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Review Paper

Artificial Intelligence in Epileptic Management and Drug Optimization: Current Applications, Challenges, And Future Perspectives

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ABSTRACT

Artificial intelligence (AI) is rapidly transforming health care, and its applications in epilepsy have increased exponentially over the past decade. Integration of AI into epilepsy management promises to revolutionize the diagnosis and treatment of this complex disorder. However, translation of AI into neurology clinical practice has not yet been successful, emphasizing the need to consider progress to date and assess challenges and limitations of AI. In this Review, we provide an overview of AI applications that have been developed in epilepsy using a variety of data modalities: neuroimaging, electroencephalography, electronic health records, medical devices and multimodal data integration. For each, we consider potential applications, including seizure detection and prediction, seizure lateralization, localization of the seizure-onset zone and assessment for surgical or neurostimulation interventions, and review the performance of AI tools developed to date. AI innovations promise a transformation in epilepsy care by possibly enhancing the accuracy of electroencephalogram (EEG) interpretation and seizure prediction through machine and deep learning. In one study, abnormal EEG recordings were classified into different categories using a convolutional neural networks (CNN) model showing a specificity of 90 % and an accuracy of 88.3 %. Other models constructed to predict seizures have also achieved a sensitivity of 96.8 % and specificity of 95.5 %. Various machine learning (ML) models highlight the potential AI holds in identifying interictal biomarkers and localizing seizure onset zones aiding in epilepsy treatment decision and outcome prediction. Our goal is to provide an overview of the current state of the field and provide guidance for leveraging AI in future to improve management of epilepsy.

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INTRODUCTION

Epilepsy is one of the most common chronic neurological disorders, affecting approximately 50 million people wordwide.Despite advances in antiseizure medications ,nearly one-third of patients continue to experience uncontrolled seizures.Artificial intelligence encompassing machine learning and deep learning,has emerged as a promising tool to improve epilepsy diagnosis,seizure prediction, treatment planning,and optimization of ASM therapy. Epilepsy affects approximately 50 million individuals globally, including 10 million patients in China ,underscoring its status as one of the most prevalent chronic neurological disorders worldwide. The World Health Organization (WHO) estimates that nearly 70% of patients with epilepsy can achieve freedom from seizures with appropriate diagnosis and treatment. However, owing to diagnostic and therapeutic gaps, approximately two-thirds of epilepsy patients in China fail to receive adequate treatment. Electroencephalography (EEG) is the most critical auxiliary diagnostic tool for epilepsy, and plays a critical role in the diagnosis, classification, and localization of epileptogenic foci. Theoretically, all epileptic seizures can be associated with detectable epileptiform discharges on EEG, but the clinical application of this diagnostic tool is subject to several limitations. There are numerous ongoing initiatives to enhance the lives of individuals with epilepsy and their families in spite of these obstacles; these initiatives must go on and be reinforced in order for all individuals with epilepsy to eventually have access to the entire spectrum of coordinated health and community services that they require. Many patients with epilepsy are able to have fewer or no seizures thanks to access to modern drugs, medical gadgets, surgery, and other treatments. For those with epilepsy who do not react to current medications or who experience intolerable side effects from existing treatments, new therapy choices are required. Depending on the audience, different kinds of information and differing degrees of depth are needed for educating individuals with epilepsy, their families, medical professionals, and the general public on the condition. The deep integration of AI into neurology has been described as a “neurological revolution” spanning scientific, medical, and policy domains , with machine learning (ML) algorithms emerging as the most widely used AI technology. ML-based models have demonstrated significant value across the entire spectrum of neurological disorders, including prevention, risk stratification, monitoring, diagnosis, treatment, prognosis, and rehabilitation. These models surpass traditional clinician-patient interviews by rapidly and accurately extracting critical clinical information and generating diagnostic suggestions, thereby enhancing diagnostic efficiency and alleviating physician workload . When specifically examining AI applications in epilepsy, AI-driven wearable and implantable devices for automated seizure detection represent one of the most prominent innovations, offering pre-seizure warnings and enabling self-emergency measures to reduce unpredictable seizure-related harm. Such AI applications in epilepsy, including electroencephalogram (EEG) analysis, seizure detection, and clinical management are laying a solid foundation for future intelligent integrated epilepsy diagnosis and treatment systems powered by multimodal AI. Research has shown that the point prevalence of epilepsy ranges from 4 to 10 per 1000 individuals, establishing it as one of the most common neurological disorders. The estimated incidence rate of epilepsy is 50–60 per 100,000 person-years, and a considerable proportion of individuals, up to 8%, experience at least one seizure during their lifetime . Diagnosing epilepsy poses a significant challenge due to the

