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REVIEW

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Artificial intelligence in diagnosis and management of Huntington's disease

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Abstract

Background Huntington's disease is one of the rare neurodegenerative diseases caused because of genetic mutation of the Huntingtin gene. The major hallmarks of the condition include motor impairment, cognitive decline, and psychiatric symptoms. With no cure and only symptomatic treatments available, early detection and personalized therapy are warranted for managing the disease effectively. Artificial Intelligence has emerged as a transformational tool in healthcare, revolutionizing many parts of medical practice and research, thus holding the potential in detecting, monitoring, and managing Huntington's disease.

Main body of abstract Artificial Intelligence's role in Huntington's disease includes a variety of applications like medical image analysis and predictive analytics. AI-driven algorithms are utilized to analyze brain imaging data in medical image analysis. Deep learning and convolutional neural networks (CNNs) aid in the detection of subtle brain changes and the identification of illness biomarkers, allowing for the early diagnosis of the disease. Additionally, the predictive analytics capabilities of AI are used to analyze disease development and forecast clinical outcomes. AI models can identify illness patterns, estimate the rate of functional decline, and assist doctors in making educated decisions about treatment methods and care planning by analyzing patient data.

Conclusions With clinical practice and research integrated with Artificial Intelligence technologies, we can significantly improve the quality of life of individuals affected with Huntington's disease. This integration holds the potential to develop effective personalized interventions. Nevertheless, collaborative efforts among doctors, researchers, and technology sound developers would be key to the successful implementation of AI in HD.

Keywords Huntington's disease, Neurodegenerative disease, Artificial intelligence, Machine learning, Deep learning, Numerical simulations

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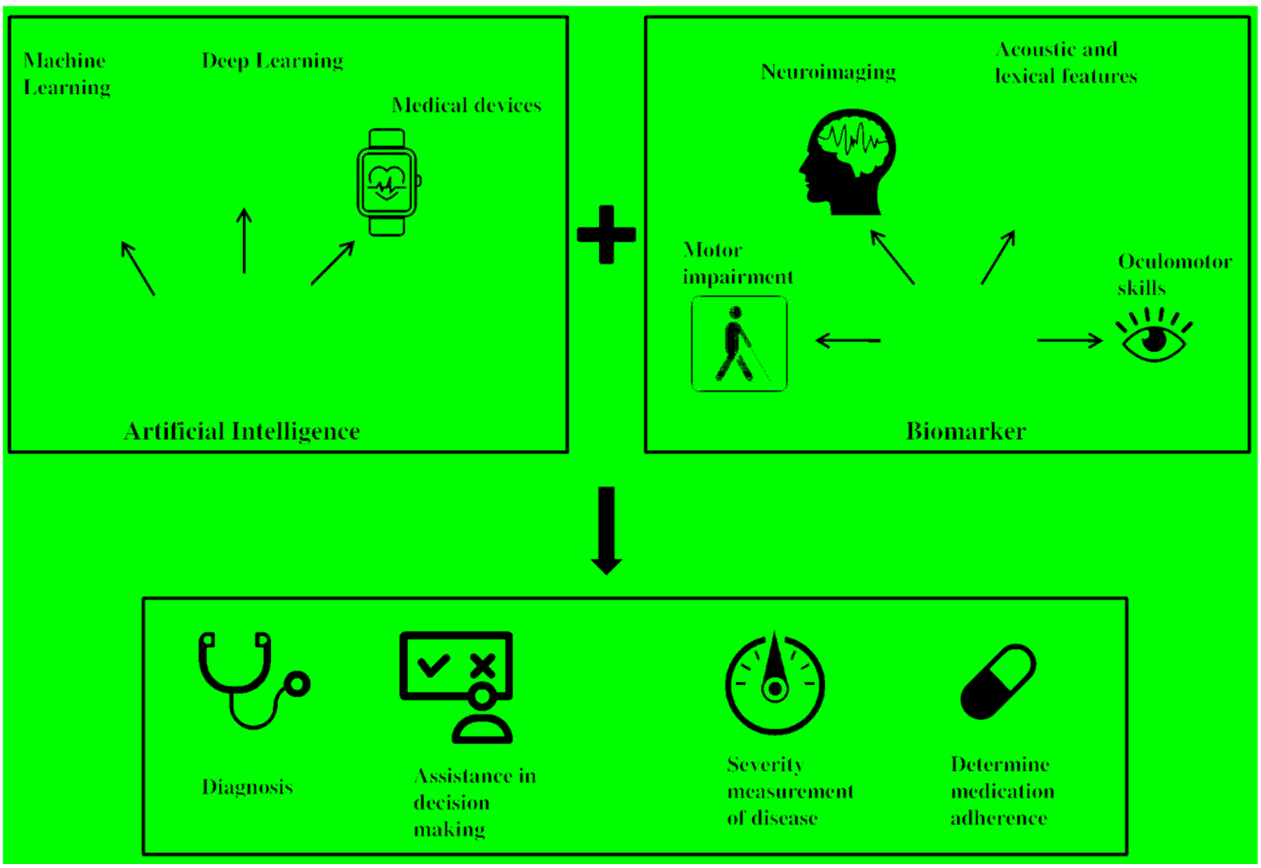
Graphical Abstract



