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Aim and Scope

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RESEARCH PAPERS

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Bidirectional Alpha Power EEG Neurofeedback During a Focused Attention Meditation Practice in Novices

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Abstract

Background. Neurofeedback and meditation practices are techniques aimed at enhancing awareness and self-regulation. Training of alpha power has been found to increase mindfulness outcomes, and increases in alpha power seem relatively consistent during focused attention meditation practices. Considering the commonalities between these self-regulation techniques, we here examined the trainability of alpha power while engaging in a focused attention meditation, allowing novice practitioners to attain self-regulation with an integrated training. In a within-subject design, 31 participants (25 women, 6 men, aged 23.16, range 18–30) engaged in two types of alpha neurofeedback training conditions, one aimed at upregulating alpha, the other aimed at downregulating global alpha absolute power. **Results**. Linear mixed-effect analyses showed a differential effect of the two neurofeedback training conditions, indicating that alpha power was overall higher during upregulation compared to downregulation training. While differential alpha power was evident "online" during training, there appeared to be no "offline" transfer, as measured during a resting-state recording posttraining. **Conclusion**. These results provide relevant insights into the applicability of alpha neurofeedback combined with focused attention meditation instructions that may guide future work into the application of neurofeedback approaches for supporting meditation practice.

Keywords: EEG neurofeedback; BCI; alpha; meditation; focused attention; self-regulation

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Background

Mindfulness entails the enactment of an attitudinal quality characterized by a state of complete presence in the ongoing moment, further distinguished by a nonjudgmental and accepting stance towards the instant emerging experience (Kabat-Zinn, 2013). This quality can be dispositional—a stable idiosyncratic tendency to be mindful—and can also be cultivated further with training (Burzler & Tran, 2022). In recent years, there has been a medical and popular increasing recognition of the relevance of mindfulness to mental health, leading to a growing focus on promoting and enhancing skills such as self-regulation as a fundamental component of overall well-being (Heatherton, 2011). The interest in improving individuals' abilities to cope with stressors and regulate one's own emotional state has further given rise to the appearance of a vast number of

mindfulness-related media, such as free guided meditations on media platforms, and mobile apps (Mani et al., 2015; Plaza et al., 2013). Altogether, these tools have facilitated the integration of mindfulness practices into daily routines, providing individuals with accessible options to reap mindfulness's positive effects independently (Cavanagh et al., 2014). The effects of regular mindfulness practice arise through processes of attention regulation, body awareness, emotion regulation, and a shift in one's perspective of the self (Hölzel et al., 2011). Moreover, evidence has demonstrated that mindfulness practices exert a beneficial influence on individuals' physical well-being, as evidenced by its ability to improve stress resilience (Creswell et al., 2019), mitigate stress reactivity (Goldin & Gross, 2010; Gotink et al., 2016; Kral et al., 2018), and lower levels of physiological stress markers (Bortolla et al., 2022; Heckenberg et al., 2018; Ooishi et al., 2021; Sun et al., 2019).

The integration of technology into mindfulness practices presents a promising avenue for enhancing the level of guidance available to individuals during meditation. Furthermore, it has the potential to enhance engagement, ultimately yielding more favorable outcomes derived from the practice. Biometric sensors and wearable devices can track physiological signals providing users with valuable insights about their physiological state during the practice. For example, electroencephalographic (EEG) sensors can detect neural patterns that indicate whether individuals find themselves in the desired meditative brain state, or whether their mind has wandered off in self-generated thoughts (Pandey et al., 2022). Through the utilization of neurofeedback training, which involves continuously monitoring and presenting changes in neural activity to the mindfulness practitioner, awareness of the neurally reflected characteristics of the mindfulness session can be expanded. Individuals can thus gain insights about the adequacy and necessary adjustments to their practice (e.g., redirecting the attention towards the intended object of focus in focused attention meditations [FAM]) and improve the quality of the mindfulness session.

Regarding candidate neural signal parameters reflecting aspects related to mindfulness practices, the neural alpha band, comprehended between 8 and 14 Hz, has been extensively studied and its changes are proposed as relevant for the development of meditative skills during early stages of learning (Cahn et al., 2013; Fell et al., 2010). Alpha synchronization, the increase in alpha band activity, has been found to reflect internally directed attention during processes such as mental imagery as opposed to externally perceived stimuli (Cooper et al., 2003). This phenomenon has been robustly observed in the context of mindfulness meditation practices (Brandmeyer & Delorme, 2018; Lee et al., 2018) which are also commonly associated in the literature with increases in relaxed alertness (Britton et al., 2014; Lomas et al., 2015). Indeed, numerous studies have consistently found mindfulness meditation to be reflected by an increase in alpha power when compared to rest, in both novices (Ahani et al., 2014; Dunn et al., 1999; Milz et al., 2014) and experienced meditators (Cahn et al., 2013; Lagopoulos et al., 2009).

Several previous studies have demonstrated increases in alpha power upon neurofeedback upregulation training (Brickwedde et al., 2019; Chikhi et al., 2023; Escolano et al., 2011, 2014; Hanslmayr et al., 2005; Nan et al., 2012; Navarro Gil et al., 2018; Nicholson et al., 2023; Radüntz et al., 2017; Su et al., 2021; Uslu & Vögele, 2023; Zoefel et al., 2011). Interestingly, some studies have targeted alpha power regulation in relation to mindfulness practices. For example, Stieger et al. (2021) investigated the effects of mindfulness-based stress reduction (MBSR) training on the volitional upregulation of alpha power with a brain computer interface (BCI). The authors found that, compared to controls, participants receiving the MBSR training learned to control the BCI faster and exhibited increased upregulation of alpha power (Cohen's d = 0.68) when in rest (Stieger et al., 2021). In a further exploration of the same dataset, Jiang et al. (2021) expanded upon this finding and showed that the association between those receiving a mindfulness training and achieving better BCI control was not evident at first but instead gradually increased over the course of the BCI task, and that with more meditation practice outside of the formal training, the better the BCI control. Along the same line, da Costa et al. (2021) primed participants with mindfulness meditation prior to an alpha neurofeedback training and found an enhanced ability to regulate when compared to those not primed. Furthermore, Navarro Gil et al. (2018) found alpha power neurofeedback to increase self-reported mindfulness scores. Taken together, the literature indicates a reciprocal relationship between mindfulness and alpha neurofeedback training, wherein the effects of one positively influence the other.

In light of the parallels between mindfulness training and alpha neurofeedback training, both of which

involve an enhanced self-regulation of alpha power, we set up a study combining both approaches. Specifically, to offer participants an integrative approach to improve their self-regulation skills, we examined the feasibility of combining alpha power upregulation neurofeedback training with a FAM practice. Additionally, we included an active control condition aimed at alpha power downregulation. The following hypotheses are hereby tested: upregulation training runs will be characterized by "online" trial-by-trial increases in global alpha power as compared to the active control downregulation training runs, where trial-by-trial decreases in alpha power are expected. Furthermore, in order to test whether the effects of training are maintained "offline" outside of the training context, we measured alpha activity during resting periods before and after the training, whereby the following hypotheses are tested: comparison between the rest period after training and before training will reflect a differential increase in alpha power during upregulation runs and a decrease during downregulation runs.

Methods

Participants

Thirty-one healthy participants (25 women, 6 men, aged 23.16, range 18–30 years) with no prior experience in meditation practices participated in this study. They were recruited via flyers on social media and using personal communication. Written informed consent was obtained from all participants prior to the start of the study. Consent forms and study design were approved by the Social and Societal Ethics Committee (SMEC) of the KU Leuven university (G-2018 12 1,463), in accordance with the World Medical Association Declaration of Helsinki. Participants were compensated for their participation at a rate of 10€ per hour.

Design and Task

EEG recordings were obtained while participants sat in a comfortable chair, facing the computer screen, and were taking part in four experimental runs in pseudorandomized order. Each run comprised an initial "pre" 3-min resting-state period, followed by six individual 2-min neurofeedback training trials and a final "post" 3-min resting-state period. A constant auditory background stimulus (the echo of a bell sound) was provided during all rest and training trials via earpods, and an additional continuous and varying feedback sound (cascade water running) was provided during neurofeedback training trials. The start and end of each rest period and training trial were indicated by a start/stop sound, prompting the participants to either close their eyes or open them and to follow instructions on the computer screen.

Prior to the start of the experiment, a short, standardized introduction was provided to the participants to familiarize them with the concept of neurofeedback and self-regulation of neurophysiological signals. This introduction included a brief explanation of autonomic nervous system activity and the objective to upregulate parasympathetic activity. Also, more detailed information regarding the specific instructions during the neurofeedback training and the structure and duration of the experiment was explained. Lastly, a volume adjustment on the to-be-presented auditory stimuli was performed individually per participant to ensure that all sounds were audible but not distracting.

Throughout the duration of the experiment, stimuli were presented to participants using PsychToolbox (Brainard, 1997). During the 3-min resting-state period (pre- and postneurofeedback training), participants were instructed to keep their eyes closed and sit comfortably while avoiding movement. During the neurofeedback training trials, and in line with FAM practices, participants were again asked to sit comfortably with eyes closed and, in addition, to focus their attention on top of the crown of their head while perceiving the feedback sound (running water) related to their brain activity. Importantly, participants were indicated not to try to influence the feedback sound directly but were informed that, by engaging in the focused attention on the crown of their head, self-regulatory processes would allow attaining the highest level of positive feedback (i.e., increasing volume of the running water sound).

In two of the four neurofeedback training runs, the running water feedback sound increased in volume with increasing global (average scalp) alpha power (alpha upregulation condition). In the other two training runs, the feedback sound increased with decreasing global alpha power (alpha downregulation condition). In every run, after each block of three training trials, participants were asked to report via a numerical keyboard their levels of tiredness, pleasantness, and calmness and the degree of focus on the crown of the head, as well as focus on the auditory stimuli.

The five questions were as follows, on a scale of 1 to 9:

(a) how tired are you?
(b) how pleasant are you feeling?
(c) how agitated are you?

(d) how well did you focus on the crown of your head?
(e) how well did you focus on the sounds?

For all questions, the response scale contained visual or textual cues. Since the study was not specifically designed to assess training-induced changes in the behavioral scores, results from these behavioral assessments are reported in supplementary information (Appendix Figure A1). In short, no significant training-specific changes were noted in any of the behavioral scores.

EEG Recordings

The Nexus-32 system (version 2015a, Mind Media, The Netherlands) was used for EEG recordings. Data was streamed to MATLAB (2019a) and recorded through the software Lab Stream Layer (LSL). The OpenVibe software was used for data quality checks during sensor placement and for data monitoring during the experiment. Continuous EEG was recorded with a 22-electrode cap (one ground electrode and two on the mastoids for reference) positioned according to the 10–20 system (MediFactory). Electrode paste (Nuprep) was used to reduce the electrode impedances during the recordings. The EEG signal was amplified using a unipolar amplifier with a sampling rate of 1024 Hz. EEG recordings were synchronized to the presented task using Matlab and Lab Stream Layer.

EEG Online Preprocessing, Feature Extraction, and Feedback

EEG preprocessing was performed through custom MATLAB scripts and EEGlab functions (Delorme & Makeig, 2004). After collection of the initial 3-min resting state at the beginning of each run, data was filtered between 1 Hz and 40 Hz to attenuate nonphysiological EEG artifacts (function *pop_eegfiltnew*). Subsequently, artifact subspace reconstruction was used with the function *asr_calibrate_r* (Chang et al., 2020) with a cutoff of 20, for further cleaning of the baseline. Lastly, points with absolute amplitudes exceeding 100 µV were set to 0. Then, short-term fast Fourier transformation (STFFT) was performed on the clean data in 1-s windows, with 90% overlap between 8 and 14 Hz (in steps of 1 Hz) per electrode. Then the absolute alpha power was averaged across electrodes and the time domain deriving a single initial resting-state alpha absolute power value. Subsequently, during each of the 2-min neurofeedback training trials, incoming data in chunks of 1 s were preprocessed with the same steps as the baseline, and resulting average absolute alpha power was used to calculate a *z*-score dependent on the resting-state period absolute power. With a table of matching *z*-score alpha power values and corresponding auditory feedback volumes, the feedback was delivered to participants by changing the volume of the sound (i.e., with continuously increasing volume in the case of alpha upregulation training trials upon increasing alpha absolute power and increasing volume upon decreasing alpha absolute power during downregulation training trials). A dynamic smoothing over time was introduced to maintain smooth feedback transitions for enhancing or diminishing the feedback sound volume.

EEG Offline Preprocessing and Analysis

Offline preprocessing was performed through custom MATLAB scripts (MATLAB version r2020b) and EEGlab functions (Delorme & Makeig, 2004). After removal of the first 3 s of the recording, raw EEG data were filtered with the *eegfiltnew* function first with a high-pass filter over the 1 Hz frequency to suppress the low-frequency noise, then with a notch filter on 50 Hz, used to remove the line noise (5th order butterworth filter with cutoff frequencies on 49–51 Hz) and lastly with a low-pass filter (40 Hz). Flat channels were detected and removed (function *clean_flatlines*) and reconstructed using spherical interpolation. The remaining epochs were then concatenated, and the continuous signals were mathematically rereferenced offline to common average. Subsequently, Independent Component Analysis (ICA) was performed (using the function *pop_runica*), to automatically reject components in the data associated with muscle, heart, or channel noise artifacts. Then data was downsampled from 1024 Hz to 256 Hz and epoched into 1-s segments.

The time-frequency representation of the EEG data was obtained using STFFT computed through the MATLAB *spectrogram* function (Hanning window length of 1 s; 90 % overlap, 1 Hz resolution between 1 and 40 Hz. A total of 29 relative amplitudes (% of overall power, in µV) within the alpha (8–14 Hz) band were estimated per participant, electrode, resting-state recording (prerest and postrest), neurofeedback training trial (trial 1 to 6) and run (run 1 and 2).

Statistical Analyses

All statistical analyses were executed with Statistica version 14 (Tibco Software Inc.). Linear mixed-effect models were used to test the training intervention effect on alpha absolute power (8–14 Hz), with the random factor *participant*, and fixed factors *training condition* (up- vs. downregulation), *run* (first vs. second), *training trial* (1, 2, 3, 4, 5, and 6) and

electrode (19 scalp electrodes), as well as interactions amongst all fixed factors.

To explore whether training-induced up- or downregulation of alpha power would persist outside the explicit training context (i.e., to the resting-state period recorded posttraining), the 3-min pre- and post-resting-state period recordings were subjected to a linear mixed-effect model with the random factor *participant*, and the fixed factors *training condition* (up- vs. downregulation), *run* (first vs. second), *rest period* (pre- vs. posttraining period) and *electrode* (19 scalp electrodes), as well as interactions amongst all fixed factors. These analyses allowed examining whether the up- and downregulation of alpha power upon the experimental training session were transferable to the subsequent resting-state recording, indicating transfer of the trained neural parameter outside the explicit training context.

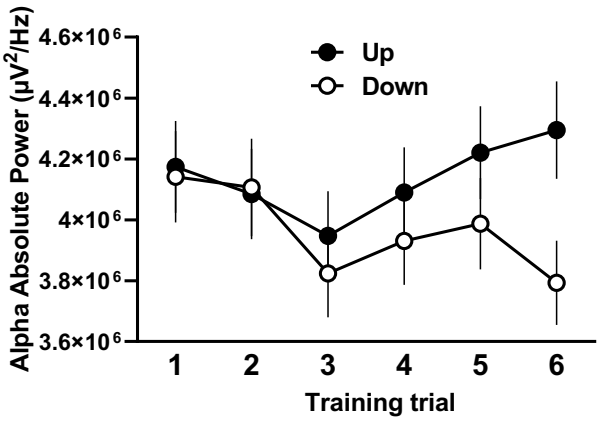
Results

Alpha Up- and Downregulation Across Neurofeedback Training Trials

The linear mixed-effect model revealed a significant main effect of training, $F(1, 30) = 10.49$, $p < .001$, $\eta^2 < .001$. This indicated an overall higher alpha power for the upregulation (mean up = $4.14x10^{+6}$ µV, $SD = 2.25x10^{+5}$) compared to the downregulation training condition (mean down = $3.96x10^{+6}$ µV, $SD = 2.32x10^{+5}$). In addition, as visualized in Figure 1, a tentative but nonsignificant trial by training interaction effect was found, $F(18, 30) = 2.05$, $p = .07$, $\eta^2 < .001$. This suggested a differential effect of training across trials. Post hoc analyses confirmed that only at the last, sixth trial ($p_{Bonferroni} = .007$) but not at the first training trial ($p_{Bonferroni} = 1.00$), alpha power was significantly higher in the upregulation when compared to the downregulation training condition.

In addition to the main effect of *training*, a main effect of *electrode* was also found, $F(18, 30) = 591.97$, $p < .001$, $\eta^2 = .44$. This indicated overall higher levels of absolute alpha power at occipital and temporal electrodes (O1, O2, T5, and T6), as well as a main effect of *run*, $F(1, 30) = 34.36$, $p < .001$, $\eta^2 = .002$. This indicated an overall higher alpha power during the second run when compared to the first run (mean run 1 = $3.89x10^{+6}$ µV, $SD = 1.48x10^{+5}$; mean run 2 = $4.20x10^{+6}$ µV, $SD = 2.15x10^{+5}$). However, these factors did not yield any significant interactions with the factor *training* (all $p > .05$), indicating that training effects were not significantly different between conditions, with respect to electrode effects and for the first compared to the second training run (see Appendix Figure A2 for a visualization of the training effects over trials, separately for the first and second training runs). Lastly, for the *trial* factor, a trend but nonsignificant main effect was found, $F(5, 30) = 2.16$, $p = .06$, $\eta^2 < .001$.

Figure 1. *Change in Alpha Absolute Power During Neurofeedback Training*.



Note. Average global alpha absolute power recorded during neurofeedback training is visualized separately for each of the six training trials, across the two runs, and separately per training condition (white: downregulation training; black: upregulation training). Vertical bars denote ± standard errors.

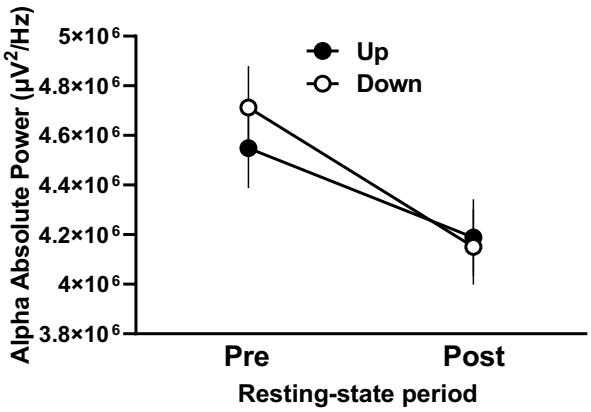
Further, to specifically explore the change in alpha power over trials for each training condition, mixed-effect models testing the main effect of *trial* were employed separately per condition. For the downregulation condition, a significant main effect of *trial* was present, $F(5, 30) = 2.46$, $p = .03$, $\eta^2 = .002$. This indicated a reduction in alpha absolute power across trials (mean trial 1 = $4.14x10^{+6}$, $SD = 5.16x10^{+6}$; mean trial 6 = $3.79x10^{+6}$, $SD = 4.76x10^{+6}$). For the uptraining condition, however, no significant main effect of *trial* was identified, $F(5, 30) = 1.77$, $p = .12$, $\eta^2 = .002$. This indicated a nonsignificant increase in alpha absolute power over trials (mean trial 1 = $4.17x10^{+6}$, $SD = 5.18x10^{+6}$; mean trial 6 = $4.29x10^{+6}$, $SD = 5.51x10^{+6}$).

Transfer of Alpha Up- and Downregulation Training Effects Outside of the Training Context

To examine whether the induced up- or downregulation of alpha power was transferable to the subsequent resting-state recording, we investigated differences in alpha power from pre- to posttraining rest periods (see Figure 2). A significant

main effect of *rest period* was identified, indicating an overall lower alpha power at the post- compared to the pre-resting-state recording, $F(1, 30) = 6.70$, $p = .01$, $\eta^2 = .1$, mean pre = $4.63x10^{+6}$, SD = $5.65x10^{+6}$, mean post = $4.17x10^{+6}$, SD = $5.08x10^{+6}$). No significant *rest period x training condition* interaction effect was identified, $F(1, 30) = 1.11$, $p = .29$, $\eta^2 < .001$. This indicated that the pre-to-post decrease in resting period alpha power was evident for both the up- and downregulation training condition. Additionally, no significant main effect of *run,* $F(1, 30) = 2.78$, $p = .09$, $\eta^2 < 0.001$, or any interactions with this factor were identified (all $p > .05$). See Appendix Figure A3 for a visualization of the training effects over rest periods, separately for the first and second training runs.

Figure 2. *Alpha Absolute Power Recorded During a Resting-State Period, Pre- and Postneurofeedback Training*.



Note. Average global alpha absolute power is visualized separately for the resting state period recorded pre- and postneurofeedback training, across the two runs, and separately per training condition (white: downregulation training; black: upregulation training). Vertical bars denote ± standard errors.

Discussion

In this study we developed and implemented an EEG neurofeedback protocol to train alpha power in the context of a FAM practice. In a single training session, 31 young adults took part in two runs aimed at training alpha power upregulation, and an additional two runs aimed at alpha power downregulation, serving as an active control condition. We hypothesized that upregulation training runs would induce "online" trial-by-trial increments in global alpha power in contrast to the active control downregulation training runs, which were anticipated to induce trial-by-trial reductions in alpha power. Moreover, to assess the "offline" persistence of training effects beyond the training environment, we examined alpha activity during periods of rest prior to and following the training. We hypothesized that the comparison between the rest period after training and the rest period before training would reveal a distinct increase in alpha power during upregulation runs and a decrease during downregulation runs.

With respect to online neurofeedback training effects, we revealed a significant difference between the up- and down-training condition, indicating higher alpha power levels during the upregulation, compared to the downregulation neurofeedback training. Particularly for the alpha power downregulation, significant alpha power decreases were evident from the first to the last training trial.

Previous studies have consistently found increases in alpha power upon upregulation training (Brickwedde et al., 2019; Chikhi et al., 2023; Escolano et al., 2011, 2014; Hanslmayr et al., 2005; Nan et al., 2012; Navarro Gil et al., 2018; Nicholson et al., 2023; Radüntz et al., 2017; Su et al., 2021; Uslu & Vögele, 2023; Zoefel et al., 2011). Similarly, other studies have found successful downregulation of alpha power during training (Brickwedde et al., 2019; Deiber et al., 2020; Kluetsch et al., 2014; Ros et al., 2010, 2013). Similar to our study, Kluetsch and colleagues (2014) succeeded to reduce alpha amplitude during a single 30-min session desynchronization neurofeedback when comparing training to baseline.

