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Management of post-stroke depression (PSD) by electroencephalography for effective rehabilitation

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ABSTRACT

Post-stroke depression (PSD) has negative impacts on the daily life of stroke survivors and delays their neurological recovery. However, traditional post-stroke rehabilitation mainly focused on motor restoration, whereas little attention was given to the affective deficits. Effective management of PSD, including diagnosis, intervention, and follow-ups, is essential for post-stroke rehabilitation. As an objective measurement of the nervous system, electroencephalography (EEG) has been applied to the diagnosis and evaluation of PSD. In this paper, we reviewed the literature most related to the clinical applications of EEG for PSD and offered a cross-section that is useful for selecting appropriate approaches in practice. This study aimed to gather EEG-based empirical evidence for PSD diagnosis, review interventions for managing PSD, and analyze the evaluation approaches. In total, 33 diagnostic studies and 19 intervention studies related to PSD and depression were selected from the literature. It was found that the EEG features analyzed by both band-based and nonlinear dynamic approaches were capable of quantifying the abnormal neural responses on the cortical level for PSD diagnosis and intervention evaluation/prediction. Meanwhile, EEG-based machine learning has also been applied to the diagnosis and evaluation of depression to automate and speed up the process, and the results have been promising. Although brain-computer interface (BCI) interventions have been widely applied to post-stroke motor rehabilitation and cognitive training, BCI emotional training has not been directly used in PSD yet. This review showed the need for understanding the cortical responses of PSD to improve its diagnosis and precision treatment. It also revealed that future post-stroke rehabilitation plans should include training sessions for motor, affect, and cognitive functions and closely monitor their improvements.

1. Introduction

Traditional post-stroke rehabilitation mainly focuses on motor restoration. The routine diagnosis and treatment also mainly emphasize the motor functions, with the purpose of helping the survivors regain their independence in daily tasks as early as possible. However, there are complex interactions among various stroke-induced impairments, such as motor, cognitive, and affective deficits. Their interrelationship could aid or hinder recovery during post-stroke rehabilitation. Post-stroke depression (PSD), defined as depression taking place in the context of a clinically apparent stroke (different from silent cerebrovascular disease) [1], occurs in almost half of stroke survivors [2]. Depression has a huge negative impact on patients' daily life. It not only caused long-lasting low mood, decreased motivation, and even suicide, but also postponed the recovery of neurological functions, such as motor, cognition, memory, and language functions [3]. Studies have indicated that patients treated for PSD can achieve better motor and cognitive rehabilitation outcomes than untreated patients [4] because a high level of motivation was usually associated with better functional recovery [5,6]. Therefore, effective management of PSD, including diagnosis,

Abbreviations: BCI, Brain-computer interface; DP, Depressed participants; DFA, Detrended fluctuation analysis; ECT, Electroconvulsive therapy; EEG, Electroencephalogram; ERP, Event-related potential; fNIRS, Functional near-infrared spectroscopy; FD, Fractal dimension; fMRI, functional Magnetic Resonance Imaging; HC, Health controls; LLE, Largest Lyapunov exponent; LZC, Lempel–Ziv complexity; MDD, Major depression disorder; PSD, Post-stroke depression; PSND, Post-stroke non-depression; SampEn, Sample entropy.

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intervention, and follow-ups, could facilitate post-stroke rehabilitation in other physiological dimensions (e.g., motor restoration).

Timely and objective diagnosis is the first step toward choosing the proper treatment for PSD. Traditionally, the diagnosis of PSD mainly uses diagnosis interviews to evaluate the symptoms subjectively. Clinicians observe and interpret explicit symptoms and then provide diagnoses with categorical scores. This method was widely adopted clinically for diagnosing depressive symptoms because the assessment operation was simple and did not require additional equipment or a special experimental setting. It was useful, informative, somewhat reliable, and effective for PSD diagnosis. However, the traditional method has some drawbacks. First, it is mostly based on ordinal scales such as the Hamilton Depression Rating Scale (HDRS) and behavioral symptoms such as those described in the Diagnostic and Statistical Manual of Mental Disorders and the International Statistical Classification of Mental Disorders [7,8]. Some assessments use numerical scales (e.g., 0 to 10), but their scale resolutions are relatively low. The diagnosis could also be influenced by post-stroke linguistic disorders in communication (like aphasia), cognitive impairment (like anosognosia), emotional liability, or even the overlap between symptoms of depression and post-stroke neurological impairments [9]. Second, psychiatric diagnoses for PSD rely on observation by the clinician and/or complaints from the patient, and it heavily depends on professional experience [10]. Sometimes, human and environmental factors (e.g., experience and knowledge of professionals, unpleasant/repetitive noise of medical instruments in clinics) can lead to misdiagnosis [11]. Thus, it might not be sufficiently objective during the diagnosis interview for professionals. Third, this method is time-consuming and requires well-trained, experienced professionals, leading to the high cost of long-term PSD treatment services. Therefore, it is necessary to develop efficient, cost-effective, and objective approaches to diagnose PSD more effectively and affordably.

Histological and physiological indicators reflect the neurological changes of PSD [12]. Clinical and experimental evidence has shown that there was a difference between the neural structure of patients with depression and that of healthy subjects [13]. The ischemic brain lesions that disrupt the aminergic pathways, or neural circuits, involved in mood regulation could directly cause PSD [1]. Neuroimaging techniques such as electroencephalography (EEG) [13,14], functional near-infrared spectroscopy (fNIRS) [15,16], and functional Magnetic Resonance Imaging (fMRI) [17,18], have revealed neurological changes in individuals with depression. For example, it has been found that the frontal cortex is associated with the complex neuronal process of depression, those with depression exhibit decreased frontal cortex function [19,20], and there are variations in electrical brain activity in various brain regions of PSD patients, and brain connectivity is also changed in patients with PSD [13,14]. Moreover, interhemispheric frontal alpha asymmetry has been considered a key sign of structural alternation of the brain in depressed patients [21]. In this regard, neuroimaging techniques have enhanced the diagnosis of PSD by offering objective evaluations of the nervous system. However, their current applications in routine practice are hindered by several technical and logistic difficulties (e.g., instruments requiring technical operations and additional professional interpretation for a large amount of data from the instrument-based assessments).

As one of the non-invasive neuroimaging techniques without radiation, EEG reveals a large amount of physiological and psychological information and could reflect the complex electrophysiological activity of neuronal populations at the cortical level. It is also sensitive to various functional states in the human brain with high temporal resolution. Compared with fMRI, EEG is more cost-effective and more accessible to patients, because it can work in less strict environments, and it requires shorter recording time at a lower cost [22]. Meanwhile, EEG signal has higher temporal resolution than both fMRI and fNIRS, which is particularly suitable for the evaluation of transient dynamics of brain functions [23]. With the above advantages, EEG has been widely adopted to investigate neurophysiological changes in general depression. Therefore, EEG has also been a frequent measure added to the clinical scales for the diagnosis of PSD. With the introduction of EEG, electrophysiological measures of brain functions have been developed. Based on modern signal processing techniques, quantitative features of EEG signals (e.g., specific frequency bands, signal complexity, functional connectivity, and brain networks) have been widely applied to dynamic brain exploration[19]. EEG has also been applied to precision treatments for PSD, for instance, designing individualized interventions for patients, determining specific biomarkers, seeking technical solutions, and playing a key role in EEG-based biofeedback training for PSD [19]. However, EEG signals could be contaminated by several sources of noise (e.g., environmental noise, cardiac signals, and motion artifacts) [3]. Modern signal processing methods are mature and available to minimize the EEG noises in real-time processing [24].

