitivity of DL models is 97%, whereas the manual interpretation by ophthalmologists is only 8.3% [34]. A major milestone in prospective assessment of AI was the United States Food and Drug Administration approval of IDx-DR. The first complete autonomous AI-based DR diagnostic system for detecting more than mild DR and diabetic macular oedema [35]. Recently a study has evaluated an offline AI on a Remidio Fundus-on Phone and it displays high sensitivity (93%) and high specificity (92.5%) [36,37]. Offline AI facilities would make this technology more reachable in areas having poor network connectivity. The intelligent retinal imaging system is another breakthrough in the field of AI in Ophthalmology. This tele retinal DR screening program compares non-mydriatic fundus retinal images with a standard set of images from early DR study, to recommend referral in cases of severe non-proliferative DR (NPDR) or advanced DR [38].

AMD is an irreversible macular disease, caused due to various genetic and epigenetic changes affecting people above the age of 50 years [39]. Advances in image recognition and classification had enabled the recognition of retinal pigment changes, choroidal neovascularization, drusen, haemorrhage, exudation, and atrophy [23]. Colour fundus images are used as data for interpretation in DL. Although the results of

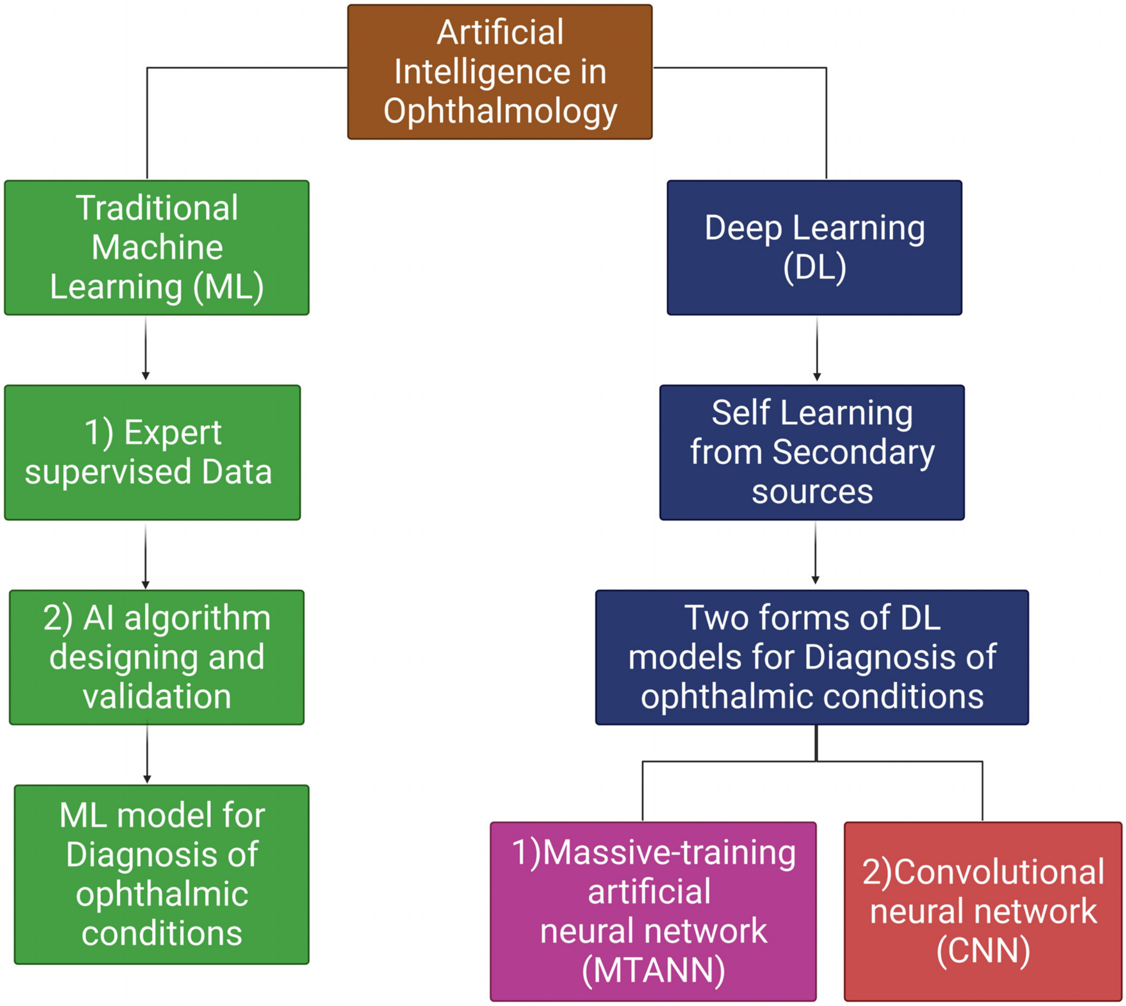

Fig. 1. AI algorithms in the traditional ML and DL models for the diagnosis in Ophthalmology.

DL application in the AMD are preliminary, many studies and clinical trials with greater study groups are ongoing for successful application [40,41]. From the observed studies, the test sensitivity of DL in AMD is > 87% [42]. But the application of OCT images of AMD in the DL model increased sensitivity, specificity, and accuracy [43]. The OCT enables the DL to detect the variations in morphology, intraretinal or subretinal fluid accumulations. The recent evaluation of OCT images obtained from the larger patient groups to develop the CNN platform in the DL model for diagnosis has shown accuracy greater than 90% [44,45]. Bogunovic et al. tested an algorithm to observe the anti-VEGF treatment responders using OCT images [46]. Incorporating ML in OCT images predicts the possibility of retreatment and it achieves significant performance in predicting low and high retreatment requirements [47]. Another study reported a deep convolution neural network (DCNN) using OCT images for decision making on anti-VEGF injection [48] and these studies are important in the image-guided prediction of treatment intervals in the management of AMD. Recently, scientists created and validated an AI model for AMD screening and predicting late dry and wet AMD progression. This model has 99.2% accuracy for AMD screening [49].

