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A Novel Neurofeedback Paradigm: First Implementation of Cordance-Based Training for Anxiety and Mood Recovery

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Abstract

This study presents the first implementation of a neurofeedback (NF) protocol based on cordance targeting mood and anxiety disorders. Cordance, a multivariate measure of brain activity, integrates both power within frequency bands and interfrequency relationships, providing a unique perspective on neural synchronization and connectivity. Using a single-case design, a 44-year-old male patient with anxiety, depression, and insomnia was selected based on left frontal discordance. Seven NF sessions were conducted, reinforcing increases in cordance in the left anterior quadrant. The results showed significant improvements in psychometric measures, including reductions in depression, anxiety, and insomnia scores, alongside a marked shift in cordance values toward normative levels. This study introduces cordance-based NF as a potential tool for mood and anxiety regulation, offering promising preliminary evidence for its efficacy. Future research should explore larger sample sizes and longer follow-ups to confirm these findings and expand the clinical applications of cordance-based interventions.

Keywords: concordance; neurofeedback; anxiety; depression

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Introduction

The analysis of electroencephalography (EEG) and quantitative electroencephalography (qEEG) has become a powerful tool in brain function research and in clinical practice for diagnosing various neurological and psychiatric disorders (Babiloni et al., 2020; Chiarenza, 2021; Höller & Nardone, 2021; Niedermeyer & Lopes da Silva, 2005; Schomer & Lopes da Silva, 2017). However, traditional approaches based on univariate analyses of EEG or qEEG have shown significant limitations in consistently and accurately detecting pathologies or in identifying specific therapeutic targets at the physiological level (Livint Popa et al., 2020; McVoy et al., 2019). These methods, which often focus on univariate measures such as the amplitude of frequencies, coherence, or spectral power across different frequency bands, may not adequately capture the complexity of the neurophysiological mechanisms underlying the clinical alterations (Cohen, 2014; Dede et al., 2023; Faiman et al., 2023; Thatcher, 2016). Univariate markers, though informative, are insufficient to fully reflect the complex and multidimensional organization of the human brain. This highlights the need for more robust and sophisticated analytical approaches for identifying specific pathological markers.

This raises the possibility that a more sophisticated approach, such as the use of multivariate analyses or nonlinear methods, could provide a more

comprehensive and representative view of the patient's neurophysiological state. Multivariate analyses allow for the exploration of interactions and activation patterns involving multiple brain regions and various frequency bands, thereby facilitating a more holistic assessment of functional connectivity and brain dynamics in pathological states (Bassett & Sporns, 2017; Friston, 2009; Medaglia et al., 2015; Michel & Murray, 2012). For example, techniques such as complex network analysis, functional connectivity, and multichannel synchronization have proven useful in uncovering interaction patterns that would remain invisible with a univariate approach (Bastos & Schoffelen, 2016; Rubinov & Sporns, 2010).

One of the multivariate measures developed for brain activity analysis is cordance, a complex measure in EEG analysis (Leuchter et al., 1999; Leuchter, Cook, Lufkin, et al., 1994; Leuchter, Cook, Mena, et al., 1994). Unlike simple linear measures, such as amplitude or spectral power, which examine a single feature of the signal, cordance combines multiple aspects of brain activity to provide an integrated view. Specifically, cordance evaluates both the absolute power within a frequency band and its relationship to total power over a broader range, allowing for interpretation of synchronization status and the relative change between different frequencies and brain areas. By combining these elements, cordance provides a perspective on neural connectivity and synchronization that cannot be captured with isolated linear measures such as correlation or power spectral analysis, which assume direct, proportional relationships between variables, making it particularly useful in complex clinical contexts where integrated and robust indicators of brain activity are needed. Cordance has been used as a biomarker of pathology, primarily for depression (Tas et al., 2015) but also for other conditions as Alzheimer's disease, multi-infarct dementia, multiple sclerosis, or frontal lobe degeneration (Cook & Leuchter, 1996; Leuchter, Cook, Lufkin, et al., 1994), as a marker of response to psychopharmacological treatment in depression (Adamczyk et al., 2015; Broadway et al., 2012; Hunter et al., 2006) and also as a marker of response to neuromodulation techniques (Erguzel et al., 2015; Hunter et al., 2018).

