

Original Research

Multiscale Neurodynamic Alterations in Major Depressive Disorder Revealed by Lempel–Ziv Complexity of Multi-Paradigm Resting-State EEG

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Academic Editor: Bettina Platt

Submitted: 11 March 2026 Revised: 20 May 2026 Accepted: 11 June 2026 Published: 27 October 2026

Abstract

Background: Electroencephalography (EEG) abnormalities in major depressive disorder (MDD) have predominantly been examined through single-frequency band analyses or single-scale nonlinear measures, and largely within a single resting-state paradigm, which limits the characterization of regulatory interactions across temporal scales. In this study, we investigated dynamic transitions and integrative patterns of multiscale EEG activity in MDD across multiple resting-state paradigms, with a focus on characterizing alterations in multiscale neural dynamic organization. **Methods:** Based on multiscale Lempel–Ziv Complexity (LZC), we derived two classes of features quantifying the Scale-Dependent Variation Slope and the Cross-Scale Correlation Coefficient. Resting-state EEG from the MDD Patients and Healthy Controls EEG Data (MPHC) was analyzed under eyes-open and eyes-closed conditions to compare multiscale regulatory dynamics between patients with MDD and healthy controls. **Results:** Patients with MDD showed impaired complexity transitions from low to high frequencies and disrupted delta-centered cross-scale integration. Distinct coupling reconfiguration patterns emerged across resting states, indicating a systemic imbalance in multiscale integrative organization. Classification models built from statistically selected features performed consistently across Support Vector Machine, K-Nearest Neighbor, and Decision Tree algorithms, reaching a maximum accuracy of 85.71% with a balanced sensitivity–specificity profile. Convergent results across models further suggested the preliminary discriminative value of the proposed features within the present dataset. **Conclusions:** These findings provide a preliminary multiscale neurodynamic framework for EEG characterization in MDD and suggest that cross-scale integration differences may provide a quantitative basis for characterizing multiscale EEG dynamics in depression.

Keywords: electroencephalography; major depressive disorder; resting-state; nonlinear dynamics

1. Introduction

Depression remains a major global health challenge and is among the leading causes of disability worldwide [1]. Therefore, timely and accurate diagnosis is essential, as early identification and intervention are associated with improved treatment outcomes [2]. Current diagnostic practice, however, relies mainly on symptom-based criteria and clinician-administered assessments, and substantial heterogeneity exists in how patients meet diagnostic thresholds, which may undermine reliability and consistency [3]. These limitations underscore the urgent need for objective, biologically grounded assessment tools. Electroencephalography (EEG), a non-invasive direct measure of neural activity, shows considerable promise for identifying neurophysiological biomarkers of depression [4]. Its high temporal resolution enables dynamic characterization of brain function, potentially overcoming the static and subjective constraints of traditional diagnostic frameworks.

In recent years, EEG has shown substantial progress in the diagnostic assessment of major depressive disorder (MDD), with increasing application of machine learning techniques to characterize aberrant neural dynamics. For example, Mulc et al. [5] analyzed EEG recordings from patients with major depressive disorder and healthy controls using various machine learning models, reporting classification accuracies of up to approximately 80%. Beyond overall classification performance, converging evidence indicates that alterations in specific frequency bands may serve as neurophysiological biomarkers of depressive states. In particular, Liu et al. [6] investigated spectral power and hemispheric asymmetry across multiple frequency bands in resting-state EEG, finding that beta-band subcomponents (e.g., 16–24 Hz and 24–40 Hz) in prefrontal, occipital and frontal regions, as well as interhemispheric asymmetries, were significant predictors of MDD, reflecting disorder-related neurophysiological dysfunction.



EEG signals are inherently complex, nonlinear, and nonstationary, and conventional linear spectral analysis methods (e.g., power spectral analysis) often fail to fully capture their dynamic behavior [7]. Nonlinear measures quantify signal complexity and irregular dynamics, offering insights into the neurophysiological mechanisms underlying MDD and revealing abnormal EEG activity patterns associated with the disorder [8]. Common nonlinear indices such as Lempel–Ziv Complexity (LZC), Higuchi’s fractal dimension (HFD), detrended fluctuation analysis (DFA), sample entropy, approximate entropy, and wavelet entropy, have all been employed to differentiate patients with MDD from healthy controls (HC) through machine learning classifiers [9]. For example, Bachmann et al. [10] conducted classification analyses based on single-channel EEG recordings using a range of linear and nonlinear features. The highest classification accuracy achieved by an individual nonlinear method was approximately 77%. When two nonlinear indices were combined, the accuracy increased to 85%. The integration of both linear and nonlinear features further improved performance, yielding a classification accuracy of approximately 92%. Saeedi et al. [11] employed wavelet packet decomposition to extract nonlinear features, including sample entropy and approximate entropy, for classification analysis. The results demonstrated a classification accuracy of 94.2%, which outperformed the frequency-based feature approach that yielded an accuracy of 91.3%. Collectively, these findings indicate that nonlinear features exhibit a distinct advantage in capturing depression-related alterations in brain activity.

As a representative nonlinear complexity measure, LZC has been widely used to characterize the temporal structure and information content of EEG signals. Conventional EEG biomarkers, such as spectral power measures and entropy-based indices, typically quantify specific aspects of neural activity, including oscillatory amplitude within predefined frequency bands or signal irregularity over time. In contrast, LZC quantifies the emergence of new patterns within a signal sequence, thereby providing an index of dynamical variability and the diversity of neural information processing [12]. Functional connectivity metrics provide complementary information by describing statistical relationships between distributed brain regions; however, they do not directly reflect the intrinsic temporal organization of local neural signals. Owing to its ability to capture the evolution of temporal patterns in a model-free manner, LZC offers a concise and computationally efficient representation of neural dynamics that is well suited for clinical EEG analysis [13]. Evidence from recent studies of major depressive disorder supports the discriminative capability of this feature. For example, Yang et al. [14] extracted four EEG features—LZC, power spectral density (PSD), sample entropy (SE), and Kolmogorov complexity (KC)—from both eyes-open and eyes-closed resting-state EEG recordings. Among these single EEG features, LZC

achieved the highest classification accuracy of 91.36% under the eyes-open condition.

MDD is associated with abnormal brain activity spanning multiple frequency bands from delta to gamma oscillations [15]. Nonlinear features derived at a single scale are therefore insufficient to comprehensively characterize the complex cross-frequency dynamics underlying the disorder. For example, when traditional LZC is computed at a single time scale, particularly under conditions dominated by low-frequency components, it may fail to adequately capture high-frequency information, thereby limiting its capacity to represent intricate brain dynamics [16]. Moreover, the neurophysiological manifestations of depression are often reflected in dynamic alterations across hierarchical neural networks, which cannot be fully captured by single-scale metrics. To overcome these limitations, growing research attention has focused on multiscale analytical methods represented by Multiscale Lempel–Ziv complexity (MLZC). This approach enables the quantification of EEG signal complexity at multiple temporal scales and enhances the detection sensitivity of high-frequency components. Kaley et al. [16] reported that incorporating high-frequency information enabled MLZC to achieve superior performance in distinguishing depressed patients from healthy controls. Furthermore, Xu et al. [17] achieved highly accurate detection of depression based on two types of multiscale entropy, thereby providing additional evidence for the advantage of multiscale analytical strategies in capturing complex brain dynamics.

In research on diagnostic biomarkers of MDD, the resting-state paradigm has been widely adopted due to its low task demands, ease of implementation, and ability to capture spontaneous neural activity [18]. In clinical populations, resting-state EEG minimizes performance-related confounds and reflects intrinsic brain dynamics that may index trait-like neurophysiological alterations. However, most studies involving MLZC have relied on a single resting-state paradigm (e.g., eyes-closed), thereby overlooking potential state-dependent modulation effects between eyes-open (EO) and eyes-closed (EC) conditions. Substantial neurophysiological evidence indicates that EO and EC paradigms differ significantly in visual input, attentional engagement, and baseline oscillatory activity [19]. Moreover, EEG studies suggest that depression is associated with alterations in large-scale brain network dynamics [20], which may become more pronounced during condition-dependent modulation or state transitions. Therefore, integrating EO and EC paradigms and systematically comparing MLZC patterns across resting-state conditions may offer novel insights into state-dependent neural dysfunction in MDD and improve the characterization of its context-sensitive neurophysiological signatures.

Based on the above considerations, the present study systematically investigated scale-dependent dynamic patterns of MLZC under both EO and EC resting-state

paradigms for the identification of MDD. Specifically, we examined MLZC profiles across multiple cortical regions in patients with MDD and HC, focusing on scale-related variations in complexity. To characterize these multiscale dynamics, we introduced two novel features: the Scale-Dependent Variation Slope (SDVS), quantifying the slope of MLZC variation across scales, and the Cross-Scale Correlation Coefficient (CSCC), capturing inter-scale coordination patterns of complexity fluctuations. Statistical testing was employed to identify frequency-scale intervals with significant discriminative power. Furthermore, multiple classification models—including Support Vector Machine (SVM), K-nearest neighbors (KNN), and Decision Tree (DT)—were comparatively evaluated to elucidate potential abnormal patterns of MDD across distinct resting-state conditions.

The principal contributions of this study can be summarized as follows:

(1) From the perspective of multiscale complexity gradients, this study proposes the SDVS to quantify the dynamic modulation of EEG complexity across frequency scales, thereby expanding the analytical scope of conventional frequency-domain power analysis.

(2) This study further constructs the CSCC to systematically characterize the statistical dependency structure among different temporal scales, providing a novel quantitative index for examining cross-scale integration abnormalities in MDD.

