Proceedings of ICBioMed 2025 Symposium: Computational Modelling and Simulation for Biology and Medicine
DOI: 10.54254/2753-8818/2025.LD25941

Advances in the Application of Brain Computer Interface in Seizure Detection and Prediction and Epilepsy Treatment

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Abstract. Epilepsy is a prevalent neurological condition impacting nearly fifty million individuals around the world. Traditional diagnosis based on clinical symptoms and neural monitoring can be inefficient or inaccurate. Pharmacotherapy is the first-line treatment, but about one-third of patients are drug-resistant and may experience adverse effects. Surgical resection is another option but is not suitable for all patients. Brain-computer interfaces (BCIs) create a direct communication link between neural activity and external systems, enabling more effective automated seizure detection, forecasting, and individualized therapeutic interventions. Among the various BCI modalities, ranging from implanted electrodes to external sensors, non-invasive, EEG-based systems remain the most widely adopted due to their safety, cost-effectiveness, and ease of use. AI algorithms are used in BCI to process data and detect biomarkers like recently discovered high frequency oscillations (HFOs), brain connectivity, and microstates automatically before sending targeted stimulations or keeping track of the patients' status remotely. Responsive neurostimulation (RNS) is a neuromodulation system that allows adaptive stimulation, meaning that it is closed-loop, which has the potential of minimizing side effects. This review aims at discussing and evaluating the effectiveness of BCI in seizure detection, prediction, and patient-specific treatments while providing enlightenment on future trends.

Keywords: epilepsy, brain-computer interfaces, BCIs, responsive neurostimulation

1. Introduction

Epilepsy is a widespread, long-term neurological condition marked by irregular brain electrical activity, impacting roughly 50 million people worldwide [1-3]. A diagnosis is confirmed when a person experiences at least two unprovoked seizures separated by a minimum of 24 hours, or after a single unprovoked seizure if the estimated risk of recurrence within ten years exceeds 60 percent, or when a recognized epilepsy syndrome is identified [4]. Epileptic seizures can be divided into focal or generalized. Epilepsy's burden is unevenly distributed, with approximately 80% of those affected residing in low- and middle-income nations [5]. Males are proven to have higher prevalence, incidence, and mortality rates than females, while children and older adults each have the highest incidence and mortality rates. Epilepsy diagnoses currently involve checking the patient's medical history and carrying out electrophysiological tests. Common electrophysiological tests include electroencephalography (EEG), which detects abnormal neural activities by monitoring and

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recording electrical activities of the brain, and extra imaging tests like magnetic resonance imaging and computed tomography scans, which can be used to detect structural abnormalities.

Epilepsy is mainly treated using antiseizure drugs (ASDs), which achieve full seizure control in roughly two-thirds of patients, but the remaining one-third develop drug-resistant epilepsy (DRE) and continue to experience seizures despite optimized medication regimens [6]. Meanwhile, conventional pharmacotherapy is also facing problems like not being regional-specific and having undesirable adverse effects, ranging from cognitive impairment and mood disturbances to hepatotoxicity and teratogenicity [7,8]. Therefore, alternative methods are required for the treatment of DRE patients. Surgeries that remove or disconnect brain tissue responsible for epilepsy are an option for DRE patients. However, epileptic surgeries may contain risk of surgical complications, including infection and disruption of the eloquent cortex [9]. Meanwhile, certain patients are not eligible for these resection surgeries due to factors like epilepsy-induced areas located in the eloquent cortex or lack of localization. Neurostimulation, ranging from continuous, open-loop approaches such as deep brain stimulation (DBS) and vagus nerve stimulation (VNS) to adaptive, closed-loop systems like responsive neurostimulation (RNS), represents a widely utilized and highly effective treatment modality. Nevertheless, these invasive neurostimulation methods require long periods of programming and long-term treatments and offer progressive improvement [5]. Non-invasive neurostimulation techniques like TMS and tDCS have also been tested to be used in epilepsy treatment.