Neurofeedback (NF) is a neuroregulation technique that enables individuals to regulate their brain activity through real-time feedback, typically obtained from EEG (Carrobles, 2016). Positioned among nonpharmacological interventions, NF differs from other methods by focusing on the direct training of specific patterns of brain activity, facilitating self-regulation of neural processes. In most cases, NF targets univariate variables, such as power in different frequency bands, to guide training. This technique has demonstrated utility in managing disorders such as anxiety and depression (Hammond, 2005), obsessive compulsive disorder (Sürmeli & Ertem, 2011), attention-deficit/hyperactivity disorder (Arns et al., 2009; Bakhshayesh et al., 2011; Pérez-Elvira et al., 2020), insomnia (Hammer et al., 2011; Pérez-Elvira et al., 2019), fibromyalgia (Kayiran et al., 2007; Pérez-Elvira & Jiménez Gómez, 2020), and epilepsy (Walker, 2005), among others, offering an alternative or complement to conventional pharmacological interventions.

Given that cordance has never before been used as a dependent variable or target for change in NF interventions, the aim of this study is to explore the implementation and efficacy of an NF protocol specifically designed to train cordance, applied in this case to a patient with mood and anxiety difficulties. This experimental protocol seeks to evaluate changes in EEG cordance metrics associated with targeted training, in order to provide preliminary evidence of the feasibility and clinical utility of cordance training as an intervention. To the best of our knowledge, this research represents the first application of a cordance-based training approach, thereby laying the groundwork for future studies in broader clinical contexts.

Methods

Participant

A 44-year-old male patient presented to the neuropsychophysiology clinic with emotional and cognitive complaints. He reported that, after the 2020 pandemic, he had experienced a marked increase in feelings of anxiety and unease, accompanied by persistent fatigue and significant mood fluctuations. These episodes included periods of emotional downturn alternating with moments of greater stability. Overall, he described a constant sense of restlessness and lack of motivation. Over the past year, these symptoms had intensified, affecting his ability to concentrate and sleep. Additionally, he had experienced episodes of insomnia, further exacerbating his fatigue. For anxiety management, he had been prescribed rescue anxiolytic medication, though he reported using it only during critical moments. His medical history also included a previous diagnosis of migraine with aura, which had first appeared during his university years, although these episodes had

been sporadic and were not part of the patient's current primary concerns. We selected this patient based on his cordance profile (left frontal discordance) and the presence of a conventional qEEG with *Z*-scores within the normal range. This selection was made for two main reasons: first, the discordance suggested a potential responsiveness to cordance-based NF, which was the novel intervention being tested; and second, the lack of other abnormal findings in the conventional qEEG minimized the likelihood that any observed improvements could be attributed to unrelated or uncontrolled variables. This made the patient an appropriate candidate to isolate and evaluate the specific effects of the cordance training protocol.

The patient provided written informed consent for the intervention and the publication of this study, which was undertaken at NEPSA Rehabilitación Neurológica, a neurologic rehabilitation clinic authorized by the Regional Department of Health (Castilla y León, Spain. Authorization Code: 37-C24-0216). The Regional Department of Health provided approval for this kind of intervention.

Psychometric Assessment

Beck Depression Inventory-II (BDI-II). The BDI-II (Beck et al., 1996; Sanz et al., 2003) is a self-administered questionnaire designed to assess the severity of depressive symptoms. Some items were updated by Beck et al. (1996) to better align with the DSM-IV diagnostic criteria for major depressive disorder. It consists of 21 items covering both emotional and physical symptoms of depression such as sadness, loss of interest, changes in appetite, fatigue, and feelings of guilt. Each item is rated on a 0 to 3 Likert-type scale, with higher scores indicating greater severity of depressive symptoms. Total scores range from 0 to 63 and are categorized into ranges to determine the level of depression: 0–13 indicates *minimal* depression, 14–19 *mild* depression, 20–28 *moderate* depression, and 29–63 *severe* depression (Beck et al., 1996). It is widely used in both clinical and research settings due to its high reliability and validity in measuring depression severity (Kendall et al., 1987; Sanz & García-Vera, 2013).

Hamilton Anxiety Rating Scale (HARS). The HARS (Hamilton, 1959; Lobo et al., 2002) is one of the most widely used tools in clinical and research settings designed to assess the severity of anxiety symptoms. It consists of 14 items covering both psychological and somatic symptoms. Each item is rated on a 0 to 4 Likert-type scale, with higher scores indicating greater symptom severity. Total scores range from 0 to 56, and results can be classified into mild, moderate, or severe levels of anxiety. A total score of 0–17 indicates *mild* anxiety, 18–24 *moderate* severity, and 25–56 *severe* anxiety (Hamilton, 1959; Lobo et al., 2002). The HARS is a reliable and valid instrument, widely used in clinical studies and in assessing the efficacy of treatments for anxiety (Bech, 2009; Maier et al., 1988; Sugarman et al., 2014; Thompson, 2015).

