Evaluating Frontal Alpha Asymmetry as a Biomarker for Major Depressive Disorder: A Spectral Analysis of Resting-State EEG

Abstract

Frontal Alpha Asymmetry (FAA) is a quantitative electroencephalography (EEG) measure of the difference in activity between the left frontal and right frontal lobes. It has been proposed that activity in the left frontal lobe is associated with "approach" (reward-seeking or goal-directed behavior), while activity in the right frontal is associated with "withdrawal" (avoidance or inhibition) - this is known as Davidson's Approach-Withdrawal model. Based on current research, the evidence linking Frontal Alpha Asymmetry (FAA) directly to Major Depressive Disorder (MDD) is inconsistent. Nonetheless, the objective of this study is to evaluate FAA as a biomarker for depression using a publicly available dataset, by comparing resting-state alpha activity in patients with MDD versus healthy controls.

Methods: The data were processed using the MNE-Python library. Preprocessing included bandpass filtering (1–40 Hz), notch filtering (50 Hz), and artifact rejection through amplitude thresholding. Power Spectral Density (PSD) was estimated using Welch's method to extract alpha band power (8–13 Hz). FAA scores were calculated using the difference in natural logarithms of right and left electrode activity, i.e. ln(F4) – ln(F3).

Results: T-tests revealed a statistically significant difference in asymmetry scores between groups ($t = -2.40$, $p = 0.023$). The healthy control group exhibited a higher mean FAA score ($M = 0.22$) compared to the MDD group ($M = 0.06$). The findings indicate significantly reduced relative left-frontal activity in the MDD group compared to the Healthy group. This supports the hypothesis that there exists a deficit in "approach" mechanisms in depressed subjects.

Introduction

Major Depressive Disorder (MDD) is a leading cause of disability worldwide. It is characterized by persistent low mood and a diminished interest in daily activities.[1] Despite its prevalence, diagnosis lacks standardized, objective, biomarkers and heavily relies on subjective clinical interviews and self-report questionnaires.

One proposed framework for understanding the neural underpinnings of depression is the approach-withdrawal model of hemispheric asymmetry (Davidson, 1998; Henriques & Davidson, 1991).[2][3] This theory states that the left frontal cortex mediates approach-related

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[1] **Jerry L. Halverson, "Depression," *StatPearls*, last modified January 7, 2024, https://www.ncbi.nlm.nih.gov/books/NBK559078/.**

[2] Jeffrey B. Henriques and Richard J. Davidson, "Left Frontal Hypoactivation in Depression," *Journal of Abnormal Psychology* 100, no. 4 (1991): 535–45.

[3] Richard J. Davidson, "Affective Style and Affective Disorders: Perspectives from Affective Neuroscience," *Cognition & Emotion* 12, no. 3 (1998): 307–30.

behaviors and positive affect, while the right frontal cortex mediates withdrawal behaviors and negative affect. Correspondingly, in the context of MDD, this model predicts a pattern of hypoactivity (reduced activity) in the left frontal region. Electroencephalography (EEG) provides a means to quantify this cortical activity through spectral power analysis. Power in the alpha band (8–13 Hz) is inversely related to cortical activation: higher alpha power indicates lower activity in a given brain region.

It is crucial to mention that a recent meta-analysis of resting frontal alpha asymmetry (FAA**)** across 23 studies found small but significant differences between MDD and controls.[4] The analysis concludes that FAA may provide some diagnostic utility, however it is limited as a standalone biomarker. Another meta-analysis of FAA as a diagnostic marker of depression found that Frontal Alpha Asymmetry (FAA) did not differ significantly between groups, yielding a negligible effect size.[5] It suggests that FAA lacks sufficient sensitivity as a diagnostic biomarker for MDD. However, as Allan and Reznik state in their review of frontal EEG asymmetry as a depression biomarker, these inconsistencies may stem from methodological differences and a reliance on resting-state data alone[6]. Instead of viewing FAA strictly as a diagnostic tool, these authors suggest it may serve as a biomarker for *depression vulnerability*.

While the present study acknowledges that recent meta-analyses reveal inconsistencies regarding association between FAA and depression, it simply aims to provide supplemental evidence by exploring whether a link remains observable within this specific dataset using the methodologies described hereafter.

Methodology

Data

This study utilized a publicly available electroencephalography (EEG) dataset obtained from the Figshare repository (Mumtaz et al., 2017)[7]. The participants are separated into two groups: patients diagnosed with Major Depressive Disorder (MDD) and healthy control subjects.

