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Artificial Intelligence for Motor Neuron Diseases: A Comprehensive Review of Detection, Diagnosis, and Prognosis

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ABSTRACT

Motor Neuron Diseases (MNDs), particularly Amyotrophic Lateral Sclerosis (ALS), are progressive neurodegenerative disorders characterized by the degeneration of motor neurons, resulting in progressive muscle weakness and loss of motor function. Early and accurate diagnosis remains a major challenge due to heterogeneous clinical presentations, overlapping symptoms with other neurological disorders, and the limited sensitivity of conventional diagnostic approaches during the early stages of disease. Artificial Intelligence (AI), including Machine Learning (ML) and Deep Learning (DL), has emerged as a promising approach for identifying subtle disease-related patterns from diverse clinical and biomedical data. This review examines and analyses existing AI-based approaches for the early detection and diagnosis of MNDs using different data modalities, including electromyography (EMG), magnetic resonance imaging (MRI), neuro-physiological signals, speech and voice characteristics, wearable sensor data, genetic information, and other digital biomarkers. The reviewed studies are compared based on the AI techniques employed, data modalities, diagnostic performance, advantages, and limitations. Particular attention is given to multimodal AI, explainable AI, and emerging approaches for patient-specific diagnosis and disease prediction. The review also identifies major challenges, including limited datasets, data heterogeneity, and lack of external validation, interpretability, and difficulties in translating research models into clinical practice. Finally, potential future directions are discussed for developing robust, interpretable, and clinically applicable AI frameworks for earlier and more precise detection of Motor Neuron Diseases.

KEYWORDS: *Motor Neuron Diseases; Amyotrophic Lateral Sclerosis; Artificial Intelligence; Machine Learning; Deep Learning; Early Diagnosis; Digital Biomarkers; Multimodal AI.*

INTRODUCTION

Motor Neuron Diseases (MNDs) are a group of progressive neurological disorders characterized by the degeneration of motor neurons responsible for controlling voluntary muscle movement. Among these disorders, Amyotrophic Lateral Sclerosis (ALS) is one of the most severe and rapidly progressive forms. The disease gradually affects muscle strength and motor function and can eventually lead to difficulties in movement, speech, swallowing, and respiration. Early identification of MND is therefore important for appropriate clinical management, patient monitoring, therapeutic intervention, and improving the quality of life of affected individuals. However, early diagnosis remains a major challenge because the initial symptoms can be heterogeneous and may overlap with those of other neurological and neuromuscular disorders. The transition from conventional, group-level disease characterization toward patient-specific interpretation has consequently become an important objective in MND research.

Conventional diagnosis of MND generally involves clinical assessment together with neurological examination, electromyography (EMG), nerve conduction studies, magnetic resonance imaging (MRI), genetic investigations, and other biomarker-based assessments. Although these approaches provide important information for diagnosis and disease monitoring, their interpretation can depend considerably on clinical expertise, and some biomarkers may not provide sufficiently distinctive information during the early stages of disease. The complexity and heterogeneity of MND further make it difficult to distinguish ALS from clinically overlapping motor neuron and neuromuscular disorders. Recent research has therefore focused on developing computational approaches capable of identifying subtle patterns that may not be readily recognized through conventional assessment.

Artificial Intelligence (AI) and Machine Learning (ML) have emerged as promising tools for addressing these challenges. The increasing availability of clinical, electrophysiological, imaging, genetic, molecular, and digital health data provides opportunities for computational models to identify disease-associated patterns and support individualized diagnosis. ML

techniques have been investigated using clinical variables, EMG signals, MRI-derived features, wearable sensor measurements, voice characteristics, metabolomic profiles, lipidomics, genetics, and transcriptomic data. Studies have reported promising results in disease classification, phenotype identification, progression prediction, survival prediction, and biomarker discovery.

Recent advances in Deep Learning (DL) have further expanded the application of AI in MND research. Deep learning models can learn complex patterns directly from high-dimensional data, reducing the dependence on manually selected features. AI-based analysis of muscle ultrasound, MRI, and electrophysiological signals has demonstrated potential for distinguishing closely related neuromuscular conditions and supporting more objective disease assessment. For example, recent work using deep learning for muscle ultrasound classification reported an accuracy of 0.9502 and an AUC of 0.9776, while machine-learning approaches applied to MRI radiomics demonstrated improved differentiation between Duchenne and Becker muscular dystrophy compared with radiologist assessment in the reported cohort.

Despite these advances, the clinical application of AI for MND remains challenging. Many existing studies are based on relatively small, single-center datasets, while differences in data acquisition protocols, imaging equipment, electrophysiological procedures, and patient populations can affect model performance. External and multicenter validation remains limited, and many models rely on a single data modality rather than integrating complementary clinical, imaging, electrophysiological, genetic, and molecular information. Issues related to missing data, data harmonization, interpretability, privacy, regulation, and clinical integration also need to be addressed before AI-based systems can be routinely implemented in clinical practice.