Cataract causes opacification of the lens in the eye with a prominent cloudy appearance. The early diagnosis of cataracts is crucial for management, which is a challenging task through clinical observation. Hence the DL finds the application in cataracts by the development of CNN algorithms for slit-lamp images for diagnosis of the early stage of cataract. The performance of the DL model in cataracts compared to the traditional clinical grading was achieved only 70% [50]. Another DL model developed for paediatric cataracts, enabled automatic localization of the region of interest in the lens for identification using CNN. The pre-processing of images has enhanced the sensitivity and specificity of the DL model up to 97% and enabled the classification and grading of cataracts [51]. Another study has reported risk prediction for posterior capsule opacification (PCO) using AI with 87% accuracy [52].

Glaucoma is caused due to increased intraocular pressure that damages the optic nerve. The early management of glaucoma is necessary to avoid irreversible compilations, but technical challenges are attributed to the clinical diagnosis of early glaucoma [53]. In the face of glaucoma diagnosis in the clinics, measurement of intraocular pressure, optic disc cupping, visual fields & OCT for RNFL and ganglion cell layer (GCL) thickness is examined [54]. Algorithms of ML were developed for the identification of glaucoma by optic disc thickness using OCT. The neural networks enabled quantitatively OCT images to classify glaucoma based on severity [55]. In the fundus images, few studies targeted cup disc ratio to apply CNN for DL [56]. The thickness of the RNF through OCT examination in glaucoma was studied in 102 patients. The DL model using CNN for the classification of glaucoma has an accuracy of over 87% [57]. The studies based on the RNF and optic disc thickness open a broad scope for future application of AI in optic neuropathy, especially in LHON, where the RNF layer and optic nerve vary upon the disease progression. Martin et al. used 24 prospective clinical trial data of a contact lens sensor for IOP monitoring using a random forest model [58]. Omodaka et al. developed an algorithm for the parameter such as optic disc cupping, neuroretinal rim thickness, and ganglion cell thick-