1 Background

About 15% of the global population today suffers from neurological illnesses, which are the most common cause of both physical and mental impairment [21]. The burden of chronic neurodegenerative diseases is only expected to double over the next 20 years because of the increasing aging population in the world. Given this, maintaining universal access to neurological treatment will be a tremendous task [67]. Alzheimer's Disease and Parkinson's Disease are the two most prevalent neurodegenerative diseases affecting the elderly population [31].

On the other hand, Huntington's disease (HD), which is not often discussed, is one of the rare neurodegenerative diseases having a wide neuropsychiatric clinical spectrum [45]. It is a progressive neurodegenerative disorder that is mostly characterized by motor incoordination, tremors (chorea) and affects cognitive ability. It is caused by a mutation in the 'Huntingtin' (HTT) gene, located on chromosome 4, leading to an expanded CAG (Cytosine, Adenine, and Guanine) repeat sequence [13, 33, 60]. It has an autosomal dominant pattern of inheritance. The typical CAG repetition range length is from 10 to 35. Patients with 36 to 39 repeats have a low penetrance range, whereas those with 40 or more repeats are more likely to manifest the condition. Degeneration of neurons is observed due to the accumulation of this toxic mutant protein [45]. Its prevalence and distribution vary geographically. The highest prevalence of HD is reported in European, Australian, and North American populations and lower amongst Asian populations [54, 59].

HD has a complex pathophysiological understanding and a complicated diagnosis. Despite enormous attempts by the medical community to comprehend and treat HD, there is presently no cure, and available treatments are mostly symptomatic [66]. Thus suggesting that new techniques are required to effectively diagnose, manage, and treat this degenerative disease. In this regard, Artificial intelligence (AI) has made enormous strides in the healthcare industry, revolutionizing several areas of medical practice and study. AI is a fast-growing field in

computer science that mimics human intelligence including memory, learning, analysis, and even innovation using computers [27]. AI possesses the potential for automation of processes requiring human interference hence its applications in many fields are possible [69].

A wide range of technologies, including machine learning, natural language processing, and computer vision, are included in AI. These tools can analyze enormous volumes of data, finding patterns, and making predictions. Using sophisticated algorithms, AI can learn features from a given set of healthcare data, and use the insights obtained from this analysis to assist clinicians. Based on the feedback mechanism, it can also learn and self-correct itself. It can also assist physicians by providing updated information from journals, clinical practices, and textbooks to giving information on patient care. AI is also capable of drawing useful information from the data of a large population and predicting health risk alerts and health outcomes. It also plays a vital role in diagnosis, patient monitoring, and care, robotic surgery, electronic health records (EHR), development of treatment protocol and health management systems [20, 29, 59].

Numerical simulation, sometimes referred to as computational simulation, is a potent method for approximating and resolving challenging physical, biological, or engineering problems by employing mathematical models and computer algorithms. It enables scientists and engineers to investigate systems and phenomena that are difficult or impossible to explore using conventional analytical techniques. Various mathematical models have been developed and have wide applications which are emerging, particularly in the fields of medicine and surgery. One of them being the Elzaki Transform Homotopy Perturbation Technique (ETHPT) which can solve the nonlinear Emden–Fowler systems. The Elzaki Transform and the Homotopy Perturbation technique are combined to generate ETHPT. The outcomes demonstrate that ETHPT is dependable and efficient in resolving these equations. Similar nonlinear equations in numerous branches of science and engineering can be resolved using ETHPT [37]. Further, it is possible to solve $(1+1)$ dimensional mixed-difference integro-differential equations with variable coefficients under mixed conditions using a novel method based on the Bernoulli polynomial method and the separation of variables [39, 42]. Additionally, another analysis involves using Reduced Differential Transform Method (RTDM) in order to solve systems of fractional order biological systems. The study proves the use of this method to be simple and reliable with a broad range of application to linear and non-linear problems [6].