(3) By adopting a dual resting-state fusion strategy that integrates EO and EC conditions, this study evaluates the complementarity of multiscale dynamical features under distinct functional backgrounds and further validates the effectiveness of the SDVS and CSCC features.

(4) Finally, this study establishes a unified analytical framework from the perspective of multiscale neural dynamic integration, offering a new methodological avenue for objective EEG-based identification of MDD and for investigating its underlying neurophysiological mechanisms.

2. Materials and Methods

2.1 Dataset and Data Preprocessing

The MDD Patients and Healthy Controls EEG Data (MPHC) (https://figshare.com/articles/EEG_Data_New/4244171) [21] used in this study was collected by the Centre for Intelligent Signal and Imaging Research (CISIR) at Universiti Teknologi PETRONAS, Malaysia. The dataset comprises resting-state EEG recordings from 34 patients with MDD (17 males and 17 females; mean age = 40.3 ± 12.9 years) and 30 HC (21 males and 9 females; mean age = 38.3 ± 15.6 years). No significant difference in age distribution was observed between the two groups. All MDD participants met the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV). EEG data were recorded under resting-state conditions, including EO and EC paradigms, each last-

ing 5 minutes. During acquisition, participants were seated in a semi-reclined position. EEG signals were recorded from 19 scalp electrodes positioned according to the International 10–20 System, with a sampling rate of 256 Hz.

The electrode configuration is illustrated in Fig. 1. Raw EEG data were preprocessed using EEGLAB 2022.0 (Swartz Center for Computational Neuroscience, Institute for Neural Computation, University of California San Diego, La Jolla, CA, USA) [22]. Bad channels were identified through visual inspection of the signal waveforms and subsequently interpolated with the average of neighboring electrodes. The data were then re-referenced to the common average reference. A finite impulse response (FIR) filter was applied with a high-pass cutoff at 0.1 Hz and a low-pass cutoff at 45 Hz to remove slow drifts and high-frequency noise, including power line interference. Independent component analysis (ICA) was further performed to eliminate ocular, muscular, and other physiological artifacts. Finally, residual noisy segments were manually rejected after visual inspection.

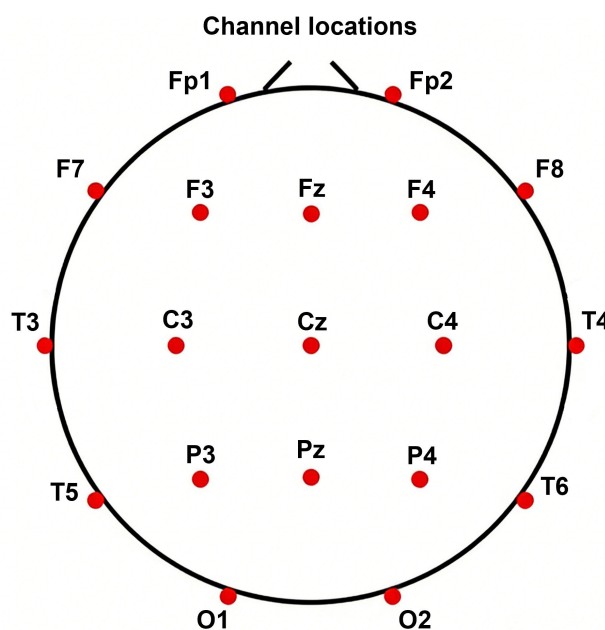


Fig. 1. Nineteen-channel brain electrode distribution map. The scalp locations of the 19 EEG electrodes used in this study are shown according to the International 10–20 System. The electrode montage includes frontal, central, temporal, parietal, and occipital channels, which were used for whole-brain MLZC calculation and subsequent regional analyses. Fp, frontopolar; F, frontal; C, central; T, temporal; P, parietal; O, occipital; z, midline; EEG, electroencephalography; MLZC, Multiscale Lempel–Ziv Complexity.

After preprocessing and denoising, subjects with incomplete EO/EC recordings and insufficient data lengths were excluded. The final dataset consisted of 25 healthy controls and 24 patients with MDD, each contributing 4

minutes of EO and 4 minutes of EC resting-state data. All recordings were segmented into non-overlapping 10-second epochs, corresponding to 2560 sampling points per segment. For MLZC estimation, this epoch length provides a sufficiently long sequence for complexity calculation while preserving an adequate number of segments for stable subsequent analysis. The use of non-overlapping epochs further reduces redundancy and statistical dependence between adjacent segments. This segmentation strategy is consistent with previous resting-state EEG MLZC research [23]. This procedure yielded 600 EO and 600 EC segments for the control group, and 576 EO and 576 EC segments for the MDD group.

Based on the International 10–20 System, the scalp electrodes were grouped into anatomically defined brain regions to facilitate whole-brain and region-specific analyses, as summarized in Table 1.

Table 1. Brain region division based on the International 10–20 System.

No.	Brain region	Channels
1	Frontal	Fp1, Fp2, F3, F4
2	Temporal	F7, F8, T3, T4, T5, T6
3	Central	C3, C4, Fz, Cz, Pz
4	Parietal-occipital	P3, P4, O1, O2

Based on the International 10–20 System, electrodes were grouped into frontal, temporal, central, and parietal-occipital regions to facilitate both whole-brain and region-specific analyses. The parietal and occipital electrodes were analyzed jointly because both are located over posterior cortical areas and can be considered within a broader posterior scalp region in scalp-level EEG topographic analyses. Functionally, however, these regions are not always interchangeable: the occipital cortex is primarily involved in visual processing, whereas the parietal cortex contributes to spatial integration and attentional regulation. Neuroimaging evidence has shown that the occipital and parietal cortices are jointly engaged in visuospatial processing, yet they play complementary rather than identical functional roles [24]. Accordingly, the combined parietal-occipital region was adopted in this study to provide a regional summary of posterior scalp activity, without implying strict functional equivalence between these two cortical areas. This regional grouping is also consistent with previous resting-state EEG research under EO and EC conditions, in which parietal and occipital electrodes were analyzed within posterior scalp regions [19].

2.2 Multiscale Nonlinear Feature Extraction

MLZC features were extracted in order to characterize the evolution of EEG signal complexity across temporal scales. LZC, a widely used measure of sequence complexity [25], was computed at multiple temporal scales follow-

ing the multiscale framework described in previous EEG studies [26].

For each EEG time series $X(t)$, a set of 45 temporal scales was defined. At scale k , the window length w_k was determined as:

$$w_k = \left\lceil \frac{f_s}{k} \right\rceil \quad (1)$$

where f_s denotes the sampling frequency. If the resulting w_k was even, it was increased by one to ensure an odd window length.

For each time point, a symmetric sliding window of length w_k centered at the current sample was applied. The median value within the window was used as the adaptive threshold:

$$T_k(n) = \text{median}\{X(n - \lfloor w_k/2 \rfloor : n + \lfloor w_k/2 \rfloor)\} \quad (2)$$

The signal was then transformed into a binary sequence:

$$Y_k(n) = \begin{cases} 1, & X(n) \geq T_k(n) \\ 0, & X(n) < T_k(n) \end{cases} \quad (3)$$

LZC was subsequently calculated for each binary sequence via the classic incremental parsing algorithm proposed by Lempel and Ziv [25]. In this approach, the complexity index is defined by the number of distinct substrings identified during sequential scanning. To minimize the influence of sequence length on complexity estimation, the raw LZC value c_k was normalized as:

$$NLZC_k = \frac{c_k}{N/\log_2 N} \quad (4)$$

where N denotes the length of the binary sequence at scale k .

Repeating this procedure across all 45 scales yielded a scale-dependent MLZC profile for each EEG channel, which was used for subsequent feature construction and visualization.

2.3 Extraction of Cross-Scale Features

To intuitively illustrate the whole-brain spatial distribution of MLZC, scalp topographic maps of mean LZC values were constructed for each of the 45 scales derived in the analysis. Then representative scales corresponding to the central frequencies of canonical EEG frequency bands were selected to characterize the spatial distribution patterns of neural complexity within each band. Specifically, scales 3, 6, 10, 20, and 35 were chosen as seed scales to represent

