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Aim and Scope

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Effects of Pulsed Electromagnetic Field on Reactive Performance

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Abstract

Pulsed electromagnetic field (PEMF) stimulation has been widely used in clinical settings for injury recovery and pain reduction; however, little is understood on its ability to modulate cortical activity, specifically in enhancing reactive performance. We hypothesized that stimulation of the FpZ site (Brodmann areas 10, 11, and 32), would upregulate activity in the prefrontal cortex, namely, the attentional network, which controls volitional movement. Twenty healthy subjects completed six trials on the Dynavision D2 interactive light board to establish a baseline for reactive performance (10 experimental and 10 sham). All participants donned a Bellabee wearable device and underwent (or did not undergo, if designated to the sham condition) 40 min of beta stimulation at the 10-20 FpZ location. Six trials were completed again after stimulation. A paired *t*-test revealed significant differences in the visual (p = .003) and physical (p = .011) components for the experimental condition. A student's *t*-test revealed the motor component to be significant (p = .023) when evaluating the postreaction time between the two conditions. Our findings suggest that a single dose of PEMF stimulation was sufficient to elicit significant changes in increasing reactive performance.

Keywords: T-PEMF; electromagnetic stimulation; perceptual motor speed; reactive performance

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Introduction

Characterization of interventions that elicit desirable perception, cognition, and action outcomes is crucial for optimizing the input-processing-output schema that defines the human operating system (HOS; Durkee et al., 2013). Increasing efficiency via augmentation of human perceptual and cognitive performance can be achieved by modulation of an individual's perceptual-motor processing, attentional resource allocation, and reaction timing, which resultantly produces considerable positive impacts with respect to an individual's readiness, workload, and recovery (Parsons et al., 2016).

Perception-reaction responses have been largely defined as an autonomic function, governing perceptual processes, including, action understanding and allocation of attentional resources (Parasuraman et al., 2009). Reactivity responses are governed by neuromuscular processes, where the nervous system receives an input (external stimulus) that then sends an efferent signal, causing the body to output a response. Reaction time describes the duration in time to respond to the stimulus. Quantification of an individual's reaction time can provide insight into how an individual responds to a stimulus or event (Parasuraman & Galster, 2013). Furthermore, optimization of an individual's attentional network could result in significant positive implications for sports and military performance outcomes via the optimization of goal directed behaviors (Lepsien & Nobre, 2006).

Attentional modulation is largely controlled by the frontoparietal attention control networks in the brain

(Petersen & Posner 2012). The frontal lobes are known to be responsible for higher-level cognitive function including planning, decision-making, cognitive flexibility, attention, and memory (Friedman & Robbins, 2022). Recent evidence suggests that the entire frontal lobe (beyond the previously established premotor cortex Brodmann area 6) is involved in premotor action such as planning and regulating higher-level motor skills (Fine & Hayden, 2022).

The 10-20 location FpZ lies over the medial prefrontal cortex (PFC) and consists of Brodmann areas (BA) 10, 11, and 32. These neuroanatomical locations play a critical role in analyzing and encoding task-relevant information and exhibiting cognitive control (Friedman & Robbins, 2022; Miller & Cohen, 2001). BA 10 (rostral PFC) is found to be active during simple and complex cognitive tasks involving planning and judgment (Koechlin et al., 1999), memory (Burgess et al., 2001), problem-solving (Christoff et al., 2001), and motor learning (Jenkins et al., 1994). Damage to BA 10 has been associated with decreased performance in time-based memory tasks (Burgess et al., 2013). BA 11 is anatomically inferior to BA 10 and is part of the orbitofrontal cortex (OFC) which is active during decision-making and plays a role in processing reinforcement and in working memory (Elliott et al., 2010). BA 32 is considered part of the ventromedial PFC and cytoarchitecturally defined as the dorsal anterior cingulate gyrus. This region has implications in decision-making and initiating goal-directed behaviors (Bechara et al., 1994; Holroyd & Yeung, 2012).

There exists an extensive amount of literature exploring the optimization of reaction time; however, little is understood regarding the modulation of key variables that promote increased perceptual-motor processing to increase reactive performance. One potential intervention used for modulating cortical activity, and subsequently, performance-related outcomes, is pulsed electromagnetic fields (PEMF). PEMF uses electromagnetic currents to induce restorative changes within the tissue at the cellular level. It has been shown to reduce inflammation after soft tissue injuries (Rasouli et al., 2012) and is FDA approved for treating pseudoarthrosis, complications from diabetes mellitus, delayed wound healing, pain, and neurodegenerative disorders (Funk, 2018). Though the majority of PEMF literature surrounds injury recovery, there are strong indications for use of PEMF in performance enhancement. Specifically, PEMF is used transcranially (T-PEMF) as a form of noninvasive brain stimulation; this type of neuromodulation introduces a weak electromagnetic current to the cortex and enhances cortical excitability (Capone et al., 2009). The pacing of the magnetic pulses may be used to help steadily guide the cortex into more synchronous, regulated rhythms to target performance-related cognition via transcranial magnetic stimulation (Fuggetta et al., 2005; Wang 2010); however, little is understood about the effects of transcranial PEMF stimulation.

This present study aimed to evaluate the effect of PEMF stimulation at increasing reaction time. It was hypothesized that due to the high frequency stimulation at the FpZ site, participants that received stimulation would have faster reactive performance. To our best knowledge, no present studies have examined the effect of PEMF stimulation on reactive performance in healthy populations.

Methods

Participants

A total of 21 healthy adults participated in the study; 11 participants received stimulation, and 10 participants were given a placebo. One participant from the placebo group had to be excluded from analysis resulting in a final count of 11 participants receiving stimulation and 9 participants given a placebo. The unequal number of participants in each group was a result of participant noncompliance. Prior to participation, all individuals completed a written informed consent that was approved by the West Virginia University Institutional Review Board (Protocol #: 2112489062); all procedures abided by the Declaration of Helsinki Guidelines. Participants were excluded from the study if they met any of the following exclusion criteria: has a metallic or electronic implanted device, currently on antihistamines or medication for attentional deficit disorders, those that were pregnant or trying to become pregnant, and those with histories of open skull traumatic brain injury, hemiparesis, epilepsy, seizures, orthostatic hypotension, Bell's palsy, or cranial nerve dysfunction.

Study Design

Participants were randomly assigned to the experimental or sham group. The Dynavision Reaction Test (defined below) procedure was explained to all participants. After the assessments of baseline perceptual motor speed and accuracy, the participants underwent (or did not undergo if assigned to the sham group) 40 min of stimulation using the commercially available, Bellabee device (Bellabee, Austin, TX). To keep the participants' focus and limit discrepancies, all participants completed up to 15 word searches during the 40 min. Then the

participants completed the Dynavision Reaction Test to assess pre-post performance outcomes.

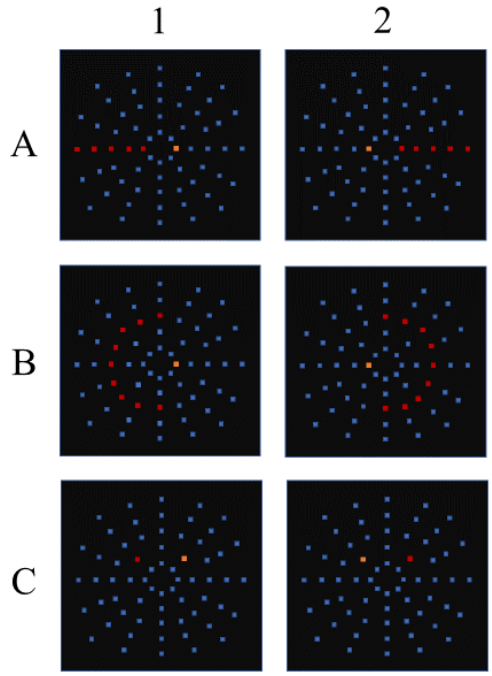
Reactive Performance

Reactive performance was assessed using the Dynavision D2 board (Dynavision Global Holdings LLC, West Chester, OH) which contains a total of 64 buttons arranged in five concentric rings. Each participant completed a total of three reaction tests with each hand, each containing a total of six trials. The participants were instructed to hold down a predefined reference button until they saw another light appear at a different location on the board, at which point they would subsequently release the reference button and hit the light as quickly as possible. Arrangement of the light patterns varied amongst the three trials, where the lights were arranged in the following patterns for trial 1, 2, and 3, respectively: straight line, half-circle, and two options. Please refer to Figure 1 for details. The Dynavision automatically outputs the physical, visual, and motor reaction times. The physical reaction time is a summation of the visual and motor reaction times, which represent the time the light illuminated to the moment that the reference button was released, and the time from the release of the reference button to the dismissal of the light, respectively.

Statistical Analyses

Data analysis and visualizations were produced in R (R Foundation for Statistical Computing, Vienna, Austria), where alpha levels were set *a priori* at 0.05. Paired *t*-tests were performed to determine differences in pre- and postsham and experimental average reaction times. Student's *t*-tests were performed to assess the difference between poststimulation average reaction times in sham versus experimental conditions. Each of the measured differences met the assumption for a normal distribution, which was determined by the Shapiro-Wilk goodness of fit test.

Figure 1. *Arrangement of Light Patterns on the Dynavision D2 Board for (A) Straight Line Condition, (B) Half-Circle Condition, and (C) Two Options Condition*.



Note. Each trial was repeated five times with the participants' dominant and nondominant hand.

Results

All reaction times were averaged across all the trials and configurations. Average reaction times for each component (physical, motor, and visual) and each condition (experimental, sham) can be found in Table 1 below.

A paired *t*-test was conducted to examine pre- versus poststimulation averaged reaction time for the sham and experimental conditions. There were no significant differences in visual, motor, or physical reactive performance in the sham condition. However, there existed significant differences in the visual (p = .003) and physical (p = .011) components, but not the motor component (p = .190) for the experimental condition.

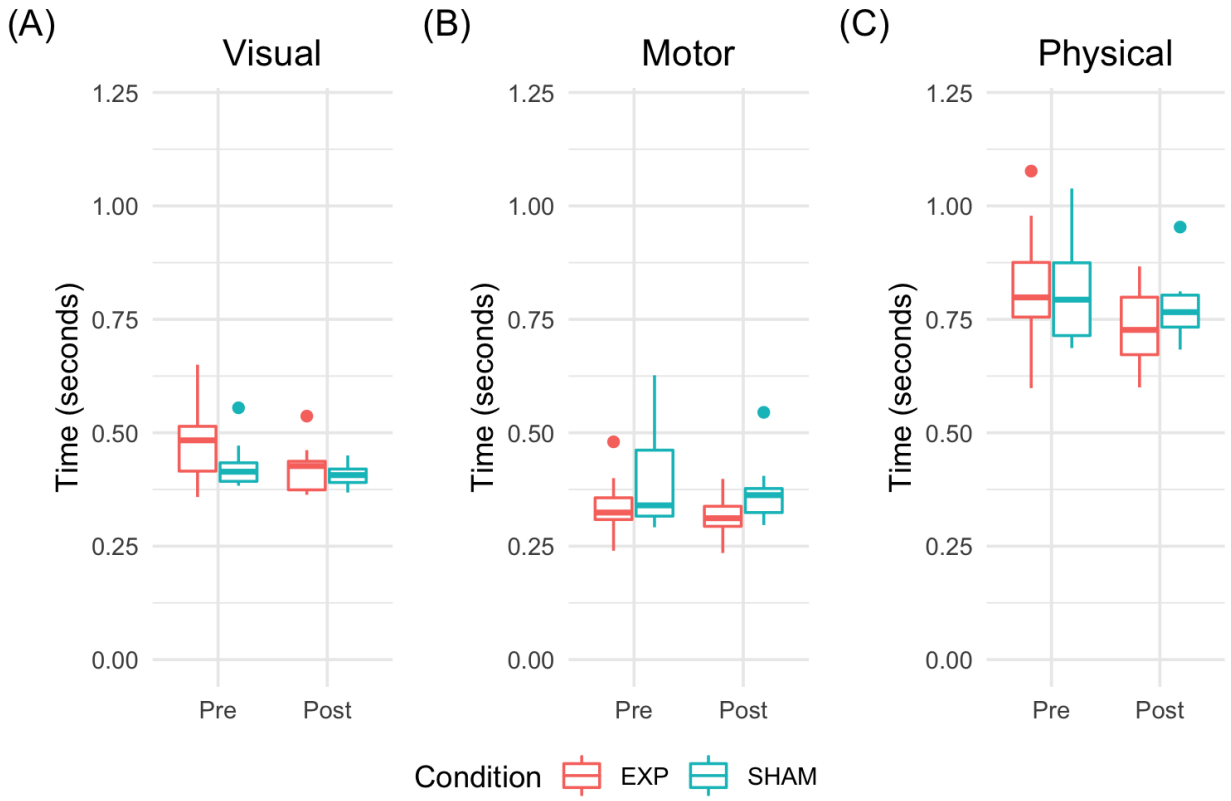
Table 1

Reaction Times for Physical, Motor, and Visual Components of Dynavision Reaction Test Between SHAM and EXP Groups

Condition	Pre/Post	Physical	Motor	Visual
Experimental	Pre	0.82 ± 0.13	0.34 ± 0.07	0.48 ± 0.09
	Post	0.74 ± 0.09	0.32 ± 0.05	0.42 ± 0.05
Sham	Pre	0.82 ± 0.13	0.39 ± 0.11	0.43 ± 0.05
	Post	0.77 ± 0.08	0.37 ± 0.07	0.41 ± 0.03

A student's *t*-test examining the postreaction time between the sham and experimental condition was found to be significant for the motor component (p = .023), but not the visual or physical components p = .348 and p = .174, respectively). As shown in Figure 2, reaction times for the experimental condition were found to be faster in the visual and physical components.

Figure 2. *Reaction Times for Experimental and Sham Conditions*.



Note. Organized by (A) visual, (B) motor, and (C) physical components of the Dynavision Reaction Time Test.

Discussion

This study aimed to examine the effects of cortical PEMF stimulation on reactive performance. Findings suggested that individuals who received 40 min of stimulation at the FpZ 10-20 site had significantly quicker reaction times than their sham counterparts. Compared to other reactive performance studies (Bagurdes et al., 2008; Kwak et al., 2020), this is the first study of its kind to examine the effects of deliberate modulation on the attentional network, using a form of external stimulation. Our findings suggest positive trends in reactive performance, which we attribute to three of our reported results. First, there were no significant differences between pre- and postreaction times in the sham condition. This suggests that a learning effect did not play a predominant role in reactive performance, establishing more credibility to the effectiveness of PEMF. Second, the aforementioned conclusion is further supported by the significant difference in postsham versus experimental reactive performance. Namely, individuals who received stimulation demonstrated quicker reaction times. Lastly, the pre- versus postreaction times were significantly different in the physical and visual components of the experimental condition, following stimulation.

Although pre- vs. poststimulation reaction time was significantly different in the experimental condition when averaging across all three components (visual, physical, and motor), when examining the components independently, the motor component did not exhibit any significant differences. The visual and motor components of the Dynavision reaction tests were defined as the time the light was illuminated to when the movement was initiated and the initiation of movement to the successful dismissal of the light, respectively, whereas the physical component was the summation of the visual and motor components. As shown in Figure 1 and Table 1, the visual component drives approximately half of the total summative time in the physical component. This suggests that PEMF stimulation may have more significance on the processing component of reactive performance rather than motor speed itself. One possible reason could be the target location. Namely, the anterior cingulate cortex controls volitional movement, and although its location is not superficial, cortical excitability at the FpZ site could potentially upregulate its effect at the BA 32 location which may play a role in the anticipation and detection of targets.

Shifting individuals towards peak performance via training or external forms of modulation, such as cortical PEMF stimulation, could have widespread implications in human performance settings; opening the door for use in populations (e.g., athletes, warfighters, etc.) where enhanced reactivity is highly sought. Enhancing perceptual-motor processing could aid in improving reaction time, thus optimizing cognitive loading, motor coordination, and ultimately resulting in injury prevention.

We envision that this preliminary study will be the first of many in understanding the effects of cortical PEMF stimulation on performance-based outcomes. The results obtained from this study are not intended to make conclusions on the use of cortical PEMF on individuals to enhance reactivity, but rather to demonstrate the existence of positive effects from stimulation. Future studies examining the prolonged effects of stimulation alongside subjective measures, quantitative electroencephalography (qEEG), or other performance-based measures (physiological trends, accuracy, etc.) to corroborate the findings from this study are warranted.

Despite the limited and unequal sample size, the results found in this study have demonstrated positive trends in reaction timing related to PEMF stimulation at the FpZ 10-20 site. To our best knowledge, this is the first study to examine the effects of cortical PEMF stimulation related to a performance-based outcome. These preliminary findings suggest that PEMF could provide a low-intensity, cost-effective, and user-friendly solution to regulating cortical activity in nonlaboratory environments.

Author Disclosure

The authors have no disclosures.

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Resting-State EEG Alteration Over the Loreta *Z*-Score Neurofeedback in Aphasia

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Abstract

Objectives. Aphasia is an acquired language disorder resulting from a brain injury which affects the brain's electrical activity. Neurofeedback (NFB) is known to synchronize neural oscillations and normalize brain wave abnormalities in several disorders. In this study, we aimed to investigate EEG signals in aphasia and the possible positive effect of Loreta *z*-score neurofeedback (LZNFB) treatment on improving EEG disturbances and symptoms in aphasia. **Methods**. Thirteen chronic aphasics and 10 unimpaired nonaphasic subjects were investigated in this study. Clinical assessments were used for the aphasic group at baseline and after 15 sessions of LZNFB to illustrate behavioral improvement. To estimate signal disruption and its alteration over the treatment, EEG signals were acquired referred to as resting-state eyes-closed condition in aphasic group during pretreatment and posttreatment as well as in the nonaphasic control group. We then investigated brain complexity and phase-amplitude coupling (PAC) in groups and compared the results. **Results**. Our EEG findings were congruent with clinical improvement and showed that after treatment, complexity and PAC changed to a normal level. **Conclusion**. We conclude that LZNFB treatment was effective in decreasing EEG disturbances and symptoms in aphasia. We think that our findings in complexity and PAC could provide important insights into the electrophysiological profile in aphasia and its alterations after treatment.

Keywords: aphasia; phase-amplitude coupling; complexity; neurofeedback; loreta

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Introduction

Aphasia is a clinical syndrome characterized by progressive speech and language deficits caused by selective neurodegeneration of particular brain networks. Several studies reported brain abnormalities in aphasia. For example, increased delta and theta activity in damaged linguistic regions within the left hemisphere of a patient with different aphasic diagnostic has been reported in previous studies (Szelies et al., 2002). It has been shown that increased delta and theta activity in aphasia can also affect EEG signal complexity (Shah-Basak et al., 2020; Takahashi et al., 2010). Wu et al. (2015) estimated approximate entropy (ApEn) in aphasia and showed higher complexity in the left hemisphere. On the other hand, phase-amplitude coupling (PAC), which is shown to be associated with brain processing (Canolty & Knight, 2010), is also reported as an aberrant feature in aphasia. Liu et al. (2019) applied the PAC algorithm to investigate multimodal neuro signals including CBF and EEG in stroke aphasia, estimated the hemispherical asymmetry of PAC, and compared the differences between the left and right hemispheres. Their result showed excessive PAC at the left occipital region in aphasia. They also analyzed PAC in the survival group as compared to the deceased group and found the deceased group showed smaller PAC than the survival group. Moreover, they showed that the PAC asymmetry between two brain hemispheres correlates with the degree of disorder.

EEG in patients with aphasia can also be distinguished from healthy controls by measuring differences in the functional connectivity of resting

networks (Marebwa et al., 2017; Yang et al., 2018). Shah-Basak et al. (2020) estimated brain network connectivity and reported reduced left hemisphere connectivity in aphasia. On the other hand, neuroimaging studies investigated brain connectivity in aphasia and its alteration during recovery. Nicolo et al. (2015) associated the coherence of neural oscillations in language networks with clinical improvement. The authors showed that the beta-band weighted node degree at the ipsilesional (Broca) area was correlated with better language improvement. Recovery was further associated with contra-lesional theta band weighted node degree (Nicolo et al., 2015). It is observed that the magnitude of alpha-band functional connectivity is correlated with behavioral performance in stroke aphasia patients (Mottaz et al., 2018). Another study investigated the association between the brain's structural connectivity and recovery and found anterior temporal connectivity can predict future recovery (Warren et al., 2009).

As aphasia lowers functional independence and health-related quality of life and increases the vulnerability to other diseases such as cancer, Alzheimer's, and Parkinson's (Lam & Wodchis, 2010), there is a need to improve currently available therapeutic options for aphasia. Neuromodulation, represented by neurofeedback (NFB), has been known as a potential therapeutic modality for many years. It uses real-time displays of electroencephalogram (EEG) to illustrate brain activity and allows for self-regulating brain activity by diminishing excessive fast or slow waves, which may frequently be seen in several disorders (Mottaz et al., 2018; Ramot et al., 2017). Growing evidence shows that NFB generates oscillations extending to distinct brain areas, such as the cortical and subcortical regions (Bichsel et al., 2021; Nicholson et al., 2016; Ros et al., 2014). Several studies show the effectiveness of NFB both behaviorally and at the network level (Cortese et al., 2017; Enriquez-Geppert et al., 2019; Grin-Yatsenko et al., 2018; Hirano & Tamura, 2021; Koush et al., 2017). Moreover, previous case studies reported the efficiency of NFB in the reduction of aphasia symptoms (Mroczkowska et al., 2014; Nan et al., 2019; Rozelle & Budzynski, 1995).

Low-resolution electromagnetic tomography analysis (LORETA) *z*-score NFB (LZNFB) has been introduced to the market relatively recently (Applied Neurosciences, Inc., USA). This system has the potential to provide faster results due to the application of a larger number of electrodes during treatment (Koberda et al., 2012). Furthermore, it can receive instant comparisons using a reference database of healthy individual *z*-scores. These instant comparisons enable finding a link between patients' symptoms and Brodmann areas (BA) in the brain (Thatcher, 2010). This technology has recently been shown to be an effective treatment for many neuropsychiatric disorders and cognitive dysfunction (A. Faridi et al., 2022; Frey & Koberda, 2015; Koberda, 2014, 2015; Prinsloo et al., 2019). Our recent case report (F. Faridi et al., 2021), suggested the potential of LZNFB in language rehabilitation for a TBI aphasia.

To date, much work has focused on local dysfunction in aphasia, but so far little is known about the electrophysiological abnormalities in aphasia and its alteration after NFB treatment as compared to a healthy control group. In this study, we aimed to estimate EEG disturbances in aphasia and possible improvement in EEG abnormalities and symptoms over the LZNFB treatment. To this end, we acquired clinical assessment in the aphasia group at baseline and after 15 sessions of treatment. We also investigated EEG signals, referred to as the resting-state eyes-closed condition in the aphasia group (during pre- and posttreatment) as well as in the nonaphasia control group. Then we analyzed EEG complexity and PAC and compared the results in groups. The hypothesis of the current study is as follows:

- Increased complexity and decreased PAC are shown in aphasia as compared to the nonaphasic group.
- Increased complexity and decreased PAC in aphasia change to nonaphasic control group level after LZNFB.

Materials and Methods

Participants

The study group included 13 aphasic patients (five females and eight males with ages of 46.53 ± 12.95 and 10 nonaphasic control individuals (four females and six males with ages of 34.46 ± 5.99). Aphasic patients were selected according to the following criteria: a) they had been diagnosed as nonfluent aphasic patients during the acute phase (Table 1), and b) at the time of the study, all patients had to be in a chronic state, as attested by an average time from the lesion of 27.84 ± 5.55 months (range: 7–60 months).

Table 1

Patient's Demographic Data, Along With the Severity of Their Condition, Etiology, Post-Onset, Lesion Location, Education, Gender, and Age

Name	Severity	Etiology	Post-onset (months)	Lesion location	Education (years)	Gender	Age
MA	Moderate	Stroke	10	Left frontal	5	Female	57
AZ	Mild	Stroke	25	Left frontal	12	Male	58
MM	Moderate	Stroke	12	Left frontal	12	Female	56
ZB	Mild	Stroke	8	Left frontal	2	Female	58
PF	Mild	Trauma	11	Left frontal	14	Male	22
HS	Medium	Stroke	18	Left frontal	5	Male	53
FA	Mild	Stroke	19	Left frontal	12	Female	48
FK	Mild	Trauma	48	Left frontal	16	Male	34
HA	Mild	Trauma	60	Left frontal	12	Female	50
MK	Mild	Trauma	60	Left frontal	7	Male	23
MR	Severe	Trauma	48	Left frontal	14	Male	38
AM	Mild	Stroke	36	Left frontal	12	Male	54
NO	Mild	Stroke	7	Left frontal	12	Male	54

Ethical Statement

All ethical principles are considered in this article. The participants were informed of the purpose of the research and its implementation stages. They were also assured about the confidentiality of their information and were free to leave the study whenever they wished and, if desired, the research results would be available to them. Written informed consent was provided by patients' next of kin. The study was approved by the Ethics Committee at Tarbiat Modares University (IR.MODARES.REC.1400.249).

Intervention

The EEG was recorded from 19 scalp locations based on the international 10-20 system of electrode placement and the linked ear as a reference. These electrodes positions were Fp1, Fp2, F3, F4, C3, C4, P3, P4, O1, O2, F7, F8, T3, T4, T5, T6, Fz, Cz, and Pz. Recordings were sampled at 256 HZ. The qEEG data were collected using a Medicom amplifier and the EEG Studio Acquisition software. Editing and digital analysis of the qEEG data were carried out using NeuroGuide software and comparative databases. The protocol included LZNFB within the language network. In the language network, BA included 22, 39, 40, 41, 42, 44, and 45. Moreover, learning reinforcement in NFB was provided using television shows or animations that increased in size when meeting the defined difficulty thresholds.

EEG Analysis

In this study, we used five indexes of complexity in time series which are described as the following: Katz, Higuchi, Sevcik, spectral entropy (SpEn), and approximate entropy (ApEn).

Fractal dimension (FD) analysis was performed using MATLAB on EEG data. FDs reflect the chaotic character of nonlinear signals and also show complexity and self-similarity in EEG signal. In this study, we used four indices of FDs, SpEn, and ApEn. Therefore, 10-s duration of the EEG channels for each index was taken. We finally computed the average of all windows.

Katz's Fractal Dimension (KFD). One of the algorithms to calculate the FD and complexity of a one-dimensional time series is KFD which is calculated by the distance between two successive points (Katz, 1988; Salimi et al., 2022; Sho'ouri et al., 2019).

$$\mathrm{KFD} = \frac{\log(N)}{\log(N)+\log(\frac{d}{L})}$$

Where the maximum distance from the first point is measured as *d* computed as following:

$$d = \max\left(|x1 - xj|\right) ; \mathrm{j} = 2, 3, \ldots, \mathrm{N}$$

and the total length of the time series taken as

$$L = \sum_{(i=2)}^{N} X_i - X_{i-1}$$

Higuchi's Fractal Dimension (HFD). Another known way to calculate the FD of time series is HFD (Mohammadi et al., 2016) in which the original time series is defined as

$$X_m^k = X(m).X(m+k).X(m+2k). \ldots X(m+int(\frac{N-m}{k}) \times k$$

Where N is the length of the time series, m showed the initial time, and k denotes the interval time. We consider k_{max} = 20 for this study. Accordingly, the length $L_m(k)$ of the curve X_m^k is computed as follows:

$$L_m(k) = \frac{\sum_{i=1}^{int(\frac{N-m}{k})} |X(m+ik) - X(m+(i-1)k| \times (N-1)}{k \times int\left[\frac{N-m}{k}\right]}$$

where $\frac{(n-1)}{k \times int\left[\frac{N-m}{k}\right]}$ is normalization coefficient.

Stochastic signals are more fractal-like with a higher length $L(k)$ than periodic time series.

Sevcik Fractal Dimension (SFD). A method to estimate another FD from a set of N values in a one-dimensional signal between time 0 and t_{max} (Sevcik, 2010). The time series was subjected to a double linear transformation that maps it into a unit square. The normalized abscissa of the square is x_i^* and the normalized ordinate is y_i^*, both of them defined as

$$x_i^* = \frac{x_i}{x_{max}}$$
$$y_i^* = \frac{y_i - y_{min}}{y_{max} - y_{min}}$$

where x_{max} is the maximum x_i and y_{min} and y_{max} are the minimum and maximum y_i. The fractal dimension of the waveform (SFD) is then approximated by D as

$$\mathrm{SFD} \approx \mathrm{D} = 1 + \frac{\ln(L)}{\ln(2.N')}$$

where L is the length of the curve in the unit square and $N' = \mathrm{N} - 1$.

Spectral Entropy (SpEn). SpEn quantifies the spectral complexity of the EEG signal. If the EEG signal consists of a wide range of dominant frequencies, the SpEn will be high; otherwise, it will be low. As an example, white noise has higher SpEn than a sine wave because a sine wave is predictable and it has information. SpEn quantifies the regularity or randomness of the power spectrum during a period of time, and it can be used as a biomarker in studies (Tian et al., 2017). We use the entropy function in MATLAB 2020b to calculate spectral entropy. The equations for SpEn arise from the equations for the power spectrum and probability distribution for a signal. For a signal $x(n)$, the power spectrum is $S(m) = |X(m)|^2$, where $X(m)$ is the discrete Fourier transform of $x(n)$. The probability distribution $P(m)$ calculates as follows:

$$P(m) = \frac{S(m)}{\sum_i S(i)}$$

And the SpEn H follows as

$$H = -\sum_{m=1}^{N} \mathrm{P(m)}\ log_2 P(m)$$

Approximate* Entropy *(ApEn). ApEn is an index that denotes the regularity, complexity, and predictability of nonlinear time series, which quantifies the irregularity, and complexity of a signal. (Delgado-Bonal & Marshak, 2019).The ApEn of the perfectly regular time series like a sinusoidal signal is significantly smaller than the stochastic time series. So regular signal containing repetitive patterns has a relatively small value of ApEn, while the less predictable stochastic signal has a higher value of ApEn. A lower entropy value indicates predictability and high regularity of a signal. Conversely, a higher entropy value shows irregularity and lower self-similarity in a signal. In this research, the ApEn of the EEG signals was calculated. ApEn calculates from the correlation integral $C_i^m(r)$ related to the embedded signal in an m-dimensional space.