As indicated, our design included bidirectional alpha power up- and downregulation. Although literature about training bidirectional regulation of alpha power is scarce, Brickwedde et al., (2019) successfully trained somatosensory alpha power and found facilitation of tactile perceptual learning upon alpha upregulation and hindering of learning upon alpha downregulation. In this study, they also showed that higher baseline alpha activity was required to achieve the behavioral learning outcome. This is in line with other studies predicting trainability of alpha based on baseline alpha activity (Chikhi et al., 2023; Nan et al., 2018; Su et al., 2021; Wan et al., 2014).

Regarding the retention of 'offline' training effects, as measured comparing pre- to post-rest periods, our analyses revealed that, for both conditions, a significant overall reduction of alpha power was evident following the training. Although this transfer effect was expected for the downregulation condition, it contrasted with our hypothesis regarding

upregulation training. Previous studies investigating the offline transferability of upregulation alpha power training to subsequent rest recordings have found increases in alpha power (Escolano et al., 2011; Nicholson et al., 2023; Zoefel et al., 2011) as compared to the control group, whereas others have not (Escolano et al., 2014; Nan et al., 2012; Navarro Gil et al., 2018; Uslu & Vögele, 2023). With respect to downregulation trainings, other studies have demonstrated that downregulation of alpha can lead to decreases in the resting alpha power level (Ros et al., 2010, 2013). However, other studies have found no influence of downregulation on the alpha power on subsequent recordings of resting periods (Nan et al., 2018; Ros et al., 2017). It might be the case that, for neurofeedback effects to be maintained, the intervention requires several training sessions, in particular when addressing clinical as opposed to nonclinical populations (Dekker et al., 2014; Nicholson et al., 2023). Interestingly, regarding nonclinical populations, Uslu and Vögele (2023) argue that instead of the number of sessions, self-paced neurofeedback, providing participants with the possibility to arrange the timing of their training, has a positive impact on cognitive performance changes upon neurofeedback.

While our work adds new insights into the application of alpha neurofeedback during FAM, the following limitations and directions for future research are highlighted.

With respect to the control condition choice in neurofeedback experiments, there is a plethora of options (Sorger et al., 2019), and the optimal one depends on the objectives of the experiment. In this study, we found significant differences between the active alpha up- and alpha downtraining condition. Although an active control condition allowed for assessing the specificity of our training with respect to regulation direction, future studies should address whether training-specific effects are also evident in comparison to a sham control condition. Further, neurofeedback studies frequently encounter subgroups of participants that are not able to control the target parameter (i.e., nonresponders or BCI illiterates). Future studies should warrant the assessment of predictors of individual trainability as recommended in previous literature (Alkoby et al., 2018). For example, there is growing evidence that alpha power levels at baseline predict the ability to further self-regulate alpha during a neurofeedback protocol (Chikhi et al., 2023; Nan et al., 2018; Su et al., 2021; Wan et al., 2014). Additionally, mindful skills and their priming have also been regarded as a possible predictors and facilitators for neurofeedback training (da Costa et al., 2021; Stieger et al., 2021).

Finally, the observation that particularly alpha downtraining was successful indicates that upregulation of alpha might require more training trials and/or sessions. Indeed, it can be anticipated that particularly for individuals who are new to the practice of mediation and/or self-regulatory neurofeedback, establishing a parallel relationship between the targeted upregulation of alpha power during neurofeedback and meditation expertise might necessitate a higher intensity or longer duration of the training.

Conclusion

The present study provides initial evidence that up- versus down-training of global alpha power during a focused attention meditation practice yielded a significant differential pattern, particularly indicating a significant decrease in alpha power upon downregulation. Training effects did however not sustain during a subsequent resting-state recording, indicating no transfer of upregulated alpha power outside the active training context. Together, these results provide important insights into the applicability of alpha neurofeedback training as an adjunct to and in support of meditation practice.

Author Disclosure

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Author Contributions

Javier R. Soriano: conceptualization, methodology, software, validation, formal analysis, writing original draft, visualization, investigation, resources, data curation, supervision, project administration, writing review and editing.

Eduardo Bracho Montes de Oca: methodology, software, writing review and editing.

Angeliki-Ilektra Karaiskou: formal analysis, writing review and editing.

Hendrik-Jan de Vuyst: data curation, writing review and editing.

Julio Rodriguez-Larios: funding acquisition.

Naishi Feng: data curation.

Carolina Varon: supervision, writing review and editing.

Kaat Alaerts: conceptualization, formal analysis, visualization, writing review and editing, supervision, funding acquisition.

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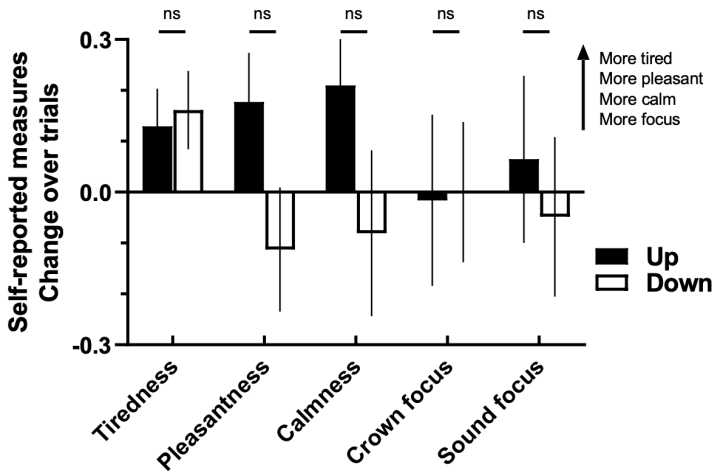
Appendix A

Changes in Self-Reported Measures Across Neurofeedback Training Trials

On an exploratory basis, differential changes in levels of self-reported measures of tiredness, pleasantness, calmness, focus on the crown of the head, and focus on the sounds upon receiving alpha up- or downregulation feedback were assessed. To do so, change scores were calculated for each self-reported measure (change from mid [after Trial 3] to end reports [after Trial 6] within each run) and subjected to a linear mixed-effect model with the random factor *participant*, and fixed factors *training condition* (up vs. downregulation) and *run* (first vs. second), as well as interactions amongst the fixed factors.

Analyses revealed no significant main effects of *training* for self-reported tiredness, $F(1, 30) = .1$, $p = .76$, $\eta^2 < .01$; calmness, $F(1, 30) = 2.01$, $p = .16$, $\eta^2 = .02$; focus on the crown, $F(1, 30) < .01$, $p = .94$, $\eta^2 < 0.01$; or focus on the feedback sound, $F(1, 30) = .23$, $p = .63$, $\eta^2 < .01$. For self-reported pleasantness, a trend but nonsignificant main effect of *training*, $F(1, 30) = 3.13$, $p = .08$, $\eta^2 = .03$, indicated tentative increases in reports of pleasantness over trials during alpha upregulation compared to downregulation. None of the remaining main or interaction effects were significant (all $p > .05$).

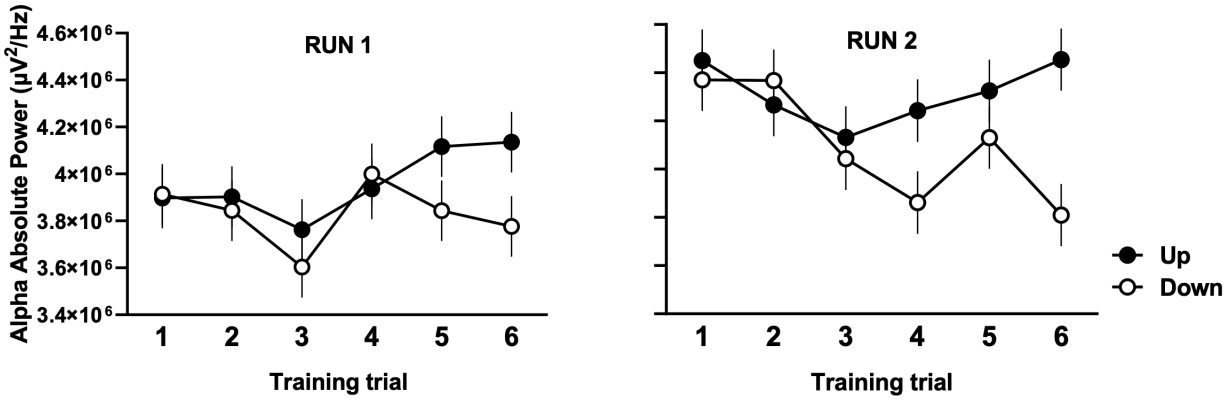
Figure A1. *Changes in Self-Reported Measures Across Neurofeedback Training Trials.*



Note. Changes in self-reported scores (change from mid [after Trial 3] to end [after Trial 6] are depicted across runs, separately per training condition (white: downregulation training; black: upregulation training). Vertical bars denote ± standard errors; "ns" indicates nonsignificant effects ($p > .05$).

Alpha Absolute Power Recorded During Neurofeedback Training Trials in Run 1 and Run 2

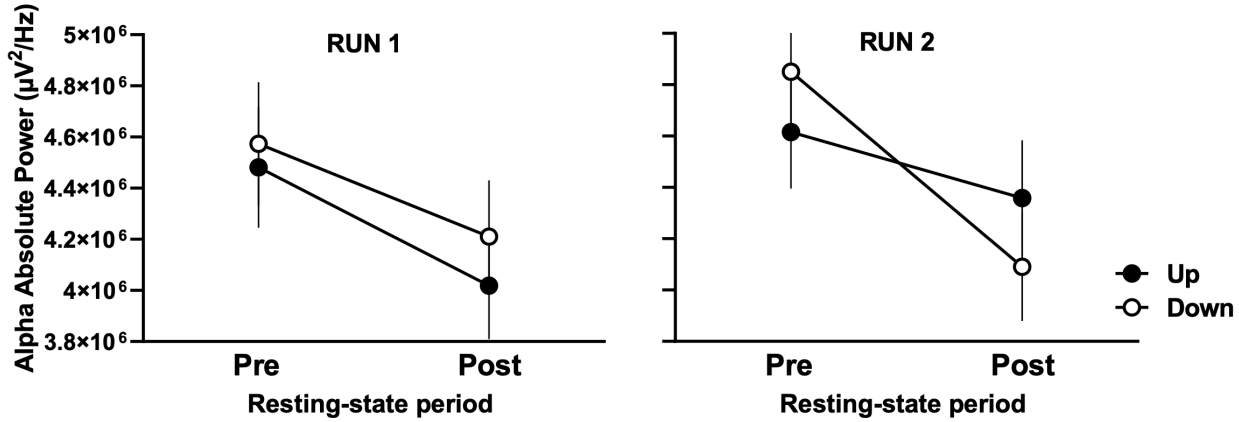
Figure A2. *Alpha Absolute Power Recorded During Neurofeedback Training Trials in Run 1 and Run 2.*



Note. Average global alpha absolute power recorded during neurofeedback training is visualized separately for each of the six training trials, separately for each run and training condition (white: downregulation training; black: upregulation training). Vertical bars denote ± standard errors.

Alpha Absolute Power Recorded During a Resting-State Period, Pre- and Postneurofeedback Training During Run 1 and Run 2

Figure A3. *Alpha Absolute Power Recorded During a Resting-State Period, Pre- and Postneurofeedback Training During Run 1 and Run 2.*



Note. Average global alpha absolute power is visualized separately for the resting-state period recorded pre- and postneurofeedback training, separately for each run and training condition (white: downregulation training; black: upregulation training). Vertical bars denote ± standard errors.

NeuroRegulation

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Effect of High-Intensity Intermittent Exercise on Cortical Hemodynamic Changes in Response to Recognition Memory and Visuospatial Tasks

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Abstract

We investigated the acute effects of high-intensity intermittent exercise (HIIE) on cortical hemodynamic changes and sex differences during recognition memory and visuospatial tasks. Forty-six healthy adults (18–30 years) were randomly assigned to HIIE (*n* = 23, including 11 males and 12 females) or control groups (*n* = 23, including 10 males and 13 females). Functional near-infrared spectroscopy measured prefrontal cortex (PFC) activation during Warrington's word and facial Recognition Memory Test (RMT), and Shipley-2 test before and after the intervention. HIIE resulted in improved word recognition memory scores, but no significant changes in face recognition or visuospatial scores. PFC activation during tasks did not significantly differ following HIIE. Sex differences were observed, with males showing greater word recognition memory scores and associated hemodynamics compared to females, but no sex differences in face recognition or visuospatial tasks in response to HIIE. In summary, HIIE improved word recognition memory without affecting PFC activation. Moreover, sex differences in PFC activation during word recognition tasks were evident following HIIE. These findings contribute to our understanding of the acute effects of HIIE on cognitive performance and highlight the potential influence of sex on cortical hemodynamics during word recognition memory tasks.

Keywords: recognition memory; visuospatial functions; cortical hemodynamics; prefrontal cortex

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Introduction

It has been established that exercise yields cognitive benefits. Regular exercise not only improves cognition but also preserves neuroplasticity and prevents neurodegeneration (Berchtold et al., 2001; Bonanni et al., 2022; Cotman et al., 2007; Hillman et al., 2003; Mahalakshmi et al., 2020; Marques-Aleixo et al., 2021). Studies have examined the effects of physical exercise on executive functions (Alves et al., 2012; Bonanni et al., 2022; H. Chang et al., 2017; Y. K. Chang et al., 2012), memory (Hötting et al., 2016), and attention (Alves et al., 2014). Animal studies have demonstrated the positive effects of physical exercise on recognition memory and nonspatial memory (Hopkins & Bucci, 2010), while exercise has also been found to benefit visuospatial ability in elderly individuals (Tsai et al., 2016). However, the number of available studies investigating the impact of exercise on recognition memory and visuospatial functions is limited, and they present conflicting evidence.

This conflict may arise from variations in exercise type (Loprinzi et al., 2021), duration (Zou et al., 2020), exercise intensity (Taverniers et al., 2010), and participants' fitness levels (Wang et al., 2015). A recent study suggests that memory functions are influenced by exercise intensity, with high-intensity exercise demonstrating the greatest benefits (Kovacevic et al., 2020). However, the relationship between high-intensity intermittent exercise (HIIE) and changes in these cognitive functions remains unclear. HIIE involves brief exercise bouts at

maximal intensities followed by low-intensity exercise or rest intervals (Boutcher, 2011). Additionally, HIIE has been associated with the maintenance of cognitive health and has shown multidimensional cognitive benefits (Matthews et al., 2009; Tsukamoto et al., 2016). However, the impact of HIIE on recognition memory and visuospatial functions in young adults has yet to be evaluated.

Recognition memory refers to the process of identifying previously encountered objects, events, or faces (Gardiner & Parkin, 1990). It relies on the familiarity of the stimulus being recognized. The stages of recognition memory involve perceiving the stimulus, comparing it to stored data, and generating related verbal and nonverbal responses (Kim et al., 1999). Various types of stimuli can be perceived, including words, faces, objects, and sounds. Emotional associations, such as pleasant or unpleasant perceptions, can enhance this memory (Herbert et al., 2008). On the other hand, visuospatial ability entails perceiving objects and cues in relation to space and the capacity to manipulate or reorganize their spatial arrangement (Mumaw et al., 1984). It involves visualizing and manipulating spatial dimensions. Visuospatial ability enables an individual to visualize an object or image, break it down into components, and then reconstruct it using those components (Mervis et al., 1999), thereby applying this information to interact with the environment (Trojano & Conson, 2008).

Converging evidence from various neuroimaging studies including functional magnetic resonance imaging (fMRI) and functional near-infrared spectroscopy (fNIRS) has revealed specific regions within the prefrontal and parietal cortices that play a role in visuospatial working memory (Herrmann et al., 2005; Spaniol et al., 2009) and recognition memory tasks (Fusar-Poli et al., 2009; Rugg et al., 1999). Cortical activation patterns have been studied through fNIRS studies (Baker et al., 2018) showing activation of prefrontal cortex (PFC) more as compared to parietal cortex. Notably, fMRI-based investigations have shown significant activation in the bilateral dorsolateral (DLPFC) during visuospatial tasks (D'Esposito et al., 1998). Further evaluation is warranted to examine whether the activation patterns of these brain areas are modulated by physical exercise interventions such as acute HIIE.

Recognition memory is typically assessed using Warrington's Recognition Memory Test (RMT) while visuospatial functions can be evaluated using the Block Patterns subset of the Shipley-2 test. The RMT is a convenient memory test that offers advantages such as easy scoring, minimal reliance on verbal responses, and low demands on other cognitive functions like attention, organization, and motor skills (O'Bryant et al., 2003). It is a reliable and valid measure for the assessment of word and facial recognition memory (O'Bryant et al., 2003; Soukup et al., 1999). The Shipley-2 Block Patterns subset, on the other hand, assesses visuospatial abilities and requires participants to mentally manipulate and transform different patterns to complete a design. This test is a reliable and valid test as well (Lodge, 2013). In our study, we employed 24-channel fNIRS to monitor cortical hemodynamic changes over the PFC during recognition memory and visuospatial cognitive tasks. This allowed us to examine the effects of exercise interventions on cortical hemodynamic functions (Kujach et al., 2018). Previous research has shown significant increases in oxygenated hemoglobin concentration, indicating cortical activation, in the left PFC regions during recognition memory retrieval (Kubota et al., 2006), and physical exercise has been shown to enhance cerebral cortex activation (Endo et al., 2013). However, the specific impact of HIIE on these activation patterns in the cerebral cortex during recognition memory and visuospatial functions has yet to be investigated.

Evidence from the previous literature indicates presence of sex differences in memory functions (Loprinzi & Frith, 2018), with females exhibiting better performance on recognition memory tasks compared to males (Coleman et al., 2018). Nagamatsu et al. (2012) previously demonstrated that 6 months of twice-weekly aerobic exercise training significantly improved executive functions in cognitively healthy women 65 to 75 years old. Sex difference and the type of exercise regime moderates the role of exercise intervention in changing the cognitive performance (Barha et al., 2017). Regular walking activity has been shown to be associated with large volume of posterior hippocampus in females only (Varma et al., 2016). Similarly, sex differences have been observed in spatial cognitive functions and their associated cortical activation (Bao et al., 2022; Munion et al., 2019). However, sex difference in the effect of acute exercise intervention on cognitive changes and their associated brain activation pattern has not been explored. Further, no specific study has examined the impact of acute HIIE on recognition memory, visuospatial functions and their associated cortical activation in a sex-specific manner.

While specific cognitive abilities may vary with age, studying young adults can provide insights into

fundamental mechanisms underlying cognition that are applicable to other age groups. Hence, young adults were chosen as the participants of this study.

We hypothesize that there will be a significant difference in the scores of recognition memory and visuospatial functional tasks following HIIE. Additionally, we expect an increase in PFC activation during the performance of these tasks in response to HIIE. Thus, the primary objective of our study was to assess recognition memory and visuospatial functional task scores, as well as the associated hemodynamic response of the PFC before and after the HIIE intervention. Furthermore, our secondary objective was to investigate potential sex differences in the scores of recognition memory and visuospatial functions, along with the related PFC activation, in response to HIIE among young adult males and females.

Methods

Participants

The study utilized a randomized two-group pre–post experimental design. A priori power analysis was conducted using G*Power software (version 3.1.9.4, Germany), with medium effect size (0.5), alpha probability error margin of 0.05 and 80% power of the test. This analysis provided a total sample size of 42. To reduce the likelihood of type-I error, a sample size of 46 (more than the calculated sample size) was taken for further analysis. Thus, a total of 46 healthy adults aged between 18 and 30 years volunteered for the study. They were randomly assigned to either the HIIE group (n = 23, including 11 males and 12 females) or the control group (n = 23, including 10 males and 13 females) using lottery method of simple random sampling. The testing protocol was thoroughly explained to all participants, and written informed consent was obtained from each individual. Table 1 provides details of the participants' meanage, height, weight, BMI, resting heart rate, and physical activity levels. The HIIE group underwent the intervention, as described in the subsequent methods section, while the control group was instructed to rest in a seated position for duration similar to the HIIE session. Participants provided written informed consent before the initiation of the testing procedures. The study received approval from the Institutional Ethics Committee of Guru Nanak Dev University, Amritsar (approval number 158/HG, dated 1 October 2019).

Study Criteria

University students with normal or corrected normal vision and no color blindness were selected for participation. They were matched based on their IQ using the Multidimensional Aptitude Battery-II (MAB-II). Participants were instructed to consume only one cup of tea or coffee before each testing session, following the breakfast instruction sheet provided during their initial visit to the laboratory. On their first visit, they were also given the International Physical Activity Questionnaire (IPAQ) for the assessment of level of physical activity during the past week (Papathanasiou et al., 2010), Physical Activity Readiness Questionnaire (PARQ) for ruling out any cardiac, respiratory, or neurological history before the exercise testing (Agarwal et al., 2016), and Pittsburgh Sleep Quality Index (PSQI) to assess the sleep quality in the past one month (Pilz et al., 2018).

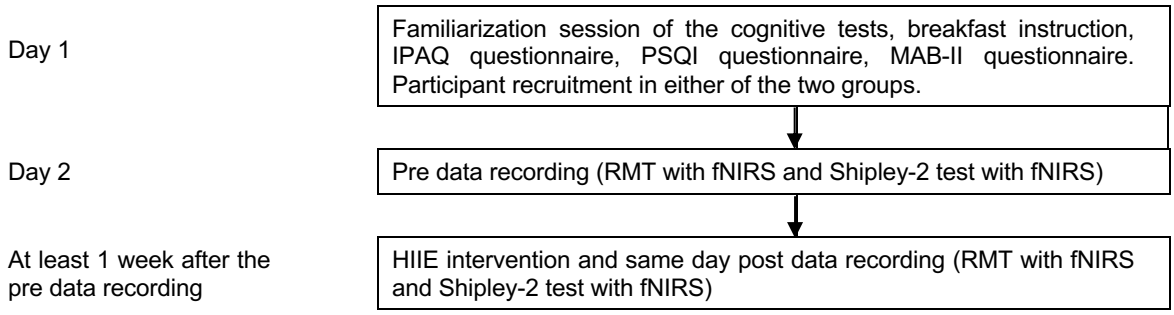
Inclusion criteria consisted of healthy male and female participants between the ages of 18 and 30, with an IQ ranging from 90 to 119 as measured by the MAB-II. Exclusion criteria included answering "yes" to any of the PARQ questions, having a history of cardiorespiratory or cerebrovascular disease, having a psychiatric or neurological condition, engaging in strenuous activity, or consuming alcohol within 24 hr prior to testing, experiencing poor sleep (as measured by the PSQI), consuming two or more cups of caffeine on the same day, or consuming a large meal within 2 hr before exercise.

