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A Multidataset Investigation of Resting-State and Event-Related EEG Correlates of Major Depressive Disorder

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Abstract
Introduction: Major Depressive Disorder (MDD) is a prevalent psychiatric condition which lacks reliable biomarkers for diagnosis and treatment. Electroencephalography (EEG) offers a non-invasive and cost-effective method to identify potential biomarkers of MDD. However, findings vary widely across studies due to differences in patient populations, analytic methods, and brain states. To investigate these issues, this study evaluates the consistency and reproducibility of EEG biomarkers of MDD across two datasets with both resting-state and task-based data.
Methods: We analyzed EEG data from two publicly available datasets of healthy controls and MDD patients. The MODMA dataset provided resting-state EEG data; the Cavanagh dataset included both resting-state and task-based data. Spectral power was extracted for canonical frequency bands, and task-evoked components were computed from feedback-locked event-related potentials (ERP). Group-level comparisons and brain-behaviour correlations were assessed using t-tests, Spearman correlations, and FDR correction.
Results: In the MODMA dataset, MDD patients showed increased beta power and reduced alpha power in frontal and temporal regions, with beta power having the strongest positive correlation with depression severity. In the Cavanagh dataset, spectral and ERP amplitudes did not differ significantly between MDD and control groups. Reward-Positivity (RewP) amplitudes were reduced in MDD patients, and time-frequency analyses showed altered theta and delta responses. However, none of the findings were significant after FDR correction. Cross-dataset comparisons revealed significant variability in spectral profiles, particularly in the beta band.
Discussion: Our findings highlight the challenges in identifying consistent EEG biomarkers of MDD across datasets and brain states. While trends in beta power and RewP amplitudes aligned with prior literature, they failed to replicate across datasets or remain significant after FDR correction. These results suggest that commonly reported neural markers may not generalize well across populations. This also highlights the need for greater standardization and cross-dataset validation in EEG biomarker research for MDD.
Conclusion: This study found limited consistency in EEG biomarkers for MDD across two datasets and brain states. Future research should investigate why spectral features like beta power show significance in some datasets but not others and assess how factors such as EEG hardware and recording conditions contribute to this variability.

Keywords: major depressive disorder; MDD; EEG; resting-state; ERP; beta power; FRN; RewP; biomarkers

Introduction

Major Depressive Disorder (MDD) is a prevalent and debilitating psychiatric condition characterized by measurable disruptions in brain activity [1]. Over 280 million individuals are affected with MDD, making it a leading cause of disability globally. MDD is also a costly illness, as researchers estimate that 12 billion productive workdays are lost each year to depression and anxiety alone [2]. Measures of neural activity, such as EEG, can provide valuable insight into the cognitive function and mental state of the brain, which can help diagnose and monitor treatment. EEG is widely used to investigate biomarkers associated with MDD, as it offers a non-invasive and cost-effective method to measure real-time brain activity with high temporal resolution [3]. EEG measures the brain's electrical oscillations across various frequency bands, each reflecting a distinct aspect of neural function making it a valuable tool for identifying potential MDD biomarkers and understanding the disorder's underlying neurophysiological mechanisms.

Various EEG changes have been identified in MDD patients during the resting state. Individuals with MDD often show reduced alpha power (8–12 Hz), particularly in the frontal region of the brain [4]. Similarly, the theta band

(4–8 Hz) often shows decreased power in the prefrontal cortex in more severely depressed individuals, which is linked to impaired limbic frontal integration [3]. Conversely, increased delta power (1–4 Hz) in the prefrontal and temporal regions has been associated with greater depressive symptoms, including both cognitive slowing and emotional distress [3]. Increased beta levels (13–30 Hz) have also been observed in MDD, especially in the frontal and temporal regions, and have been linked to increased rumination, anxiety, and dysregulated executive control [5]. These changes point to a broad disruption in the brain's baseline activity in individuals with MDD, demonstrating the importance of investigating resting state EEG as alterations in neural wave patterns may serve as potential biomarkers for identifying and monitoring MDD.

Complementary to resting state brain signals are task-based signals where EEG activity is studied in relation to a stimulus, called event-related potentials (ERP) [6]. ERPs are composed of various components that make up their overall complex waveforms. These include P300, a positive deflection occurring ~300–600 milliseconds after stimulus onset, and N200, a negative deflection occurring ~200–350 milliseconds after a given stimulus. P300 and N200 are almost always captured at frontocentral electrodes (FCz, Cz) [7]. In individuals with MDD, P300 amplitude is often reduced, especially in response to emotionally salient or task-relevant stimuli [8]. Further, individuals with MDD often show altered or diminished N200 responses, which may reflect deficits in cognitive control and impaired error monitoring [9]. The difference between P300 and N200 is used to calculate Feedback-Related Negativity (FRN), which is an ERP component typically elicited by punishment or negative feedback [10]. In MDD, FRN is typically enhanced, indicating a hypersensitivity to negative outcomes or punishment [11]. RewP is another ERP component given by the mean amplitude between 250–350 ms at the FCz electrode, and is dominated by delta-band (2–3 Hz) activity. It is negatively correlated to MDD, where a smaller RewP is often a marker for more severe MDD [12].

In relation to each other, resting-state EEG provides a neural "default" context in which task-related activities occur. Therefore, if resting activity is abnormal, the brain's reactivity or adaptability shown in task-related ERPs may also be impaired [13–15].

Many studies have examined resting-state EEG or task-evoked ERPs in individuals with MDD, and a few have directly assessed the reproducibility of EEG biomarkers across independent datasets or brain states. However, findings from these studies have been inconsistent [16]. Understanding whether biomarkers generalize across cohorts and contexts is critical for developing clinically meaningful EEG markers of depression. Moreover, exploring how resting-state and task-evoked features relate to one another can offer insight between baseline neural predispositions and stimulus-driven cognitive processing. In this study, we analyzed two publicly available datasets: MODMA [17] and those provided by Cavanagh et al. [18]. These contain resting-state and task-based ERP data from individuals with and without MDD. Using consistent preprocessing pipelines and statistical controls, we evaluated group-level differences, brain–behaviour correlations, and the reproducibility of spectral and ERP biomarkers across datasets and states.