Although EEG is useful for investigating neurophysiological changes in PSD, it generates a large amount of complex time-point data during recording. Since PSD recovery is a long-term and progressive process, it requires tremendous manual investigations to analyze these data in current practice. Thus, the automatic evaluation of the condition of patients and the intervention effect is desirable. Machine learning can realize the automatic recognition of EEG features so that the application of EEG becomes more practical and less reliant on the manual investigation by trained professionals. As a part of artificial intelligence, machine learning was developed during the 1960s for pattern classification [25], and it is currently being used in a wide variety of applications. It builds automatic learning models based on a large set of a priori data, and it extracts useful information from input data to make predictions or decisions [26]. Therefore, EEG is suitable for machine learning because of its highly structured data [27]. Since the 1990s, numerous machine learning and pattern recognition algorithms have been developed to extract abstract features from EEG data without manual investigations [28]. In line with this, in the last few years, machine learning has been explored using EEG signals for the automatic and timely diagnosis of depression [29].

In recent years, the number of research studies using EEG techniques in PSD applications has increased dramatically. In this paper, we reviewed the literature most relevant to the clinical applications of EEG for PSD and offered a cross-section that is useful for selecting appropriate approaches in practice. The first purpose of the study was to gather EEG-based empirical evidence on brain oscillations and to review EEG-based approaches for the diagnosis of PSD. The second purpose was to review EEG-based approaches for the evaluation of the effects of interventions to manage PSD.

2. Review methods and results

In the identification of relevant studies, we searched the databases MEDLINE, Web of Science, PubMed, and PubPsych from 2005 to 2022 using the following keywords: (EEG or electroencephalography) AND (post-stroke depression or depression or emotion) AND (stroke) OR (data mining or machine learning or classification) OR (brain-computer interface (BCI) or rehabilitation) OR (prediction or diagnosis or evaluation or detection). English language papers related to the diagnosis, prediction, evaluation, and/or treatment of PSD were reviewed. Due to the limited papers on PSD, additional papers on major depression disorder (MDD) were obtained from the references of these papers through the mentioned databases. In total, 33 diagnostic studies and 19 intervention studies were selected.

3. EEG features for PSD detection/diagnosis

3.1. Studies on relationships between EEG features and depression

Resting-state EEG, which is associated with the fundamental brain state at rest [30], can denote spontaneous neural activity to evaluate intrinsic neural activity that is not elicited through a task. It could reveal brain dynamics and identify depressive symptom-related changes.

Table 1
Depression diagnostic studies: main findings derived from band-based approaches and nonlinear dynamical measures of EEG.

Studies	Analysis approaches	Brain areas	Frequency bands/ bandwidth	Main findings
Frequency analysis				
Doruk et al. [35]	Power asymmetry, inter-hemisphere coherence	Frontal, central	α,θ,β	1) $\alpha,\beta\uparrow$ in frontal, $\alpha,\theta\uparrow$ in central; 2) $\alpha\downarrow$.
Wang et al. [7]	Spectral power	Whole brain	$\delta,\alpha,\theta,\beta2,\beta1$	↑ in temporal regions
Lee et al. [34]	Spectral power	Whole brain	$\delta,\alpha,\theta,\beta$	↑ in C3
Wang et al. [12]	Absolute spectral powers	Whole brain	$\delta,\alpha,\theta,\beta1,\beta2$	$\beta2\uparrow$ in frontal, central areas(left-hemisphere); $\theta,\alpha\uparrow$ in temporal, occipital regions, (right-hemisphere)
Zheng et al. [36]	Power ratio	Whole brain	$\delta,\alpha,\theta,\beta$	Low amplitude α activity, θ activity ↓
Li et al. [3]	Absolute spectral powers	Whole brain	$\delta,\alpha,\theta,\beta$	$\alpha1\uparrow$ in frontal, parietal, temporal regions; $\alpha2\uparrow$ in left frontal pole; $\theta\uparrow$ in central, temporal, occipital regions
Nonlinear dynamics				
Nandrino et al. [44]	Informational (LZC)	Frontal, central and parietal	Broadband	↑
Pezard et al. [48]	Informational (Information index S_0, Kolmogorov-Sinai entropy)	Frontal, central, and parietal	Broadband	↑ when comparing with first-episode depressives
Linkenkaer-Hansen et al. [53]	Invariant (DFA α)	Occipitoparietal and temperamental	θ	↓
Lee et al. [49]	Invariant (DFA α)	Frontal, central, temporal, and occipital	Broadband	DFA < 1 for both groups, ↑ (except in C4)
Li et al. [45]	Informational (LZC)	Whole brain	Broadband	↑across study stages, but no differences in frontal areas under the emotion induction task
Mendez et al. [46]	Informational (LZC)	Whole brain	Broadband	↑, more complexity
Ahmadlou et al. [52]	Invariant (Higuchi FD, Katz FD)	Frontal	Broadband,δ,β,γ	↑ in frontal areas; $\delta\uparrow$in frontal areas, globally and in the left Hemisphere; $\beta\uparrow$in frontal areas; $\gamma\uparrow$ (but not in the right hemisphere)
Bachmann et al. [50]	Invariant (FD)	Whole brain	0.3–70 Hz	↑
Zhang et al. [41]	Informational (LZC); Spectral power	Whole brain	Broadband, slow waves	↓ LZC values in the whole brain regions
Acharya et al. [29]	Invariant (LLE, Hurst exponent, Lacasa FD); Informational (SampEn, EntPh, BiEnt); Geometric (recurrence plot measures)	Frontal, temporal, central, and parietal	Broadband	↑ for recurrence plot measures; ↓ for LLE and FD
Akar et al. [42]	Invariant (Katz FD, Higuchi FD); Informational (Shannon entropy, LZC, KC)	Frontal, temporal, central and parietal	Broadband	↑ in frontal, central, and parietal areas under resting. ↑in frontal and parietal areas under the music stage for invariant measures and LZC. ↑ in frontal and parietal areas under noise stage for invariant measures, KC and LZC;
Akar et al. [51]	Invariant (Higuchi FD, Katz FD)	Frontal and parietal	Broadband, β,γ, δ	$\delta\uparrow\beta,\gamma\uparrow$invariant (Katz FD, Higuchi FD) in frontal, parietal.
Bachmann et al. [47]	Invariant (Higuchi's FD, DFA); Informational (LZC); Spectral power	Whole brain	0.3–200 Hz, γ, δ	↑

Note: Nonlinear measures: BiEnt = Bispectrum entropy; DFA = Detrended fluctuation analysis; EntPh = Bispectrum phase entropy; FD = Fractal dimension; KC= Kolmogorov complexity index; LLE = Largest Lyapunov exponent; LZC = Lempel Ziv complexity index; MSE = Multiscale entropy; SampEn = Sample entropy. ↑refers to higher values in an index for a depression group in comparison to a healthy control one. ↓refers to lower values.