The interaction between immune system (IS) cells and glioblastoma multiforme (GBM) cells is modeled in a study using fractional order. To model the disease spreading systems, the Caputo–Fabrizio fractional derivative kernel is the ideal choice. The proposed fractional-order GBM illness paradigm's stability and distinctiveness are established. The Adams–Bashforth–Moulton (ABM) approach's numerical integrations demonstrate how the behavior of the model can change as parameters are changed [38]. Another study demonstrates that the nonlinear fractional Rubella illness model may be solved using the numerical technique using shifted second Chebyshev polynomials type (SSCPT) which explores the model's dynamic system and establishes that the fractional model has a stable solution both before and after control. Furthermore, the study concludes that the suggested method is new and practical for examining the internal methodology of different nonlinear biological models [40, 41]. Another work, in a similar vein, focuses on using the moved Vieta-Lucas polynomials type (SVLPT) as part of the basic collocation technique. It analyzes and resolves nonlinear Rubella disease tributes using a numerical technique. The existence of a continuously stable solution, disease equilibrium, and stability balance points are also covered [40, 41].

Other models include replicating the Kernel Hilbert space method, which is used to solve fuzzy Fredholm–Volterra integrodifferential equations. To model the actual situations involving uncertainty, the study of fuzzy IDEs with fuzzy beginning conditions is helpful [1]. In a different work, a brand-new and effective technique for solving three-dimensional mixed Volterra–Fredholm integral equations of the second class (3D-MVFIEK2) using Lucas polynomials are presented. These equations are converted into a system of linear algebraic equations using this method. The Lucas polynomial method produces better results when compared to other numerical techniques, particularly the Haar wavelet technique. In conclusion, this approach may be modified to solve singular 3D-VFIEK2 and can also be modified to use the finite difference method to solve different kinds of integral equations [42]. Another study suggests numerical analytical methods for examining fuzzy approximations of nonlinear fuzzy solutions using the extended reproducing kernel Hilbert space method, duffing oscillators and fuzzy fractional differential equations [5]. In other similar study, the replicating kernel technique is used to solve groups of fuzzy fractional integrodifferential equations with Atangana-Baleanu-Caputo fractional distributed order derivatives [2]. Thus while dealing with complicated and ambiguous patient data, the application of fuzzy mathematical models and AI techniques can result in disease detection systems that are more accurate and understandable.

Recent advances involving computational models and simulations are also used to study brain function, neural connectivity, and neurological disorders. Brain simulations help to understand illnesses like epilepsy and aid in the development of brain-computer interfaces [7]. The role of AI and numerical simulations in neurodegenerative diseases is multifaceted and holds significant promise for improving our understanding, diagnosis, treatment, and management of these complex conditions. AI algorithms can analyze diverse data sources, such as genetic information, neuroimaging scans, and clinical assessments, to identify early biomarkers and patterns indicative of neurodegenerative diseases. The development of computational models of disease progression is aided by numerical simulations, which also assist researchers comprehend the subtle changes that take place in the pilot stages and enable prompt diagnosis [12, 49]. Machine learning, which aims at developing algorithms to discover repetitions or trends in present data and form new prediction data, the repetitive motor, historical patterns, and other features of HD could be used to predict the disease. It can also classify HD from other neurodegenerative disorders and provide information on the progression of the disease, as well as measure the effectiveness of the drug thereby confirming medication adherence. This could only be done by computational statistics and mathematical optimization [15, 74].

Thus, this review aims to elucidate various methodologies of AI that have been implemented or are being developed for the determination of HD and its contribution to patient care. A disease such as HD requires regular and frequent observation by clinicians, but irregularities are seen in real conditions. Hence, the collection of such medical data using sensors along with analysis and management of the huge amount of generated data is carried out with the help of artificial intelligence. In the following sections, we have highlighted the recent studies utilizing AI and classified them based on different biomarkers of HD such as motor impairment, neuroimages and EEG, emotional imbalance, speech disability, and eye movements which are collected with the help of simple medical devices that are cost-effective and easy to use.