ApEn of signal with N data points x(1), x(2), . . ., x(N) is calculated as follows:

$$ApEn(m,r,N) = \frac{1}{N-m+1}\sum_{i=1}^{N-m-1} logC_i^m(r) - \frac{1}{N-m}\sum_{i=1}^{N-m} logC_i^{m+1}(r)$$

where, $C^m(r)$ is the probability that two sequences will match for m points, and $C^{m+1}(r)$ is the probability that two sequences will match for m+1 points. In this research, m is set to 2 and r is set to 0.20% of each signal variance.

Phase* Am*plitude* Co*upling (PAC). We calculate PAC by direct PAC estimator (dPAC; Özkurt & Schnitzler, 2011). Let $\boldsymbol{a_H(n)}$ be the amplitudes of high-frequency oscillation $\boldsymbol{z_H(n)}$ and also $\boldsymbol{\varphi_L(n)}$ the phase of low-frequency oscillation $\boldsymbol{z_L(n)}$, where $\boldsymbol{z_L}$ and $\boldsymbol{z_H}$ are bandpass filtered complex form representations from two frequency band signals such that

$$\boldsymbol{z_L(n) = |z_L(n)|e^{i\varphi_L(n)} \quad , \quad a_L = |z_L(n)|}$$
$$\boldsymbol{z_H(n) = |z_H(n)|e^{i\varphi_H(n)} \quad , \quad a_H = |z_H(n)|}$$

$$\boldsymbol{dPAC = \frac{1}{\sqrt{N}} \frac{|\sum_{n=1}^{N} a_H(n)e^{i\varphi_L(n)}|}{\sqrt{\sum_{n=1}^{N} a_H(n)^2}}}$$

The low- and high-frequency oscillations are obtained by bandpass filtering the signal $s(t)$ in delta (0–4 Hz), theta (4–8 Hz), alpha (8–13 Hz), beta (13–30) and gamma (30–60 Hz).

Statistical Analysis. All analyses were made using MATLAB software. The normality assessment was done using the Shapiro-Wilk test. Since the null hypothesis of normality could not be rejected, a parametric paired *t*-test was performed to assess the significance of the difference between the pretreatment and posttreatment aphasia group, while an unpaired *t*-test was used for analyzing differences between aphasia and control groups.

Clinical Assessments

The behavioral analysis included the Persian version of the aphasia battery (Nilipour et al., 2016), the forward and backward digit/word/nonword span (Conway et al., 2005), and the Stroop test (Siegrist, 1997), which were acquired at baseline and the final LZNFB session for the aphasic group. Each exam contained multiple questions. For each subtest, the Shapiro-Wilk test was used to examine the normality of the data. For normal and nonnormal distributions, the paired *t*-test (T) or Wilcoxon (Z) was subsequently used. * indicates significant changes ($p < .05$) in Table 3.

Statistical assessments were made with parametric *t*-test and nonparametric Wilcoxon signed ranked test for data showing normal and nonnormal distribution respectively.

Results

Our results involved both clinical and EEG assessments, which are described as the following.

Results Derived From Clinical Assessments

Clinical assessments were applied just for the experimental aphasic group to show the clinical recovery over the LZNFB treatment. Our clinical assessments showed improvement in language, working memory, and attention scores in aphasic patients after treatment (Table 2). Significant changes ($p < .05$) were starred.

Results Derived From EEG Metrics

In our EEG analysis, we estimated complexity and PAC in three groups including pretreatment aphasic, post-treatment aphasic, and nonaphasic control group. Then we compared the results to see whether LZNFB helped to normalize EEG disruption in aphasia.

Complexity

A remarkable change in EEG complexity was observed in association with LZNFB treatment. Complexity analysis were performed by Katz, Higuchi, and Sevcik fractal dimension methods as well as SpEn and ApEn in three groups. We differentiated the left and right hemispheres in our analysis and found more dominant differences in the left rather than the right hemisphere. Table 3, Figure 1 shows EEG complexity in three groups in the left hemisphere. Significant differences ($p < .05$) were observed between pretreatment and two other groups (pretreatment and posttreatment, pretreatment and normal). No significant differences were observed between the posttreatment aphasic group and nonaphasic group. That means posttreatment aphasic complexity gets much close to the nonaphasic control group. Significant changes were shown by * for $p < .05$) and ** for $p < .01$.

Table 2

Systolic and Diastolic Blood Pressure Changes (Postingestion – Preingestion)

Behavioral test	Subtest	Pretreatment (mean)	Posttreatment (mean)	*p*
Language	Auditory perception	171	182	.028*
	Lexical richness	0.75	0.863	.011*
	Speed	34.27	52.25	.003*
	Repeat	80.30	94.30	.003*
	Utterance	8.23	12.30	.003*
Working memory	Forward digit	6.15	8.84	.004*
	Forward word	5.15	6.46	.003*
	Forward nonword	3.15	4.53	.002*
	Backward digit	2.30	5	.000*
	Backward word	2.84	4.92	.000*
	Backward nonword	0.92	1.69	.000*
Attention	Congruent error	3.92	1.53	.166
	Incongruent error	11	2.23	.003*
	Congruent correct	31.46	38.46	.004*
	Incongruent correct	21	36	.002*

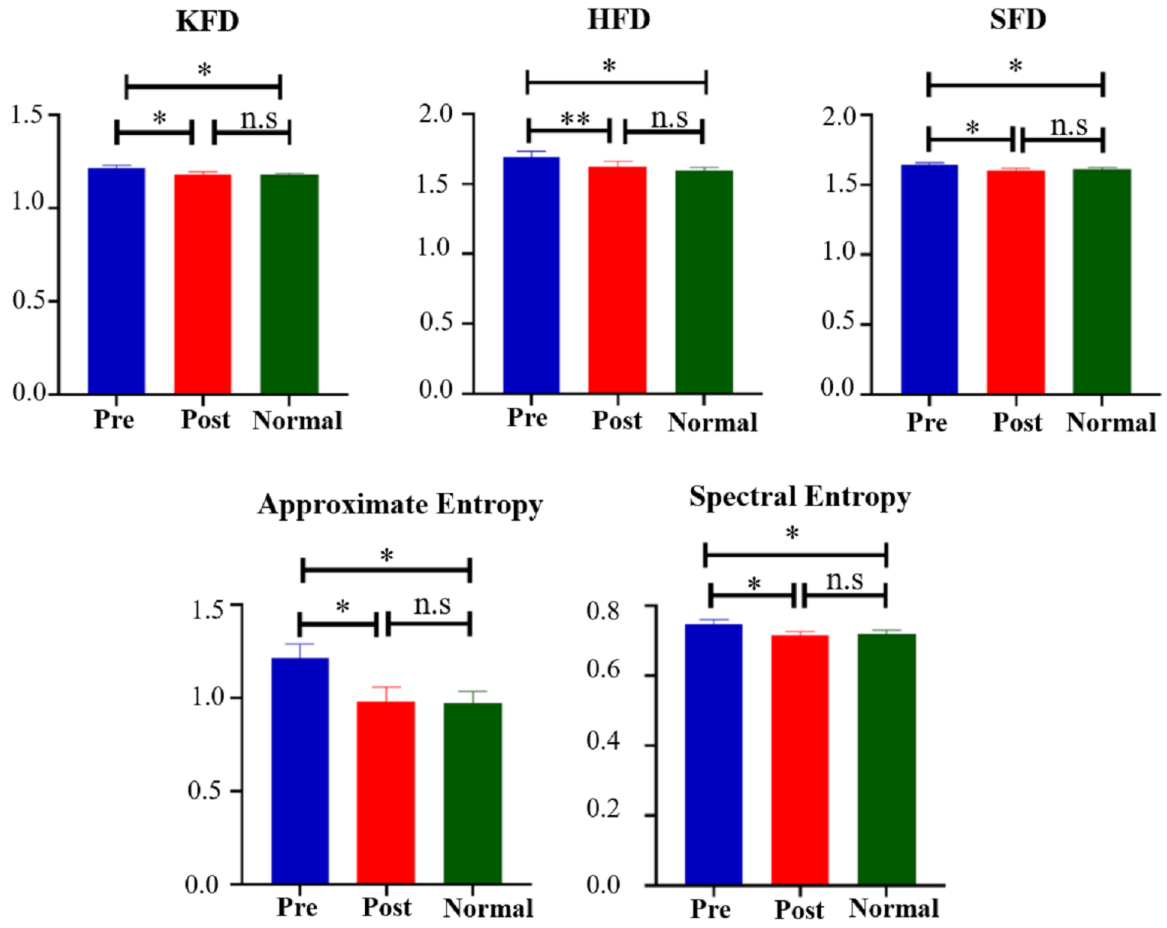
Table 3

EEG Complexity Analysis in Three Groups at the Left Hemisphere

Left	Pretreatment		Posttreatment		Control		*p*		
	Mean	*SD*	Mean	*SD*	Mean	*SD*	Pre vs. Post	Pre vs. Control	Post vs. Control
KFD	1.212	0.067	1.177	0.069	1.170	0.037	.040*	.0500	.9000
HFD	1.692	0.133	1.623	0.119	1.599	0.067	.009**	.0422*	.7381
SFD	1.646	0.041	1.604	0.046	1.609	0.042	.002**	.0500	.7861
SpEn	0.749	0.040	0.716	0.035	0.715	0.040	.001**	.0407*	.5369
ApEn	1.212	0.256	0.983	0.249	0.974	0.235	.005**	.0217*	.9299

Pre: pretreatment group; Post: posttreatment group; *SD*: standard deviation; SpEn: spectral entropy; ApEn: approximate entropy.

Figure 1. *EEG Complexity Analysis in Three Groups at the Left Hemisphere.*



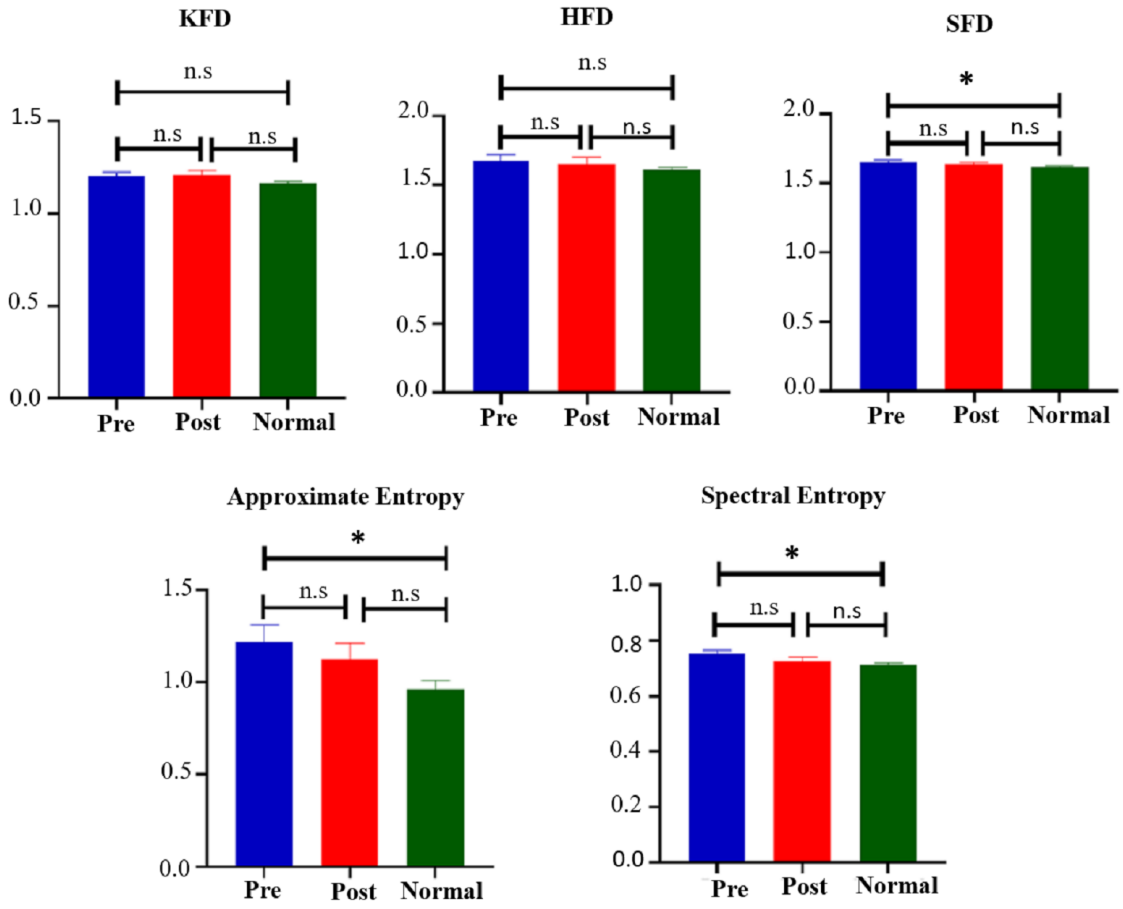
In the right hemisphere, KFD and HFD values were not significantly different between groups. However, SFD, Approximate Entropy, and Spectral Entropy showed significant differences between pretreatment aphasic and nonaphasic groups. No significant differences were observed between pretreatment and posttreatment aphasic groups and between posttreatment aphasic and nonaphasic groups (Table 4, Figure 2).

Table 4

EEG Complexity Analysis in Three Groups at the Right Hemisphere

Right	Pretreatment		Posttreatment		Control		*p*		
	Mean	*SD*	Mean	*SD*	Mean	*SD*	Pre vs. Post	Pre vs. Control	Post vs. Control
KFD	1.202	0.074	1.209	0.079	1.165	0.035	.698	.0902	.0554
HFD	1.674	0.156	1.651	0.167	1.608	0.086	.736	.1692	.3836
SFD	1.651	0.045	1.635	0.049	1.616	0.030	.398	.0203*	.2272
SpEn	0.750	0.051	0.726	0.052	0.713	0.029	.150	.0237*	.4003
ApEn	1.216	0.328	1.124	0.305	0.963	0.191	.306	.0161*	.0974

Figure 2. *EEG Complexity in Three Groups at the Right Hemisphere.*



Phase-Amplitude Coupling (PAC)

We estimated theta-gamma PAC in groups and compared the results. Significant changes have been shown in Table 5. The most significant change between the pretreatment and the posttreatment group was observed at Fp2-C4 (p = .0083), Cz-Fp1 (p = .0155), and Cz-F3 (p = .0175). Pretreatment versus control groups showed the most significant difference at C3-Fp2 (p = .0009), Fp1-O2 (p = .0084), and Fp1-T6 (p = .0132) and posttreatment versus control group showed the most significant change at C3-Fp2 (p = .0024), Cz-Fp1 (p = .0047), T5-F4 (p = .0057).

Figure 3. *Theta-Gamma PAC in Pre-Treatment, Post-Treatment, and Normal Group.*

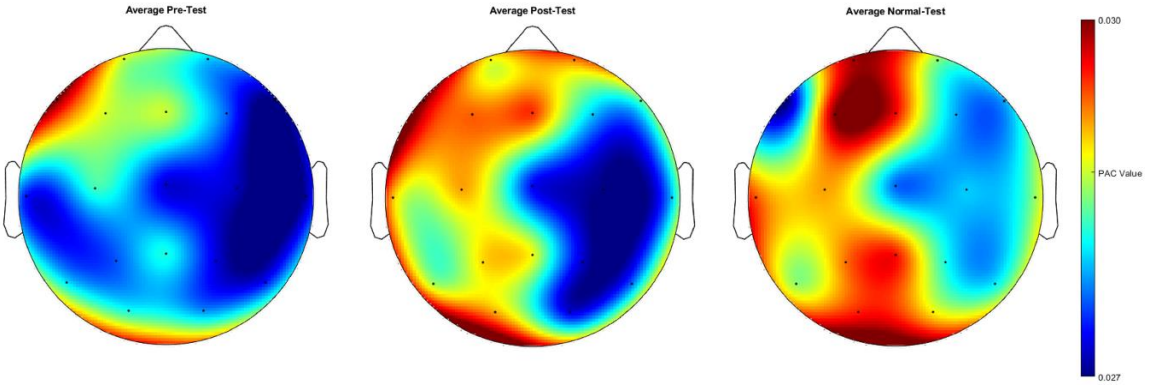


Table 5

EEG Complexity Analysis in Three Groups at the Right Hemisphere

Pretreatment vs. Posttreatment			Pretreatment vs. Control			Posttreatment vs. Control		
Amplitude channel	Phase channel	*p*	Amplitude channel	Phase channel	*p*	Amplitude channel	Phase channel	*p*
Cz	Fp1	**.0155**	F3	Fp2	.0150	Fz	Fp1	.0126
F4	F3	.0229	C3	Fp2	**.0009**	F4	Fp1	.0098
Cz	F3	**.0175**	Fp1	F4	.0376	C3	Fp1	.0458
F4	Fz	.0457	Fp2	F4	.0270	Cz	Fp1	**.0047**
Fp2	F4	.0301	T5	F4	.0386	C3	Fp2	**.0024**
Fp2	Cz	.0445	Fp1	Cz	.0381	F4	F3	.0460
Fp2	C4	**.0083**	Pz	Cz	.0429	T5	F4	**.0057**
Fp2	P4	.0427	O1	Cz	.0380	T5	F8	.0099
Fp1	O2	.0278	Fp1	C4	.0476	P4	C4	.0369
F3	O2	.0321	F8	T4	.0466	Fz	T4	.0125
---	---	---	Fp1	P4	.0380	T4	T4	.0428
---	---	---	Fp1	T6	**.0132**	T5	T4	.0242
---	---	---	Fp1	O2	**.0084**	P3	T4	.0259
---	---	---	---	---	---	F7	P4	.0446
---	---	---	---	---	---	T3	P4	.0408
---	---	---	---	---	---	C4	P4	.0405
---	---	---	---	---	---	F3	O2	.0245
---	---	---	---	---	---	T3	O2	.0146

Discussion

In aphasia, cognitive performance becomes poor and the organization of the brain network architecture is affected. In this study, we aimed to show EEG disruptions in aphasia and the possible effect of LZNFB on improving EEG abnormalities and clinical symptoms. Therefore, we used behavioral and EEG assessments at baseline and after 15 sessions of LZNFB. Our behavioral assessments showed improvement in language, working memory, and attention scores in our aphasic group after LZNFB and implied as decreased aphasia symptoms. Our EEG findings were congruent with clinical improvement and showed that complexity, PAC, and coherency changed to a normal level after treatment. We think that this study may pave the way to provide biomarkers for treatment targets in chronic aphasia.

Complexity

In this study, we reported NFB-induced changes in the EEG complexity in aphasia. In fact, the brain is a complex nonlinear system, and the EEG signal is demonstrated nonlinearity at the neuronal level. Therefore, it would be appropriate to use nonlinear methods to analyze EEG signals (Klonowski, 2009). Moreover, a nonlinear dynamic approach could provide novel insights into brain diseases and could be a useful tool in understanding the mechanisms of neuronal plasticity after injury and during rehabilitation (Sun et al., 2017).

Brain damage can result in dysfunction of particular parts of the brain and can be reflected in the complex dynamics of its neural activity (McBride et al., 2014), loss of synaptic connections, and neurotransmitter deficiency (Sun et al., 2017). Therefore, we hypothesized that the complexity of

the experimental group would be improved with training and decrease to a normal level.

According to Figure 1, the complexity in the pretreatment group was the most among the groups, but it decreased over the LZNFB. So posttreatment aphasic complexity was much closer to the nonaphasic group. We estimated complexity in the left and right hemispheres separately and found more dominant differences in the left rather than right hemisphere, which is in line with the study of Wu et al. (2015). At left hemisphere, KFD, HFD, SFD, ApEn, and SpEn showed that complexity in the aphasia group at baseline was significantly different from that of in posttreatment aphasia and nonaphasic control group. However, the differences between groups in the right hemisphere were less significant. Considering the fact that the experimental group had an injury in the left hemisphere and this hemisphere plays a great role in language performances, EEG signal alteration in this hemisphere may add support for the effectiveness of LZNFB treatment and decreased EEG complexity can be implied as clinical improvement. In line with our findings, several studies associated decreased complexity with improvement. For example, decreased complexity after recovery has been reported in depression (Okazaki et al., 2013) and autism (Okazaki et al., 2015). Nevertheless, our findings are opposed to the study of Sun et al. (2017), showing increased complexity in the contralesional hemisphere after treatment in stroke patients (Sun et al., 2017). To clear up these diversities in results, several factors such as lesion size, affected hemisphere, and postonset should be taken into account. If the affected region of the brain is large, there might be insufficient cortical tissue left in the ipsilesional hemisphere. Therefore, the right hemisphere is more probable to activate in order to help the defiant and weakened left hemisphere. Our participants had the right hand affected, suggesting a lesion in the left hemisphere. Moreover, our participants were in the chronic phase and their EEG data were assessed at least 7 months after brain damage (Table 1). By showing decreased complexity to normal levels over the LZNFB treatment we provide evidence of the potential of using complexity as an indicator of improvement in aphasia.

PAC

With the present study, we showed significant differences in theta-gamma coupling after treatment (Table 5, Figure 3). Our findings provide evidence that LZNFB can enhance PAC in aphasic patients to a normal level. This enhancement was found over various cortical sites, especially in the left hemisphere. It is necessary to consider that the human brain is unlikely to be a composition of neatly separated neural modules whose oscillatory signatures can be manipulated independently from each other. Rather, its essence lies in a myriad of dynamic neural interactions that serve the integration of information across various temporal and spatial processing scales (Tononi, 2010). One promising mechanism for how such integration may be implemented in the brain is through a nested hierarchy of neural oscillations (Lakatos et al., 2005). Studies have shown that the phase of oscillations arising from slower global computations can flexibly modulate the amplitude of faster local oscillations (Bonnefond & Jensen, 2015). As oscillations in the human brain are known to interact within nested hierarchies via PAC, and PAC increment has been reported in neuromodulation techniques (Helfrich et al., 2016; Noda et al., 2017), we expected NFB might also be able to increase the macroscopic detectability of such coupling.

Increased PAC in our study, over the LZNFB, has two major implications. On the one hand, it implies improved cognitive performance in aphasia. Our findings were in line with previous studies showing the association between PAC and visual perception (Händel & Haarmeier, 2009), feedback processing (Cohen et al., 2008), memory recall (Tort et al., 2009), and visual (Okazaki et al., 2013) and motor mapping (Tzvi et al., 2016). Similarly, the association between increased PAC coupling with improved task performance was reported (Vivekananda et al., 2021).

On the other hand, increased PAC in our study is relevant for language performance in aphasia. In fact, theta-gamma cross-frequency coupling in the left hemisphere has been proposed to subserve the concatenation of phonemes to syllables (Canolty et al., 2006), and it adopts to speech rate (Lizarazu et al., 2019). Notably, the increase in PAC could not have been due to an increase in the number of neurons, as lost neurons cannot be regenerated during rehabilitation training. However, following the neuronal death, spared neural structures in adjacent tissue, and remote structures in the ipsileisional and contralateral hemispheres, undergo significant functional changes.

Previous studies also associated dysfunction in PAC with several clinical conditions such as Parkinson's disease (de Hemptinne et al., 2013), autism spectrum disorder (Khan et al., 2013), and epilepsy (Edakawa et al., 2016). Here, by demonstrating

enhanced theta-gamma PAC to normal levels over the NFB treatment, we provide evidence in potential of using PAC as an indicator of improvement in aphasia.

Taken together, by demonstrating enhanced theta-gamma PAC and decreased complexity to normal levels over the LZNFB treatment, we provide evidence of the potential of using PAC, and complexity as an indicator of improvement in aphasia. We have shown here the ability of LZNFB to be used as a neuromodulatory tool in decreasing symptoms and EEG disturbances in aphasia. Our finding of NFB efficacy in aphasia is supported by previous case studies (Mroczkowska et al., 2014; Rozelle & Budzynski, 1995).

Limitations

There were some limitations in this study. First, the data were collected from aphasic subjects in the chronic phase with homogenous lesion locations and clinical impairment, which could limit the generalization of our findings to other variations in aphasia. Small sample size is another limitation of our study. Future studies that evaluate a greater number of patients and healthy subjects will be necessary to verify the conclusions of the present study.

Conclusions

We conclude that LZNFB treatment was effective in decreasing EEG disturbances and symptoms in aphasia. We think that our findings in complexity and PAC could provide important insights into the electrophysiological profile in aphasia and its alterations after treatment.

Author Disclosure

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Exploring Single-Case Research Design With Individualized Anxiety-Based Neurofeedback Protocols and Session Data

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Abstract

Individuals' experiences of anxiety differ in manifestation, development, and severity. Using retrospective neurofeedback session data which included quantitative electroencephalography (qEEG)-based anxiety protocols, we examined four participants' data. We employed a single-case research design (SCRD) methodology to highlight the individual variations or change across participants' neurofeedback session data. We assessed effect size using visual analysis, nonoverlap of all pairs, and simulation modeling analysis. Considering the novel concept of applying SCRD to physiological data, we compare and contrast our findings while also suggesting limitations and future areas for research.

Keywords: neurofeedback; single-case research design; anxiety

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Introduction

In 2017, the National Institute of Mental Health (NIMH), reported that approximately 31.1% of adults in the United States will experience some type of anxiety during their lifetime. Additionally, researchers conducted a systematic review and meta-analysis of studies assessing the prevalence of anxiety disorders during the COVID-19 pandemic, revealing a rate of 35.1%, or one in three adults (Delpino et al., 2022). Although the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition Text Revision* designates anxiety concerns to include intrusive thoughts, tightness in the jaw, clenched fists, headaches, or other physiological and psychological dysregulation, individuals do not always experience anxiety in similar fashions (American Psychiatric Association [APA], 2022). Adding to the complexity, anxiety can also co-occur with depression or other mental health diagnoses and, depending on individual development, vary due to culture, genetics, environment, social climate, and various other ecological dynamics (NIMH, 2023). Whereas treatment methods using talk therapy (e.g., Carpenter et al., 2018) and neurofeedback demonstrate positive outcomes for reducing anxiety concerns (e.g., Cheon et al., 2015; Gregory et al., 2020; Walker, 2012), evaluating treatment efficacy utilizing methodologies that capture individual experiences of anxiety is warranted.

A methodology primarily applied in education research, yet with a growing interest among researchers in other disciplines within the last 10 years, are single-case research designs (SCRD; Ganz & Ayres, 2018; Gregory, 2022). SCRDs can also exist in literature as single-case designs, single-case experimental designs, or time series data research. Currently, scholars are developing SCRDs best practice guidelines which include recommendations for methodological approaches, data analyses, and ethical considerations (Kratochwill et al., 2023). Researchers gravitate toward SCRDs when there are numerous intervention data points and an interest in evaluating individual changes.

Method

Authors, La Vaque et al. (2002) recognize best practices for neurofeedback methodologies and studies. One of their recommendations encourages researchers to add multiple observations (La Vaque et al., 2002). Adding multiple observations to research studies includes various methodologies-including single-case research designs (SCRDs). SCRDs, also known as time series designs, utilize participants as their own baseline (Kazdin, 2021). Characteristics of SCRDs include (a) repeated measurement of the dependent variable, (b) a measurement that occurs across time, and (c) the identified "case" is either an individual, organization, business, or other group (Kazdin, 2021; Lobo et al., 2017). SCRD researchers utilize multiple baselines (i.e., participants begin the intervention at varying times), reversal designs, and multiple treatment designs based on their desired data outcomes and research goals. For example, the baseline is the "A" phase containing repeated measures but no intervention. The "B" phase involves the intervention and uses the same repeated measurement (i.e., assessment or neurofeedback intervention as the "A" phase). The overall concept is to assess if an intervention has any effect on the independent variable.

As variations of SCRDs reflect various strengths for evaluating intervention effects, the literature emphasizes the need for researchers to exercise care in analyzing their data. A similar mentality may also benefit neurofeedback researchers and clinicians considering the vast differences and intricacies in subjects' individual life experiences, physiological development, and presenting brain patterns. In addition to these factors, we measured participants' self-reported anxiety symptoms by administering pre and post Zung assessments (Zung, 1971). Since retrospective was utilized, we did not need to acquire additional IRB approval as the university has an ongoing blanket approval for the neurofeedback anxiety data. Using retrospective neurofeedback session data with anxiety-based protocols, our research questions ask:

1. Is there a change over time in participants' mean magnitude (i.e., band 1, band 2, and band 3 in BioExplorer) of their neurofeedback session-to-session data, based on their corresponding brain wave frequencies?
2. Is there a change over time in participants' anxiety as measured by pre and post Zung scores?

Clinicians

The current study utilized student clinicians, which consisted of clinical mental health masters-level students and counselor education and supervision doctoral-level students within counseling programs nationally accredited by the Council for Accreditation of Counseling and Related Education Programs. These students had previously completed the Biofeedback Certification International Alliance requirements for didactic coursework for neurofeedback and were under the supervision of a certified and licensed supervisor at the time of data collection. Volunteer clinicians (e.g., faculty, alumni) with neurofeedback training were also utilized.

Measures

Demographic Information and Treatment Record. The demographic data utilized in this study include gender, age, ethnicity, highest level of education completed, and current or previous experience with counseling. Additional data collected using session-to-session treatment records include number of sessions attended, average length of sessions, treatment protocol, average amplitude measures per frequency band trained from BioExplorer, and electrode sites (based on the international 10-20 system).