Athens Insomnia Scale (AIS). The AIS (Gómez-Benito et al., 2011; Soldatos et al., 2000, 2003) is a self-administered questionnaire designed to assess the severity of insomnia based on the criteria of the International Classification of Sleep Disorders (Sateia, 2014). The questionnaire consists of eight items, each rated on a 0 to 3 Likert-type scale, with a total score ranging from 0 to 24 and higher scores indicating greater insomnia severity. A total score of 6 or higher is considered indicative of clinically relevant insomnia problems (Shahid et al., 2011).

Neuropsychophysiological Assessment (qEEG)

EEG Acquisition and Preprocessing. For the collection of the EEGs the patient was fitted with an EEG cap, Electro-Cap (Electro-cap International) with 19 channels located according to International System 10–20 (Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, and O2) and using a Linked Ears montage. For 5 min, EEG signals from all 19 channels were simultaneously obtained and collected using a Discovery24 amplifier from BrainMaster Technologies, Inc. Impedances of less than 5 kΩ were maintained, and a constant temperature and humidity of less than 25°C and 50%, respectively, were maintained in the laboratory. EEG recordings were made in the closed-eye state with the use of Brain Avatar 4.6.4 software (BrainMaster Technologies, Inc.). The EEG signal preprocessing was performed using MNE-Python (version 1.8.0). The signal was band-pass filtered between 1 and 40 Hz, and artifacts were handled using Artifact Subspace Reconstruction (Blum et al., 2019; Kothe & Jung, 2016).

EEG Analysis and Processing. All EEG data processing were performed using Python (version 3.12.1) and the MNE-Python package (1.8.0; Gramfort et al., 2014). These tools were used for signal processing, cordance computation, and graphical representation. Additionally, data visualization and the generation of Microsoft Excel tables with the numerical cordance data were accomplished using SciPy (Virtanen et al., 2020), NumPy (Harris et al., 2020), and Pandas (The

Pandas Development Team, 2024). EEG recordings were processed using Linked Ears montage.

Cordance Calculation.

1. Hjorth Power Calculation of the Alpha Band. Hjorth power was calculated in the alpha band (8–13 Hz), a frequency band frequently studied in EEG due to its association with resting activity and cognitive functions (Başar et al., 2001). A filter between 8 and 13 Hz was applied to the EEG data using MNE-Python's filtering tools, ensuring the extraction of information specific to the alpha band.

Hjorth power in each channel was obtained by calculating the mean square of the alpha-filtered signal, according to the following equation:

$$Hjorth\ power_i = \frac{1}{N}\sum_{t=1}^{N} x_{i,t}^2$$

where:

N is the number of samples,

$x_{i,t}^2$ represents the amplitude at time *t* in channel *i*, and

$Hjorth\ power_i$ corresponds to the alpha band power for channel *i*.

This quadratic power is a common measure to assess the intensity of activity within a specific band, providing an approximation of the signal power in the selected frequency range (Teplan, 2002).

2. Calculation of Total Broadband Power (1–30 Hz). To normalize the power values in the alpha band, the total power in the range of 1–30 Hz was calculated for each channel, encompassing low-frequency components (1 Hz) up to the upper limit of the beta band (30 Hz). This approach follows established practices in EEG quantification, where total power serves as a reference for relative power analyses and normalization (Nunez & Srinivasan, 2006).

Total power was calculated as the mean square of the signal filtered in the 1–30 Hz range:

$$Total\ power_i = \frac{1}{N}\sum_{t=1}^{N} k_{i,t}^2$$

Where $Total\ power_i$ represents the power of the signal for channel *i* across the full frequency range, and $k_{i,t}^2$ represents the amplitude at time *t* in channel *i*.

3. Normalization of Alpha Hjorth Power and Calculation of Relative Power. Two normalization indices were used to assess cordance in each channel, based on the comparison of power in the alpha band with total power.

Alpha normalization (a_{norm}): The Hjorth power of each channel in the alpha band was normalized by dividing it by the maximum Hjorth power value across all channels, as shown in the following formula:

$$a_{norm,i} = \frac{Hjorth\ power_i}{max(Hjorth\ power)}$$

Normalized relative power (r_{norm}): The relative power in the alpha band was defined as the ratio between Hjorth power and total power in each channel, subsequently normalized by dividing it by the maximum relative power value across channels:

$$r_{norm,i} = \frac{\frac{Hjorth\ power_i}{Total\ power_i}}{max\left(\frac{Hjorth\ power}{Total\ power}\right)}$$

This normalization allows for consistent comparison of power levels across channels, regardless of absolute intensity differences (Cohen, 2014).