Brain–computer interfaces (BCIs) are advanced technologies that establish a direct link between neural activity and external systems by capturing and interpreting brain signals to drive device functions, offering great promise for improving epilepsy diagnosis and treatment. BCIs are classified into two types: invasive and non-invasive. Invasive systems achieve high-quality, reliable recordings through electrodes implanted in the cerebral cortex, making them well suited for long-term monitoring and intervention; non-invasive approaches rely on surface sensors such as electroencephalography (EEG) and functional magnetic resonance imaging (fMRI), providing lower risk and greater patient comfort [6]. BCI has made great progress in the field of epilepsy diagnosis and treatment within recent years, with research showing the great sensitivity and accuracy of the machines during tests. Responsive neurostimulation (RNS) exemplifies a closed-loop BCI therapy: through stimulating the brain adaptively when epileptiform activity is detected, it can abort emerging seizures while minimizing unnecessary pulses [5]. With the emergence of sufficient AI algorithms, there may be greater potentials in closed-loop neurostimulation in providing more efficient and personalized treatment. Accordingly, this review will critically examine recent progress in BCI-based seizure detection and prediction, evaluate the clinical readiness of closed-loop neurostimulation platforms, and discuss the challenges and opportunities for translating AI-driven BCIs into standard epilepsy management.

2. Traditional diagnosis and treatment

2.1. Pharmacotherapy

Pharmacotherapy using ASDs is still considered the mainstream treatment of epilepsy at the moment [6]. ASDs suppress seizures by modifying intrinsic excitability properties of neurons or altering fast inhibitory or excitatory neurotransmission, which involves interacting with a range of cellular targets, including modulating voltage-gated ion channels and synaptic release, enhancing GABA-mediated inhibition, and inhibiting ionotropic glutamate receptor-mediated synaptic excitation [1]. Although there are many antiseizure medications on the market, roughly one third of individuals

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with epilepsy continue to experience uncontrolled seizures due to drug-resistant epilepsy, substantially undermining the benefits of pharmacotherapy. Meanwhile, traditional ASDs lack regional specificity and may lead to adverse drug reactions such as sedation, depression, obesity, and gastrointestinal and liver-related problems [8]. Therefore, for patients with DRE or low drug tolerance, alternative methods are demanded.

2.2. Surgery

Surgical intervention remains a mainstay for managing drug-resistant epilepsy when seizures originate from a well-defined cortical focus. Conventional resective procedures remove the epileptogenic tissue to interrupt seizure generation, often yielding substantial improvements in seizure control for appropriately selected patients. This approach is particularly well suited to individuals whose lesions are tightly localized and do not overlap with critical functional areas. However, brain surgery carries inherent risks, including bleeding, infection, and potential damage to surrounding neural structures, which can lead to cognitive, motor or sensory deficits. Moreover, patients whose seizure foci are diffuse, multifocal or situated within eloquent cortex are generally deemed poor candidates for resection due to the unacceptable risk of postoperative neurological impairment.

2.3. Traditional neuromodulation treatments

In addition to medical and surgical treatment, neuromodulation technique is also a critical option for epilepsy treatment. Vagus Nerve Stimulation (VNS) is a technique that modulates neural activity to alleviate seizures by stimulating what is usually the left vagus nerve through an implanted electrode [5]. Deep brain stimulation (DBS) employs implanted electrodes to deliver electrical pulses to brain regions such as the anterior (ANT) and centromedian (CM) thalamic nuclei, achieving seizure reduction in approximately half of treated patients. However, its invasive nature carries risks of infection and other surgical complications, and clinical responses vary widely across individuals.

3. BCI in recording and detecting

3.1. Invasive brain monitoring techniques

Common BCI recording devices in epilepsy detection can be divided into invasive and non-invasive. Intracranial electroencephalography (iEEG), which includes ECoG and Stereotactic EEG (sEEG), is an invasive method that is commonly used in epilepsy-related evaluation. ECoG is a semi-invasive measure in detecting epileptic features that involves placing flexible silicone sheets imbedded with 1D or 2D electrode arrays named strips and grids onto the cortical surface, while sEEG is an invasive measure that involves penetrating probe-like electrodes deeply into the brain. Compared to sEEG, which takes samples from various tissues and potentially different cortical layers of throughout the brain, ECoG has a higher spatio-temporal mapping since it records signals from the grey matter orthogonal to the surface and covers a broad cortical surface area. ECoG covers a large cortical surface area and records the signals from the grey matter orthogonal to the surface, giving them a high spatio-temporal mapping compared with sEEG, which samples from different tissues and potentially different cortical layers throughout the brain [10]. While ECoG may have had higher spatial and temporal resolution, they do not access deep cortical structures and are less sensitive to activities within sulci compared to sEEG [11].