Zung Self-Rating Anxiety Scale for Adults. The Zung Self-rating Anxiety Scale (SAS) is a 20-item self-report assessment instrument, which includes measures of state and trait anxiety based on scoring in four groups of manifestations: cognitive, autonomic, motor, and central nervous system symptoms. Items are measured on a 4-point Likert type scale (1 = *None or A little of the time* to 4 = *Most or All of the time*). Example items include "I get upset easily or feel panicky," "I can breathe in and out easily," and "I feel that everything is all right and nothing bad will happen." Raw scores range from 20 to 80, which are converted to index scores by dividing the sum of the raw scores by 80 and multiplied by 100. Higher scores indicate greater severity of anxiety symptomatology (Zung, 1971). The SAS continually displays good internal consistency with a Cronbach's alpha of .82 (Tanaka-Matsumi & Kameoka, 1986); fair concurrent validity, correlating significantly (.30) with the Taylor Manifest Anxiety Scale (Zung, 1971); and to distinguish both between clinical and nonclinical groups and between patients diagnosed with anxiety disorders and those with other psychiatric diagnoses (Zung, 1971).

Instrumentation

Quantitative Electroencephalography (qEEG). Prior to beginning neurofeedback treatment, a qEEG was computed to identify an individual's standard brainwave patterns and the areas that would benefit from conditioning. At least a 24-hr window prior to the qEEG recording was suggested for clients to restrict consumption for nonessential substances, unless otherwise medically directed. All medically directed substances were factored into qEEG interpretation and protocol development.

The 19-channel qEEGs were acquired using one of two systems: (a) a BrainMaster Discovery 24 high-impedance amplifier (BrainMaster Technologies, Inc., Bedford, OH) and NeuroGuide (Applied Neuroscience, Inc., Largo, FL) software, or (b) a Mitsar BT 201 high-impedance amplifier with WinEEG software (Mitsar Co. Ltd., St. Petersburg, Russia). Recordings were captured in the eyes-closed and eyes-opened conditions using a properly sized Electro-Cap (Electro-Cap International, Inc., Eaton, OH) which was fitted as per manufacturer's guidelines with ear-clip leads. Preparation of electrodes was performed in a manner adequate to achieve impedance levels of less than 5K Ω (Jones, 2015).

Neurofeedback. For the neurofeedback sessions, clinicians utilized the BrainMaster Atlantis two-channel amplifiers (BrainMaster Technologies, Inc., Bedford, OH) and BioExplorer software (Cyberevolution, Inc., Seattle, WA). Electrode site preparation was done by cleaning the site, ground, and reference locations with rubbing alcohol and abrading using PDI sterile alcohol prep pads and Nuprep skin prep gel. Gold-plated electrodes were attached to the clients using Ten-20 conductive paste. Impedance measurements were taken to ensure that interelectrode impedance was less than 5K Ω (Jones, 2015).

Participants (Including Neurofeedback Protocols, Statistical/Data Analysis, Results)

Participant data were collected from retrospective neurofeedback data at a southern university in the United States. Participants of interest included individuals with at least 14 neurofeedback sessions during a semester and a continuation of the same protocol. For organizational purposes, we display our participants' demographic information and results from data analyses under their corresponding participant number.

Data Analysis

First, we entered data into Microsoft Excel to produce graphs which serve as our visual representation of the participants' data and resulting trend lines. Next, our analysis consisted of nonoverlap of all pairs (NAP; Parker & Vannest, 2009). NAP is not contingent on trend lines or averages, is prevalent in SCRD research, and is popular with AB Phase designs. Some researchers criticize NAP analysis and suggest its limitation of distinguishing between the two phases (Manolov & Solanas, 2018); however, with neurofeedback sessions participants continually receive the intervention instead of having a distinct treatment phase and a no-treatment phase. NAP scores are the result of comparing all data points between two phases (Fielenbach et al., 2019). For the current study, Phase A consists of the first defined group of neurofeedback sessions and Phase B the last (i.e., or successive) defined group of sessions. Resulting NAP scores produce effect sizes that range from 0.00–0.65 (i.e., 65%) a weak effect, 0.66–0.92 a medium effect, and 0.93–1.0 a large effect (Parker & Vannest, 2009).

To bolster the NAP results, we used simulation modeling analysis (SMA; Clinical Research Solutions, 2021)—a free and downloaded software program for SCRD data with <30 time points (Borckardt, 2006). The software program allows for controlling for autocorrelation, testing the slope and trend lines of the session data, and runs a 5,000-simulation test for determining the best fit trend line or most correlated model. The five models are (a) Model 1 suggests a Phase A increase in outcome measure with a decrease during Phase B; (b) Model 2 suggests a stable or level Phase A and an increase in Phase B; (c) Model 3 indicates a Phase A increase that levels out and is stable during Phase B; (d) Model 4 suggests a Phase A increase that continues into Phase B; and (e) Model 5 indicates an increase in Phase A, and immediate decrease, and an additional increase in Phase B. SMA illuminated deeper insight to participants neurofeedback session data. Specifically, this analysis can predict subtle changes within the data and how the participant might have responded to sessions if clinicians had continued the intervention.

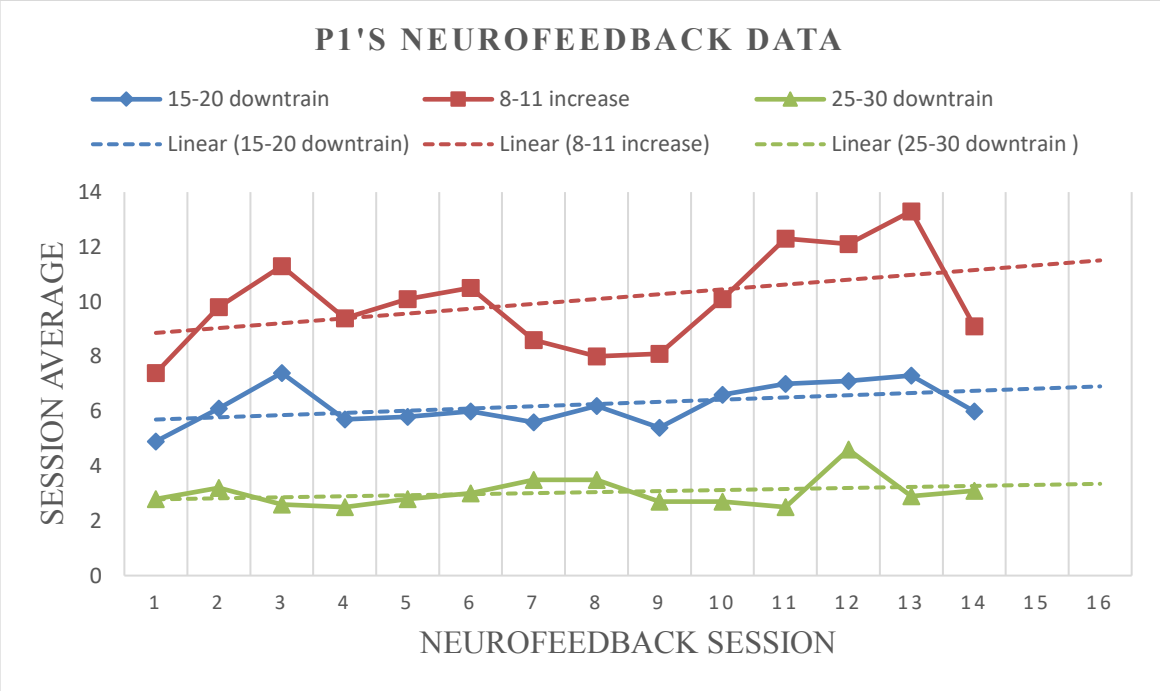
For our final analysis, we calculated change score percentage using the *Statistical Package for the Social Sciences (SPSS) software version 28* (SPSS, 2021). We compared each participant's percentage of change from their pre and post Zung raw scores. These data outcomes serve as the participants' self-report data, which Wigton and Krigbaum (2015)

strongly recommend to collect and then compare with physiological data.

Participant 1

Participant 1 (P1) identified as a 45-year-old, Caucasian, Hispanic/Latino female. During P1's first semester of neurofeedback treatment, her sessions included the protocol of downtraining 15–20, increasing 8–11, and downtraining 25–30 at PZ with eyes closed. Her sessions were an average of 23 min in length and utilized audio feedback. A visual of her session data is presented below.

Figure 1. *P1's Visual of Neurofeedback Data.*



According to P1's protocol, the visual outcomes of her downtraining bands appear to slightly increase, while the 8–11 Hz band shows an overall increasing trend. Hence, according to her protocol, the participant shows a desired trend of increasing the 8–11 Hz band. To further examine the data, we divided the 14 session averages of each band into Phase A (n = 7) and Phase B (n = 7) for determining the NAP scores and their corresponding effect sizes. These results are in Table 1.

Table 1

Nonoverlap of All Pairs Statistical Outcomes for P1

	S	*Pairs*	*NAP*	VARs	*z*	*p*	90% CI
15–20 Hz	22	49	0.725	245	1.41	.160	[−0.076, 0.974]
8–11 Hz	10	49	0.602	245	0.64	.522	[−0.321, 0.730]
25–30 Hz	5	49	0.551	245	0.32	.749	[−0.423, 0.628]

Note. S = distribution; Pairs = total pairs comparisons; NAP = nonoverlap of all pairs effect sizes; VARs = variance; z = z-score; p = p value (p = .05); CI = confidence interval.

The NAP scores support the visual trend lines of the increase in all three of the participant's bands. Also, the 8–11 Hz and 25–30 Hz bands both produced the NAP score equivalent of a weak effect, while the 15–20 Hz band is in the medium effect range.

Simulation Modeling Analysis. We ran the SMA on P1's three training bands. For P1's 15–20 Hz band, the data best fit with (Slope Vector) Model 4 (R = .33, p = .32). Model 4 is indicative of an increase in Phase A that continues during Phase B. This is an opposite desirable outcome according to P1's protocol. Her 8–11 Hz band also was most correlated with Model 4 (R = .23, p = .51), which does align with her protocol and visual graph; however, the increase was not significant. P1's 25–30 Hz band fit best to Model 3 (R = .26, p = .30). Model 3 denotes a Phase A increase and a leveling out during Phase B. Hence, if P1 had continued with sessions, this could suggest a future trend toward her protocol goal.

Zung Scores. P1 reported Zung raw scores of 44 (pre) at the start of services and 35 (post) at the conclusion of her neurofeedback treatment. Using *SPSS 28*, we calculated the percentage of change. Her change score percentage shows a 20.45% decrease in her self-reported anxiety concerns. To further interpret P1's self-reported data, we calculated P1's SAS index following Zung's procedure (Zung, 1971). P1's initial score demonstrated a SAS index of 55 (mild to moderate anxiety) at pre and a decrease in symptomology at post with a SAS index of 44 (normal range).

Participant 2

Participant 2 (P2) identified as Caucasian, Hispanic/Latino, and a 52-year-old male at the beginning of his neurofeedback treatment. His protocol included downtraining 4–7 Hz, increasing 12–15 Hz, and downtraining 25–30 Hz at CZ with EO. His feedback included audio/visual displays of episodes of a TV series and movie clips. Most of his sessions were 20 minutes in length. Figure 2 visually displays his band averages after his first university semester of neurofeedback sessions. P2's duration of neurofeedback treatment is represented in Figure 3.

Examining P2's first 14 sessions show only a positive trend that aligns with his protocol in the downtraining of 25–30 Hz. P2 continued with his neurofeedback treatment for a total of 47 sessions, which included missing band averages for session 21 and a continuation of the same protocol. These session data are in Figure 3.

Figure 2. *P2's Visual of Neurofeedback Data for His First Semester of Sessions.*

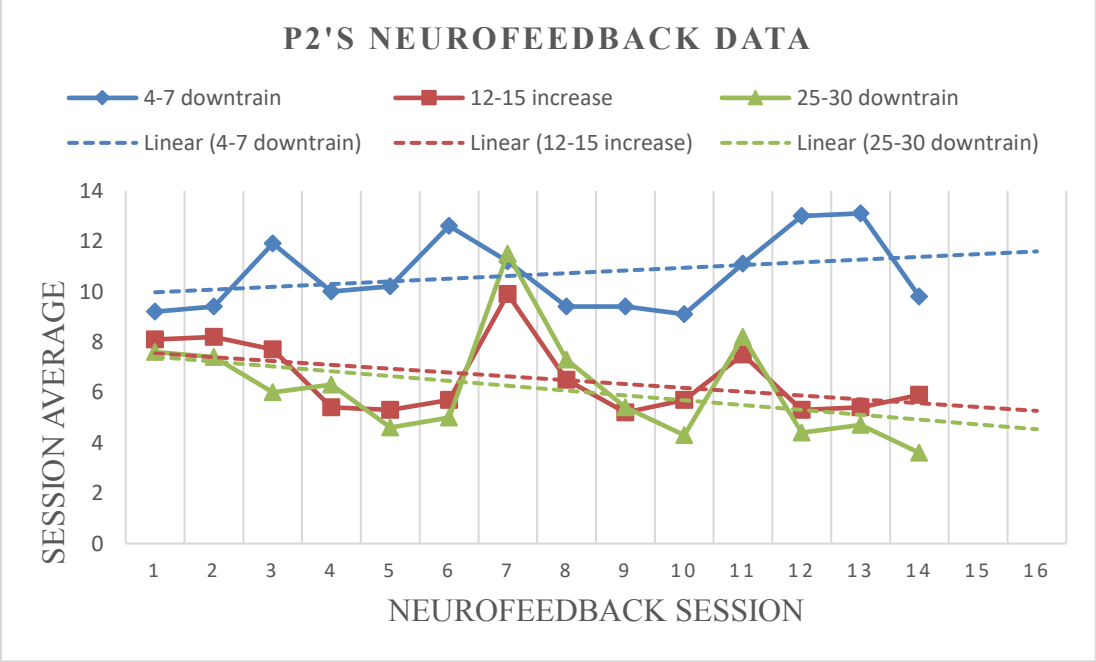
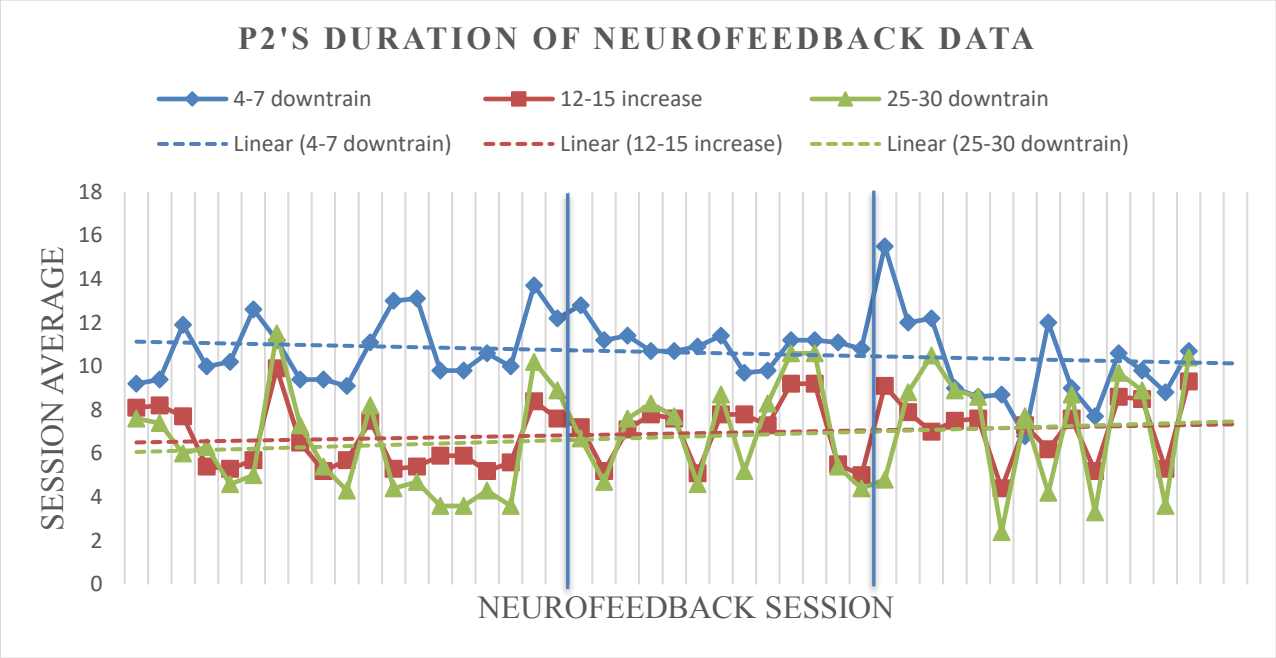


Figure 3. *P2's Visual of Neurofeedback Data for His Duration of Sessions.*



When we explored the duration of P2's data, we can see positive trend toward his protocol in downtraining 4–7 Hz and increasing 12–15 Hz. In full disclosure of data reporting, P2's data includes university semester breaks in treatment between sessions 19 to 20 and 32 to 33. These breaks in treatment were around 3–4 weeks and are marked in Figure 3. While it is vital to report the visual trends of data in SCRD, researchers also encourage further exploration of data change with statistical analyzes (Kratochwill et al., 2023).

Table 2
Nonoverlap of All Pairs Statistical Outcomes for P2

	S	*Pairs*	*NAP*	VARs	*z*	*p*	90%CI
4–7 Hz	−119	529	0.388	8287	−1.31	.191	[−0.508, 0.058]
12–15 Hz	112	529	0.606	8287	1.23	.219	[−0.071, 0.495]
25–30 Hz	134	529	0.627	8287	1.47	.141	[−0.030, 0.536]

Note. S = distribution; Pairs = total pairs comparisons; NAP = nonoverlap of all pairs effect sizes; VARs = variance; *z* = *z*-score; *p* = p value (*p* = .05); CI = confidence interval.

We performed NAP analyses for P2 using the duration of his neurofeedback treatment data. This displayed a corresponding correlation to the visual analysis and an overall decrease in his 4–7 Hz band; however, the effect was low. Additionally, P2's 12–15 Hz band also had a trend toward his protocol with an overall increase, but with a weak effect.

Simulation Modeling Analysis. Per the SMA creator, Borckardt (2006), the program was designed for data with < 30 time points. Hence, we did not utilize SMA for P2's duration of neurofeedback session data.

Zung Scores. P2's Zung scores were 29 pretreatment and 29 posttreatment. Since there was no change, we did not perform a change score computation. P2's SAS Index of 36 fell within the normal range of anxiety.

Participant 3

Participant 3 (P3) identified as a non-Hispanic, Caucasian female, age 55. Her protocol consisted of downtraining 6–10 Hz, increasing 12–15 Hz, and downtraining 25–30 Hz at FZ with EO. Her feedback included audio/visual displays of movie clips and simple balloon popping games. P3's duration of sessions took place over one university semester and totaled 18 sessions with an average length of 28 min.

P3's visual display of neurofeedback is challenging to interpret. The similar trend lines of her 12–15 Hz and 25–30 Hz bands both appear to be slightly increasing. P3's 6–10 Hz band also appears to be increasing. The difficulty in interpreting the visual analysis trends solidify the need for furthering analyzing data. Ideally data analyses will illuminate supplemental data trends.

Both of P3's bands, 6–10 Hz and 25–30 Hz, displayed medium effects in their changes. These trends were not in the desired directions. Her 12–15 Hz SMR band resulted in a large effect change and a significant result that aligned with her protocol.

Figure 4. *P3's Visual of Neurofeedback Data.*

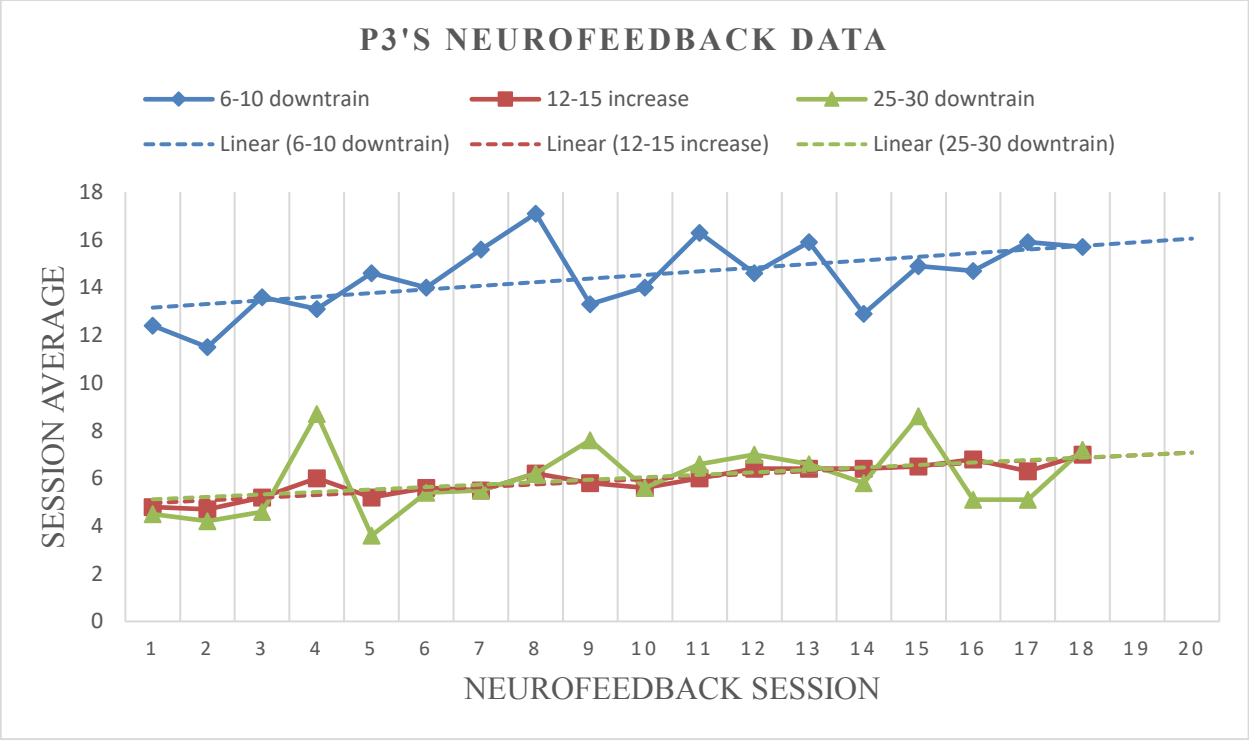


Table 3

Nonoverlap of All Pairs Statistical Outcomes for P3

	S	*Pairs*	*NAP*	VARs	*z*	*p*	90%CI
6–10 Hz	39	81	0.741	513	1.72	.085	[0.022, 0.941]
12–15 Hz	71	81	0.938	513	3.13	.002	[0.417, 1.000]
25–30 Hz	31	81	0.691	513	1.37	.170	[−0.077, 0.843]

Note. S = distribution; Pairs = total pairs comparisons; NAP = nonoverlap of all pairs effect sizes; VARs = variance; *z* = *z*-score; *p* = *p* value (*p* = .05); CI = confidence interval.

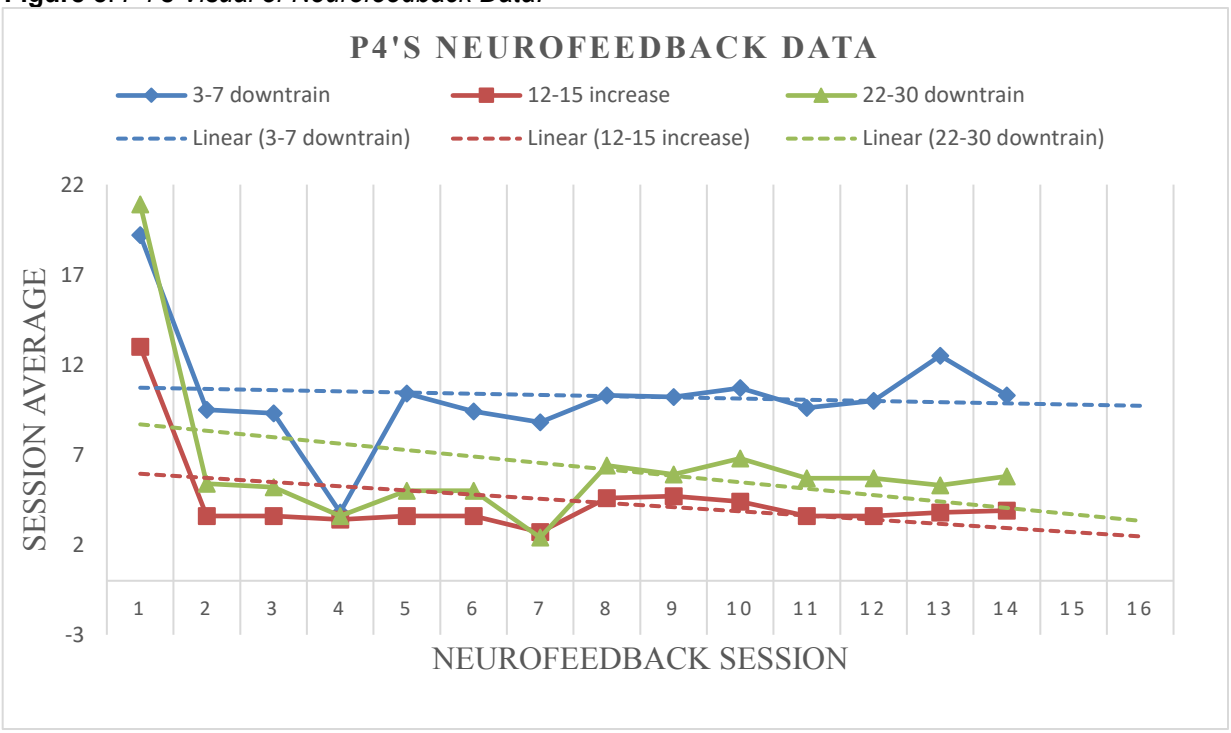
Simulation Modeling Analysis. P3' SMA results for band 6–10 Hz correlated best with Model 3 (R = .62, p = .02) and is significant, which is not ideal for her protocol considering Model 3 indicates an increase during Phase A and a leveling out effect during Phase B. However, similar to P1, if P3 had continued with neurofeedback session, a potential trend toward her protocol decreasing might have been achieved. P3's SMR band of 12–15 Hz produced the best fit with Model 4 (R = .90, p < .001). Model 4 is an ongoing increase in the data. This aligns with the participant's protocol of increasing his SMR band. For P3's 25–30 Hz band, her data best fit with Model 3 (R = .45, p = .03). Neither Model 3 nor the significant finding is the preferred trend for P3's data. Like her 6–10 Hz band, if she continued with sessions there is the potential for her to meet her protocol goal.

Zung Scores. P3 self-reported a Zung score of 43 pretreatment and 40 at the conclusion of her neurofeedback treatment. This resulted in a percentage change of −6.97%. P3's initial and post scores demonstrated a SAS index of 54 (pre) and 50 (post) both of which indicate mild to moderate anxiety.

Participant 4

P4 was a 46-year-old, who identified as female and Caucasian. She completed 14 neurofeedback sessions with a protocol of downtraining 3–7 Hz, increasing 12–15 Hz, and downtraning 22–30 Hz at Cz. Her feedback consisted of EO training with TV show clips and a waterfall visual with calming music. The majority of her sessions were 30 min in length.

Figure 5. *P4's Visual of Neurofeedback Data.*



Inspecting P4's visual graph, all her bands appear to be decreasing over time. However, the linear trend lines are potentially altered due to the first session data points being outliers. The NAP scores and SMA may prove more insightful than the visual trends. When outliers exist in SCRDs, some authors believe NAP scores as being less sensitive (Ledford et al., 2018). We opted to include all P4's session data points for the NAP analysis and removed them for her SMA.

All of P4's NAP scores produced a medium effect. Also, each of her bands showed an increase over time, which is opposite of her visual graph. This is due to her first session outliers. Her 22–30 Hz band results were significant; however, not in the direction that aligned with her protocol.

Table 4
Nonoverlap of All Pairs Statistical Outcomes for P4

	S	*Pairs*	*NAP*	VARs	*z*	*p*	90%CI
3–7 Hz	25	49	0.755	245	1.60	.11	[−0.015, 1]
12–15 Hz	27	49	0.776	245	1.73	.08	[0.026, 1]
22–30 Hz	33	49	0.837	245	2.11	.04	[0.148, 1]

Note. S = distribution; Pairs = total pairs comparisons; NAP = nonoverlap of all pairs effect sizes; VARs = variance; *z* = *z*-score; *p* = *p* value (*p* = .05); CI = confidence interval.

Simulation Modeling Analysis. For P4's SMA data analyses, we removed the first session data points for all her brain bands and included the first six sessions for Phase A and the last seven for Phase B. Her 3–7 Hz band displayed highest correlation with Model 4 (*R* = .51, *p* = .08) indicating a Phase A increase that continues into Phase B. Her 12–15 Hz band best fit with Model 5 (*R* = −.49, *p* = .15) which states an increase in Phase A with an immediate decrease and an additional increase in Phase B. P4's 22–30 Hz band best fit with Model 2 (*R* = .43, *p* = .16). Model 2 represents a stable or level Phase A with an increase in Phase B. P4's SMA analyses offered us more insight into her session data. Her 3–7 Hz and 22–30 Hz bands appear to not be responding to her protocol. Her SMR band of 12–15 Hz may or may not be responding to her uptraining protocol.

Zung Scores. P4's Zung scores were 37 at the start of services and 36 at the conclusion of neurofeedback treatment. Hence, her semester percentage change score was −2.70%. P4's initial and post scores demonstrated a SAS index of 46 (pre) and 45 (post) both of which are indicative of mild to moderate anxiety.

Discussion

Our goals for this study were to utilize a SCRD approach to examine participants' change over time through neurofeedback session data averages from their individualized neurofeedback protocols and self-report data. For the first research question, we created and reviewed a visual representation of the participants' session data and resulting trend lines, computed NAP scores, and performed SMA. Considering the NAP scores, the participants' sessions displayed mainly small to medium effect sizes or changes between Phase A and Phase B, with a few significant findings trending in the intended direction. However, in P3's SMR band, her protocol asked her to increase this area which resulted in her NAP scores showing a large effect size and her SMA displaying significant results. For all participants, we used SMA and their session data. Results were varied within each participant and their three bands. Additionally, outcomes varied across participants; yet it appears for some of their training bands, if participants had continued neurofeedback sessions, an alignment toward their protocol goals might have been achieved. Further, some participant NAP scores were significant while their SMA results using the same data did not display significance. For the final research question, all participants self-reported their Zung score decreasing or staying the same after their neurofeedback treatment.

