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Application of Brain-Computer Interface in Generalized Tonic-Clonic Seizures

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Abstract. Generalized Tonic-Clonic Seizures (GTCS), or grand mal seizures, are a severe type of epileptic seizure with high morbidity and mortality. Traditional treatment methods, such as Anti-seizure Medication (ASM) and surgical intervention, have limited efficacy, and long-term medication may lead to adverse reactions. Brain-Computer Interface technology provides a new potential approach for the treatment of GTCS by real-time monitoring and regulating abnormal brain electrical activity. Through the closed-loop regulation mechanism, it shows significant potential in the monitoring and early warning of GTCS. This article, in the form of a review, summarizes and analyzes the research results on the pathological mechanism of GTCS, the technical principles of Brain-Computer Interface, and its clinical applications, aiming to lay a foundation for the clinical application of Brain-Computer Interface technology in the treatment of GTCS and other neurological diseases. In addition, Brain-Computer Interface technology also has application value in other neurodegenerative diseases such as Parkinson's disease, post-stroke paralysis, and Amyotrophic Lateral Sclerosis (ALS). Despite technical challenges such as the biocompatibility of invasive devices and signal noise of non-invasive devices, with policy support and the deepening of interdisciplinary cooperation, Brain-Computer Interface is expected to become a revolutionary treatment for patients with refractory epilepsy.

Keywords: Generalized Tonic-Clonic Seizures (GTCS), grand mal seizures, Brain-Computer Interface (BCI), clinical application, neurodegenerative diseases

1. Introduction

Epilepsy is a chronic neurological disease characterized by sudden abnormal discharge of brain neurons, resulting in transient brain dysfunction. Its core feature is recurrent "epileptic seizures", which can manifest as abnormalities in movement, sensation, consciousness, autonomic nerves, and mental aspects. The etiology of epilepsy is complex, including genetic factors, brain diseases (such as traumatic brain injury, stroke, tumors, infections, etc.), metabolic abnormalities, poisoning, etc. The etiology of some idiopathic epilepsy patients is still unknown. According to statistics, currently about 20% to 30% of patients with idiopathic epilepsy in the world cannot be treated with drugs [1].

"Grand mal epilepsy" is not a disease independent of epilepsy but a type of epileptic seizure, medically known as "generalized tonic-clonic seizure (GTCS)", which was formerly commonly called "grand mal seizure".

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GTCS is one of the types of neurological diseases with high morbidity and mortality, affecting about 50 million people, of whom about 30%-40% will experience grand mal seizures [2]. Grand mal seizures can occur at any age, but the incidence rate is higher in children and the elderly. Traditional treatment methods such as Anti-seizure Medication (ASM) and surgical intervention have limited effects on some patients with refractory epilepsy, and long-term medication can lead to liver and kidney function damage and cognitive decline [2]. For the population with drug-resistant epilepsy (DRE), Brain-Computer Interface (BCI), Vagus Nerve Stimulation (DBS), and Responsive Neurostimulation (RNS) have become more popular treatment methods [3]. In recent years, Brain-Computer Interface (BCI) technology has provided a new direction for the treatment of GTCS by real-time monitoring and regulating abnormal brain electrical activity. This article analyzes the pathological mechanism of grand mal epilepsy, the technical principles of BCI, clinical applications, and challenges in the form of a review, and then explores the potential value of BCI in GTCS and neurological diseases, laying a foundation for future clinical treatment of GTCS.

2. GTCS

GTCS is the most serious type of epilepsy, manifested as loss of consciousness, generalized tonic-clonic convulsions, which may cause acute complications such as trauma, asphyxia, and fractures. Repeated grand mal seizures may lead to cognitive decline, psychological disorders (such as depression, anxiety), and impaired social function. Patients with GTCS have a higher risk of sudden death (SUDEP), especially those with uncontrolled GTCS [4]. The core mechanism of GTCS is excessive synchronous discharge of neurons, involving weakened γ-aminobutyric acid (GABA) ergic inhibitory transmission and enhanced glutamatergic excitatory transmission [5]. Long-term epileptic activity can induce neural network remodeling. Functional magnetic resonance imaging (fMRI) confirmed that during epileptic seizures, the connection between the default mode network (DMN) and the thalamocortical network is enhanced, promoting the spread of abnormal electrical activity. About 30% of epilepsy is related to gene mutations in ion channels such as SCN1A and KCNQ2, leading to decreased stability of neuron membrane potential [6]. Whole-exome sequencing studies have shown that gene mutations can affect the inactivation characteristics of sodium channels and increase the risk of burst discharge. GTCS is the result of the combined action of neuronal excitation-inhibition imbalance, network reorganization, and genetic factors, which provides a biological basis for targeted intervention of BCI.