Exercise Protocol

HIIE protocol of four bouts of 4 min (4*4) at 90–95% HR max with 3 min of active recovery at 70% HR max (Helgerud et al., 2007) interspersed with the intense bouts on a cycle ergometer (Lode Corival BV, Groningen-The Netherlands) was applied. Polar heart rate monitor (Polar Vantage V Pro Multisports Watch) was used to monitor heart rate during the whole exercise session. HR max (beats/min) was calculated by the formula (Fox et al., 2013).

$$\text{HR max} = 206.9 - 0.67 \times \text{age (year)}$$

Figure 1. *Study Design*.



Note. The above figure describes the study design and the timeline used for the procedure of the study. IPAQ – International physical activity questionnaire; PSQI – Pittsburgh Sleep Quality Index; MAB-II – Multidimensional Aptitude Battery-II; RMT – Recognition memory testing; fNIRS – functional near-infrared spectroscopy; HIIE – High-intensity intermittent exercise.

Participants cycled against a workload of 100–150 W at an average rate of 120 RPM and between 15 and 18 on Borg's Rating of Perceived Exertion (RPE) scale during each high-intensity bout and, with no workload, an average 91 RPM and 8–12 Borg's RPE during the recovery period. Borg's RPE was noted after 1 min of start of high-intensity bout and after the end of each of the four high-intensity bout sessions. The HIIE protocol was preceded by a 3-min warm-up and followed by a 2-min cooldown, at a pedaling frequency and intensity as per each participant's preference between 8 and 12 grading of the 20-pointed Borg's RPE scale. All the participants were able to complete the whole test with no dropouts. Interparticipant variations were seen during the exercise intervention because of the high intensity of the exercise, but the whole exercise intervention was well tolerated. All training sessions were conducted in a neurophysiology lab of MYAS-GNDU Department of Sports Sciences and Medicine of Guru Nanak Dev University, Amritsar.

Cognitive Testing

Cognitive functions were assessed using two tests: Warrington's word and face RMT and the Block Patterns test of Shipley-2. The administration order of the tests was counterbalanced between the pre- and postsessions for both groups to eliminate bias. There was a minimum gap of 1 week between the pre and postsessions to minimize the impact of learning on the cognitive tests.

Warrington's Recognition Memory Test (RMT)

This test evaluates recognition memory for both words and faces. The RMT was utilized to assess deficits in material-specific recognition memory. It consisted of two subtests: Recognition Memory for Words (RMW) and Recognition Memory for Faces (RMF). Each subtest included 50 target stimuli displayed for 3 s. Participants were required to rate each stimulus as pleasant or unpleasant, responding with a "yes" or "no" accordingly. Subsequently, participants were presented with each of the 50 target stimuli paired with a distracter and asked to identify the target stimulus by either pointing to it or reading it aloud. The number of correct responses was recorded as raw data for subsequent analysis of accuracy.

Block Patterns Test of Shipley-2

This scale is utilized to evaluate visuospatial ability (Lodge, 2013). It consisted of two parts: Part A and Part B, each containing 12 block patterns. Multiple blocks within a specific pattern were queried, resulting in a total of 26 items to be scored. Part A consisted of simple blocks to be answered, while Part B increased the difficulty level by rotating the blocks to 90 or 180 degrees. Participants were provided with multiple choices to indicate which block option would fit in the gray square within the given block pattern. The number of correct responses for both parts was recorded as raw data for subsequent analysis.

Hemodynamic Testing Using Functional Near-Infrared Spectroscopy

Hemodynamic changes, specifically oxyhemoglobin (oxyHb) and deoxyhemoglobin (deoxyHb) levels in µmol, were measured using the portable Brite Artinis fNIRS (version 24; Artinis Medical Systems, The Netherlands) brain imaging system. The measurements were taken before and after the HIIE sessions, during the cognitive testing. After the intervention, a 6- to 10-min gap was followed, right before the postintervention cognitive and fNIRS assessments. This time interval allowed the

physiological artifacts to decline, which are known to be enhanced by an increased heart and respiratory rates (Pinti et al., 2019).

Participants were in a sitting position during the measurements. The purpose of collecting fNIRS data during the RMT and Shipley-2 testing was to examine the hemodynamic changes associated with acute HIIE. To establish a baseline, 10 s of fNIRS data was collected immediately before starting the cognitive tests and also before the HIIE session, as recommended by Fox et al. (2013). During baseline data acquisition, participants were instructed to sit quietly and relax. Post-HIIE data was collected 10 min immediately after the HIIE session.

The fNIRS data was collected using a 24-channel Brite Artinis fNIRS system configured into a 3x3 optode pattern on each lateral side of the PFC, following the topographic probe layout map of the 10–20 International Standard Coordinate system (Herwig et al., 2003; Homan et al., 1987). A soft neoprene cap, selected based on the participant's head diameter, was used to secure the optodes on the participant's head. This configuration provided a total of 24 channels (12 on each side) with an overall emitter and detector separation of approximately 3 cm (Kalia et al., 2018). The channel grids were placed to cover specific regions of interest (ROI) for each hemisphere, including the DLPFC, ventrolateral prefrontal cortex (VLPFC), and frontopolar area (FPA) over the PFC. A differential path length factor was calculated based on the exact age of each participant. A sampling rate of 10 Hz was used, which is consistent with the literature (Yanagisawa et al., 2010)

For the fNIRS data, preprocessing was performed using the open-source software HOMER 2, which is implemented in MATLAB (MathWorks). All recorded signals were initially converted to optical density for processing in the HOMER 2 software. Channels with low amplitudes were excluded from group processing. The signals were then processed using the principal component analysis method to eliminate any systematic artifacts, following the methods described in previous literature (Tak & Ye, 2013). Motion artifacts exceeding a threshold of more than 15 standard deviations from the mean were identified and replaced with spline interpolation based on the preceding and subsequent segments of the signals. Wavelet filtering was applied to remove motion-induced sharp spikes, as suggested by previous literature (Jahani et al., 2018). After this processing, the signals were bandpass filtered within the frequency range of 0.02–0.5 Hz to eliminate baseline drift and physiological noise. Finally, the filtered signals were converted to oxyHb and deoxyHb concentration (μmol) data using the modified Beer-Lambert law (Cope & Delpy, 1988). To infer changes in the hemodynamic response across the participants, a block averaging method was employed.

Statistical Analysis

The cognitive data obtained was subjected to Shapiro-Wilk test in order to determine the normality distribution of the data. An independent sample *t*-test was used to compare the data of the demographic variables of the two groups at baseline. A two-way ANOVA was utilized to evaluate the main and interaction effects, with group (control/HIIE) and session (pre/post) considered as between-subject factors for RMT word, RMT face, and Shipley-2 scores. Two-way ANOVA was also used to analyze main and interaction effect of HIIE on oxy and deoxyHb concentrations with group (control/HIIE) and session (pre/post) as between the subject factors. Three-way ANOVA was used with group (control/HIIE), session (pre/post), and sex (female/male) for the evaluation of sex difference in the cognitive scores and PFC hemodynamics in response to HIIE amongst the participants. Partial η^2 values were used to report the effect sizes for the significant main and interaction effects. Bonferroni's post hoc test was used for pair-wise comparison.

Results

Word Recognition Memory

On two-way ANOVA analysis, we found a significant ($p < .05$) effect of group for the scores of RMT word, $F(1,88) = 4.44$, $p = .034$, partial $\eta^2 = 0.045$; and session, $F(1,88) = 64.98$, $p = .0001$, partial $\eta^2 = 0.35$; and a significant interaction of group*session, $F(1,88) = 13.85$, $p = .0001$, partial $\eta^2 = 0.136$ (Figure 2). These findings indicate an improvement in RMT word scores in response to HIIE intervention.

Face Recognition Memory Scores

RMT face scores showed a significant effect of session, $F(1,88) = 14.25$, $p = .001$, partial $\eta^2 = 0.139$; but no significant effect of group, $F(1,88) = 0.125$, $p = .725$, partial $\eta^2 = 0.001$; and group*session, $F(1,88) = 0.060$, $p = .807$, partial $\eta^2 = 0.001$, was observed (Figure 2). These results show no significant change in RMT face performance in response to HIIE.

Table 1
Demographic Variables of the Participants of Control and HIIE Group

	Control group	HIIE group	*t*-value	*p*-value
Number (*n*)	23	23	-	-
Male: female	10:13	11:12	-	-
Age (years)	23.95 ± 1.36	23.62 ± 1.55	0.762	.450
Height (m)	1.62 ± 0.08	1.63 ± 0.07	−0.534	.596
Weight (kg)	60.46 ± 9.32	60.08 ± 8.74	0.143	.887
BMI (m/Kg^2)	23.00 ± 3.07	22.47 ± 2.27	0.675	.503
Resting heart rate (beats/min)	81.72 ± 2.62	80.37 ± 4.78	1.172	.247
Physical activity level (measured by IPAQ in MET*min / week)	2024.93 ± 1113.95 (Moderate physical activity level)	2400.22 ± 1207.34 (Moderate physical activity level)	−1.093	.281

Note. The above table shows values of variables as mean ± standard deviation.

Shipley-2 Scores

Shipley-2 scores showed a significant effect of session, $F(1,88) = 5.69$, $p = .019$, partial $\eta^2 = 0.057$; but no significant effect of group, $F(1,88) = 3.006$, $p = .086$, partial $\eta^2 = 0.031$; and group*session was observed, $F(1,88) = 0.506$, $p = .478$, partial $\eta^2 = 0.005$. It shows that visuospatial functions were improved in both control as well as HIIE group, but HIIE did not affect the scores of Shipley-2 scale (Figure 2).

Hemodynamic Response to HIIE

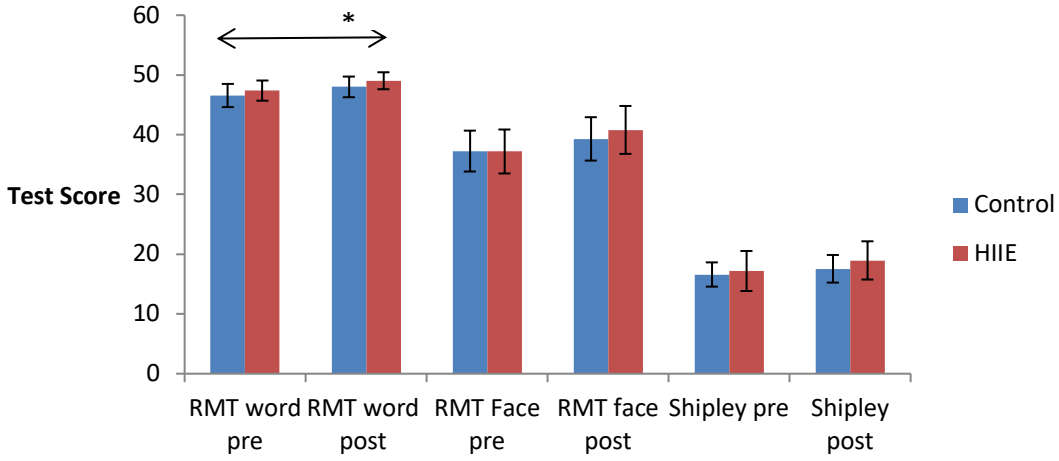
Hemodynamic Response During Warrington's Word and Face Recognition Memory Task. Pre values of oxy and deoxyHb concentration showed no significant difference between the control and HIIE group. A significant difference ($p < .05$) in the oxyHb concentration was observed in the right FPA during both RMT word ($p = .007$) and RMT face test ($p = .039$) in response to HIIE. However, deoxyHb concentration in the right FPA did not show a significant change. Activation of a particular area has been shown as an increase in the oxyHb and a decrease in the deoxyHb concentration (Lachert et al., 2017) and, thus, we cannot state the changes in the activation in response to HIIE in our study.

Hemodynamic Response During Shipley-2 Test. Post mean values of oxyHb concentration during Shipley-2 did not show a significant change in the right FPA and in any other region of interest of PFC in response to HIIE in our study. DeoxyHb concentration also showed no significant difference in response to HIIE in any of the area of interest in the PFC.

Effect of Sex of the Participant on the Cognitive and Hemodynamic Scores in Response to HIIE. A significant effect of sex was observed on word recognition memory scores ($p = .035$) shown in Table 3, with females getting more benefited with HIIE intervention compared to males. No significant effect of sex was shown on face recognition memory ($p = .989$) and Shipley-2 scores ($p = .936$).

We found a significant increase in the activation (an increase in oxyHb and a decrease in deoxyHb) in females during RMT word task in response to HIIE, where no such increase was seen in males in response to HIIE (Table 4). No significant interaction of group*session*sex was observed for oxyHb and deoxyHb concentration in any of the ROI during RMT face and Shipley-2 task, in response to HIIE in our study. It indicates that no significant sex effect of HIIE was present for the PFC activation during the performance of face recognition and visuospatial task.

Figure 2. *Changes in Cognitive Scores in Response to HIIE*.



Note. The above figure shows the variation in the mean scores of recognition memory test scores (RMT face and words) and Shipley-2 scores before and after HIIE session. Error bars represent standard deviation values. * = Indicates a significant difference between pre and post values of RMT word scores in response to HIIE.

Table 2
Changes in Cortical Hemodynamics in Response to HIIE

Test-Associated Hemodynamics	OxyHb Control (mean ± *SD*) (μ mol)	OxyHb HIIE (mean ± *SD*) (μ mol)	*p*-value	Partial η^2 values
RMT word	−9.234 ± 1.19	1.779 ± 0.14	**.007***	**0.326**
RMT faces	−4.988 ± 1.59	1.60 ± 0.06	**.039***	**0.161**
Shipley	−4.810 ± 1.63	1.233 ± 1.21	.104	0.079

Note. The above table presents the difference of post mean values of oxyHb concentration between the control and HIIE group during RMT and Shipley-2 block test in the right FPA region. * = Represents a significant difference at $p < .05$ level of significance.

Discussion

Cognitive Response to HIIE

This study aims to evaluate the effects of HIIE on recognition memory and visuospatial functions, as well as the associated hemodynamic changes. We observed a significant improvement in word recognition memory performance following the acute HIIE protocol. This finding differs from a previous study (Rattray & Smee, 2016) which reported no effect of HIIE on simple recognition memory accuracy in young adults. The disparity in results may be attributed to the difference in exercise duration, as the mentioned literature used a 1-hr protocol compared to our study's 25-min protocol. Longer durations of high-intensity exercise can deplete the body's energy stores and lead to diminished performance. In contrast, our results suggest that HIIE with a shorter duration is effective in enhancing word recognition memory.

The memory process is influenced by various neurotransmitters, including acetylcholine, glutamate, gamma amino butyric acid (GABA), adrenaline, and noradrenaline (Miranda, 2007). Improvement in recognition memory is attributed to changes in the noradrenergic system of brain. Previous studies in humans and in animal models demonstrated noradrenaline mediating recognition memory process by the activation of subcortical structures such as amygdala and hippocampus (Barsegyan et al., 2014; van Stegeren et al., 2005). Improvement in the performance of recognition memory is associated with the increase in the concentration of noradrenaline neurotransmitter in response to acute exercise intervention (da Silva de Vargas et al., 2017; Kitaoka et al., 2010; Kliszczewicz et al., 2017).

Table 3
Warrington's Recognition Memory and Shipley-2 Scores in Males and Females

Group	Control				HIIE			
Session	Pre		Post		Pre		Post	
Sex	Female	Male	Female	Male	Female	Male	Female	Male
RMT Word	46.13 ± 1.99	47.37 ± 1.68	47.53 ± 2.83	46.12 ± 2.41	44.81 ± 1.92	46.13 ± 1.80	**49.00 ± 1.03**	48.42 ± 1.13
RMT Face	36.86 ± 3.77	37.12 ± 3.22	40.86 ± 4.13	38.87 ± 2.28	38.18 ± 3.15	35.71 ± 3.48	41.37 ± 4.37	37.71 ± 4.23
Shipley-2	16.26± 2.21	17.25 ± 3.01	17.53 ± 2.72	17.62 ± 3.08	17.23 ± 1.58	17.11 ± 4.13	19.67 ± 1.40	17.66 ± 3.20

Note. The above table shows mean ± standard deviation of pre and post values of RMT and Shipley test results in males and females of control and HIIE group. Bold value represents a significant difference between pre and post values at $p < .05$ level of significance.

Table 4
Hemodynamic Changes in the Right VLPFC in Response to Word Recognition Task in Males and Females

Sex	Female				Male			
Group	Control		HIIE		Control		HIIE	
Session	Pre	Post	Pre	Post	Pre	Post	Pre	Post
OxyHb (μ mol)	0.139 ± 0.197	0.119 ± 0.10	0.023 ± 0.08	**0.565 ± 0.10**	0.100 ± 0.07	0.043 ± 0.10	0.366 ± 0.08	0.224 ± 0.06
DeoxyHb (μ mol)	−0.282 ± 0.22	0.092 ±0.29	0.509 ± 0.073	**−0.161 ± 0.026**	0.074 ± 0.01	−0.005 ±0.04	0.076 ± 0.005	−0.088 ± 0.029

Note. Bold values indicate a significant difference (at $p < .05$ level of significance) between pre and post values.

Our results of an increase in word recognition memory in response to acute HIIE in young adults are in agreement with these findings.

The enhancement in recognition memory observed in our study suggests a potential influence of changes in the noradrenergic system of the brain. This suggests a potential mechanism through which HIIE affects cortical hemodynamic changes in response to recognition memory tasks, as explored in our study.

We did not find a significant improvement in the performance of facial recognition memory. Facial recognition is a crucial cognitive domain for social interaction. It has been recently studied in depth for its role in security of electronic devices and cyber security. Facial recognition is divided into input, processing, and output stages (Anwarul & Dahiya, 2020). Input phase involves observing the identifying features of the face such as nose, eyes, lips, and cheeks. These features vary on the basis of depth, breadth, and length in the population, and these are very precisely registered in three-dimensional image forms in the brain, when an individual is seen in person. Whereas, by looking at an image of the person, only two-dimensional features are registered in the brain in the input phase. Many factors such as color, resolution, contrast, pose, expression, and light in the image affect facial identification (Sharif et al., 2017), and therefore it is a more difficult task as compared to identifying the person by direct viewing. The next phase comprises of perception of face stimuli by neurobiological mechanism of the brain. This involves several areas of brain such as hippocampus, left prefrontal cortex, inferior frontal gyri, cingulate cortex, and fusiform face area (FFA) situated in the temporoparietal area (Haxby et al., 1996). In the third phase, memory retrieval is done from the stored information in the brain areas and recognition of familiar faces, that engages PFC (Rugg et al., 1999).

Like word recognition, face recognition memory is also mediated by neurochemicals such as oxytocin (Bate et al., 2015). The changes in the facial recognition memory in response to physical exercise are attributed to the changes in the central and peripheral concentration of oxytocin. However, the concentration of this neurochemical is only increased after exercise of longer duration (more than an hour; Hew-Butler et al., 2008) and not by the

exercise of lesser duration such as high-intensity continuous exercise of 20-min duration (Gilbert & Loprinzi, 2022). Consistent with these evidences, we did not find a significant difference in the performance of facial recognition memory in our study, attributing to no change in the concentration of oxytocin.

An increase was seen in our study in the post scores of Shipley-2 test, but the effect of intervention on visuospatial scores was not clear because no interaction of sessions with group was seen. The previous literature has shown a positive effect of acute aerobic exercise on visuospatial functions in older adults and in physically fit individuals who exercised regularly; whereas, no significant effect was observed in the lower fitness group (Tsai et al., 2016). The participants of the two groups in our study belonged to the same lower fitness group, having similar IPAQ scores (Table 1) as that of this mentioned study. The findings of no significant effect of acute HIIE in our study were consistent with their results of acute aerobic exercise intervention in the lower fitness group. Fitness level is maintained by a long-term physical activity level, and it has been found to increase processing speed of central nervous system by increasing angiogenesis and blood volume in the cerebral cortex (Swain et al., 2003). Processing speed has a direct correlation with mental rotation skills and visuospatial ability (Heppe et al., 2016). Thus, it can be postulated that long-term physical activity training would be associated with a greater visuospatial performance. However, we used intervention with only one session to look for these effects in the central processing-related visuospatial improvements, which was not found significant. It seems that a single session of acute HIIE was not sufficient to raise the performance level of visuospatial ability in young adults. Further research with long-term HIIE training is warranted to look for the same.

Hemodynamic Response to HIIE

A significant effect of HIIE was observed in the change of oxyHb concentration of right FPA during both recognition of words as well as during recognition of faces in our study, but we did not find a significant effect on deoxyHb concentration in the PFC. This indicates no significant change in the activation, as we previously mentioned that activation of any area involves increase in the oxyHb and a decrease in the deoxyHb concentration. Selective response of the PFC has been observed in response to facial recognition in previous studies (Nelson, 2001; Ó Scalaidhe et al., 1999), but the effect of acute exercise intervention on PFC activation during visuospatial functions has not been studied to date. Our study was the first one to evaluate this effect in young adult males and females. However, we did not find a significant change in the PFC activation in response to acute HIIE intervention in our study. Recognition memory functions involve activation of many brain areas such as hippocampal, parahippocampal, and occipital gyrus (Yonelinas et al., 2001). PFC area also plays an important role in the formation of recognition memory (Zhou et al., 2016). Physical exercise has been shown to improve functional connectivity in PFC during recognition memory task in animal models (Dong et al., 2018). Previous research (Friedl-Werner et al., 2020) has shown that a long-term HIIE training program of 5–6 times weekly for a duration of 60 days has shown improvements in the activation of hippocampal area in participants during recognition memory task. Perhaps a single exercise session was not sufficient to raise neural responses in the PFC during recognition memory task in our study, and a prolonged training intervention is required. We also evaluated PFC response during visuospatial functions, and the findings showed that HIIE did not affect the changes in the concentration of oxyHb and deoxyHb of the PFC during visuospatial activity. Further research is needed to identify the cortical neural correlates of recognition memory and visuospatial ability in response to HIIE training protocol.