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3.2. Non-invasive brain monitoring techniques

Scalp electroencephalography (EEG) is one of the most commonly used non-invasive techniques for monitoring brain activity. Electroencephalography records the brain's electrical activity by positioning electrodes on the scalp. According to several studies, it is considered a highly preferred option due to its ability to capture rapid neural changes as a result of high temporal resolution and Additional non-invasive neuroimaging modalities include magnetoencephalography (MEG), functional magnetic resonance imaging (fMRI), and functional near-infrared spectroscopy (fNIRS). practicability coming from low cost, high portability, and wide utilization. Other non-invasive brain monitoring techniques include magnetoencephalography (MEG), functional magnetic resonance imaging (fMRI), and functional near-infrared spectroscopy (fNIRS). While MEG provides high spatial and temporal resolution, its widespread use is limited by its high cost and complex setup. In contrast, fMRI and fNIRS, though valuable for certain applications, are restricted by their own limitations. fMRI, for example, requires large, expensive equipment and is sensitive to patient movement, while fNIRS, although portable, has a limited spatial resolution compared to more advanced techniques [6].

3.3. Hybrid EEG-fNIRS technology

To address the limitations inherent in each of these individual techniques, researchers have developed hybrid systems that combine EEG with fNIRS. These hybrid systems take advantage of the high temporal resolution of EEG alongside the better spatial resolution of fNIRS, thus providing enhanced capabilities for capturing brain activity. These combined approaches also improve synchronization between the two modalities, offering more comprehensive data with higher accuracy. Li et al. designed a compact, lightweight EEG–fNIRS wearable patch that simultaneously records co-localized EEG and fNIRS signals with noise levels around 0.89 μVrms and amplitude and frequency distortions under 2% and 1%, respectively, while supporting comfortable, long-duration monitoring [12]. It is noticeable that there is an increasing trend in developing safer and more portable monitoring techniques [13]. As the demand for accessible and reliable brain monitoring systems increases, researchers are focusing on making these devices smaller, more comfortable, and easier to use in diverse settings. This shift not only holds promise for advancing clinical applications but also for expanding the use of brain monitoring technologies in everyday life, from personal health tracking to neurofeedback training.

3.4. Biomarkers in BCI-based epilepsy detection

Reliable biomarkers are essential for automated seizure detection and prediction in BCI systems. Although interictal epileptiform discharges (IEDs) remain the gold-standard marker of epilepsy, they are not consistently observable on EEG recordings even in clinically diagnosed patients. Although several studies have been focusing on identifying IEDs undetectable by EEG, it still remains a challenge which leads to the demand for identifying alternative biomarkers. High-frequency oscillations (HFOs) are one of the EEG biomarker candidates and are short oscillatory field potentials (80-500 Hz) that can be categorized into physiological HFOs (80 -250 Hz) and fast HFOs (250 - 500 Hz), which are associated with epilepsy [6]. Analyses of brain connectivity patterns have also emerged as potential biomarkers, effectively distinguishing individuals with epilepsy from healthy controls [14]. Microstates, which arise from the concept of a finite number of brain activity

DOI: 10.54254/2753-8818/2025.LD25941

maps changing over time, has given us a potential biomarker in the means of identifying epilepsy through the duration of the maps.

4. Seizure detection and prediction algorithms

To identify epileptic seizure automatically and alert patients or provide information for treatment planning, various BCI-based epilepsy seizure detection algorithms have been developed to classify epileptic seizure features and determine the seizure status of the patient [14]. Effective seizure detection pipelines start with comprehensive preprocessing to eliminate noise and artifacts from raw EEG data. Standard denoising procedures encompass band-pass filtering, application of independent component analysis (ICA) to segregate and remove ocular and myogenic interference, and wavelet-based techniques to retain transient epileptiform features. Following cleanup, informative features—such as time-domain statistics, spectral power in canonical frequency bands, high-frequency oscillation (HFO) counts, and nonlinear measures (e.g., entropy, fractal dimension)—are extracted to characterize both interictal and preictal states [15].

Common AI algorithms employed may be divided into machine learning (ML) and deep learning (DL). Traditional machine-learning classifiers, such as artificial neural networks, support vector machines, and random forest models, have long underpinned automated seizure detection systems. Despite showing impressive accuracies in the laboratory, these techniques may have lacked practicability when employed in real-life situations [16]. Deep learning approaches, particularly convolutional neural networks and recurrent neural networks, are increasingly being adopted for seizure detection [15]. The most widely used models at the moment are 2D-CNN and 1D-CNN, with 2D-CNN being the most employed model [17]. Nevertheless, deployment in clinical practice faces hurdles: inter-center data heterogeneity, artifact-laden real-world recordings, and the need for real-time inference on resource-limited hardware. Addressing these challenges will require domain-adaptation strategies, explainable AI techniques, and federated learning frameworks to protect patient privacy while improving generalizability.