Methods

MODMA Dataset

The MODMA resting state dataset includes 128-channel recordings from individuals diagnosed with Major Depressive Disorder (MDD_1, n = 24) and healthy controls (HC_1, n = 29) [17]. Metadata, including diagnosis, age, gender, and Patient Health Questionnaire (PHQ-9) scores, were extracted from the accompanying Excel file. Five minutes of eye-closed EEG recordings were collected using a 128-channel HydroCel Geodesic Sensor Net (HCGSN) with a Cz reference and a sampling rate of 250 Hz. EEG data were loaded using Python 3.11.13. Channel labels were assigned using the GSN-HydroCel-129 montage provided by MNE-Python 1.10.0.

Cavanagh et al. Dataset

Resting state and task EEG data were obtained from Cavanagh et al.'s public dataset [18] hosted on the PRED+CT repository [19]. The dataset included EEG data from individuals diagnosed with depression (MDD_2, n = 46) and healthy controls (HC_2, n = 71) recorded at a 500 Hz sampling rate. Resting state lasted 5 minutes. Participants were divided into HC and MDD groups based on Beck Depression Inventory (BDI) scores, where HC_2 = BDI < 8 and MDD_2 = BDI > 8 [18]. Participants with missing or poor-quality data were excluded (see Supplementary Methods for full details). In the task, participants learned probabilistic reinforcement contingencies from Japanese Hiragana symbol pairs with varying reward probabilities (A/B: 80/20%, C/D: 70/30%, E/F: 60/40%). Trials began with a jittered inter-trial interval (300–700 ms), followed by stimulus presentation (up to 4,000 ms) and then feedback (500 ms). EEG was time-locked to feedback onset, and ERP components were extracted at electrode FCz [18].

Resting State Preprocessing

MODMA Dataset preprocessing was conducted using MNE-Python. Each EEG recording was downsampled to 250 Hz, underwent an IIR notch filter at 50 Hz, and a Butterworth IIR bandpass filter from 0.5–45 Hz. Bad channels were identified via statistical rejection if their z-scored amplitude, variance, or average correlation distance fell outside ±3. All marked bad channels were interpolated using MNE spherical spline interpolation. Resting state data in the Cavanagh dataset was preprocessed according to the same methods as Cavanagh task-based data, except resting-state data was epoched into 2-second window according to Cavanagh et al's method. Independent component analysis

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(ICA) was applied prior to spectral analysis to remove artifacts. ICA was fitted on the preprocessed EEG data using the FastICA algorithm to retain 99% of the explained variance. Components were evaluated based on z-scored kurtosis, and those exceeding a threshold of ±2.5 were marked as artifacts and excluded.

Task-Based Preprocessing

Task-based preprocessing and analysis followed Cavanagh et al. [17] (see Supplementary Methods for full pipeline details).

Resting State Analysis

For each subject, the power spectral density (PSD) was computed using Welch's method with 2-second windows. Frequency band power was extracted for the four standard bands delta (1–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), and beta (12–30 Hz). Per-channel band power was averaged and stored with metadata in a structured pandas DataFrame. Topographic plots were generated using MNE to show spatial distributions of average band power across channels, along with the difference between those with MDD_1 and HC_1. The same methods were used to compute PSD and extract band powers for MDD_2 and HC_2.

Task-Based Analysis

Following Cavanagh et al.'s methods, [17] ERP data were bandpass filtered between 0.1 and 20 Hz and baseline-corrected to the mean voltage from −200 to 0 ms relative to feedback onset. Analyses focused on feedback-locked ERPs at electrode FCz. For punishment trials, the Feedback-Related Negativity (FRN) component was quantified using a peak-to-trough measure: the difference between the N2 (276 ms) and P3 (376 ms) amplitudes. For reward trials, the RewP component was quantified as the average voltage from 250 to 350 ms post-feedback.

To assess the relationship between ERP components and depressive symptoms, Spearman correlations were computed between ERP amplitude (at each time point) and BDI scores for HC_2 and MDD_2, separately. Time-frequency (TF) power dynamics were plotted for HC_2 and MDD_2 participants at electrode FCz for punishment and reward conditions.

Statistical Tests

Group-level statistical analyses were conducted for both resting-state and task-based data. For resting-state EEG, independent-samples t-tests were used to compare MDD_1 vs. HC_1 and MDD_2 vs. HC_2 for each channel × frequency band. For MDD_1 vs. HC_1, both raw and FDR-corrected p-values were computed, and binary significance maps ($p < 0.05$) were visualized as heatmaps. Pearson correlations between resting-state band power and PHQ-9 scores were computed across all participants, with FDR correction applied across all channel × band correlations (Benjamini–Hochberg). For MDD_2 vs. HC_2, unequal-variance t-tests with FDR correction were performed, and topographic plots displayed spatial distributions of mean band power and group differences. Spearman correlations were also computed between resting-state band power and the FRN–RewP difference score across MDD_2 participants.

For task-based EEG, correlations between punishment and reward ERPs and BDI scores were plotted over time with bootstrap-based SEMs, and significance at each time point was FDR-corrected ($q < 0.05$). Between-group differences in correlation strength were tested using Fisher's z-transformation with FDR correction. Time–frequency analyses involved Spearman correlations between BDI scores and TF power at each time–frequency point, with cluster-based correction (neighbourhood thresholding) applied to control for multiple comparisons.

Resting State Comparison Between Datasets

Group-level comparisons of mean band power were conducted between the MODMA and Cavanagh et al. datasets for both MDD and HC participants. For each group, mean power across all electrodes was computed for each canonical frequency band. Independent sample t-tests were performed to assess statistical differences between datasets within each group (MDD_1 vs. MDD_2 and HC_1 vs. HC_2). To further evaluate dataset-level differences, Fisher's r-to-z transformations were applied to compare correlations between band power and normalized depression scores (PHQ-9 for MODMA, BDI for Cavanagh).

Results

MDD_1 Showed Increased Beta Power and Reduced Alpha Power Relative to HC_1 but These Effects Were Not Significant

PSDs and topographs at each band power across MODMA (Figure 1A,C) and Cavanagh datasets (Figure 1B,D) demonstrated minimal differences between MDD and HC groups within each dataset, though beta power displayed visible trends with being higher power in MDD than HC.