4. Cordance Classification. To classify cordance, three main categories were established based on the normalized values of a_{norm} and r_{norm}, following the approach proposed in previous studies (Leuchter, Cook, Lufkin, et al., 1994; Leuchter, Cook, Mena, et al., 1994; Kappenman & Luck, 2010):

Discordant: channels where a_{norm} <0.5 and r_{norm} >0.5

Concordant: channels where a_{norm} >0.5 and r_{norm} >0.5

Neutral: channels that do not meet any of the above conditions

This classification was implemented using logical comparisons and allowed categorization of each channel's states based on cordance, providing a three-level objective interpretation of the alignment

between normalized power and relative power in each channel.

5. Cordance Magnitude Calculation. Finally, cordance magnitude was calculated to quantify the degree of concordance or discordance in each channel. This value reflects the degree of deviation of each channel from a reference value of 0.5 in both normalizations, using the following formula:

$$\text{Cordance Magnitude}_i = \left(\left|a_{\text{norm,i}} - 0.5\right| + \left|r_{\text{norm},i} - 0.5\right|\right) \times 100$$

For graphical representation, and by convention (Leuchter, Cook, Lufkin, et al., 1994), discordance values are transformed to negative values, and concordance values to positive values. This cordance analysis was implemented in Python using the MNE-Python library (Gramfort et al., 2013) for EEG signal processing and filtering, whilst NumPy (Harris et al., 2020) was used for mathematical operations and data normalization.

Generation of Comparison Data for Cordance Comparison. To develop a reference database for cordance interpretation, data from 10 EEGs were used from the database: resting-state EEG data before and after cognitive activity across the adult lifespan and a 5-year follow-up, version 1.9.0 (Wascher et al., 2024). The selected EEGs belonged to subjects with characteristics similar to the study subject, allowing for a meaningful comparison in terms of physiological variability and demographic characteristics. Each EEG file, in EDF format, was imported and analyzed in Python using the MNE-Python library (Gramfort et al., 2013). Cordance variables were calculated using the same procedure explained above. The normality of the produced data was checked and organized in a tabular format using Pandas (The Pandas Development Team, 2024). The variables that did not follow an approximate normal distribution (Table 4) were subjected to a logarithmic transformation $X' = log_{10}(x)+1$ to approximate normality and stabilize variance (Bland & Altman, 1996). The addition of 1 was applied to avoid negative values in the transformed data, especially when dealing with original values smaller than 1, for which logarithms yield negative results. Subsequently, the same logarithmic transformation was applied to the subject's data that were to be compared with the comparison database, thereby ensuring homogeneity in the measurement scale. This strategy enabled the derivation of *Z*-scores, facilitating a direct comparison between individual values and the parameters of the comparison database.

Intervention. For the implementation of the NF protocol, the BrainAvatar software (Collura, 2012) was used, which was specifically configured in its Event Wizard to calculate and provide real-time feedback based on cordance parameters. This setup included the creation of bipolar virtual channels, ensuring a montage consistent with Hjorth's (1975) online transformation of EEG potentials into orthogonal source derivations and employed by Leuchter, Cook, Mena, et al. (1994) in cordance calculation.

The cordance calculation procedures were applied using the previously defined metrics, which involve the assessment of Hjorth power in the alpha band (8–13 Hz) and total power in the range of 1–30 Hz. These calculations were conducted according to the methods established in previous studies (Leuchter et al., 1999; Leuchter, Cook, Lufkin, et al., 1994; Leuchter, Cook, Mena, et al., 1994), thus ensuring the consistency and validity of the approach.

The selection of the intervention area was based on cordance measurements. Rather than defining a specific location, an entire quadrant was designated. The quadrant chosen for intervention was determined upon the initial assessment prior to the intervention by comparing the subject's cordance values with those of the comparison database. Specifically, the quadrant that exhibited the greatest average deviation from the normative values, expressed in terms of *Z*-scores and indicating a more pronounced alteration, was selected for intervention (Tables 2, 3, and 4).

The software was set up to integrate the results of the cordance calculations into the feedback provided to the patient, thereby facilitating a real-time training process that responded to variations in brain activity. The setup NF protocol provided reinforcement to the patient each time their current cordance magnitude increased compared to the average of the previous 10 s. This is represented as follow:

$$Reinforcement = \begin{cases} 1, if\ Cordance_{current} > Average\left(Cordance_{prev\ 10}\right) \\ 0, otherwise \end{cases}$$

where:

$Cordance_{current}$ is the current cordance magnitude, and

$Average\left(Cordance_{prev\ 10}\right)$ is the average cordance magnitude over the previous 10 s.