Utilizing the SCRD approach to examine individual changes throughout the duration of the neurofeedback treatment afforded us the opportunity to see the more nuanced changes by viewing the data points from different perspectives. For instance, visually, there seems to be an increase in all three bands for P1, one of which appears to be trending in the intended direction (8–11 Hz); however, the NAP score and SMA do not suggest a significant change within the evaluated window of treatment. Conversely, when reviewing P1's self-reported SAS scores, P1 reported experiencing a 20.5% decrease in anxiety concerns moving from a mild to moderate level of anxiety to within the normal range of anxiety. This study seeks to contribute new information concerning the use of SCRD to examine neurofeedback outcomes.

Limitations and Implications for Research

The neurofeedback sessions were primarily conducted by students and in an academic setting verses a research facility. Some factors to consider may be variations in student-run sessions using different threshold settings and possessing various neurofeedback skill levels. Also, participants might

have been receiving other forms of mental health support (i.e., counseling) or biofeedback before or during their neurofeedback intervention and the effects could have altered or been responsible for the data changes. The session averages were not artifacted and due to this, data could be distorted.

SCRD for neurofeedback session data is a novel approach and future researchers may consider a similar format to this study or utilize other SCRD methods and analyses. We recommend interested researchers to view the article by Kratochwill et al. (2023) and consider their suggestions for SCRD best practices. A considerable strength of SCRD approaches may highlight subtle changes in participants' data over time (Lenz, 2015) which may provide neurofeedback professionals with insight into when a protocol shift may be necessary. Currently, neurofeedback professionals are advocating for its evidence-basis and credibility and are accordingly conducting larger sample size neurofeedback studies with double-blind procedures or control groups. This research is extremely vital for neurofeedback advocacy. However, examining individual change in physiological interventions could prove beneficial for neurofeedback professionals and their clients. Assessing individual changes may also be more meaningful to professional counselors or psychologists offering neurofeedback services.

Conclusion

This SCRD study incorporated individual-based anxiety protocols and examined neurofeedback data on an individual level. We performed a visual analysis of each participants' band averages and computed NAP scores and SMA. Results were varied within participant data and among participants. Employing SCRD and different analyses allowed us to compare and contrast significant findings while acknowledging individual protocols and individual change.

Author Disclosure

All authors disclose that this was an unfunded study and there are no conflicts of interest.

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A Preliminary Study Investigating the Acquisition of Valid qEEG Data While Wearing a Virtual Reality (VR) Headset

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Abstract

The use of virtual reality (VR) therapy is being utilized and promoted for a wide range of treatment applications. Yet, the majority of clinical evidence that supports the efficacy of VR treatment has been established utilizing reports of subjective outcome variables, such as rating scales or a reduction of symptoms reported by the patient. Instead, the present study supports the use of quantitative electroencephalography (qEEG) as a more precise and objective method for assessing treatment efficacy involving the use of VR-based treatments. Although a few studies have attempted to establish physiological evidence from qEEG recordings to strengthen the efficacy of pre-post treatment effects for VR-based treatments, these attempts have been based upon very small sample sizes or case studies. Therefore, to the best of our knowledge, prior studies have failed to uniformly account for ingenuine treatment effects that could arise from merely wearing a VR headset while acquiring qEEG. The current preliminary study sought to systematically measure any potential confounding effects that wearing a VR headset could produce by measuring and comparing the baseline qEEG recordings for the eyes-open, resting condition (staring at a dot) with and without the VR headset for 28 participants. The present results revealed very minimal significant differences between the two conditions when analyzed collectively and no significant differences for the male participants. The implications of these findings are discussed and provide preliminary support for confidently reporting qEEG efficacy data involving the use of a VR headset. Additionally, the current study is believed to have successfully established a valid and standardized approach for reliably obtaining active or real-time qEEG data while wearing a VR headset in order to confidently report the physiological effects of VR immersion on electrical brain activity.

Keywords: qEEG; virtual reality; VR therapy.

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Introduction

As virtual reality (VR) devices have grown in availability and use, so too has the body of literature on the effects and possible implications that VR can have. Current research efforts have explored VR's effectiveness in education, the treatment of mental health conditions, pain relief, training of practical skills, developing procedural knowledge, improving athletes' understanding of and intention to report concussions, enhancing conceptual knowledge, and enhancing meditation and presence (Baceviciute et al., 2021; Daneshvar et al., 2021; Hufnal et al., 2021; Tran et al., 2022). With the increase in this research, the methods for evaluating effectiveness and impact have also advanced. More studies on VR are beginning to employ quantitative electroencephalography (qEEG) data to further analyze cognitive impacts of the VR platform (Baceviciute et al., 2021; Tarrant et al., 2018; Tremmel et al., 2019). Employing qEEG measurement allows researchers to move away from subjective questionnaires rating the individual's experience in VR, and instead allows for more objective and continuous data that is collected in

real time during the exposure (Hertweck et al., 2019).

While the application of qEEG measurements in studying the impact of VR has increased, there is currently a lack of understanding of the potential impacts VR devices may have on qEEG data acquisition. Of recent studies that have either analyzed qEEG data during VR experiences (Tarrant et al., 2018; Tremmel et al., 2019) or compared qEEG data for 2-D versus VR videos (Xu & Sui, 2021), few have established validity for acquiring accurate qEEG data while wearing a VR headset. That is, thus far this new and growing body of research has yet to assure the scientific community whether certain factors present during qEEG acquisition (i.e., the weight of the headset, interference with electrode signal detection, artifact produced by physical movements during interactive VR experience) interfere with the reliability and validity of VR-based qEEG data.

While understanding of the validity of qEEG in VR technology is limited, current research has established some understanding of the interaction of qEEG and VR. One study investigating the potential impacts of electrical signals from the VR device did not find any significant impacts on qEEG readings (Cattan et al., 2018). While this study helps to provide evidence that the impact of the VR headset alone may not impede qEEG readings, the study used a more primitive VR device (one using smartphones), that is not representative or fully generalizable to the current state of advanced VR technology. A second study investigated qEEG signal quality obtained while using two popular VR head-mounted displays. Results revealed qEEG data being fairly consistent across experimental groups which consisted of eyes-open and eyes-closed trials with VR headsets and without (Hertweck et al., 2019). While this study suggested the viability of qEEG acquisition, it did not compare traditional brain-mapping procedures to ensure validity and suggested further analysis of conditions is needed for the field (Hertweck et al., 2019). Hence, there remains a gap in the literature and the research field on the validity of acquiring qEEG data with recent VR technology. Over the past several years the application of VR for mental health treatment has increased and is also supported by the American Psychiatric Association (APA, 2021). VR therapy is being promoted nationally and internationally by companies such as Amelia Virtual Care (Gurr & Laitz, 2023) based upon clinical case studies that rely upon subjective outcome variables. Another company, EaseVRx, recently received FDA approval for the marketing and use of VR therapy for patients 18 years or older diagnosed with chronic lower back pain (FDA, 2021).

The present study seeks to fill the gaps in our understanding of the reliability and validity of qEEG data collection with VR technology and adds several novel contributions to the field. The current study expands upon previous studies that have suggested qEEG data is viable with VR (Cattan et al., 2018; Hertweck et al., 2019) by collecting data under longer intervals using an eyes-open baseline condition in VR. An analysis of brain mapping is also utilized to compare eyes-open baseline with and without VR. Previous studies that have acquired baseline data have done so using immersive 3D experience compared to 2D screen applications using the same virtual environment (Tran et al., 2022). This study, however, will be one of the first to add an understanding of whether or not the VR headset itself (in this experiment, the Meta Quest 2, formerly called the Oculus) causes any difference in qEEG data by comparing a task in VR with a natural environmental condition. Additionally, many previous studies of qEEG and VR have been completed with small sample groups or as case studies, while the present study was able to recruit a larger sample size. Given previous research, we hypothesize that there should not be a significant difference when comparing the baseline data collected with and without the VR headset.

Materials and Methods

Participants

The study consisted of 30 participants ranging from 19–72 years of age (57% male, 43% female). No demographic data, other than gender and age, was obtained from the participants. This study was conducted in an empty classroom located in the college. The study was approved by the Bryn Athyn Institutional Review Board (Bryn Athyn College, PA). Participants were recruited through posted advertisements using digital or paper flyers posted throughout the college campus and community. Additionally, students enrolled in introductory psychology courses at the college were offered extra credit in their course for participating in the study.

Equipment

Virtual Reality (VR) Headset. The experiment was conducted using the Meta Quest 2 (formerly the Oculus) VR headset. The headset comes equipped with two handheld controllers. The Meta Quest 2 is typically used for gaming and watching 360-degree VR videos with 20 pixels per degree visuals and a

Fast-Switch LCD display spanning 1832 x 1920 pixels per eye with a 120 Hz refresh rate. The headset weighs 503 grams and measures 224 x 450 mm.

Electro-Cap. qEEG data was obtained utilizing a standard Electro-Cap 19-channel EEG with ear lead attachments (Bio-Medical Instruments, Clinton Township, MI). They are made of an elastic spandex-type fabric with recessed, pure tin electrodes attached to the fabric. The electrodes on the standard caps are positioned to the International 10–20 method of electrode placement. The sizes utilized for the current experiment ranged from 52–56 cm (medium) to 58–62 cm (large) depending upon the size of the participants' head circumference.

Measures

EEG Data Collection. The EEG data in this study was obtained using a Discovery 24 Series amplifier (BrainMaster Technologies, Bedford, OH). The Discovery 24 offers 1024 samples per second on 22 channels, with 24-bit resolution, and an amplifier bandwidth from DC (0.000 Hz) to 80 Hz. The EEG data in this study was sampled with 19 electrodes in the standard 10–20 International placement using a standard electrode cap plus two additional channels used for separate references attached to the right and left ears. Automatic artifacting was conducted using qEEG-Pro (qEEG Pro B.V., Verdunplein, The Netherlands) software's Standardized Artifact Rejection Algorithm (S.A.R.A). The files were then converted to enable NeuroStat and NeuroBatch (Applied Neuroscience, Inc., St. Petersburg, FL) to generate group mean statistics and paired-group *t*-test analyses.

Procedures

Upon replying to the digital or paper recruitment flyers, participants scanned the QR code contained on the flyer in order to select an available 60-min time slot. Participants received an email 1 to 2 days prior to their scheduled appointment which explained what to expect during their appointment as well as standard instructions for the proper clinical preparation for having a qEEG conducted (i.e., not using product other than basic shampoo when washing their hair prior to the appointment).

Upon their arrival on the day of their scheduled appointment, all participants read a written description of the study process contained in the IRB consent form requiring their signed consent. Once their consent was obtained, participants were asked to sit in a comfortable chair facing a whiteboard situated 5 feet from the chair. The study sessions took place in a secluded classroom away from noise and visual distractions. The participants were informed that the procedure for placing the Electro-Cap on their head and establishing "clean recordings" would take approximately 20–25 min followed by two conditions lasting approximately 6 min each. All participants were asked to turn off their phones and leave them with their personal items in a chair located in the back of the room to prevent distraction.

The participants then were prepared for the active qEEG recording by ensuring the Electro-Cap was securely fitted on their head adhering to standard qEEG acquisition protocol involving the application of Electro-Gel and Nuprep skin prepping gel to ensure low electrode impedance. In general, impedance levels up to 10 Ω are acceptable involving the use of qEEG recordings in clinical and research applications. The current researchers obtained impedance levels less than 5 Ω for the majority of the participants in each of the 19 locations on the scalp and less than 10 Ω impedance for all participants. Once the participant's qEEG reading was deemed to be suitable for valid data acquisition and recording, each participant was briefly taught how to minimize eye blinking and muscle artifact, such as jaw or shoulder tension. Participants were provided with real-time visual feedback from a laptop screen to demonstrate how eye blinking and muscle artifact affect the qEEG data acquisition, along with suggestions of how to minimize these artifacts during the recording (i.e., take a deep breath and then exhale, take a long and slow blink when necessary).

Following these steps, the participant was then instructed to stare at a black dot that was placed on a whiteboard located at eye level at a 5-foot distance for 6 min (Condition 1: eyes open). Upon completion of the first condition, the participant was provided with a 2- to 3-min break to relax while remaining in the chair and still wearing the Electro-Cap. During the brief break, the experimenter powered up and synched the Meta Quest 2 VR headset for the second condition (Condition 2: eyes open with VR headset). Then, the VR headset was placed directly upon the Electro-Cap (see Figure 1) and impedance readings were again measured to ensure that all 19 scalp locations maintained an impedance less than 10 Ω.

Figure 1. *VR Headset Placement for qEEG Recording*.

Once again, the current researchers obtained impedance levels less than 5 Ω for the majority of the participants and less than 10 Ω impedance for all participants. Once the VR headset was properly secured, the participants were asked to stare at a black dot that appeared in the VR headset, which was a still image of the black dot that they were asked to stare at on the whiteboard during the first condition. The black dot was placed at eye level by the experimenter using a synched iPad or iPhone with verbal feedback provided by the participant to confirm that the black dot, based upon the participant's visual perception, was at eye level and the same distance from view as experienced during the first condition. Once confirmation of the dot placement was confirmed, the participant was again asked to stare at the dot for 6 min. Following the completion of the study, all participants were provided with paper towels and provided a washroom where they could remove some of the excess Electro-Gel from their hair before leaving.

Data Analysis

qEEG is produced through statistical analysis of the EEG; that is, conversion of the time domain EEG record (voltage plotted against time) to the frequency domain (amplitude or power plotted against frequency) using the fast Fourier transformation (FFT). The qEEG bands we considered were delta (1–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), and beta (12–25 Hz). In this study, raw EEG data were collected noninvasively from the participant's scalp during the two experimental conditions using a BrainMaster Discovery 20-channel EEG (BrainMaster Technologies, Bedford, OH). Electrode caps were used to place recording electrodes over the 19 standard regions defined by the International 10/20 system referenced to linked ears: Fp1, Fp2, F3, F4, F7, F8, T3, T4, C3, C4, P3, P4, T5, T6, O1, O2, Fz, Cz, and Pz. All channels of EEG were acquired with 24-bit resolution at the sampling rate of 256 Hz.

The EEG was recorded for 6 min for each of the two conditions. Automated artifacting using SARA was uniformly applied without exception in order to remove human error or bias in the analysis and selection of which data should be rejected. The NeuroGuide EEG and qEEG analysis system software (Applied Neuroscience, Inc., Largo, FL) was used for the signal processing of the qEEG. Quantitative data were presented using absolute power group means comparison between the two experimental conditions utilizing a within-subjects design for the following four EEG frequency bandwidths: delta (1–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), and beta (12–25 Hz). Quantitative data analysis was also performed utilizing NeuroStat's paired-group *t*-test for comparing the absolute power differences between the two experimental conditions across the 19 scalp locations acquired for each of the four aforementioned frequency bandwidths.

Automated artifacting using S.A.R.A. was uniformly applied without exception in order to remove human error or bias in the analysis and selection of which data should be rejected. Finally, the Bonferroni correction was applied to adjust for the number of paired-group *t*-tests conducted for each set of analyses to properly adjust the critical *p*-value for determining levels of significance.

Results

There were 30 participants recruited (17 males, 13 females). The age range was 19–72 years old (*M* = 39.3) years old. Out of these 30 participants, 2 females were eliminated from the study due to the presence of excess noisy channels. According to the qEEG-Pro manual, noisy channels are defined as channels that contain a disproportional amount of high-frequency power due to muscle artifacts, and the manual recommends that an individual's qEEG data be rejected when five or more noisy channels are present. The final sample included 28 participants consisting of 61% male and 39% female participants.

Group Means Analysis

Eyes-Open Resting Without VR Headset. Group means were recorded for this condition. This condition revealed absolute power measures with high activity levels in delta (1–4 Hz) and theta (4–8 Hz) in the central region of the brain. High activity levels were detected in alpha (8–12 Hz) and in beta (12–25 Hz) in the occipital region of the brain (see Figure 2).

Eyes-Open Resting With VR Headset. Similar patterns of activity were detected in the eyes-open condition with the Meta Quest 2 headset. Absolute power measures revealed high activity levels in delta (1–4 Hz) and theta (4–8 Hz) in the central region of the brain. High activity levels were detected in alpha (8–12Hz) and in beta (12–25 Hz) in the occipital region of the brain. High activity was also detected in beta (12–25 Hz) in the frontal region of the brain (see Figure 3).

Paired-Group *t*-test

Eyes-Open Resting Without VR Headset vs. Eyes-Open Resting With VR Headset. To compare the differences between the two conditions a paired-group *t*-test was performed using data from the 28 subjects (see Figure 4). However, the topographic maps in Figure 3 do not represent the significant *p*-value levels after the Bonferroni correction was applied as the NeuroStat software applications allow the user to manually adjust the *p*-values. Instead, the current researchers divided the critical *p*-value ($p = .05$) by the number of comparisons ($N = 28$) to determine the adjusted critical *p*-value ($p < .002$). Therefore, only regions depicted in dark red in Figure 4 below indicate possible significant difference since the dark red represents *p*-values ranging from 0.00 to 0.005.

Figure 2. *Eyes-Open Resting Without VR Headset.*

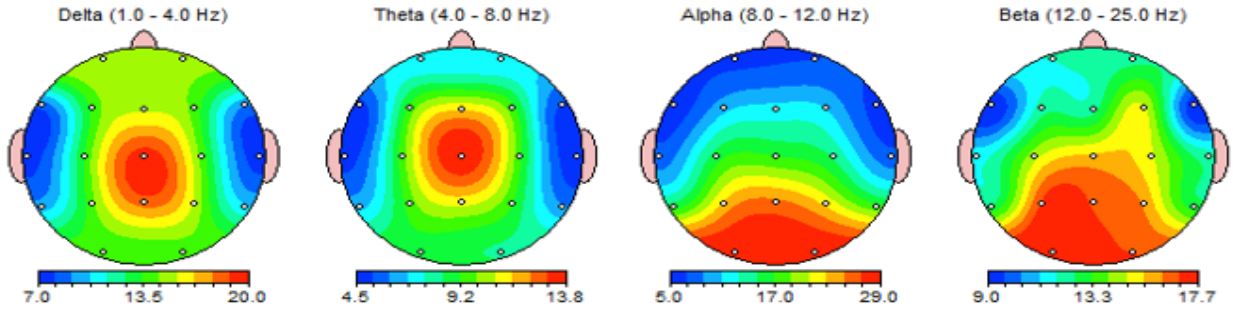


Figure 3. *Eyes-Open Resting With VR Headset.*

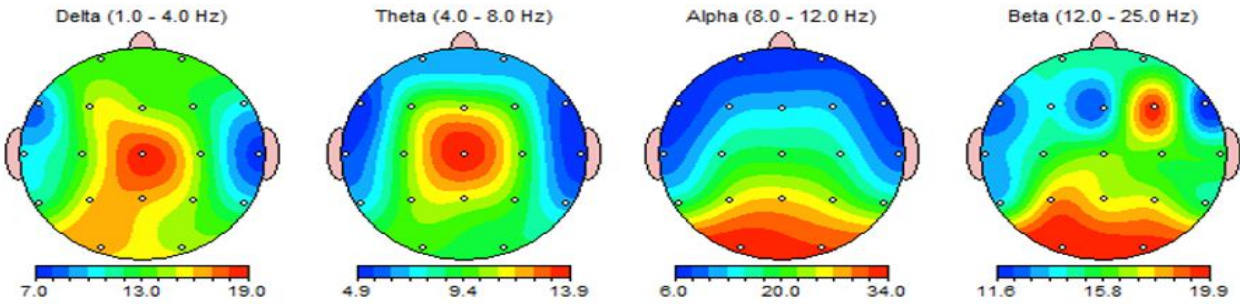
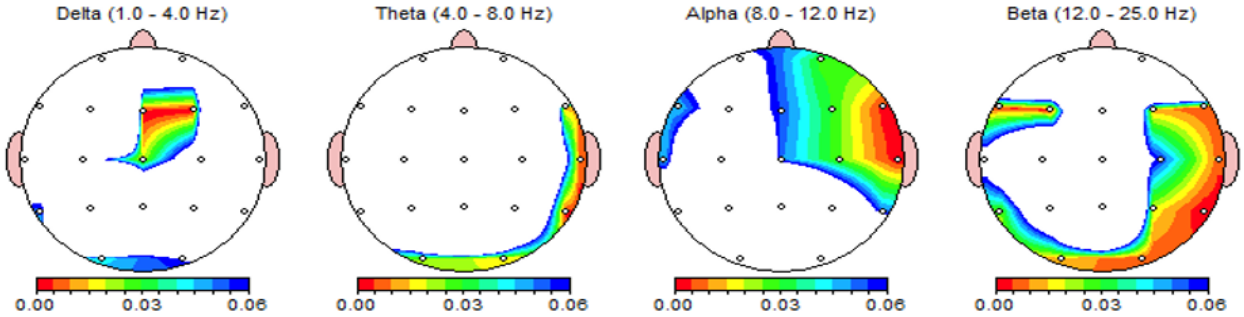


Figure 4. *Paired-Group t-test. FFT Absolute Power (uV Sq).*



After applying the Bonferroni correction to the NeuroStat automated paired *t*-test report, the results were analyzed and significant findings for the adjusted *p*-values were more specifically identified and highlighted according to the 19 electrode locations in the standard 10–20 International placement (see Tables 1 and 2).

The paired-group analysis revealed significant differences in the right hemisphere absolute power of delta (1–4 Hz) in the frontal regions ($p < .002$; see Table 1). Furthermore, significant differences were found in alpha (8–12 Hz) and beta (12–25 Hz), in the temporal regions of the brain. In the fronto-central of the brain, significant differences were found in delta (1–4 Hz), mainly in the frontal region of the brain ($p < .002$; see Table 1). No significant differences were found in the left hemisphere (see Table 1).

Table 1

Paired-Group t-test for Eyes Open With vs. Without VR Headset.

FFT Absolute Power Group Mean (uV Sq)

Post hoc Bonferonni Paired *t*-test Correction ($N = 28$, $p < .002$)*

	Intrahemispheric: LEFT			
	Delta	Theta	Alpha	Beta
Fp1 – LE	0.144	0.611	0.074	0.291
F3 – LE	0.995	0.708	0.084	0.002
C3 – LE	0.070	0.590	0.204	0.179
P3 – LE	0.703	0.253	0.251	0.118
01 – LE	0.042	0.025	0.192	0.013
F7 – LE	0.554	0.318	0.045	0.005
T3 – LE	0.117	0.116	0.046	0.077
T5 – LE	0.051	0.141	0.127	0.026

Table 1

Paired-Group t-test for Eyes Open With vs. Without VR Headset.

FFT Absolute Power Group Mean (uV Sq)

Post hoc Bonferonni Paired *t*-test Correction ($N = 28$, $p < .002$)*

	Intrahemispheric: RIGHT			
	Delta	Theta	Alpha	Beta
Fp2 – LE	0.126	0.646	0.028	0.377
F4 – LE	0.000*	0.444	0.030	0.012
C4 – LE	0.097	0.274	0.026	0.056
P4 – LE	0.253	0.207	0.120	0.019
02 – LE	0.061	0.016	0.202	0.006
F8 – LE	0.426	0.012	0.003	0.006
T4 – LE	0.402	0.006	0.001*	0.007
T6 – LE	0.159	0.003	0.051	0.000*
	Intrahemispheric: CENTER			
	Delta	Theta	Alpha	Beta
Fz – LE	0.000*	0.374	0.054	0.253
Cz – LE	0.019	0.834	0.051	0.102
Pz – LE	0.172	0.770	0.226	0.365

Gender Effect

To investigate whether there were any differences between males and females in the two conditions a paired *t*-test was performed. Bonferroni *p* values were adjusted for males ($p < .0027$) and females ($p < .005$) due to smaller sample size. For males, there were no significant differences between the two conditions (eyes open with or without VR headset) in the absolute power of delta (1–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), and beta (12–25 Hz; see Table 2).

Table 2

Paired-Group t-test for Eyes Open With vs. Without VR Headset (Male Participants).

FFT Absolute Power Group Mean (uV Sq) Post hoc Bonferonni Paired *t*-test Correction (N = 17, p < .0029)*				
	Intrahemispheric: LEFT			
	Delta	Theta	Alpha	Beta
Fp1 – LE	0.646	0.992	0.248	0.668
F3 – LE	0.234	0.283	0.507	0.048
C3 – LE	0.560	0.853	0.848	0.489
P3 – LE	0.415	0.562	0.647	0.568
01 – LE	0.023	0.163	0.446	0.130
F7 – LE	0.856	0.895	0.369	0.013
T3 – LE	0.170	0.634	0.435	0.084
T5 – LE	0.094	0.487	0.478	0.315
	Intrahemispheric: RIGHT			
	Delta	Theta	Alpha	Beta
Fp2 – LE	0.611	0.981	0.155	0.922
F4 – LE	0.041	0.376	0.223	0.168
C4 – LE	0.368	0.725	0.223	0.253
P4 – LE	0.887	0.368	0.382	0.382
02 – LE	0.029	0.130	0.486	0.486
F8 – LE	0.506	0.071	0.048	0.048
T4 – LE	0.126	0.049	0.032	0.032
T6 – LE	0.042	0.037	0.199	0.199
	Intrahemispheric: CENTER			
	Delta	Theta	Alpha	Beta
Fz – LE	0.025	0.240	0.327	0.630
Cz – LE	0.317	0.806	0.302	0.306
Pz – LE	0.708	0.998	0.590	0.980

Table 3

Paired-Group t-test for Eyes Open With vs. Without VR Headset (Female Participants).

FFT Absolute Power Group Mean (uV Sq) Post hoc Bonferonni Paired *t*-test Correction (N = 11, p < .005)*				
	Intrahemispheric: LEFT			
	Delta	Theta	Alpha	Beta
Fp1 – LE	0.042	0.170	0.388	0.375
F3 – LE	0.525	0.343	0.098	0.027
C3 – LE	0.095	0.470	0.050	0.016
P3 – LE	0.297	0.373	0.169	0.104
01 – LE	0.783	0.153	0.134	0.061
F7 – LE	0.250	0.178	0.046	0.106
T3 – LE	0.476	0.118	0.019	0.261
T5 – LE	0.193	0.144	0.047	0.021
	Intrahemispheric: RIGHT			
	Delta	Theta	Alpha	Beta
Fp2 – LE	0.052	0.176	0.207	0.348
F4 – LE	0.002*	0.937	0.062	0.039
C4 – LE	0.391	0.211	0.061	0.043
P4 – LE	0.252	0.594	0.177	0.042
02 – LE	0.798	0.231	0.221	0.048
F8 – LE	0.546	0.218	0.060	0.015
T4 – LE	0.249	0.201	0.031	0.009
T6 – LE	0.541	0.106	0.132	0.034
	Intrahemispheric: CENTER			
	Delta	Theta	Alpha	Beta
Fz – LE	0.004*	0.821	0.085	0.184
Cz – LE	0.047	0.799	0.054	0.194
Pz – LE	0.237	0.958	0.215	0.154

For females, there were significant differences in the right and central hemispheres. In the right hemisphere, there was a significant difference in the absolute power of delta (1–4 Hz) in the frontal region (p < .005; see Table 3). There was also a significant difference in the absolute power of delta (1–4 Hz), in the fronto-central region (p < .005; see Table 3). No significant differences were found in the left hemisphere (see Table 3).

Discussion

To our knowledge, this is the first study to systematically consider and examine the validity and reliability of qEEG data acquisition involving a VR interface beyond a single or small sample size research design. Specifically, the current study was designed to provide researchers, mental health clinicians, and neurofeedback therapists

implementing VR-based therapy a standardized and valid approach to scientifically examining the effects of such therapy modalities. The current research was designed to investigate two primary objectives: a) determine whether simply wearing a VR headset during the eyes-open resting qEEG recording significantly alters baseline levels of electrical brainwave patterns, and b) establish a standardized method for properly securing the VR headset on top of the Electro-Cap when performing qEEG data acquisition to secure valid recordings.

To address the first objective, the findings of the present study revealed some minimal differences in brainwave patterns during the resting eyes-open condition with the VR headset when compared to the standard eyes-open resting baseline condition employed by qEEG clinicians. A comparison of the absolute power differences in regional brainwave activity across frequency bands for both conditions provided the ability to determine directionality for the significant differences indicated by the paired-group *t*-test. The significant decrease in delta activation suggests an activation of the anterior cingulate corresponding to an increase in focus and attention. Increased beta activation in the right occipito-temporal area suggests an increase in visual sensation activation and processing. Furthermore, increased alpha activation in the right hemisphere suggests a suppression of avoidance related to a sense of being comfortable and unafraid. Therefore, it would appear that when participants were asked to establish a resting, eyes-open baseline qEEG by staring at a dot placed inside the VR headset, the research design resulted in a group effect suggesting a greater orientation response in the brain associated with an increase in visual attention while being in a safe environment.

While these findings suggest some measurable effect on the resting qEEG while wearing the VR headset, the majority of the location-specific bandwidth power values were not significantly different than the comparison eyes-open, resting baseline condition without the VR headset. These findings would generally support prior and future research studies which measure VR efficacy without the need to conduct a separate baseline qEEG recording with the VR headset, particularly when attention is given to the few location-specific changes (right: F4 delta, T4 alpha, T6 beta, and central: Fz delta). Additionally, the few significant changes observed in the current study could arguably be considered part of the cumulative VR effect that cannot and possibly should not be excluded or controlled. However, future replication group studies are warranted to provide further assurance to the qEEG community of these findings.