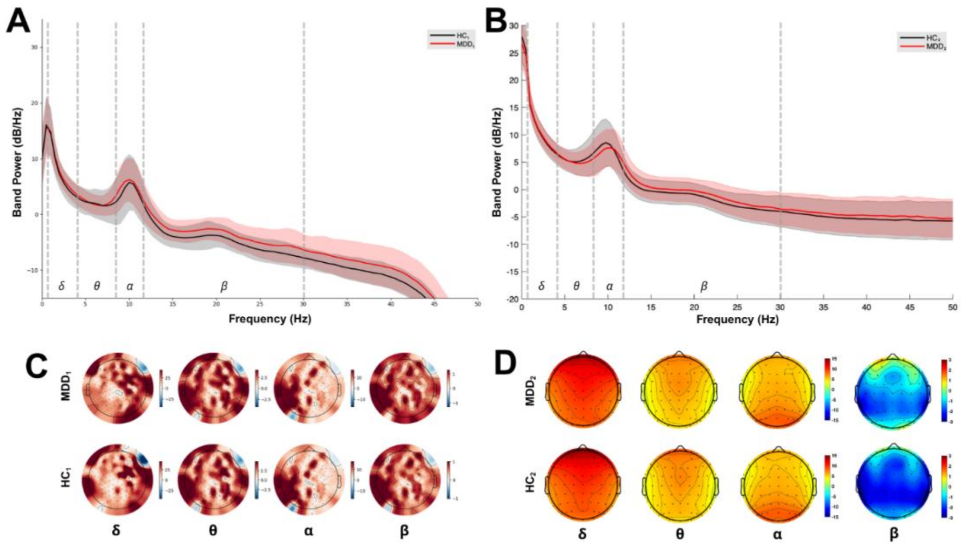

Figure 1. *Average Resting-State EEG Power Spectra and Topographies Across MODMA and Cavanagh Datasets*. **A)** Average PSD across all channels of HC$_1$ (black) and MDD$_1$ (red) from the MODMA dataset. **B)** Average PSD across all channels of HC$_2$ (black) and MDD$_2$ (red) from the Cavanagh dataset. **C)** Band specific topographs of HC$_1$ and MDD$_1$. **D)** Band specific topographs of HC$_2$ and MDD$_2$. Shaded regions reflect the standard deviation (SD). Dashed vertical lines indicate canonical frequency band boundaries. Figure created using Python (A and C), MATLAB (B and D), and Canva.

MDD$_1$ Showed Non-Significant Increased Beta Power and Reduced Alpha Power Relative to HC$_1$

Topographic maps of band power differences (MDD$_1$ − HC$_1$) revealed distinct spatial patterns across canonical EEG bands (Figure 2A). MDD$_1$ displayed increased beta power in the bilateral frontal and temporal regions when compared to HC$_1$($q > 0.05$). Alpha power was also lower in the parieto-occipital areas ($p > 0.05$), whereas delta and theta bands had more diffuse differences. Independent samples t-tests were conducted across all 128 channels and four frequency bands. At an uncorrected threshold ($p < 0.05$), 14 beta-band channel x group comparisons were significant (Table 1). However, after FDR correction ($q < 0.05$), none of the comparisons were significant.

Group-level resting-state comparisons of mean band power at resting state were conducted between MDD$_2$ and HC$_2$ but revealed no strong correlation or significant differences for any of the canonical power bands.

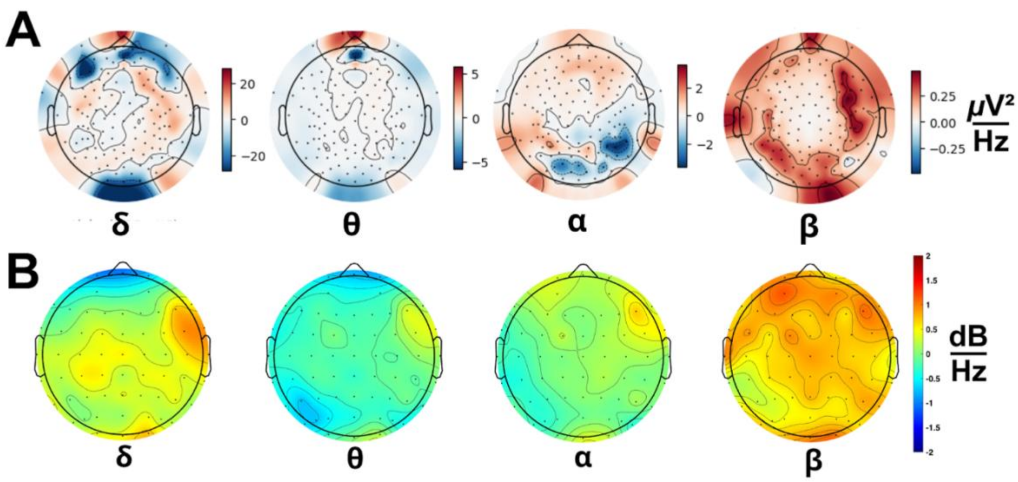

Figure 2. *MDD and HC Resting-State EEG Power Spectra Differences within MODMA and Cavanagh Datasets.* **A)** Topographic maps showing EEG power differences (MDD$_1$ − HC$_1$) across delta, theta, alpha, and beta bands (MODMA). **B)** Topographic maps showing EEG power differences (MDD$_2$ − HC$_2$) across delta, theta, alpha, and beta bands (Cavanagh). Figure created using Python (A), MATLAB (B) and Canva.

Table 1. Uncorrected significant differences in Beta Band Power between MDD_1 and HC_1

Electrode	p-value	Percent Difference	Electrode	p-value	Percent Difference
E2	0.0485	40.7%	E65	0.0349	41.9%
E13	0.0390	48.1%	E76	0.0496	40.8%
E17	0.0196	46.2%	E77	0.0498	36.6%
E40	0.0416	69.8%	E116	0.0465	102.5%
E51	0.0438	44.8%	E120	0.0415	42.2%
E58	0.0367	50.2%	E124	0.0362	55.7%
E59	0.0137	55.1%	E127	0.0485	33.0%

<u>Beta Power Showed the Strongest Positive Correlations With Depression Severity but Were Not Significant</u>

Topographic maps of Pearson correlation coefficients between EEG band power and PHQ-9 scores revealed frequency-specific spatial patterns (Figure 3). Beta power showed the strongest positive associations with depression severity. Alpha and theta bands exhibited weaker and more variable correlations. Across all 128 channels and four frequency bands, 66 beta-band channels × correlation comparisons were significant at an uncorrected threshold ($p < 0.05$), but not after FDR correction ($q < 0.05$).