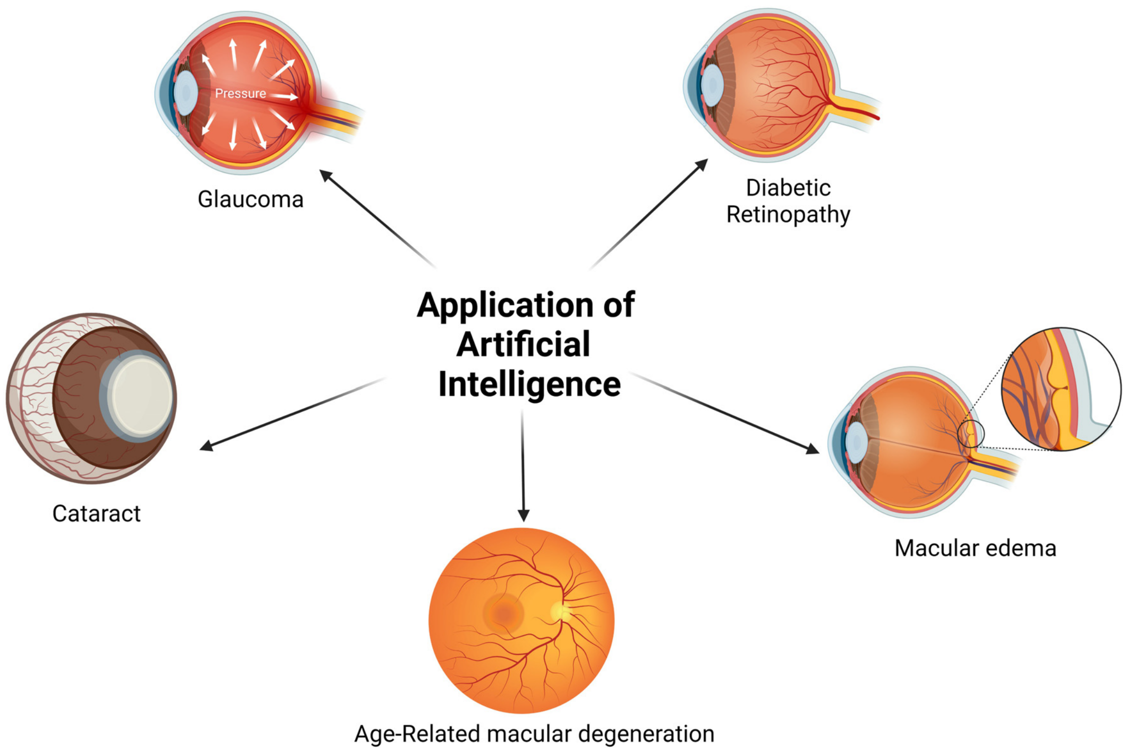

Fig. 2. The major areas of application of AI models in Ophthalmology.

ness based on segmentation technique using OCT images and it showed 87% accuracy [55]. Another study designed a fully automated model to classify angle-closure glaucoma using OCT scans and it reported 89.2% accuracy [59]. Studies have evaluated the DL algorithm to detect glaucomatous optic disc changes using fundus images and it shows high sensitivity and specificity [60,61]. Visual fields are very difficult to interpret and AI in the interpretation of visual field have been reported using a feed-forward neural network to identify pre-perimetric visual fields [62,63].

In other ocular diseases, Ohsugi et al. developed DL which can detect rhegmatogenous retinal detachment from ultra-wide-field fundus images with high sensitivity and specificity [64]. Xu et al. designed a dual-stage DL system to identify pigment epithelial detachment in polypoidal choroid vasculopathy (PCV) from OCT images [65]. Another study from retinitis pigmentosa and Leber congenital amaurosis patients has employed an ML-based approach to predict perimetry from OCT images [66]. The ML decision tree model has been introduced to predict the complexity of reconstructive surgery after the excision of periocular basal cell carcinoma [67]. In Ophthalmology, AI holds many advantages like corneal topography, IOL power prediction, predicting the outcome of the treatment, screening, and diagnostics. Artificial Intelligence has not only proven to be efficient and structured but also cost-effective when compared to high-end screening and diagnostic techniques [68].

Current status of AI in the diagnosis of optic neuropathy

Optic neuropathy occurs when the optic nerve is damaged causing structural changes in the eye and variations in the blood flow [69]. In most cases, optic neuropathy leads to vision loss starting with fading of vision, loss of colour vision, blurriness, peripheral vision loss, and clouding. It is important to detect optic nerve damage early and treat it. Researchers are trying to study various methods to derive better and quick diagnoses using AI. [70]. Currently, some studies support the use of AI in various diseases related to optic neuropathy. Recent studies on ML system attempts in detecting optic disc abnormalities through retinal fundus, focusing on optic disc atrophy and papilledema. The combination of DL systems along with new innovative hardware solutions could bring revolution in the neuro-ophthalmic conditions and healthcare [71].