Also, there were some noteworthy limitations to our design and data analysis. First, the current research design did not counterbalance the two conditions. Instead, all participants' resting, eyes-open qEEG was measured first without the headset for 6 min followed by the resting, eyes-open qEEG with the VR headset. This may have caused an order effect and should be considered in future research. Secondly, the current data analysis was conducted according to traditional methodologies employed in qEEG comparison studies for treatment efficacy or group comparison. That is, employing the Bonferroni correction as the most conservative measure for protecting against Type 1 errors to minimize the chances of falsely indicating valid significant results or efficacy of the intervention (i.e., efficacy of neurofeedback intervention). However, the current study did not guard equally against Type 2 errors or failure to reject a null hypothesis. Therefore, future replication studies may wish to include such corrections or consistently apply the Bonferroni correction whenever attempting to claim a significant treatment effect, especially for VR-based interventions.

Additional analysis of a possible gender effect was significant in the current study, indicating that females showed significant delta activation in the right and central hemisphere, but males did not show any significant differences in any of the location-specific qEEG bandwidth power values across both conditions. Additionally, unsolicited anecdotal statements made by participants after removing the VR headset may be of qualitative interest for future studies to measure. For example, some participants noted feeling calmer and more relaxed while wearing the headset and, on the contrary, others indicated feeling more tense in the VR headset condition. Some participants expressed their familiarity with using a VR headset, while others indicated it was their first time wearing a VR headset. It is also noteworthy to mention that anecdotal evidence suggested that far more males were more familiar and experienced with the VR headset than females, which could have contributed to the gender effect. Therefore, future studies may wish to systematically investigate participants' subjective experience while wearing the VR headset and account for prior VR experience as a potential contributing factor.

In regard to the second objective, we believe this to be one of the first studies to have systematically

designed a standardized approach for recording qEEG for group research designs involving a VR headset. Specifically, we developed a framework for assuring consistent placement of the VR headset bands on top of the Electro-Cap sensors at Fz, Cz, Pz, T7, P7,01, T8, P7, and 02 (see Figure 1) and the actual headset resting on Fp1 and Fp2 (see Figure 1). The acquisition of valid and reliable qEEG recordings was established by measuring and assuring the impedance levels were below 10 Ω for each electrode sensor, both before and after placing the VR headset on participants. Also, rather than having participants stare at a blank wall with a dot through a grainy passthrough (see-through) option provided by the VR headset, the present study utilized a still picture of the same dot and wall inside the VR headset to control as much as possible for differences in visual stimuli across the two conditions. Finally, the qEEG data were processed using an automated artifact rejection procedure (S.A.R.A) to eliminate any potential experimenter bias or error that hand-artifacting methods could present. Therefore, we believe the current study will help provide an essential framework for future researchers wishing to replicate and further validate the present research findings as well as acquire real-time qEEG data to determine the efficacy of VR-based interventions.

Although the results of this study provided preliminary evidence suggesting that it is not necessary to obtain a separate resting qEEG baseline measure while wearing the VR headset, future replication studies are required that address the limitations of the current study and continue to systematically adapt and adjust methodological qEEG acquisition procedures for real-time qEEG recordings for VR-based interventions as the VR technology advances and changes. For example, the latest version of the Meta Quest VR headset (Meta Quest Pro) released in October 2022 has the battery pack situated on the only securing headset strap located and resting on the back of the head.

Author Disclosure

Authors have no grants, financial interests, or conflicts to disclose.

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A Scoping Review on Integration of Electroencephalogram Neurofeedback Training for Alcohol Use Disorder: Clinical and Neurocognitive Outcomes

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Abstract

Background. The conventional treatment for alcohol use disorder (AUD) consists of dual treatment encompassing pharmacotherapy and psychotherapy. Nonetheless, the impact of these treatments on clinical and neurocognitive outcomes is only low to medium efficacy. Research studies substantiate the integration of electroencephalogram neurofeedback training (EEG-NFT) as an add-on tool with significant improvements in clinical and neurocognitive outcomes. **Methods**. A scoping review of the existing literature on EEG-NFT and AUD, which are open access, including review papers and empirical studies in the English language, and with human subjects are deemed worthy of the scope of this study. The keywords *electroencephalogram neurofeedback training*, *alcohol use disorder*, *stress*, *neurocognition*, and *relapse* were used. The primary sources of the literature search were Science Direct, Scopus, PubMed, and Google Scholar. A total of 35 articles have been included in the scoping review. Studies from the last 15 years were considered for the same. **Results**. This review revealed that EEG-NFT is a promising tool with significant improvements in stress levels, cognitive deficits, and relapse rates for individuals with AUD when used in integration with conventional treatments. **Conclusion**. Chronic alcohol use affects cognitive functions, escalates relapse rate, and increases stress experienced by the individual. The present study highlights the significance of NFT as a potent add-on treatment modality to improve clinical and cognitive outcomes, thereby facilitating abstinence and reducing relapse rates in individuals with AUD.

Keywords: neurofeedback training; alcohol use disorder; stress; response inhibition; relapse

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Introduction

Alcohol use disorder (AUD) is a serious public health concern, with chronic use resulting in 3.3 million deaths worldwide every year, which as a causal factor exceeds global death rates caused by HIV/AIDS or tuberculosis (Althaus et al., 2021; Dousset et al., 2020). Despite the growing number of research on preventing relapse and reinforcing abstinence, AUD has an astonishingly high relapse rate of approximately 80% within a year postwithdrawal, which is why relapse occurring from the consumption of alcohol after prolonged periods of withdrawal is still of interest for understanding addiction (Dacosta-Sánchez et al., 2021; Dousset et al., 2020).

Chronic alcohol use is associated with a wide range of clinical comorbidities, of which stress has been constantly reviewed in the literature. Adverse experiences such as early social deprivation, isolation and abandonment, and parental use of alcohol exceed an individual's coping capacity, increasing his or her risk for AUD (Sebold et al., 2021). By the same token, long-term use of alcohol also dysregulates the brain's effector system such as the hypothalamic-pituitary-adrenal (HPA) axis, leading to the pathophysiology of AUD (Uscinska et al., 2021). Additionally, stress has long been known to increase the risk of relapse among individuals with AUD (Breese et al., 2011). For instance, evidence shows

differences in stress responsivity in individuals with AUD and without AUD, wherein the former demonstrated alterations in stress pathways that could explain the significant contribution of stress-related mechanisms on relapse (Sinha, 2012).

Likewise, chronic use of alcohol also has profound neurocognitive effects mainly affecting executive functions, episodic memory, and visuospatial capacities related to multiple brain lesions (Bernardin et al., 2014). While the literature strongly establishes that chronic use of alcohol leads to cognitive deficits, there have been efforts to understand the relationship between various parameters of alcohol use and associated cognitive deficits (Dacosta-Sánchez et al., 2021). For example, a study analyzed cognitive profiles of patients according to the pattern of substance use and found that there is a significant association between the age of onset of alcohol use (early age of use; before 25 years) and executive dysfunctions, likewise, the duration of alcohol use (more than 10 years) is related to attentional deficits, and quantity of alcohol use increased impairment in working memory (Madhusudhan et al., 2021). The transition to habit theory by Everitt et al. (2008) states that addiction consists of a series of transitions from voluntary and hedonic-driven drinking habits at first to strongly automatized habitual use of the substance that is characterized by compulsive behavior and loss of control, which explains consumption of alcohol despite the negative consequences or relapse (Czapla et al., 2016).

The classic treatment model for AUD consists of a combination of pharmacotherapy and psychotherapy, where the former addresses the neurotoxic effects of alcohol, and the latter deals with the psychosocial dimensions of the disorder. Nonetheless, the efficacy of this dual treatment providing significant changes in the individual is still low to medium with limited impact on drinking behavior and quality of life (Dousset et al., 2020). Furthermore, alcoholism involves the alteration of brain electrophysiology such that researchers and clinicians are considering the alteration of brain rhythmic activity as a viable mode of treatment option for individuals with AUD (Dalkner et al., 2017; Heilig et al., 2019; Rangaswamy & Porjesz, 2014).

Thus, the main objective of the present paper is to review the merits of neurofeedback training (NFT) as a tool that has been gaining momentum for its efficiency-cum-effectiveness in clinical and research areas (Marzbani et al., 2016). This article highlights the evidence that is in favor of the application of electroencephalogram neurofeedback training (EEG-NFT) as an add-on tool for altering the deficient brain wave patterns of AUD patients with significant improvements in clinical such as reduced stress levels and relapse rates and enhanced neurocognitive abilities to maintain long-term abstinence when used in combination with other forms of treatments.

Methods

The primary aim of the review paper is to present arguments in favor of the application of EEG-NFT neurofeedback as an add-on tool for the treatment of AUD with other adjunct therapies such as psychotherapy and pharmacotherapy. A scoping review of the existing literature on NFT and AUD, which are open access, including review papers and empirical studies in the English language, and with human subjects are deemed worthy of the scope of this study. The keywords *electroencephalogram neurofeedback training*, *alcohol use disorder*, *stress*, *neurocognition*, and *relapse* were used to identify relevant publications. The primary sources of the literature search were Science Direct, Scopus, PubMed, and Google Scholar. A total of 35 articles have been included for scoping review. Studies from the last 15 years were considered for the same.

Results and Discussion

EEG Function in AUD

Literature shows that both acute and chronic use of alcohol results in significant brain wave alterations that are observable with quantitative electroencephalogram (qEEG). The qEEG reports in AUD patients mainly describe brain wave alterations that are mainly within the alpha, theta, and beta bands (Sokhadze et al., 2008). For example, a higher theta (4–8 Hz) power has been reported in alcoholics when compared with control subjects indicating a reduction or blocking capability of the individual to encode new information (Mumtaz et al., 2018). The abnormal elevation of theta in the posterior region is also associated with deficient inhibition and excitation (Mohan & Rajeshwaren, 2015). Additionally, a decrement in alpha (8–12 Hz) oscillatory powers especially in the occipital regions of AUD patients is an indication of impaired memory and attention, in addition to dysregulated stress response (Mumtaz et al., 2018).

In like manner, elevated beta (12–30 Hz) band power is observed in the whole brain of AUD patients and such abnormal elevations at the posterior region can predict relapse in alcoholics (López-Caneda et al., 2017). Hence, chronic use of alcohol leads to

increased activity of the autonomous nervous system, resulting in increased physical and psychological stress and anxiety marked by decreased alpha and increased high beta respectively, which are clinically important as they are related to the severity and relapse of AUD (Ko & Park, 2018). These altered brain wave patterns and associated impairments compromise the treatment outcome in favor of individuals by hampering good decision-making, and further accelerating cognitive and behavioral dysfunctions heightening the propensity to relapse in the face of drug and drug-related stimuli (Le Berre et al., 2017).

EEG Neurofeedback Training in AUD

Yonah (2023) mentions the efficient-cum-effective use of NFT for various psychological and neuropsychiatric disorders. Neurofeedback is a noninvasive, self-regulation technique that utilizes a brain-computer interface (BCI) to facilitate neural plasticity and neural efficiency (Cannon, 2015). It provides feedback to the individual on the localized brainwave activity with a specific frequency range (Cannon, 2015). The feedback here is similar to the feedback provided in other modes of treatment, which empowers the person to make necessary changes in their behavior that often results in therapeutic gains (Russo et al., 2023). Neurofeedback of the operant conditioning type consists of EEG activity to hit the threshold fixed before the feedback is delivered (Cannon, 2015; Yonah, 2023).

The major advantage of neurofeedback is that it safely harnesses internal brain processes, facilitates voluntary control of brain oscillations, and enhances long-term induction of brain plasticity (Ros et al., 2014). Also, EEG-NFT is purely endogenous in nature and the reorganization of oscillations is facilitated by the system itself based on the conscious feedback signals unlike pharmacotherapy (Dousset et al., 2020; Ros et al., 2014). Thus, repeated training of the specific brain oscillations further strengthens the synaptic connections (“neurons that fire together, wire together”), encouraging them to produce the same pattern in an open environment. It means that NFT enables implicit volitional control of covert brain activity inducing enhanced attention and motor cortical activation yielding coherent and stimulus-specific brain activity than an unregulated mental practice (Ros et al., 2014).

The two neurofeedback protocols that are commonly used in the treatment of AUD are the Peniston-Kulkosky (alpha/theta protocol) and Scott-Kaiser modification (beta/sensorimotor rhythm [SMR]) protocol. Literature shows that neurofeedback protocols are designed to reduce anxiety and stress levels through the alpha-theta protocol, and impulsivity, through the beta-SMR protocol, with significant results in maintaining abstinence (Russo et al., 2023). Study shows that the application of the Peniston-Kulkosky protocol induced a profound state of relaxation for the participants with AUD (Sokhadze et al., 2008). It was seen to amplify the effect of psychotherapy by enhancing self-efficacy and personal insight, and by inducing a sense of control among patients diagnosed with AUD (Dalkner et al., 2017).

Hence, training alcohol-dependent individuals to increase their alpha and theta rhythms is associated with a decrease in alcohol intake and relapse (Mohan & Rajeshwaren, 2015). Furthermore, unlocking the direct control of the brain also induces changes at the neurochemical level by increasing beta-endorphins (a stress index), which is related to the stress of abstinence (Ross, 2013). Research demonstrates that the baseline alpha brainwaves increased substantially after the first five sessions of the Peniston-Kulkosky training, which called for the need for multiple sessions of NFT to elicit lasting changes in the EEG metrics of the individual. Accordingly, 15 sessions of the Peniston-Kulkosky training showed significant positive changes in the overall quality of life and long-term abstinence among individuals with AUD (Ross, 2013).

Together with the Peniston-Kulkosky protocol, the Scott-Kaiser modification is found to show substantial improvements in attention, reduction in hyperactivity, and impulsivity in facilitating thalamic inhibitory mechanisms, thus helping individuals to override automatic behaviors facilitated by the drug-wanting system such as ventral striatum, and further strengthening the drug-denying system governed by the prefrontal cortex (Rangaswamy & Porjesz, 2014). Over the course of learning via neurofeedback, the individual gains control over the physiological process which also used to be in automatic action schemata mode (Ros et al., 2014). Thus, participants report improved confidence and reduced emotional stress, feelings of inadequacy, and insecurity, which are potential dispositional factors that are used to increase the risk of relapse among AUD patients (Dalkner et al., 2017).

Correspondingly, alcoholism is also characterized by a lack of control over drinking patterns despite negative consequences; such abnormal behavioral patterns may be attributed to structural and functional abnormalities of the prefrontal cortex responsible for decision-making (Fein & Cardenas, 2015).

Accumulation of evidence shows that EEG-NFT enhances cognitive functions by facilitating brain plasticity through structural and functional changes over the course of learning (Loriette et al., 2021). A meta-analysis on neurofeedback affirms that all neurofeedback protocols have shown improved activation of the striatum, which is responsible for reinforcement learning, and increased volume of putamen indicating an ability to integrate learned behaviors and benefit from the training (Emmert et al., 2016). The neural network held by neurofeedback consists of both cortical and subcortical structures in which basal ganglia play an important role, in addition to dopaminergic and glutamatergic synapses that play an essential role in the neurobiology of AUD (Yonah, 2023).

Participants learn to associate the feedback provided during training with the behavior they are producing, initiating direct activation of specific brain regions underlying the behavior (Loriette et al., 2021). EEG-NFT has yielded positive behavioral outcomes such as reduced intensity of adverse symptoms and improved specific cognitive functions. For example, a case study on the efficacy of neurofeedback on AUD patients showed that as the sessions progressed, the patient showed improvements in working memory index and executive functions, in addition to decreased intake of alcohol and improved quality of life with improved assertiveness and self-confidence (Ghosh et al., 2014).

Integration of EEG Neurofeedback

A large number of data have shown EEG alterations in addition to impaired quality of life among AUD patients. The low to moderate efficacy of conventional treatments with significantly high relapse rates call for interventions that address the neuropsychophysiological conditions of the disorder from the point of view of Rostami and Dehghani-Arani (2015). Similarly, Dousset et al. (2020) emphasize the importance of a novel treatment modality that is multimodal in nature, suggesting that the typical psychological and pharmacological treatments need to be complemented with neuromodulation techniques considering the viability of neural networks to reduce symptoms.

Dalkner et al. (2017) show that alpha/theta training has shown beneficial effects on AUD pathology such as decreased stress-related craving, fear of relapse, and depressive symptoms, in addition to changes in clinical personality traits and that the beta-SMR protocol has improved the cognitive deficits experienced by individuals, which can be further maintained with the help of adequate psychological interventions. The improvements in AUD pathology facilitate a neurocognitive shift that enhances an individual's capability to deal with stressors in a healthy way (Feldstein Ewing, Filbey, et al., 2011).

As stress levels decrease, individuals learn better coping mechanisms with the help of treatments such as psychotherapy governed by the hippocampus, extended amygdala, reduced activation of the HPA axis, and subsequently lower cortisol levels. Psychotherapies such as motivational interviewing (MI) have been successfully used among individuals with AUD, as motivation and change talk (individuals using languages of change from the current state) indicate a neurocognitive shift and inhibition of impulsive responses to drug related-cues (Feldstein Ewing, Filbey, et al., 2011; Ewing, Yezhuvath, et al., 2014).

Such change in perception of alcohol use indicates activation of the prefrontal cortex over the motivational and reward circuitry of the brain which can be further amplified with the help of neurofeedback protocols such as beta-SMR that facilitates top-down processing that dominates over sensory information such as craving responses of the individual (Feldstein Ewing & Chung, 2013). The importance of interpersonal context in group psychotherapy reduces hopelessness and stress levels which in turn enhances the efficacy of alpha-theta protocol on stress reduction and improved relaxation with better coping in the face of stress (Feldstein Ewing & Chung, 2013). Furthermore, NFT involves gaining control over physiological processes which is likely to enhance self-confidence and reduce emotional stress, feelings of inadequacy, insecurity, and fear among patients (Dalkner et al., 2017).

Conclusion

An integrative and multimodal approach is needed, for AUD has been proven difficult to treat with psychological or pharmacological interventions alone. Nonetheless, it would be unfair to believe that alteration of brain waves alone would be sufficient, considering the psychosocial context of the disorder. Therefore, EEG-NFT can be considered a promising add-on tool for the treatment of AUD in addition to medication and psychotherapy. EEG-NFT would facilitate a symbiotic interplay of biopsychosocial aspects of the disorder when used in conjunction with other treatment modalities.

To conclude, given the complexity of substance use disorder in general and AUD in particular, any one form of treatment will seldom work for the individual considering the multiple dynamics associated with AUD. Although evidence strongly states that EEG-NFT is efficacious in reducing the symptomatology associated with AUD, there is still the need for additional counseling/psychotherapy to address the psychosocial factors that can impact an individual's setbacks in the journey of recovery. The focus of the study is to understand the effective utility of EEG-NFT as an add-on treatment tool for addressing the neurophysiological factors that are found in individuals with AUD. EEG-NFT acts as an additional course of action to support clients' long-term recovery addressing clinical and neurocognitive outcomes related to AUD. The inclusion of EEG-NFT could prove to be beneficial and may align with the biopsychosocial model of addiction.

Limitations and Future Scope

This article attempts to explain the application of NFT that mostly involves electroencephalogram neurofeedback, as it is widely preferred by researchers for the treatment of AUD due to its affordable, noninvasive, and high temporal resolution (= 1 ms), and convenience compared to other modes (Mumtaz et al., 2018). The main objective of this scoping review is to focus on the merits of EEG-NFT. Nonetheless, NFT has widespread other interfaces such as functional magnetic resonance imaging neurofeedback (fMRI-NF), which is also used among AUD and relies on real-time processes, localizing brain signals to specific regions of the brain in response to specific stimuli and has not been reviewed intensively due to the limited scope of the study (Dousset et al., 2020).

Future research should focus on the functional specificity of EEG-NFT by delving into the trainability (desired changes in the trained brain wave oscillations), independence (lack of changes in untrained bands), and interpretability (differences in the treatment group only; Gadea et al., 2020). Research shows that a substantial population of participants (almost one-third of the nonresponders) does not benefit from EEG-NFT as the success of EEG-NFT is heavily dependent on the participant's ability to actively control their brain activity based on the given feedback (Loriette et al., 2021). Having clarity on trainability, independence, and interpretability will help clinicians understand the nonresponders and design protocols according to the individual characteristic needs that might help reduce the percentage of nonresponders (Yonah, 2023).

It is equally important to check the training effect of neurofeedback beyond laboratory conditions through systematic evaluations such as follow-ups similar to psychotherapy, to ensure that the improvements produced are not state-dependent (Gadea et al., 2020). Prospective studies with a larger sample size are also recommended to further generalize the transition effect produced by EEG-NFT (Dalkner et al., 2017; Loriette et al., 2021). Most importantly, the scope of EEG-NFT as a preventive tool can also be explored as the majority of the evidence is based on clinical samples compared to early-stage problem drinkers, who are far more numerous than dependent drinkers (Subramanian et al., 2021). Last but not least, a meta-analysis on the efficacy of integrated NFT adjunct to psychotherapy and/or pharmacotherapy will help clinicians to understand individual differences in the treatment outcome and also the effectiveness of a multimodal approach for the treatment of AUD.

Author Disclosure

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Effectiveness of Low Frequency Noninvasive Brain Stimulation Therapy for Improving Neuropsychological and Neurophysiological Functions: A Systematic Review

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Abstract

Introduction. Cranial electrotherapy stimulation (CES) is a technique used to address various mental disorders symptoms. However, it is recently concluded that the quality of clinical trials involving CES is not standardized and lacks sufficient evidence to support its use for improving mental health. The purpose of this study was to undertake a systematic examination of evidence of CES in improving mental health. **Method**. From inception to April 2022, systematic review was conducted using electronic databases MEDLINE (accessed via PubMed), CENTRAL (Cochrane Library Central Register of Controlled Trials), and Web of Science to retrieve relevant studies. Methodology of all the identified randomized controlled trials (RCTs) was assessed using an 11-point PEDro scale by two independent reviewers. **Results**. Sixteen RCTs were identified to be relevant and their characteristics were evaluated. Thirteen studies concluded CES has favorable effect on variety of mental disorders, particularly on anxiety and depressed symptoms in varied groups. **Conclusions**. While these positive effects were observed, limitations included insufficient detail about existing treatments, lack of using standardized objective outcome measures for quantifying mental health dysfunction, and uneven representation of CES limiting the generalizability and making it difficult to carry out the pooled quantification and meta-analysis. Despite its shortcomings, literature suggests that CES warrants more research.

Keywords: cranial electrotherapy stimulation (CES); mental disorders; mental health; psychological health; cognitive health

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Mental disorders are an all-time high as a more important topic in the world, particularly in most of the developed countries (Murray et al., 2012). Common mental health disorders (CMD) are mainly comprised of depressive disorders and anxiety disorders (World Health Organization, 2017). Following depression and anxiety, mood disorders have been demonstrated as a highly prevalent disorder among the general population by numerous large epidemiologic surveys in developed countries (Kessler, Berglund, et al., 2005). The high prevalence estimates of these mental disorders are associated with a heavy burden on the health of the community and disruption to their daily life (Kessler, Chiu, et al., 2005), and are the leading cause of disability worldwide (Vos et al., 2012). In addition, it has been found that these mental disorders are associated with cognitive dysfunctions, and there is an invariable and mutual association between cognitive dysfunction and mental disorders such as depression, anxiety (Castaneda et al., 2008), and mood disorders (Wolf et al., 2010), affecting each other in a bidirectional manner.

The trend is such that, even among the most serious disorders, people are left untreated. In industrialized countries, 36–50% of serious cases remain untreated, whereas in developing countries the

situation is even worse, with 76–86% are left untreated. It has been proposed that treatment services need to be expanded to reduce the prevalence and impact of mental disorders (Wang et al., 2007), as they seem to impact significantly both the patient's functioning and quality of life as well as increase the risk of recurrence of CMD (Perini et al., 2019). Despite this, relatively few interventions for the condition have been developed in recent years. Although there are many pharmacological interventions for improving mental health, they are quite exorbitant or present with considerable side effects. Up to half of such population do not respond to first-line antidepressant treatment and one-third do not respond to two or more treatments (Trivedi et al., 2006), making it prevalent and therefore resulting in added patient suffering, disability, and suicide risk (Crown et al., 2002). These relatively poorer clinical outcomes and limitations with pharmacotherapy heighten the need to optimize and develop brain modulation treatments, which have the potential to modulate brain activity and which may constitute safe and efficacious treatment options for mentally disturbed individuals in the future. Such established treatments include neuromodulation techniques and ablative neurosurgery. A number of new neuromodulation techniques over the past several years have been investigated with the goal of achieving efficacy of established mental disorder treatments with better neurocognitive safety. Noninvasive brain stimulation (NIBS) is a technique to achieve neuromodulation without surgical treatment through safe local stimulation of specific brain areas using magnetism or electricity (In et al., 2017). Reports in animals and humans have described changes in certain neurotransmitters, neurochemicals, and brain activity on electroencephalography as a mechanism of action of these NIBS techniques (Antal & Paulus, 2008; Kirsch, 2002; Zaghi et al., 2010). Repetitive transcranial magnetic stimulation (rTMS), transcranial direct current stimulation (tDCS), and cranial electrotherapy stimulation (CES) are used clinically for the improvement of brain functioning and mental health (Fregni & Pascual-Leone, 2007; Kirsch & Nichols, 2013).

Of these, CES has been approved by the US Food and Drug Administration (FDA) as a noninvasive, prescriptive medical intervention for treating insomnia, depression, anxiety, stress, (Rosa et al., 2011, Sevilla-Llewellyn-Jones et al., 2018) and mood-related symptoms as well (Kirsch, 2002). While on the one hand the relatively stronger current modalities such as electroconvulsive therapy (ECT) that are being used as adjuncts to pharmacological and psychotherapeutic treatment plans have both cardiovascular complications and cognitive side effects (Andrade et al., 2016) and TMS adverse effects including headaches (O'Connell et al., 2018) and seizures (Rossi et al., t2009), CES on the other hand tends to be a more efficient, user-friendly, cost-effective, and easily tolerable noninvasive type of device that can be safely used by patients at home. It is being used as an adjunct to medication or psychotherapy or as a stand-alone treatment (George, 2019). CES now has a foundation of more than 50 years of research and clinical use in the USA which proves its safety and effectiveness (Price et al., 2021).

Rationale for Systematic Review

An issue recently concluded by Cochrane review is that there are no high-quality clinical trials comparing CES with sham-CES in people with mental disorders such as depression and that there is insufficient evidence to support the use of CES in the treatment of depression (Kavirajan et al., 2014; Price et al., 2021; Shekelle et al., 2018) and low strength evidence to support the use of CES in the treatment of anxiety (Shekelle et al., 2018). However, numerous systematic reviews and meta-analyses have appeared over the past two decades. Klawansky and colleagues focused on anxiety and other conditions but not on other mental disorders (Klawansky et al., 1995). Kirsch and Gilula (2007) investigated CES in depression, but their meta-analysis had several flaws: they did not specify the search strategy or specific study eligibility criteria; their summary effect size was based only on active CES treatment and did not compare CES to sham; they combined data from open uncontrolled trials and blinded randomized control trials (RCTs), which likely overestimated effect sizes; and they included trials with a variety of primary diagnoses, which limits generalizability (Kirsch & Gilula, 2007). A study by Kavirajan and colleagues, led in 1974 and later invalidated in a Cochrane review, possibly had inefficient CES equipment (Kavirajan et al., 2014). Shekelle et al. (2018) focused on anxiety, depression, insomnia, and pain but did not cover the other mental health aspects. Their study lacked explicit study inclusion, and for a few other studies the data was insufficient to determine an effect size, preventing a quantitative assessment of publication bias. As a result, the likelihood of its occurrence remains hypothetical.

Small samples, symptom and demographic variability, overlap of diseases, large variety of marketed CES devices, varied treatment regimens, and the fact that published trials do not usually offer

detailed stimulation settings make it challenging to interpret these findings. Given the gaps in the current literature, the goal of this study was to conduct a systematic assessment of the evidence and provide a clear picture of the usefulness of CES in improving mental health. Furthermore, to our knowledge, this is the first time that the body of evidence in favor of CES (RCTs) for the treatment of the majority of mental diseases has been comprehensively investigated. We believe that the work's uniqueness adds to our understanding of various mental health treatment techniques.

Methods

Search Strategy

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards were followed for this review, and it is registered in Prospero with the registration number CRD42021273171. To find papers on the impact of CES on mental health, we devised the following search strategy. A systematic search was performed on the electronic databases MEDLINE (accessed via PubMed), CENTRAL (Cochrane Library Central Register of Controlled Trials), and Web of Science starting from the earliest records available. Random search items used were a combination of keywords (i.e., cranial electrotherapy stimulation, cranial electrical stimulation, cranial electrostimulation, CES, mental health, psychological health, cognitive health, depression, anxiety, stress, mood, brain drive neurotrophic factor, and BDNF) in various combinations. To provide more concentrated results and to widen or narrow the search, the keywords were joined with Boolean operators 'OR' and 'AND' from inception to April 2022. Figure 1 shows a diagram of the PRISMA flowchart.

Eligibility Criteria

The inclusion criteria involved RCTs, the CMD pathology, or any other mental health disorder diagnosed in the subjects. This review included RCTs investigating the effect of CES with one or more treatment sessions on mental disorders assessed by either qualitative measures (e.g., clinical observation, questionnaires, self-report), quantitative measures (e.g., neuropsychological battery test [NBT], electroencephalography [EEG], event-related potentials [ERP, P300]), or any biomarkers such as cortisol, adrenocorticotropic hormone [ACTH], brain-derived neurotrophic factor [BDNF], nerve growth factor [NGF] or any other peripheral biomarkers supported by convincing and highly suggestive evidence across major mental disorders. Studies examining the effect of CES on other conditions such as sleep, pain, incontinence, and fibromyalgia were excluded. Furthermore, studies on healthy subjects or animal models using other forms of neuromodulation, such as ECT and TMS, or other forms of invasive spinal stimulation, were excluded. There was no limit on the number of samples taken. This review did not include studies conducted and reported in languages other than English.