Studies have shown impairment of large-scale brain networks, decreased frontal cortex function, and increased limbic system function in patients with MDD [20], and several studies have also used EEG to explore the neural responses of PSD patients [3,7,12]. Thus, features identified by resting-sate EEG could help to elucidate the neural responses of PSD. The two main analysis approaches for resting-state EEG were linear frequency/spectral analyses (band-based approaches) and nonlinear dynamic measures. In this review, six band-based approach studies and 13 nonlinear dynamic studies for depression were examined, and they are summarized in Table 1.

3.1.1. EEG frequency band-related depression features

Frequency/spectral analysis (band-based approach) is a common linear method to analyze resting EEG oscillations. The brain oscillations are divided into several narrow bands—delta (from 0.5 to 4 Hz), theta (from 4 to 8 Hz), alpha (from 8 to 13 Hz), beta (from 13 to 30 Hz), and gamma (from 30 to 45 Hz)—ranging from the slowest to the fastest waves. (1) Delta is related to the deep stage of sleep, known as the slow-wave stage of sleep. It is associated with attentional processes and large-scale cortical integration with homeostatic processes. This oscillation is also related to autonomic regulation and reacts to motivationally salient stimuli, especially in frontal areas. It sensitively reflects structural brain damage (lesions) and a wide range of neurodegenerative disorders [31]. (2) Theta is engaged in active motor behavior linked to memory formation and navigation [32]. Its pathological changes are mainly reported in association with memory deficits. (3) Alpha represents the activity of the visual cortex in an idle state, and it can be further divided into alpha1 (from 8 to 10 Hz) and alpha2 (from 10 to 13 Hz). Alpha1, as a characteristic oscillation of the resting state, is shown to be abnormal in dementia, Alzheimer's disease, and mild cognitive impairment [30]. (4) Beta is associated with normal waking consciousness over the motor cortex and muscle contractions, and it can also be further divided into beta1 (from 13 to 20 Hz) and beta2 (from 20 to 30 Hz). (5) Gamma is related to brain network activity and cognitive phenomena. The resting state relative power (RP) of the five EEG bands, delta/alpha ratio (DAR), and delta/theta ratio (DTR) can be recorded from EEG electrodes over the whole brain, and these EEG features derived from different brain areas have also been widely investigated. The cortical region of the brain consists of four lobes, known as the frontal, parietal, temporal, and occipital lobes. In general, each lobe handles different functions, whereas emotion processing requires the involvement of multiple brain regions [33].

A total of six studies used band-based approaches to investigate the neural response of depression (shown in Table 1). Among them, four papers revealed the abnormal spectral power in patients with depression. For MDD patients, Lee et al. [34] revealed that the origination of high alpha and beta power could differentiate the depressive group from the euthymic group, especially in the left central cortex (C3). In line with the above MDD study, Li et al. [3] found that the absolute powers of the alpha and theta bands could be distinguished between PSD patients and post-stroke non-depression (PSND) subjects, and the absolute alpha1 power increased with the severity of depression [3]. Wang et al. [12] also reported that theta and alpha powers increased in the occipital and temporal regions of PSD patients with lesions in the right hemisphere. They also observed increased beta2 power in the frontal, central, and right parietal regions of PSD patients with lesions in the left hemisphere [12]. In addition, Wang et al. [7] found that delta, theta, and beta2 powers in stroke subjects increased with depressed mood, especially in temporal regions. The theta and beta2 powers in the right temporal area were relevant to depressed mood. These authors also studied the relationship among post-stroke depression, functional status, lesion side, and post-stroke time. They concluded that the lesion location and the time since stroke onset did not affect depression. Only the patient’s functional status was associated with emotional symptoms [7]. The other two papers used other EEG spectral features (power ratio, power asymmetry, coherence, etc.) to predict depression. Doruk et al. [35] found that lower scores on the Stroke Impact Scale–Emotion were related to some features of the following bands: (1) the alpha and beta bands (frontal EEG power asymmetry), (2) the alpha and theta bands (central EEG power asymmetry), and (3) the alpha band (lower interhemispheric coherence). Zheng et al. [36] used the activity of alpha and theta as independent predictors for post-cerebral infarction depression.

Based on the above findings, theta, alpha, and beta bands were the most representative EEG frequency bands for PSD patients, and their powers could be positively associated with the severity of depression. Meanwhile, the EEG power features could vary according to the left/right hemispheric lesion side of the stroke.

3.1.2. Nonlinear dynamical measures related to depression

Although the linear band-based approach has revealed useful characteristics of neurophysiological changes, it has strict requirements for the stability, linearity, and signal-to-noise ratio of the signal, which EEG cannot completely satisfy [37]. In contrast to the conventional band-based approach, nonlinear analytic methods require lower stability of the processed signal because they focus more on the EEG features that change with time [37], which makes them potential supplementary and compensatory approaches to frequency-power analysis. Recently, nonlinear analytic methods—that is, nonlinear features—have been applied to model the brain as a complex system and describe the complex and chaotic characteristics of EEG signals. They could provide new insights into aberrant neural connectivity and physiological processes in pathological conditions like depression [38]. The physiological complexity could thus be studied by vast families of analysis approaches in information theory [22]. Torre-Luque et al. [19] classified the nonlinear measures of brain oscillations into three categories: geometric, informational, and invariant measures. For instance, a recurrence plot is a geometric technique that quantifies the times when a system’s trajectory arrives at approximately the same area in the phase space. Entropy-related measures were applied to the informational domain (e.g., sample entropy and Lempel–Ziv complexity (LZC)), while features like Largest Lyapunov exponent (LLE), detrended fluctuation analysis (DFA) and fractal dimension (FD) were classified as invariant measures. The five most widely adopted characteristic measures of a complex system for depression investigation are presented below. (1) LLE was the first essential property of complex systems to measure a system’s predictability and sensitivity to changes in its initial conditions. It can estimate the level of chaos presented in the EEG signals, and higher LLE values imply more complex signals [39]. (2) The second property was “entropy” in information theory, which describes the generation rate of new information in a system. Complex systems usually achieved high entropy values because they generate a large amount of information and are less predictable. Approximate entropy, sample entropy, permutation entropy, and Kolmogorov–Chaitin complexity are examples of entropy indices [40]. (3) Closely associated with entropy measures, the LZC of finite sequences was the third property. It indicates how new elements are captured in a time series (e.g., an EEG epoch), and it is utilized to examine the data repetition. A higher LZC value usually implies that the signal is more repetitive and more complex [41]. (4) The fourth property was long-range temporal correlations (LRTCs), which are commonly measured by scaling exponent and calculated using DFA [19]. LRTCs detect inherent self-similarity features of EEG [39]. (5) The FD of the EEG system was the fifth measure. Several algorithms have been applied to the estimation of FD (e.g., Katz’s and Higuchi’s algorithms). It can be used to compare the EEG complexity and detect EEG signal patterns and details [39]. More nonlinear biomarkers of depression can be found in the review papers of Torre-Luque et al. [19] and Akdemir Akar et al. [42].