Recently, A study reported an unsupervised data-driven technique to quantify measurement of RNFL structure covering a large region using swept-source optical coherence tomography(SS-OCT) images for detection of glaucoma and to predict future glaucomatous progression [72]. In another study, using RNFL thickness spatial patterns were used for predicting visual field loss in glaucoma [73]. Mariotonni et al. developed a novel segmentation-free DL algorithm that can measure accurate RNFL thickness on spectral-domain optical coherence tomography (SDOCT), without requiring segmentation of retinal layers [74]. Another scientist modified the ResNet-152 DCNN system to determine the optic disc laterality, to characterize between right and left optic discs in presence of neuro-ophthalmic pathologies [75]. Al-Aswad et al. evaluated the performance of the DL system for the identification of glaucomatous optic neuropathy using colour fundus photographs and its high sensitivity makes it a valuable tool for screening this disease [61]. One of the DL systems can diagnose optic nerve abnormalities specifically for papilledema from fundus photographs with dilated pupils differentiate amongst optic disc with papilledema, normal disc, and disc with non-papilledema abnormality [76]. Machine Learning techniques can be combined with fundus images as an effective approach to distinguish between Pseudopappiledema (PPE) and elevated optic disc associated with optic neuropathies [77]. AI-based DL algorithm for detecting optic disc abnormalities showed significant performance in differentiating non-glaucomatous optic neuropathy and glaucomatous optic neuropathy using colour fundus photographs [78].

Pathophysiological changes observed in LHON

LHON is an inherited optic neuropathy caused due to mitochondrial dysfunction. The point mutations *MT-ND1, MT-ND4,* and *MT-ND6* in the mitochondrial DNA (mtDNA) affect the respiratory complex I subunits [79]. The mutation impairs NADH-ubiquinone oxidoreductase chains and increases reactive oxygen species (ROS) leading to oxidative dam-

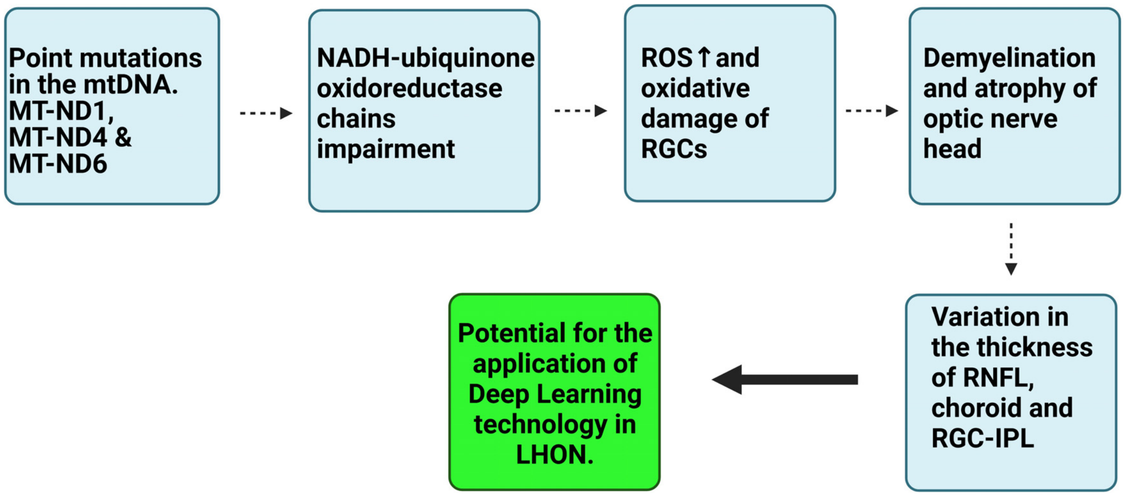

Fig. 3. Stepwise pathophysiological changes in LHON from mtDNA mutation level to optic nerve atrophy for understanding DL application.