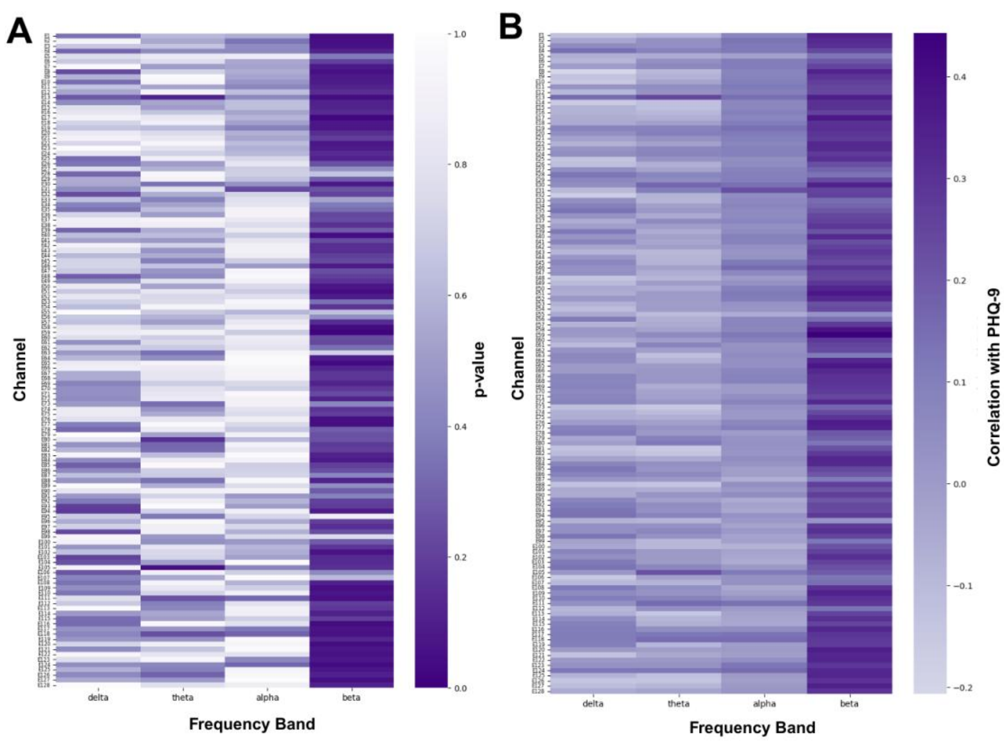

Figure 3. *Uncorrected Differences in Power Spectral Bands Between MDD_1 and HC_1 Groups and Band Power Correlation with PHQ-9.* Each row represents one of the 128 EEG channels, and each column corresponds to a canonical frequency band. **A)** Corresponding heatmap of raw p-values across all channels and frequency bands. Lighter shades represent higher p-values, while darker shades indicate lower (more significant) q-values. **B)** Pearson correlation between band power at each channel and PHQ-9 scores. Positive correlations are shown in darker shades. Figure created using Python and Canva.

FRN and RewP Amplitudes Showed Correlations With Depression Scores

Participants completed a probabilistic reinforcement learning task during EEG recording. In the training phase, they chose between Hiragana symbol pairs that were associated with fixed reward probabilities and received probabilistic feedback. EEG was time-locked to feedback, and ERPs were analyzed at FCz. FRN and RewP ERP amplitudes were correlated with BDI depression scores (Figure 4). Significant within-group Spearman correlations ($p < 0.05$) were found; however, following FDR correction, no relationship reached statistical significance ($q < 0.05$). HC_2 show a reduced P3 amplitude compared to the depressed group within the punishment window. MDD_2 showed significant positive correlations within and beyond the punishment P3 window.