5. Responsive neurostimulation (RNS)

Among the three commonly used neuromodulation techniques, RNS differs from DBS and VNS as it is closed-loop, which means that it responds to neural activities instead of continuously stimulating (open-loop). The RNS system, approved for clinical use in 2013, is an implantable intracranial device specifically designed to manage focal seizures. The only FDA approved closed-loop neurostimulation device is the RNS system of NeuroPace [18]. It consists of a neurostimulator attached to electrodes that are implanted at the site of the seizure onset zone SOZ or seizure spread (more recently), which record ECoG data for a period of time known as the programming epoch without stimulation and store them into the patient data management system (PDMS) by the patient uploading it through the remote monitor and help with the settings of the programmer. After the programming epoch, the RNS device is programmed with the stimulation settings for it to deliver stimulation when detecting epileptiform activity [19].

In essence, RNS sends electrical stimuli through the implanted neurostimulator upon detecting electrographic activity predetermined to be epileptiform activity. It also allows access to analyzing long-term ECoG data for physicians to review. Long-term studies indicate that over 50% of patients treated with RNS experience a sustained reduction in seizure frequency at the five-year mark, a level of efficacy that mirrors outcomes reported for DBS [19]. Compared with open-loop techniques like DBS and VNS, RNS may reduce unnecessary stimulation, which may disrupt normal functions, and

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provide more patient-specific treatments, which may have a promising future with the development of AI to improve the stimulation settings. However, RNS, DBS, and VNS are still invasive approaches that are under the risk of infection and other surgical complications. With the growing trend of safer and more user-friendly treatments, patients are offered an option that is low risk and doesn't require surgical intervention with the arrival of noninvasive brain stimulation (NIBS) provides. Two commonly utilized techniques are TMS and tDCS. 24 DRE patients treated with TMS and tDCS at Mayo Clinic in Rochester showed a median seizure reduction of 50%, proving that it is a potential treatment [20].

6. Conclusion

Brain-computer interfaces (BCIs) are gaining prominence in the medical field, particularly in the diagnosis and treatment of epilepsy. BCIs have shown promising potential in seizure detection, prediction, and personalized intervention. By integrating artificial intelligence (AI), BCIs can automatically analyze data such as EEG recordings to identify biomarkers like high-frequency oscillations (HFOs), functional connectivity, and EEG microstates. These systems enable time-efficient, automated monitoring and support real-time closed-loop neurostimulation. In clinical practice, BCIs not only assist conventional diagnostic procedures but also offer potential applications in presurgical assessments and localization of epileptogenic zones, thus improving treatment precision.

Among available BCI technologies, EEG-based systems—particularly non-invasive scalp EEG—are widely preferred due to their high temporal resolution, ease of use, and minimal risk compared to invasive alternatives. BCI algorithm development leverages both classical machine-learning techniques and modern deep architectures; in particular, convolutional and recurrent neural networks have gained widespread adoption, enabled by high-performance computing resources such as GPU acceleration. One notable clinical application is responsive neurostimulation (RNS), a closed-loop system that delivers stimulation only when epileptiform activity is detected, thereby reducing unnecessary stimulation and minimizing side effects associated with continuous methods like deep brain stimulation (DBS) and vagus nerve stimulation (VNS).

In spite of the achievements so far, several limitations are still to be addressed, which include the lack of sample size and Multicenter study as well as the challenge of data heterogeneity and the need to improve generalization. Meanwhile, a few possible future focuses and considerations are listed below. First, a further study of integrated monitoring systems such as EEG-fNIRS can be crucial for the providing of higher quality recordings, as it combines two techniques, despite having to solve the problem of crosstalk. Second, to allow more personalized treatment planning and treatment, further study on AI-driven adaptive closed-loop systems should be carried out, as should the same for remote monitoring platforms, which may improve real-time intervention and epileptiform activity recording. Third, with the growing need for less risky and more convenient options, non-invasive techniques as well as portable monitoring devices are growing more popular and therefore may require more attention. Last, future researches should consider to prioritize large-scale and collaborative trials to validate BCI systems across diverse cohorts. Ethical problem should also be under concerned, leading to the need of establishing better regulations.

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