age of the cells [80]. As the nerve cells are vulnerable to mitochondrial dysfunction, the retinal ganglion cells (RGC) in the axonal region of the optic nerve disc degenerates due to apoptosis [81,82]. This causes optic neuropathy and affects the visual pathway for image perception. The following events contribute to bilateral visual loss in the individual and pathological changes observed at the optic nerve. The pathophysiological changes at the optic nerve disc include demyelination and atrophy. In the acute stage, the RNFL swells in the area surrounding the optic nerve head. It is then followed by persistent thinning of these layers due to compensatory response in the chronic LHON. These changes were studied in OCT imaging [83]. Few studies suggested that, in acute LHON, both RNFL and choroidal thickening were observed. On the other hand, in chronic LHON, both RNFL and choroidal become thin [84]. The pathological changes in the RGCs affect the vascularity of the retinal ganglion cell-inner plexiform layer (RGC-IPL). Both the macular and peripapillary choroid thinning in progressed LHON correlates with the RGC-IPL thickness [85]. Evaluation of retinal vasculature in acute LHON using OCT angiography (OCT-A) outlines the marked vascular dilatation and tortuosity clinically. In fundus examination after dilation, peripapillary telangiectasias with hyperaemic optic nerve are observed and serve for clinical diagnosis of LHON. In the chronic stage, optic atrophy is seen at the nerve head [83]. To exclude the other causes of demyelination and compressive lesions from LHON, Magnetic resonance imaging (MRI) aids to narrow down the differential diagnosis. In LHON, increased T2 signals are noted in the chiasm and optic nerve tract. Optic nerve and chiasmal enhancements mimic optic neuritis in MR. Following pathological changes observed on LHON in comparison with the healthy individual and it may serve as a tool for the application of DL in face of LHON diagnosis (Fig. 3).

Potential of DL in the diagnosis of LHON

Currently, DL models are widely used only in the diagnosis of DR, AMD, cataract, and glaucoma [86,87]. Its application is not yet investigated in LHON. Although the demand for the data exists to train the DL models, since LHON is a rare disease, a targeted multi-centric study can provide enough information to feed the DL system. Successful application of DL in LHON will revolutionize the diagnosis and precision in neuro-ophthalmology. In recent years, DL technology is well established especially in the DR, and enables the classification of them based on the types and severity [88]. In DR, fundus examination shows microaneurysms, dot hemorrhages, intraretinal microvascular abnormalities, neovascularization which serves as an essential tool for clinical diagnosis [89]. The colour fundus images displaying these peculiar changes in DR are taken into consideration by the DL algorithm to form CNN and can classify them into proliferative or non-proliferative DR or macular oedema and mild, moderate, the severe scale of severity [3]. Similarly, in LHON, OCT examination revealed changes in the width of the RNFL, choroid, and RGC-IPL due to demyelination and atrophy. The thickness of RNFL and choroid studied were found to progress along with the severity of LHON. In acute LHON, these layers appear thick and after progression of LHON to the chronic stage, it gets significantly thin [84,85]. These changes were examined through many observational studies for enabling ophthalmologists to diagnose LHON and its prognosis. But considering the minor observational changes through OCT, MRI, and fundoscopy and its non-specificity, it remains difficult for manual interpretation. Conditions like optic neuritis and other sources of inflammation in the optic nerve tract mimic the optic nerve pathology of LHON and lead to many other differential diagnoses, hindering the ophthalmologist to decide on genetic testing and counselling for LHON. Hence the DL model with black box algorithm can create neural networks for accurate identification of width and other structural changes observed in the OCT. For more precision in the clinical picture of LHON, DL can augment ophthalmologists to decide on further proceedings.

Virtual assessment of LHON by various AI techniques

Many observational studies in LHON are currently focused on understanding optic nerve pathology, as it causes loss of central vision in most cases [90]. Here, we discuss how AI systems can potentially help the virtual assessment of LHON. In recent years, researchers worked on different ways of visualizing the white matter tracts like optic radiation and optic tract using diffusion tensor imagining (DTI) [91]. After this discovery, understanding morphometric changes near the subcortical area of the brain has increased. This would help the clinicians to correlate how the subcortical area could be associated with the prognosis of LHON. For observation of subcortical area in optic neuropathy, ultra-high-field imaging data requires 7T magnetic resonance. Artificial Intelligence DL system running on various installed algorithms, takes the core control and made it possible for high-resolution visualization of the cortical area [91].