2 Main text

2.1 Methodologies of AI

AI is classified into two main branches: virtual and physical as shown in Fig. 1. The physical branch of AI comprises medical devices and robots that assist in complex surgeries and healthcare delivery. The virtual branch majorly consists of machine learning (ML) and deep learning (DL). ML is further classified into 3 types: (1) Unsupervised learning (2) Supervised learning and (3) Reinforcement learning. [35, 69]

ML is a learning and predictive technique that finds a meaningful pattern in each set of data with little human interference. However, a part of ML is dependent on human knowledge for the selection of features in data, multitasking, and transferring knowledge [22]. The major difference between the three subclasses of ML is the data interpretation method. For supervised learning techniques, the data, which is labeled with features can only be interpreted, however for the unsupervised

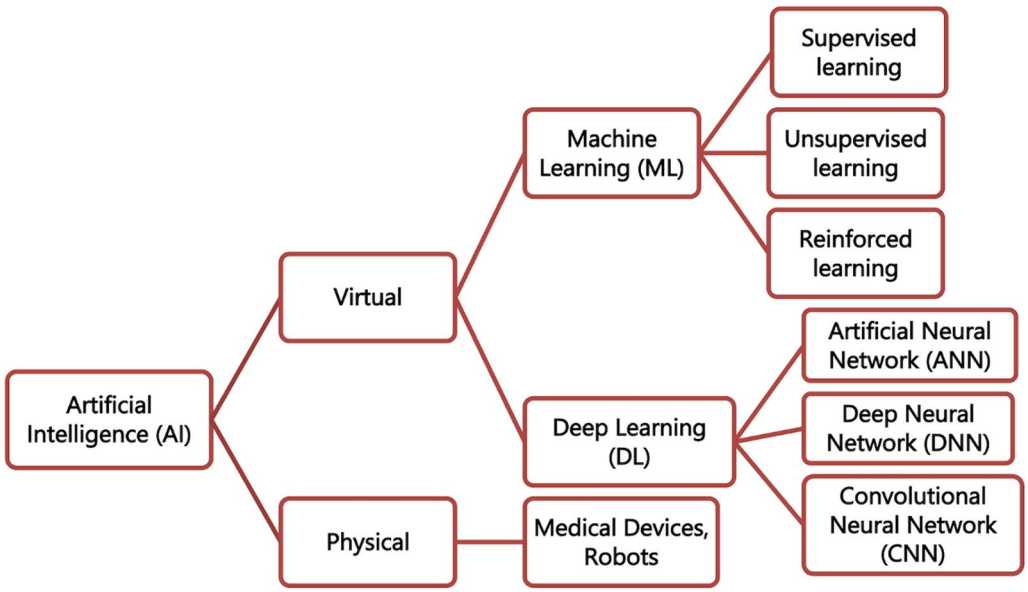


Fig. 1 Various branches of artificial intelligence

technique,the interpretation is conducted based on learning and data structure. In the case of reinforced learning, the algorithm learns from its own experiences in an interactive system with the data with the help of a feedback loop [11, 65, 73]. Supervised learning consists of various regression and classification algorithms such as logistic regression, linear regression, decision trees, random forest, *K*-nearest and support vector machine (SVM). In order to split the data points into distinct classes or forecast their values, SVM, a prominent machine learning technique for classification and regression issues, seeks to identify the best hyperplane. The maximization of margin, linear separability, margin and support vectors, cost parameter, kernel trick, convex optimization, binary and multiclass classification, and scalability are some of the rules of the SVM. Clustering algorithms in unsupervised learning consist of k-means, and hierarchical clustering are a few examples [8, 35].

DL is a part of ML that employs multiple-layer artificial neural networks (deep architectures) to learn and represent complicated patterns in data. The structure and function of the human brain, notably the linked neurons that process and send information, influenced the design of these deep neural networks. Artificial Neural Network (ANN) involves the unidirectional flow of information from the input layer to the output layer via the hidden layers. A deep Neural Network (DNN) is an extension of ANN with multiple hidden layers. Adding more layers helps in learning and representing complex data patterns. Convolutional Neural Networks (CNN) are specially designed for image and video analysis. Convolutional layers are used to automatically learn and extract spatial hierarchies of features from images. These scan the input image to detect local patterns, edges, and textures [14, 35].

Description of methodologies of AI as discussed above and a few other approaches used in HD diagnosis and assessment are described in Table 1 below.