restricted availability of diagnostic modalities such as electroencephalography (EEG), magnetic resonance imaging, computed tomography, and supplementary tests such as lumbar puncture and genetic testing. The treatment of epilepsy presents a significant challenge not only in terms of diagnosis but also because of the adverse effects associated with antiepileptic drugs (AEDs), which include cognitive impairment, nausea, Stevens–Johnson syndrome, behavioural changes, and osteopenia. Moreover, these medications are known to induce hepatotoxicity, pancreatitis, leukopenia, and thrombocytopenia and exhibit teratogenic effects when administered during pregnancy. AED resistance, a condition affecting approximately one-third of individuals with epilepsy, is characterized by seizures persisting despite adequate trials of two or more AEDs. For individuals suffering from drug-resistant epilepsy, there are various alternatives available beyond conventional AEDs. Implantable devices provide supplementary options; for example, for vagus nerve stimulation, electrical impulses are administered to the vagus nerve to alleviate the occurrence of seizures. Moreover, responsive neurostimulation supervises brain activity, and stimulation is administered when seizures are anticipated. The technique of deep brain stimulation (DBS) entails the insertion of electrodes in specific brain areas to regulate neural activity. Non-invasive devices such as transcranial magnetic stimulation (TMS) utilize magnetic fields to provoke brain activity, potentially lessening seizures. Moreover, non-invasive devices such as TMS, accelerometers, and wearable devices apply magnetic fields to increase brain function, reducing seizures. Novel technologies such as optogenetics, focused ultrasound, and artificial intelligence/machine learning operate on fundamental principles and contribute to the management and identification of seizures through EEG data, although they necessitate comprehensive validation and the resolution of challenges concerning safety, availability, and clinical confirmation. Neuromodulation can be described as using electrical or magnetic stimuli to modify nerve activity, particularly to address neurological disorders such as epilepsy. The main goal of employing neuromodulation techniques for epilepsy is to hinder or reduce the frequency and severity of seizures by precisely targeting specific brain regions or pathways [6]. Implantable devices used as neuromodulators are specialized medical devices designed to modulate or alter the activity of the nervous system through electrical stimulation or drug delivery. In the domain of epilepsy, implantable devices are surgically implanted into the body to assist in the management of seizures and improve the quality of life for patients with drug-resistant epilepsy. These devices commonly deliver electrical stimulation to nerves or specific areas of the brain that play a role in initiating or modifying seizures [7]. The primary types of implantable devices employed in epilepsy are explained below. The vagus nerve is a crucial component of the autonomic nervous system that significantly influences various bodily functions. The vagus nerve, after originating from the medulla oblongata, exits the cranium through the jugular foramen and travels down the neck within the carotid sheath along the common carotid artery and the internal jugular vein. Compared with the other cranial nerves, the vagus nerve connects many visceral organs with the brainstem and the cortex, given its widespread course and distribution through the autonomic nervous system interface [8]. The evolution of VNS therapy advanced through initial experimental investigations in animals, which revealed encouraging outcomes in reducing the frequency of seizures. The debut of the initial implantable VNS device was authorized by the U.S. Food and

Drug Administration (FDA) in 1997 to manage epilepsy in individuals aged 12 years and older.

VNS, an open-loop device, administers scheduled electrical stimulation to the vagus nerve, typically for durations of 30–60 s at regular intervals. The intensity of the current is adjusted gradually to a minimum of 1.50 mA within 10–12 weeks postimplantation, depending on the patient's tolerance levels. Additionally, a wrist magnet is provided to the patient to activate the pulse generator and administer supplementary stimulation. VNS functions are based on the premise that mild electrical stimulation of the vagus nerve can interfere with or regulate abnormal brain activity, leading to seizures [9]. The VNS device is typically surgically inserted beneath the skin in the thoracic region, with a connecting lead wire linking it to the left vagus nerve in the cervical area. Owing to efferent projections to the sinoatrial node, the left vagus nerve is preferred for stimulation.The antiseizure effects of VNS are facilitated by the modulation of neurotransmitter release (e.g., GABA, glutamate) and changes in synchronization within thalamocortical networks, encompassing phase-amplitude coupling across various frequency bands [10]. This modulation facilitates cortical desynchronization and neuroplasticity, with activation of noradrenergic $\alpha 2$ receptors and astrocytic calcium signaling playing a role in long-term effects [11].VNS results in a variety of negative outcomes, as elucidated in the literature. Common adverse events include alterations in voice quality, tingling sensations, coughing, breathlessness, and discomfort. Moreover, laryngeal complications such as changes in voice characteristics and partial or complete loss of voice function have been observed, which are frequently linked to issues with the device, such as high resistance and incorrect frequency allocation. In exceptional instances, uncontrollable episodes of hiccups have been recorded post-VNS insertion, leading to serious repercussions such as Mallory–Wiss syndrome and the necessity for intensive medical attention [5]. RNS has emerged as a valuable treatment option for patients with drug-resistant epilepsy, particularly those with focal epilepsy or multifocal epilepsy who are ineligible for surgical intervention. The NeuroPace RNS system not only provides safe and well-tolerated stimulation but also collects crucial long-term electrocorticographic data, aiding in seizure risk assessment, treatment response evaluation, and future surgical planning [6]. The RNS system, developed by NeuroPace, possesses a significant historical background that originated in the late 1990s with the emergence of the idea of utilizing targeted electrical stimulation to regulate brain activity for the treatment of epilepsy. In 2013, the FDA approved the RNS system, allowing its utilization for clinical purposes in the United States. DBS, which is primarily utilized in the management of movement disorders such as Parkinson's disease, is now being employed as a therapeutic approach for individuals suffering from drug-resistant epilepsy [7]. The potential of DBS as a treatment option for epilepsy has been under investigation, especially for patients who exhibit poor responses to traditional medications or alternative surgical procedures. The history of employing DBS in the treatment of epilepsy traces back to initial experiments and clinical trials conducted in the early 2000s. Imaging tools such as ultrasound, MRI, and CT provide intricate visualizations of internal structures, aiding in the identification and characterization of illnesses without the necessity of surgical intervention. Monitoring equipment such as ECGs, pulse oximeters, and continuous glucose monitors measures essential physiological parameters over a period, enabling immediate evaluation of health conditions and disease advancement (1). Non-invasive devices for epilepsy, such as optically pumped magnetometers (OPMs) and non-invasive