Sex Difference in the Performance and Neural Correlates of the Cognitive Tasks

We found a significant increase in the activation in both males and females in the right VLPFC in response to HIIE during the performance of recognition memory word task. However, females showed a greater activation compared to males after HIIE. More activation of the right VLPFC during word recognition task in females attributes to a significantly better performance in RMT word scores compared to males in our study. Our findings support previous studies demonstrating a better object recognition memory in women as compared to men after a moderate intensity exercise (Coleman et al., 2018).

No significant sex difference was observed for the activation during the performance of face recognition task, indicating a similar ability to recognize faces in men and women. These results of similar facial recognition memory in males and females and an associated similar activation of PFC are consistent with the findings of similar activation of other brain areas such as amygdale, insula, and hippocampus

in men and women, observed in a previous fMRI study (Ino et al., 2010). Our study was the first one to evaluate the sex difference in the effect of HIIE on the facial recognition and its associated prefrontal cortical activation. However, we did not find any significant difference in the same variables.

No difference in the visuospatial task performance and associated PFC activation was observed between males and females in the current study. Men generally outperform women in visuospatial task, which was also shown by a longitudinal study in middle and old-aged adults (de Frias et al., 2006), but our findings were not in agreement with theirs. Similar PFC activation during this task is attributed to the similarity in performance of visuospatial task between men and women in our study.

Conclusion

We conclude that improvement in the word recognition memory occurs in response to HIIE. Face recognition memory remains unaffected by a single bout of HIIE session. Visuospatial ability does not show a significant effect, in response to HIIE. Improvement in the PFC hemodynamics is shown through oxyHb concentration during recognition memory task but deoxyHb concentration remains unchanged in response to HIIE. Effects of a single session of HIIE are not translated to an improvement in prefrontal activation. Word recognition memory shows a greater benefit for women in response to HIIE, as compared to men. No sex difference was found in the scores of face recognition, visuospatial functions, and their associated PFC hemodynamic functions.

Author Disclosure

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A Quasi-Experimental Study on the Effectiveness of Integrated Electroencephalogram Neurofeedback Training and Group Psychotherapy for Harmful Alcohol Use: Neurocognitive and Clinical Outcomes

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Abstract

Introduction. This study investigates the efficacy of integrating electroencephalogram (EEG) neurofeedback training and group psychotherapy for individuals with harmful alcohol use (AUDIT-10 scores 10–13). **Methods**. Seventy-six participants were purposively sampled and divided into treatment (EEG neurofeedback training and group psychotherapy) and control groups. Baseline assessments measured alcohol consumption (AUDIT-10), stress (perceived stress scale [PSS]), neurocognition (NIMHANS neuropsychological battery), craving (PACS), and visual analog scale. The treatment group underwent 20 sessions of EEG neurofeedback (Peniston-Kulkosky and Scott-Kaiser modification protocols) and four sessions of group psychotherapy (motivational interviewing [MI], psychoeducation). **Result/Discussion**. A repeated measures ANOVA showed significant improvement in postcondition scores for the treatment group compared to controls, who exhibited deterioration over time. The study provides evidence supporting the efficacy of integrated EEG neurofeedback training and group psychotherapy in mitigating harmful alcohol use progression. **Conclusion**. By addressing stress, cognition, and cravings, this intervention offers crucial support to individuals with problematic drinking.

Keywords: craving; executive functions; harmful alcohol use; neurofeedback; psychotherapy; stress

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Introduction

Alcohol is the most common psychoactive substance used by Indians with about 15% (160 million) of the population between 10 and 75 years of age using alcohol of which 5.2% are problem users. That is, more than 50 million individuals are affected by harmful alcohol use (Ambekar et al., 2019). Harmful alcohol users experience harm associated with their alcohol use but do not meet the criteria for alcohol use disorder (Whitlock et al., 2004). Johnson et al. (2013) gave a concrete definition of harmful alcohol users as individuals scoring between 10 and 13, who fall within Zone III of the Alcohol Use Disorder Identification Test 10-Item (AUDIT-10) experiencing negative effects from alcohol use and require brief intervention to reduce or abstain from usage.

Role of Stress and Neurocognition

Stress is one of the several factors contributing to harmful alcohol use. The stress-coping model states that individuals use alcohol as a coping mechanism to deal with stressors and their associated emotional distress (Wittgens et al., 2022). However, this does not clearly explain the association between stressful experiences and harmful alcohol use. Environmental, biological, and psychological factors can explain the relationship between stress and harmful alcohol use. For instance, observational studies show that childhood maltreatment moderates the association between stress and harmful alcohol use and alcohol

use disorder in the later stages of the individual (Kim et al., 2014). The prolonged and excessive activation of the hypothalamic-pituitary-adrenal (HPA) axis causes individual differences in basal cortisol secretion explaining the development of harmful alcohol use behavior (Lijffijt et al., 2014). At the later stages of alcohol use, excessive alcohol consumption causes neuroadaptations in stress and reward pathways promoting increased salience of alcohol-related cues called attentional bias that further increases alcohol craving (Sinha, 2008). This is further accompanied by impaired response inhibition and executive deficits causing a lack of self-regulation in harmful alcohol use consumption (Madhusudhan et al., 2021; Sinha, 2012).

Integrated Intervention: A Biopsychosocial Approach

Harmful alcohol use treatment requires an integrated intervention approach due to the multitude of factors contributing to it. Combining and integrating interventions leads to superior treatment outcomes compared to a single approach alone. Conventional dual models, such as pharmacotherapy and psychotherapy, have demonstrated only modest efficacy among alcohol users, with high relapse rates (Dousset et al., 2020). To address this gap, the present study adopts an integrated approach by combining electroencephalogram (EEG) neurofeedback training and group psychotherapy for the treatment of harmful alcohol users.

The EEG reflects various mental states by recording the brain's electrical activity via electrodes placed on the human scalp (Heinrich et al., 2007). EEG neurofeedback training utilizes this technology to train individuals to self-regulate their brain activity in real time (Masterpasqua & Healey, 2003; Niv, 2013). For instance, a relaxed state is characterized by slow brain wave frequency alpha (8–12 Hz), which is often deficient in individuals with alcohol use behavior (Enriquez-Geppert et al., 2013; Kelly & Daley, 2013; Rangaswamy & Porjesz, 2014; Sokhadze et al., 2008). The Peniston-Kulkosky protocol (also known as alpha-theta neurofeedback) employs feedback of alpha (8–12 Hz) and theta (4–8 Hz) brain waves, teaching participants to increase the amplitude of alpha and theta brain waves and enhance the coherent interaction between the two, inducing a state of profound relaxation and reverie (Phneah & Nisar, 2017; Rangaswamy & Porjesz, 2014). This method was seen as useful in improving stress levels and promoting individual insight.

EEG studies have shown that chronic alcohol consumption can alter brain wave patterns leading to increased beta activity in certain regions of the brain. These changes contribute to cognitive impairments such as impulsivity, attentional bias, and deficits in working memory and executive functions (Rangaswamy & Porjesz, 2014). The Scott-Kaiser Modification protocol, called the beta (12–30 Hz) sensorimotor rhythm (SMR; 12–15 Hz), addresses these cognitive deficits by uptraining the SMR frequency band and regulating beta waves. This intervention aims to improve attention, concentration, response inhibition, and executive functions in individuals affected by harmful alcohol use consumption (Logemann et al., 2010).

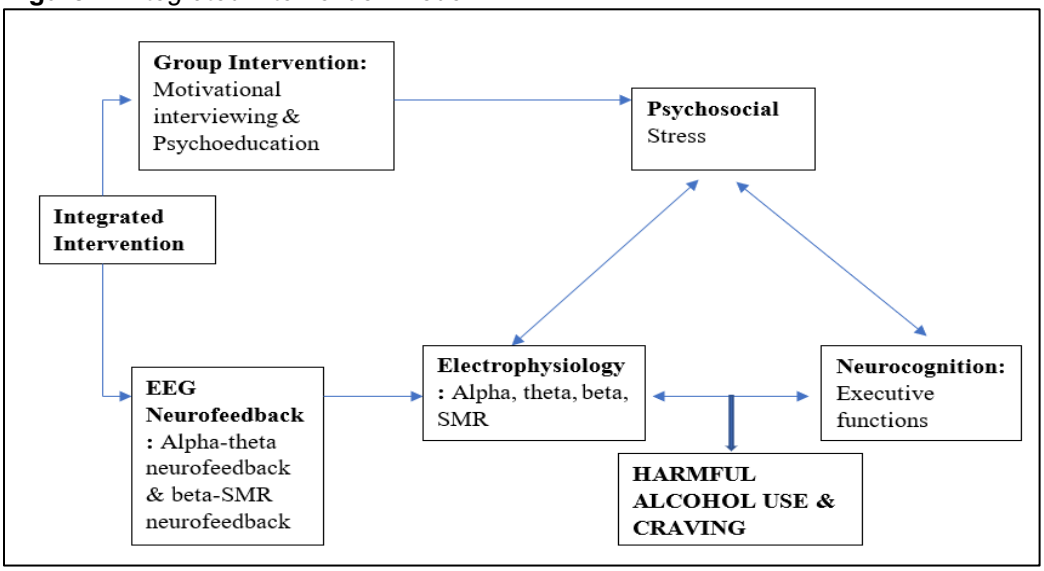
Thus, EEG neurofeedback training helps in addressing biological factors such as altered EEG patterns observed in individuals with harmful alcohol use (Dehghani-Arani et al., 2013; Kadosh & Staunton, 2019; Phneah & Nisar, 2017; Sitaram et al., 2017). However, while EEG neurofeedback training can be considered an efficacious treatment, it alone may not suffice to address the complex psychosocial factors contributing to harmful alcohol use. For instance, stress, which fluctuates over time, can significantly impact motivation, treatment retention, and overall recovery of individuals undergoing EEG neurofeedback training (Kadosh & Staunton, 2019).

This study integrated group psychotherapy incorporating motivational interviewing (MI) and psychoeducation, with EEG neurofeedback training to create a supportive environment for individuals to explore psychosocial factors such as stress and associated emotional distress contributing to their harmful alcohol use (Feldstein Ewing et al., 2011). Within the group setting, participants have the opportunity to share experiences, gain insight, and receive feedback and encouragement from one another (Pombo et al., 2016; Santa Ana et al., 2021; Valeri et al., 2018). Group psychotherapy addresses the psychosocial dimension of harmful alcohol use behavior, complementing and reinforcing the positive changes induced by EEG neurofeedback training (Kadosh & Staunton, 2019; Morgenstern et al., 2017). Integrating the supportive environment, shared learning, and emotional regulation provided by group psychotherapy with the neurobiological intervention of EEG neurofeedback training, individuals are afforded enhanced treatment outcomes and an increased likelihood of sustained recovery from a biopsychosocial perspective of harmful alcohol use behavior.

The Proposed Model of the Study

The intervention comprises a structured program consisting of 20 sessions, including 10 sessions of the Peniston-Kulkosky protocol and 10 sessions of the Scott-Kaiser modification protocol for EEG neurofeedback training. The group psychotherapy incorporates MI and psychoeducation. The proposed model of the integrated intervention is provided in Figure 1.

Figure 1. *Integrated Intervention Model*.



The objective of the study is to understand whether the integration of EEG neurofeedback training and group psychotherapy leads to improved stress levels, neurocognitive functioning, and reduced craving among harmful alcohol users. Therefore, this study comes with three hypotheses:

- **Hypothesis 1**: The integration of EEG neurofeedback and group psychotherapy will lead to decreased stress levels among individuals with harmful alcohol use.
- **Hypothesis 2**: The integration of EEG neurofeedback and group psychotherapy will lead to improvement in neurocognition among individuals with harmful alcohol use.
- **Hypothesis 3**: The integration of EEG neurofeedback and group psychotherapy will lead to a reduction in alcohol cravings among individuals with harmful alcohol use.

Methods

Participants

The inclusion criteria were participants with a history of alcohol use who meet the criteria of the AUDIT-10 with scores of 10 to 13 indicating harmful alcohol use consumption between the age range of 18 to 50 from Bangalore, India. A general health questionnaire (GHQ-12) was used to evaluate and understand the mental health status of the individuals. The participants were to be literate to perform the screening tests and participate in the intervention. The exclusion criteria consisted of people who are already seeking treatment for alcohol use and people with a history of significant psychiatric, neurological, and neurosurgical conditions. The study assessed the eligibility of 90 participants in total. A total of 76 participants met the inclusion criteria of the study. All of the recruited participants went abstinent for 14 days before the commencement of the intervention and were abstinent during the intervention.

The 14-day abstinence period aligns with clinical guidelines and research findings indicating that withdrawal symptoms typically peak within the first few days of alcohol cessation and gradually subside over the following week or two (Kattimani & Bharadwaj, 2013). By ensuring that participants are abstinent for 14 days before the intervention, researchers can minimize the potential confounding effects of acute withdrawal symptoms on the outcomes of the study.

Recruitment

The study was conducted in the Clinical Assessment and Training Lab in CHRIST (Deemed to be University), Bangalore. The participants were recruited with the assistance of the Centre for Counselling (CHRIST, Bangalore). Recruitment efforts included the distribution of brochures on the university campus and through social media channels, accompanied by clear communication of the study's purpose and procedures.

Informed Consent

The informed consent form had three parts: the information sheet (to share information about the research with participants), information on the integrated intervention, and a certificate of consent (for signatures if the participant is willing to take part in the study). The individuals self-recruited themselves into treatment and control groups. The intervention took place between September 2022 and June 2023 in the university lab after obtaining approval from the Research Conduct and Ethics Committee of Centre for Research, CHRIST, Bangalore with referral number RCEC/00394/01/22.

Sampling

The study used a purposive sampling technique. The G power software version 3.1 suggested a sample size of 28 each in the treatment and control groups to attain the effect size of .7. The treatment group consisted of 37 participants, and the control group consisted of 39 participants.

Research Design

This is a quasi-experimental study that includes a treatment group and a control group of harmful alcohol use individuals. A flowchart showing the sequence of recruitment, assessment, and intervention is shown in Figure 2.

Experimental Procedure

The intervention consisted of 20 sessions of neurofeedback training, incorporating 10 sessions of the Peniston-Kulkosky protocol and 10 sessions of the Scott-Kaiser modification protocol, and four sessions of group psychotherapy consisting of MI and psychoeducation. Every five sessions of EEG neurofeedback training was followed by group psychotherapy. This design facilitates ongoing monitoring of psychosocial factors throughout the treatment process. By initiating the Peniston-Kulkosky protocol, the intervention prioritizes addressing stress due to its significant influence on individuals' overall performance during treatment. The participants in the treatment group underwent all 20 sessions of neurofeedback and four sessions of group psychotherapy (see Table 1).

Materials

General Health Questionnaire. The 12-item GHQ is used for detecting psychological distress (Hystad & Johnsen, 2020). The items on GHQ-12 are rated on a 4-point Likert scoring method (0-1-2-3) which is commonly used in research (Anjara et al., 2020). The test–retest reliability ranges from 0.70 to 0.95 and the concurrent validity is 0.80 (Kirmani & Suman, 2010).

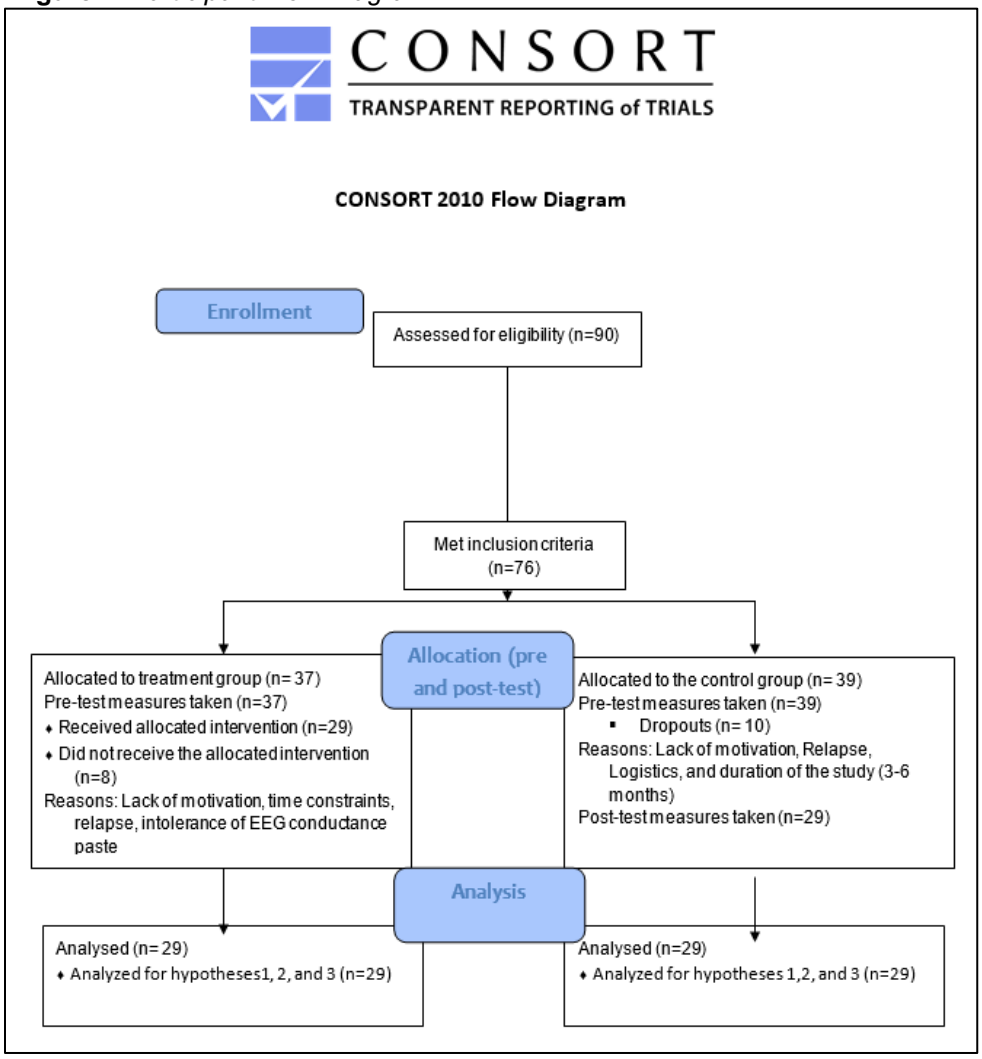
Alcohol Use Disorder Identification Test 10-Item (AUDIT-10). The AUDIT-10 questionnaire is a screening instrument developed by the World Health Organization (WHO) to screen for a range of drinking problems. The scale has a reliability of .84 (Endsley et al., 2017).

Perceived Stress Scale (PSS). The PSS, developed by Sheldon Cohen, is used as a self-appraisal measure for individuals to assess the extent of the perceived stressfulness of their various life situations (Pangtey et al., 2020). Six items of the scale measure stress and four items measure coping strategies for stress (Manzar et al., 2019). The scale has an internal reliability of .84 (Lee, 2012).

Penn's Alcohol Craving Scale (PACS). The PACS is a five-item questionnaire that measures the frequency, intensity, and duration of craving, the ability to resist drinking, and asks for an overall rating of alcohol craving in the past week (Flannery et al., 1999). The 0.92 Cronbach's alpha coefficient obtained from the prerandomization PACS scores shows that the PACS possesses a high degree of internal consistency (Flannery et al., 1999).

The National Institute of Mental Health and Neuroscience (NIMHANS) Neuropsychological Battery. The NIMHANS neuropsychological battery is used to study and understand cognitive impairments associated with substance use disorders. It is a lobe-based test focusing on lateralization and localization of higher mental functions (Porrselvi & Shankar, 2017). The tests used in the study are of mental speed (Digit Symbol Substitution Test [DSST]), of sustained attention (Digit Vigilance Test [DVT]), of executive functions (Animal Naming Test [ANT]), of working memory (*N*-back tasks), of planning (Tower of London [ToL]), of set-shifting (Wisconsin Card Sorting Test [WCST]), of response inhibition (Stroop test), of verbal learning and memory (Rey Auditory Verbal Learning

Figure 2. *Participant Flow Diagram*.



Test [RAVLT]), and of visuospatial working memory (Rey Complex Figure Test [RCFT]).

Visual Analog Scale (VAS). This study uses 0 to 10 cm VAS, which considers the scores to be at an ordinal level of measurement, where a lower numerical value of VAS reflects less severity of symptoms and a higher numerical value reflects more severity of symptoms for the following factors urge to drink, quality of sleep, and anxiety.

EEG Neurofeedback Training. The EEG neurofeedback was administered to the patients using the Brain Avatar 4.0 software acquired on the Brain Master Discovery 24E. The EEG and other signals are sampled at higher rates and high resolution and are processed and reconstructed for transmission of the same to the personal computer. The signals sent to the personal computer are already processed to remove any interference and provide wide bandwidth signals. For EEG acquisition and processing, the Brain Avatar modules are supported by the Brain Master Discovery 24E software. The Notch filler will be set at 50 Hz, and the EEG sampling rate at 256 sps.

The alpha-theta protocol focuses on the augmentation of alpha and theta activity simultaneously at Occipital (O_1 and O_2) locations and the beta-SMR neurofeedback protocol helps the augmentation of beta and SMR activity simultaneously at C_3 and C_4 locations. The ground electrodes were placed at A_1 and A_2 (Mastoids) locations, and the reference electrode was placed at Nasion.

Table 1
Experimental Procedure

Intervention	Description	Objectives	Duration	Measures
Peniston/Kulkosky (Alpha/Theta Protocol)	Learning to uptrain alpha and theta O_1-O_2 location of the brain	To voluntarily regulate brain waves associated with stress	Sessions 1–5, lasting 30 min each	Nil
Group psychotherapy	Group members narrate their experiences of harmful alcohol use	Facilitate decisional balance	Session 1, 1 hr 30 min	VAS
Peniston/Kulkosky (Alpha/Theta Protocol)	Learning to self-regulate alpha and theta at the occipital region of the brain	To voluntarily regulate brain waves associated with stress	Sessions 6–10, lasting 30 min each	Nil
Group psychotherapy	Educate on stress and neurocognitive risk factors associated with alcohol use behavior	Decrease the erroneous rationalization	Session 2, 1 hr	VAS
Scott-Kaiser Modification (beta-SMR Protocol)	Learning to uptrain SMR and regulate beta at C_3-C_4 location of the brain.	To voluntarily regulate brain waves associated with cognition	Sessions 1–5, 37 min each	Nil
Group psychotherapy	Activity: Change Plan Worksheet	To enhance autonomy, competence, and self-efficacy by setting realistic goals.	Session 3, 1 hr	VAS
Scott-Kaiser Modification (beta-SMR Protocol)	Learning to uptrain SMR and regulate beta at C_3-C_4 location of the brain.	To voluntarily regulate brain waves associated with cognition	Sessions 6–10, 37 min each	Nil
Group psychotherapy	Increase the conviction and confidence to sustain a behavior change.	Review progress, Renewing the motivation, Redoing commitment	Session 4, 1 hr	VAS

Note. VAS: visual analog scale.