Thus, by utilizing such techniques as discussed above, AI can detect patterns in the huge set of provided data. Prediction and stages of classification of disease help in early and accurate diagnosis and better patient care [35].

Table 1 List of various AI techniques and Huntington's disease scale

Sr. no	AI method or various approach	Description	References
1	Regression	Finding a correlation between independent and dependent variables	[16]
2	Decision tree	Divides the data into two or more homogenous sets	[64]
3	Random forest (RF)	Classification of a new object from a set of data which is a forest, and each tree is classified from that collection	[44]
4	KNN (*k*- Nearest Neighbor	Sorting is done by storing all cases which are available and then classifying via k-neighbor majority voting	[23]
5	Logistic regression	Deals with the probable finding of the occurrence of an event through a logical function	[26]
6	K-mean	Classification of a set of data using a cluster	[62]
7	Naive Bayes	Prediction is done by an assumption of the existence of a unique feature in a set that is different from other features	[17]
8	Support Vector Machine (SVM)	Classifies labeled data into two groups employing the n-dimensional hyperplane	[56]
9	Deep Learning (DL)	Used for huge data sets. The required features are automatically selected by the algorithm, unlike other techniques of ML	[34]
10	Artificial Neural Networks (ANN)	It is a technique where computational units are like neurons of the brain. ANN can perform complex analyses including multiple factors	[68]
11	Deep Neural Network (DNN)	It is a type of ML algorithm that can be trained. Here layers of the neural network are stacked to form a deep structure	[63]
12	CNN (Convolutional Neural Network)	Designed for analyzing multidimensional images such as 2D. Hence these are applied to data with a spatial arrangement	[34]
13	Linear Discriminant Analysis (LDA)	It is a technique to reduce the dimension and perform class separation	[48]
14	Adaptive Neuro-fuzzy Interference System (ANFIS)	Combination of neural network adaptive capabilities and the fuzzy logic qualitative approach	[70]
15	Long Short-term Memory (LSTM)	Deep model based on a 'memory cell' that can maintain information for a prolonged period	[72]
16	Unified Huntington's disease Rating Scale (UHDRS)—Total Motor Score	Used for rating eye movements, gait, speech, bradykinesia, dystonia, and rapidly alternating movements	[25]

2.2 Use of AI methodologies in Huntington's disease studies

HD includes characteristic symptoms such as psychiatric decline, cognitive impairment, and movement disorders like chorea (involuntary and jerky movements), motor incoordination, and bradykinesia [25]. Detection or diagnosis of HD at an early stage is difficult and mostly the symptoms are considered the normal symptoms of aging and dismissed. In addition to this, the similarity in symptoms of major neurodegenerative diseases also makes it difficult to correctly diagnose a particular disease [28]. At present, one of the commonly used methods for identification and assessment of HD is questionnaires of various kinds which is more of a subjective approach. Hence it is crucial to objectively evaluate the patient's physical functions for clinical use which can assist clinicians to make better clinical decisions and develop suitable treatment algorithms. Recently, different AI techniques including machine learning, methods of feature extraction, and methods of classification have been developed and employed to make an automatic and more precise diagnosis using available clinical data [70].

Additionally, Genetic Algorithms (GAs) and Swarm Intelligence could also be utilized in HD diagnosis and management. GAs is influenced by biological evolution and natural selection. They emulate the ideas of genetic heredity and the survival of the fittest to solve optimization and search challenges. GAs can be utilized for genetic risk assessment, illness progression modeling, feature selection, and medication development in the context of HD. GAs can detect high-risk genotypes, help simulate illness progression, choose pertinent genetic features, and assist in refining chemical molecules for potential therapeutic interventions by analyzing different combinations of genetic markers. Each member of the population that GAs represent as potential answers to the optimization problem has a different potential solution to the problem. Fitter people are more likely to pass on their inherited features, simulating the natural selection process. Through crossover (recombination), GAs enables the combining of advantageous features from several individuals, and through random mutations, they increase population diversity. The GA continues for a predetermined number of generations or until a stopping requirement is satisfied, and it improves over time [24].

Swarm intelligence is an AI approach that takes its cues from social insects, in which groups collaborate to complete challenging tasks. It helps with solving optimization issues. Swarm intelligence can improve parameter tuning, illness progression modeling, ideal treatment approaches, and image analysis in the study of HD. It is possible to fine-tune computational models to describe disease dynamics or therapeutic results as accurately as possible. Swarm intelligence can calibrate computer models to empirical data to forecast how the disease will develop. By simulating the results of various interventions, it helps improve treatment regimens for patients. In order to identify alterations caused by the disease and track the evolution of the condition in HD patients, swarm intelligence can segment and analyze brain images [30, 55].