A value of 1 indicates reinforcement is provided, while 0 indicates no reinforcement. The reinforcer was given to the patient every time the cordance value exceeded a preset threshold. Movies selected by the patient were used as reinforcement, ensuring they were engaging enough to sustain attention. This approach was based on evidence suggesting that self-chosen and personally satisfying reinforcers are optimal for facilitating learning through NF (Pérez-Elvira et al., 2021). A dimmer was applied to the movies, which increased in opacity (obscuring the screen) when the patient failed to meet the criterion and became more transparent (allowing the movie to be visible) when the criterion was met. Seven 30-min sessions were conducted, twice per week, following this procedure. This decision to use seven sessions, as opposed to the 10 sessions employed in our previous studies (Pérez-Elvira et al., 2020, 2021), was made to minimize the number of sessions required, thereby avoiding unnecessary burden on the patient within the context of this purely experimental procedure.

Statistical Analysis. To evaluate changes in the scores of the psychological tests administered, the reliable change index (RCI) of Jacobson and Truax (1991) was used.

The RCI is calculated using the following formula:

$$RCI = \frac{X_2 - X_1}{S_{diff}}$$

where:

X_1 is the score obtained in the posttreatment assessment,

X_2 is the score obtained in the pretreatment assessment, and

S_{diff} is the standard error of the difference between the two scores and is calculated as:

$$S_{diff} = \sqrt{2\ x\ SE}$$

The SE or standard error of measurement is obtained using the following formula:

$$SE = SD\ x\ \sqrt{1 - r}$$

where:

SD is the standard deviation of the test scores in the reference population (Gómez-Benito et al., 2011; Lobo et al., 2002; Sanz et al., 2003), and

r is the reliability of the test (such as the test-retest reliability coefficient or Cronbach's alpha).

To interpret the RCI, if the value is greater than 1.96 or less than −1.96, the change is considered statistically significant at the 95% confidence level. If the value is between −1.96 and 1.96, the change is not considered significant.

To apply a paired samples *t*-test and study changes in cordance, a similar approach to that expressed by Thatcher (2021) was used. A sliding window approach was employed to segment the EEG data into overlapping chunks. Chunks of 30 s were generated. A window of the specified length was set and slid across the entire EEG recording, advancing 1 s for each new segment. Specifically, the first segment included data from $t = 1$ to $t = n$, where t represents the time points of the segment and n is the theoretical upper limit of the segment interval. The second segment would then encompass data from $t = 2$ to $t = n + 1$, and so on, covering the entire dataset.

Mathematically, for the EEG time series $X(t)$, where $t = 1, 2, \ldots, T$ represents the time points in the EEG recording, each segment S_i is defined as:

$$S_i = X(i{:}\ i + \omega - 1),\ i = 1, 2, \ldots, T - \omega + 1$$

where:

S_i represents the i-th segment,

$X(i{:}\ i + \omega - 1)$ denotes the subset of the EEG signal from the time point i up to $i + \omega - 1$,

ω is the length of the window, and

T is the total number of time points in the EEG recording.

Both EEGs (pre and post) had the same recording duration but different edited durations. The first had an artifact-free duration of 1 min and 20 s, while the second had an artifact-free duration of 1 min and 2 s. Thus, 51 samples were generated for the pre-EEG and 33 for the post-EEG. To match the comparisons and avoid issues with the different number of samples, the number of samples for the shorter EEG was selected, meaning that 33 samples were used for both measurements.

For the analyses, which involved multiple comparisons, we applied Storey's *q*-value method (Storey, 2002), which estimates the proportion of true null hypotheses (π_0) and provides adjusted *p*-values (*q*-values) that control the false discovery rate. The λ parameter was set to 0.5 for π_0 estimation. Statistical significance was set at α = .05 for all analyses, with results considered significant when $q < .05$ after correction.

Results

Baseline Psychometric Assessment

In the baseline psychometric assessment of this subject, scores indicative of psychological distress and insomnia were found (Table 1).

Specifically, regarding mood assessment, a BDI-II score of 28 points was obtained, suggesting the presence of clinical depression symptoms such as low mood, feelings of hopelessness, and decreased interest in activities. Regarding anxiety symptoms, the total score of 23 suggested moderate levels of anxiety. On the AIS, the subject scored 12 points, suggesting a moderate intensity of insomnia.

Posttreatment Psychometric Changes

The subject's scores for each scale, as well as the results of their statistical analysis, are shown in the table (Table 1).