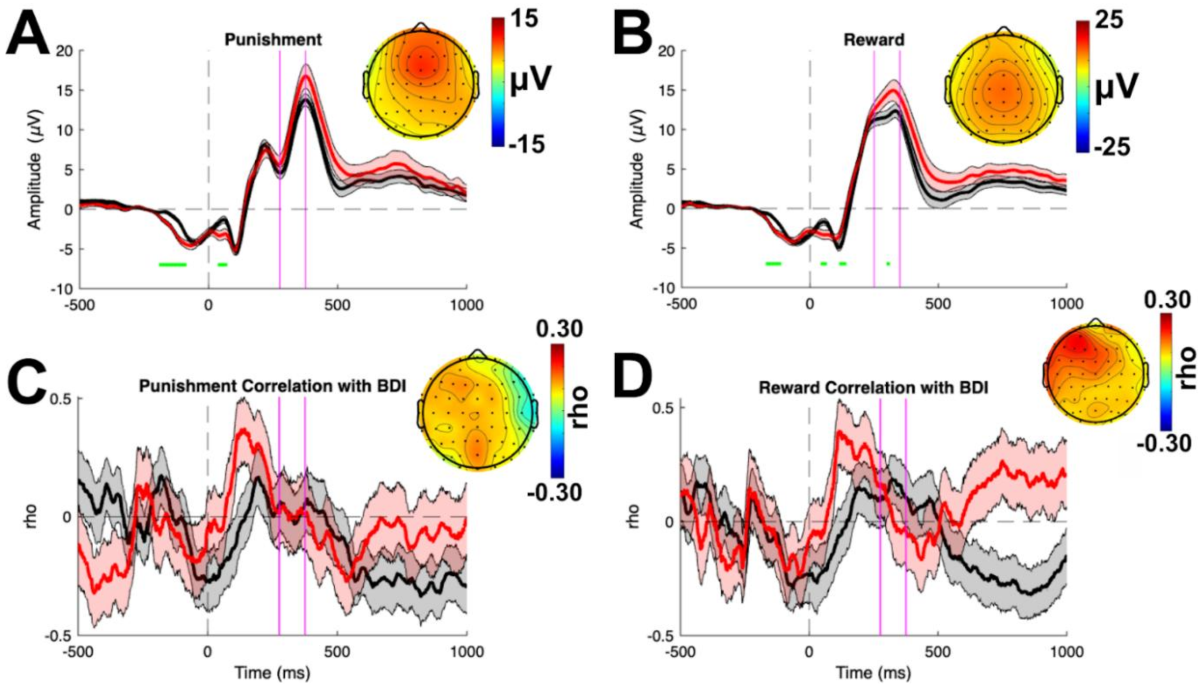

Figure 4. *ERP Group Differences and Correlations with BDI During Punishment and Reward Feedback.* All plots display time in milliseconds (ms) on the x-axis, with stimulus onset at 0 ms (dashed vertical line). Magenta vertical lines mark predefined ERP windows used for analysis (Punishment: 276–376 ms; Reward: 250–350 ms). Horizontal green ticks indicate FDR-corrected significant group differences ($q < 0.05$). All data are from electrode FCz; shaded areas around traces represent standard error of the mean (SEM). Black and red lines denote HC_2 and MDD_2, respectively. **A)** Average ERPs during punishment trials for HC_2 and MDD_2. The topographical inset shows the scalp distribution of the mean voltage difference (376–276 ms), with a central positivity. **B)** Average ERPs during reward trials for each group. MDD_2 exhibited blunted RewP relative to controls within the 250–350 ms window. The topographic inset shows frontocentral positivity during the reward window, with attenuated responses in the depressed group. **C)** Time-resolved Spearman correlations between punishment ERP amplitude and BDI scores. The topographic map shows the scalp distribution of average rho values across the punishment window, with the strongest correlations over frontocentral regions. **D)** Time-resolved Spearman correlations between reward ERP amplitude and BDI scores. The scalp map indicates that these reward-related BDI correlations are centred over frontocentral sites. Subplots A and B are the intellectual property of Cavanagh et al [18]. Figure created using MATLAB and Canva.

MDD_2 Demonstrated Stronger Theta and Delta Responses than Hc_2, Though Reward-Evoked Theta Activity was Reduced and More Diffuse

TF Power Dynamics (Figure 5) demonstrated that punishment feedback increased theta power in HC_2 and that reward feedback increased delta power. MDD_2 showed similar results; however, MDD_2 showed more pronounced and intense theta and delta activity following both punishment and reward, respectively. Notably, MDD_2 had more theta band activity than HC_2 following punishment feedback. Positive correlations are evident in the beta range (~15–25 Hz) around 200–500 ms, while significant negative correlations are seen in the theta band (~4–6 Hz). A significant negative correlation cluster is observed in the theta range (~4–6 Hz) post-feedback. Compared to HC_2, MDD_2 reward-evoked theta activity appears reduced, with a more diffuse temporal profile.

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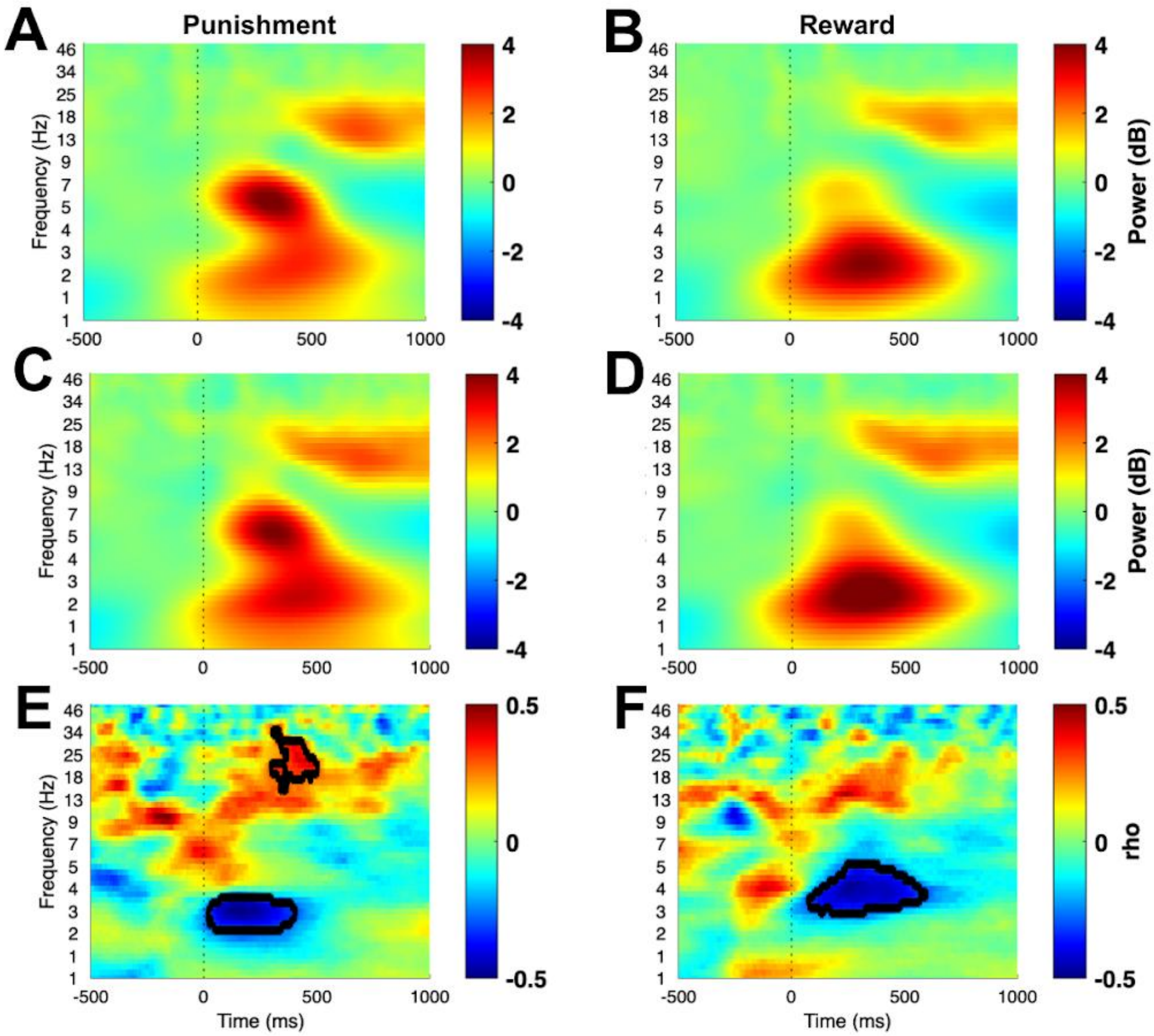