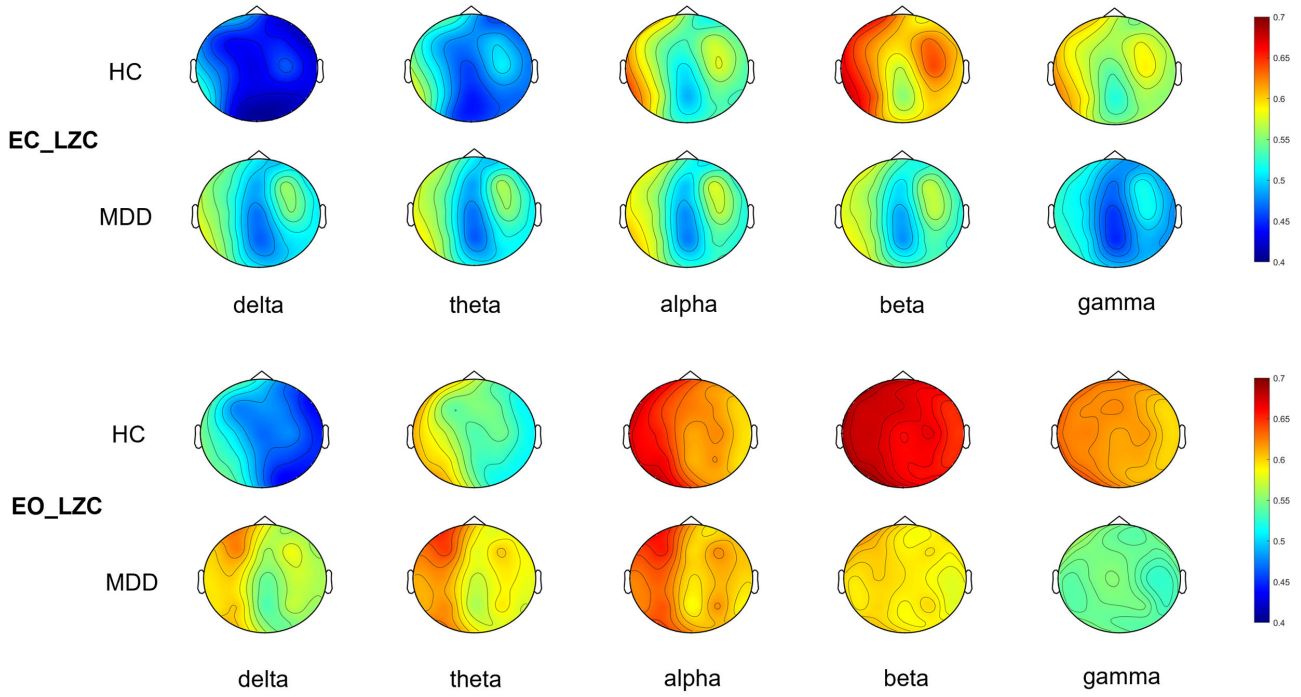


Fig. 2. Mean LZC topographic maps at representative scales under EO and EC conditions. From left to right, maps correspond to representative scales 3, 6, 10, 20, and 35, representing the delta (1–4 Hz), theta (5–8 Hz), alpha (9–13 Hz), beta (14–30 Hz), and gamma (31–45 Hz) bands, respectively. The upper and lower panels show the EC and EO conditions, respectively. Within each condition, the upper row represents the HC group and the lower row represents the MDD group. Each map illustrates the scalp distribution of group-averaged LZC values at the corresponding scale. Warmer colors indicate higher LZC values, whereas cooler colors indicate lower LZC values. The color scale was fixed across maps to facilitate direct visual comparison of spatial complexity patterns across groups and conditions. LZC, Lempel–Ziv Complexity; EO, eyes-open; EC, eyes-closed; HC, healthy controls; MDD, major depressive disorder.

the delta (1–4), theta (5–8), alpha (9–13), beta (14–30), and gamma (31–45) frequency bands, respectively. The corresponding mean LZC topographies are presented in Fig. 2. This visualization approach facilitates whole-brain comparisons of spatial complexity distributions across frequency bands and provides an intuitive foundation for subsequent quantitative analyses.

When comparing group differences at individual scales, distinct scale-dependent patterns were observed between the MDD and HC groups. At lower scales (corresponding to delta and theta bands), LZC values in the MDD group were generally higher than those in the HC group. In contrast, at higher scales (e.g., beta and gamma bands), the MDD group exhibited overall lower LZC values relative to HC. These findings indicate that information derived from a single scale may provide only limited insight into group differences. Notably, both the MDD and HC groups demonstrated a non-monotonic trend across temporal scales: LZC values initially increased and then gradually declined as the scale number rose. However, the patterns of increase and subsequent decrease differed between groups under both EO and EC paradigms. Specifically, MLZC variations across scales appeared relatively stable in the MDD group, whereas the HC group exhibited more

pronounced scale-dependent fluctuations. To quantitatively characterize these dynamic changes, SDVS features were constructed to capture the slope of MLZC variation across scales. Two multiscale slope indices were defined: the Rising Slope (RS) and the Falling Slope (FS).

(1) The RS reflects the slope from low scales to the scale at which the peak MLZC value occurs, thereby characterizing the stability of neural regulatory capacity during the ascending phase of scale-dependent complexity modulation.

$$RS = \frac{LZC_{peak} - \min(LZC_{1:peak-1})}{peak - \arg\min(LZC_{1:peak-1})} \quad (5)$$

(2) The FS reflects the slope from the peak-value scale to higher scales, thereby characterizing the stability of neural regulatory capacity during the descending phase of scale-dependent complexity modulation.

$$FS = \frac{LZC_{peak} - \min(LZC_{peak+1:end})}{\arg\min(LZC_{peak+1:end}) - peak} \quad (6)$$

In the above formulations, RS and FS denote the Rising Slope and Falling Slope, respectively. LZC_{peak} corresponds to the maximum MLZC value across the entire scale range, and peak indicates the associated scale index at which this maximum occurs. The notation $\min(LZC_{1:peak-1})$ denotes the minimum MLZC value observed prior to the peak scale, and $\operatorname{argmin}(LZC_{1:peak-1})$ specifies the corresponding scale index. For the Falling Slope, $\min(LZC_{peak+1:end})$ represents the minimum MLZC value observed after the peak scale, and $\operatorname{argmin}(LZC_{peak+1:end})$ denotes its associated scale index.

In addition, inspection of the mean topographic maps revealed that, at two non-adjacent scales, the MDD group exhibited highly similar spatial activity patterns (e.g., theta- and beta-associated scales), whereas the HC group demonstrated more pronounced scale-dependent variations. To quantitatively assess this difference, a scale-association feature was introduced to characterize the statistical dependency between multiscale complexity measures. Specifically, mean LZC values at each scale were extracted, and the CSCC was computed by evaluating Pearson's correlation coefficients between pairs of scales, thereby establishing inter-scale coupling relationships.

The CSCC between scale X and scale Y was calculated as:

$$r_{xy} = \frac{\sum_{i=1}^n (x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\sum_{i=1}^n (x_i - \bar{x})^2} \sqrt{\sum_{i=1}^n (y_i - \bar{y})^2}} \quad (7)$$

where x_i and y_i denote the mean feature values of the i -th data segment at scales X and Y, respectively. In this study, each subject's data were divided into 24 segments, yielding, $n = 24$. Pairwise correlations were then computed across all scale combinations.

To reduce feature redundancy and retain the most informative variables for subsequent classification analysis, a statistical feature screening procedure was performed following feature extraction. Specifically, independent-samples t -tests were employed to assess between-group differences in each candidate feature derived from the multiscale MLZC measures under EO and EC conditions. Importantly, to prevent potential information leakage, feature screening was strictly performed within the training data of each cross-validation fold, i.e., the feature selection procedure was nested within the cross-validation process. Only features exhibiting statistically significant between-group differences in the training data were retained as candidate discriminative variables, while non-significant features were excluded from further analysis.

2.4 Multi-Paradigm Feature Fusion and Ablation Design

To investigate whether different resting-state paradigms provide complementary neurodynamic information for MDD identification, a multi-paradigm feature

fusion framework was introduced. Resting-state EEG signals recorded under EO and EC conditions were analyzed both separately and jointly to evaluate their respective contributions to classification performance.

Specifically, three feature configurations were constructed: (1) EO Only features, derived exclusively from EEG signals under the EO condition; (2) EC Only features, derived from the EC condition; and (3) EO–EC fusion features, obtained by concatenating features extracted from both conditions to form a unified subject-level feature vector. This design enabled a systematic comparison between single-condition and cross-condition representations.

To further assess the contribution of each resting-state paradigm, an ablation-style experimental design was adopted. By comparing classification performance across the three feature configurations, the proposed framework allowed evaluation of the relative contribution of EO and EC conditions and examination of whether feature fusion across multiple paradigms enhances the discriminative capability for MDD detection.

2.5 Feature Classification

Supervised learning methods were employed to discriminate patients with MDD from HC. Classification was conducted at the subject level, whereby each subject was represented by a single feature vector for model training and evaluation.

Three commonly used machine learning algorithms were adopted: SVM [27], KNN [28], and DT [29]. The SVM classifier employed a linear kernel with the regularization parameter (BoxConstraint) set to 1. The number of neighbors in the KNN model was set to 5. For the decision tree model, the minimum leaf size was set to 5, while all other parameters were kept at default values. No additional hyperparameter tuning procedures were performed, and fixed parameter settings were used throughout all experiments to ensure methodological consistency and reproducibility. To prevent bias caused by differences in feature scales, data standardization was performed within each fold of cross-validation. Specifically, normalization of the test set was performed using mean and standard deviation derived exclusively from the training set, thereby preventing information leakage and enhancing generalizability.

To ensure robustness and reliability of the results, a 10-fold cross-validation strategy was adopted. The dataset was randomly partitioned into ten subsets. Random partitioning was performed with a fixed random seed to ensure reproducibility. In each iteration, one subset was used for testing and the remaining nine for training. This procedure was repeated ten times so that each subject was included in the test set once. Final performance metrics were obtained by averaging results across the ten folds.

All experiments were conducted on a Lenovo Legion R9000P laptop computer (Lenovo, Beijing, China) equipped with an AMD Ryzen 9 7945HX processor (2.50

GHz; AMD, Santa Clara, CA, USA), 16 GB Micron Technology DDR5 RAM (5200 MHz; Micron Technology, Boise, ID, USA), and an NVIDIA GeForce RTX 4060 GPU (NVIDIA Corporation, Santa Clara, CA, USA), running a 64-bit Windows 11 25H2 operating system (Microsoft Corporation, Redmond, WA, USA). Model training and cross-validation were implemented in MATLAB R2024a (MathWorks, Natick, MA, USA).