EEG signals were acquired using a standard 19-channel configuration positioned according to the International 10-20 system. Recordings were conducted in a resting-state environment. While the original dataset contains both eyes-open and eyes-closed conditions, this study restricted

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[4] Yiwen Luo, Mingcong Tang, and Xiwang Fan, "Meta analysis of resting frontal alpha asymmetry as a biomarker of depression," *npj Mental Health Research* 4, no. 1 (2025): art. 2, https://doi.org/10.1038/s44184-025-00117-x.

[5] Nika van der Vinne et al., "Frontal alpha asymmetry as a diagnostic marker in depression: Fact or fiction? A meta-analysis," *NeuroImage: Clinical* 16 (2017): 79–87, https://doi.org/10.1016/j.nicl.2017.07.006.

[6] Allen, J. J. B., & Reznik, S. J. (2015). Frontal EEG Asymmetry as a Promising Marker of Depression Vulnerability: Summary and Methodological Considerations. [cite_start]*Current Opinion in Psychology*, 4, 93–97. https://doi.org/10.1016/j.copsyc.2014.12.017

[7] Wajid Mumtaz et al., "EEG Data New," Figshare, November 23, 2016, https://doi.org/10.6084/m9.figshare.4244171.

analysis exclusively to the eyes-closed (EC) recordings because the alpha rhythm is most prominent during eyes-closed resting states. As a result, 30 MDD subjects and 28 healthy subjects were analyzed. The raw data were provided in European Data Format (.edf).

Data Processing

The MNE-Python library was used for signal processing and analysis. First, raw data files were imported, and channel labels were renamed to map correctly to the international 10-20 system. Non-relevant channels were excluded, retaining only the 19 standard scalp electrodes. To isolate the relevant physiological signals, a bandpass filter (1–40 Hz) was then applied. A notch filter at 50 Hz was also applied to eliminate power line interference. The data were then segmented into epochs of 4 seconds. Artifact rejection was performed using amplitude thresholding: any epoch containing voltage fluctuations exceeding ±100 μV was automatically excluded to minimize the impact of ocular movements and muscle artifacts.

Spectral Analysis

Power Spectral Density (PSD) was computed for each valid epoch using Welch's method. This transformation resulted in a power structure comprising dimensions for epochs, channels, and frequency bins, and contained power values restricted to the Alpha band, defined here as 8–13 Hz.

To derive a single metric of alpha activity for each electrode, a two-step averaging process was employed. First, power values were averaged across the frequency bins within the 8–13 Hz range. Second, these values were averaged across all epochs for a given subject. This yielded a single mean alpha power value for each channel per participant. These final values were used to create a pandas dataframe that was used to calculate FAA scores and T-tests. FAA scores were calculated as follows.

$$FAA = \ln(Power_{F4}) - \ln(Power_{F3})$$

To get a sense of magnitude, the equation can be manipulated as follows to obtain the ratio of F4 alpha power to F3 alpha power (as an indication of *how much more* alpha activity there is in the right vs. left frontal regions).