Figure 5. *Time–Frequency Power Dynamics and BDI Correlations During Punishment and Reward Feedback.* All plots display time (ms) on the x-axis (stimulus onset at 0 ms, dotted vertical line) and frequency (Hz) on the y-axis, with power plotted using a jet colormap. Panels A–D show average power (in dB), while Panels E–F display Spearman rho values between power and BDI scores in the depressed group. **A)** Average time–frequency power (in dB) at electrode FCz in HC_2 during punishment feedback. A prominent increase in theta (4–8 Hz) and lower-beta (~13–20 Hz) power emerges post-feedback, peaking ~300–500 ms. **B)** Average time–frequency power (in dB) at electrode FCz in HC_2 during reward feedback. Strong theta power increases are observed post-reward, particularly in the 4–7 Hz range, along with later beta activity. **C)** TF power in MDD_2 during punishment trials. Similar temporal and spectral profiles are observed as in HC_2, but with subtle reductions in magnitude, particularly in theta and low-beta bands. **D)** TF power during reward feedback in MDD_2. **E)** Time–frequency map of Spearman rho values between punishment-evoked power and BDI scores in MDD_2. Black contours denote statistically significant clusters ($p < 0.05$). **F)** Time–frequency map of Spearman rho values between RewP power and BDI scores in MDD_2. Black contours denote statistically significant clusters (corrected $p < 0.05$). Subplots A and B are the intellectual property of Cavanagh et al [18]. Figure created using MATLAB and Canva.

No Correlation Between MDD_2 Band Powers and ERP Amplitude Difference

In the MDD_2 group, correlation analyses revealed no significant associations between the FRN–RewP amplitude difference and power in canonical frequency bands. Although slight positive trends were observed across all bands (Figure 6A–D), none reached statistical significance, indicating that variations in ERP-based feedback processing were not reliably related to resting-state spectral power in these frequency ranges.

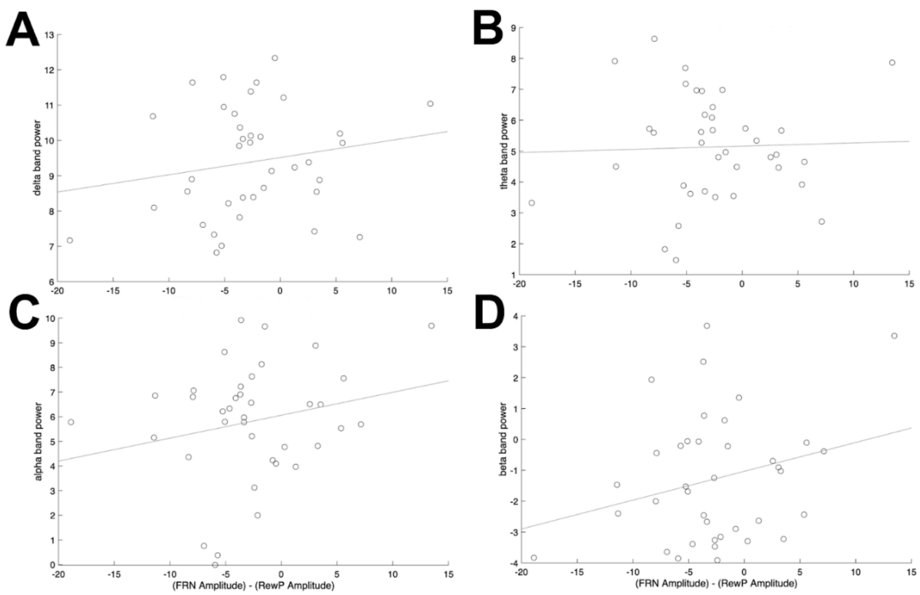

Figure 6. *Correlation Between MDD_2 Band Powers and FRN-RewP Amplitude Difference.* Scatter plots show the relationship between the ERP difference value (FRN amplitude minus RewP amplitude) and band power for each frequency band. No significance or strong correlation was found across any relationship. Each point represents one participant. Gray lines show the linear regression fit. Figure created using MATLAB and Canva.

<u>MDD_1 Exhibited Higher Delta, Theta, and Beta Power Than MDD_2, While Healthy Controls Also Differed Significantly in Delta and Theta Power Across Datasets</u>

Group level comparisons of mean band power at resting state were conducted between the MODMA (MDD_1, HC_1) and Cavanagh et al. (MDD_2, HC_2) datasets across delta, theta, alpha, and beta bands (Figure 7). For MDD participants, there was a significant difference in the delta ($p = 0.0119$), theta ($p < 0.0001$), and beta power bands ($p < 0.0001$), with MDD_1 participants exhibiting higher average powers in these bands. There was no significant difference in alpha power. Among healthy controls, delta ($p = 0.0138$) and theta ($p = 0.0056$) power were significantly higher in HC_1 compared to HC_2, whereas alpha and beta power were not significantly different.