Psychosocial Intervention. The psychosocial intervention consisted of MI and psychoeducation conducted in groups as explained (see Table 1). The treatment group was divided into four separate groups comprising eight in two groups and six and seven members in the other two groups. The groups formed were closed as no new members were added once the groups were formed.

Results

Descriptive Analysis, Categorical Comparison of Variables, and Test of Normality

Table 2 shows the demographic characteristics of the participants in the treatment and control groups. Table 3 shows the categorical comparison of demographic variables using the Chi-square test between the treatment and control groups. Based on demographic factors, there is no significant difference between the two groups. Table 4 represents Shapiro-Wilk's Normality test of the variables under study. The normally distributed variables have a significance level higher than .05, whereas those with a significance level lower than .05 are not normally distributed.

Analyses of Hypothesis

Hypothesis 1. Hypothesis 1 states that the integration of EEG neurofeedback and group psychotherapy will lead to decreased stress levels among harmful alcohol users in the treatment group. A repeated measures analysis of variance (ANOVA) was conducted to examine the effect of conditions (pre vs. post) on perceived stress levels within the treatment group (Table 5). The results revealed a significant effect of conditions on perceived stress, $F(1, 27) = 437$, $p < .001$, $\eta^2 = .88$. This indicates that there was a substantial difference in perceived

stress levels between the pre- and postconditions within the treatment group.

A post hoc analysis using Tukey's honestly significant difference (HSD) test further demonstrated significant differences between the pre- and postconditions, in which participants exhibited significantly lower perceived stress levels in the posttreatment condition showing the effectiveness of the intervention ($p < .001$).

Table 2
Participant Demographic Variables

	Group	Mean	Median	*SD*	Minimum	Maximum
Age	Treatment	23.6	22	5.20	19	46
	Control	24.8	24	4.28	20	34
General Health	Treatment	16.2	16	1.44	14	19
	Control	15.9	16	1.51	12	19

Demographics	Treatment group		Control group	
	n	%	*n*	%
Gender				
Male	10	17.2	14	24.1
Female	19	32.8	15	25.9
Occupation				
Employed	12	20.7	16	27.6
Unemployed	17	29.3	13	22.4
Marital status				
Married	5	8.6	6	10.3
Single	24	41.4	23	39.7
Parental alcohol use				
Yes (Disorder)	8	13.8	10	17.2
Moderate use (Social drinking)	12	20.7	9	15.5
No	9	15.5	10	17.2
Previous treatment failures (if any)				
Yes	1	1.7	3	5.2
No	28	48.3	26	44.8
Age of first alcohol use				
13–16	3	5.2	3	5.2
17–20	23	39.7	26	44.8
20+	3	5.2	0	0

Table 3
Chi-Square Test of Categorical Variables Between Treatment and Control Groups

Characteristics	Categories	Treatment (29)	Control (29)	χ^2	*p*
		M ± *SD* or *n* (%)	*M* ± *SD* or *n* (%)		
Age (years)		23.6 ± 5.20	24.8 ± 4.28		.3
Age of first alcohol use					
	13–16	(5.2)	(5.2)	3.18	.2
	17–20	(39.7)	(44.8)		
	20+	(5.2)	(0)		
Gender					
	Male	(17.2)	(24.1)	1.14	.2
	Female	(32.8)	(25.9)		
Occupation					
	Employed	(20.7)	(27.6)	1.10	.2
	Unemployed	(29.3)	(22.4)		
Marital Status					
	Married	(8.6)	(10.3)	.11	.7
	Single	(41.4)	(39.7)		
Parental alcohol use					
	Yes (Disorder)	(13.8)	(17.2)	.70	.7
	Moderate use (Social drinking)	(20.7)	(15.5)		
	No	(15.5)	(17.2)		
Previous treatment failures					
	Yes	(1.7)	(5.2)	1.0	.3
	No	(48.3)	(44.8)		

Table 4
Shapiro Wilk Test of Normality

Variables	Treatment group						Control group					
	Pre			Post			Pre			Post		
	M	*SD*	*w*	*M*	*SD*	*w*	*M*	*SD*	*w*	*M*	*SD*	*w*
Harmful alcohol use	11	1.16	.79	4.55	2.27	.88	10.48	.94	.55	11.7	1.16	.82
Perceived stress	27.8	3.18	.95*	14.24	1.64	.94*	25.4	2.42	.93*	28.7	2.40	.91
Alcohol craving	7.2	1.67	.75	3.24	1.05	.48	6.3	1.23	.70	8.8	2.17	.87
Cognitive flexibility (PE)	11.4	7.85	.84	10	3.13	.96*	18	5.02	.97*	19.1	4.97	.97*
Concept formation (TCF)	13.7	4.93	.71	12.1	1.67	.91	19.6	5.40	.95*	21.3	7.20	.89
Ability to maintain set (FMS)	.8	2.08	.48	.03	.18	.18	.06	.25	.28	.03	.18	.18
Stroop effect (Response inhibition)	315.6	88.8	.96*	177.13	73.6	.94*	324.2	71.33	.96*	352.2	66.25	.96*
Learning (IR)	12.6	2.61	.84	14.8	.40	.28	14.6	.77	.56	14.6	.80	.43
Learning (DR)	12.1	2.55	.88	14.5	.68	.69	13.9	1.03	.84	13.6	1.13	.85
Long-term memory retention	88.5	14.72	.89	97	4.43	.67	93.2	6.34	.85	91.6	6.53	.86

Table 4
Shapiro Wilk Test of Normality

Variables	Treatment group						Control group					
	Pre			Post			Pre			Post		
	M	*SD*	*w*	*M*	*SD*	*w*	*M*	*SD*	*w*	*M*	*SD*	*w*
Visuospatial working memory (IR)	17.7	6.29	.96*	22.5	3.12	.94*	15.9	2.67	.95*	14.5	2.45	.94*
Visuospatial working memory (DR)	16.5	5.95	.95*	22.9	3.94	.96*	13.8	2.18	.95*	13.4	1.84	.90
Mental speed	173.4	41.93	.91	123.9	39.52	.92	149.2	42.70	.97*	153.2	27.37	.97*
Sustained attention (time taken)	441.5	134.4	.94*	374	158.8	.87	441.4	91.9	.91	474.4	55.10	.97*
Category fluency	15	3.25	.87	16.8	2.39	.82	13.7	1.66	.94*	13.2	1.25	.92
Verbal working memory (hits)	6.8	1.98	.83	8.9	.18	.18	8.7	.43	.53	8.8	.40	.28
Planning	9.0	1.03	.92	12.1	.91	.89	9.4	1.37	.89	9.3	1.77	.84

Table 5
Repeated Measures ANOVA Within the Treatment Group for Perceived Stress

Variables		Treatment group Mean/Median ± *SD*	*F*/χ^2	*df*	*p*	Effect size (η^2)	$p^{\text{Tukey/Durbin Conover}}$
Perceived stress	Pre	27 ± 3	437	1,27	< .001*	.88	< .001*
	Post	14 ± 1.6					

*$p < .05$

Hypothesis 2. Hypothesis 2 states that the integration of EEG neurofeedback and group psychotherapy will lead to improved neurocognition among harmful alcohol users in the treatment group. The repeated measures ANOVA showed a significant effect on Stroop effect scores, $F(1, 27) = 47.6$, $p < .001$, $\eta^2 = .42$ indicating a notable difference in Stroop effect scores between the two conditions. A post hoc analysis using Tukey's HSD demonstrated significant differences between the pre- and postconditions ($p < .001$) wherein, the posttest scores were reduced compared to the of pretest scores suggesting that the intervention had a significant impact on reducing Stroop effect scores. This shows that the intervention has been effective in improving response inhibition among the treatment group (Table 6).

For visuospatial working memory, the repeated measures ANOVA showed a significant effect on immediate recall (IR) scores, $F(1, 27) = 22.7$, $p < .001$, $\eta^2 = .19$, and on delayed recall (DR) scores, $F(1, 27) = 34.9$, $p < .001$, $\eta^2 = .29$, indicating that there is a significant effect on visuospatial working memory scores between the pre- and posttest conditions. The post hoc analysis using Tukey's HSD shows significant improvements in posttest conditions compared to pretest conditions ($p < .001$) for both the immediate and delayed recall scores within the treatment group indicating improved visuospatial working memory (Table 6).

For the tests of mental speed and sustained attention, a significant effect was observed with $F(1, 27) = 31.9$, $p < .001$, $\eta^2 = .27$ and $F(1, 27) = 6.25$, $p < .01$, $\eta^2 = .05$, showing a significant difference on mental speed and sustained attention scores between pre- and posttest conditions within the treatment group. A post hoc analysis using Tukey's HSD further showed that the postcondition scores improved compared to preconditions with $p < .001$ and $p = .01$ respectively showing mental processing capacity and sustained attention (Table 6).

A Friedman test was conducted for those variables that violated normality, to examine the effect of conditions (pre vs. post) on cognitive flexibility, concept formation, and ability to maintain set scores within the treatment group. The analysis revealed a nonsignificant effect on cognitive flexibility scores, $\chi^2(1) = .14$, $p = .7$, and concept formation scores, $\chi^2(1) = 1.50$, $p = .2$. The post hoc analysis using the Durbin-Conover test did not show any significant pairwise differences between the pre- and postconditions for cognitive flexibility ($p = .7$) and

concept formation (p = .2). The ability to maintain set scores showed a significant difference between the pre- and postconditions, $\chi^2(1) = .7$, p = .008. The post hoc analysis also showed that the posttest conditions significantly improved compared to the pretest conditions (p = .006; Table 6).

The Friedman test for learning (IR, DR, long-term memory retention) showed a significant difference between the pre- and postconditions, $\chi^2(1) = .20$, p = .001; $\chi^2(1) = .14.7$, p = .001; and $\chi^2(1) = 8.05$, p = .005, respectively. The postanalysis showed a significant improvement in postconditions compared to the preconditions for IR, DR, and long-term memory retention (p < .001, p < .001, and p = .003, respectively). Likewise, the Friedman test for category fluency, verbal working memory (B2 hits), and planning also showed a significant difference between pre- and postconditions within the treatment group, $\chi^2(1) = 14.1$, p = .001; $\chi^2(1) = 25$, p = .001; and $\chi^2(1) = 29$, p = .001, respectively. The post hoc analysis showed that the postcondition scores improved significantly for category fluency, verbal working memory (B2 hits), and planning (p < .001, p = .001, and p = .001, respectively; Table 6).

Table 6

Repeated Measures ANOVA Within the Treatment Group for Neurocognition

Variables		Treatment group Mean/Median ± *SD*	*F*/χ^2	*df*	*p*	Effect size (η^2)	$p^{\text{Tukey/Durbin Conover}}$
Cognitive flexibility[a]	Pre	10 ± 7	.14	1	.7	-	.7
	Post	9 ± 3					
Concept formation[a]	Pre	12 ± 4	1.50	1	.2	-	.2
	Post	12 ± 1					
Ability to maintain set[a]	Pre	0 ± 2	7	1	.008*	-	.006*
	Post	0 ± 1					
Stroop effect (Response Inhibition)	Pre	316 ± 88	47.6	1, 27	<.001*	.42	<.001*
	Post	177 ± 73					
Learning (IR)[a]	Pre	13 ± 2	20	1	<.001*	-	<.001*
	Post	15 ± .4					
Learning (DR)[a]	Pre	12 ± 2	14.7	1	<.001*	-	<.001*
	Post	15 ± .6					
Long-term memory retention[a]	Pre	92 ± 14	8.05	1	.005*	-	.003*
	Post	100 ± 4					
Visuospatial working memory (IR)	Pre	17 ± 6	22.7	1, 27	<.001*	.19	<.001*
	Post	22 ± 3					
Visuospatial working memory (DR)	Pre	16 ± 5	34.9	1, 27	<.001*	.29	<.001*
	Post	22 ± 3					
Mental speed (Time taken)	Pre	173 ± 41	31.9	1, 27	<.001*	.27	<.001*
	Post	123 ± 39					
Sustained attention (Time taken)	Pre	442 ± 134	6.25	1, 27	.01*	.05	.01*
	Post	374 ± 159					

Table 6
Repeated Measures ANOVA Within the Treatment Group for Neurocognition

Variables		Treatment group Mean/Median ± *SD*	*F*/χ^2	*df*	*p*	Effect size (η^2)	$p^{\text{Tukey/Durbin Conover}}$
Category fluency[a]	Pre	14 ± 3	14.1	1	<.001*	-	<.001*
	Post	17 ± 2					
Verbal working memory (B2-hit)[a]	Pre	8 ± 1	25	1	<.001*	-	<.001*
	Post	9 ± .18					
Planning	Pre	9 ± 1	29	1	<.001*	-	<.001*
	Post	12 ± .9					

[a] Violation of normality; * $p < .05$

Hypothesis 3. Hypothesis (3) states that the integration of EEG neurofeedback and group psychotherapy will lead to decreased clinical outcomes among harmful alcohol users in the treatment group. A repeated measures ANOVA on harmful alcohol use and alcohol craving scores also showed a significant difference between pre- and postconditions, $\chi^2(1) = 29$, $p = .001$ and $\chi^2(1) = 29$, $p = .001$, respectively. The post hoc analysis of paired comparison showed that the postcondition scores for harmful alcohol use and alcohol craving significantly improved ($p = .001$ and $p = .001$, respectively) within the treatment condition (Table 7).

Table 7
Repeated Measures ANOVA Within the Treatment Group for Clinical Outcomes

Variables		Treatment group Mean/Median ± *SD*	*F*/χ^2	*df*	*p*	Effect size (η^2)	$p^{\text{Tukey/Durbin Conover}}$
Harmful alcohol use[a]	Pre	11 ± 1	29	1	<.001*	-	<.001*
	Post	5 ± 2.2					
Alcohol craving[a]	Pre	6 ± 1	29	1	<.001*	-	<.001*
	Post	3 ± 1					

[a] Violation of normality; * $p < .05$

Repeated measures ANOVA and its nonparametric alternative have been done for the control group to understand the overall effect between the two conditions (pre vs. post) on the variables and pairwise comparison to see any notable difference between the conditions (Table 8). The results show that there is a significant difference between the two conditions (pre and post) on perceived stress, neurocognition, and clinical outcomes within the control group. The post hoc analysis show that the posttest conditions have deteriorated over time compared to that of the pretest conditions in stress, neurocognition, and clinical outcomes.

Table 8
Repeated Measures ANOVA Within the Control Group

Variables		Control group Mean/Median ± SD	*F*/χ^2	*df*	*p*	Effect size (η^2)	$p^{\text{Tukey/Durbin Conover}}$
Perceived stress	Pre	25 ± 2	52	1, 27	<.001*	.33	<.001*
	Post	28 ± 2					
Cognitive flexibility	Pre	18 ± 5	2.95	1, 27	.09	.01	.09
	Post	19 ± 4					

Table 8
Repeated Measures ANOVA Within the Control Group

Variables		Control group Mean/Median ± SD	F/χ^2	*df*	*p*	Effect size (η^2)	$p^{Tukey/Durbin\ Conover}$
Concept formation	Pre	19.7 ± 5	5.76	1, 27	.02*	.01	.02*
	Post	21 ± 7					
Ability to maintain set[a]	Pre	0 ± .25	.33	1	.5	-	.57
	Post	0 ± .18					
Stroop effect (Response Inhibition)	Pre	324 ± 71	4.03	1, 27	.05	.04	.05
	Post	352 ± 66					
Learning (IR)[a]	Pre	15 ± .7	.66	1	.4	-	.42
	Post	15 ± .8					
Learning (DR)[a]	Pre	14 ± 1.03	4.45	1	.03*	-	.03*
	Post	14 ± 1.13					
Long-term memory retention[a]	Pre	93 ± 6.3	6.23	1	.01*	-	.01*
	Post	93 ± 6.5					
Visuospatial working memory (IR)	Pre	15 ± 2	7.40	1, 27	.01*	.06	.01*
	Post	14.6 ± 2					
Visuospatial working memory (DR)	Pre	13.9 ± 2	1.17	1, 27	.2	.01	.28
	Post	13.4 ± 1.8					
Mental speed (Time taken)	Pre	149 ± 42	1.05	1, 27	.3	.003	.31
	Post	153 ± 27					
Sustained attention (Time taken)	Pre	441 ± 92	6.88	1, 27	.01*	.04	.01*
	Post	483 ± 55					
Category fluency	Pre	13 ± 1	2.66	1, 27	.1	.02	.11
	Post	13 ± 1.2					
Verbal working memory (B2-hit)[a]	Pre	9 ± .4	2.91	1	.08	-	.08
	Post	9 ± .4					
Planning[a]	Pre	9 ± 1	2	1	.15	-	.16
	Post	9 ± 1					
Harmful alcohol use[a]	Pre	10.5 ± .9	13.8	1	<.001*	-	<.001*
	Post	12 ± 1.16					
Alcohol craving[a]	Pre	6 ± 1	21	1	<.001*	-	<.001*
	Post	9 ± 2					

[a] Violation of normality; *$p < .05$

A visual analog scale assessment for the urge to drink, quality of sleep, and anxiety was taken from the treatment group postpsychotherapy. Friedman's test for the urge to drink, quality of sleep, and anxiety was measured considering the complex relationship of stress with the urge to drink, quality of sleep, and anxiety among harmful alcohol users. The results show that there is a significant difference in the urge to drink, quality of sleep, and anxiety scores between the two conditions within the treatment group collected at four time points, $\chi^2(3) = 77$, $p < .001$; $\chi^2(3) = 81$, $p < .001$; and $\chi^2(3) = 80$, $p < .001$, respectively. The post hoc analysis using the Durbin Conover test showed that the urge to drink, quality of sleep, and anxiety levels improved significantly across different conditions ($p < .001$, $p < .001$, and $p = <.001$, respectively; Table 9).

Table 9
Friedman Test for VAS Within the Treatment Group

Variables	Conditions	Median ± *SD*	χ^2	*df*	*p*	$p^{\text{Durbin-Conover}}$
Urge to drink	UD1	7 ± .9	77.7	3	<.001*	<.001*
	UD2	5 ± 1				
	UD3	4 ± 1.47				
	UD4	2 ± 1.1				
Quality of sleep	QS1	4 ± .8	81.4	3	<.001*	<.001*
	QS2	5 ± .7				
	QS3	7 ± .7				
	QS4	8 ± .7				
Anxiety	Anxiety1	8 ± .9	80.3	3	<.001*	<.001*
	Anxiety2	6 ± .9				
	Anxiety3	4 ± .8				
	Anxiety4	3 ± .9				

*$p < .05$

A visual analog scale for the assessment of the urge to drink, quality of sleep, and anxiety was taken from the control group on the same day as that of the treatment group. Friedman's test for the urge to drink, quality of sleep, and anxiety shows that there is a significant difference across the conditions, $\chi^2(3) = 28.6$, $p < .001$; $\chi^2(3) = 25.2$, $p < .001$; and $\chi^2(3) = 28.8$, $p < .001$, respectively. The post hoc analysis shows that the urge to drink varied significantly across the different conditions with the most notable difference observed in first and third ($p < .001$) and first and fourth ($p < .001$) time points. The quality of sleep showed notable difference in first and third ($p < .001$) and first and fourth ($p < .001$) time points. Anxiety showed significant differences across first and fourth ($p < .001$) and second and fourth ($p < .001$) time points (Table 10).

Table 10
Friedman Test for VAS Within the Control Group

Variables	Conditions	Median ± SD	χ^2	*df*	*p*	$p^{\text{Durbin-Conover}}$
Urge to drink	UD1	7 ± 1	28.6	3	<.001*	UD1–UD3 (<.001*)
	UD2	7 ± 8				
	UD3	8 ± 8				UD1–UD4 (<.001*)
	UD4	8 ± 8				
Quality of sleep	QS1	4 ± 0.9	25.2	3	<.001*	QS1–QS3 (<.001*)
	QS2	4 ± 0.9				
	QS3	4 ± 0.9				QS1–QS4 (<.001*)
	QS4	3 ± 1.1				
Anxiety	Anxiety1	7 ± 1.1	28.8	3	<.001*	Anxiety1–Anxiety4 (<.001*)
	Anxiety2	7 ± 1.30				
	Anxiety3	8 ± 1.15				Anxiety2–Anxiety 4 (<.001*)
	Anxiety4	8 ± 0.88				

*$p < .05$

Discussion

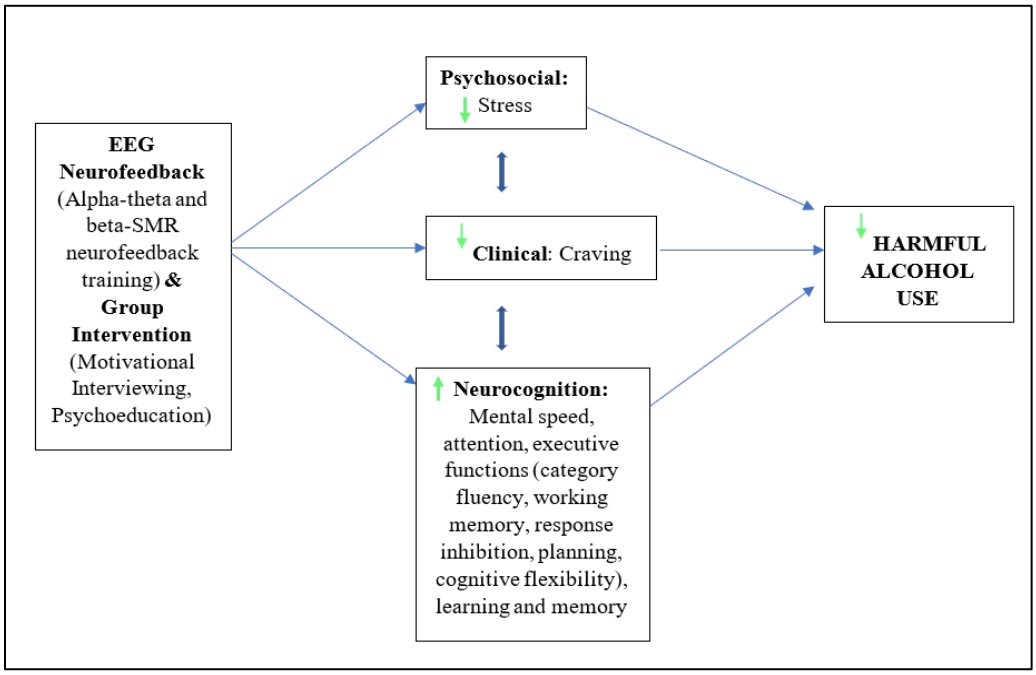
This study aimed to investigate the effectiveness of EEG neurofeedback training and group psychotherapy on harmful alcohol users. Although researchers have previously combined and integrated EEG neurofeedback with psychotherapy, this study has been integral in explaining how the integration mechanism works. Significant improvements were observed in stress, neurocognition, and clinical outcomes of harmful alcohol users in the treatment group following the intervention compared to the control group (see Figure 3).