In this study, 13 studies that mainly adopted nonlinear dynamic measures of EEG on depression were examined. Among them, eight studies applied entropy-related measures in the informational domain, eight studies used invariant measures, and one study adopted geometric measures. Several studies utilized multiple nonlinear measures in different categories and some of them also applied band-based approaches for correlation and comparison.

The EEG complexity of depression has been frequently studied via entropy-related measures in the informational domain. In a study by Zhang et al. [41], LZC was utilized to measure EEG complexity in PSD patients. The authors observed that PSD patients exhibited lower neural complexity and decreased LZC values in all brain regions when compared to PSND and healthy subjects. Meanwhile, for stroke survivors, a significant correlation was further found between the severity of depression and the LZC values in all brain regions, particularly in the temporal and frontal areas [41]. The lower neural complexity of stroke patients might be related to their declined capability of neural processing since the inter-neuronal connectivity was impaired due to stroke [43], further resulting in less functional recovery. On the contrary, the LZC values for MDD patients were reported to be significantly higher in all brain regions than those for the controls [42,44–47]. Other informational parameters, such as the Kolmogorov index [42,48], Shannon entropy [42], and sample entropy [29], were also higher in MDD patients when compared to control participants. The evidence above implied that the neural complexity of patients with PSD and MDD was varied and that MDD patients mainly presented high neural complexity, whereas PSD patients showed low neural complexity. However, only one study on the neural complexity of PSD was found and examined; thus, this conclusion requires more literature support in the future.

In the above entropy measures of the informational domain, “complexity” might not have a single, unique meaning. Extensively used measures like LZC might not be able to determine the differences between complex systems and random, albeit simple systems. EEG dynamics for patients with depression might appear more complex and more random than the dynamics for healthy participants without depression. Thus, more sensitive and reliable measures with clearer definitions, such as invariant measures (e.g., DFA, FD, and LLE) in EEG oscillations, have been widely applied to the research on the EEG complexity of depression [19]. Most of the literature reached a consensus that MDD patients present higher levels of EEG complexity via LLE, DFA, and FD with broadband up to 50 Hz than control participants [42,47,49–52]. Akar et al. [51] and Ahmadlou et al. [52] further pointed out that higher FD values of MDD patients were mainly observed in the frontal and parietal areas for beta and gamma bands. Some contradictory findings have also been reported. Linkenkaer-Hansen et al. [53] confirmed the presence of LRTC (hidden in alfa, beta, and theta rhythms) in patients with depression in occipitoparietal and temporocentral areas, where the DFA exponent of control participants was higher in the theta band. Acharya et al. [29] found that the control participants exhibited higher FD and LLE in both hemispheres when compared with those depressed patients, which is likely due to the higher EEG variability in the normal class. They also applied geometric measures with broadband up to 50 Hz and obtained higher recurrence plot values for MDD patients than for control participants [29]. Nevertheless, all the current studies on the EEG complexity of depression via invariant and geometric measures targeted MDD, whereas the application to PSD was scarce. These measures should thus be extended to PSD in future studies.

Two studies included both linear band-based analysis and nonlinear measures to explore their relationship and compare their depression detection sensitivity. In the study by Zhang et al. [41], PSD patients showed slow wave rhythms, and there was a clear correlation between neuronal complexity and spectral powers of the delta, theta, alpha, and beta bands. On the other hand, Bachmann et al. [47] compared the sensitivity of depression detection between the linear and nonlinear EEG analysis approaches. They concluded that the combination of multiple measures from a single EEG channel could increase the sensitivity of depression detection [47]. Their findings suggested that both linear and nonlinear measures are useful for investigating the EEG features of depression, and the combination of multiple measures would enable a more comprehensive understanding of the neural responses of patients with depression.

3.2. EEG-based machine learning diagnostic models

In recent years, machine learning has been widely applied to the classification and identification of patterns in EEG signals [13]. These studies have usually consisted of the following processing stages: (1) recording EEG, (2) pre-processing EEG signals, (3) standard filtering via sampling frequency selection and artifact removal, (4) defining exact epochs for analysis, (5) feature extraction, (6) feature selection (or dimensionality reduction), (7) classification, (8) validation, and (9) machine learning testing [22]. Generally, EEG-based machine learning studies can be classified with three criteria: EEG features, sample size, and classifiers. If the number of both depressed participants (DPs) and healthy controls (HCs) was larger than 30, the sample size was defined as large; otherwise, it was viewed as moderate [22]. Feature extraction created features by calculating different fractal and nonlinear measures from selected epochs (time series) of raw signals. In EEG-based studies, band-based/spectral and dynamic measures were the most widely applied features. Classifiers were used for classifying features and discriminating EEG between HCs and DPs. Some popular classifiers are artificial feedforward neural networks (ANN), linear discriminant analysis (LDA), random forest, convolutional neural network (CNN), support vector machine (SVM), decision tree (DT), Naïve Bayes classification (NBC), Gaussian mixture model (GMM), K-nearest neighbor (KNN), probabilistic neural network (PNN), and Fuzzy Sugeno Classifier (FSC).

In this review, 15 EEG-based machine-learning studies on depression were selected, and they are summarized in Table 2. Among them, one study examined the emotional states of post-stroke patients for their potential usage in early PSD diagnosis. Yean et al. [33] used higher-order spectra features of EEG signals and machine learning-based classifiers (i.e., KNN and PNN) to classify six emotional states for both stroke patients and unimpaired controls. They found that the beta band was the best EEG band to classify emotion, with the emotion of sadness obtaining the highest classification. However, the classification accuracies for sadness using PNN were relatively low at around 60% for both stroke and unimpaired participants [33]. Furthermore, the authors did not directly investigate PSD patients and classify their EEG features with PSND patients or controls, leading to a lack of information on their actual or potential classification performance in early PSD diagnosis.

The other 14 studies investigated general depression. During the stage of EEG feature extraction, nine studies mainly applied nonlinear dynamic EEG measures, two studies applied band-based measures, and three studies applied other EEG features, such as synchronization likelihood and spectral-spatial EEG features. The majority of machine learning-based studies extracted EEG features with nonlinear dynamic measures. Four studies applied a single classifier to discriminate the EEG signals of normal and depressed patients. Acharya et al. [29] presented a method for automated EEG-based diagnosis of depression using the following nonlinear approaches: FD, DFA, LLE, SampEn, higher order spectra, Hurst's exponent, and recurrence quantification analysis. These features were fed to the SVM classifier and yielded an average classification accuracy of 98%. Puthankattil et al. [54] used ANN and relative wavelet energy to discriminate the EEG signals of normal controls from those of depressed patients. Ahmadlou et al. [52] utilized enhanced PNN for the classification of MDD and non-MDD EEGs via Katz's and Higuchi's FDs. They found that Higuchi's FDs of the beta band achieved a high accuracy of 91.3%. Kalatzis et al. [55] developed an event-related potential (ERP) and SVM classification system to discriminate depression, which achieved high classification accuracy. Some authors used multiple classifiers with multiple EEG features to obtain higher classification accuracy. Bairy et al. [56] applied five significant nonlinear features and four classifiers, and they found that the SVM classifier with a radial basis function obtained the highest classification accuracy. Faust et al. [57] utilized four nonlinear features and seven classifiers, and they reported that the PNN classifier had better performance than the other classifiers. Cai et al. [58] extracted a total of 270 linear and nonlinear features. They suggested that KNN with theta absolute power had the highest accuracy for classifying depression. In terms of feature selection, SampEn was reported by Čukić et al. [59] to have better performance than Higuchi's FD for seven classifiers. Meanwhile, Hosseinifard et al. [60] calculated the EEG powers and nonlinear features—DFA, LLE, Higuchi fractal, and correlation dimension—and used three classifiers to discriminate DPs and HCs. The authors concluded that combining multiple nonlinear features could enhance the performance of classification.