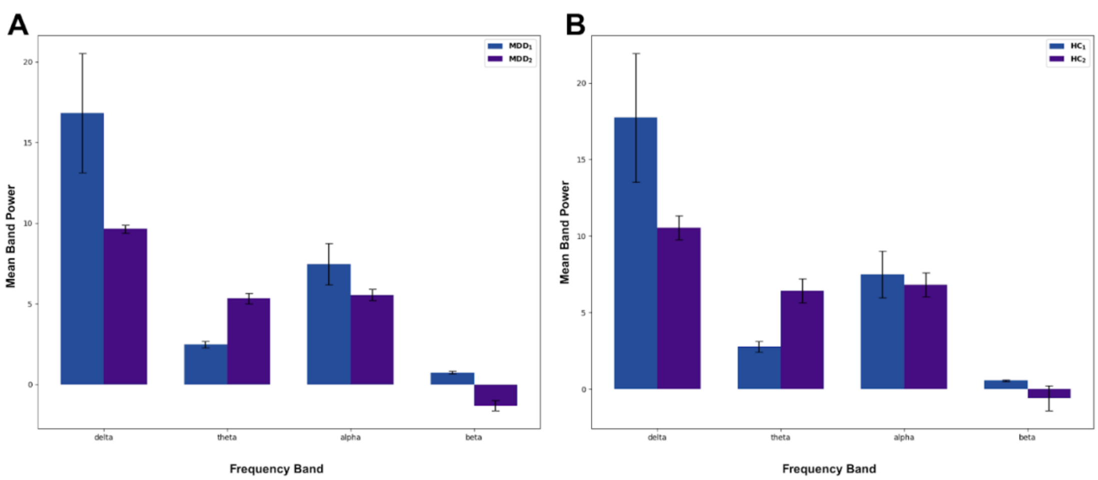

Figure 7. *Group-Level Comparisons Between the MODMA and Cavanagh et al. Datasets.* **A)** Mean band power across all 128 electrodes for MDD participants in each dataset (MDD_1: MODMA, MDD_2: Cavanagh). **B)** Mean band power across all electrodes for HC participants in each dataset (HC_1: MODMA, HC_2: Cavanagh). Each bar represents the average power within a canonical frequency band (delta, theta, alpha, beta), and error bars denote the standard error of the mean (SEM) across participants. These plots highlight between-dataset variability in spectral power profiles within both clinical and healthy control groups. Figure created using Python and Canva.

Beta Band Correlations With Depression Scores Were Stronger in the MODMA Dataset Than Cavanagh, but Neither Reached Significance

Fisher's r-to-z tests were conducted to compare the strength of correlation between EEG band power and normalized depression scores across datasets (PHQ-9 in MODMA vs. BDI in Cavanagh). Beta band power exhibited the largest difference, with a higher mean correlation in MODMA ($r = 0.263$) than in Cavanagh ($r = 0.045$), though this difference did not reach statistical significance ($z = 1.321$, $p = 0.1864$). Alpha band correlations differed in direction between datasets ($r = 0.049$ vs. -0.105), but the difference was also not significant ($z = 0.911$, $p = 0.3625$). Delta and theta band differences were minimal ($p > 0.85$).

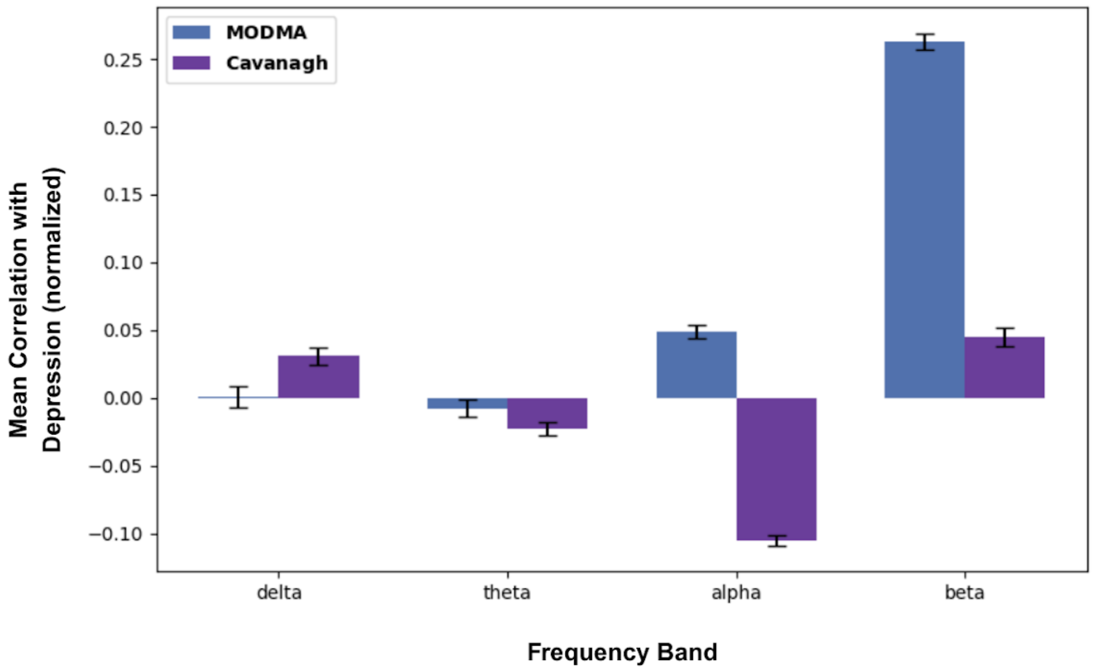

Figure 8. *Band Power Correlation with a Normalized Depression Metric for Both Datasets.* Mean Pearson correlation coefficients between EEG band power and normalized depression scores (PHQ-9 for MODMA; BDI for Cavanagh) are shown across canonical frequency bands. Depression scores were normalized to a 0–1 scale to allow comparison across instruments. Each bar reflects the average correlation across all available electrodes in the respective dataset, and error bars represent the standard error of the mean (SEM). Figure created using Python and Canva.

Discussion

EEG has long been considered a promising modality for identifying neural biomarkers of Major Depressive Disorder due to its direct measurement of brain activity, high temporal resolution, and clinical accessibility. Despite decades of research, however, no EEG based marker has demonstrated sufficient robustness or reproducibility to support routine clinical use. A central unresolved issue is whether commonly reported EEG signatures of depression, including resting state spectral power alterations and reward related ERPs, generalize across independent datasets, recording contexts, and analytic pipelines. This question is critical because biomarkers that fail to replicate across cohorts or brain states may reflect dataset specific characteristics rather than stable neurophysiological processes. In this study, we directly evaluated the consistency of resting state and task evoked EEG features across two independent datasets to assess their reproducibility and potential clinical relevance.

In the MODMA dataset, there was a clear trend in the beta power band, where both topographic and statistical heat maps highlighted increased beta power in MDD_1 participants, specifically in the bilateral frontal and temporal regions. Although not significant following FDR multiple comparisons correction, 14 channels showed a trend towards higher beta power among MDD_1 patients relative to the healthy control, while 66 beta-band channels exhibited a positive association trend with PHQ-9 scores. This is in line with previous research showing that elevated beta power has been associated with ruminative thought, heightened arousal, and cognitive inflexibility among depression patients [20]. Previous studies have also reported that increased beta power and reduced alpha power may serve as EEG biomarkers of affective dysregulation [21]. Although not statistically significant, our results echo this literature suggesting beta power may quantitatively reflect depressive symptoms severity in some populations. Taken together, these findings suggest that beta power

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alterations may reflect cohort-specific sensitivity rather than a stable, generalizable biomarker of depression.