Table 1
Psychometric Assessment

Test	X_1	X_2	*r*	*SD*	RCI
BDI-II	28	15	.91	10.9	−2.81
HARS	23	14	.92	9.45	−2.38
AIS	12	6	.90	3.24	−4.14

Note. BDI-II**:** Beck Depression Inventory-II; HARS: Hamilton Anxiety Rating Scale; AIS: Athens insomnia scale; X_1: Pretreatment assessment; X_2: Posttreatment assessment; *r*: reliability coefficient; *SD*: standard deviation; RCI: Reliable Change Index.

Cordance Baseline

In Table 5, the pretreatment cordance calculated and its associated magnitude can be found. In Table 2, the average magnitude of the cordance can be observed in a classification by quadrants (Gazzaniga, 2000; Hammond, 2005).

Quadrant A was selected for intervention as it had the highest average *Z*-score, deviated the most from the comparison values, and therefore exhibited the least optimal functioning (Northoff & Tumati, 2019), in addition to its connection with the patient's symptoms (Grimm et al., 2008; Thibodeau et al., 2006), the left anterior quadrant, particularly the FP1, F3, and F7 electrodes, is associated with emotional regulation and has been linked to mood and anxiety disorders. Altered alpha and theta activity in this region reflect impaired emotion processing, with studies showing reduced cortical activity in individuals with depression and anxiety disorders (Pokorny et al., 2024; Wutzl et al., 2024).

Table 2
Average Cordance by Quadrant

	Quadrant A	Quadrant B	Quadrant C	Quadrant D
Pre	−40.27	−29.56	−12.95	13.17
Post	−20.90	−6.71	27.15	48.80

Note. Quadrant A: Fp1, F7, F3, Fz, C3; Quadrant B: Fp2, F8, F4, Fz, C4; Quadrant C: C3, P3, T5, Pz, O1; Quadrant D: C4, P4, Pz, T6, O2.

Table 3
Average Pre-Post Z Scores by Quadrant

	Pre	Post
Quadrant 1	−0.795	−0.475
Quadrant 2	−0.652	−0.395
Quadrant 3	−0.407	0.212
Quadrant 4	0.247	0.296

Note. Although the subject's *Z*-scores fall within the statistically normal range (±1.98 *SD*), when analyzed categorically (the only prior criterion available for cordance), the majority were discordant, with negative scores as shown in Table 2. In contrast, in the control group, almost all values were neutral or positive, approaching zero.

Posttreatment Cordance

Table 5 presents the changes in cordance scores pre- and postintervention, as well as the statistical significance of these changes. Overall, an increase in cordance values was observed across all channels compared to the pretreatment measurement (Figure 1). Table 3 shows the change in the average *Z*-scores for each quadrant. All quadrants exhibited a noticeable trend toward the mean, except for Quadrant 4, which, however, was the closest to the mean in the pretreatment phase (Table 3).

Figure 1. *Pre- and Posttreatment, Difference Pre-Post Cordance Topomaps and P-Values Topomap.*

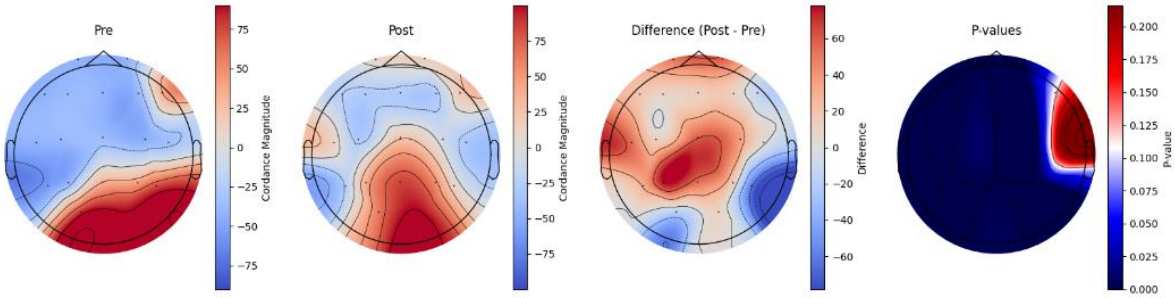

Table 4

Comparison Database Statistics and Individual Cordance Scores (Log-Transformed Values)