Therefore, this review examines the current applications of Artificial Intelligence and Machine Learning in the early detection and diagnosis of Motor Neuron Diseases, with particular emphasis on multimodal biomarkers, electrophysiological signals, medical imaging, digital biomarkers, genetic and molecular data, and emerging Deep Learning approaches. Existing techniques are reviewed and compared according to their data modalities, algorithms, diagnostic performance, advantages, and limitations. The review further identifies current

research gaps and discusses future directions toward developing robust, explainable, multimodal, and clinically applicable AI systems for earlier and more precise detection of Motor Neuron Diseases.

RESEARCH AREA

Motor Neuron Diseases (MNDs) represent an important research area in neurology because of their progressive nature, complex clinical presentation, and difficulties associated with early diagnosis. Among these disorders, Amyotrophic Lateral Sclerosis (ALS) is one of the major areas of research, where early identification of disease-related changes is particularly important. Conventional diagnostic assessment relies on clinical examination, electrophysiological investigations, neuroimaging, genetic testing, and biological biomarkers. However, the heterogeneous nature of MND and the overlap between different neurological and neuromuscular disorders make accurate and timely diagnosis challenging.

The increasing availability of large and heterogeneous biomedical datasets has created opportunities for the application of Artificial Intelligence (AI), Machine Learning (ML), and Deep Learning (DL) in MND research. AI-based approaches can analyze complex patterns obtained from different sources, including electromyography (EMG), magnetic resonance imaging (MRI), muscle ultrasound, EEG, clinical information, speech and voice characteristics, wearable sensors, genetics, transcriptomics, metabolomics, and other biomarkers. Machine learning has already been investigated for disease classification, phenotype identification, progression prediction, survival prediction, and biomarker discovery.

Within this research area, early detection using multimodal AI is becoming particularly important. Instead of depending on a single clinical or biomarker measurement, multimodal systems can potentially combine information from clinical observations, electrophysiological signals, imaging, molecular biomarkers, and digital health technologies. Recent reviews highlight the potential of AI to integrate heterogeneous data streams and support more precise diagnosis and disease progression assessment.

The major research focus of this review is therefore the development and application of AI techniques for early detection, differential diagnosis, and patient-specific assessment of

MNDs. Particular attention is given to the different data modalities, AI algorithms, diagnostic performance, advantages, limitations, and challenges associated with existing approaches. The research area also includes emerging directions such as explainable AI, multimodal learning, digital biomarkers, and integration of clinical and molecular information.

RELATED WORK

Several Artificial Intelligence and Machine Learning techniques have been investigated for the detection, classification, and prediction of Motor Neuron Diseases (MNDs), particularly Amyotrophic Lateral Sclerosis (ALS). Researchers have explored different clinical, electrophysiological, imaging, molecular, and digital biomarkers as input to computational models. These studies demonstrate the potential of AI to identify disease-related patterns and assist in diagnosis and prognosis.

Among the different approaches, machine learning-based clinical prediction models have been investigated for identifying disease progression and patient outcomes. Clinical variables and routinely collected patient information can be used to develop models for prognostic categorization and prediction of functional decline. Such approaches are particularly relevant because they can potentially support patient-specific assessment rather than relying exclusively on population-level clinical measures.

Researchers have also investigated electrophysiological data, particularly EMG, for AI-assisted MND assessment. Electrophysiological signals contain information associated with motor-unit activity and can therefore provide useful features for computational classification. Machine learning and deep learning approaches have been explored to distinguish MND-related abnormalities from other neuromuscular conditions and to support more objective interpretation of neurophysiological measurements.

Another important research direction is medical imaging-based AI. MRI and other neuroimaging modalities have been investigated for identifying structural and functional changes associated with MND. Machine learning approaches can extract quantitative imaging features that may not be readily apparent through conventional visual assessment. AI-based neuroimaging therefore provides an opportunity for objective disease characterization and potentially earlier identification of pathological changes. The reviewed literature also

emphasizes the importance of combining imaging information with other clinical and biomarker data rather than treating imaging as an isolated source.

Researchers have further explored muscle ultrasound and deep learning for neuromuscular disease classification. Deep learning models applied to muscle ultrasound have demonstrated promising classification performance, indicating that image-based AI may provide a non-invasive method for supporting differential diagnosis. However, the performance of such models depends on the quality and representativeness of the available training data.

AI has also been applied to speech and voice characteristics as potential digital biomarkers. Changes in speech, articulation, and bulbar function can occur in MND, providing an opportunity to develop computational models capable of identifying disease-associated patterns. Such approaches are particularly interesting for early and remote assessment because speech data can potentially be collected without specialized clinical equipment.

Another emerging area is the use of wearable devices and digital biomarkers. Sensor-derived information related to movement, gait, activity, and motor performance can provide continuous measurements of functional changes. AI algorithms can analyze these measurements to estimate disease burden and monitor changes over time. Such objective measurements may complement conventional functional rating scales, particularly in clinical trials and longitudinal monitoring.

Researchers have also examined genetic and molecular data using AI-based methods. Genomics, transcriptomics, metabolomics, proteomics, and other molecular datasets can contain information related to disease mechanisms and patient heterogeneity. Machine learning can be used to identify patterns within these high-dimensional datasets and potentially identify molecular signatures associated with specific phenotypes or disease progression. The integration of molecular information with clinical and imaging data represents an important direction for personalized MND assessment.