Selection of Studies

To retrieve records to be reviewed, 206 duplicates were deleted from the total records (392) identified. Two reviewers (ZK and AS) independently read the titles and abstracts of 58 records during the screening procedure. Based on the predesigned eligibility criteria, 16 papers (RCTs) were deemed to be relevant and were examined for study features by two independent reviewers (ZK and AS) who assessed the quality of each of the 16 RCTs' methodology (Figure 1). Conflict at any stage during the process was resolved by consensus with the third reviewer (AP).

Data Extraction

Two of the authors (ZK and AS) extracted data on trial characteristics (e.g., author, year of trial conduction, design, duration), the participants (e.g., age, information on other medical comorbidities), and the intervention (e.g., device used, duration, dosimetry, safety, follow-up), and their results are summarized in Table 2. If any of the reported data was ambiguous, then it was resolved in consultation with the third reviewer (AP).

Measurement of the Treatment Effect

Effect size for the predecided outcome measures (eligibility criteria) was calculated for the RCT reporting point measures and variability using Cohen's *d* (Barclay & Barclay, 2014), two-tailed test (Padjen et al., 1995; Wu et al., 2020), and nQuery power analysis software (Rose et al., 2009).

Figure 1. *PRISMA Flowchart Showing Identification and Selection of Trials for the Systematic Review.*

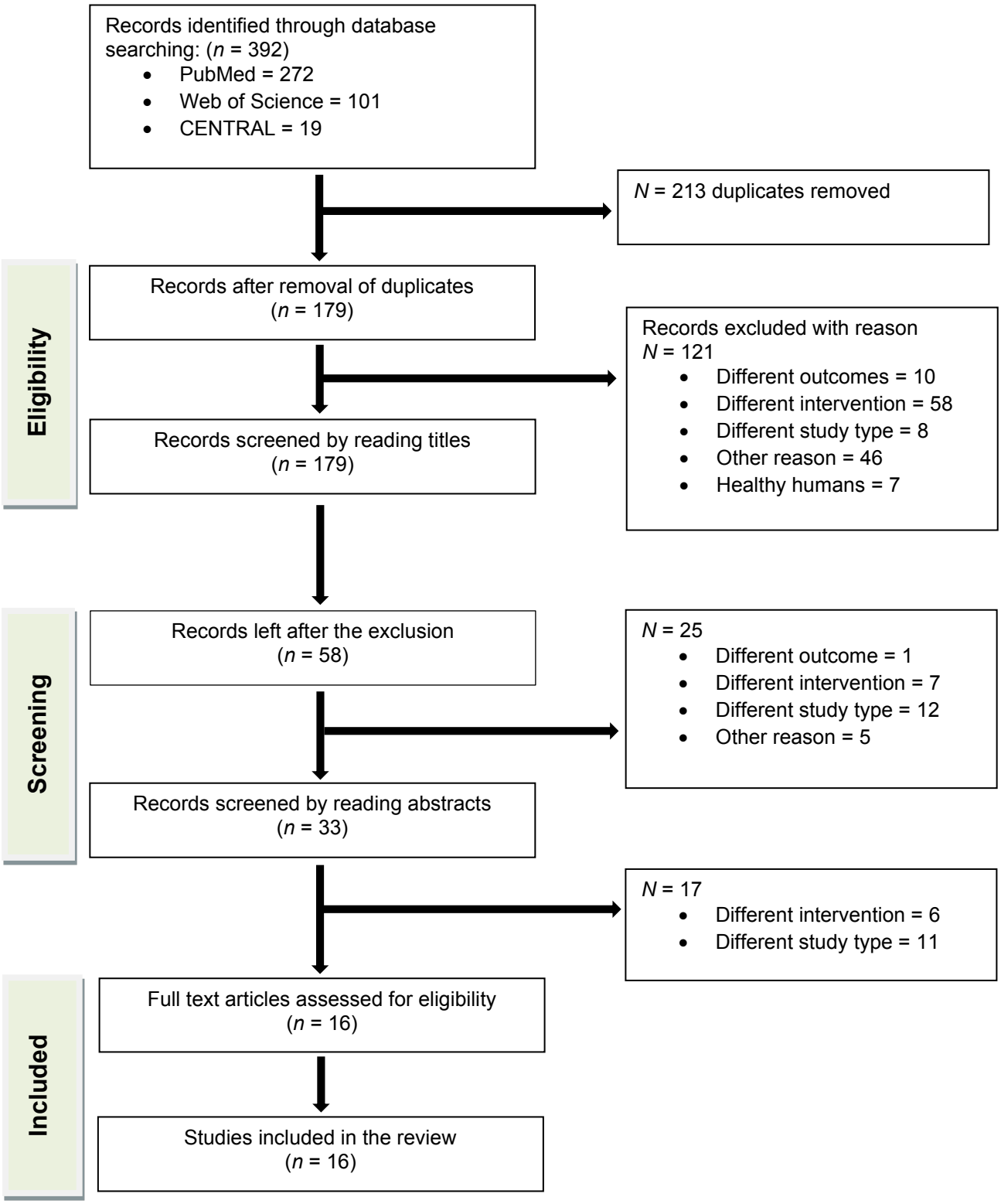

Table 1

Quality Scoring of Randomized Controlled Trials (RCTs) Including Pilot RCTs (n = 16).

Study	Eligibility Criteria	Random Allocation	Concealed Allocation	Group Similarity at Baseline	Blinding of Subjects	Blinding of Therapist	Blinding of Assessor	Dropouts < 15%	Intention to Treat Analysis	Between-Group Differences Reported	Point Estimate and Variability Reported	Total Score	Quality
Barclay & Barclay, 2014	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	Yes	Yes	8	Excellent
Kang et al., 2020	Yes	Yes	No	Yes	No	No	No	Yes	No	Yes	No	5	Good
Lee et al., 2013	Yes	Yes	No	Yes	No	No	No	Yes	No	Yes	No	5	Good
Lyon et al., 2010	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	Yes	No	7	Good
McClure et al., 2015	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	9	Excellent
Michoulon et al., 2015	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	9	Excellent
Padjen et al., 1995	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes	No	8	Excellent
Roh & So, 2017	Yes	Yes	No	Yes	No	No	No	Yes	No	Yes	No	5	Good
Rose et al., 2009	Yes	Yes	No	No	Yes	Yes	No	Yes	No	Yes	No	6	Good
Scherder et al., 2003	Yes	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes	6	Good
Scherder et al., 2006	Yes	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes	6	Good
Schmitt et al., 1986	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	Yes	No	7	Good
Smith et al., 1994	Yes	Yes	No	No	Yes	Yes	No	Yes	No	No	No	5	Good
Southworth et al., 1999	Yes	Yes	No	No	Yes	Yes	No	Yes	No	No	No	5	Good
Winick, 1999	Yes	Yes	No	No	Yes	Yes	No	Yes	No	Yes	No	6	Good
Wu et al., 2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	9	Excellent

Table 2

Quality Scoring of Randomized Controlled Trials (RCTs) Including Pilot RCTs (n = 16)

Study	Participants; *N*	Design	CES Mode, Safety and Dropouts	Patient Evaluation and Follow-up	Interventions	Duration of Intervention	Area of Application of CES and CES Parameters (current density, frequency) in Experimental/Active CES Group	Outcome	Results
Barclay & Barclay, 2014	*N* = 115; both males and females, 18–65 years old, with anxiety and comorbid depression.	Double-blind, randomized sham-controlled trial.	Alpha-Stim CES device. Safety reported: FDA approved. 6% dropout.	At baseline, week 1, week 3, and week 5. No follow-up.	Two arms: Group 1 – EG (*n* = 60). Group 2 – SCG (*n* = 55).	60-min daily CES treatment for 5 weeks.	CES was placed at both earlobes, with a frequency of 0.5 Hz and a current intensity at 100 μA, a subsensory level.	Anxiety measured using HAM-A. Depression measured using HAM-D17.	Significant reduction in anxiety symptoms. Improved depressive symptoms.
Kang et al., 2020	*N* = 80; both male and female patients undergoing general anesthesia.	Computer generated RCT.	Alpha-Stim CES device. Safety not reported. 11% dropout.	3 times: day before the surgery, pre-operative and on the day of surgery. No follow-up.	Two arms: Group 1 – CG (*n* = 40). Group 2 – EG (*n* = 40).	20-min preoperative CES, 2 sessions, both on the day before and morning of day of surgery.	A clip-type electrode of a microcurrent stimulator was attached to the earlobe, and a microcurrent of less than 200 μA and 0.5 Hz was delivered via the electrode.	Anxiety scores measured using 5-point Likert scale.	Reduced both preoperative anxiety levels.
Lee et al., 2013	*N* = 50; female patients undergoing thyroidectomy.	Prospective RCT.	Alpha-Stim CES device. Safety not reported. 0 to 1% dropout.	Before and after the surgery. No follow-up.	Group 1 – CG (*n* = 25). Group 2 – EG (*n* = 25).	20-min CES, 2 sessions, between 20:00–22:00 on day before surgery, and between 07:00–09:00 on day of surgery.	All treatments were given via electrodes clipped to the patients' ear lobes. A CES was preset to provide microcurrents of 100 μA intensity and frequency of 0.5 Hz.	Anxiety scores measured using a 5-point Likert scale. Stress level measured using ACTH and cortisol.	Reduced level of preoperative anxiety. No effects on stress hormone responses.

Table 2

Quality Scoring of Randomized Controlled Trials (RCTs) Including Pilot RCTs (n = 16)

Study	Participants; *N*	Design	CES Mode, Safety and Dropouts	Patient Evaluation and Follow-up	Interventions	Duration of Intervention	Area of Application of CES and CES Parameters (current density, frequency) in Experimental/Active CES Group	Outcome	Results
Lyon et al., 2010.	*N* = 36; women with stage I-IIIA breast cancer scheduled to receive chemotherapy.	Prospective, three-group, randomized, double-blinded, longitudinal *pilot* feasibility study	Alpha-Stim CES device. Safety reported: FDA approved. 0 to 1% dropout.	At baseline, week 3 and week 6. After completing the protocol, participants completed a follow-up interview.	3 groups: Group 1 – EG. Group 2 – SCG. Group 3 – Usual comparison group.	For participants receiving chemotherapy every 3 weeks (total CES duration use of 8 weeks, daily for 60 min) and for every 2 weeks (total CES duration use of 6 weeks, daily for 60 min).	CES delivers the electrical stimulation via electrodes attached to the earlobes, with a stimulus intensity of less than 1.0 μA at 100 Hz frequency from a 9-volt battery source. CES in this study were set at a subsensory intensity.	Depression was measured using HADS.	Decreased depressive symptoms.
McClure et al., 2015	*N* = 16; male and female outpatients aged 23–71 years diagnosed with bipolar II disorder.	*Pilot* double-blind, sham-controlled study	Alpha-Stim CES device. Safety reported: FDA approved. 0 to 1% dropout.	At baseline, weeks 1, 2, 4, and 12. Follow-up of participants at weeks 4 and 12.	2 Groups: Group1 – EG (*n* = 7). Group 2 – SCG (*n* = 9).	20-min CES treatments, 5 days per week for 2 weeks.	The CES treatment was delivered by two electrodes covered with damp sponges and placed over the temples bilaterally with 2 μA of alternating current, with a frequency ranging from 5 Hz to 15,000 Hz.	Cognitive functions measured by CFQ, 3MS, and AMI. Depression measured by BDI, HAM-D-17, and YMRS, at baseline, weeks 2, 4, and 12. Mood measured by PANAS subscale.	Improved cognitive functioning was found on CFQ. Decreased symptoms of bipolar depression. No significant changes on PANAS score.

Table 2

Quality Scoring of Randomized Controlled Trials (RCTs) Including Pilot RCTs (n = 16)

Study	Participants; *N*	Design	CES Mode, Safety and Dropouts	Patient Evaluation and Follow-up	Interventions	Duration of Intervention	Area of Application of CES and CES Parameters (current density, frequency) in Experimental/Active CES Group	Outcome	Results
Mischoulon et al., 2015	*N* = 30; adults of both genders, with MDD and inadequate response to standard antidepressants.	Double-blind sham-controlled *pilot* study.	FW-100 Fisher-Wallace device. Safety reported: FDA approved. 6.6% dropout.	At baseline, weeks 1, 2, and 3. No follow-up.	2 Groups: Group 1 – EG (*n* = 17). Group 2 – SCG (*n* = 13).	20-min CES treatments, 5 days per week for 3 weeks.	The headset of CES (15/500/15,000 Hz, symmetrical rectangular biphasic current of 1–4 μA and 40 V) was placed on the scalp (one current applicator on each side), over the two dorsolateral prefrontal cortex areas.	Depression measured using HAM-D-17.	Improved depressive symptoms.
Padjen et al., 1995	*N* = 64; alcohol-dependent males (25 and 60 years, younger alcoholics with antisocial personalities and 60 above older alcoholics having too frequent cognitive impairment).	*Pilot* double-blind randomization sham-controlled study.	N-S, Inc. C stimulator. Safety not reported. 7.4% dropout.	Baseline, weeks 1, 2, 3, and 4. No follow-up.	2 Groups: Group 1 – EG (*n* = 28). Group 2 – SCG (*n* = 34).	30-min CES treatment, between 5:00 and 8:00 p.m., for 5 days per week for 4 weeks.	CES was administered by placing 4 electrodes; 2 at frontal and 2 at each mastoid with a current intensity of less than 100 μA and frequency of 100 Hz at 50% duty cycle.	Depression measured using Hamilton Depression Scale, Montgomery Asberg Scale, and SCL-90-R39. Anxiety measured by Hamilton Anxiety Scale and the SCL-90-R39.	Significant reduction in depressive symptoms. Significant improvement in anxiety symptoms.
Roh & So, 2017	*N* = 50; healthy postmenopausal women.	Randomized sham-controlled trial study.	Alpha-Stim CES device. Safety reported: FDA approved. 0 to 1% dropout.	Baseline and after 8 weeks. No follow-up.	2 Groups: Group 1 – SCG (*n* = 25). Group 2 – EG (*n* = 25).	20-min CES treatments, 3 times per week for 8 weeks.	Clip-shaped electrodes were attached to both earlobes of patients with a current of 100 μA and frequency of 0.5 Hz.	Cognition measured by BDNF and NGF levels. Stress measured by ACTH and cortisol. Mood measured by POMS.	No changes in BDNF and NGF or stress levels were found. Significant reduction in Tension-Anxiety and Depression-Dejection scores on the POMS; however, no changes were seen on other mood measures.

Table 2

Quality Scoring of Randomized Controlled Trials (RCTs) Including Pilot RCTs (n = 16)

Study	Participants; *N*	Design	CES Mode, Safety and Dropouts	Patient Evaluation and Follow-up	Interventions	Duration of Intervention	Area of Application of CES and CES Parameters (current density, frequency) in Experimental/Active CES Group	Outcome	Results
Rose et al., 2009	*N* = 38; AD patients of both genders, age 65 years or older.	Randomized, double-blind, controlled *pilot* study.	Alpha-Stim CES device. Safety not reported. 0 to 1% dropout.	Baseline, weeks 2 and 4. No follow-up.	2 Groups: Group 1 – EG (*n* =19). Group 2 – SCG (*n* =19).	60-min CES intervention each day for 4 weeks.	A single cable attaches the CES device to two ear clips worn by the participant. The device was preset at an intensity level of electrical stimulation 100 μA; timer was preset at 60 min and the pulse rate at 0.05 pps.	Depressive symptoms measured by GDS.	Reduced depressive symptoms.
Scherder et al., 2003	*N* = 16; AD patients of both genders, with clinical symptoms of dementia present for at least 6 months.	RCT	Alpha-Stim CES device. Safety not reported. 0 to 1% dropout.	Before and after 6 weeks of intervention. No follow-up.	2 Groups: Group 1 – EG (*n* = 8). Group 2 – SCG (*n* = 8).	30-min CES stimulation each day, 5 days per week for 6 weeks.	CES applied involved the bipolar asymmetric rectangular waves, with an intensity between 10 and 600 μA and frequency of 0.5 Hz. The electrodes were clipped to the earlobes.	Cognition measured by neuropsychological tests including digit span, visual memory, face and picture recognition, and word fluency test. Stress level measured using salivary cortisol level.	No beneficial effects on cognitive functions. Increase instead of a decrease in the level of cortisol.
Scherder et al., 2006	*N* = 21; patients of AD of both genders with mean age of 84 years.	RCT	Alpha-Stim CES device. Safety not reported. 0 to 1% dropout.	Before and after 6 weeks of intervention. No follow-up.	2 Groups: Group 1 – EG (*n* = 11). Group 2 – CG (*n* = 10).	30-min CES stimulation administered each day, 5 days per week, for 6 weeks.	CES applied involved the bipolar asymmetric rectangular waves, with an intensity between 10 and 600 μA and frequency of 100 Hz. The electrodes were clipped to the earlobes.	Cognition measured by neuropsychological tests including digit span, visual memory, face and picture recognition, and word fluency test. Mood measured by SCL-90, BDI and the BOP.	No improvement in cognition status. No significant effects for any of mood and behavior scales.

Table 2

Quality Scoring of Randomized Controlled Trials (RCTs) Including Pilot RCTs (n = 16)

Study	Participants; *N*	Design	CES Mode, Safety and Dropouts	Patient Evaluation and Follow-up	Interventions	Duration of Intervention	Area of Application of CES and CES Parameters (current density, frequency) in Experimental/Active CES Group	Outcome	Results
Schmitt et al., 1986	*N* = 40; inpatient alcohol or poly drug users of both genders.	Double-blind, RCT	Alpha-Stim CES device. Safety not reported. 0 to 1% dropout.	Before and after 3 weeks of intervention. No follow-up.	2 Groups: Group 1 – EG (*n* = 30). Group 2 – SCG (*n* = 10).	30-min CES stimulation each day, 5 days per week for 3 weeks.	The current with a series of low intensity, sinusoidal electric impulses at 100 pps on a 20% duty cycle with current variable from 0.0 to 1.0 mA was applied to the head of the patient through two ear stethoscope electrodes placed just behind the earlobe at the maxillo-occipital juncture.	Cognition measured by revised beta examination, subscales of WAIS including digit span, digit symbol, object assembly. Anxiety measured by STAI and IPAT. Mood measured by POMS.	CES improved all WAIS subscales. Significantly greater improvement in all anxiety measures. No significant gains on any POMS measures.
Smith et al., 1994	*N* = 10; CHI patients, both genders with average age of 30 years.	Double-blind, RCT	CES Lab device. Safety not reported. 0 to 1% dropout.	Before and after 3 weeks of intervention. No follow-up.	Group 1 – PCG. Group 2 – SCG. Group 3 – EG.	45-min CES intervention daily, 4 days per week for 3 weeks.	CES intervention used, involves the alternating current, pulsing 100 times per second (100 Hz) on a 20% duty cycle, with a maximum of 1.5 mA output.	Mood measured by POMS.	Significant reduction in all the negative mood factors of mood states.
Southworth, 1999	*N* = 21; non-clinical healthy participants (age 18–60 years).	RCT	LISS Body Stimulator Bipolar Model No. SBL-502-B. Safety reported: FDA approved. 0 to 1% dropout.	Before and after 20–60 min single CES intervention session. No follow-up.	Group 1 – CG. Group 2 – EG.	Single session, 20-min CES intervention.	For giving CES intervention, the electrodes were placed below the temples to deliver the CES. Frequency and intensity not mentioned.	Cognition measured using neuropsychological tests including continuous performances task.	CES intervention improved the attention on continuous performances task.

Table 2

Quality Scoring of Randomized Controlled Trials (RCTs) Including Pilot RCTs (n = 16)

Study	Participants; *N*	Design	CES Mode, Safety and Dropouts	Patient Evaluation and Follow-up	Interventions	Duration of Intervention	Area of Application of CES and CES Parameters (current density, frequency) in Experimental/Active CES Group	Outcome	Results
Winick, 1999	*N* = 33; subjects of both genders who underwent to dental procedures in last 1 month.	RCT	Alpha-Stim CES device. Safety not reported. 0 to 1% dropout.	Before and after the single stimulation. No follow-up.	2 Groups: Group 1 – EG (*n* = 17). Group 2 – Placebo control group (*n* = 16).	Active CES treatment given 5 min before starting dental procedure.	CES applied during routine dental procedure, using micro-current cranial electrotherapy stimulator to deliver the modified byphasic square waveform of varying pulse width at 50% of duty cycle. Clip-shaped electrodes were attached to both earlobes with a current of 200 μA at a frequency of 0.5 Hz.	Anxiety measured by VAS (rated as not anxious at the left and very anxious at the right by 7-point Likert scale).	Improved anxiety symptoms.
Wu et al., 2020	*N* = 53; patients of both the genders, aged 6–17 years with TD and lack of clinical response to 4 weeks of pharmacotherapy.	Randomized, double-blind, sham-controlled trial.	CES American neuro-fitness by LLC. Safety not reported. 17% dropout.	Before and after 4 weeks of intervention. No follow-up.	2 Groups: Group 1 – EG (*n* = 29). Group 2 – SCG (*n* = 24).	30-min CES stimulation therapy, 40 sessions applied for 4 weeks (twice daily on weekdays from Monday to Friday).	The devices used in this study provided the bipolar, asymmetric, rectangular waves. Frequency and intensity not mentioned.	Anxiety measured by HAMA-14.	Significant reduction in the anxiety symptoms.

Note. RCT = randomized controlled trial; % = percent; Hz = hertz; μA = microampere; mA = milliampere; min = minutes; pps = pulses per second; V = volt; MDD = major depressive disorder; AD = Alzheimer's disease; CHI = closed head injuries, TD = tic disorder; CES = cranial electrical stimulation; EG = experimental group; SCG = sham control group; CG = control group; HAMA = Hamilton Rating Scale for Anxiety; HAM-D17 = Hamilton Rating Scale for Depression - 17 items; ACTH = adrenocorticotrophic hormone; HADS = Hospital Anxiety and Depression Scale; BDI = Beck Depression Inventory; YMRS = Young Mania Rating Scale; CFQ = Cognitive Failures Questionnaire; 3MS = Modified Mini-Mental State; AMI = autobiographical memory inventory; SCL-90-R39 = Symptom Check List; BDNF = brain-derived neurotrophic factor; NGF = nerve growth factor; POMS = Profile of Mood States; GDS = Geriatric Depression Scale; BOP = behavior observation scale; WAIS = Wechsler Adult Intelligence Scale; STAI = State Trait Anxiety Index; IPAT = Institute for Personality and Ability Testing Anxiety Scale; VAS = visual analogue scale; HAMA 14 = Hamilton Anxiety Scale - 14 items; FDA = Food and Drug Administration.

Quality Assessment of Included Trials

The authors utilized an 11-point PEDro scale with a set of general core elements for quality assessment of RCTs to assess the methodological quality of all the collected RCT evidence (Verhagen et al., 1998). The two authors separately rated the quality of the trials (ZK and AS). If there was a disagreement on a criterion, each reviewer separately reevaluated it. Unresolved issues were found and discussed in a meeting in order to obtain a final agreement. Ten out of 11 criteria (when giving ratings, factors regarding the specification of eligibility criteria in the paper were not taken into account because all of the included studies had stated their inclusions and exclusions) were used for quality assessment on PEDro and each criterion was rated either *Yes* (score = 1) or *No* (score = 0) to minimize ambiguity in responses. The total score for the methodological quality of each included study was calculated by summing all the responses (maximum score = 10). Studies were then classified as *poor* (score of < 4), *fair* (score of 4–5), *good* (score of 6–8), and *excellent* quality (score of > 8) based on total scores obtained on PEDro scale (Hariohm et al., 2015). In Table 1, the overall score for methodological quality is shown.

Quality of Trials

Quality scoring was performed for all the RCTs included in the review. Average PEDro score for all the trials was approximately 7/10 (good quality). Three trials scored 9/10 (McClure et al., 2015; Mischoulon et al., 2015; Wu et al., 2020), two scored 8/10 (Barclay & Barclay, 2014; Padjen et al., 1995), three scored 7/10 (Lyon et al., 2010; Scherder et al., 2003; Schmitt et al.,1986), three scored 6/10 (Rose et al., 2009; Scherder et al., 2003; Winick, 1999), and five scored 5/10 (Kang et al., 2020; Lee et al., 2013; Roh & So, 2017; Smith et al., 1994; Southworth et al., 1999). All of the studies randomly allocated the subjects into groups, but only one maintained a concealed allotment (Wu et al., 2020). Four of the trials (Lee et al., 2013; Roh & So, 2017; Scherder et al., 2003, Scherder et al., 2006) did not blind either of the subject, the therapist, or the assessor; however, six studies followed the double-blind procedure with blinding the subject and therapist (Lyon et al., 2010; Rose et al., 2009; Schmitt et al., 1986; Smith et al., 1994; Southworth et al., 1999; Winick, 1999). Four studies carried out triple-blinding for the subjects, the therapist as well as the assessor in their carefully conducted trials (McClure et al., 2015; Mischoulon et al., 2015; Padjen et al., 1995; Wu et al., 2020). Five out of 6 RCTs reported very well about the between-group differences postintervention with point estimates and measures of variability (Barclay & Barclay, 2014; McClure et al., 2015; Mischoulon et al., 2015; Scherder et al., 2003, Scherder et al., 2006). On the other hand, except two (Lyon et al., 2010; Mischoulon et al., 2015) no other studies applied intention to treat analysis on dropouts (Table 1).

Results

We devised a search technique that comprised three databases, and we found 392 studies, including 272 in PubMed, 19 in CENTRAL, and 101 in Web of Science. There were 179 articles left after the 213 duplicates were removed. After screening the titles and abstracts, the remaining articles were culled for full texts, and 16 were chosen based on the inclusion criteria. The summarized results of the selected articles are shown in Table 2.

Characteristics of the Studies

The important characteristics of the selected articles are shown in Table 2.

Study Design. Randomized controlled trial (RCTs) including pilot RCTs.

Participants. Fifteen included RCTs consisted of 690 participants with different types of pathologies: 115 subjects with anxiety and comorbid depression in one study (Barclay & Barclay, 2014), 30 patients with depression only (Mischoulon et al., 2015), 28 subjects undergoing general anesthesia (Kang et al., 2020), 25 patients undergoing thyroidectomy (Lee et al., 2013), 36 breast cancer patients (Lyon et al., 2010), 16 bipolar disorder patients (McClure et al., 2015), 124 patients were alcoholics and drug abusers (Padjen et al., 1995; Schmitt et al., 1986), 50 postmenopausal women (Roh & So, 2017), 70 Alzheimer's patients (Rose et al., 2009; Scherder et al., 2003; Scherder et al., 2006), 21 patients of close head injuries (CHI; Smith et al., 1994), 33 dental patients (Winick, 1999), 62 tic disorder patients (Wu et al., 2020), and 21 nonclinical healthy participants (Southworth, 1999). However, a common limitation in all studies was the lack of information on sample size and power calculation, except for four studies (Barclay & Barclay, 2014; Padjen et al., 1995; Rose et al., 2009; Wu et al., 2020). The majority of studies included all age groups (6–88 years old) and both genders, with one study assessing only females (Lee et al., 2013; Lyon et al., 2010; Roh & So, 2017) and another study assessing only males (Padjen et al., 1995).

CES Mode and Safety. All studies investigated the effect of cranial electrical stimulation using different commercially available devices, like various derivative models of Alpha-Stim (Barclay & Barclay, 2014; Kang et al., 2020; Lee et al., 2013; Lyon et al., 2010; McClure et al., 2015; Roh & So, 2017; Rose et al., 2009; Scherder et al., 2003; Scherder et al., 2006; Schmitt et al., 1986; Winick, 1999), FW-100 Fisher-Wallace device (Mischoulon et al., 2015), N-S, Inc. C stimulator (Padjen et al., 1995), CES Lab device (Smith et al., 1994), CES American by Neuro-Fitness by LLC (Wu et al., 2020), and LISS Body Stimulator Bipolar Model No. SBL-502-B (Southworth, 1999). Some of these studies reported on safety of the CES intervention (Kang et al., 2020; Lee et al., 2013; Lyon et al., 2010; McClure et al., 2015; Mischoulon et al., 2015; Wu et al., 2020; Winick, 1999). However, few of these studies have reported if the device was FDA approved or not (Barclay & Barclay, 2014; Lyon et al., 2010; McClure et al., 2015; Mischoulon et al., 2015; Roh & So, 2017; Southworth, 1999).

Duration. Duration of CES treatment ranged from a single session to 8 weeks, with each session varied from 20 min to 1 hr. One study involved a single 20-min CES session (Southworth, 1999). Other studies involved treatment sessions as: 1 hr daily for 5 weeks (Barclay & Barclay, 2014); 20 min on day before surgery and 20 min on morning of surgery (Kang et al., 2020; Lee et al., 2013); 1 hr daily for 6–8 weeks (Lyon et al., 2010); 20 min per day for 5 days each week for 2 weeks (McClure et al., 2015); 20 min per day for 5 days each week for 3 weeks (Mischoulon et al., 2015); 30 min per day for 5 days each week for 4 weeks (Padjen et al., 1995); 20 min per day for 3 days each week for 8 weeks (Roh & So, 2017); 60 min per day for 4 weeks (Rose et al., 2009); 30 min per day for 5 days each week, for 6 weeks (Scherder et al., 2003; Scherder et al., 2006); 30 min per day for 5 days each week, for 3 weeks (Schmitt et al.,1986); 45 min per day for 4 days each week, for 3 weeks (Smith et al.,1994); 30 min twice per day for 5 days each week, for 4 weeks (Wu et al., 2020); and one study did not reported any details regarding the duration for which current was used (Winick, 1999).