In contrast, Mohammadi et al. [61] used band power as an EEG feature. They mapped a new feature space via LDA and applied an algorithm to recognize the features that were most related. The DT algorithm was then used to discover rules and hidden patterns based on selected features; however, the classification accuracy (MDD vs. HCs) was only 80%. Duan et al. [13] used spectral power to calculate the asymmetry and cross-correlation of interhemispheric function, and they applied several classifiers (i.e., KNN, SVM, and CNN) to identify MDD. They found that using mixed features with CNN could achieve the best classification accuracy of 94.13%.

The final three studies applied other EEG features. After using three classic classifiers, Mumtaz et al. [62] verified that EEG-derived synchronization likelihood features could be a promising approach for detecting depression. In addition, Liao et al. [63] developed a kernel eigen-filter-bank common spatial pattern extractor (KEFB-CSP) to classify MDD patients and HCs via three common classifiers. An EEG classification accuracy of 81.23% was obtained when electrodes from the temporal areas and an SVM classifier were applied. The KEFB-CSP also outperformed other widely applied EEG features like spectral power and nonlinear fractal dimension [63]. It should also be noted that some studies did not require any separate features because the model could learn from obtained features during algorithm training. For instance, Sharma et al. [64] presented an EEG-based computer-aided hybrid neural network for depression screening. It used a CNN for temporal learning, and the developed hybrid method attained an accuracy of 99.10%.

Most EEG-based machine learning diagnostic studies examined in this review obtained a high classification accuracy in discriminating between DPs and HCs. A variety of machine learning classifiers, multiple EEG features, and their combinations were utilized, and high

Table 2
EEG-based machine learning studies on depression diagnosis.

Studies	EEG features	Sample size	Classifiers	Main findings
Kalatzis et al. [55]	ERP (P600)	Moderate: 25DP+25HC	SVM	When using all channels, the classification accuracy was 94%; when using right scalp channels, the classification accuracy was 92%; when using left scalp channels, the classification accuracy was 82%.
Ahmadlou et al. [52]	Wavelet-chaos methodology, Katz's and Higuchi's FD	Moderate: 12DP+12HC	Enhanced PNN	A high accuracy of 91.3% was achieved for MDD and non-MDD EEGs based on HFDs of the beta band.
Puthankattil et al. [54]	Relative wavelet energy	Moderate: 30DP+30HC	ANN	A classification accuracy of 98.11% was achieved.
Hosseinifard et al. [60]	Spectral power, DFA, Higuchi fractal, CD, LLE	Large: 45DP+45HC	KNN, LDA, and LR	A classification accuracy of 90% was obtained by the LR classifier with all nonlinear features.
Faust et al. [57]	ApEn, SampEn, REN, and Ph	Moderate: 30DP+30HC	PNN, SVM, DT, KNN, NBC, GMM, and FSC	PNN classifier achieved the best discriminating performance with a classification accuracy of 99.5%.
Mohammadi et al. [61]	Spectral power	Large: 53DP+43HC	DT	An average classification accuracy (MDD vs. HC) of 80% was achieved.
Bairy et al. [56]	SampEn, CD, FD, LLE, H, and DFA	Moderate: 30DP+30HC	DT, SVM, KNN, and NBC	The SVM classifier with radial basis function resulted in a classification accuracy of 93.8%.
Acharya et al. [29]	FD, LLE, SampEn, DFA, H, higher order spectra, and recurrence quantification analysis	Moderate: 15DP+15HC	SVM	The SVM classifier yielded an average classification accuracy of about 98%.
Liao et al. [63]	KEFB-CSP, band-specific CSP, GPFD, and spectral power,	Moderate: 12DP+12HC	SVM, KNN, and LDA	EEG classification accuracy of 81.23% was obtained with electrodes from the temporal areas and the SVM classifier.
Mumtaz et al. [62]	Synchronization likelihood features	Moderate: 34DP+30HC	SVM, LR, and NB	SVM classifier obtained the highest classification accuracy of 98%.
Cai et al. [58]	Adaptive predictor filter, discrete wavelet transformation, and Kalman derivation formula	Large: 92DP+121HC	SVM, KNN, CT, and ANN	The highest accuracy of 79.27% was obtained in KNN.
Wen et al. [33]	Higher order spectra	Moderate: 15DP+14HC	KNN and PNN	The beta band showed the best performance in emotion classification.
Čukić et al. [59]	Higuchi's FD and SampEn	Moderate: 23DP+20HC	MLP, LR, SVM, DT, Random Forest, and NB	The average accuracy among classifiers ranged from 90.24 to 97.56%.
Duan et al. [13]	Fusing interhemispheric asymmetry and cross-correlation	Moderate: 16DP+16HC	KNN, SVM, and CNN	CNN achieved the highest accuracy of 94.13% with mixed features.
Sharma et al. [64]	Hybrid neural network	Moderate: 21DP+24HC	CNN and LSTM	The developed hybrid CNN-LSTM model attained an accuracy of 99.10%.

Note: ANN=artificial feedforward neural networks, ApEn=approximate entropy, CNN=convolutional neural network, CD=correlation dimension, DT=decision tree, DFA=detrended fluctuation analysis, FD=fractal dimensions, FSC=Fuzzy Sugeno Classifier, GMM=Gaussian mixture model, GPFD=Grssberger and Procaccia fractal dimension, H=Hurst exponent, KEFB-CSP=kernel eigen-filter-bank common spatial pattern, KNN=k-nearest neighbor classifier, LLE=Largest Lyapunov exponent, LDA=linear discriminant analysis, LR=logistic regression, LSTM=long short-term memory, MLP=Multilayer Perceptron, NBC=naive bayes classification, PNN=probabilistic neural network classifier, Ph=bispectral phase entropy, REN=renyi entropy, SVM=support vector machine, SampEn=sample entropy.

classification accuracy and sensitivity were achieved. Among various classifiers, SVM seemed to be more prominent, as it presented the highest classification accuracy in several studies [29,56,62,63]. Noticeably, compared to classical spectral power, nonlinear features of EEG could increase the accuracy of all classifiers. This implied that the nonlinear dynamic features were more suitable in the machine learning-based depression diagnosis. Additionally, several studies suggested that the adoption of multiple features was beneficial for enhancing classification accuracy [13,60]. Therefore, the EEG-based machine learning diagnostic models could be a useful tool for psychiatrists to diagnose depression. Nevertheless, only one machine learning study related to PSD diagnosis was found, so more studies should be conducted to support potential early diagnosis of PSD.

4. EEG-based interventional studies

In addition to the depression diagnosis, EEG can also be applied to interventional studies for symptom management; for example, it can evaluate/predict the effects of interventions to ameliorate depression or act as a key biofeedback tool in the treatment design, like a brain-computer interface (BCI).