The size of the optic nerve head can be useful in LHON [92]. The size of the optical disc can be captured in the image using AI/DL system. Various algorithms were designed to work on the pedigree of an individual by exploring the genetic history of their family. This makes it easier for clinicians to understand the background of the patient, their family, and their genetic capabilities to accept and increase the rate of early diagnosis of inherited genetic disorders like LHON [93]. Not much has been explored using AI in treating and understanding LHON; nevertheless, there is a great potential in quantitative analysis in combination with *in*

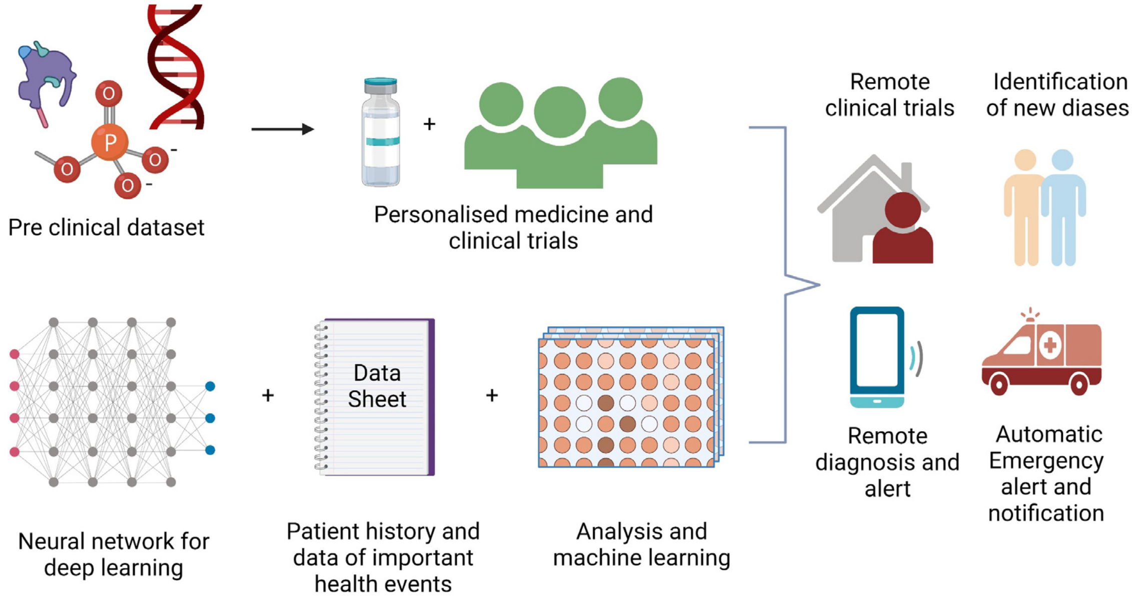

Fig. 4. Remote assessment in Ophthalmology. Telemedicine employing AI technology as a prospective for longitudinal diagnosis of ocular conditions.

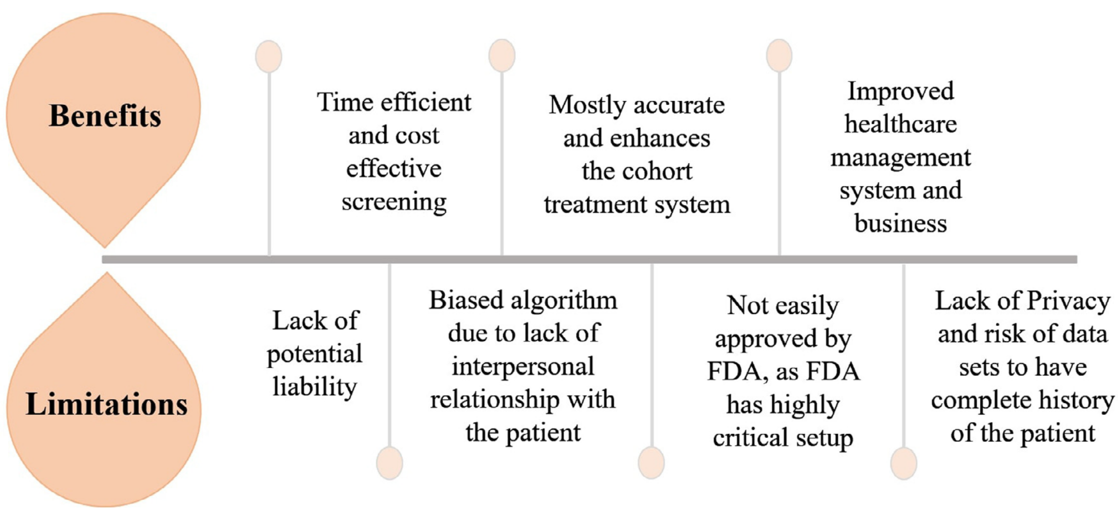

Fig. 5. This figure depicts the major benefits and limitations of AI in healthcare.

vitro studies to track down the morphological changes, progression, and understanding of LHON.