		FP1	FP2	F3*	F4*	C3	C4*	P3	P4*	O1*	O2*	F7	F8	T3	T4	T5	T6*	Fz*	Cz*	Pz*
Group	*M*	11.77	8.29	0.35	−0.02	−10.00	−0.01	−7.94	−0.29	1.52	1.47	19.91	−2.39	2.56	2.62	38.64	1.48	0.36	0.68	−0.66
	SD	44.59	51.19	1.75	1.84	55.30	1.83	52.08	1.74	1.16	1.14	47.20	48.70	41.30	45.21	56.30	1.16	1.87	1.73	1.62
Subject	*Pre X*	−42.67	−43.60	−1.61	−1.63	−43.60	−1.69	−45.00	1.63	1.88	1.98	39.27	39.04	−44.80	−37.02	−57.36	1.84	−1.67	−1.62	1.63
	Pre Z	−1.22	−1.01	−1.12	−0.88	−0.61	−0.91	−0.71	1.10	0.31	0.44	0.41	0.85	−1.15	−0.88	−1.71	0.31	−1.09	−1.33	1.42
	Post X	25.06	28.36	−1.47	−1.49	28.36	−1.46	41.28	1.74	1.85	2.00	−28.93	28.43	−30.09	−34.84	−43.23	1.68	−1.47	1.59	1.93
	Post Z	0.30	0.39	−1.04	−0.80	0.69	−0.79	0.95	1.16	0.28	0.46	−1.03	0.63	−0.79	−0.83	−1.45	0.17	−0.98	0.53	1.60

Note. *M*: Group mean, *SD*: group standard deviation, Pre *X*: subject´s pretreatment cordance direct value, Pre *Z*: subject´s pretreatment cordance *Z*-Score, Post *X*: subject´s posttreatment cordance direct value, Post *Z*: subject´s posttreament cordance *Z*-Score. The values obtained from the channels marked with * did not follow a normal distribution, and a logarithmic transformation was applied to both the group data and the individual subject data.

Table 5

Statistical Comparison of Pre- and Postcordance Values Based on 33 EEG Subsamples

Channel	Cordance magnitude Pre (*SD*)	Cordance magnitude Post (*SD*)	Diff. (Post-Pre)	*t*-statistic	*p*-value	*q*-value BH
C3	−38.58 (2.63)	−29.24 (1.12)	9.34	−21.49	.010	**.0173**
C4	−44.30 (1.68)	−7.79 (28.88)	36.51	−8.09	.010	**.0173**
Cz	−36.51 (2.16)	22.51 (31.80)	59.02	−11.68	.010	**.0112**
F3	−37.43 (1.94)	−29.53 (1.33)	7.90	−21.40	.010	**.0173**
F4	−38.91 (2.05)	−28.90 (9.08)	10.01	−6.69	.010	**.0173**
F7	−41.78 (1.04)	−24.90 (14.48)	16.87	−7.68	.010	**.0173**
F8	29.56 (25.92)	17.41 (33.03)	−12.15	1.62	.112	.1182
Fp1	−42.13 (1.45)	8.17 (32.20)	50.30	−10.49	.010	**.0173**
Fp2	−42.00 (1.44)	14.76 (33.18)	56.76	−11.20	.010	**.0173**
Fz	−41.43 (2.02)	−29.03 (1.44)	12.40	−29.68	.010	**.0112**
O1	81.02 (6.26)	64.33 (13.26)	−16.69	5.89	.010	**.0173**
O2	90.13 (1.41)	99.97 (0.22)	9.84	−42.60	.010	**.0173**
P3	−38.87 (11.79)	39.38 (8.49)	78.25	−31.50	.010	**.0173**
P4	40.95 (7.02)	54.32 (6.31)	13.36	−7.32	.010	**.0173**
Pz	29.69 (22.84)	83.56 (6.49)	53.87	−12.91	.010	**.0112**
T3	−42.12 (1.43)	9.97 (31.03)	52.08	−10.95	.010	**.0158**
T4	−33.70 (1.79)	−31.04 (13.69)	2.66	−1.26	.216	.2160
T5	−54.09 (2.27)	−22.25 (39.66)	31.84	−5.08	.010	**.0112**
T6	71.65 (3.60)	13.96 (46.67)	−57.69	7.93	.010	**.0112**

Note. *DE* = Standard Deviation; Diff. = Post-Pre; BH *q*-value = *p*-value adjusted using the Benjamini-Hochberg False Discovery Rate method; Significant: BH *q*-value < .05. The values with a significant *q*-value have been highlighted in bold.

Discussion

In this study we aimed to analyze the utility of a new NF paradigm—cordance-based NF—for alleviating anxious and depressive symptoms. Notably, to the best of our knowledge, this is the first time that real-time cordance calculation has been implemented and applied in NF.