4.1. Evaluation/prediction studies on the intervention outcome

EEG could be used as a biomarker to evaluate the treatment effectiveness after an intervention, as well as for the prognosis phase. In this review, we did not specifically distinguish the literature on prediction and evaluation, since they were frequently combined. The EEG interventional studies were mainly delivered via cross-sectional designs based on responder analysis (comparing intervention responders and non-responders), comparisons of pre-/post-tests, or comparisons of different doses of the same intervention. Most literature focused on general depression treatment rather than PSD.

4.1.1. Evaluation/prediction studies with band-based approaches and nonlinear dynamic measures

In this review, 12 studies for the evaluation/prediction of intervention outcomes using nonlinear dynamic measures and/or band-based approaches were selected, and they are summarized in Table 3. In clinical practices, electroconvulsive therapy (ECT) and pharmacotherapy were the most widely applied interventions for depression.

Four studies used EEG changes to evaluate and predict the treatment effects of depression after ECT. In early research, one depressed patient who underwent ECT sessions to ameliorate the depression was

Table 3
Evaluation/prediction studies: main findings derived from band-based approach and nonlinear dynamic measures.

Studies	Frequency bands	Type of treatment	Studied areas	Measure	Main findings
Nandrino et al. [44]	Broadband	Pharmacotherapy	Frontal, central, and parietal	Informational (Correlation coefficient ρ)	After the intervention, first-episode depressed patients could achieve comparable levels to the controls.
Pezard et al. [48]	Broadband	Pharmacotherapy	Frontal, central, and parietal	Invariant (Kolmogorov-Sinai entropy), Informational (Information index S_0)	After the intervention, first-episode depressed patients could achieve comparable levels to the controls.
Thomasson and Pezard [65]	Broadband	ECT	All areas	Informational (Kolmogorov entropy)	Decreasing entropy from pre-test to post-test (high correlations with symptomatology reductions)
Gangadhar et al. [67]	Broadband	ECT	Frontal	Invariant (Katz FD)	The closest predictor for treatment effects was the post-seizure FD.
Jagadisha et al. [68]	Broadband	ECT	Frontal and temporal	Invariant (Katz FD)	Lower post-seizure FD was obtained in early responders than in late responders.
Lee et al. [69]	100Hz	Pharmacotherapy	Frontal temporal	Connectivity strength	Stronger connectivity strength indicated poorer treatment response.
Cavanagh et al. [71]	0.5–100 Hz	Probabilistic reinforcement learning task	Whole brain	EEG response to error feedback	Depressed participants had large EEG responses to error feedback.
Mendez et al. [46]	Broadband	Pharmacotherapy	All areas	Informational (LZC)	Younger participants had significantly decreased complexity in anterior areas.
Okazaki et al. [66]	Broadband	ECT	All areas	Informational (MSE)	Lower MSE (especially in lower scale factors)
Arns et al. [8]	α	rTMS + PSY	Frontal and occipital	Informational (LZC)	EEG complexity was decreased after the treatments.
Shahaf et al. [72]	δ	Pharmacotherapy	Frontal	Brain engagement index by EEG/ERP	It can detect treatment-resistant depression.
Jaworska et al. [70]	$\delta,\alpha,\theta,\beta,\gamma$	Pharmacotherapy	All areas	Informational (MSE)	At coarser temporal scales, MSE was increased diffusely; at fine temporal scales, MSE was decreased.

Note: ECT=Electroconvulsive therapy; PSY=Psychotherapy; rTMS=Repetitive transcranial magnetic stimulation. Nonlinear measures: DFA=Detrended fluctuation analysis; FD=Fractal dimension; LZC=Lempel Ziv complexity index; MSE=Multiscale entropy.

monitored [65]. The results showed a reduced EEG entropy after the ECT sessions and revealed that the relief of symptomatology was positively correlated with the decreased entropy [65]. The decreased entropy was further confirmed by Okazaki et al. [66]. They studied three patients with depression who received bilateral ECT, and all of them showed decreased multiscale entropy in the gamma oscillations, especially in multiscale entropy factor scales 1–5 [66]. In addition, Gangadhar et al. [67] studied the effects of bilateral ECT with different types on depressed patients. Their FDs were calculated via Katz's algorithm at three seizure EEG stages, i.e., early, middle, and post, respectively. They found the best biomarker to predict the ECT effect was the post-seizure FD. Jagadisha et al. [68] also used FD to investigate EEG fractal properties in early or late responders with depression during the first week of ECT (the sample with remitted symptoms). They observed that the post-seizure FDs of early responders to ECT were significantly lower than those of late responders. Meanwhile, the post-seizure FD and the percentage of symptom amelioration were closely correlated.

Five studies analyzed the pharmacotherapy benefits via EEG features. Nandrino et al. [44] and Pezard et al. [48] analyzed the effects of pharmacotherapy on inpatients with depression. Those inpatients showed decreased Kolmogorov–Sinai entropy, Kolmogorov complexity, and correlation coefficient ρ (broadband up to 40 Hz). The treatment effects of taking six months of mirtazapine via informational properties of brain oscillations were investigated by Mendez et al. [46]. A significantly declined LZC was achieved by younger participants, reaching levels similar to those seen in the control group. Lee et al. [69] designed an experiment to predict the treatment response of medication (selective serotonin reuptake inhibitors, SSRIs) for MDD. They advised that connectivity strength in the frontotemporal region might be a promising predictor to categorize the responders and non-responders with MDD. Jaworska et al. [70] compared the multiscale entropy before and after 12 weeks of anti-depressive treatment among responders, non-responders, and controls. They found that the anti-depressive treatment effects for responders were characterized as decreased mental state examination (MSE) on fine temporal scales and augmented MSE on coarser temporal scale diffusely. Moreover, the combination of pharmacotherapy and repetitive transcranial magnetic stimulation (rTMS) was studied. Méndez et al. [46] investigated the effect of an intervention delivering rTMS alongside psychotherapy via nonlinear features in alpha band. The results showed that treatment responders obtained decreased LZC in frontal and occipital areas, whereas there was no difference in LLE levels (7–12 Hz).

Two pure EEG-based evaluation studies for depression were also examined. One study compared the neural responses during probabilistic reinforcement learning tasks between MDD patients without medication and HCs via ERP analysis, to examine their cognitive and sensory functions [71]. The authors investigated the EEG responses to error feedback and calculated time-frequency measures for spectral bands, which demonstrated selective alteration of avoidance learning [71]. Another study used auditory oddball stimuli to develop a novel electrophysiological attention-associated biomarker [72]. They calculated the average ERP and brain engagement index of the delta band from a single channel using 1-min samples and successfully utilized these EEG features to recognize treatment-resistant depression in the early stage [72].

All of the above studies concluded that the EEG profiles, especially dynamic complex features, could examine the benefits of interventions for ameliorating depressive symptoms. The reason behind this is that dynamic complex EEG features could reveal the nonlinear dynamic system characteristics in the brains of patients with depression.

4.1.2. Evaluation/prediction studies using machine learning models

In the previous sections, we introduced machine learning-based investigations on the automatic diagnosis of depression. The related techniques could also be used to evaluate and predict the effects of interventions for depression. Five studies in this category were reviewed, and they are summarized in Table 4.