Frequency. Frequency was used between 0.5 and 15,000 Hz. Frequency of 0.5 Hz was set in most of the studies (Barclay & Barclay, 2014; Kang et al., 2020; Lee et al., 2013; Roh & So, 2017; Rose et al., 2009; Scherder et al., 2003; Scherder et al., 2006; Winick, 1999). A few studies reported the frequency of 100 Hz (Lyon et al., 2010; Padjen et al., 1995; Smith et al., 1994). Whereas two studies have used frequency ranging between 5 Hz and 15,000 Hz (McClure et al., 2015; Mischoulon et al., 2015), one study used three frequency ranges 0.5 Hz, 1.5 Hz, or 100 Hz (Wu et al., 2020). However, two studies failed to give details of the frequency of current utilized during the experiment (Schmitt et al., 1986; Southworth, 1999).

Intensity. Intensity of current used for giving intervention, ranged from 10 μA to 2 mA. Intensity of less than 100 μA was used in two studies by (Lyon et al., 2010; Padjen et al., 1995). Intensity of 100 μA was used in majority of the studies (Barclay & Barclay, 2014; Lee et al., 2013; Roh & So, 2017; Rose et al., 2009). Intensity of 200 μA was used in three studies (Kang et al., 2020; McClure et al., 2015; Winick, 1999). One study reported the range of intensity between 100–400 μA (Mischoulon et al., 2015), another study set the intensity between 500 μA – 2 mA (Wu et al., 1992020). Two studies used the intensity of current between 10–600 μA (Scherder et al., 2003; Scherder et al., 2006), whereas one study reported an intensity of 1.5 mA (Smith et al., 1994). However, two studies failed to give details of the intensity of current utilized during the experiment (Schmitt et al., 1986; Southworth, 1999).

Electrode Placement. The placement of electrodes varied between the studies, however, majority of the studies used clip electrodes and attached them to earlobes (Barclay & Barclay, 2014; Kang et al., 2020; Lee et al., 2013; Lyon et al., 2010; Roh & So, 2017; Rose et al., 2009; Scherder et al., 2003; Scherder et al., 2006; Winick, 1999; Wu et al., 2020), whereas in one study electrodes were placed at ear temples (McClure et al., 2015) and in another study, the electrodes were placed below the temples (Southworth, 1999). One study applied the stimulation through headsets with wet electrodes sponges (Mischoulon et al., 2015), another one uses the four electrodes (two at frontal and two on each mastoid) for delivering the stimulation. Two studies did not mention any details regarding the electrode placement (Schmitt et al., 1986; Smith et al., 1994).

Sham Group and Other Comparison Group Protocols. In all 15 selected studies, the experimental or active group was either compared with the control group (Kang et al., 2020; Lee et al., 2013; Scherder et al., 2003; Scherder et al., 2006; Southworth, 1999), with other intervention groups such as sham CES group (Barclay & Barclay, 2014; McClure et al., 2015; Mischoulon et al., 2015; Padjen et al., 1995; Roh & So, 2017; Rose et al., 2009; Schmitt et al., 1986; Wu et al., 2020), or with a

placebo CES group (Winick, 1999). Further, in studies having three groups, the experimental group was compared with two other stimulation groups such as a sham CES and usual comparison group (Lyon et al., 2010), or with a sham CES and placebo CES group (Smith et al., 1994). However, protocol parameters for other stimulation, such as sham CES stimulation (Barclay & Barclay, 2014; Roh & So, 2017; Rose et al., 2009), control CES stimulation (Kang et al., 2020; Lee et al., 2013; Scherder et al., 2003, Scherder et al., 2006), and placebo CES stimulation (Winick, 1999), were identical to the active CES stimulation, and the electrodes were attached in the same way as in the CES group except the ear clip electrodes did not emit electricity, the power was turned off, or the current was not given (Barclay & Barclay, 2014; Kang et al., 2020; Lee et al., 2013; Roh & So, 2017; Rose et al., 2009; Scherder et al., 2003, Scherder et al., 2006; Winick, 1999). Interestingly, in one study, SCS (sham Alpha-Stim Stress Control System) CES devices were constructed for the placebo treatment with nonconductive wires; otherwise, the device, settings, and batteries were identical in both the active and the sham groups. Further, no details regarding the usual control group were mentioned (Lyon et al., 2010). In another study, the sham CES treatment was performed by a trained technician who did not take part in any other aspect of the study, by turning the current on until the patient experienced a tingling sensation on the scalp and then turning it off. The treatment itself was a subthreshold for the above sensation (McClure et al., 2015). In another study, the sham CES devices were identical to the active device except that the sham devices were modified to not deliver current to the headset (Mischoulon et al., 2015). In a study by Padjen and colleagues, the treatment group involved the flow of the current between the frontal and mastoid electrodes; whereas, in the sham group, the current was arranged to flow between the adjacent frontal electrodes so that the stimulation was limited to the frontal skin and there was no transcranial current flow (Padjen et al., 1995). In a study by Schmitt, the treatment procedure was exactly the same in both active CES group and sham group except that the current was turned off completely for the patients who were in the sham treatment condition (Schmitt et al., 1986). In a study by Smith and colleagues, Group 1 served as placebo controls and continued in their ordinary activities during the study with no access to CES devices; whereas Group 2 served as sham treatment controls and were placed on CES devices via double-blinding boxes but received no treatment (Smith et al., 1994). In a study by Wu and colleagues, the sham CES device was identical to the active device, except the ear clip electrodes emitted electricity of intensity lower than 100 μA (Wu et al., 2020).

Patient Evaluation and Follow-Up. Patient evaluation varied in all the studies. In one study the patient evaluation was done before and after 20–60 min after a single session of CES intervention (Southworth, 1999); however, in a study by Kang et al. (2020), the evaluation was done three times per day before the surgery, preoperative, and on the day of surgery. In another study, the assessment was done before and after the surgery (Lee et al., 2013). In other studies, the evaluation was done before the intervention and 3 weeks postintervention (Lyon et al., 2010); at baseline, weeks 1, 3, and 5 (Barclay & Barclay, 2014); at baseline, weeks 2, 4, and 12 (McClure et al., 2015); at baseline, weeks 1, 2, and 3 (Mischoulon et al., 2015); at baseline, weeks 1, 2, 3, and 4 (Padjen et al., 1995); at baseline and after 8 weeks (Roh & So, 2017); at baseline, weeks 2 and 4 (Rose et al., 2009); before and after 6 weeks of intervention (Scherder et al., 2003; Scherder et al., 2006); before and after 3 weeks of intervention (Schmitt et al., 1986; Smith et al., 1994); before and after a single stimulation (Winick, 1999); and before and after 4 weeks of intervention (Wu et al., 2020). However, only two studies took the follow-up of participants postintervention (Lyon et al., 2010; McClure et al., 2015).

Dropouts and Side Effects. Discontinuations of the study by the subjects were quite rare overall (Table 1), with proportions of subjects completing each study around 99–100% with only 0–1% dropout in some studies (Lee et al., 2013; Lyon et al., 2010; McClure et al., 2015; Roh & So, 2017; Rose et al., 2009; Scherder et al., 2003; Scherder et al., 2006; Schmitt et al., 1986; Smith et al., 1994; Southworth, 1999; Winick, 1999) for both active and control groups. Some studies had dropout in between 5–17%, such as 6% (Barclay & Barclay, 2014), 7.4% (Padjen et al.,1995), 11% (Kang et al., 2020), and 17% (Wu et al., 2020). However, discontinuations of the study by the subjects were either due to personal issues or some other issues and not because of the side effects of CES.

Outcome Measures

Cognition. Cognitive measures included questionnaires or a self-rating scale such as the Cognitive Failures Questionnaire (CFQ), Modified Mini-Mental State (3MS) exam, and autobiographical memory inventory (AMI; McClure et al., 2015). In another study, neurotrophic factors such as brain-derived neurotrophic factor (BDNF) and nerve

growth factor (NGF) levels for cognitive assessment were used (Roh & So, 2017). Whereas three studies utilized the neuropsychological tests like digit span and visual memory span, the eight-words test, face and picture recognition, and word fluency (Scherder et al., 2003, Scherder et al., 2006) and continuous performance test (Southworth, 1999) for quantifying the changes in cognitive functions parameters.

Depression and Anxiety. The most common outcome measures used by the majority of studies for quantifying depression level were questionnaires and self-rating such as the Hamilton Depression Rating Scale 17 (HAM-D17; Barclay & Barclay, 2014; Mischoulon et al., 2015); Hospital Anxiety and Depression Scale (HADS; Lyon et al., 2010), Hamilton Depression scale (HDS) and Montgomery Asberg Scale (Padjen et al., 1995), and the Geriatric Depression Scale (GDS; Rose et al., 2009).

Similar to depression, many studies rely on questionnaires or a self-rating scale for measuring anxiety levels. A study by Barclay and colleagues used the Hamilton Rating Scale for Anxiety (HAM-A) for measuring anxiety (Barclay & Barclay, 2014), whereas another study quantified anxiety levels by using a 5-point Likert scale (1 = *not at all*; 2 = *mild*; 3 = *intermediate*; 4 = *moderate*; 5 = *severe*; Kang et al., 2020). Lyon and colleagues incorporated the Hospital Anxiety and Depression Scale (HADS) for quantifying anxiety level (Lyon et al., 2010). On the other hand, Padjen and colleagues used the Hamilton Anxiety Scale for measuring anxiety levels (Padjen et al., 1995). Another study by Schmitt utilized a variety of scales for assessing anxiety levels such as the State Trait Anxiety Index (STAI) and Anxiety scale of the Institute for Personality and Ability Testing (IPAT; Schmitt et al., 1986). One study incorporated the visual analogue scale (VAS), a 7-point Likert scale (Winick, 1999), whereas the study by Wu and colleagues utilized the Hamilton Anxiety Scale - 14 items (HAMA-14) for quantifying anxiety levels (Wu et al., 2020). A study by Lee and colleagues incorporated the 5-point Likert scale (Lee et al., 2013).

Mood and Stress. Mood measures were assessed with the Beck Depression Inventory (BDI), Hamilton Rating Scale for Depression (HAM-D17), Young Mania Rating Scale (YMRS), and Positive and Negative Affect Schedule (PANAS) in a study by McClure and colleagues (McClure et al., 2015). Three studies incorporated the Profile of Mood States (POMS) for the assessment of mood (Roh & So, 2017; Schmitt et al., 1986; Smith et al., 1994). However, one study utilized the behavior observation scale (BOP), Anxiety and Depression subscales of the Symptom Checklist (SCL-90), and the Beck Depression Inventory (BDI) for measuring the mood status (Scherder et al., 2006).

For quantifying stress, stress-related hormone such as adrenocorticotrophic hormone (ACTH) and cortisol were used by two studies (Lee et al., 2013; Roh & So, 2017), whereas one study involved only salivary cortisol for assessing the stress level (Scherder et al., 2003).

Effect of CES Intervention On

Cognition. A study by McClure and colleagues demonstrated an improved cognitive functioning on one of their cognitive function scales (Cognitive Failures Questionnaire [CFQ]), from baseline to week 4 in an active group (p = .045) compared to sham group (McClure et al., 2015). Similarly, a study by Schmitt and colleagues showed improved in all the subscales of WAIS including digit span, digit symbol, object assembly CES following CES intervention of 30 min each day, 5 days a week, for a period of 3 weeks (Schmitt et al., 1986). Along the same lines, one study reported improved continuous performances task for attention following 60 min of CES intervention (Southworth et al., 1999). In contrast, a study by Roh and So revealed no significant changes (p > .05) with regard to levels of serum BDNF and serum NGF, or interaction between time and groups following 8 weeks of CES treatment (Roh & So, 2017). Likewise, another study demonstrated no beneficial effects on neuropsychological tests including digit span test, visual memory, recognition, and word fluency following CES treatment for a period of 6 weeks (Scherder et al., 2003). The same authors showed no significant interaction effects between the groups over time during the study for any of the neuropsychological tests after treating with CES for a period of 6 weeks (Scherder et al., 2006).

Depression. Majority of the studies stated the reduced depression symptoms after CES treatment. Barclay and colleagues revealed a significant reduction in depressive symptoms (HAM-D17) in active CES group (p = .001, d = .78) as compared to sham group following an intervention of 5 weeks, suggesting CES as an efficient tool for treating symptoms of depression (Barclay & Barclay, 2014). Likewise, there was significantly greater improvement (end score − baseline) in depressive symptoms in the active treatment group (t = −2.56, df = 60, p = .013) compared to sham group after an intervention of 4 weeks, suggesting results again in favor of the CES for treating depression (Padjen et

al., 1995). However, Mischoulon and colleagues showed improvement in 3 to 5 points in HAM-D17 scores ($p < .05$) and reduced depression remission rates in both the treatment groups without any significant differences between these groups following 3 weeks of CES treatment (Mischoulon et al., 2015). Additionally, in a study (of over 4 weeks) by Rose and colleagues, decreased depressive symptoms scores with final depressive scores falling below baseline were seen in both groups without any significant differences between the groups ($F = 9.022$, $p = .224$; Rose et al., 2009). In a study by McClure and colleagues, following 2 weeks of intervention, active CES but not sham treatment was associated with significant decrease in BDI and HAM-D scores, from baseline to the second week ($p = .003$), maintaining significance until week 4 ($p = .002$), and then reducing to a trend ($p = .09$) by week 8. However, there was no significant difference between the groups for HAM-D scores. For YMRS, the total and subscale scores did not change through the study, and no significant differences were found between and within the groups at any of the time points (McClure et al., 2015). In contrast, in a study of a 6- to 8-week period of intervention by Lyon and colleagues, the symptoms of depression increased over time ($p = 0$), as the depressive symptoms went from mild to a potentially clinically significant level in week 6. However, greater increases (not statistically significant) occurred in the depression symptoms in sham and standard care groups than occurred in CES group from baseline at 3 weeks (Lyon et al., 2010).

Anxiety. Most of the studies showed lower anxiety scores in the CES group as compared to other groups following CES intervention (Barclay & Barclay, 2014; Kang et al., 2020). A study by Barclay, revealed a significant reduction in anxiety symptoms in the CES group ($p = .001$, $d = .94$) as compared to sham group, after an intervention of 5 weeks (Barclay & Barclay, 2014). Further, a study by Kang and colleagues signified lower anxiety scores and a smaller number of patients with higher anxiety levels in the CES group as compared to control group, following 20 min of CES stimulation, both on the day before surgery and on the morning of the day of surgery (Kang et al., 2013). Additionally, a study by Padjen and colleagues reported greater improvement (end score − baseline) in the active CES group (not statistically significant) as compared to sham group in anxiety subscales following CES treatment of over 4 weeks (Padjen et al., 1995). A study by Schmitt and colleagues showed that both the alcoholic and polydrug abusers responded significantly and experienced the same level of improvement in anxiety symptoms with CES, but the control group did not show any improvement in the same, following 3 weeks of intervention (Schmitt et al., 1986). Furthermore, a study by Winick and colleagues (in which CES treatment was administered during a dental procedure) exhibited significant improvement on anxiety symptoms in active CES group compared to placebo group at the conclusion of various dental procedures (Winick, 1999). Likewise, a study by Wu and colleagues demonstrated a significant difference in anxiety scores between the groups over time during the study of 4 weeks of treatment ($F = 10.64$, $p = .001$). Anxiety scores at week 4 decreased significantly according to baseline in active group ($t = 1.01$, $p = .001$), and not in the sham group ($F = 1.11$, $p = .34$; Wu et al., 2020). Lyon and colleagues demonstrated no significant increase in the level of anxiety symptoms in any of the three groups (active, sham, and usual care group) from baseline at 3 weeks, with no statistically significant differences between the groups (Lyon et al., 2010).

Mood and Stress. Three (Roh & So, 2017; Schmitt et al., 1986; Smith et al., 1994) out of six studies showed positive results of CES for improving the mood status**.** Following a 3-week intervention program, Schmitt and colleagues reported that the CES group significantly reduced on every anxiety subscale of the POMS used, the sham-treated CES group improved on only two of the six scales of the POMS, and the normal treatment program controls did not post significant gains on any measure of POMS (Schmitt et al., 1986). In another study, the pretreatment and posttreatment means of the three groups were compared, in which the CES treatment group showed significant improvement on every subtest of the POMS while control groups (placebo and sham group) did not, following 3 weeks of intervention (Smith et al., 1994). Further, in a study by Roh and So, following CES treatment of 8 weeks, the CES group exhibited a significant decline in depression-dejection subscores ($p < .05$) of POMS as compared to sham group (Roh & So, 2017). In contrast, a study by Scherder and colleagues showed no significant interaction effects ($p > .05$), between the groups for any of the mood and behavior scales following 6 weeks of CES therapy (Scherder et al., 2006). The same authors showed no significant effect on mood functions measures following a 6-week CES intervention (Scherder et al., 2003). Additionally, in a study by McClure and colleagues, following 2 weeks of CES intervention, PANAS subscale scores and total score did not change appreciably and no significant differences

were found between and within the groups (p > .05) at any of the time points (at weeks 2, 4, and 8; McClure et al., 2015).

None of the included studies showed a positive effect of CES on improving stress level. In one study by Lee and colleagues, there were no significant differences in serum ACTH and cortisol levels in between the patients undergoing thyroidectomy given with CES and patients undergoing thyroidectomy without CES, measured at 1-, 4-, 12-, and 24-hr postsurgery (Lee et al., 2013). A study by Roh and So,revealed no significant differences with regard to levels of plasma cortisol and plasma ACTH or interaction between time and groups following CES treatment of 8 weeks (p > 0.05; Roh & So, 2017). In addition, a study by Scherder and colleagues demonstrated that low-frequency CES did not reduce stress in AD patients. Further, both groups showed an increase instead of a decrease in the level of cortisol, following 6 weeks of CES stimulation therapy (Scherder et al., 2003, Scherder et al., 2006).

Discussion

Prior systematic reviews, found in our literature searches up to April 2022, revealed beneficial results for anxiety and depression but suggest that there is an inadequate literature for methodologically eligible or high-quality trials for anxiety (Shekelle et al., 2018) or depression (Kavirajan et al., 2014; Shekelle et al., 2018). In addition, to the best of our knowledge, the advantages of CES on other outcome parameters such as mood functions, stress levels, and cognitive functions in a range of settings were not studied in the prior review. As a result, our analysis adds fresh research, additional settings, and extra outcome characteristics to these previous reviews. Based on data from 669 participants, this is the first systematic review to provide full information on the findings, features, and quality of RCTs, investigating the effect of CES on variety of mental health conditions such as cognitive dysfunction, depression, anxiety, mood, and stress disorder in various populations. We have mixed findings from different results and therefore limited evidence to support the use of CES for treating variety of mental disorders, as indicated by various qualitative and quantitative methods.

Cognitive Functions, Depression, and Anxiety

In the present review, we found limited evidence to support the use of CES for improving the cognitive function parameters, as three out of six RCTs reported no changes or improvement in cognitive functions parameters after using CES (Roh & So, 2017; Scherder et al., 2003, Scherder et al., 2006). However, three studies demonstrated an improved cognitive functioning on one of their cognitive function scales (McClure et al., 2015; Schmitt et al., 1986; Southworth, 1999). Therefore, our overall result has inconclusive findings regarding the effect of CES on cognitive functions.

We examined the efficacy of CES for the treatment of depressive disorders in a methodological review of six RCTs. Most of the studies on different population show that CES is an effective treatment and a useful adjunctive to other ongoing treatments, including pharmacotherapy and psychotherapy for treating depression (Barclay & Barclay, 2014; McClure et al., 2015; Mischoulon et al., 2015; Padjen et al., 1995; Rose et al., 2007). However, a study by Lyon and colleagues showed no significant changes and therefore no improvement in depressive symptoms (Lyon et al., 2010). Overall, our review suggests that CES helps in improving the depressive symptoms in a variety of population. The findings from this systematic review are in line with a prior review: CES as an effective treatment for depression, showing a cumulative treatment effect with repeated use and observable improvements following the first course of treatment (Kirsch & Nichols, 2013); a meta-analysis of CES for the treatment of depression (Price et al., 2021); and a systematic review showing low strength evidence suggesting modest benefit in patients with anxiety and depression (Shekelle et al., 2018).

Regarding anxiety, preceding systematic reviews identified in our literature searches to November 2021 reported beneficial effects for anxiety but with inadequate evidence (Shekelle et al., 2018). We analyze the effect of CES for the treatment of anxiety in a precise review of seven RCTs. The majority of RCTs demonstrated improvement in anxiety symptoms post-CES intervention (Barclay & Barclay, 2014; Kang et al., 2020; Lyon et al., 2010; Schmitt et al., 1986; Winick, 1999) but not significant enough (Padjen et al., 1995; Wu et al., 2020) to report any convincing results.

Mood and Stress

Three RCTs (Roh & So, 2017; Schmitt et al., 1986; Smith et al., 1994) showed positive results of CES for improving mood status. In contrast, the study by Scherder and colleagues showed no significant effects of CES for the improvement of any of the mood and behavior parameters (Scherder et al., 2003). Another study by the same authors revealed no improvement in mood status following CES

intervention (Scherder et al., 2006). Additionally, a study by McClure and colleagues showed no improvement on any of the mood total scores and mood subscale scores throughout the study period (McClure et al., 2015). In total, findings were not substantial to make any conclusive results concerning mood treatment by CES. Concerning stress, none of the included RCTs (Lee et al., 2013; Roh & So, 2017; Scherder et al., 2003, Scherder et al., 2006) showed any positive changes on stress level quantified by serum or plasma ACTH and cortisol levels, following 6 weeks of CES stimulation therapy (Scherder et al., 2003; Scherder et al., 2006), therefore warranting further research for making any conclusion.

Speculated Underlying Mechanism

CES mechanism of action on mental health is a topic of discussion, as a growing body of evidence advocated different theories and approaches for explaining the same. The mechanisms underlying the effect of CES are not well understood, but several theories can be used in an attempt to explain the scientific findings and clinical usefulness of CES in treating various mental diseases. A review of early literature (Bystritsky et al., 2008) stated that neurotransmitter levels are affected as a result of CES therapy; however, the animal studies had difficulties in scaling from exam animal anatomy to human neuroanatomy, and thus acquaintances were incomparable. Others have speculated that CES devices might interpose ongoing (pathologic) brain activity by introducing “cortical noise” and that this may impede with electrical oscillatory performance within the brain (Zaghi et al., 2010). Functional magnetic resonance imaging was used in recent research of the mechanistic effects of CES on brain activity on healthy adult volunteers to assess short-term effects (Feusner et al., 2012). Significant deactivation of the midline frontal and parietal regions, as well as changes in connectivity within the default mode network, were discovered by the researchers. Nonetheless, according to one study, the mechanisms of action of externally applied CES have been found in the limbic system (which is involved in emotional regulation and memory), as well as in the cingulate gyrus, insula, and prefrontal cortex (which is involved in pain processing; Taylor et al., 2013) by a variety of process including: transcranial and cranial nerve stimulation, pathways like cortical and subcortical region activation, effects on endogenous brain oscillations and cortical excitability, impact on neurotransmitters, hormones and endorphins, and impact on autonomic nervous system in the desired frequency (Mindes et al., 2014). Overall, it's unclear if CES has a single mechanism of action or whether clinical effects are caused by different methods of action of different CES devices in different disorders; therefore, more thorough research is needed to resolve these questions.

Limitations and Future Implications of Research

The widely held studies included in this review revealed improvements in anxiety, depression, and mood functioning to some level. However, in addition to the limitations already mentioned in terms of the quantity and quality of trials in previous literature, this study contains a number of other flaws. For a few research studies, the data was insufficient to compute an impact size; hence, those studies contributed less to the overall outcome. Because the data did not support a quantitative assessment of publication bias, its existence is still questionable. Importantly, many of the published RCTs were pilot studies, had uncertain validity and power, and were restricted by a lack of blinding assessment. Many studies reported small effects or did not provide sufficient detail about patients’ existing treatments, such as two studies that did not mention any details regarding the electrode placement (Schmitt et al., 1986; Smith et al., 1994), two studies that failed to give details of the intensity and frequency of current utilized during the experiment (Schmitt et al., 1986; Southworth, 1999), and one study that did not describe any information regarding the duration for which current was used (Winick, 1999). Besides, some studies included single gender in their studies, with only females (Lee et al., 2013; Lyon et al., 2010; Roh & So, 2017) or only males (Padjen et al., 1995). Importantly, the number of treatment sessions of CES was significantly less in two studies (Kang et al., 2020; Lee et al., 2013). To end, all the included studies used a diverse population, mixed symptoms, overlapping conditions, variety of outcome measures and treatment program, making it difficult to perform meta-analysis. As a result, future studies should take into account the aforementioned constraints to back up their conclusions and to carry out the further pool analysis.

Conclusions

The evidence from this systematic review for the effectiveness of CES is sparse. None of the studies favored the use of CES for improving cognitive function or treating stress. Due to the paucity of RCTs, limited evidence supports the use of CES for treating mood disorder and an average amount of evidence suggests a beneficial effect of CES for treating anxiety and depression symptoms.

Therefore, proof of benefit requires larger RCTs of higher quality, better execution, and longer follow-up. In addition, more gold standard and objective outcome measures such as EEG, ERPs, NBT, BDNF, serotonin, cortisol, and ACTH level to quantify mental health dysfunction are required to provide us with more high-level evidence regarding the efficacy of this treatment. Such standardized outcome measures would also allow an appropriate meta-analysis of future studies in this field. To give clear proof for the same, more trials with optimum controls and randomization protocols are required.

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Documenting the Effects of Noninvasive Prefrontal pIR HEG Neurofeedback in the Treatment of Common Mental Health Problems

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Abstract

Clients with mixed diagnoses were provided passive infrared hemoencephalography (pIR HEG) neurofeedback in a mental health private practice treatment setting. This is the first formally documented investigation of pIR HEG neurofeedback applied to a mental health population. Both qualitative and quantitative data were collected. Results from 66 clients showed that five sessions of neurofeedback resulted in statistically significant changes in anxiety, depression, limbic overload, and coping self-efficacy. For clients who completed 10 or 15 sessions, results showed robust changes in anxiety, depression, limbic overload, general self-efficacy, coping self-efficacy, and dissociation. The impact of neurofeedback on self-efficacy is discussed as well as limitations and implications for future research.

Keywords: neurofeedback; pIR HEG; prefrontal cortex (PFC); self-efficacy; data-driven practice; limbic overload

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Introduction

Technology has been suggested as a mechanism to influence the accessibility, efficiency, and effectiveness of mental health care (Magnavita, 2018). At least 20% of people in the United States are currently suffering with a mental health disorder, and almost half of all people will suffer with mental health difficulties in their lifetime. In assessing the impact of the COVID-19 pandemic, 41% of 5,500 adults surveyed in 2020 reported having an adverse mental health impact, and an alarming 11% had considered suicide in the last month (Czeisler et al., 2020). The full mental health impact of a postpandemic world is still filtering into view with scores of people struggling with anxiety, social isolation, financial difficulties, COVID-related medical trauma, and ongoing stress about gun violence, the environment, and the postpandemic geopolitical state. With telehealth sessions and health-related digital apps becoming commonplace, the integration of technology into mental health services is inevitable. Further understanding technology's influence on the efficiency and effectiveness of services in this time of extensive need has become critical. This study examines the use of noninvasive prefrontal cortex (PFC) neurofeedback technology to treat common mental health difficulties.

Neurofeedback technology represents a different type of mental health treatment. The last 50 years in the mental health field have been dominated by the innovation of psychiatric medication and cognitive behavioral psychotherapy approaches. Although evidence from many studies show that antidepressants and psychotherapy produce a reliable small treatment effect over placebo, we know that many people do not get better from these traditional treatments. A 12-year prospective study estimated that in depression, 90% of people have persistent symptoms despite treatment (Judd et al., 1998). Many people do not have access to treatment

that is delivered systematically or optimally, thereby reducing an already small margin of effectiveness. In addition, side effects of medications and the difficulties clients report in finding a comfortable psychotherapy fit can be deterrents to people receiving relief from these treatments. From the clients' perspective, neurofeedback presents a notably different method and if shown to be useful, such novelty can be attractive to those who have not responded or benefitted enough from other approaches.

As an alternative treatment, neurofeedback is noninvasive and without the systemic side effects of psychiatric medication. Unlike psychotherapy, it does not rely on the person's interest or ability to work out problems through verbal communication. Neurofeedback works through implicit learning in the targeted brain area which results in new automatic capacity and function associated with that brain region. This is notably different from the explicit teaching of emotion regulation skills in psychotherapy. Explicit teaching of skills requires clients to learn, remember, and choose to implement skills when their brains are reacting emotionally. In addition, this way of explicitly teaching skills is mostly done in the context of clients' past coping difficulties. In neurofeedback, clients learn through observing their new abilities and behavioral accomplishments. In this way, neurofeedback empowers clients and instigates a natural openness and efficacy around emotional skills.

Theoretically, neurofeedback can help across diagnoses through influencing the executive brain, the PFC. As the brain evolved over time, the emphasis shifted from a brain with rigid, fixed functions to one that is capable of flexible adaptation. Although neurofeedback systems target a variety of brain areas, most approaches show frontal changes regardless of which brain area is targeted. The PFC's role is one of oversight, coordination, inhibition, and integration (Goldberg, 2009). Given its role, the PFC must be malleable. Activation of the PFC relates to the mental and behavioral capacity for rational thinking, self-awareness, initiation of action, integration of emotion and rational thought, and inhibition of stress reactivity. When the PFC is dominant, the limbic system becomes less dominant. The amygdala, the brain's threat detector, becomes less active when the prefrontal area is more active. By instigating change in the PFC, we target a process of greater self-regulation that may result in amelioration of symptoms and improved executive capacity across mental health diagnoses.