Additionally, to understand the role of AI in HD, we have described different studies using AI techniques and have classified them according to the biomarkers of the disease discussed below.

2.2.1 Motor impairment

Gait pattern and mobility are affected in HD and observation of changes in the trend can be used for assessment. A few early motor signals of HD include a balance disorder, slowness, and random jerking movements [4, 53]. For classification and measurement of the severity of the disease, data is gathered, selected, then preprocessed followed by extraction of certain features, and then assessment of features is conducted to support the decision-making process. Data is attained with the help of several sensors. A few of the common classifiers used are linear, non-linear, Bayes, SVM, and Random Forest among many more. A fusion of various classifiers to obtain more accurate results has also been observed [28, 70]. Along with sensors, wearable and non-wearable devices incorporating accelerometers, photo sensors, and gyroscopes can also be used to gather data. The application of smartphones could be for data collection, reminders, or drug-intake reports by the patient itself and evaluating patient compliance [15].

Another method used for gait classification is Adaptive Neuro-Fuzzy Interference System (ANFIS). Various gait dynamics are taken into consideration such as stride intervals, stance intervals, and double support intervals and these were used as inputs for classification models. Here sensitivity, accuracy, and specificity were considered using the leave-one-out-cross validation method where one subject is left out and used for testing while the remaining subjects are used to train the data [70]. Few factors play a role in gait analysis including fatigue, hence one of the methods includes this parameter for gait recognition using a deep model based on Long Short-term Memory (LSTM) for analysis where a combination of time series and force series is included [72]. Arm gait analysis (arm choreiform movements) is also done for diagnosis using ANN [4].

The severity of chorea can also be determined clinically using the UHDRS– Total Motor Score. In one of the methods used, the measurement of chorea was conducted with the help of a smartwatch and a smartphone

for in-house and in-clinic study. The volunteer's smartwatch accelerometer data were collected daily, and his/her smartphone accelerometer and gyroscope data were collected during chorea assessments. A rating of chorea was given by both volunteers and doctors. A two stacked random forest classifier model was used for chorea prediction in this method. All data from both the smartwatch and smartphone sensors, output from the initial models (single smartwatch or single smartphone model) was used for assessment. With the use of these devices and the model, the progression of HD was evaluated and adherence to medication by patients was found out [25].

The use of UHDRS-TMS is also seen as another method where matching of the upper and lower limb with impaired isometric force is conducted. In this method, the subject is evaluated for generating and maintaining isometric forces with the use of a force transducer which is pre-calibrated. The different target levels are displayed on the monitor as a straight black line for the subject concerning force applied by him/her depicted as a moving red line. The matching of the target must be for at least 20 s. The generated data were analyzed for decision-making [46]. UHDRS is used for scoring finger tapping and pronation/supination with the use of a tailor-made smartphone having an in-built motion sensor and gravity detection software. It recognizes and counts the number of taps on the screen at a particular time. It also senses the rotation performed if the smartphone is held while performing the task. The generated data was sent to a software program and database on a laptop nearby. The number of taps, pronation/supination cycles, and the time during the interval were recorded and plotted as a graph. This task is beneficial in differentiating an HD patient from a healthy individual [10].

Motor diagnosis is one of the important bases for HD determination. Most of the gait analysis distinguishes HD from other neurodegenerative disorders, whereas sensor-enabled medical devices are used for measuring the severity of the disease along with monitoring patient compliance. However, sensors attached device at the ankle and finger-tapping study are specifically used to determine HD. The motor activity of subjects is an important parameter for HD and hence it should be considered for better diagnostic purposes. A study demonstrates that individuals with neurological movement disorders like HD can have their functional capacity level and stage of reaction predicted by a hybrid model that combines an artificial neural network and a fuzzy logic system [32]. In another study, it was discovered that combining age at study admission, clinical factors, and the length of the cytosine-adenine-guanine (CAG) repeats significantly improves the accuracy of the motor diagnosis in HD patients. The data analysis, which employed the machine learning technique known as random survival forests (RSF), discovered that anticipated probabilities can be utilized to describe the advancement level and support the selection of study samples in the future [36].