2.6 Performance Evaluation Metrics

As this study addressed a binary classification problem, model predictions resulted in four possible outcomes: true positive (TP), false positive (FP), true negative (TN), and false negative (FN). Based on these quantities, Accuracy, Sensitivity, and Specificity were used as performance evaluation metrics. These metrics assess overall discriminative ability, positive-class detection capability, and negative-class detection capability, respectively. To further characterize the variability and reliability of classification performance, 95% confidence intervals (95% CIs) were estimated for each evaluation metric. Specifically, the 95% CIs were calculated using percentile bootstrap resampling with 2000 iterations, based on the fold-wise performance estimates obtained from the 10-fold cross-validation procedure.

$$\text{Accuracy} = \frac{TP + TN}{TP + TN + FP + FN} \quad (8)$$

$$\text{Sensitivity} = \frac{TP}{TP + FN} \quad (9)$$

$$\text{Specificity} = \frac{TN}{TN + FP} \quad (10)$$

3. Results

3.1 Multiscale Nonlinear Feature Curve Analysis

To characterize the overall scale-dependent variation of MLZC, mean LZC values across scales 1–45 were computed, and scale-wise trajectories were plotted for the MDD and HC groups under both EC and EO conditions, at the whole-brain level and across individual brain regions (Fig. 3).

Under the EC condition, clear group differences were observed across scales. At lower scales, corresponding to the delta-band-related range, the MDD group exhibited overall higher mean LZC values than the HC group, with relatively stable variation, whereas the HC group maintained comparatively lower levels within this range. As the scale transitioned from low to intermediate ranges (i.e., scales associated with the theta and alpha frequency bands),

the trajectories of the two groups diverged markedly. The HC group demonstrated a steeper upward trend, whereas the MDD group showed a comparatively slower increase. As a result, the pattern shifted from higher LZC values in the MDD group at lower scales to higher values in the HC group at intermediate scales. This difference was primarily reflected in the slope of complexity increase across scales, suggesting that patients with MDD may exhibit a less pronounced increase in neural complexity during the transition from lower to intermediate scales. At higher scales (corresponding to beta- and gamma-band-related ranges), both groups reached peak LZC values around the beta-associated scales and subsequently showed a gradual decline with further scale increase. However, the overall LZC levels in the MDD group remained lower than those in the HC group. Overall, although the general scale-dependent trajectory under the EC condition appeared similar between groups, the MDD group exhibited a significantly reduced slope of complexity increase from low to intermediate-high scales and maintained lower complexity levels at higher scales. These findings suggest altered scale-dependent complexity dynamics in MDD, which may be related to differences in cross-scale neural regulation.

Under the EO condition, similar scale-dependent trends were observed at both whole-brain and regional levels. Specifically, LZC values in the MDD group were higher than those in the HC group at delta- and theta-associated scales, but lower at alpha-, beta-, and gamma-associated scales. Compared with the EC condition, LZC values under EO were consistently higher across scales at the whole-brain and regional levels. This pattern suggests enhanced global neural activation and elevated oscillatory activity across frequency bands during the EO condition.

Based on the overall scale-wise MLZC trajectories described above, distinct transition patterns between low and intermediate scales were observed in the MDD and HC groups, particularly in the extent to which complexity increased with scale. To quantitatively characterize these scale-dependent dynamic variations and evaluate their discriminative potential between MDD and HC, the RS and FS of the MLZC curve were extracted as feature indices. Group comparisons were conducted at both the whole-brain and regional levels. The corresponding mean values and statistical results are presented in Fig. 4.

Under the EC condition, significant group differences were observed in RS. The HC group exhibited significantly higher RS values than the MDD group. Specifically, RS values in the HC group were concentrated around approximately 0.015, whereas those in the MDD group were centered around 0.005, indicating a markedly reduced slope of complexity increase in MDD. In contrast, FS values were largely comparable between groups, with the exception of the temporal region, where a significant difference was detected. No significant differences were observed at the whole-brain level or in other regions.

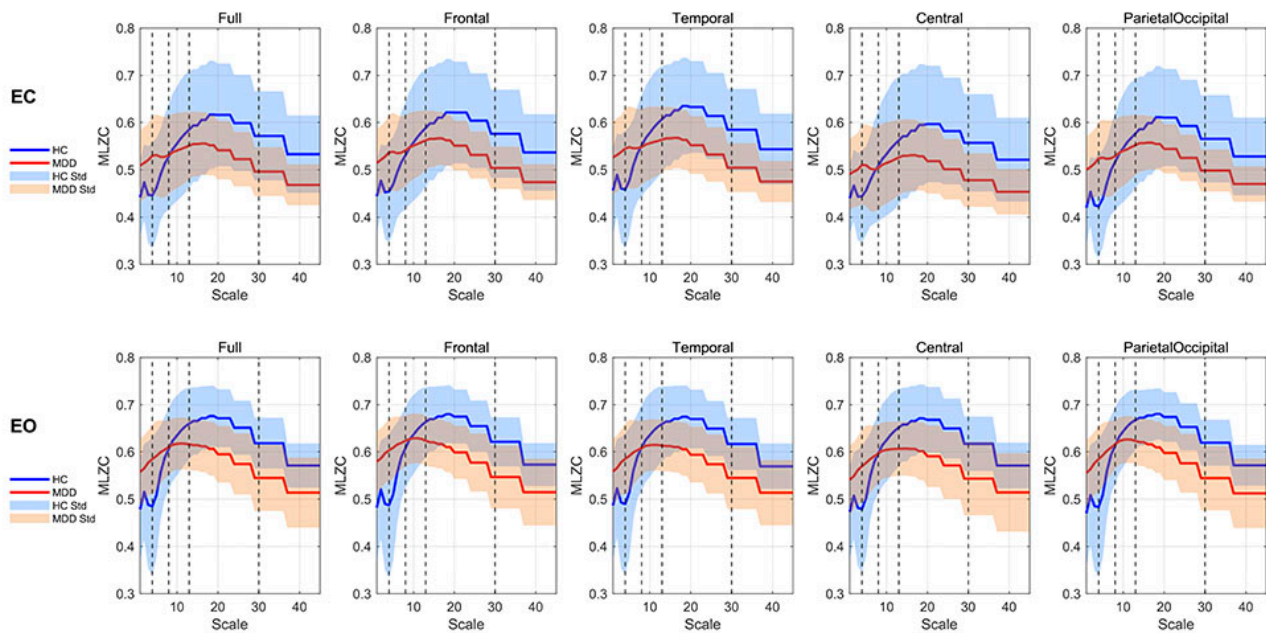


Fig. 3. Mean LZC scale-wise curves at the whole-brain and regional levels under EC and EO conditions. The x-axis denotes scale number from 1 to 45, and the y-axis denotes the mean LZC value at each scale. The four dashed vertical lines at scales 4, 8, 13, and 30 divide the scale range into delta (1–4), theta (5–8), alpha (9–13), beta (14–30), and gamma (31–45) bands. Shaded areas indicate standard deviations.

Under the EO condition, RS again showed significant group differences. The HC group demonstrated higher RS values (approximately 0.017) compared with the MDD group (approximately 0.005), and this difference reached statistical significance across the whole brain and multiple regions. For FS, group differences were generally less pronounced. Except for the parietal-occipital region, where no significant difference was observed, FS values showed significant group effects at the whole-brain level and in several regional comparisons.

Taken together, these findings indicate that the RS feature consistently distinguishes MDD from HC within the present dataset under both EC and EO conditions. The reduced RS observed in MDD suggests attenuated scale-dependent increases in neural complexity, which may indicate differences in the modulation of neural dynamics across temporal scales and may contribute to the discrimination between groups within the present dataset.

3.2 Analysis of Cross-Scale Correlation Features

Based on the MLZC profiles across scales, the HC group exhibited greater differentiation across scales corresponding to canonical EEG frequency bands, whereas the MDD group showed reduced variability across these scales and a comparatively more homogeneous scale-dependent pattern. To further characterize coordinated variations between scales, Pearson correlation coefficients were computed between MLZC values across all scale pairs. The resulting cross-scale correlation patterns at the whole-brain

and regional levels for both HC and MDD groups are illustrated in Fig. 5.

As shown in Fig. 5, under both EC and EO conditions, the HC group exhibited strong correlations primarily between adjacent scales within low- and high-scale ranges, whereas correlations between low and high scales were comparatively weak. This pattern suggests a structured and locally organized inter-scale coupling profile. In contrast, the MDD group demonstrated elevated correlations between low and high scales, with cross-scale association values markedly higher than those observed in HC. However, correlations between adjacent high scales were reduced relative to HC as scale increased. Similar correlation patterns were observed across the four regional subdivisions and were largely consistent with whole-brain results. Collectively, these findings suggest differences in cross-scale coupling patterns in MDD, particularly in the association between low- and high-frequency-related scales. Such reorganization of inter-scale dependency may be associated with differences in the coordination of neural dynamics across frequency bands.