mobile EEG solutions, represent promising advancements in the realm of epilepsy diagnosis and management. The utilization of OPMs positioned directly on the scalp serves to increase the signal-to-noise ratio, thereby improving sensitivity toward deep sources and facilitating the recording of seizures with heightened levels of patient-friendliness and cost-effectiveness (2). Conversely, non-invasive mobile EEG solutions offer a convenient and dependable approach to monitoring patients with chronic conditions, demonstrating positive feedback from both patients and healthcare providers, satisfactory signal integrity, and ongoing research endeavors aimed at enhancing the accuracy of seizure detection. Ambulatory EEG, also known as Amb EEG, is a technique developed for the extensive monitoring of cerebral activity in natural environments beyond the confines of conventional clinical settings. This approach uses a mobile recording device equipped with scalp electrodes, which allows individuals to wear the equipment comfortably for extended periods, typically lasting anywhere from 24 to 72 h or even longer. By adopting this strategy, a continuous stream of EEG data is captured during various routine activities, including sleep, work, and physical exercise, thereby offering valuable insights that may elude detection in brief clinical EEG sessions. The application of ambulatory EEG is particularly advantageous in the diagnostic process of epilepsy and other neurological disorders characterized by sporadic symptoms or infrequent episodes. By providing real-time data acquisition and visualization on mobile devices, mobile EEG systems enhance the diagnostic capabilities for epilepsy, enabling personalized and efficient treatment decisions based on the patient's specific needs and condition [33]. TMS is a nascent modality employed in the management of epilepsy. This pioneering method involves the application of magnetic fields to provoke neuronal activity in the brain. Approval from the FDA for the treatment of major depressive disorder was granted to TMS in 2008, signifying a notable milestone in acknowledging TMS as a viable therapeutic option for patients with treatment-resistant depression. The duration of TMS sessions may vary depending on the specific protocol utilized and the condition under treatment. Typically, a single TMS session lasts between 20 and 40 min (2). Nevertheless, the total duration and frequency of sessions may differ based on the treatment plan recommended by the healthcare provider. tDCS is a form of non-invasive neuromodulation that delivers a weak electric current to the brain via electrodes placed on the scalp, generating a subtle electric field that influences cortical neuron polarization. Research findings have suggested that tDCS shows promise in enhancing cognitive functions, particularly numerical skills, by modulating cortical excitability through synaptic mechanisms (5). Anodal stimulation is thought to increase cortical excitability, whereas cathodal stimulation is believed to decrease it. The transformative potential of AI in advancing neuroscience lies in its ability to increase diagnostic accuracy, predict disease progression, and enhance imaging techniques. Future research should focus on refining AI methods to enhance generalizability and foster collaborations between AI practitioners and neuroscientists.

CONCLUSION

Artificial intelligence (AI) is transforming epilepsy management by improving the accuracy of seizure detection, prediction, diagnosis, and treatment planning. Recent advances in machine learning and deep learning algorithms have enabled rapid analysis of EEG, neuroimaging, and wearable device data, facilitating earlier diagnosis, continuous patient monitoring, and personalized therapeutic strategies. AI-driven systems also

assist clinicians in identifying epileptogenic zones, predicting seizure onset, optimizing antiseizure medication selection, and supporting surgical decision-making, thereby improving clinical outcomes and patients' quality of life.

Despite these promising developments, AI is not yet a replacement for clinical expertise. Current challenges include limited interpretability of AI models, lack of standardized and diverse datasets, concerns regarding data privacy, algorithm bias, and the need for multicenter prospective validation before widespread clinical implementation. Most experts recommend that AI should function as a clinical decision-support tool, with all recommendations interpreted in conjunction with comprehensive clinical assessment by neurologists.

In conclusion, AI has the potential to revolutionize epilepsy care by enabling precision medicine through individualized diagnosis, real-time seizure forecasting, and optimized treatment strategies. As explainable AI, robust validation studies, and regulatory frameworks continue to evolve, AI is expected to become an integral component of routine epilepsy management, complementing rather than replacing clinician judgment and ultimately improving patient safety and long-term outcomes.

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