Effect on Stress

The literature is replete with compelling evidence on the role of stress in the initiation and maintenance of alcohol use behavior (Becker, 2017; Blaine & Sinha, 2017; Keyes et al., 2011; Koob & Colrain, 2020; Mohan et al., 2015; Sinha et al., 2009). The treatment group was first subjected to alpha-theta neurofeedback training due to heightened stress levels and high levels of stress impact the overall performance of the individual in neurofeedback training and treatment retention in general. The group showed improvement in stress levels following the neurofeedback training as the alpha-theta neurofeedback is reported to have beneficial effects on stress, anxiety, and fear of relapse (Dalkner et al., 2017). The intervention facilitated individuals to think of strategies that help them to self-regulate their brain waves imparting a sense of self-efficacy. Such voluntary regulation allowed subjects to better tolerate stress and anxiety, which are prominent during the initial stages of recovery. Additionally, the enhanced alpha and theta during the training support individuals to be calm, tolerate stress, and impart a sense of inner empowerment (Dave & Tripathi, 2023). Gaining control over physiological processes helps in increased self-confidence, and reduces emotional stress and anxiety, feelings of inadequacy, insecurity, and fear (Lackner et al., 2016). Neurofeedback as a procedure helps reduce subjective stress and anxiety that could interfere with the HPA axis by impacting the stress-related systems of the brain directly (Mohan et al., 2015; Moss, 2022; White & Richards, 2023).

Improvements in stress may have caused improvements in neurocognition and clinical outcomes considering the bidirectional relationship between the variables. However, stress and related anxiety, are psychological variables that vary over time and hence need monitoring throughout the treatment conditions (Kadosh & Staunton, 2019). Group psychotherapy amplifies the effect of neurofeedback training by keeping a check on the psychosocial factors that could affect the overall performance of the individuals.

Figure 3. *A Diagram Showing the Effectiveness of Integrated Intervention in Reducing Harmful Alcohol Use*.



The group psychotherapy helped participants manage emotions in a social setting, overcoming the shame and fear of relapse associated with alcohol use which can act as potential stressors. Group support in times of pain and trouble can help people grow in ways that are healthy and creative (Valeri et al., 2018). This was true for our female participants to overcome the stigma associated with gender while seeking treatment for alcohol use. Once the individual learns emotional regulation and adaptive coping it engages the prefrontal cortex quieting the hyperactivation of the limbic system that governs the emotional response of the individual (Baxter et al., 1992; Rostami & Dehghani-Arani, 2015)

The collaborative approach of the group considers resistance to change or ambivalence as a normal aspect of human nature taking the blame away from clients that in turn aggravates stress-related relapse among individuals who are in the initial stages of their recovery (Ehret et al., 2015). Psychoeducation facilitated risk perception of alcohol use behavior that further increased the discrepancy between individual's behavior and resulting consequences motivating individuals to take accountability for their harmful alcohol use behavior (Magill et al., 2021). It was also helpful in addressing the repercussions of self-treating stress, anxiety, and poor sleep using alcohol. The improved levels of sleep can be attributed to better management of stress and anxiety through the intervention.

Effect on Neurocognition

The treatment group showed improvements in executive functions such as response inhibition, cognitive flexibility, learning and memory, working memory (visuospatial and verbal), mental processing capacity, sustained attention, and executive functions following the intervention. The beta-SMR facilitated uptraining of SMR brain wave activity that is associated with increased perceptual sensitivity, sustained attention, and decreased impulsivity (Logemann et al., 2010).

During the neurofeedback training, participants were encouraged to think of a mental strategy that would help them in improving their attention and other cognitive domains. The autonomy of identifying and controlling their brain waves (to self-decisively choose to start, maintain, or stop an action) and competence (to act efficiently) by gradually regulating the impulsive responses have been instrumental in improving participant compliance and acquisition of positive results (Ko & Park, 2018). The participants reported the ability to visualize the cons of alcohol use behavior far more than the pros which facilitated a neurocognitive shift. Study reports clinical improvements in patients' postneurofeedback training and the effects can last up to 12 months depending on the ability of the brain to learn (neuroplasticity; Loriette et al., 2021). Studies have reported electrophysiological, structural, and functional changes that result in reinforcement learning and brain plasticity on neurofeedback training (Hinterberger et al., 2005; Sherlin et al., 2011). Literature shows that EEG neurofeedback can be used as an add-on tool to enhance cognitive abilities that are pertinent to maintaining abstinence among individuals with alcohol use behavior (Dousset et al., 2020).

The group psychotherapy utilized improved cognition to facilitate neurocognitive shifts by tapping the decisional balance, which was inclined towards alcohol use and the urge to drink before the intervention. Verbalizing change talk further gave clarity to the cost-benefit analysis by maximizing the cognitive dissonance of harmful alcohol use behavior. Brain imaging studies show that change talk impacts the inferior frontal gyrus which is a key regulator in the brain's inhibitory control circuit (Ma et al., 2022; Zhuang et al., 2023). Understanding the consequences of alcohol use through psychoeducation and experiences shared by fellow participants motivated individuals to come for subsequent sessions of the intervention. The need to complete the intervention systematically became the priority of the clients. Literature shows that when patients are provided information on the nature of their alcohol use behavior, it enhances their treatment compliance with better retention and improvements in treatment outcomes (Ekhtiari et al., 2017). The therapy sessions enhance psychological integration that is, cognitive functions of the executive brain to have increasing access to information across networks of sensation, behavior, and emotion that in turn impacts cognition in psychotherapy (Malhotra & Sahoo, 2017).

Effect on Clinical Outcomes

The preoccupation/anticipation (third stage of the addiction cycle) stage is commonly linked to craving and the urge to drink and the prefrontal activation of craving reported executive deficits that interfere with decision-making, self-regulation, inhibitory control, and working memory (Koob & Volkow, 2016). The treatment group showed a marked reduction in the urge to drink following the intervention. The alpha-theta neurofeedback training helped in reducing the stress and anxiety levels and the group psychotherapy increased awareness of stress and related cravings that could trigger the individual to

alcohol use. The integrated intervention facilitated the identification of triggers which helped them to be aware of the same and take appropriate actions that work best for them. The beta-SMR sessions followed by group psychotherapy enhanced the cognitive flexibility through a neurocognitive shift that directed the attention to reducing alcohol use rather than craving the substance in general. Neurofeedback reduces drug seeking symptoms, improves psychological and neurophysiological variables, and results in longer periods of abstinence (Dehghani-Arani et al., 2013). The integrated intervention had a positive effect on decreased craving (Dave & Tripathi, 2023; Fahrion et al., 1992; Hashemian, 2015)

The affective component of craving involves the activation of motivational systems associated with specific subjective, behavioral, physiological, and cognitive correlates (Pombo et al., 2016). Fox et al. (2007) report that exposure to stress and alcohol cues can significantly increase craving, anxiety, and negative emotions. The group psychotherapy provided the role of a social setting to understand and manage emotion regulation healthily. The administration of alpha-theta neurofeedback and group psychotherapy significantly reduced the levels of craving by improving the stress, anxiety, and fear of relapse among individuals in the treatment group. It also facilitated the adoption of healthy strategies that can be used in times of stress-related craving rather than resorting to alcohol use as a coping mechanism.

Scope and Future Implications

This study was able to address one of the major gaps associated with gender in the diagnosis and treatment of harmful alcohol use. It ensures equitable access to care and tailored support for individuals of all genders affected by harmful alcohol use. To an extent, the nonclinical setting offered a promising avenue for reducing the stigma attached to treatment seeking and enhancing treatment accessibility. Future efforts should explore innovative approaches to destigmatizing harmful alcohol use and promoting help-seeking behaviors within community-based settings, fostering a supportive and inclusive environment for individuals seeking treatment recovery. The group sessions presented a unique opportunity to reach out to a greater number of people within a short period without compromising the effectiveness of the same. Furthermore, individuals felt less burdened to change in a group setting.

Limitations

This study did not specifically look into the impact of group dynamics and group cohesion on the psychosocial variables of the study. It has been found that some of the dropouts' demotivation was due to their inability to self-regulate their brain waves. Nonresponders and nonregulators should be further studied to understand the factors that could explain the inability to self-regulate and further improve the efficacy and administration of EEG neurofeedback among alcohol and other drug use behavior.

Conclusion

The integration of EEG neurofeedback training with group psychotherapy represents a promising approach to addressing harmful alcohol use. Our study demonstrates that this integrated intervention leads to significant reductions in stress levels, improvements in neurocognition, and reductions in craving among individuals with harmful alcohol use compared to those who did not receive the intervention. These findings underscore the potential of combining neurobiological interventions with psychosocial support to effectively address the multifaceted challenges associated with harmful alcohol use. Moving forward, further research is warranted to explore the long-term effects and mechanisms underlying this integrated approach, with the ultimate goal of optimizing treatment strategies and improving outcomes for individuals struggling with alcohol-related problems.

Author Disclosure

The authors declare no conflict of interest concerning the research, authorship, and publication of this article. There is no financial interest or benefit that has arisen from this research.

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Unraveling the Risk Landscape of Mild Cognitive Impairment: A Pilot QEEG Study With *Z*-Score and Cordance Analysis

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Abstract

Introduction. Mild cognitive impairment (MCI) is the decline in cognitive function among individuals aged over 60, and the transitional phase between normal aging and dementia. The Mini-Mental State Examination and Montreal Cognitive Assessment (MoCA) may not detect early dementia, hence the importance of identifying MCI or early dementia through biomarkers, such as EEG. **Objectives**. Evaluating EEG quantification in raw values, EEG quantification in *z*-scores, and cordance measures as potential differential biomarkers to discriminate MCI. **Method**. The study involved 20 subjects: 10 healthy individuals and 10 with memory complaints. An EEG was obtained from each participant and raw scores, *z*-scores, cordance, and three-dimensional data were analyzed. **Results**. No differences were found in absolute power in raw scores, three-dimensional analysis and cordance variables. A significant difference was found between the groups regarding the Delta1 *z*-scores at the F7 location, where the memory complaints group exhibited a higher *z*-score. **Conclusions**. Normalized EEG quantification data, converted into *z*-scores, could serve as potential markers to distinguish between cognitively healthy individuals and those at risk of MCI. Using qEEG normative databases may reveal useful differences for identifying subjects at risk of MCI. Further research into intermediate states, between normal cognitive function and established MCI, is needed to clarify this aspect.

Keywords: qEEG; mild neurocognitive disorders; *z*-score; cordance; sLORETA

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Introduction

Mild neurocognitive disorder (NCD) due to unknown etiology, previously known as mild cognitive impairment (MCI), is the decline and deterioration in cognitive functions among people over 60 years (5th ed.; DSM-5-TR Neurocognitive Disorders Supplement; American Psychiatric Association [APA], 2022). It is also viewed as the preclinical and transitional stage between healthy aging and dementia. Currently, the overall worldwide prevalence of mild NCD is 15.56% in adults aged 50 years and older (Bai et al., 2022).

According to Zhuang et al. (2021), mild NCD is a clinical condition with a high risk of progression to dementia. Hence, the importance of early detection, particularly at the mild NCD stage as a critical strategy in disease management, could potentially affect long-term outcomes (Zhuang et al., 2021). In this sense, the advice is to have a clinical neuropsychological examination that facilitates early detection of dementia, pointing to a pathway for care planning and disease education (Weintraub, 2022).

The detection of mild NCD is a complex clinical task because of its different manifestations or subtypes (amnestic, multidomain, etc.). However, the evolutionary nature of the pathological aging process, especially in the preclinical stage, advises

the use of screening strategies to determine the early risk of developing dementia. Since the sentinel units of epidemiologic surveillance are the primary health care systems, the use of rapid and simple screening tools (brief cognitive tests) is required to objectively identify patients at risk (Jorm & Jacomb, 1989).

However, there is controversy regarding the most advisable instruments for screening in primary care, depending on the time, the cognitive processes evaluated, and the applicability according to the educational level (Carnero-Pardo et al., 2022), or the psychometric quality and discriminative sensitivity among the tests (Costa et al., 2022; Jannati et al., 2024).

For this reason, it is necessary to use combined strategies that evaluate the older adult (cognitive functionality) and contrast the evolution with a key informant, whether a family member or a caregiver. In addition, face-to-face or teleneuropsychology modalities should be used to reach the highest percentage of the population (Sánchez Cabaco et al., 2023).

On the other hand, in the prodromal or earliest stages of dementia, especially in those with high prior levels of cognitive achievement and education, the routine screening accomplished with such tests as the Mini-Mental State Examination (MMSE), the Montreal Cognitive Assessment (MoCA), or the cursory bedside clinical mental status examination may yield no abnormalities (Nasreddine et al., 2005). Hence, the importance of differencing mild NCD from early stages of dementia through biomarkers, being EEG techniques, is helpful in this matter. The sensitivity of EEG to detect brain disorder correlates has been enhanced through quantitative methods of analysis such as quantitative EEG (qEEG). Additionally, qEEG data can be logarithmically transformed to achieve Gaussianity and undergo age regression and transformation into *z*-scores relative to population reference norms (normative databases), thereby mitigating intersubject variations due to variables such as age (Deslandes et al., 2004).

Finally, given the limitations and controversies mentioned above, the need to use neurophysiological markers (EEG measurements) combined with brief neuropsychological tests should be emphasized to increase the safety of screening (avoidance of false positives and negatives). These markers are an effective complementary tool because of their simplicity, noninvasiveness, few limitations in the measurement environment, and ease of use. Recent studies in this direction have shown that they detect specific changes in elderly people with MCI (Katayama et al., 2023).

The objective of this study was to examine certain quantitative features derived from EEG recordings in both healthy individuals and those with subjective memory complaints. Specifically, we aimed to evaluate EEG quantification in terms of raw values, EEG quantification in terms of *z*-scores, and cordance measures as potential differential biomarkers that could discriminate between healthy individuals and those experiencing subjective memory complaints.

Methods

Participants

The focus of this study is on biomarkers, but participants were recruited from the MCI Screening Unit. So, it is important to note that *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; DSM-5-TR; APA, 2013) diagnostic criteria for mild NCD due to unknown etiology are based on four criteria and two specifiers. The four criteria relate to cognitive changes, functional activities, and excluding delirium and competing mental disorders. The two specifiers are the presumed etiologies of mild NCD and the presence or absence of behavioral problems (Stokin et al., 2015).

The inclusion criteria for this study were as follows. Participants must be:

- registered in the city of Salamanca, Spain.
- at least 60 years of age at the time of selection.
- able to give informed consent.
- absent of medical conditions that could significantly affect participation in the study.
- willing to attend the scheduled appointments and complete the required questionnaires.
- fluent in Spanish to understand and complete the assessment tools used in the study.
- screened for MCI.

Participants were selected from the population already attending the Mild NCD Screening Unit of the Pontifical University of Salamanca. Twenty participants were invited to participate in this study (mean age 75.4 years) with the sociodemographic characteristics described below (Table 1). Although 20 participants were invited, not all of them were able to complete the EEG measurements due to various circumstances such as poor understanding

of the task during the test (producing nonreductible muscular and movement artifacts which created massive noise to the recordings), nonattendance at the appointment, or illness, among others, including 14 for data analysis.

Study participants were divided into two categories: (a) cognitively healthy and (b) with subjective memory complaints (SMC) or with mild NCD indicator according to MoCA scores (Table 2; Rosenzweig et al., 2023). The Yesavage scale was used to get a better context of the emotional status of the participants, and its implication on the qEEG measurements (Table 3; Greenberg, 2023).

This study protocol was reviewed and approved by the Institutional Review Board of Universidad Pontificia de Salamanca (ei-MEMO+AYsal 03/11/2023). Before the experiment, written informed consents were obtained from all the participants according to the Declaration of Helsinki. Neuropsychophysiology assessments were conducted in one of our neuropsychophysiology laboratories, properly equipped and isolated during the EEG recording.

Table 1
Demographics and Psychometric Data

Variable	HC	MCG	*P*
Gender (M:F)	4:5	1:4	.360
Age	74.56 (4.79)	77.80 (4.32)	.147
Education (years)	19 (5.61)	16.80 (3.63)	.518
GDS	1.11 (2.42)	0.20 (0.44)	.898
MoCA	27.22 (1.39)	16.60 (6.02)	**.040**

F = female; M = male; HC = healthy controls group; MCG = memory complaints group; GDS = Yesavage Geriatric Depression Scale; MoCA = Montreal cognitive assessment. Gender: chi-square test of independence. Age/Education/GDS/MoCA: Mann-Whitney test.

Table 2
MoCA Scores

Interpretation	Score range
Normal cognition	26–30 points
Mild NCD	18–25 points
Moderate NCD	10–17 points
Major NCD	Under 10 points

Table 3
Yesavage Depression Scale Scores

Interpretation	Score range
Normal condition	0–4 points
Mild depression	5–8 points
Moderate depression	9–11 points
Severe depression	12–15 points

EEG Acquisition and Preprocessing

An EEG was obtained from each participant. For the collection of the EEGs each patient was fitted with an electroencephalography cap, Electro-Cap, (Electro-cap International) with 19 channels located according to the 10–20 International System (Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, and O2) and using a linked-ear montage. For 5 min, EEG signals from all 19 channels were simultaneously obtained and collected using a Discovery24 amplifier from BrainMaster Technologies, Inc. Impedances of less than 5 kΩ were maintained, and a constant temperature and humidity of less than 25 °C and 50%, respectively, were maintained in the laboratory. EEG recordings were made in the closed-eye state with the use of BrainMaster Technologies, Inc. Brain Avatar 4.6.4 software, where artifacts were visually inspected and removed.

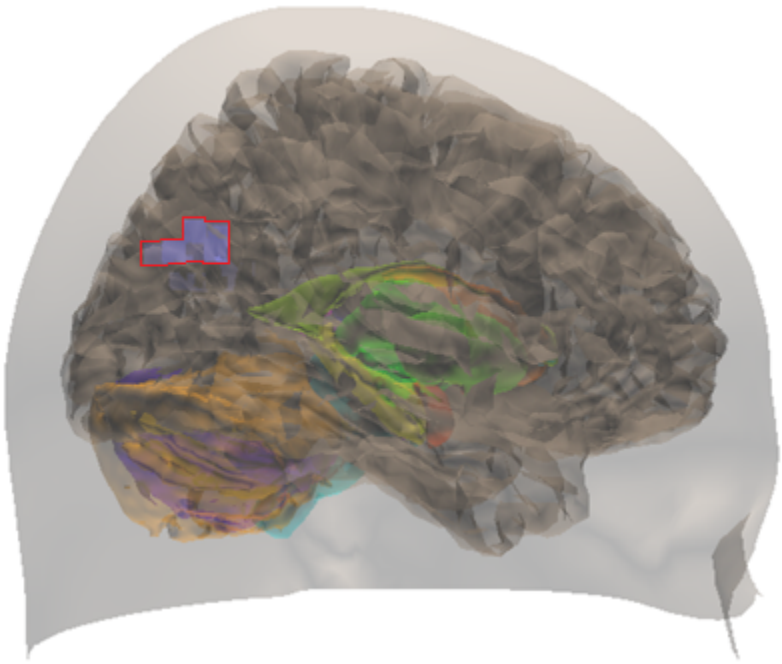
EEG Analysis and Quantification

EEG recordings were processed using a linked-ear montage and compared to the BrainDx normative database (John et al., 1977; John et al., 1987), from

which surface *z*-score values were obtained. Ten frequency bands were selected with the following ranges: Delta1 = 0.5–1.5 Hz, Delta = 1.7–3.7 Hz, Theta = 3.7–7.7 Hz, Alpha = 7.7–12.7 Hz, Beta = 12.7–25.2 Hz, Beta-2 = 25.2–35.2 Hz, Gamma = 35.2–50 Hz, Alpha1 = 7.7–10.2 Hz, Alpha2 = 10.2–12.7 Hz, and Sum = 1.7–25.2 Hz, as they appear in the Brain Avatar 4.6.4 BrainDx normative database implementation. Relative power was excluded because it was a calculation of the absolute power distribution of the entire spectrogram. This avoided redundant data (Stoller, 2011) and allowed each wave to be treated as a variable independent of the other variables.

In addition, *z*-scores for voxels, structures, Brodmann areas, and networks were calculated using BrainMaster standardized low-resolution electromagnetic tomography (sLORETA). This software allows the source of EEG activity within the cortex to be triangulated. Its bark model consists of 6,239 voxels, cubes of 5 mm^3. In each voxel, the current density source (CDS) is 1–45 Hz, whose estimates can be converted into a three-dimensional image (Gracefire, 2016). Each structure is formed by a set of voxels (see Figure 1) that are considered or designated as regions of interest (ROI) and displayed for monitoring through the screen (Collura, 2012, 2017).

Figure 1. *Brain Avatar sLORETA Projector*.



Note. The angular gyrus is displayed as an ROI (blue-colored and red-highlighted marked area).

Additionally, concordance was calculated using the method proposed by Leuchter et al. (1994). Cordance is known to be a metric highly correlated with metabolism and perfusion (Leuchter et al., 1994; Leuchter et al., 1999). This was important to this study, given the fact that different studies (Austin et al., 2011; Sperling et al., 2010) have revealed reductions in metabolism and perfusion, along with the accumulation of amyloid deposits, in regions such as parietal areas, lateral temporal areas, precuneus, posterior cingulate gyrus, and the dorsolateral frontal cortex in patients with cognitive decline.