To further characterize group differences in the MLZC association structure between HC and MDD, independent-samples *t*-tests were performed for each pairwise scale combination within the 1–45 scale range under both EC and EO conditions. Given the large number of comparisons (990 unique scale pairs, corresponding to the upper triangular part of the scale-to-scale matrix excluding the diagonal), the resulting *p*-values were corrected using the

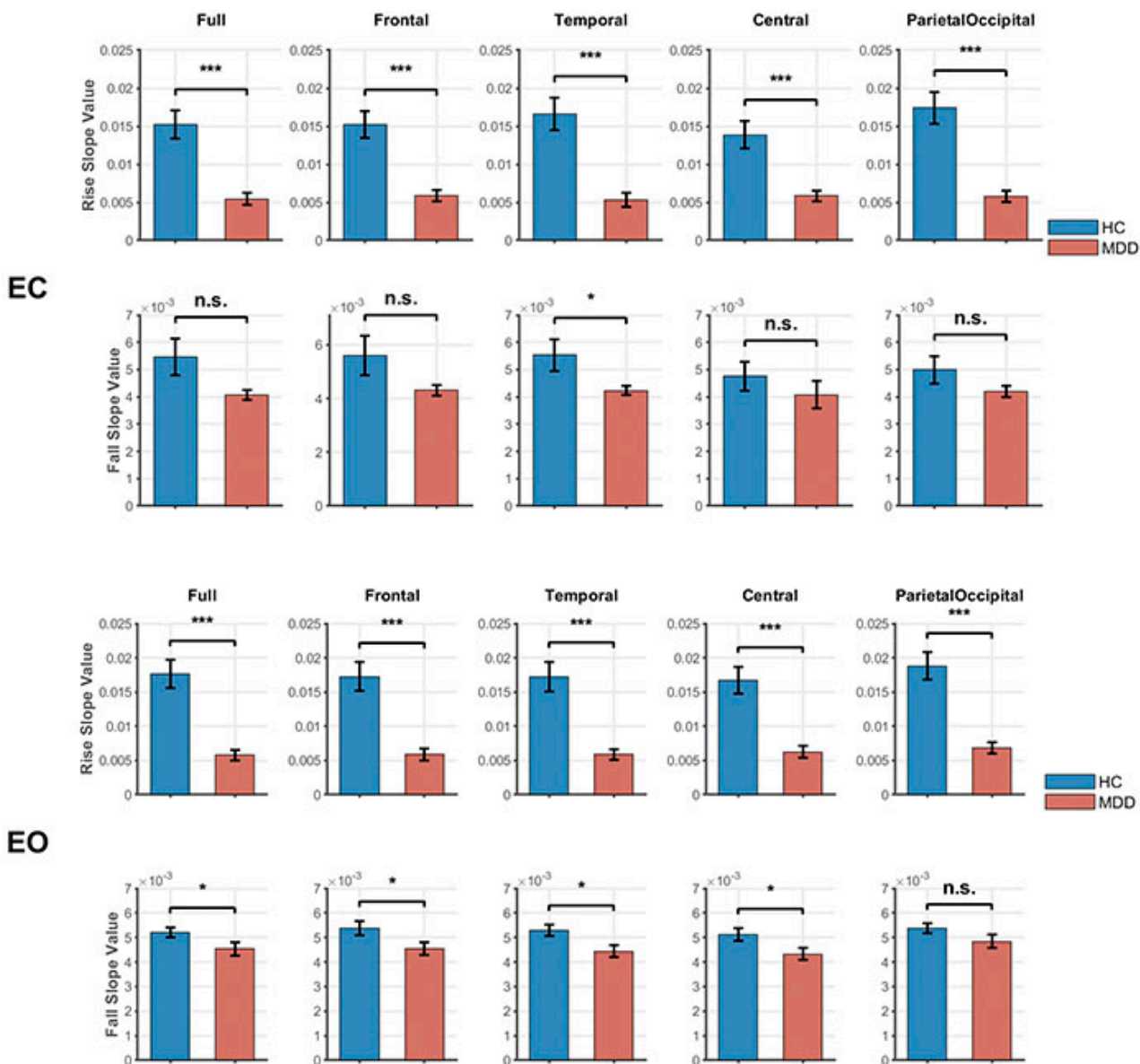


Fig. 4. Group comparisons of RS and FS under EC and EO conditions at the whole-brain and regional levels. Bar heights represent mean feature values, and error bars indicate within-group variability. Statistical significance was determined using independent-samples *t*-tests. Significance levels are denoted as follows: *** $p < 0.001$, * $p < 0.05$, n.s., not significant; RS, Rising Slope; FS, Falling Slope.

Benjamini–Hochberg False Discovery Rate (FDR) procedure ($q = 0.05$). Based on the FDR-corrected results, significance matrices were constructed to visualize between-group differences in scale-to-scale associations, as shown in Fig. 6.

Under the EC condition, FDR-corrected results revealed frequency-band-dependent patterns of group differences in scale associations across the whole brain and within individual regions. Scale associations involving delta-band-corresponding scales exhibited widespread significant differences when paired with scales from other frequency-band-related ranges. In contrast, associations restricted to intermediate- and high-frequency-related

scales showed comparatively fewer significant differences. These results indicate that, during the EC resting state, group differences are predominantly driven by cross-scale associations involving low-frequency-related scales. This pattern suggests altered multiscale coordination of neural complexity in MDD under internally driven resting conditions.

Under the EO condition, between-group differences in CSCC were more extensive compared with EC, as reflected by a larger number of FDR-significant scale pairs across the whole brain and regional analyses. Scale associations between delta-band-corresponding scales and other band-related scales remained robustly different between

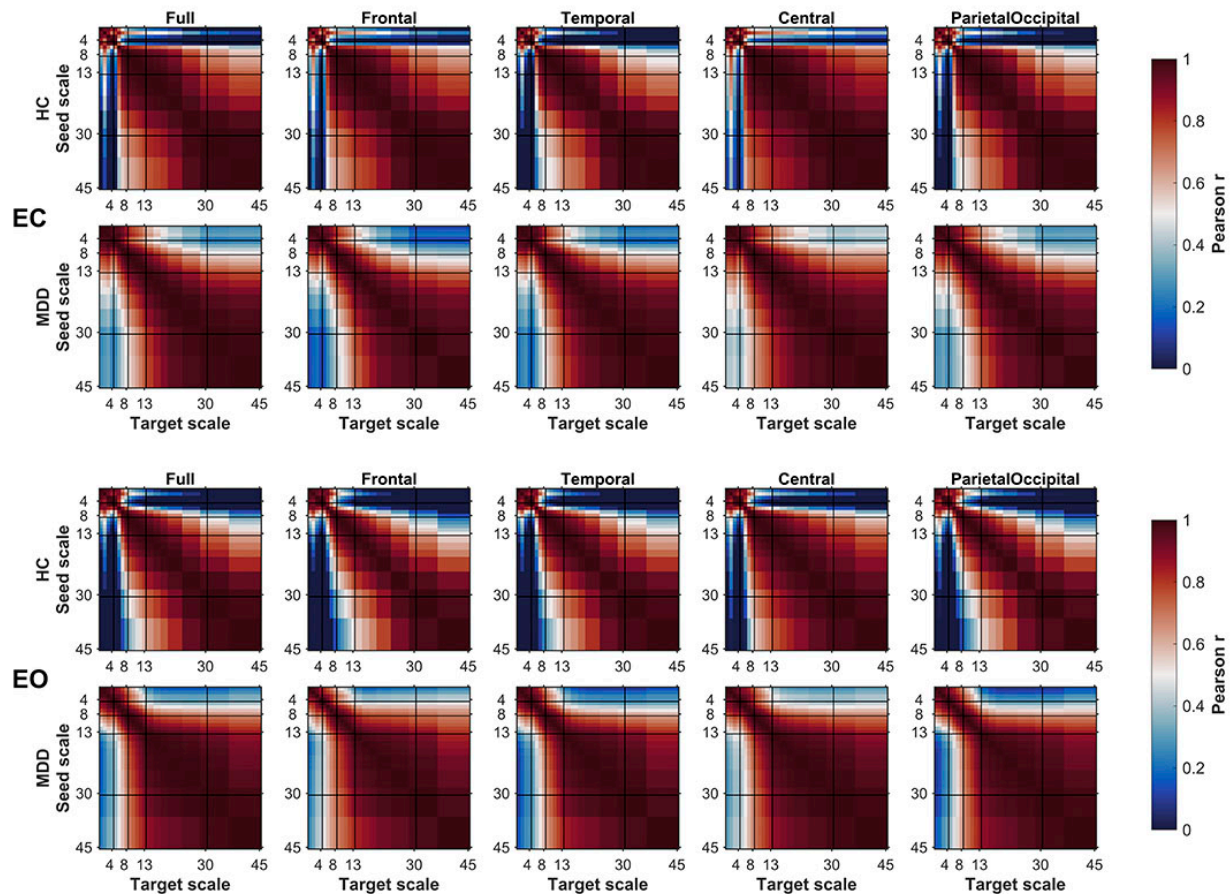


Fig. 5. Cross-scale correlation maps of MLZC under EC and EO conditions at the whole-brain and regional levels. The upper row shows HC and the lower row shows MDD within each condition. Columns correspond to the whole-brain level and four regional subdivisions, including frontal, temporal, central, and parietal-occipital regions. Both the horizontal and vertical axes denote scales from 1 to 45. In the figure, vertical and horizontal demarcation lines after scales 4, 8, 13, and 30 divide the scale range into five intervals (1–4, 5–8, 9–13, 14–30, and 31–45), corresponding to the delta, theta, alpha, beta, and gamma frequency bands. Pearson correlation coefficients (r) were computed between scale-wise LZC values, with the diagonal corresponding to self-correlations. The color scale ranges from 0 to 1 and displays only the positive portion of the original Pearson correlation coefficients, with warmer colors indicating stronger cross-scale associations and cooler colors indicating weaker associations. Overall, the MDD group exhibits altered cross-scale coupling patterns, particularly characterized by stronger associations between low- and high-scale ranges than the HC group does.

groups. Additionally, significant differences linking low- and high-frequency-related scales were prominent, and associations among intermediate-frequency-related scales were also more frequently affected compared with EC.

Collectively, group differences in CSCC between HC and MDD were more pronounced under the EO condition than under the EC condition. Across both conditions, scale associations involving delta-band-corresponding scales consistently showed significant between-group differences across the whole brain and regional subdivisions. Overall, the MDD group exhibited a reorganization of cross-scale association patterns, particularly involving low-frequency-related scales. Such alterations in multiscale coordination may reflect disrupted integration of neural dynamics across frequency bands and highlight systematic differences in cross-scale organization between HC and MDD.