Other clinical studies using motor impairment are summarized in Table 2 below.

2.2.2 Neuroimaging and EEG (electroencephalogram)

The use of MRIs (Magnetic Resonance Imaging), fMRI (Functional Magnetic Resonance Imaging), EEG, and qEEG (Quantitative EEG) as biomarkers for HD has proven to be valuable in the diagnosis and evaluation of HD. MRI scans could be defined as imaging formed due to the magnetic field (typically brain images), whereas fMRI takes images of resting and active states of the brain separately. Hence fMRI can give information on dynamic brain activity. Many regions of the brain suffering from any kind of neurodegenerative disorder are depicted as signal-intensity abnormalities on MRIs. The presence of specific patterns of such signal intensity abnormalities in MRI or such an indication at a specific location suggests a particular kind of disease [61]. One of the potential markers for HD is MRI measurement of grey and white matter along with functional MRI (fMRI). Characteristic neurodegeneration of sub-cortical features within the basal ganglia, early striatal atrophy, abnormalities in grey regions, white matter, and fMRI signals have been observed in HD and pre-HD patients [58].

Another technique, EEG, is used to understand subcortical pathology. Quantitative electroencephalography acts as a technique to provide parameters for evaluating sub-cortical malfunctioning which is observed earlier or is accompanied by motor or cognitive impairment in HD. With the use of clinical measures [UHDRS-TMS, TFC, Symbol Digit Modalities Test (SDMT) Stroop Word Reading (SWR) and Beck Depression Inventory-II (BDI-II)] and EEG recordings along with a classifier, the subjects are divided for diagnosis of HD. The SDMT and SWR measure neurocognitive functions in HD, independent of motor impairments [18, 50]. Distinguishing HD patients from control and progression of the disease is also done using neuroimaging data by implementing SVM and Linear Discriminant Analysis (LDA) [51, 58]. Here novelty in analysis methods has been implemented using machine learning techniques to examine these neuroimaging datasets in new ways, hence ML could be used as a technique to successfully assist clinicians in making decisions. A few clinical studies using neuroimaging and EEG are shown in Table 3 below.

2.2.3 Oculomotor performance

As generally observed, one of the pre-symptoms of HD is a change in oculomotor performance. Quantified

Table 2 Clinical studies involving motor impairment for HD determination

Serial No	Characteristic symptom	No. of subjects involved	Method used	Outcome	References
1	Gait discrimination	59	Linear, Non-linear, Bayes	Classification from Alzheimer's, Parkinson, and ALS (Amyotrophic Lateral Sclerosis)	[28]
2	Gait Dynamics	64	K*, RF	Classification of HD and other neurodegenerative diseases (ND)	[9]
3	Gait rhythm	64	SVM, RF, kNN, MLP (Multilayer Perceptron neural network)	Classification of HD and other neurodegenerative diseases	[70]
4	Remote digital trials	17	Intel® Pharma Analytics Platform (In association with Teva Pharmaceuticals)	Measure patient compliance	[15]
5	Quantification of motor function	17	RF, Logistic regression	Patient adherence, assisting in treatment decisions	[25]
6	Abnormal movements	39	UHDRS	Differentiation of HD patients from control	[10]
7	Movement sensors in the ankle	14	iPhone sensors	HD patient classification	[3]
8	Gait dynamics	64	Fuzzy logic, SVM	Classification of HD and other neurodegenerative diseases	[53]
9	Gait dynamics via deterministic learning	64	Radial Basis Function (RBF) neural network	Classification of HD and other neurodegenerative diseases	[71]
10	Finger Tapping	10	Fuzzy logic, ANN	HD determination	[32]
11	Upper and lower limb assessment	53	UHDRS-TMS	Severity of HD	
12	Multi-feature extraction in gait	64	LTSM	Classification of HD and other neurodegenerative diseases	[72]
13	Motor diagnosis for 12 years	1078	Random survival forest	Variables other than CAG repeat length and age (and their interaction) enhanced the prediction of HD	[36]
14	Gait classification using sensors	42	SVM, UHDRS	Discriminate abnormal gait patterns	[43]

Table 3 Clinical studies involving neuroimaging and EEG for HD determination

Serial No	Characteristic symptom	Number of subjects involved	Method used	Outcome	References
1	Subclinical brain electrical activity changes	26	ANN	HD determination	[19]
2	Imaging biomarkers	64	SVM, LDA	Classify between pre-HD and controls	[58]
3	EEG	51	UHDRS-TMS	Separate HD gene carriers from healthy controls with good specificity and sensitivity	[50]

performance of eye movements could be used as a biomarker for diagnosis and progression of HD in pre-symptomatic and early symptomatic HD patients. Clinical data of HD patients have shown increased saccade latencies and directional error errors. These results suggest the use of saccadic movement as a biomarker for HD.