To implement the NF protocol based on concordance, we selected a patient with anxiety, mood disturbances, and insomnia. This patient also met the requirement of exhibiting left frontal discordance (Bench et al., 1992; Leuchter, Cook, Mena, et al., 1994; Videbech, 2000) and did not exhibit any other relevant abnormalities in their qEEG expressed in *Z*-scores. The patient was evaluated psychometrically, with results consistent with mood disturbances, anxiety, and insomnia. Additionally, as previously mentioned, the patient underwent neurometric assessment, which revealed no significant findings in the commonly measured qEEG parameters. Cordance was calculated for the patient's EEG and divided by quadrants. The patient exhibited marked discordance (low concordance) in the left anterior quadrant. A NF protocol was designed to reinforce the patient every time cordance increased. Seven sessions of this protocol were applied, and it was found that there was a general increase in cordance, resulting in a statistically significant change across all regions except for the right frontotemporal region, which already exhibited positive concordance during the pretreatment phase. This change was accompanied by a significant shift in the desired direction in the psychometric variables, with improvements in depression (from *moderate* to *mild*), anxiety (from *moderate* to *mild*) and insomnia (reduced to half of the initial score; Gómez-Benito et al., 2011; Lobo et al., 2002; Sanz & García-Vera, 2013).

Cordance has been shown to correlate significantly with cerebral perfusion and metabolism. In his seminal study, Leuchter et al. (1999) demonstrated that cordance values, particularly in frontal regions, were highly correlated with regional cerebral blood flow measured by SPECT. This suggests that cordance may serve as a noninvasive electrophysiological proxy for assessing metabolic activity in the brain, providing a valuable tool for neuropsychiatric research and clinical monitoring.

In this regard, our results suggest that NF based on cordance may be an effective intervention for patients with mood and anxiety disorders and are consistent with previous research identifying patterns of hypoperfusion and hypometabolism in the left frontal region among individuals with affective disorders (Bench et al., 1992; Drevets et al., 2008; Videbech, 2000). Mayberg et al. (2000, 2005) reported on a correlation between left frontal metabolic activity and depressive symptoms, showing that normalization of activity in the left dorsolateral prefrontal cortex is strongly associated with clinical remission. Their studies using positron emission tomography (PET) revealed that increases in glucose metabolism and cerebral blood flow in these regions are significantly correlated with reductions in depression scores, as measured by standardized instruments such as the Hamilton Depression Rating Scale (Hamilton, 1960). In this regard, Cook et al. (2002) reported that prefrontal cordance may serve as a useful biomarker for predicting treatment response in depression. Cook et al. (2002) observed that changes in prefrontal cordance preceded clinical improvement in patients with depression treated with psychotropic medications. Our approach, compared to theirs, differs in that we employed NF to directly modify cordance, rather than merely observing it as a passive biomarker.

Regarding the number of sessions required for improvement to appear, our results align with those highlighted by Baker (2023), who applied passive infrared hemoencephalography (pIR HEG) to a sample of individuals with mental health conditions, primarily emotional and anxiety-related issues, finding positive results around the fifth session. The pIR HEG reflects underlying cerebral blood flow and metabolic activity (Carmen, 2004; Coben & Padolsky, 2007) and focuses on enhancing prefrontal cortex function through noninvasive NF, measuring changes in thermal activity as a byproduct of cerebral blood flow. Both techniques, pIR HEG and cordance, assess brain function but approach the analysis from different angles. Cordance not only offers a more detailed frequency-based view of brain activity but also provides greater versatility in terms of the regions and structures that can be evaluated. In any case, the number of sessions appears significantly lower than the typical number reported in the scientific literature using conventional amplitude NF (Hammond, 2005; Marzbani et al., 2016) or other modalities such as slow cortical potentials (Sitaram et al., 2017).

This study presents limitations that must be considered when interpreting its results. First, as it employs a single-case design, the generalizability of the findings to a broader population is limited. In

addition, the reduced number of sessions, may restrict the long-term efficacy of the intervention when compared with conventional amplitude-based NF protocols. Therefore, future research is recommended to include larger samples, follow-up assessment, and a comparison intervention to confirm and expand these preliminary findings and to examine their long-term maintenance. Our data analysis was based on statistical changes, which might fail to appraise clinically meaningful changes for smaller effect sizes than the one reported in the present work. Additional research using more sophisticated statistical methods than the RCI (McAleavey, 2024) is needed.

The present work introduces an innovative NF paradigm based on real-time cordance calculation. To our knowledge, this is the first application of this methodology. The results obtained suggest that this technique can effectively modulate brain activity, which is associated with improvements in symptoms of anxiety and depression. Despite the inherent limitations of the single-case design, this contribution opens new perspectives for the clinical application of this type of NF and lays the groundwork for future investigations.

Author Disclosure

The authors declare that they have not used AI during the writing of this paper.

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