Building upon the cross-scale correlation maps and the corresponding significance analyses, we further sought to clarify the specific contributions of different frequency bands to the overall cross-scale coupling architecture. To this end, representative seed scales were selected to approximate canonical frequency bands: scales 3, 6, 10, 20, and 35 were chosen to represent the delta, theta, alpha, beta, and gamma bands, respectively. For each seed scale, CSCC with all scales (1–45) were extracted. Slice trend curves were then constructed to characterize the coupling patterns of specific frequency bands across the full scale range (Fig. 7).

As shown in Fig. 7, under both EC and EO conditions, the delta seed scale exhibited the most extensive between-group differences across multiple target scales. Under the EC condition, the delta slice revealed a rapid

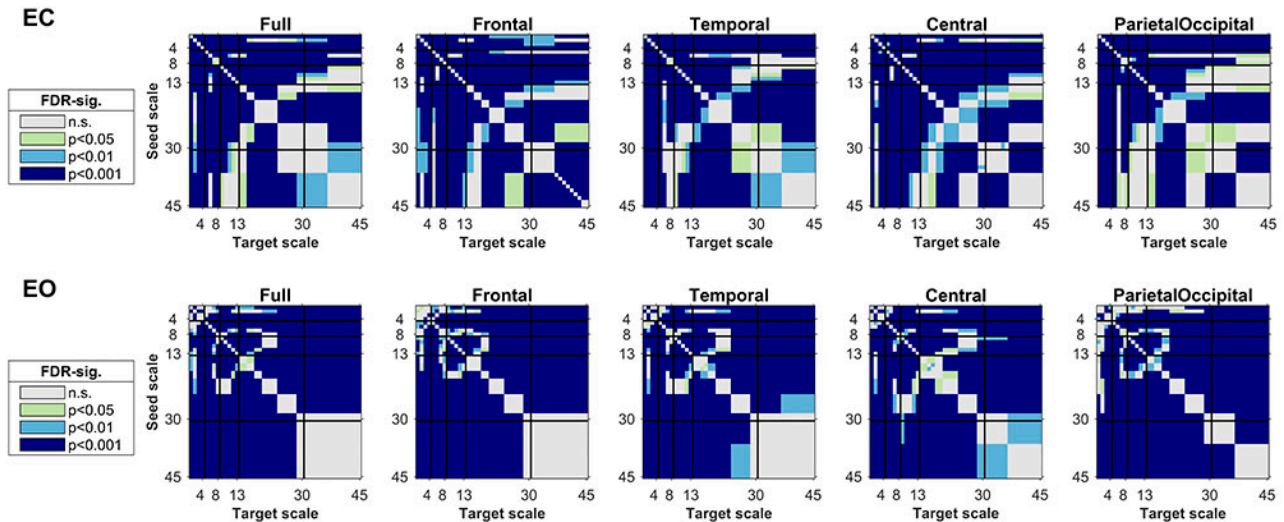


Fig. 6. Differences in MLZC scale-to-scale associations across the whole brain and brain regions under EC and EO conditions. Rows correspond to EC and EO conditions, and columns represent the whole brain and four regional subdivisions, including frontal, temporal, central, and parietal-occipital regions. Each map shows the between-group significance pattern of CSCC between HC and MDD across the 45 MLZC scales. In the figure, vertical and horizontal demarcation lines after scales 4, 8, 13, and 30 divide the scale range into five intervals (1–4, 5–8, 9–13, 14–30, and 31–45), corresponding to the delta, theta, alpha, beta, and gamma frequency bands, respectively. Gray cells represent non-significant results after FDR correction, whereas colored cells indicate scale pairs that survived FDR correction, with color intensity denoting the nominal p -value level among significant pairs. This figure shows that group differences in cross-scale coupling are predominantly concentrated in scale interactions involving delta-band-related ranges. CSCC, Cross-Scale Correlation Coefficient; FDR, False Discovery Rate; n.s., not significant.

decline in correlation strength in the HC group when transitioning from lower to middle-higher scales, forming a clearly stratified scale-dependent structure. In contrast, the MDD group showed a markedly attenuated decline, with significantly higher correlations than HC across the low-to-mid scale range. Notably, significant differences were primarily distributed within the alpha-band interval. Further inspection of the alpha seed slice demonstrated significant group differences at lower scales, particularly within the delta-band interval, thereby corroborating the delta-slice findings. These results suggest that, during EC condition, between-group differences predominantly arise from cross-frequency coupling structures involving low-frequency scales, especially within the delta–alpha interaction range.

Under the EO condition, the delta slice again demonstrated the most widespread and pronounced group separation. Compared with EC, the range of significant differences extended further toward higher scales, with especially prominent effects within the gamma-band interval. The HC group maintained a relatively well-defined hierarchical correlation structure across low-to-high scales, whereas the MDD group exhibited globally elevated correlations within the middle-to-high scale range, significantly exceeding those of HC. Correspondingly, the gamma seed slice also showed between-group differences at lower scales, particularly within the delta-band interval, consistent with

the delta-slice results. These findings indicate that, under EO resting conditions, the cross-scale coupling strength from low-frequency to high-frequency scales is abnormally enhanced in MDD, with group differences primarily concentrated in the delta–gamma cross-scale coupling structure.

Taken together, the slice trend analysis further substantiates the patterns observed in the multiscale coupling matrices and significance maps. Specifically, within the present dataset, delta–alpha cross-scale coupling under EC and delta–gamma cross-scale coupling under EO showed relatively prominent group-separating patterns.

3.3 Classification Performance

Based on the preceding statistical feature analyses, four features with significant discriminative capacity were identified. These included the MLZC-derived RS under both EO and EC conditions, the delta–alpha CSCC under EC, and the delta–gamma CSCC under EO. Subject-level feature vectors were constructed using these variables. Comparative classification experiments were then conducted under three feature configurations—EO Only, EC Only, and Fusion (EO+EC)—using three classifiers: SVM, KNN, and DT. The results are summarized in Table 2.

Overall, cross-state feature fusion outperformed single-state configurations in most cases. For the SVM

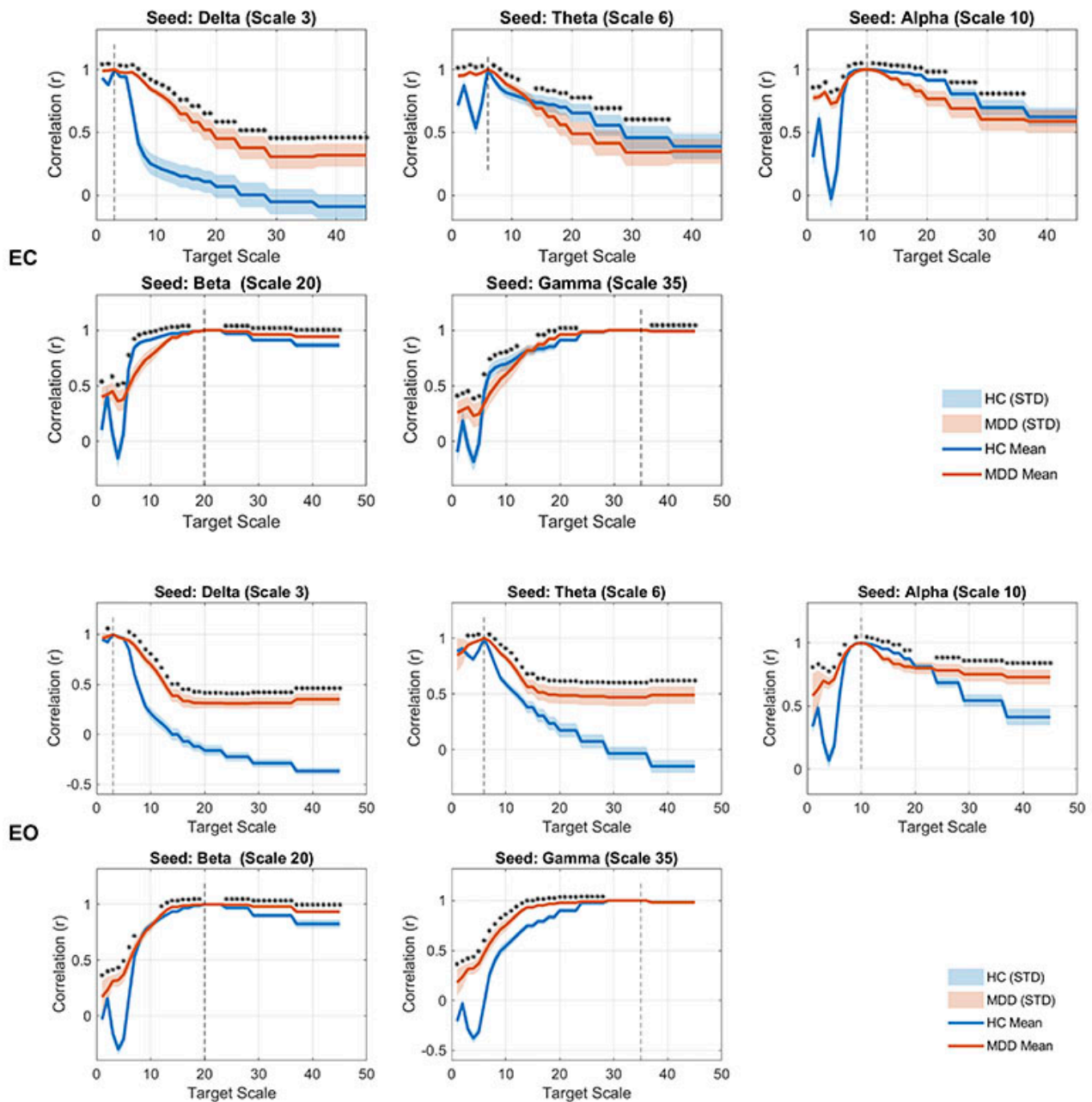


Fig. 7. Slice trend curves of representative frequency bands under EC and EO conditions. Representative seed scales 3, 6, 10, 20, and 35 were chosen to represent the delta (1–4), theta (5–8), alpha (9–13), beta (14–30), and gamma (31–45) bands. For each seed scale, CSCC between the seed scale and all target scales from 1 to 45 are shown. The vertical dashed line marks the corresponding seed scale. Solid lines represent group means and shaded areas denote standard deviations. Asterisks indicate significant group differences after FDR correction. The slice trend analysis illustrates frequency-band-specific differences in cross-scale coupling, with delta–alpha interactions under EC and delta–gamma interactions under EO showing relatively prominent group differences within the present dataset. Significance levels (*) are denoted as follows: $p < 0.05$. STD, standard deviation.