Advantages of employing telemedicine in Ophthalmology

Trials are ongoing to expand AI platforms via digital innovations in the internet of things, 5th generation telecommunication networks, and the creation of an ecosystem that is self-dependant and provides the prospect to advance the latest models related to Ophthalmology addressing various challenges [94]. One of the major advantages of using telemedicine is that it made possible for clinicians to evaluate the patient from any given location. Replicating routine clinical examination, AI and telemedicine are improvising to be better by incorporating vast information about the progression of diseases, longitudinal data usage, and real-time calculation of incidences in the real-world [95,96]. The application of AI can make data collection possible and store big data of patients. Many digital innovations run from diagnostics to helping in the treatment of eye diseases. Screening of eye diseases was majorly carried with the help of AI. Tele-screening through AI has expanded its application towards ophthalmological issues like DR, ROP, glaucoma, myopia, cataract, and AMD [23]. It can help in capturing the ocular conditions and make remote screening possible in Ophthalmology. Incorporating telemedicine for screening and understanding genetic diseases would be of great advantage (Fig. 4). Research has proven the use of AI in various genetically inherited diseases and similarly, this theory could successfully be applied for patients diagnosed with LHON. Genotypic and phenotypic correlation in LHON is a bit challenging task, but it is important clinically to decide on the treatment.

Limitations of AI

In the face of technology, AI has a major contribution towards diagnosis, assisting surgery, biomedical research, and biomedical information processing [97]. We have discussed the important role of AI in revolutionizing the future, however, it has several drawbacks in medicine and diagnosis [98]. The most challenging work involving the AI systems would be studying the intrinsic aspects of ML, concerning diseases with several possibilities and outcomes. To begin with, the regulation of various algorithms is a tedious task. AI is widely accepted, yet doesn't easily receive approval from FDA [99]. Few assistive algorithms have been approved by the FDA, which has critical acceptance criteria for the majority of the systems including clinical trials and transparency.

There are slight chances that AI commits minor errors which may be a hindrance in the process of operations and disease diagnosis considerably [99]. To originate various ways for gathering data as well as analysing them considering the legal formality is one amongst the principal challenges to be confronted by the upcoming AI system. Artificial Intelligence uses different approaches to assign ground labels which are AI reference standards, and they are subjected to human error. With evidence, it can be easily stated that there is a high risk of AI system producing biased assessment by the methodological index for nonrandomized studies (MINORS), which is yet to be used completely as an application due to testing [100]. Every new system and algorithm must go through a large amount of testing and trials which is time-consuming as it must cross many approvals, as the whole system is dependant on a trial-and-error procedure.

Neural networking in DL, also known as AI paradigms, trains dataset depending on the input fed. In some cases, the variability may occur in the output data which is termed as a black-box problem [101]. The AI would efficiently work only if the database has all the sufficient information to understand the particular condition [102]. The biased algorithm is not a very common mistake of AI but occurs in three different forms of components namely Model variance (Insufficient dataset), Model bias (selected majority and under-represented groups), and outcome noise (Interaction through model predictions unaffected by subpopulation) [99]. Despite various challenges and risks, AI/DL system is still changing the face of the healthcare ecosystem universally (Fig. 5).

Conclusion

Accurate and efficient image interpretation and satisfactory preliminary outcome of AI have a significant impact on Ophthalmology. The fusion of automatic diagnostics through AI with the traditional system of Ophthalmology would help ophthalmologists in understanding the pathophysiology of ocular conditions. Diagnosis of LHON requires complex genetic tastings which is time-consuming. Therefore, the application of AI in the observation of clinical images increases precision in the provisional diagnosis and helps in the early management.

Declaration of Competing Interest

The authors declare that there are no conflicts of interest.

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