Statistical Analyses

Mann-Whitney *U*-test and *t*-test were used to analyze continuous variables (age, absolute power, absolute power *z*-scores, etc.) computing the means, standard deviation, and chi-square (χ^2) for gender and cognitive abilities distribution between groups. Statistical significance was set at $\alpha = 0.05$ for all analyses. The effect size was calculated using Hedges' *g*.

Results

For an overview of the results of group comparisons for demographic data and screening psychometric scale data, refer to Table 1. In the healthy controls (HC) group, there were nine subjects (55.55% female) and five in the memory complaints group (MCG) group (80% female). No statistically significant differences in the distribution were found either by gender or condition (χ^2 = .837, p = .360). There were no differences between the groups for age (U = 33.50, p = .0147), years of education (U = 17.00, p = .518), or GDS scale (U = 21.00, p = .898). A statistically significant difference between the groups was found in the MoCA scores (U = 2.00, p = .004), in which the MCG group scored lower than the HC.

In terms of neurometric variables, no differences were found between the groups in any variable of absolute power in raw scores, cordance (Tables 4 and 5) or sLORETA. Regarding the *z*-scores, a single statistically significant difference was found between the groups (see Table 6), particularly in Delta1 activity at the F7 location, where the MCG group exhibited a higher *z*-score (U = 4.00, p = .048, ES = .573).

Discussion

This pilot study focused on exploring the potential of brain mapping, including analysis of cordance and transformations in *z*-scores of qEEG variables, in the detection of MCI. Our sample consisted of cognitively normal individuals and individuals with subjective memory complaints, suspected of cognitive impairment. No significant differences were found in the demographic variables, but differences were observed in the performance on the MoCA screening test, with subjects reporting memory complaints scoring lower. This finding was expected, as previous literature documented similar results (Hong & Lee, 2023). Subjective memory complaints in healthy individuals are a risk factor for the development of cognitive impairment, and individuals with cognitive complaints have been found to perform worse on memory tests (Han et al., 2021; Mills et al., 2020; Xiao et al., 2021).

Regarding the neurometric measures, we found no significant differences in the raw qEEG values between the groups. In this regard, it is worth mentioning that previous studies have found differences in raw qEEG between healthy subjects and those with Alzheimer's disease (Musaeus et al., 2018; Shim et al., 2022; Tomasello et al., 2023), or between healthy subjects and patients with established cognitive impairment (Musaeus et al., 2018; Tomasello et al., 2023). One possible explanation for this discrepancy in results between our study and previous research is that our subjects with memory complaints did not have a confirmed diagnosis of cognitive impairment but only a suspected diagnosis.

On the other hand, although there were no differences in age between the groups, it is known that there are developmental changes in qEEG scores, and therefore, age is a crucial factor in interpreting the results of such neuropsychophysiological tests (John et al., 1980; Ko et al., 2021; Matthis et al., 1980). For that, we decided to transform the raw qEEG scores into *z*-scores by comparing each subject to a normative database based on age and using these transformed scores as the dependent variable. The *z*-score minimizes the influence of variables that could affect the EEG in each subject, such as age.

When comparing between groups, we found that subjects in the MCG exhibited a higher *z*-score than controls in the left frontal region, specifically at the F7 location. This was the only noteworthy finding regarding the results of quantification and comparison with normative databases in our study. These results are consistent with previous studies that have found greater EEG slowing in individuals with impairment compared to healthy subjects. For example, Shim et al. (2022), investigated early detection of Alzheimer's disease in individuals with memory complaints and found an excess of delta activity in frontal, temporal, and parietal regions in subjects with subjective complaints and positive amyloid PET. Furthermore, they found that the greatest slowing of the EEG was in the left frontal regions. In another study focused on frontal event-related oscillations using oddball tasks as a reflection of neurodegeneration in the continuum between normality and mild NCD, Yener et al. (2016) found that frontal volume was lower in subjects with mild NCD compared to healthy individuals, and that there was a positive correlation between frontal volume and frontal event-related oscillations. They explain this correlation by assuming that an increase in frontal delta activity at rest could lead to lower frontal event-related oscillations during the performance of tasks like those used in their study.

Table 4
P-Values for Each Frequency Band and Channel of the Raw Scores

	Frontal Lobe							Central Area			Parietal Lobe			Temporal Lobe				Occipital Lobe	
	Fp1	Fp2	Fz	F3	F4	F7	F8	Cz	C3	C4	Pz	P3	P4	T3	T4	T5	T6	O1	O2
Delta1	.833	.833	.435	.622	.435	.524	.065	.524	.222	.127	.171	.724	.524	.354	.354	.435	.093	1.00	1.00
Delta	.622	.724	.943	.943	.833	.435	.435	.622	.284	.524	.354	.943	.724	.833	.724	.622	.127	.622	.724
Theta	.622	.833	.524	.622	1.00	.171	.833	.622	.833	.833	.724	1.00	.833	.833	.833	.724	.943	.724	.833
Alpha	1.00	1.00	.622	1.00	.833	.524	1.00	1.00	.943	1.00	.622	.833	.943	.622	.943	.622	.284	.524	.284
Beta	.622	.524	1.00	.943	.622	.354	.284	.833	.833	.833	.524	1.00	.833	.284	.222	.724	.127	.435	.524
Sum	1.00	1.00	.833	.943	.943	.222	.724	.943	.622	.943	.171	.622	.622	.833	.622	.524	.065	.435	.354
Beta2	.435	.354	.724	1.00	.524	.093	.065	.435	1.00	.724	.724	.724	.524	.435	.127	.622	1.00	.724	.833
Gamma	1.00	.284	.127	1.00	.943	.354	.354	.524	.622	.171	1.00	.524	.833	.524	.524	.943	1.00	.354	.833
Alpha1	1.00	1.00	1.00	.943	.833	.524	1.00	1.00	.943	.943	.435	.724	.724	.435	.833	.724	.354	.524	.222
Alpha2	.724	.524	.284	.724	.524	.354	.724	.354	1.00	.833	.724	.724	1.00	.622	.833	1.00	.354	.724	.435

Table 5
P-Values for Each Channel of the Cordance

	Frontal Lobe							Central Area			Parietal Lobe			Temporal Lobe				Occipital Lobe	
	Fp1	Fp2	Fz	F3	F4	F7	F8	Cz	C3	C4	Pz	P3	P4	T3	T4	T5	T6	O1	O2
Cordance	.524	.354	1.00	.724	.284	1.00	.524	.524	.943	1.00	1.00	.435	.171	.622	.943	1.00	.833	.524	.622

Table 6
P-Values for Each Frequency Band and Channel of the Z-Scores

	Frontal Lobe							Central Area			Parietal Lobe			Temporal Lobe				Occipital Lobe	
	Fp1	Fp2	Fz	F3	F4	F7	F8	Cz	C3	C4	Pz	P3	P4	T3	T4	T5	T6	O1	O2
Delta1	.808	.368	.570	.570	.808	.048	.214	.683	.368	.368	.570	.683	.683	.933	.933	1.00	.808	.933	.683
Delta	.570	1.00	.368	.933	.214	.461	.154	.570	.570	.808	.283	.214	.154	.933	.808	.933	.683	.808	.283
Theta	.368	.461	.683	.570	.933	.109	1.00	.214	.154	.154	.160	.073	.214	.461	.570	.109	1.00	.808	1.00
Alpha	.933	1.00	1.00	.570	.808	.933	.808	.808	.461	.808	1.00	.570	.461	.683	.808	.368	.461	.570	1.00
Beta	.283	.368	.808	.808	.808	.283	.368	.683	1.00	.808	.683	.683	.808	.933	.368	.808	.368	.368	.570
Sum	1.00	.808	.808	.683	.570	1.00	1.00	.808	.368	1.00	.283	.808	.683	.808	1.00	.283	1.00	.933	1.00
Beta2	.214	.400	.570	.808	.808	.933	.683	.368	1.00	.368	.109	.933	.808	.283	.214	1.00	.461	.073	.280
Gamma	.368	.933	.368	.808	.214	1.00	.683	.933	.283	.808	1.00	.570	1.00	1.00	.368	.570	1.00	.570	.214
Alpha1	.933	.933	.933	.933	.933	.808	.570	1.00	.683	.808	.808	.368	.461	.808	.683	.214	.461	.461	.933
Alpha2	.808	.808	1.00	.461	.570	1.00	1.00	1.00	.214	.808	.283	.808	.368	1.00	.570	.808	.368	.368	.808

In a study conducted by Li et al. (2017), P300 was collected during a working memory task in individuals with amnestic mild NCD and healthy subjects, and it was found that subjects with mild NCD exhibited larger P300 amplitudes in the left frontal region. They interpretated this, according to previous literature, as an explanation that those individuals with mild NCD recruit more neural resources than individuals without impairment in various cognitive tasks, including memory and attention, to attempt to compensate for their cognitive deficits; hence, larger amplitudes of this component were observed.

The concept of using cordance in this pilot study stems from the well-established fact that there are changes in perfusion in patients with cognitive impairment (Alexopoulos et al., 2012). Given that cordance is a measure highly correlated with perfusion (Leuchter et al., 1994; Leuchter et al., 1999), it would not be surprising to uncover relevant findings in this regard. To the best of our knowledge, there have been few or no studies to date that have focused on the use of cordance measurement for the identification of markers of cognitive decline. In this regard, our research is pioneering. However, we did not uncover any significant findings related to cordance. One reason for the lack of findings in this metric could lie in the intermediate state (between normal cognitive functioning and established mild NCD diagnosis) in which the mild NCD group was situated. Although some studies (Sierra-Marcos, 2017) have found alterations in perfusion in patients with mild NCD compared to healthy controls, others have shown that there are no differences between individuals with and without subjective memory complaints (Funaki et al., 2019). Further research in intermediate states, between normal cognitive functioning and established cognitive impairment, is likely necessary to clarify this aspect.

No differences were found between the groups in sLORETA. Despite a significant difference being found in F7, we did not find anything relevant in the three-dimensional analysis. The structures represented by the sLORETA projector are created based on voxels (units of 5 mm^3). One possible explanation for this is that only part of some structures may exhibit significant elevations, but the averaging effect of the activity recorded in those voxels could dilute the elevation. In other words, one or several nearby structures may show elevations in a group of voxels, but the remaining portion of them may not show such elevations and therefore fail to generate sufficient deviating data. In one of our studies (Pérez-Elvira & Jiménez Gómez, 2020), we found that some voxels within a structure could exhibit elevations expressed in *z*-scores, while the remaining voxels of the structure could fall within the norm.

In summary, our work has presented as main innovations the testing of normalized data, transformed into *z*-scores, and concordance metrics as potential markers that differentiate cognitively healthy individuals from those at risk of cognitive decline. According to our results, and contrary to comparing healthy subjects with patients with Alzheimer's or with established cognitive impairment, raw qEEG values would not be informative. However, qEEG data transformed into *z*-scores through normative databases could reveal differences that assist in discriminating subjects at risk of cognitive decline. In this regard, it appears that changes in the frontal region, specifically the left frontal area, is a relevant location for detecting the risk of cognitive decline.

It should be noted that this study had significant limitations, being the sample size with the primary one. On the other hand, voxel-by-voxel data calculations were also not conducted in the case of sLORETA, which could have provided more information. It would be interesting for future research to increase the sample size and record information on a voxel-by-voxel basis.

Author Disclosure

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Neurofeedback Beta Down Training in Women With High State-Trait Anxiety and Elevated Beta Patterns in Temporal Lobes: A Pilot Study

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Abstract

This study intends to evaluate the effect of neurofeedback beta downtraining in the treatment of anxiety as a personality trait, measured in the State-Trait Anxiety Inventory (STAI), and to estimate the changes in the beta and high-beta rhythms in the left (T3) and right (T4) temporal lobes. An intrasubject analysis was carried out with six right-handed female university students who were submitted to a control and experimental condition (five neurofeedback seasons). In the results, it was observed that no significant changes were presented in the control stage. In turn, a significant reduction in the scores of the inventory was found in the experimental stage. On the other hand, even though in the experimental stage there was a decrease in the relative power of the beta and high-beta frequency bands, this was statistically significant in the beta band in T3 and T4 and in the high-beta band in T3. In conclusion, according to the results, neurofeedback had a significant effect on both reducing anxiety as a state and a personality trait, as well as reducing beta and high-beta patterns in the temporal lobes. The need for more studies with greater methodological rigor that can reassert or refute these results is noted.

Keywords: neurofeedback; state-trait anxiety; temporal lobes; electroencephalogram

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Introduction

According to the World Health Organization (World Health Organization [WHO], 2017), anxiety and depression are the two diagnostic categories of mental disorders with the highest prevalence in the world population and with the greatest impact on people's lives. In 2015, the WHO estimated that 3.6% of the world population had some type of anxiety disorder. This percentage corresponds to an approximate total of 264 million people who lived with the disease during that year (WHO, 2017).

State-Trait Anxiety Inventory

According to the dimensional model of anxiety proposed by Spielberger (1966), it is important to distinguish between anxiety as a person's transient state and anxiety as a relatively stable personality trait. Anxiety as a state (State-A) can fluctuate in intensity depending on daily events and is characterized by concern, muscle tension, and agitation associated with the momentary increase in the autonomic nervous system activity, such as increased heart rate, blood pressure, sweating, and sphincter control loss, among others (Forte et al., 2021). On the other hand, anxiety as a personality

trait (Trait-A) is characterized as a person responding constantly to a wide range of objectively nonhazardous situations as if they were threatening throughout various everyday situations. Such responses are disproportionate in intensity and frequency when compared to the objective magnitude of the threat (Spielberger, 1966).

The State-Trait Anxiety Inventory (STAI) is a self-report psychometric test that aims to assess the two previously mentioned anxiety components as a state and as a personality trait (Spielberger et al., 1983). It is one of the most used questionnaires in the study and detection of anxiety and has been widely leveraged in clinical and academic contexts from different cultures (Fioravanti-Bastos et al., 2011). It was translated into Portuguese and validated to be used with the Brazilian population by Biaggio et al. (1977).

State-A by itself does not represent a problem for people, as it works like an alert-sign warning about environmental threats and provides the necessary resources to face them. In this sense, State-A can be considered as a set of normal responses to the various situations of everyday life that generate stress. On the contrary, Trait-A is characterized by State-A intensity levels and response frequencies that outdo a person's capacity, causing clinically significant discomfort (Garcia et al., 2007). In such a way, Trait-A can be associated with difficulties in quality of life such as constant concern, low self-esteem, sleep disorders, emotional instability, hypervigilance, thoughts of vulnerability, exaggerated emotional reactions to real or imaginary threats, and excessive and constant levels of sympathetic autonomic activation of the nervous system (Rodríguez Landa et al., 2012).

Currently, there are various pharmacological and nonpharmacological approaches to treating anxiety, according to the intensity and characteristics of the symptoms. Psychotherapy and medications, such as antidepressants or anxiolytics, are among the main treatment modalities (Podea & Ratoi, 2011).

To early detect and implement the necessary measures for its timely treatment, a major focus of research and clinical practice has been on the study and detection of psychophysiological markers that reflect the neural and physiological characteristics of anxiety as a personality trait (Lee & Park, 2011). Based on the need for evidence-based intervention treatments, technological tools for neuromodulation have been developed since the 1960s to treat different clinically relevant symptoms such as anxiety (Nowlis & Kamiya, 1970). Neuromodulation tools can be understood as technological devices for direct intervention in the nervous system, developed to modify neuronal structure and/or function (Coben & Evans, 2011; Othmer, 2009).

Neurofeedback in the Treatment of Anxiety

Neurofeedback is a noninvasive neuromodulation tool focused on assessing and training brain electrical activity patterns (Bielas & Michalczyk, 2021; Hampson et al., 2020; Price & Budzynski, 2009). Between 1960 and 1970, it was discovered that it was possible to condition and train the brain wave patterns. Some of these papers started with alpha-wave training for concentration and relaxation (Kamiya, 2011; Nowlis & Kamiya, 1970). Others were focused on handling sensorimotor rhythm waves to control epilepsy (Sterman & Friar, 1972).

During a neurofeedback session, the person receives constant audiovisual feedback about the spectral parameters corresponding to specific EEG frequency ranges (Dessy et al., 2020). This tool works as a noninvasive modality of conditioning brain activation itself (Larsen & Sherlin, 2013), as feedback works as a contingent reinforcement to the neural adjustments that are presented during the session, thus generating the conditioning of new patterns (Yucha & Montgomery, 2008).

According to Larsen and Sherlin (2013), on an efficacy rating scale of 1 to 5, neurofeedback is rated at level 4 of moderate efficiency in treating diagnoses such as anxiety, as multiple studies with this technique showed positive results in improving clinically relevant symptoms for various forms of anxiety disorders (Choi et al., 2023; Hammond, 2005; Kerson et al., 2009; Micoulaud-Franchi et al., 2021). Likewise, according to the systematic review by Santana and Bião (2018) and Choi et al. (2023), neurofeedback is effective in the treatment of anxiety, although the need for more studies that may reassert or refute these results is noted.

Neurofeedback, also known by the name of EEG biofeedback, has proved to be potentially effective in reducing mood disorders among post-COVID-19 patients. The technique was demonstrated to be capable of improving cognitive and executive functions and reducing the anxiety, panic, and fear symptoms (Kopańska et al., 2022).

Neurofeedback treatment can be divided into two stages: (a) an evaluation stage, in which a quantitative electroencephalogram (qEEG) is performed and the brain activation patterns are

identified; and (b) an intervention stage, in which the corresponding protocols are applied according to the needs demonstrated in the brain activation patterns recorded by the qEEG (Patil et al., 2023).

The results of a qEEG reflect consciousness statuses and different levels of physiological and cognitive excitation. That is, activity in the delta (2–4 Hz) and theta (4–8 Hz) frequencies is known as slow waves that are associated with sleep, drowsiness, or relaxation states, whereas activity within the alpha (8–12 Hz), beta (12–23 Hz), high-beta (23–38 Hz), and gamma (38–42 Hz) frequency ranges refers to fast waves, which are associated with alertness and cognitive activation (Faller et al., 2019; White & Richards, 2009).

As a personality trait, anxiety is closely related to constant stress statuses and high levels of cognitive and physiological excitation. Thus, Trait-A is highly associated with higher cortical activity levels in the beta and high-beta waves in a qEEG (Micoulaud-Franchi et al., 2021; Thompson & Thompson, 2007).

The amygdala and hippocampus are subcortical structures that have been widely associated with the classical response of struggling or escaping as a fast way of responding to environmental threats (Verbitskii, 2019). In the various anxiety disorders, an increase has been found both in the amygdala functional activity and in its volume (Barrós-Loscertales et al., 2006). Therefore, a hyperactive amygdala can be an indicator of constant emotional responses of fear, aversion, and stress (Wheelock et al., 2021). However, the amygdala is not the only structure in charge of producing the entire emotional response. For this, all the cortical regions interact with several subcortical structures in the process to perceive and elaborate the different components of the emotional response (Barreto & Silva, 2010). Of all the brain cortex areas, the most extensively connected to the limbic system are the temporal and frontal lobes (Kamali et al., 2023). In anxiety disorders (e.g., phobia, panic, and generalized anxiety, etc.), high-beta activity levels have been observed in the lateral prefrontal and anterior temporal cortical areas (Davidson, 1992). Therefore, beta and high-beta activity levels in the temporal lobes in a qEEG are highly correlated with negative emotional states, associated with amygdala hyperactivation levels (Gordeev, 2007), mainly when these irregular activity levels are found in the right anterior frontotemporal portion (Davidson et al., 2000).

According to the results obtained in the study by Ribas et al. (2018) based on the learning curve model proposed by Peter Van Dausen (Ribas, Ribas, & Martins, 2016), there is a statistically significant correlation between the symptoms associated with anxiety, insecurity, fear, panic, and phobia with high levels of beta and high-beta waves in the temporal lobes when compared to the respective control. Thus, the anxiety response can be observed when the relative power of the beta waves (12–23 Hz) is greater than 17% and that of the high-beta ones (23–38 Hz) is greater than 10% in the temporal lobes. According to the learning curve model, this pattern is known as “hot temporals” and is associated with the idea that the temporal lobes present excessive levels of fast activity.

EEG data analysis employs two primary methodologies: population-based and pattern-based approaches. In the former, client measures undergo comparison with a database spanning 3 decades, yielding *z*-scores that highlight deviations in specific brain regions from the population norm. However, the interpretation of these deviations as positive or negative, adaptive or maladaptive, remains ambiguous. Conversely, the pattern-based approach identifies consistent activation patterns associated with problematic aspects of individuals' lives through quantitative EEG research. These patterns are discerned by contrasting individuals with specific concerns, such as anxiety or ADHD, against the broader population to ascertain recurring disparities. The learning curve model aims to discern particular brain patterns, such as the hot temporals pattern and establish tailored training objectives to address each individual's unique requirements.

Several research studies have confirmed the efficacy of neurofeedback in the treatment of anxiety (Chen & Lin, 2020; Choi et al., 2023; Hammond, 2003, 2005; Jones & Hitsman, 2018; Micoulaud-Franchi et al., 2021; Mennella et al., 2017; Moore, 2005); however, there are no studies evaluating neurofeedback interventions specifically in the beta and high-beta wave patterns in the temporal lobes, which, as mentioned, have important links with the limbic system in charge of processing emotional information and with an acknowledged connection with the development of anxiety disorders (Forte et al., 2021; Lee & Park, 2011; Ribas et al., 2018).

Based on the aforementioned, the objective of the current research was to assess the effect of the neurofeedback neuromodulation tool in the

treatment of anxiety as a personality trait. More specifically, the study aims at evaluating the possible changes generated after the neurofeedback interventions, focusing attention on two aspects: (a) the subjective perception of anxiety, as measured by STAI; and (b) brain activation patterns in the temporal lobes, as measured by a qEEG.

Method

The study procedures were approved by the Tropical Medicine Center (*Núcleo de Medicina Tropical*, NMT) at the Federal University of Pará (CAAE No.: 25068619.8.0000.5172/Opinion No.: 3,784,218) and the participants signed the Free and Informed Consent Form (FICF).