Three of them applied machine learning to predict the pharmacotherapy outcomes for depression via both spectral and nonlinear measures. Khodayari-Rostamabad et al. [73] probed the power spectral densities and magnitude coherences with a mixture of factor analysis

Table 4
Machine learning-based evaluation/prediction studies on depression.

Studies	Type of treatment	Measure	Classifiers	Main findings
Khodayari-Rostamabad et al. [73]	Pharmacotherapy	Power spectral densities and magnitude coherences	MFA	The overall classification accuracy was 87.9%.
Erguzel et al. [75]	rTMS	EEG cordance: absolute and relative power	BPNN, GA	The outcomes of the proposed approach indicated increased overall accuracy of 89.12% using the reduced feature set.
Mumtaz et al. [21]	Pharmacotherapy	Wavelet transform analysis	LR	The antidepressant's treatment outcome could be predicted by wavelet coefficients in delta and theta bands from frontal and temporal regions.
Al-Kaysi et al. [76]	tDCS	Power spectral density	SVM, ELM, and LDA	The predictive rate of mood was 80%, and the rate of cognition labels was 100%.
Jaworska et al. [74]	Pharmacotherapy	Source-localized current density and scalp-level EEG power	RF	A high predictive utility with 88% accuracy was achieved when included all features.

Note: ANN=artificial neural network; BPNN=back-propagation neural network; CT=classification trees; ELM=extreme learning machine; GA=genetic algorithm; KPLSR=kernelized partial least squares regression; KNN=K-Nearest Neighbor; LR=logistic regression, LDA=linear discriminant analysis; MFA=mixture of factor analysis; rTMS=repetitive transcranial magnetic stimulation; tDCS=transcranial direct current stimulation.

(MFA) and obtained an 87.9% overall prediction accuracy. Mumtaz et al. [21] used wavelet transform analysis and an LR classifier to predict the treatment outcomes for MDD patients. Frontal and temporal pre-treatment EEG data of the delta and theta bands were reported to hold considerable promise for depression treatment prediction. In addition, Jaworska et al. [74] applied both EEG power and source-localized current density as EEG features in an RF classifier. They found that the predictive utility could be as high as 88% when all features were included. Two studies investigated other types of depression treatment. Erguzel et al. [75] utilized EEG absolute and relative power to examine the optimal classification methods for MDD patients treated by rTMS, while Al-Kaysi et al. [76] predicted the effect of transcranial direct current stimulation (tDCS) treatment on MDD participants via power spectral density. The abovementioned studies validated that EEG-based machine learning not only could be useful to predict and monitor the treatment outcomes and recovery pace but also could be used to screen the treatment responders, with high classification and prediction accuracies.

Although promising results have been obtained with potential biomarkers via both EEG features and machine learning models, all of the current EEG-based depression studies on interventional evaluation/prediction targeted MDD patients, whereas the usage of those approaches for PSD patients was scarce.

4.2. EEG-based BCI intervention for emotion training

BCI systems provide a window to decode brain dynamics in real-time, allowing us to interact with the brain environment using control signals generated solely by brain activities [77]. BCI interventions have been widely used in post-stroke motor rehabilitation and cognitive training. For instance, in motor rehabilitation, BCI systems have been used to decode patients' intentions for motor actuation [78]. Then, these decoded intentions will be utilized to provide patients with various forms of contingent sensorimotor feedback, such as visual feedback, haptic feedback, and actual movement. In cognitive training, BCI systems have been applied to increase patients' attention index, such as prefrontal beta and theta powers [79]. Interestingly, BCI interventions for both cognitive and motor trainings have been shown to improve motivation and affect the nervous system, which might further contribute to ameliorating PSD [5,79–81]. It was reported that the performance of BCI was associated with the patients' motivation and interest [5]. Increased emotional scores were also observed after several sessions of neurofeedback-based cognitive training [79–81]. This is because there are complex interactions between post-stroke affect, cognitive, and motor deficits. BCI intervention may help patients regain their willingness and motivation for rehabilitative therapy, and these are the keys to their cognitive and motor improvements. Since a major symptom of depression is a low level of motivation, BCI intervention could be an alternative treatment for PSD.

Although BCI-based depression training treatment for stroke patients has seldom been designed and practiced, some BCI-based forms of emotion training have been applied to MDD patients [82,83]. In this review, two BCI-based studies on emotion training for major depression were examined. Zotev et al. [82] designed a form of real-time neurofeedback training for emotional self-regulation by targeting the activation of the amygdala. During a happy emotion induction task, patients learned to upregulate their blood oxygenation level-dependent activity of the left amygdala using real-time fMRI neurofeedback. The EEG asymmetry results indicated that the training targeting the amygdala was beneficial for MDD patients. Another form of emotion mediation with a non-invasive brain stimulation-based system was proposed by Ehrich et al. [83]. They established a closed-loop interaction between the participants' brain responses and the musical stimuli, enabling participants to intentionally regulate musical feedback through self-induced emotions [83]. Both studies succeeded in real-time self-emotional regulation via BCI systems, thereby providing references for the BCI-based emotion training for PSD.

5. Future research directions

After reviewing the recruited EEG-based diagnostic and interventional studies, we found that both EEG detections and interventions have been widely applied in MDD patients. The feasibility and efficacy of using EEG features to diagnose, evaluate, and predict depression or directly act as a regulator have been supported by various MDD studies. However, EEG studies for PSD patients were mainly in the diagnostic stage rather than the interventional stage. Although PSD and MDD share similar behavioral symptoms, their different pathophysiology could result in varied EEG features. PSD is mainly caused by brain lesions related to loss of neural tissues that disrupt aminergic pathways, or neural circuits, involved in mood regulation, as a result of a combination of biological (brain lesion, disruption of neural circuits & neurochemicals), psychological (presence of poor coping skills) and social factors (disability, limited social support, loss of independence) [1]. On the other hand, MDD usually is the consequence of altered endocrine function, diminished neurotransmission, and brain connectivity [84], activated by long-term emotional distances or stressful events. Thus, although the EEG patterns of PSD and MDD could be similar with the same representative frequency bands in alpha/beta bands, they could also differ in neural complexity, e.g., low complexity in PSD versus high complexity in MDD. The methods for EEG evaluation of MDD could be applied to PSD, once the respective signal features, or patterns, are well identified. Based on the current PSD research, several future research directions can be provided.

5.1. EEG studies on PSD diagnosis

Understanding the differences in EEG features among post-stroke patients with/without depression and HCs is the first step in exploring the potential for treatment. The following are some suggestions in the field of PSD detection.

First, there was no single superior EEG feature for PSD detection; both linear and nonlinear EEG features could reveal the abnormal neural responses of PSD patients from different aspects. The combination of multiple measures is thus recommended to gain a more comprehensive understanding of neural responses for PSD [47]. Second, the neural complexity of PSD should be further investigated, since different patterns in neural complexity were observed in PSD and MDD patients in the literature. Only one study found low neural complexity in PSD patients, whereas high neural complexity was observed in most studies on MDD patients. Third, investigations of brain oscillations with nonlinear features should be linked with investigations of functional connectivity, as increased functional connectivity could act as a biomarker of disorganization, which is reflected in the increased randomness/complexity of the EEG. Finally, future research should pay attention to widespread complexity alterations of the whole brain rather than specific brain areas such as parietal or temporal lobes. The brain oscillation system should be treated as a whole system that is affected by PSD [19].