In a study, saccade latency and duration along with errors conducted in performing oculomotor tasks are considered for assessment in fifty patients. SVM is used for the classification and prediction of groups provided to the classifier. The participants performed four saccadic tasks in a fixed order: prosaccade, antisaccade, 1- or 2-back memory prosaccade, and 1- or 2-back memory antisaccade. In all these tasks, the time taken by HD patients to perform the task was longer than for a healthy individual. Direction errors (like prosaccades initiated towards stimulus) or timing errors (like in 1-or 2-back memory prosaccade, the eye movements made before the signal was given) are greater in HD subjects. The task is followed by the identification of valid trials where the

errors are excluded. The extraction of 9 features of each task for each participant is done followed by classification and prediction by SVM based on these features [47].

2.2.4 Use of acoustic and lexical features

Speech impairment is one of the characteristic symptoms of HD and it could be used for distinguishing HD patients and determining the stage of the disease. In this study, data were collected from sixty-two subjects. Features of speech such as filler features (i.e., uh, um, etc.), pauses, speech rate, and Goodness of Pronunciation (GoP) were used for classifying the available data. In this method, data were obtained from human transcripts, speaker audio, and Grandfather Passages. The Grandfather Passage is a paragraph that is phonetically balanced and is used as a standard reading passage for speech-language analysis. It consists of 129 words and 169 syllables and helps to determine the number of utterances along with their size. Static features (calculated by applying statistics) and dynamic features (utterance level) were taken into consideration for analysis. Static feature sets were modeled using k-NN and DNN whereas dynamic feature set was modeled using k-NN and Long-Short-Term Memory Networks (LSTM). [52]

Another study involved the collection and analysis of 126 forward and backward-counting audio samples from 103 HD gene carriers. 60 speech features were extracted from blindly annotated samples. Machine learning models were implemented to combine various speech characteristics to predict clinical markers at an individual level. Combining speech characteristics and demographic variables allowed us to make better predictions of individual cognitive, motor, and functional scores compared to the predictions involving genetics and demographic information. From the study, standard deviation and mean of pause durations during backward counting samples and clinical scores correlated with striatal atrophy [57].

3 Conclusion

The incorporation of AI in the field of HD is an enticing and transformational strategy to address the difficulties of this neurodegenerative disorder. Significant progress has been made in understanding HD, enabling early identification, and extending new therapy pathways because of AI's tremendous skills in numerical simulations, modeling, and data analysis. The most widely utilized biomarker in many research involving many biomarkers are motor impairment, followed by neuroimages and EEG. The increased emphasis on these biomarkers could be related to their ease of measurement and prominence. Studies utilizing machine learning algorithms have been widely incorporated among the various AI methodologies. Less usage of deep learning, which could be due to low data availability because HD is one of the rare disorders, implies more research especially involving different biomarkers is further warranted. AI gives more accuracy and credibility to the physician's decisions and hence both can work in synchronization to achieve desirable outcomes. A transition from conventional to computerized technique is promising for HD and will contribute towards better patient care.

4 Future perspectives

We have a long way to go before fully utilizing AI's advantages in healthcare because it is still in its early phases of development. Significant challenges lie ahead of us, the most important being validating and optimizing the existing models to develop more resilient and robust models. Aside from this, embracing interdisciplinary collaboration and ethical issues will be crucial in maximizing AI's potential in HD as we move forward. Fostering collaborations between academic institutions, healthcare professionals, and researchers will make it possible to share large, diverse datasets, enhancing the utility of AI in HD research. Additionally, encouraging patient empowerment and ethical data practices will increase public trust, fostering acceptance of AI as an effective tool for HD management. Nevertheless, AI in Huntington's disease marks a promising era for research and development.

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GK visualized the presented idea, contributed to manuscript writing, and supervised the project. NP, AB, BR, and RSC contributed to literature search, and preparing the manuscript draft. HSB, SR, and HST provided valuable input. GK, HSB and HST corrected, revised and approved the manuscript.

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