model, the Fusion strategy achieved an accuracy of 85.71%, clearly exceeding EO Only (79.59%) and EC Only (73.47%). A similar pattern was observed for KNN, where Fusion reached an accuracy of 83.67%, surpassing both single-state settings. In terms of sensitivity and specificity, the fused features demonstrated improved balance, partic-

ularly in the SVM and KNN models. Compared with the relatively low specificity observed under the EC-only configuration, the fusion approach improved discrimination of healthy controls while retaining relatively high sensitivity for MDD detection. For the DT model, Fusion and EC Only yielded identical performance metrics, both achiev-

Table 2. Classification performance of EO, EC and fusion features using three machine learning models.

Experiment	Model	Accuracy	Sensitivity	Specificity
EO Only	SVM	79.59% [78.50–80.00]	95.83% [90.00–100.00]	64.00% [55.00–73.33]
	KNN	79.59% [72.00–88.00]	87.50% [76.67–100.00]	72.00% [60.00–83.33]
	DT	77.55% [68.00–88.00]	75.00% [53.33–91.67]	80.00% [63.33–95.00]
EC Only	SVM	73.47% [67.50–79.00]	95.83% [90.00–100.00]	52.00% [41.67–66.67]
	KNN	77.55% [68.00–88.00]	95.83% [90.00–100.00]	60.00% [39.17–80.00]
	DT	85.71% [80.00–92.00]	83.33% [73.33–96.67]	88.00% [75.00–96.67]
Fusion	SVM	85.71% [80.00–92.00]	95.83% [90.00–100.00]	76.00% [65.00–88.33]
	KNN	83.67% [76.00–92.00]	91.67% [83.33–100.00]	76.00% [61.67–88.33]
	DT	85.71% [80.00–92.00]	83.33% [73.33–96.67]	88.00% [76.67–96.67]

Table footnote. Performance values are reported as percentages. Bracketed values indicate 95% CIs, estimated using percentile bootstrap resampling with 2000 iterations. In each iteration, the performance estimates from the ten cross-validation folds were resampled with replacement, and the 2.5th and 97.5th percentiles of the bootstrap distribution were reported as the interval bounds. SVM, Support Vector Machine; KNN, K-nearest neighbors; DT, Decision Tree.

ing an accuracy of 85.71%. The underlying classification outcomes were also identical in terms of TP, TN, FP, and FN counts. This phenomenon is attributable to the splitting mechanism of decision trees: under the current parameter constraints, the model preferentially utilized the more discriminative EC-derived features for node partitioning. When the additional EO features did not provide further information gain, the resulting classification boundaries remained unchanged. Therefore, this outcome reflects differences in feature utilization rather than model failure. Taken together, compared with the best single-state configuration within each classifier, Fusion improved accuracy by 6.12 percentage points for SVM (85.71% vs. 79.59%) and by 4.08 percentage points for KNN (83.67% vs. 79.59%), and matched the best single-state configuration for DT (85.71% vs. 85.71%). As a descriptive summary across the three classifiers, Fusion yielded a mean accuracy of 85.03%, compared with 78.91% for EO Only and 78.91% for EC Only. These quantitative results suggest that EO and EC resting-state conditions may provide complementary discriminative information within the present dataset. The corresponding confusion matrices for the SVM, KNN, and DT classifiers under the Fusion condition are shown in Fig. 8.

Further comparison of the three classifiers showed that, within the present dataset, the selected features yielded broadly comparable classification performance across different model architectures. Under the Fusion condition, all three classifiers achieved accuracies exceeding 83%, with a maximum of 85.71%. Sensitivity values ranged from 83% to 96%, indicating relatively high detection performance for patients with MDD within the present dataset. Specificity reached up to 88.00%, indicating reliable discrimination of healthy controls. In addition, the 95% CIs reported in Table 2 provide an estimate of performance variability across cross-validation folds and offer additional information regarding the reliability of the observed classification results within the present dataset. The consistency of re-

sults across classifiers suggests that the MLZC-derived RS and CSCC features showed relatively consistent discriminative patterns across classifier structures within the present dataset.

4. Discussion

4.1 Neurophysiological Significance of SDVS Alterations in MDD

Taken together, the present findings indicate that, under both EC and EO conditions, HC participants exhibited higher RS values than individuals with MDD. The group differences observed in the present data demonstrate that healthy adults display a steeper rise in EEG complexity from low to intermediate temporal scales. In contrast, lower RS values in MDD reflect a reduced magnitude of complexity increase across scales. Specifically, the RS of the HC group may index more pronounced differentiation between low-frequency oscillatory activity (e.g., delta and theta rhythms) and higher-frequency oscillations (e.g., alpha and beta), whereas individuals with MDD exhibited a relatively flatter increase in complexity across these scales.

From a theoretical circuit-level perspective, reduced RS may be interpreted as being associated with reduced engagement of higher-frequency neural processes in response to slower regulatory rhythms. From a neurophysiological standpoint, this process is thought to be regulated by excitation–inhibition balance within cortical microcircuits, which governs the generation and modulation of oscillatory activity across frequency bands [30]. In major depressive disorder, dysfunction within cortical–subcortical circuits, particularly fronto–limbic pathways, has been consistently associated with impaired modulation of oscillatory activity and reduced flexibility of emotional and cognitive regulation [31]. Such circuit-level alterations may constrain the dynamic range of neural responses across temporal scales.

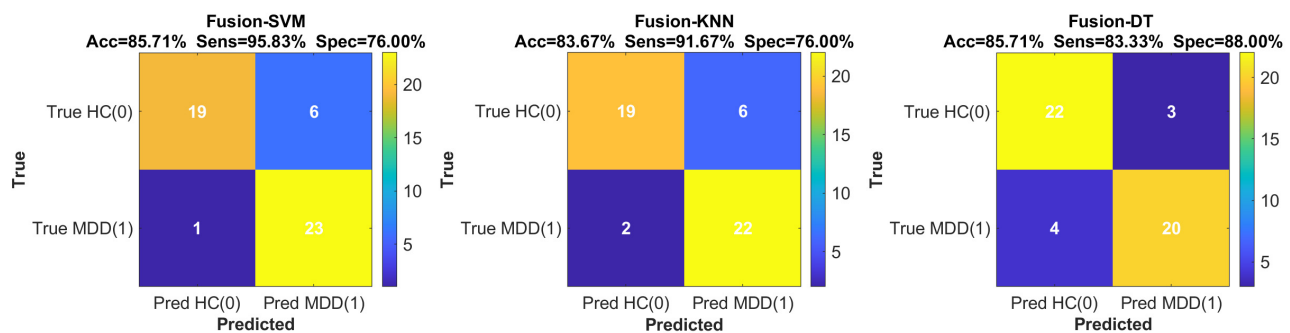


Fig. 8. Confusion matrices of the fusion-based classifiers. From left to right, panels correspond to SVM, KNN, and DT models trained on fused multiscale features. Rows indicate the true class labels and columns indicate the predicted labels. Acc, Sens, and Spec denote accuracy, sensitivity, and specificity, respectively.

Similarly, prior studies have reported that reduced increases in entropy or neural variability across temporal scales, together with shallower power spectral density (PSD) slopes, may reflect a shift toward less differentiated neural processing and increased dominance of local neural activity patterns. According to previous studies, such flattening of scale-dependent dynamics has been associated with reduced efficiency in coordinating distributed neural processes and diminished functional adaptability in aging and neuropsychiatric conditions [32]. This pattern is broadly consistent with the present findings.

These observations align with prior spectral PSD analyses showing that patients with MDD typically display increased power in low-frequency bands (e.g., delta and theta) and decreased power in certain higher-frequency bands (e.g., alpha), indicative of slowed neural dynamics and diminished flexibility in cortical activity [33]. In this context, the SDVS derived from MLZC complements these findings by capturing subtle dynamics of frequency-to-frequency transitions that PSD alone does not resolve.

A lower RS may also be associated with a reduced degree of differentiation in neural complexity between lower and higher temporal scales in MDD patients. Such adaptive differences may be related to alterations in cortical-subcortical functional interactions (e.g., prefrontal–limbic pathways), resulting in reduced cognitive flexibility and impaired emotion regulation. Dysfunctional alpha asymmetry in the prefrontal cortex has been linked to executive impairment and mood dysregulation in depression [34], and the RS results reported here are consistent with this mechanistic framework. From a theoretical neurophysiological perspective, aberrant SDVS might also be associated with altered thalamocortical functional coordination. The thalamus is thought to play a central role in generating and pacing low-frequency oscillations, and its coordinated interaction with cortical high-frequency activity is essential for flexible neural dynamics—an interaction that may be indirectly reflected in SDVS features [35]. This resonates with PSD findings of abnormal low-to-high frequency power ra-

tios in MDD [36], suggesting differences in large-scale dynamic coordination patterns.