5.2. EEG-based machine learning for PSD diagnosis and treatment evaluation

In recent decades, the use of machine learning for automatically classifying the desired discrimination tasks has become increasingly popular. Machine learning for depression diagnosis and its treatment evaluation has achieved high classification accuracy in various MDD studies, which is of great clinical significance. On the contrary, machine learning has not been well investigated for PSD diagnosis and treatment evaluation. The only EEG-based machine learning study for PSD found in the literature could not be applied to categorize the emotion states in PSD patients yet [33]. Therefore, machine learning investigations via EEG should be further explored with the target of PSD diagnosis and treatment evaluation.

Based on current machine learning studies on the MDD population, several challenges, from both statistical and methodological aspects, could be generalized for the machine learning-based prediction of clinical outcomes and should be addressed in future research. First, the sample sizes of current studies were relatively small, and the samples were commonly recruited from one clinical site, which might affect the models' generalizability. This problem could be solved by collecting more data, starting collaborative projects, using wireless EEG caps, or sharing regular medical check-up data. Second, most studies reported a classification accuracy above 90%; however, they did not provide solid evidence regarding the verification of the models' reliability or internal and external validation [22]. Third, there was a problem of model generalizability, which is the ability of a model that was trained on one dataset to predict patterns in another unseen dataset. Fourth, overfitting was common in the model development. Overfitting occurs when "a developed model perfectly describes the overall aspects of the training data, resulting in fitting error to asymptotically become zero" [85]. Then, it will be difficult for the model to make predictions on unseen (test) data.

5.3. Integrated EEG-based PSD intervention

The current BCI-based post-stroke treatments mainly concentrated on motor and cognitive recovery, whereas few interventions were delivered for emotion deficits such as PSD. In those studies of motor and cognitive recovery, several limitations could be pointed out. For instance, in neurofeedback therapy, few studies have addressed feedback timing and the modality (e.g., visual, robotic, and neuromuscular electrical stimulation), despite them being key factors in determining the effectiveness of a form of therapy. The effectiveness of an intervention may also be improved by adaptation, personalization, and fine-tuning. Moreover, the treatment effectiveness could be enhanced by adjusting the intensity, frequency, and dosage of the treatment, which should be further investigated. Furthermore, sample sizes should be increased to facilitate comparison across different studies.

There are complex interactions between affect, cognitive, and motor deficits after stroke. For example, their relationships will affect the overall outcomes of post-stroke rehabilitation. Instead of separating motor, affect, and cognitive training, we propose that future rehabilitation plans should include training sessions in all three aspects and pay attention to the improvement in each of them. An integrated and holistic form of treatment might obtain additional functional improvements due to the synergies among the affect, cognitive, and motor systems. The relationship among these deficits is critical in designing a future integrated rehabilitation plan; however, this approach has not been well investigated in the current literature.

Some integrated rehabilitation studies without EEG technologies have been reported. A case study by Van Derwerker et al. [86] combined aerobic exercise and rTMS for stroke survivors with PSD. All the recruited patients finished the treatments with good compliance and obtained improved walking capacity and relief of depression symptoms. Barbarulo et al. [87] proved the feasibility of an integrated cognitive and neuromotor rehabilitative program on emotional, cognition, balance, and walking functions for patients with multiple sclerosis, demonstrating robust positive effects in the cognitive, motor, and emotional components.

An EEG-based BCI system could serve as a common platform that could simultaneously target the multiple deficits of stroke by invoking the implicit relationship among the motor, cognitive, and affect functions. Studies have provided evidence that EEG-based BCI training could promote changes in neuroplasticity, which has been applied to improve stroke-induced deficits. However, few integrated intervention studies, such as case studies, have applied EEG. In a case study by Putman [88], a post-stroke patient received EEG biofeedback training, with its protocols including sensorimotor rhythm enhancement, theta suppression, and beta enhancement. The patient showed significant improvement in motor ability and speech, in addition to restored mood stability. Therefore, as a future direction, more EEG-based integrated intervention studies of post-stroke patients via clinical trials considering motor, cognitive, and affect functions should be conducted.

5.4. Integration of EEG-based diagnosis and intervention

EEG could be applied to both PSD diagnosis and interventional outcome evaluation. It is noted that diagnosis studies mainly used frequency and nonlinear dynamic measures, while intervention studies mainly adopted nonlinear dynamics and other measures (e.g., EEG engagement index). However, the current EEG-based diagnosis/evaluation of MDD or PSD has not been widely accepted in the routine clinical practices. One reason could be that the relevant EEG technologies are still under development, e.g., validation of standard measures for diagnosis and intervention via clinical trials. Another reason is that cross-disciplinary expertise (e.g., neurology, engineering, etc.) is required for the implementation of EEG diagnosis and evaluation in the routine practices for acquiring, processing EEG, and interpreting it with clinical meanings. However, it takes time to establish collaboration across the disciplines and to nurture the related professionals. In future studies, the integration of EEG-based diagnosis and intervention outcome evaluation could be a promising direction.

5.5. Integration of EEG and other modality imaging technologies

Multi-modality neuroimaging technologies have been applied to investigate the neurological changes in MDD. Sheepens et al. [89] provided a review of multi-modal neuroimaging studies that revealed abnormalities in brain structure and function in patients with depression. For instance, Knyazeva et al. [90] used fMRI and EEG, Köhler-Forsberg et al. [91] collected data from PET, fMRI, and EEG, and Zhang et al. [92] applied EEG and NIRS in relevant MDD studies. However, multimodality neuroimaging technologies have seldom been applied and reported for PSD. The future direction of PSD studies should also emphasize the integration of EEG and other imaging technologies on PSD, which could yield more detailed information about brain dynamics.

6. Conclusion

This study reviewed the current clinical applications of EEG for PSD. EEG-based studies related to the diagnosis, prediction, evaluation, and/or treatment of PSD and MDD were examined. EEG features analyzed by both band-based and nonlinear dynamic approaches were capable of quantifying abnormal neural responses on the cortical level for PSD diagnosis and treatment evaluation/prediction. Meanwhile, machine learning has been applied to depression diagnosis and evaluation and shows promising potential. Based on the current PSD research, future research directions have been pointed out. However, several challenges from both methodological and statistical aspects should be addressed in future EEG studies on PSD diagnosis and treatment. Additional investigations are necessary to understand the cortical responses of PSD and thereby improve its diagnosis and precision treatment. Future post-stroke rehabilitation plans should include training sessions for affect, cognitive, and motor functions and closely monitor their putative improvements. Finally, BCI emotional training could be effective and beneficial when directly applied to PSD.

Declaration of Competing Interest

The authors declare no competing interests related to this study.

CRediT authorship contribution statement

Bibo Yang: Writing – original draft, Writing – review & editing. **Yanhuan Huang:** Writing – original draft, Writing – review & editing. **Zengyong Li:** Writing – review & editing. **Xiaoling Hu:** Writing – review & editing, Conceptualization, Funding acquisition.

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