3. Brain-Computer Interface (BCI)

BCI technology is a technology that directly reads brain signals and converts them into control instructions. Its core principles include signal acquisition, signal processing, and control output. BCI systems usually rely on the acquisition of electroencephalogram (EEG) signals because EEG has the advantages of non-invasiveness, high temporal resolution, and relatively low cost. EEG signals can capture the neuronal activity of the cerebral cortex through scalp electrode arrays, and these signals reflect the electrophysiological changes of the brain in different cognitive states. The collected EEG signals usually need to go through preprocessing, feature extraction, and classification steps. Preprocessing includes filtering and noise reduction to remove interference signals. Feature extraction extracts neural markers related to specific tasks by analyzing the time-domain, frequency-domain, or time-frequency domain features of EEG signals. Deep learning is widely used in feature extraction and classification of EEG signals to improve the accuracy and efficiency of signal processing. BCI systems convert processed signals into control instructions for driving external

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devices or feeding back to users. For example, BCI-based virtual reality (VR) systems can feedback the user's EEG state in real-time for cognitive training or rehabilitation. In addition, BCI technology is also applied to assist motor function rehabilitation, driving rehabilitation equipment through motor imagery (MI) signals. Therefore, BCI technology realizes the direct interaction between the brain and external devices by collecting and processing brain signals, providing new possibilities for medical rehabilitation and cognitive enhancement. BCI technology has been widely used in the treatment of neurological diseases, such as epilepsy, Parkinson's disease, post-stroke paralysis, Amyotrophic Lateral Sclerosis (ALS), mental diseases, and other neurological diseases [7-8].

4. Application of BCI in epilepsy treatment

BCI can collect EEG signals through implantable (such as SEEG) or non-invasive (such as EEG) devices, which can be used to identify all types of signals of emotional states. Among them, EEG is widely used because it provides a non-invasive and intuitive method for measuring emotions. EEG data is the preferred method to study the brain's response to emotional stimuli because it can record neurophysiological signals and objectively reflect the activity of the cerebral cortex to a certain extent [9].

In the research on the treatment of epilepsy, EEG combined with machine learning algorithms is currently mainly used to identify epileptic characteristic waves (such as spike-and-wave complexes) and locate the epileptogenic focus based on the identification results. Tan et al. analyzed the epileptic EEG cycle based on the closed-loop BCI of the responsive neurostimulation system (RNS) and predicted focal seizures, and the results showed that the accuracy of the prediction results reached 79% [10]. In addition, BCI can accurately locate the epileptogenic area by identifying "source-sink" network markers (i.e., the "source" that continuously inhibits adjacent nodes and the "sink" that is inhibited).

In recent years, Zou et al. developed a new non-invasive closed-loop acoustic brain-computer interface (aBCI) for decoding epileptic seizures by combining EEG and ultrasound stimulation that triggers the vagus nerve [11]. In a rat model of pentylenetetrazole-induced epilepsy, acoustic radiation force induced by different acoustic parameters was used to stimulate the vagus nerve, and the results of triggering vagus nerve ultrasound stimulation through epileptic EEG signals to control epileptic seizures were obtained. In addition, Zou et al. studied the mechanism of aBCI in controlling epileptic seizures through real-time quantitative polymerase chain reaction (RT-qPCR) [11]. In the rat model of epilepsy, the aBCI system selectively activates mechanically sensitive neurons in the nodose ganglion, while inhibiting the neuronal excitability of the hippocampus and amygdala, and rapidly stops epileptic seizures after ultrasound stimulation of the vagus nerve. Physical transection or chemical blockage of the vagus nerve pathway eliminated the anti-epileptic effect of aBCI. In addition, in acute experiments, aBCI showed significant anti-epileptic effects compared with traditional vagus nerve electrical stimulation [11]. Closed-loop aBCI provides a novel, safe, and effective tool for on-demand stimulation to treat abnormal neuronal discharge, opening the door for the next generation of non-invasive BCI. In addition, Neuralink has implanted brain-computer interface chips in 3 patients and will conduct larger-scale trials in 2025 to verify the safety and effectiveness of fully implantable devices [12].

5. Application of BCI in other neurodegenerative diseases

Parkinson's disease is a neurodegenerative disease characterized by motor dysfunction. BCI technology provides precise neuromodulation for patients with Parkinson's disease by decoding

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brain signals. For example, a system combining closed-loop brain-computer interface with deep brain stimulation (DBS) (BCI-DBS) can automatically adjust stimulation parameters according to the patient's brain activity, significantly improving the patient's motor symptoms [13]. Studies have shown that the closed-loop BCI-DBS system can reduce the Unified Parkinson's Disease Rating Scale (UPDRS) score of patients with Parkinson's disease, thereby improving symptoms such as bradykinesia [14].

In addition, post-stroke paralysis is one of the main causes of long-term dysfunction in patients. BCI technology helps paralyzed patients control external devices (such as wheelchairs, robotic arms) or perform rehabilitation training by decoding their movement intentions. For example, intravascular BCI systems (such as Stentrode) have been used for the rehabilitation of severely paralyzed patients, who can control computer cursors or send emails through imagined movements [15]. In addition, the combination of BCI and functional electrical stimulation (FES) can promote the recovery of nerve function in paralyzed patients [16].