By focusing on the MLZC-derived SDVS, this study extends the dimensionality of EEG dynamic analysis. The slope of complexity variation change from low to high frequencies not only suggests abnormal dynamic modulation during frequency transitions in MDD, but also provides a novel quantitative framework for characterizing such alterations. One principal merit of this approach lies in its capacity to integrate information across multiple temporal scales and frequency domains, thereby offering a more comprehensive perspective on the neurophysiological mechanisms underlying depression.

4.2 Neurophysiological Implications of CSCC Alterations in MDD

Based on the MLZC-derived CSCC features, this study revealed systematic abnormalities in cross-scale neural integration in individuals with MDD. In neurophysiological terms, multiscale integration refers to the coordinated interaction between neural processes operating at different temporal scales, which depends on balanced excitation–inhibition dynamics and effective coordination across distributed brain networks. Disruption of these regulatory mechanisms may lead to abnormal cross-scale coupling patterns [37]. Overall, HC participants exhibited a hierarchical pattern characterized by relatively higher correlations between adjacent scales and lower correlations between distant scales, reflecting functional segregation and modular organization across temporal scales in neural activity. In contrast, individuals with MDD were characterized by abnormally enhanced correlations between low and mid-to-high scales, suggesting less differentiated relationships between neural dynamics across time scales. This pattern is consistent with previous reports of abnormal cross-frequency coupling in spectral analyses of depression [38], supporting the notion of altered multiscale neural synchronization in MDD.

Slice-trend analysis further clarified the core basis of these abnormalities. In both EC and EO conditions, the delta band emerged as a critical hub within cross-scale coupling structures. Under the EC condition, group differences were primarily manifested as abnormal coupling between delta- and alpha-related scales. Under EO, enhanced coupling between delta- and gamma-associated scales was predominant. This state-dependent reconfiguration suggests that MDD may not simply reflect global synchronization increases, but rather exhibits specific coupling pattern reorganizations contingent on functional context.

Under EC, in healthy individuals, delta and alpha typically maintain relatively differentiated hierarchical regulation [39]. However, our findings of enhanced delta–alpha cross-scale coupling in MDD suggest a blurring of regulatory boundaries driven by slow oscillations. This abnormal interaction may reflect altered coordination across distributed neural activity patterns, potentially related to large-scale functional systems such as the default mode network (DMN), which has been implicated in dysfunctional internal mentation and impaired emotional regulation in depression [40]. Previous EEG studies have also reported alpha anomalies and altered slow oscillatory modulation in MDD [41]. In addition, Kou et al. [42] reported enhanced alpha-band frontal–parietal functional connectivity during eyes-closed resting-state EEG in adolescents with MDD, and the present study complements these findings from a dynamic integration perspective.

Under EO, high-frequency activity (particularly gamma oscillations) has been associated with local processing and neural synchrony [43]. In general, healthy brains tend to maintain a functional distinction between low-frequency global regulation and high-frequency local processing. This hierarchical organization of slow global rhythms and fast local processing is a central principle of hierarchical predictive processing frameworks, in which lower-frequency activity coordinates large-scale contextual information while higher-frequency activity supports local information processing [30]. In contrast, individuals with MDD demonstrated significantly increased delta–gamma cross-scale coupling, suggesting abnormal modulation of high-frequency cognitive dynamics by slow rhythms. This pattern may be related to alterations in executive control network (ECN) function and changes in cross-network coordination [44]. Notably, recent EEG research has reported abnormal cross-frequency coupling involving low and gamma bands in depression, consistent with the present observations [38].

From a neurophysiological standpoint, delta oscillations are closely linked to thalamocortical circuit dynamics and provide a foundation for baseline rhythm regulation [45]. The consistent role of delta as a core coupling node across conditions suggests that slow-wave modulation may be closely associated with the multiscale coupling reorganization observed in MDD. Furthermore, disrupted

excitation–inhibition (E/I) balance—particularly GABAergic dysfunction—is widely documented in depression and may contribute to enhanced neural synchrony [46]. These findings collectively suggest that depression may involve systematic alterations in cross-hierarchical neural integration.

Collectively, these results indicate that MDD is characterized by delta-centric cross-scale integration abnormalities, which exhibit distinct coupling reconfigurations under different functional states: delta–alpha coupling anomalies under EC that may reflect intrinsic integration imbalance, and delta–gamma coupling abnormalities under EO that may be related to altered cross-frequency control processes during externally oriented processing.

4.3 Multi-Paradigm Feature Fusion Improves MDD Classification

In the present study, classification analyses were conducted on the MPHC dataset using single-state features derived from EO and EC conditions, as well as cross-state fusion features. The results showed that, within the present dataset, cross-state fusion features generally achieved superior classification performance across SVM, KNN, and DT classifiers.

From a neurophysiological perspective, EO and EC resting states reflect distinct modes of brain functional regulation. During EC, neural activity is often characterized by internally oriented cognitive processing associated with the DMN, accompanied by enhanced alpha oscillatory activity that reflects endogenous regulatory mechanisms [47]. In contrast, EO is typically associated with sustained visual input processing and externally oriented attentional modulation, often accompanied by increased engagement of sensory cortices and attentional networks [48]. Previous studies have demonstrated that individuals with MDD exhibit abnormalities in DMN regulation, prefrontal–limbic functional connectivity, and cross-frequency oscillatory integration [49]. Importantly, such abnormalities may manifest in state-dependent neural dynamic patterns under different resting conditions. Therefore, reliance on a single resting state may not sufficiently characterize disease-related functional imbalance. By integrating multiscale complexity measures—specifically the SDVS and the CSCC—across EO and EC conditions, the present framework enables the joint characterization of neural dysfunction under both internally and externally oriented processing modes. The findings further confirm the complementary informational value of the two resting paradigms.

Further evaluation of overall model performance revealed that, within the present dataset, the proposed cross-state fusion features yielded broadly stable classification outcomes across the three classifiers. This cross-model consistency suggests that the proposed SDVS and CSCC features exhibit relatively stable discriminative patterns across classifier architectures within the present dataset.

Compared with approaches relying solely on single-band spectral power or single-scale statistical features, the present framework is grounded in multiscale neural dynamic integration and may provide a complementary perspective for characterizing the complex modulatory characteristics of MDD-related EEG activity.

More broadly, emerging research has begun to link large-scale EEG dynamics and cortical excitability to inter-individual variability in cognitive performance and clinical symptom expression across neuropsychiatric populations. These studies suggest that variability in neural responsiveness and network-level dynamics reflects fundamental properties of cortical stability and functional adaptability that may underlie differences in behavioral and clinical outcomes [50,51]. Within this broader neurophysiological context, multiscale features such as SDVS and CSCC—by quantifying cross-scale coordination of neural activity—may provide exploratory indices of large-scale neural dynamics relevant to depression-related neurophysiological alterations.

In summary, the cross-state fusion strategy has a neurophysiological rationale and showed favorable empirical performance on the MPHIC dataset. These results provide quantitative support for future investigations into depression-related neurophysiological mechanisms and multiscale neural dynamic processes.

5. Conclusion

This study investigated multiscale complexity characteristics of resting-state EEG in major depressive disorder and proposed an MLZC-based analytical framework for multiscale neurodynamic assessment. Within this framework, four categories of cross-scale regulatory features were constructed and validated, including the RS and the delta–gamma CSCC under the EO condition, as well as the RS and the delta–alpha CSCC under the EC condition. Within the present dataset, the results showed distinct alterations in multiscale complexity regulation in the MDD group. Specifically, the RS was significantly reduced, suggesting potential differences in dynamic transitions and integrative capacity across frequency hierarchies. In addition, delta-centered cross-scale coupling architecture exhibited condition-dependent reorganization, manifested as enhanced delta–alpha coupling under the EC condition and enhanced delta–gamma coupling under the EO condition, indicating altered hierarchical coordination of neural dynamics across temporal scales. By integrating multiscale features across EO and EC conditions, the present study jointly characterized resting-state neurodynamic alterations under different paradigms and provided quantitative evidence that the two conditions may contribute complementary discriminative information within the present dataset. Classification models built upon the selected multiscale features achieved relatively high identification performance across three machine learning algorithms (SVM, KNN, and

DT) within the present dataset. Overall, within the present dataset, these findings suggest that MLZC-derived multiscale features may help characterize MDD-related resting-state EEG alterations from the perspective of multiscale dynamic regulation and cross-scale coupling.

6. Limitations

Several limitations of the present study should be acknowledged. First, the sample size of the current dataset (25 HC and 24 MDD) is relatively modest, which may limit the statistical representativeness of the findings to some extent. Although the cross-validation strategy provided an internal evaluation of model performance, future studies incorporating larger and multi-center datasets will be beneficial for further validating the robustness and generalizability of the proposed multiscale features. Second, the analysis was conducted using a conventional 19-channel scalp EEG system, which provides limited spatial coverage compared with high-density recording configurations. Expanding the recording montage or integrating complementary neuroimaging modalities in future work may help to capture more comprehensive neurodynamic information and further refine the characterization of multiscale brain activity patterns.

Availability of Data and Materials

The datasets used and analyzed during the current study is publicly available from Figshare: MDD Patients and Healthy Controls EEG Data (MPHC), https://figshare.com/articles/EEG_Data_New/4244171 (accessed on 10 February 2025).

Author Contributions

YH: writing—original draft, methodology, software and data curation. HQ: investigation and visualization. ZZ: conceptualization, software and editing. JH: conceptualization, supervision and funding acquisition. JY: data curation, writing—review & editing and resources. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

Acknowledgment

We would like to thank the data providers for providing data for this study.

Funding

This work was supported by the National Natural Science Foundation of China (U24A20280).

Conflicts of Interest

The authors declare no conflicts of interest.

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