In contrast, the Cavanagh dataset (MDD_2 vs. HC_2) showed no significant group differences in spectral power and no significant correlations between BDI scores and spectral band power. While beta power emerged as a potential biomarker candidate in MOMDA, this pattern was not present in this dataset even at uncorrected levels. We found no significant resting-state spectral differences in the Cavanagh dataset (MDD_2 vs. HC_2), nor did we observe strong correlations between BDI scores and resting-state band power. It is important to note although the Cavanagh dataset included resting-state EEG recordings, the original publication did not conduct a resting state analysis. Our analysis extends the utility of the Cavanagh data by incorporating resting state features and placing them in direct comparison with the MODMA findings contributing to a more comprehensive understanding of EEG biomarkers across states. The absence of comparable effects in this dataset indicates that resting-state spectral markers reported in single cohorts may not readily transport across samples, even when similar analytic approaches are applied.

The lack of cross-dataset consistency may stem from a few reasons. Firstly, depression is highly heterogeneous, with symptom profiles varying considerably between individuals, samples, and depression subtypes [22]. This variability may obscure consistent neural biomarkers in large and varied samples. Second, methodological differences may also contribute to the inconsistencies including EEG hardware and recording conditions [23]. When analyzing the data, subtle variances in the preprocessing may affect signal-to-noise ratios and sensitivity across the cohort. Additionally, resting-state EEG frequency band makers often overlap with other psychiatric disorders such as ADHD, OCD, and schizophrenia which could further limit the specificity of spectral markers [21].

In terms of task-evoked ERP components, our analysis focused on the FRN and RewP components during punishment and reward feedback. Although prior literature has reported blunted RewP and exaggerated FRN amplitudes in depressed individuals [24, 25] we found no statistically significant group differences between MDD_2 and HC_2 after correction, despite visible trends. Specifically, the RewP appeared reduced in MDD_2 relative to controls, consistent with anhedonic processing [24–26], characterized by diminished neural response to rewarding stimuli. Although anhedonia is a core symptom of MDD [27], the RewP reductions in MDD_2 were not significant following FDR correction. This is in line with previous research, where despite decreased RewP being associated with depression, no significant differences were found between HCs and MDD patients [28]. This pattern suggests that commonly reported ERP markers of reward processing may be more sensitive to task structure or sample characteristics than to depression diagnosis alone.

Similarly, we observed modest correlations between ERP amplitude and BDI depression scores within MDD_2 participants, with frontocentral topographies, but again, these failed to reach statistical significance after correction. In contrast, Li et al. [29] reported statistically significant P300 differences (which temporally and topographically overlap with RewP) across depressive state groups at electrode Pz. Their findings suggest that even subthreshold depressive states may elicit measurable differences in neural processing. The lack of significance in our sample, despite a larger and clinically diagnosed cohort, highlights the potential variability across paradigms and populations, and further underscores the challenges in identifying robust EEG biomarkers of depression.

TF analyses during feedback showed expected theta increases in both groups, and exploratory correlations suggested negative associations between theta power and depression severity in the reward condition. These effects were statistically weak and diffuse, suggesting limited robustness of ERP–BDI associations in this dataset.

In summary, we re-analyzed resting and task-based EEG from two independent datasets and found no statistically significant trends in either spectral or ERP measures. This emphasizes the challenges in establishing reliable EEG biomarkers for MDD.

Limitations

Our automated analysis pipeline ensures reproducibility but may miss subtle artifacts detectable by expert review. Moreover, the use of absolute (rather than normalized) resting state values, reliance on a single task paradigm, and lack of EEG standardization may limit generalizability and bias results toward a subset of MDD patients [22].

Conclusions

This study investigated EEG biomarkers of MDD using two independent datasets with both resting-state and task-based recordings. In the MODMA dataset, MDD_1 participants showed increased beta power and positive correlations with depression severity, but these findings were not significant following multiple comparisons correction. By contrast, the Cavanagh dataset showed no spectral or ERP group differences, nor correlations with BDI scores, even at uncorrected levels.

The discrepancy between datasets raises concerns about the reliability and generalizability of EEG biomarkers across populations. Differences in demographic and technical factors, depression heterogeneity, and overlap of EEG features across psychiatric disorders may contribute to inconsistent findings.

These results add to evidence that spectral features such as beta power may index depressive symptomatology but highlight the challenges of identifying consistent biomarkers. Future research should examine why spectral markers emerge in some datasets but not others, and whether demographic, clinical, or technical variables (e.g., hardware and recording conditions) drive this variability. Investigating whether specific MDD subtypes yield more consistent EEG patterns than broader diagnostic categories [29] may also improve biomarker specificity.

Addressing these issues will require standardized EEG protocols, refined clinical categorization, and direct cross-dataset comparisons. Combining automated processing pipelines with expert oversight may further enhance reliability. Together, these steps could advance the identification of EEG biomarkers that are both robust and clinically meaningful.

List of Abbreviations

BDI: Beck Depression Inventory
EEG: electroencephalogram
ERP: event-related potential
FDR: false discovery rate
FRN: feedback-related negativity
HC_1: healthy control group in MODMA dataset
HC_2: healthy control group in Cavanagh et al. dataset
HCGSN: hydrocel geodesic sensor net
ICA: independent component analysis
MDD: major depressive disorder
MDD_1: major depressive disorder group in MODMA dataset
MDD_2: major depressive disorder group in Cavanagh et al. dataset
PHQ-9: patient health questionnaire
PSD: power spectral density
RewP: reward positivity
SEM: standard error of the mean
TF: time-frequency

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Ethics Approval and/or Participant Consent

Consent from study participants was gained by those who made the original datasets.

Authors' Contributions

KS: reprocessed and analyzed the Cavanagh dataset; created Figures 1, 2, 4, 5, and 6; drafted and revised the manuscript; and gave final approval of the version to be published.
MFF: reprocessed and analyzed the MODMA dataset; created Table 1 and Figures 1, 2, 3, 7, and 8; drafted and revised the manuscript; and gave final approval of the version to be published.
RG: drafted part of the introduction, revised the manuscript, and gave final approval of the version to be published.

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