$$\Rightarrow FAA = \ln \frac{(Power_{F4})}{(Power_{F3})}$$

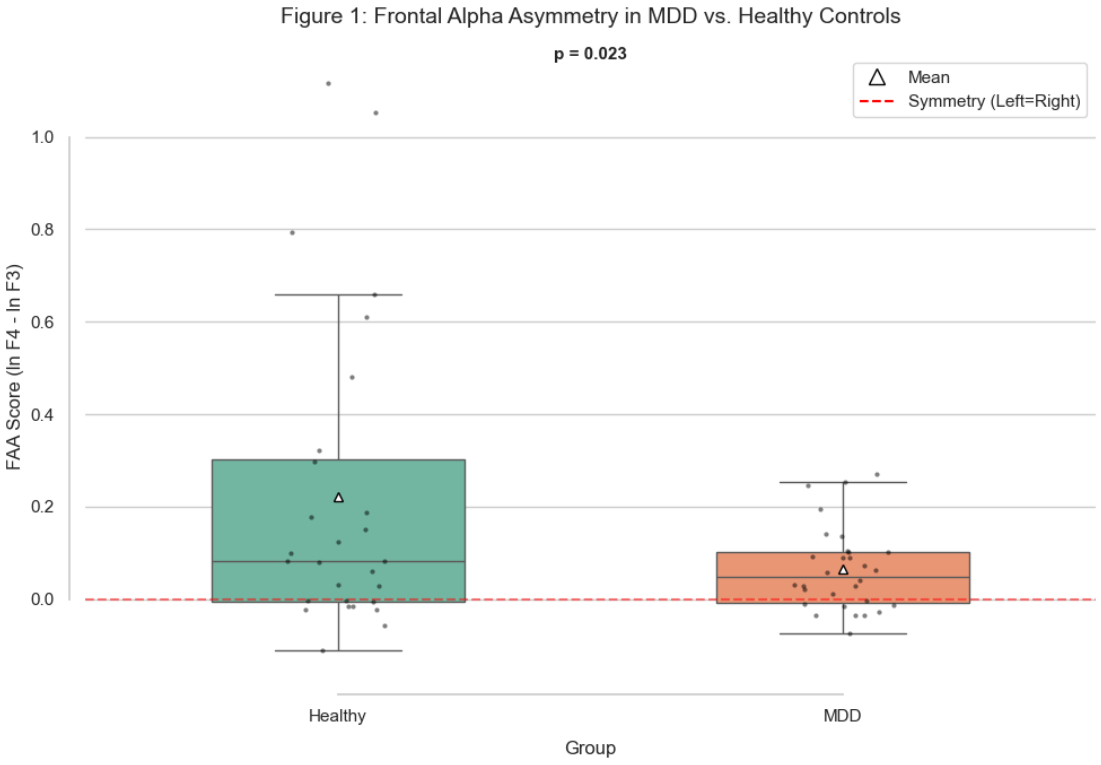
$$\Rightarrow e^{FAA} = \frac{(Power_{F4})}{(Power_{F3})}$$

Results

The analysis included resting-state EEG data from two groups: Healthy Controls and patients with Major Depressive Disorder (MDD). The Healthy Control group exhibited a mean Frontal Alpha Asymmetry (FAA) score of 0.2209, which suggests 25% more alpha activity in the F4 channel compared to F3. In contrast, the MDD group demonstrated a notably lower mean FAA score of 0.0643, suggesting 6% more alpha activity in the F4 than F3. This difference in alpha activity aligns with the theoretical expectation of reduced left-frontal activity (lower asymmetry scores) in depressed subjects.

To assess the significance of this difference, an independent samples t-test assuming unequal variance (Welch's t-test) was used. The analysis revealed a statistically significant difference in FAA scores between the MDD and Healthy groups ($t = -2.402$, $p = 0.023$), meaning the results are statistical significance ($p < 0.05$).

Figure 1 illustrates the distribution of FAA scores across both groups. As shown in the boxplot, both the median and mean asymmetry scores for the Healthy group is higher than that of the MDD group, with the MDD distribution shifted towards zero and negative values.



Discussion

This study investigated resting-state Frontal Alpha Asymmetry (FAA) as a neurophysiological biomarker for Major Depressive Disorder (MDD) using the Mumtaz et al. dataset. Because alpha power is inversely related to cortical activation, these findings align with Davidson's Approach-Withdrawal model, suggesting that MDD is characterized by a deficit in left-frontal "approach" mechanisms rather than an excess of right-frontal "withdrawal" activity.

While these results provide local validation of FAA, they must be interpreted within the context of recent meta-analyses that report inconsistent or negligible effect sizes for FAA as a standalone diagnostic tool. The robustness of this study's findings may be influenced by specific methodological choices such as the use of simple amplitude thresholding (±100 μV) for artifact rejection (rather than Independent Component Analysis (ICA)). Accordingly, while FAA demonstrates statistical significance in this specific cohort, the utility of FAA is likely as a complementary biomarker for depression vulnerability rather than a singular diagnostic determinant.

Moreover, inconsistencies within the diagnostic biomarker literature of depression likely reflect the high heterogeneity of MDD with respect to its diagnostic criteria. In other words, there are a vast amount of different profiles for MDD patients according to the DSM-5's diagnostic criteria: two patients can both be diagnosed with "Severe MDD" and share little to no symptoms (for example, Patient A has insomnia/weight loss/agitation, Patient B has hypersomnia/weight gain/retardation). Therefore, even if robust biomarkers do exist, they may only correspond to certain *kinds* of MDD. This should be taken into consideration when investigating potential biomarkers for MDD. Furthermore, future research should prioritize the identification of specific MDD subtypes, as the identification of these distinct physiological profiles may be necessary for improving the diagnostic reliability of potential neurophysiological biomarkers.

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