In addition, ALS is a progressive neurodegenerative disease that causes patients to gradually lose motor ability. BCI technology provides a new method for ALS patients to communicate with the outside world and control external devices. For example, through BCI systems, ALS patients can control cursors, synthesize speech, or operate robotic limbs through brain activity. The latest research shows that BCI technology can convert the brain signals of ALS patients into speech with an accuracy rate of up to 97%, significantly improving the patients' communication ability [17].

6. Discussion

BCI realizes precise intervention of neural activities through real-time monitoring and regulation of abnormal brain electrical activities, thus providing a new treatment direction for neurological diseases such as GTCS. In epilepsy treatment, it can identify characteristic waves, locate epileptogenic foci, and perform targeted stimulation. In other neurodegenerative diseases, it can help patients improve motor function and restore communication ability. However, the current technology is not yet mature, and there are many problems to be solved, such as the biocompatibility of devices, signal quality, and handling of individual differences in epileptogenic networks.

In addition, invasive devices can collect EEG signals more accurately with higher signal quality, which is conducive to more accurate identification and regulation of neural activities. For example, the closed-loop BCI based on the responsive neurostimulation system (RNS) has an accuracy rate of 79% in predicting focal seizures. Non-invasive devices do not require surgery, cause less damage to the patient's body, and have relatively low costs. However, invasive electrodes need to improve biocompatibility (such as Neuralink's flexible electrodes), and non-invasive devices need to solve the problem of signal noise (signal-to-noise ratio 10:1 ~ 100:1). The epileptogenic network heterogeneity of epilepsy patients is high, so it is necessary to combine fMRI and magnetoencephalography (MEG) to build personalized models. The infection risk and electrode displacement of implantable devices also need further optimization. In the future, we should focus on individualized treatment, combine fMRI and magnetoencephalography (MEG) to build personalized models for different patients to deal with the high heterogeneity of epileptogenic networks in epilepsy patients, and promote the integration of multimodal technologies to comprehensively improve the performance and applicability of BCI systems. In addition, it is necessary to strengthen policy support and interdisciplinary cooperation to accelerate the clinical transformation of BCI technology, making it a revolutionary treatment for refractory epilepsy and other diseases. It is also necessary to improve the biocompatibility of invasive electrodes, reduce the risk of infection and the possibility of electrode displacement, and improve the signal-to-noise ratio

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and the accuracy of signal processing by solving the signal noise problem of non-invasive devices. In addition, in view of the high heterogeneity of epileptogenic networks in epilepsy patients, the method of building personalized models can be optimized, and long-term safety verification can be carried out to ensure the safety and effectiveness of BCI devices in long-term use.

7. Conclusion

This article focuses on the application of BCI in GTCS, involving the pathological mechanism of GTCS (such as excessive synchronous discharge of neurons, neural network remodeling, genetic factors, etc.), the technical principles of BCI (signal acquisition, processing, control output, etc.), clinical applications in GTCS (such as identifying characteristic waves and locating epileptogenic foci through EEG combined with algorithms, the development and application of non-invasive closed-loop acoustic brain-computer interfaces, etc.), and the application of BCI in other neurodegenerative diseases (Parkinson's disease, post-stroke paralysis, ALS, etc.). It focuses on analyzing the potential value of BCI in GTCS and other neurological diseases, discusses the challenges it faces in clinical applications, and lays a foundation for the development of BCI in clinical treatment. Through the closed-loop regulation mechanism, BCI shows significant potential in the monitoring, early warning, and treatment of epilepsy. Despite technical and industrial challenges, with policy support and deepening interdisciplinary cooperation, BCI is expected to become a revolutionary treatment for patients with refractory epilepsy. Moreover, in the future, it is necessary to focus on individualized treatment, long-term safety verification, and integration of multimodal technologies to accelerate clinical transformation.

This article has some shortcomings. Firstly, it mentions little about the long-term effect data of BCI technology in the clinical application of GTCS, and lacks sufficient long-term follow-up research results to support its effectiveness and safety. In addition, this article does not conduct a more detailed comparative analysis of the specific applicable populations and scenarios of different types of BCI devices (invasive and non-invasive) in the treatment of GTCS.

In the future, this article should add content on long-term follow-up studies of BCI technology in the clinical application of GTCS, collect patient data in a longer time dimension, including seizure control effects, device safety, and changes in patients' quality of life, to more comprehensively verify its long-term effectiveness and safety. For invasive and non-invasive BCI devices, it is necessary to conduct more detailed comparative studies combined with the characteristics of different patients' conditions (such as seizure frequency, location of epileptogenic focus, physical condition, etc.). At the same time, the advantages and limitations of the two types of devices in different applicable populations (such as children, the elderly, patients with different degrees of refractoriness, etc.) and application scenarios (such as long-term home monitoring, accurate treatment in hospitals, etc.) should be clarified to improve the pertinence and clinical guiding value of the research.

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