EEG-based neurofeedback has been around since the 1960s. Despite being a diverse and misunderstood field, several key studies show the importance of a reexamination of the utility of neurofeedback in the current demand for treating unprecedented numbers of people struggling with mental health conditions. In 2020, Yu and colleagues conducted a randomized, controlled trial of neurofeedback in the treatment of depression targeting peak alpha frequency activation in the PFC. They showed that with 20 neurofeedback sessions, the treatment group had significant improvement in executive function and a corresponding decrease in rumination and depression. They posited that with greater PFC activation, it is easier to inhibit negative ruminative thinking resulting in a decrease in depression. A landmark study by Bessel van der Kolk et al. (2016) showed significant results for EEG neurofeedback applied to those with chronic PTSD (where there was no clinical improvement for 6 months). In recounting the results of the study in *The Body Keeps the Score*, van der Kolk (2015) states "most intriguing was the marked effect of neurofeedback on executive functioning … about a 60% increase … to my knowledge no other treatment has achieved such marked improvement in executive functioning, which predicts how well a person will function in relationships, in school performance, and at work" (p. 330). Several neurofeedback studies involve follow-up data and have found evidence that symptoms continue to improve for weeks or months posttreatment. Rance et al. (2018) found these gains posttreatment in two distinct data sets and postulated that brain learning in neurofeedback may instigate a process of learning consolidation and reconsolidation over time, resulting in continued brain function enhancement even once sessions have stopped. Such studies inspire curiosity about how different neurofeedback methods may be used to invoke potent and lasting neuroplastic changes in the brain, particularly in the PFC region.

Other naturalistic studies looking at neurofeedback in the treatment of mental health conditions suggest that it can be an effective intervention across diagnostic groups. Cheon et al. (2015) applied EEG-based neurofeedback to 77 clients in a naturalistic outpatient setting and reported significant changes between pretreatment and posttreatment (after a mean of 17 neurofeedback sessions) in clinician-rated global clinical improvement scores and self-rated scales measuring symptoms of depression, anxiety, and inattention. Fleischman (2022) reported on the clinical impact of applying infra low frequency neurofeedback to complex psychiatric presentations in an underserved mental health population. Fleischman

reported reductions in drug/alcohol relapse and use of ER/hospital after 20 neurofeedback sessions. Clients showed improvements in a cognitive test of attention and impulse control as well as positive changes in how well they perceived themselves coping with stress.

The current study seeks to expand our understanding of the application of neurofeedback in mental health. Its intention is to examine the possible advantage of integrating neurofeedback into treatment across diagnoses. It also assesses whether a neurofeedback system (pIR HEG) that is particularly easy to implement can produce substantial findings. If a very simple system can be used to treat underlying neurobiological mechanisms successfully, this calls even more profoundly for an examination of the use of neurofeedback and other psychophysiological approaches within the context of mental health primary care.

Hemoencephalography (HEG) is a type of noninvasive neurofeedback technology invented in 1994. Hershel Toomim developed HEG technology as a poor man's MRI. When a region of the brain is used, cellular metabolism can be detected through changes in cerebral blood flow. Rather than measuring brain activity through the traditional methods involving EEG brain waves, HEG detects brain activity through changes in cerebral blood flow in the PFC. Toomim invented the near-infrared HEG system [see Kohl et al. (2020) for a review on studies evaluating fNIRS]. In Toomim's design, increasing blood oxygen levels are detected and shown to the client as the PFC is exercised. Carmen invented a similar system in 1998. Carmen's passive infrared hemoencephalography (pIR HEG) system measures heat distally without skin contact. The pIR HEG system detects increases in thermal waste in the PFC, produced as a byproduct of cellular metabolism. Both types of HEG systems use simple headbands that allow for direct training of the PFC.

Both Toomim and Carmen (2009) addressed the focus on prefrontal training. Toomim noted that by examining literature on brain imaging, the source of most aberrant behavior can be linked to hypoperfusion in the frontal lobes. Carmen posited that through the enhanced activation of the PFC, there is a helpful inhibition on the rest of the brain, resulting in diminished expression of migraines and other brain events. Although systems were applied to various specific brain-related disorders, the impact on global brain control and self-regulation was noted by both developers.

The pIR HEG sensor sits at the Fpz brain training location and measures a relatively large area directly in the center of the forehead. Studies have demonstrated that pIR HEG shows a reduction of thermal variability in the PFC (Carmen, 2004; Coben & Padolsky, 2008). As a result, Carmen states that pIR HEG can be useful across diagnoses and can result in reductions in the rate and magnitude of behavioral responses. Despite the theorized impact on self-regulation, there are no published studies on pIR HEG applied to mental health conditions. The literature shows that it has been successfully and safely applied to clients for the treatment of migraines (Carmen, 2004; Stokes & Lappin, 2010; Walker & Lyle, 2016).

Scientist-Practitioner Approach to This Clinical Pilot Study

In applying pIR HEG to the clinical mental health population, the principal investigator adopted a scientist-practitioner approach while implementing 1400 pIR HEG sessions with 100 clients. As this first contingent received treatment, quotes were recorded that captured changes from their point of view. For a more formal evaluation of the clinical program, clients were asked to complete the same questionnaires before starting pIR HEG (baseline), after 5 sessions, after 10 sessions, and after 15 sessions. Even after questionnaires were introduced, clients continued to share their own view of stressors in their lives and observations of their own behavioral responses to them. Clients self-reported observations are organized into four types. See Tables 1–4 for a collection of direct quotes and observations by the first 100 clients.

Table 1

A Collection of Clients' Direct Quotes Related to "Quieting the Nervous System"

- "I am more present."
- "I feel better on the inside."
- "I am having fewer panic attacks and I can think my way through them. Something is different."
- "I had a conflict with my landlord, and I waited two days to respond."

Table 1

A Collection of Clients' Direct Quotes Related to "Quieting the Nervous System"

- "I used to yell and scream. I can see the things I used to react to. I used to feel like I had to say it, and now I don't have to say it."
- "Before neurofeedback I used to feel a lot of dread. My hopelessness is much better. I don't feel dark and depressive anymore."
- "My overreactivity is not controlling me anymore."
- "It feels like I can figure out stuff instead of freaking out."

Table 2

A Collection of Clients' Direct Quotes Related to "Window of Tolerance Expanding"

- "I feel more irritated rather than shut down."
- "I feel more anger than panic or hopelessness."
- "I am able to allow myself to be sad."
- "I have been tearful and experiencing more emotion, not just anger or anxiety."
- "I realize my feelings are normal. I have less doubt about being crazy."
- "Sadness, anger, disappointment, and grief are coming up. These are things I can't change, and I don't have to."
- "I am feeling, and I can tolerate the feelings. I am not numbing out."

Table 3

A Collection of Clients' Direct Quotes Related to "Self-Agency"

- "It feels like I am on the ball."
- "My focus has shifted to me."
- "I said yes to something uncomfortable that led to a promotion at my job."
- "There is more of a sense of I can handle this."

Table 3

A Collection of Clients' Direct Quotes Related to "Self-Agency"

- "I asked my boss to work from home 1 day per week."
- "I feel like I am standing up for myself."
- "My daughter got COVID, and I didn't worry. I can tackle this. I am doing the best I can."
- "I have more authority over what I want."

Table 4

A Collection of Clients' Direct Quotes Related to "Self-Observation and Awareness"

- "I was aware of my heightened state. I notice anxiety in my body when I lie down at night. It feels like an activating sensation in my chest."
- "I am more open to suggestions. I realize that many of the fights with my parents and my boyfriend are my fault."
- "This has made a huge difference coming here. My awareness of myself has increased. Noticing my own experience of working at my job, asking myself 'Why am I working here?'"
- "I realize that I am afraid of going back to pretending that I am okay, and I don't want to do that."
- "It is amazing that I had anxiety the other day and my mind went to 'isn't that interesting?' This is not the usual way I would relate to my anxiety."

The above observations led to a test construction process. In noting the types of positive changes reported by clients, items were created that described the opposite. For example, items were constructed to capture a sense of "feeling stuck" and "feeling helpless" as the opposite of self-agency. Items were created to capture "feeling on edge," "anxiety in my body," "overreacting emotionally," as the opposite of a quieted nervous system. The total scale includes 17 items created to comprise the Limbic Overload scale. This scale is meant to be a measure of the perception of one's mental state when there is a general lack of

brain control over emotions and deficits in self-regulation. After the scale was completed by 92 total clients, Cronbach's alpha was calculated to be .91–.93, showing high internal consistency for the scale. See items below in Table 5. Correlations with other measures are reported in Table 6.

Table 5

Limbic Overload (Baker, 2020)

1. I have trouble controlling my anger/irritability.
2. I feel stuck, unable to change.
3. I feel panicky and anxious in my body.
4. I feel helpless.
5. I feel on edge/hypervigilant.
6. I am scattered in my mind and can't focus.
7. I find myself overreacting emotionally.
8. I procrastinate.
9. I numb, distract, and/or avoid things.
10. I ruminate about my problems.
11. I can't make decisions.
12. I am stressed.
13. I feel like hiding rather than reaching out.
14. I am overwhelmed.
15. I am tired in my body.
16. I have symptoms of digestive problems.
17. I have pain in my body.

Note. 17 items are rated on a 10-pt scale from 0 = *Never* to 10 = *All the time*. Item scores were summed to create a total score. Please contact author for use of this scale.

Purpose of the Study

This program evaluation study examined the effectiveness of pIR HEG neurofeedback across common clinical diagnoses in outpatient mental health private practice. The goal was to determine whether clients receiving pIR HEG sessions showed significant improvement on quantitative measures collected after every five sessions of neurofeedback.

1. Is there a statistically significant difference between individuals' baseline depression, anxiety, limbic overload, and self-efficacy scores and their scores after 5 sessions, 10 sessions, and 15 sessions of pIR HEG neurofeedback?
2. For significant differences, what are the estimated effect sizes for these measures across clinical diagnoses? How many sessions result in a change? Are those changes maintained? Are there additional gains with additional sessions?

It was anticipated that clients would show significant decreases in anxiety, depression, limbic overload, and increases in self-efficacy. Hypotheses were based on the PFC's inhibitory power as well as qualitative reports from clients.

Method

This within-subjects research design occurred in a private practice setting treating adults presenting with issues related to anxiety, depression, stress, and trauma. The purpose of the data collection was to be able to evaluate the efficacy of the implementation of pIR HEG into the principal investigator's clinical practice. Prior to completing baseline questionnaires, clients were oriented to the fact that the investigator was using the data to assess the impact of pIR HEG on mental health outcomes and to document those findings. Clients were informed that questionnaire data would be used to track individual progress. With as much transparency as possible, clients were presented with pre-post graphs of the changes in their measures as part of the clinical treatment process. Clients were not required to attend a particular number of pIR HEG sessions. Data was collected through a rolling process where each person completes questionnaires at baseline, after 5, after 10, after 15, and continuing every 5 sessions while in treatment.

For the purpose of this investigation, group data is reported on 66 clients who completed baseline and after five session measures. In addition, data is reported on 46 of the 66 clients who completed baseline and after 10 measurements, as well as data on 21 of the 66 clients who completed baseline and after 15 measurements.

Participants

The present study included data from a total of 66 clients ranging in age from 19 to 66. There were 20 males and 46 females in this predominately white middle class sample in Upstate NY.

Clients' diagnoses included generalized anxiety disorder, PTSD, persistent depressive disorder, major depression, ADHD, bipolar disorder,

adjustment disorder, and panic disorder. PTSD or trauma-related issues presented as the primary problem in 28 of the 66 total individuals.

Baseline measurements revealed that this sample population presented with a mix of anxiety and depression. For depression scores (PHQ-9), 38% fell into the mild range, 23% in the moderate range, and 39% in the severe range. For anxiety scores (GAD-7), 32% of clients report none-minimal anxiety, 29% reported moderate anxiety, and 39% reported severe anxiety. Both of these measures were originally designed to screen for anxiety and depression in primary care settings. Given that this is a clinical population presenting with distress and many with trauma histories, scores skewed to the more severe side are expected.

Measures

Patient Health Questionnaire-9 (PHQ-9). The PHQ-9 is a multipurpose instrument for screening, diagnosing, monitoring, and measuring the severity of depression (Kroenke et al., 2001). The PHQ-9 incorporates DSM-IV depression diagnostic criteria with other leading major depressive symptoms into a brief self-report tool. The PHQ-9 asks clients to rate their level of each symptom over the last 2 weeks from 0 (*not at all*) to 3 (*nearly every day*). PHQ-9 scores of 5, 10, and 15 represent mild, moderate, and severe depression, respectively.

Generalized Anxiety Disorder Assessment-7. (GAD-7). The Generalized Anxiety Disorder Assessment (GAD-7; Spitzer et al., 2006) is a brief measure for symptoms of anxiety, based on the generalized anxiety disorder diagnostic criteria described in the Diagnostic and Statistical Manual of Mental Disorders (DSM). The GAD-7 assessment asks clients to evaluate their level of symptoms over the last 2 weeks. A symptom severity description is presented based upon the raw score: 0–4 = *None-Minimal*; 5–9 = *Mild*; 10–14 = *Moderate*; 15+ = *Severe*.

Limbic Overload (LO). The LO scale was developed by the author of this study through a test construction process based on clients' reports of where they felt stuck and areas of stress perception that improved with pIR HEG sessions (Baker, 2020). The scale includes items endorsed by clients who report the feeling of mental and physical overwhelm. The scale has 17 questions including three types of experiences:
a) general feelings of being stressed, overwhelmed, and stuck; b) feelings of being on edge, hypervigilant, scattered, and anxious in the body; and c) feelings of being numb, avoidant, tired, and in pain.

Each item is rated on a 10-point scale from "*Never*" to "*All the time*." Scores on the 17 items were summed to come up with a LO total score. Cronbach's alpha was calculated to be .91–.93 showing high internal consistency for the scale. Correlations between Limbic Overload and the other measures are presented in Table 6.

Table 6

Correlations Between Limbic Overload and Other Measures

	r
PHQ	.721
GAD	.682
GSE	−.549
CSE	−.634
DES	.464

General Self-Efficacy (GSE). The General Self-Efficacy Scale is a 10-item psychometric scale that is designed to assess optimistic self-beliefs to cope with a variety of difficult demands in life (Schwarzer & Jerusalem, 1995). The scale was developed in German by Matthias Jerusalem and Ralf Schwarzer in 1981 and has been used in many studies with thousands of participants. In contrast to other scales that were designed to assess optimism, this one explicitly refers to personal agency (i.e., the belief that one's actions are responsible for successful outcomes). Each of the 10 items is rated on a 4-point scale: 1 = *Not at all true*; 2 = *Hardly true*; 3 = *Moderately true*; 4 = *Exactly true*. The sum is the GSE score, ranging between 10 and 40. Internal reliability for GSE = Cronbach's alphas between .76 and .90. The General Self-Efficacy Scale is correlated to emotion, optimism, and work satisfaction. Negative coefficients have been found for depression, stress, health complaints, burnout, and anxiety.

Coping Self-Efficacy (CSE). The CSE scale provides a measure of a person's perceived ability to cope effectively with life challenges (Chesney et al., 2006). This measure focuses on changes in a person's confidence in his or her ability to cope effectively which, according to self-efficacy theory (Bandura, 1997), is an important prerequisite to

changing coping behavior. CSE was assessed with a 26-item measure of perceived self-efficacy for coping with challenges and threats. Participants were asked, "When things aren't going well for you, or when you're having problems, how confident or certain are you that you can do the following...?" They were then asked to rate on an 11-point scale the extent to which they believe they could perform behaviors important to adaptive coping, such as "sort out what can be changed, and what cannot be changed," "break an upsetting problem down into smaller parts," "look for something good in a negative situation," and "get emotional support from friends and family." Anchor points on the scale were 0 (*cannot do at all*), 5 (*moderately certain can do*) and 10 (*certain can do*). Scores range from 0–260.

Brief Dissociative Experiences Scale (DES-B). The DES-B is an 8-item measure that assesses the severity of dissociative experiences in individuals ages 18 and older (Dalenberg & Carlson, 2010). Each item asks the individual receiving care to rate the severity of his or her dissociative experiences during the past 7 days. Each item on the measure is rated on a 5-point scale (0 = *Not at all*; 1 = *Once or twice*; 2 = *Almost every day*; 3 = *About once a day*; 4 = *More than once a day*). The total score can range from 0 to 32, with higher scores indicating greater severity of dissociative experiences. The total scores were used as data in this investigation.

Data Collection Procedures

Clients were asked to complete questionnaires at baseline, after 5 sessions of neurofeedback, after 10 sessions, and after 15 sessions. Questionnaires were completed electronically as part of clients' ongoing treatment in the principal investigator's private practice. This section describes procedures for the pIR HEG neurofeedback training process.

Jeff Carmen's EZ pIR neurofeedback system was used for all clients. The system uses a headband with two infrared sensors capturing thermal activity from the center of the forehead. It captures infrared radiation within the 7- to 14-micron band, with field of view of 1.5 in. X 2.0 in. The sensor assembly records infrared light waves emitted from the forehead in much the same way that a camera records visible light waves reflected from objects. The sensor assembly has a response time of 80 ms. The data sampling rate is 30 times per second. (Carmen, 2018).

The EZ pIR protocol uses a DVD of a Hollywood film as an emotional stimulus. Clients pick from a small collection of movies in the clinician's office and are instructed to choose a movie that "resonates" with them, a movie that they find satisfying to watch. Clients were generally instructed to avoid films that are upsetting to them and films that they have seen multiple times where they can anticipate each scene. Most often clients would choose a DVD that would be used from session to session, starting wherever they left off in the prior session. Clients were able to change the movie for the next session anytime they wanted.

When the sensors on the forehead detect a decrease in thermal output in the PFC, the movie freezes and a bar graph appears on the screen. The bar graph shows whether heat coming off the PFC is rising or falling. The client then uses the information in the bar graph to voluntarily exercise the PFC, learning to return heat to this part of the brain, thereby prompting the movie to play again. In any given session, clients obtain approximately 10 min of active brain exercise over a total of approximately 30 min.

The principal investigator served as the clinician for all neurofeedback sessions. She received direct training from Jeffrey Carmen, PhD. There are very few complications to the implementation process—the way the equipment is used takes seconds to set up (put on headband and give basic instructions) and is the same for each client. The only assumption is that regardless of primary diagnosis, greater PFC activation and connectivity is the goal.

Although no side effects were reported, clients were monitored for frontal fatigue. In order to make sure pIR HEG sessions were implemented safely, a maximum of 10 min of active training time (time when movie is paused and person is exerting effort) was allowed for each neurofeedback session. Generally, the time spent in the neurofeedback training session was between 23–30 min, an approximate ratio of 1:3 active training time to overall elapsed time. In addition, sessions were spread apart by at least 1 week. The neurofeedback session was stopped if the patient reported any headache or forehead discomfort. Needing to stop the session early was not necessary in most cases with clients gaining 10 min of active prefrontal training during each session.

Results

Scores on anxiety (GAD-7) and depression (PHQ-9) at baseline and after 5, 10, and 15 sessions of neurofeedback were organized into categories of symptom severity. Table 7 shows the number (and percentage) of clients reporting minimal/mild, moderate, and severe levels of symptoms.

A series of paired one-tailed *t*-tests were conducted to compare data collected after 5 sessions, after 10 sessions, and after 15 sessions with data collected from the same clients at baseline (before neurofeedback sessions began). After 5 sessions, measures of anxiety, depression, limbic overload, and coping self-efficacy showed statistically significant changes. After 10 sessions and after 15 sessions, *t*-tests showed statistically significant changes in mean scores across all measures. While depression, anxiety, limbic overload, and dissociation decreased, general self-efficacy and coping self-efficacy increased. See Table 8 for *t*-test results as compared to clients' baseline measurements. Because the measure of dissociation was added after other measures, *t*-tests on the DES-B are reported separately in Table 11.

Table 7

Number of Clients Reporting Symptoms in the Minimal, Moderate, and Severe Ranges of Anxiety and Depression

	Score on PHQ	Baseline	After 5 sessions	After 10 sessions	After 15 sessions
Depression	Mild 0–9	25 (38%)	46 (70%)	37 (80%)	21 (100%)
	Moderate 10–14	15 (23%)	13 (20%)	6 (13%)	0
	Severe 15–27	26 (39%)	7 (10%)	3 (7%)	0
	Total subjects	66	66	46	21
	Score on GAD-7	Baseline	After 5 sessions	After 10 sessions	After 15 sessions
Anxiety	Mild 0–9	21 (32%)	38 (58%)	36 (79%)	19 (90%)
	Moderate 10–14	19 (29%)	18 (27%)	8 (17%)	2 (10%)
	Severe 15–21	26 (39%)	10 (15%)	2 (4%)	0
	Total subjects	66	66	46	21

Table 8

Paired One-Way T-Test Analyses Comparing the Same Clients at Baseline to the Same Clients After 5, 10, and 15 Sessions of pIR HEG

	Baseline	After 5 sessions	Effect size	After 10 sessions	Effect size	After 15 sessions	Effect size
PHQ	12.09	8.299***	*g* = .60	5.935***	*g* = .96	3.619***	*g* = 1.4
GAD	12.104	8.672**	*g* = .60	6.109***	*g* = 1.1	4.571*	*g* = 1.1
GSE	29.03	30.463	N/A	32.739**	*g* = −.71	33.524*	*g* = −1.0
CSE	118.015	145.149***	*g* = −.58	169.043***	*g* = −1.05	187.286**	*g* = −1.4
LO	113.418	90.567***	*g* = .76	77.652***	*g* = 1.34	64.524***	*g* = 1.55
Sample	*n* = 66	*n* = 66		*n* = 46		*n* = 21	

Statistical significance associated with *t*-tests ***$p < .001$, **$p < .01$, *$p < .05$.

Data was analyzed using a series of paired one-tailed *t*-tests to see if clients benefitted from additional sessions. Table 9 reveals results comparing patient scores after 5 sessions with their scores after 10 sessions. Table 10 shows results of comparing patient scores after 10 sessions with their scores after 15 sessions. All measures show additional statistically significant changes in client scores between 5 and 10 sessions. Between 10 and 15 sessions, all measures showed statistically significant changes except anxiety which essentially stayed stable between 10 and 15 sessions. Effect sizes were calculated for any statistically significant results. Hedges' g was used to compute effect sizes via the following link: https://effectsizecalculator.herokuapp.com/#paired-samples-t-test. See Tables 8–11 for estimated effect sizes.

Table 9

Paired One Way T-Tests Comparing Post 5 Sessions to Post 10 Sessions (n = 46)

	After 5 sessions	After 10 sessions	Effect size
PHQ	7.61	5.93**	*g* = .33
GAD	8.2	6.12**	*g* = .42
GSE	30.85	32.74***	*g* = −.46
CSE	148.96	169.04***	*g* = −.41
LO	87.43	77.65**	*g* = .35

Statistical significance associated with *t*-tests ***$p < .001$, **$p < .01$, *$p < .05$.

Table 10

Paired One Way T-Tests Comparing Post 10 Sessions to Post 15 Sessions (n = 21)

	After 10 sessions	After 15 sessions	Effect size
PHQ	5.38	3.62**	*g* = .45
GAD	4.81	4.57	N/A
GSE	32.05	33.52*	*g* = −.39
CSE	171.95	187.29**	*g* = −.34
LO	73.57	64.52*	*g* = .32

Statistical significance associated with *t*-tests ***$p < .001$, **$p < .01$, *$p < .05$.

Table 11

Dissociative Experiences Scale- Brief (DES-B) Results

	Baseline	After 5 sessions	Effect size	After 10 sessions	Effect size	After 15 sessions	Effect size
DES-B	10.0	9.0	N/A	7.41**	*g* = .59	5.73**	*g* = .49
Sample	*n* = 48		*n* = 22		*n* = 15		

Statistical significance associated with *t*-tests ***$p < .001$, **$p < .01$, *$p < .05$.

Discussion

This study demonstrates the possible advantages of integrating noninvasive prefrontal neurofeedback into the treatment of common mental health conditions. In particular, we examined the application of pIR HEG neurofeedback which has shown positive results for the safe and effective treatment of migraines but has not been formally examined in the treatment of mental health. HEG neurofeedback approaches have the dual advantage of being easily implemented in a traditional mental health office setting as well as allowing direct training of the PFC.

The current study showed significant changes in anxiety, depression, general self-efficacy, limbic overload, and coping self-efficacy after five sessions of pIR HEG when compared to baseline. The changes after five sessions yielded moderately large effect sizes (g = .58–.76) and these positive changes were both maintained and enhanced with additional sessions. Effect sizes for within-group analyses increased when comparing scores after 10 sessions and after 15 sessions with all outcome measures showing very large effect sizes (g = .71–1.55).

Limbic Overload (Baker, 2020) was created using a test construction process based on previous qualitative reports from 100 clients regarding the changes they perceived as a result of pIR HEG neurofeedback. The LO scale demonstrated high internal consistency. The LO scale shows moderate to strong positive correlations with depression and anxiety, moderate positive correlation with dissociation, and moderate negative correlations with global self-efficacy and coping self-efficacy. The LO scale scores indicated that clients felt less stuck, avoidant, and less overwhelmed as their neurofeedback sessions increased, consistent with early qualitative reports from clients.

DES-B was used to assess the impact of this noninvasive brain training on dissociative experiences. Scores decreased from a mean of 10 at baseline to a mean of 5 at 15 sessions. Clients reported fewer aberrant experiences of depersonalization and derealization after receiving neurofeedback. This also provides converging evidence of clients' qualitative reports in terms of feeling present, less reactive, and more emotionally tolerant.

The results of the current study provide some initial evidence that the impact of pIR HEG sessions on mental health outcomes is noteworthy in a few different ways. One is the robustness of clinical changes reported. The range in anxiety and depression scores reveal the scope of these changes (see Table 7). At baseline, 62% of our sample reported moderate or severe depression on the PHQ-9. After 15 sessions, 100% of clients reported depression in the mild or minimal range. A similar robust pattern was observed in anxiety. At baseline, 61% of our sample reported anxiety in the moderate or severe range on the GAD-7. After 15 sessions, 90% of clients reported that their symptoms had fallen into the minimal to mild range of anxiety.

Findings in the realm of self-efficacy are also worth noting. Both general self-efficacy (after 10 sessions and after 15 sessions) and coping self-efficacy (after 5, 10, and 15 sessions) showed significant increases. Self-efficacy is an important predictor of function in many domains. In Bandura's theory of self-efficacy, performance accomplishments are the most potent contributor to one's overall self-efficacy (Bandura, 1997). According to the theory, in the realm of coping and healthcare, somatic indicators (or what is perceived in the body) is also a significant contributor. The increases in global and coping self-efficacy seen in this study make sense in the context of neurofeedback influencing the experience of somatic indicators of safety and tolerance rather than fear and overwhelm. Even more significant is what happens when people rapidly develop coping self-efficacy. Having higher self-efficacy results in people approaching tasks that they would generally avoid or give up on. By approaching coping tasks and persisting, clients rapidly build coping accomplishments in a way they have generally not experienced before. In addition, after experiencing some success and feelings of capability, clients are more open to reflect on times where their coping is challenged. From this perspective, an intriguing aspect of neurofeedback in mental health is the possibility of creating a snowball effect with somatic changes, emotional tolerance, self-efficacy, and reflective learning enabling a new level of personal agency, coping, and health over the longer term (Baker, 2022).

Limitations

The pIR HEG system used does not produce a metric of activity in the PFC that can be compared before and after sessions. This study does not include specific data on PFC activation increasing or decreasing over time. Previous studies have used infrared camera images to show a reduction in thermal variability in the PFC with pIR HEG sessions (Carmen, 2004; Coben et al., 2008).

Although multiple measurements over time in this study present a design advantage, conclusions based

on the current study are limited by the pre-post within-subjects design. Without random assignment and control groups, we cannot conclude that the pIR HEG neurofeedback is responsible for the effects we have demonstrated here. In addition, it is possible that the clinician's attention to "change" through graphing changes in questionnaire measurements and discussing them with clients led to some of the robustness of these changes. Data-driven practice could affect outcomes through the clinician's active attention and interest in the possibility of change. If sharing continuous data with clients contributes to the robustness of the neurofeedback effects, it could be adopted by neurofeedback practitioners both to enhance care and provide validation of the method being used. We need well-designed larger scale studies on EEG and HEG neurofeedback as applied to mental health populations. In the meantime, given the number of systems being used, it makes ethical and practical sense to integrate a data-driven approach to continuously evaluate and validate the impact of neurofeedback on mental health.

In this naturalistic study, because we included people both with PTSD, without PTSD, with a trauma-focused reason for seeking care, and those seeking care for other reasons, we cannot make conclusions if results would vary in some way if these groups were looked at separately.

In addition, the present study does not look at any follow-up data. Even though it appears that 5 sessions of pIR HEG can be potent and 10 or 15 sessions even more potent, it does not assess the longevity of the effects over time.

By suggesting that a simple system like pIR HEG can have a relatively fast and powerful impact on the treatment of mental health, it would be easy to conclude that the myriad of guided meditation apps or at-home brain training devices could result in such significant changes. Although individuals may gain significant relief with self-treatment, at home treatment suffers from lack of consistency and implementation standards. Harnessing new implicit skills that come online as a result of neurofeedback can be significantly enhanced by a knowledgeable clinician. Skilled clinicians help clients interpret changes and develop a new way of observing themselves and their coping responses. Clinicians can observe how brain changes manifest in thinking and behavior and can help clients to connect the dots. Without helpful observation and guidance, clients are likely to ignore aspects of their behavior that are inconsistent with their familiar habits or historical self-beliefs (Bandura, 1997; Dana, 2018).

In summary, studies like this one do not fill the need for well-designed research studies on neurofeedback and mental health. On the other hand, such qualitative and quantitative reports can provide a clear ethical and scientific motivation to engage in further study. Through the targeted use of neuroscience technology, we may be able to consistently improve executive function across diagnoses in an effective and efficient manner. In fact, given the ease of implementation in an office setting and no side effects, the pIR HEG tool is a low-risk medical device which can teach us that we can easily target psychophysiological aspects of mental health and, when we do, treatment might be able to take a new course. In meeting the ever-increasing mental health needs of our human population, efficient and effective approaches are critical. The current study demonstrates that neurofeedback and other neuroscience informed learning technologies may be able to help providers design shorter term models that actually address underlying psychophysiology, build implicit skills, and instigate strong shifts in self-efficacy needed to live well in an ever changing, stressful world.

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