More recently, attention has shifted from single-modality AI models toward multimodal approaches. Researchers have proposed integrating clinical measurements, imaging, electrophysiological information, and biological biomarkers to improve disease

characterization. Such integration is particularly important because MND is heterogeneous and no single biomarker is sufficient to represent the complete disease state. The literature identifies multimodal data integration as one of the major opportunities for future ML applications in ALS and other MNDs.

Researchers have additionally investigated AI for differential diagnosis and disease mimics. This is an important clinical application because MND may share symptoms with other neurological and neuromuscular disorders. AI models capable of multi-class classification could therefore be more clinically useful than models restricted to a simple healthy-versus-disease classification. Existing work emphasizes the need to move toward robust multiclass models that better represent the heterogeneity encountered in real clinical practice.

Another important research direction is explainable Artificial Intelligence (XAI). Although high-performing ML and DL models can identify complex patterns, their clinical adoption is limited when the reasoning behind their predictions cannot be understood. Explainable approaches can help identify the clinical, imaging, electrophysiological, or molecular features contributing to a prediction and may therefore improve clinician confidence in AI-assisted decision-making.

The reviewed studies also highlight several limitations. Many AI models have been developed using relatively limited datasets, and models trained on data from a single institution may not generalize to other populations. Differences in scanners, laboratory measurements, clinical protocols, and patient characteristics create data-harmonization problems. In addition, underrepresentation of specific phenotypes and the absence of external validation can introduce bias into AI models.

Therefore, existing research demonstrates that AI has potential across several stages of MND assessment, including early detection, differential diagnosis, phenotypic classification, progression prediction, biomarker identification, and patient stratification. However, the literature also indicates that future systems should move beyond isolated datasets and single-domain models toward multicenter, multimodal, explainable, and externally validated AI frameworks.

COMPARATIVE ANALYSIS OF EXISTING AI TECHNIQUES

Problem Statement

Researchers have explored different clinical, electrophysiological, imaging, molecular, and digital biomarkers as input to computational models. These studies demonstrate the potential of AI to identify disease-related patterns and assist in diagnosis and prognosis.

Among the different approaches, machine learning-based clinical prediction models have been investigated for identifying disease progression and patient outcomes. Clinical variables and routinely collected patient information can be used to develop models for prognostic categorization and prediction of functional decline. Such approaches are particularly relevant because they can potentially support patient-specific assessment rather than relying exclusively on population-level clinical measures.

Researchers have also investigated electrophysiological data, particularly EMG, for AI-assisted MND assessment. Electrophysiological signals contain information associated with motor-unit activity and can therefore provide useful features for computational classification. Machine learning and deep learning approaches have been explored to distinguish MND-related abnormalities from other neuromuscular conditions and to support more objective interpretation of neurophysiological measurements.

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More recently, attention has shifted from single-modality AI models toward multimodal approaches. Researchers have proposed integrating clinical measurements, imaging, electrophysiological information, and biological biomarkers to improve disease characterization. Such integration is particularly important because MND is heterogeneous and no single biomarker is sufficient to represent the complete disease state. The literature identifies multimodal data integration as one of the major opportunities for future ML applications in ALS and other MNDs.

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CONCLUSIONS AND FUTURE WORK

Motor Neuron Diseases (MNDs), particularly Amyotrophic Lateral Sclerosis (ALS), remain challenging neurological disorders due to their heterogeneous clinical presentation, progressive nature, and difficulties in achieving early and accurate diagnosis. This review examined the application of Artificial Intelligence (AI), Machine Learning (ML), and Deep

Learning (DL) techniques for the detection, classification, prediction, and monitoring of MNDs. Existing studies demonstrate that AI can utilize clinical, electrophysiological, imaging, speech, wearable, genetic, and molecular data to identify disease-related patterns and support diagnosis and prognosis. The integration of multiple data modalities may provide a more comprehensive representation of disease status than approaches based on individual biomarkers.

Despite these promising developments, several challenges remain before AI-based systems can be widely implemented in clinical practice. Limited datasets, differences in data acquisition, data harmonization, inclusion bias, and lack of external validation, interpretability, privacy, and regulatory issues continue to affect the reliability and generalizability of existing models. Future research should therefore focus on developing large-scale, multicenter, and internationally validated datasets to reduce overfitting to individual institutions and improve model generalization. The development of multimodal AI models integrating clinical, EMG, MRI, molecular, genetic, and digital biomarker information should also be prioritized. Future models should move beyond simple binary classification toward robust multiclass systems capable of distinguishing MND from clinically similar disorders.

Further research should emphasize Explainable AI (XAI) to improve transparency and clinician confidence, together with wearable technologies and digital biomarkers for continuous and remote monitoring of disease progression. Privacy-preserving approaches such as federated learning may also help facilitate collaborative development while protecting sensitive patient information. Ultimately, the future of AI in MND lies in developing accurate, interpretable, multimodal, personalized, and clinically validated systems that can support earlier detection, improved diagnosis, and more effective patient-specific disease management.

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