Participants

The STAI questionnaire was answered by 100 university women aged between 18 and 35 years old. Fifteen of them were preselected, as they met the inclusion criteria and obtained scores above 50 points in the Trait-A form from the STAI by Biaggio et al. (1977). A qEEG was administered to assess all 15 students, and six participants were selected for the intervention process as they presented the hot temporals brain pattern, the object of the current study. All the participants selected were right-handed to avoid asymmetries in the interhemispheric brain activity influenced by hand dominance (Davidson, 1988). Table 1 summarizes the criteria to include and exclude research participants.

Table 1

Inclusion and Exclusion Criteria

Inclusion	Exclusion
• Women • Age between 18 and 35 years old • Trait-A STAI score > 50 points • Hot temporals brain pattern • University students • Right-handed	• Psychotherapeutic or psychiatric treatment • Comorbidity with other diseases: other mental disorders; hypertension; diabetes; obesity. • Using a medication known to exert an influence on the EEG measurements (antidepressants and anxiolytics, etc.)

Procedures

State-Trait Anxiety Inventory (STAI). STAI has 40 items formulated in a Likert self-report format, with scores for each individual item varying from 1 (*absolutely not*) to 4 (*very much*). The questionnaire consists of two subscales: State A and Trait A, and each one is comprised by 20 items that should be answered according to the person's perception. The State A form seeks answers based on how the person feels at that moment or on that day (e.g., I feel calm, I feel safe, I'm tense). On the other hand, the Trait A form seeks answers based on how the person generally feels (e.g., I feel good, I get tired easily, I want to cry).

The questionnaire was adapted through a digitalized version in Google Forms, although the original structure of the questions and answers was maintained. Subsequently, it was sent to the participants in the online modality. The answers were forwarded directly to the researcher.

Quantitative Electroencephalogram (qEEG). Silver electrodes (Nicolet Scientific Instruments Ltd), conductive paste (Ac Cream by Spes Medica), and abrasive gel for cleaning the scalp (NuPrep by Spes Medica) were used, in addition to the Q-Wiz electroencephalograph (Pocket Neurobics) with four simultaneous channels for individual electrodes and a 21-channel cap interface. The sampling rate was 512 Hz. Each channel has a 0.2-Hz high pass filter. Real-time acquisition, processing, and reproduction of biological signs were performed in the BioExplorer software (CyverEvolution Inc.). For data processing, the TRAINER'S QEEG (TQ-7) software (BrainTrainer, version TQ-7.5.9.2), based on the learning curve model was used, which offers high-resolution brain information such as frequency distribution maps, absolute and relative amplitude distributions, histogram graphs, asymmetry graphs and coherence tables, among other forms of EEG analysis (Ribas, Ribas, de Oliveira, et al., 2016).

Conventional EEG research commonly involves simultaneous recordings from 19 channels, necessitating at least 2 min of artifact-free EEG data for analysis. However, advancements in neurofeedback systems have aimed to enhance accessibility within clinical settings. As a result, these systems often utilize a smaller number of active channels for both assessment and training purposes. The current study sought to reproduce standard neurofeedback assessment conditions.

Considering the purpose of neurofeedback assessment is to make it easily accessible, shorter recording times are used while ensuring data quality through artifact removal. Consequently, the qEEG was recorded at rest in two conditions: (a) 1 min with the eyes closed; and (b) 1 min with the eyes open. Twelve points were measured with monopolar assembly (FZ, PZ, CZ, OZ, F3, F4, P3, P4, T3, T4, C3, and C4, with linked references on the mastoid bones behind the ears), according to the 10–20 International System (Klem et al., 1999). Following data collection, the gathered data underwent processing using the TQ-7 processing software for artifact removal and posterior analyses.

The filtering of artifacts, including electromyography (EMG) artifacts, and its differentiation from actual beta power in EEG recordings were also addressed using TQ-7 data processing software. This software utilizes an algorithm that distinguishes EMG artifacts from genuine beta activity by analyzing their amplitude and frequency characteristics. EMG artifacts generally present higher amplitudes and broader frequency ranges than neuronal signals (Yu, 2021). To confirm the reliability of these measures, the TQ-7 software sets low-frequency thresholds to filter out artifacts associated with eye blinks, eye movements, and cable movements, and high-frequency thresholds for muscle tension, movement, and electromagnetic artifacts. During the assessment, the system ensures that at least 50% of the recording is free of artifacts, requiring a minimum of 30 s of artifact-free data for each electrode placement to guarantee the data's validity. The software detects these potential artifacts and highlights epochs containing significant artifacts to discard them for further analysis. Subsequently, it conducts a detailed frequency analysis on the remaining epochs. To analyze the qEEG results, the beta (12–23 Hz) and high-beta (23–38 Hz) ranges in the left and right temporal lobes were considered.

In the context described, data analysis was conducted without relying on database comparisons, utilizing the pattern-based approach. Rather than comparing individual measures to a database, this methodology concentrates on identifying consistent activation patterns associated with specific concerns, such as the hot temporal pattern linked to anxiety, within the individual's EEG data. This approach offers a more focused and personalized analysis of the individual's brain activity, yielding insights into underlying neural changes that could serve as effective targets for neurofeedback interventions.

Neurofeedback Intervention Protocol. The protocol design was developed by the BrainTrainer company (Ribas, Ribas, de Oliveira, et al., 2016). For its execution, two separate EEG channels with monopolar assembly are used. The active electrodes were positioned on the left (T3) and right (T4) temporal lobes, with linked references on the right and left mastoid bones and ground electrode on CZ. For this protocol, it is possible to make adjustments that allow decreasing the amplitude of specific frequency bands such as beta and high beta.

For all intervention sessions, the participants wore high-definition earbuds and remained seated in a reclining chair with a headrest in front of a TV screen. During the session, the participants watched landscaping videos on the TV screen while receiving auditory feedback through the earbuds and visual feedback through the TV screen. For the research object, the training was selected to inhibit the amplitude corresponding to the 19–38 Hz frequency range. During the first 30 s of the intervention protocol, the BioExplorer software establishes a baseline to place a threshold that acts as the training range. Thus, for example, if during the first 30 s, the system establishes a threshold of 20 microvolts (μV) for the 19–38 Hz frequency range, then, throughout the protocol, each time the group of pyramidal neurons near the electrode fire below 20 μV, the patient hears a high-pitched piano note. The sounds or screen brightness acted as feedback linked to the active channels being trained. The patient only listened to the piano sound after recording the values stipulated in the baseline for the specific frequency range being trained. The more piano sounds heard by the participant, the more adequate were the trained brain waves. The same happened with screen brightness: the brighter, the better the response of the trained waves.

A single-factor intersubject pretest and posttest experimental design was used, with each participant as their own control (Kazdin, 2017). Data analysis was performed in blocks according to their mean values and standard deviations. Thus, all the participants were grouped and subjected to two conditions: control and experimental, with manipulation of the independent variable in the latter. As can be seen in Table 2, the research was developed in four phases: (a) Pretest 1; (b) Pretest 2; (c) intervention; and (d) posttest.

Table 2
Study Phases

Control			
Pretest 1	Pretest 2	Intervention	Posttest
STAI/qEEG	STAI/qEEG	Neurofeedback (five sessions)	STAI/qEEG
Experimental			

In the control stage, STAI and the qEEG were applied in order to compare their results between Pretest 1 and Pretest 2. This first research stage corresponded to the control stage, where the mean values of the tests before the intervention were compared. The experimental stage was initiated the 1st week after Pretest 2. Five sessions of the same neurofeedback protocol were applied in the temporal lobes during 2 weeks. The posttest was performed 1 week after finishing the intervention. The objective of the experimental phase was to compare the Pretest 1 and Pretest 2 results to the posttest separately.

Results

To evaluate the effect of neurofeedback in the treatment of anxiety, the STAI and qEEG variables were measured before and after the intervention. The Pretest 1 results were compared to those of Pretest 2 (control stage) and the Pretest 1 and Pretest 2 results were compared to those of the posttest (experimental stage).

Initially, basic descriptive statistics were performed to characterize the study variables; subsequently, normality tests were carried out using the Shapiro-Wilk test. Finally, to quantify and evaluate the changes between the pre and postintervention study variables, comparative statistics were applied using the calculation of comparison of related means, Student's *t* test for paired samples. The statistical decisions were calculated considering $p < .05$ as the significance level.

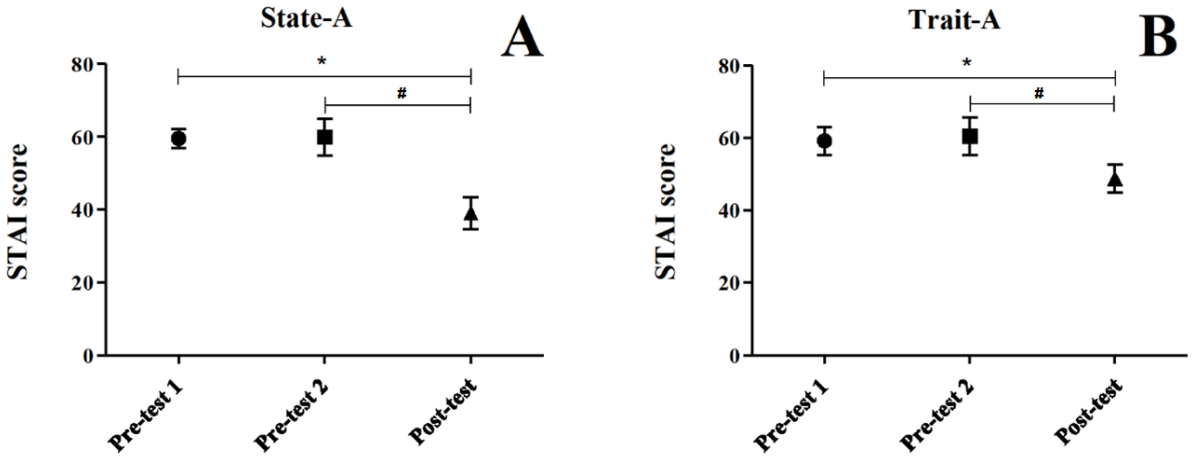
STAI Results. Table 3 shows the descriptive and comparative statistics corresponding to the STAI Pretest 1, Pretest 2, and posttest phases. Figure 1 shows the mean STAI scores in its two forms: (A) State-A and (B) Trait-A.

Table 3
Descriptive and Comparative Statistics Corresponding to the STAI Pre and Posttests

Control						
	Pretest 1		Pretest 2			
	$\bar{x}$	σ	$\bar{x}$	σ	*t*	*p*
State-A	59.50	6.53	59.83	12.37	−0.077	.471
Trait-A	59.17	9.41	60.5	12.63	−0.628	.279
Experimental						
	Pretest 1		Posttest			
	$\bar{x}$	σ	$\bar{x}$	σ	*t*	*p*
State-A	59.50	6.53	39.00	10.71	3.154	.013*
Trait-A	59.17	9.41	48.83	9.52	2.488	.028*
	Pretest 2		Posttest			
	$\bar{x}$	σ	$\bar{x}$	σ	*t*	*p*
State-A	59.83	12.37	39.00	10.71	2.486	.028*
Trait-A	60.5	12.63	48.83	9.52	2.110	.044*

* = Descriptive and comparative statistics of the Trait-A STAI scores in the Pretest 1, Pretest 2, and posttest phases.

Figure 1. *Mean Scores Corresponding to the STAI Pretest and Posttest Phases*.



Note. Mean STAI scores in its (A) State-A and (B) Trait-A form. * = Significance between Pretest 1 and posttest; # = Significance between Pretest 2 and posttest.

Analysis of qEEG Results. The analysis of the qEEG results was based on the mean values corresponding to the relative power of the wave amplitude of the frequency bands, also known as the relative power of the frequency bands, which are expressed in microvolts (μV). Data were collected from 12 evaluated EEG points but for research purposes, only data obtained about the beta (12–23 Hz) and high-beta (23–38 Hz) frequency bands at T3 and T4 were used. Table 4 shows the descriptive and comparative statistics corresponding to the Pretest 1, Pretest 2, and posttest phases of the mean values corresponding to the beta wave relative power at T3 and T4. Figure 2 shows the mean scores corresponding to the beta wave relative power at (A) T3 and (B) T4.

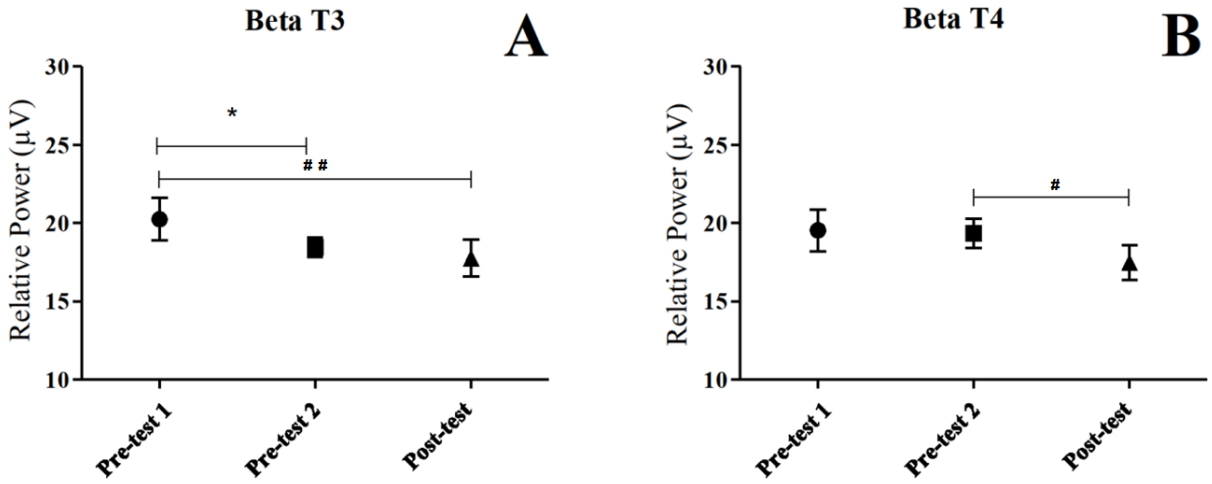
Table 4

Descriptive and Comparative Statistics Between the Pre and Posttests – Beta at T3 and T4

Control						
	Pretest 1		Pretest 2			
	$\bar{x}$	σ	$\bar{x}$	σ	*t*	*p*
T3	20.27	3.33	18.47	1.51	2.1000	.045*
T4	19.55	3.26	19.35	2.31	0.1622	.439
Experimental						
	Pretest 1		Posttest			
	$\bar{x}$	σ	$\bar{x}$	σ	*t*	*p*
T3	19.93	3.68	17.77	2.87	4.070	.005**
T4	19.55	3.26	17.47	2.70	1.916	.057
	Pretest 2		Posttest			
	$\bar{x}$	σ	$\bar{x}$	σ	*t*	*p*
T3	18.47	1.51	17.77	2.87	0.806	.229
T4	19.35	2.31	17.47	2.70	2.393	.031*

* = Descriptive and comparative statistics corresponding to the mean beta relative power at the T3 and T4 points for the Pretest 1, Pretest 2, and posttest phases.

Figure 2. *Mean Values Corresponding to the Beta Wave Relative Power at T3 and T4*.



Note. Mean beta wave relative power at the (A) T3 and (B) T4 point. * = Significance between Pretest 1 and posttest; # = significance between Pretest 2 and posttest.

Table 5 shows the descriptive and comparative statistics corresponding to the Pretest 1, Pretest 2, and posttest phases of the mean values corresponding to the high-beta wave relative power in the temporal lobes. Figure 3 shows the mean scores corresponding to the high-beta wave relative power at (A) T3 and (B) T4.

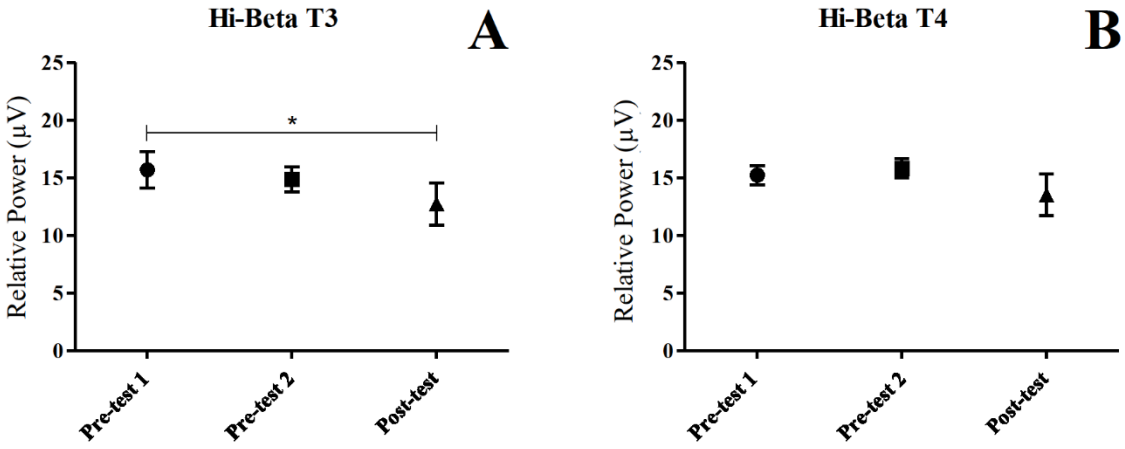
Table 5

Descriptive and Comparative Statistics Between the Pre and Posttests – High-Beta at T3 and T4

Control						
	Pretest 1		Pretest 2			
	$\bar{x}$	σ	$\bar{x}$	σ	*t*	*p*
T3	15.70	3.86	14.87	2.71	0.9245	.199
T4	15.23	2.08	15.83	2.07	0.5061	.317
Experimental						
	Pretest 1		Posttest			
	$\bar{x}$	σ	$\bar{x}$	σ	*t*	*p*
T3	15.70	3.86	12.73	4.46	2.215	.038*
T4	15.23	2.08	13.53	4.42	0.896	.206
	Pretest 2		Posttest			
	$\bar{x}$	σ	$\bar{x}$	σ	*t*	*p*
T3	14.87	2.71	12.73	4.46	1.396	.110
T4	15.83	2.07	13.53	4.42	1.098	.161

* = Descriptive and comparative statistics corresponding to the mean high-beta relative power at the T3 and T4 points for the Pretest 1, Pretest 2, and posttest phases.

Figure 3. *Mean Values Corresponding to the High-Beta Wave Relative Power at T3 and T4*.



Note. Mean high-beta wave relative power at the (A) T3 and (B) T4 point. * = Significance between Pretest 1 and posttest.

Discussion

The objective of this study was to evaluate the effect of neurofeedback interventions in the treatment of anxiety as a personality trait and to estimate the changes in brain patterns of the beta and high-beta rhythms in the left (T3) and right (T4) temporal lobes.

When analyzing the STAI results, it can be observed that in the control stage, no statistically significant differences were found between the mean scores corresponding to the Pretest 1 and Pretest 2 phases of the State-A or Trait-A forms. On the other hand, in the experimental stage, there was a statistically significant decrease in the scores between the STAI pretests 1 and 2 and posttest, both in its State-A and Trait-A forms. These results show a statistically significant difference in the STAI scores before the neurofeedback intervention process. These results coincide with research studies that acknowledge the efficacy of neurofeedback in the treatment of anxiety (Chen & Lin, 2020; Choi et al., 2023; Hammond, 2003, 2005; Jones & Hitsman, 2018; Larsen & Sherlin, 2013; Mennella et al., 2017; Micoulaud-Franchi et al., 2021) and support the hypothesis that intervention protocols focused on decreasing the relative power of the beta and high-beta frequency bands in the temporal lobes has the potential to treat and reduce the anxiety symptoms.

The results of this study evidence the participants' favorable evolution after undergoing the intervention procedure, observing significant improvements in the anxiety as measured by STAI both in its State-A (Figure 2A) and Trait-A (Figure 2B) forms. It is important to note that, although the research focused on anxiety as a personality trait, it was also possible to observe in the results that anxiety as a state response was also reduced. This result is common and logical, as a decrease or increase in Trait-A generates a decrease or increase in State-A, although this effect is not necessarily observed in the other direction. In other words, an increase or reduction in State-A not necessarily increase or reduce Trait-A (Spielberger et al., 1983).

Among the results obtained in the qEEG, in the experimental stage, a statistically significant decrease in the relative power of the beta frequency bands (Figure 3A and Figure 3B.) is observed in both temporal lobes.

When analyzing the results about the relative power of the high-beta frequency band, it can be summarized that in the control stage there was no significant difference between the mean values corresponding to the relative power of the wave between pretests 1 and 2 for T3 or T4. On the contrary, in the experimental stage there was in fact a significant reduction in the mean value between pretest 1 and the posttest at the T3 point. In turn, at the T4 point a decreasing trend can be observed in the results, although this difference was not statistically confirmed.

Limitations and Future Research

The current study elucidates several limitations that prevent the generalization of its findings. Notably, the sample is characterized by specific features, comprising only six participants. Furthermore, it is essential to emphasize that the sample selection was nonrandom and based on convenience according to the accessibility of the participants. Future research could increase the number of participants to enhance statistical accuracy, as well as explore methodologies for the random selection of participants within a larger sample.

Most of the qEEG evaluation processes present difficulties inherent to their execution, such as variations in brain patterns resulting from daily habits and other artifacts related to the measuring process, such as muscle and eye movements and even the electrical grid. In the research, the same times and conditions were always maintained, both for the evaluations and for the intervention sessions, to reduce the aforementioned interferences to the minimum possible. However, for future research studies, it is recommended to control these and other external variables that can interfere with data from tools as sensitive as an EEG.

According to the scientific literature, the number of sessions can exert an influence on the results of the changes in the brain patterns. Therefore, the proposal for future research studies is to conduct more sessions to assess data stability and trends. Although there is no consensus in scientific research on the minimum number of sessions for the treatment, the results of this study suggest that, even with five sessions, neurofeedback can produce positive effects in reducing the symptoms, in line with the results obtained in other research studies that evidence the efficacy of neurofeedback in the treatment of anxiety (Santana & Bião, 2018; Gadea et al., 2020).

An additional limitation in our study arises from the limited literature available on the use of the TQ-7 software for EEG data processing in scientific research. Originally developed for neurofeedback interventions and widely used around the world, the TQ-7 software was not specifically designed for research purposes, which presents challenges for its application in scientific studies. While the software has been utilized in some research contexts, such as the study by Ribas et al. (2018) on the hot temporals brain pattern, and in other case studies (Habib et al., 2023; Ribas et al., 2017; Solano & Basile, 2020), comprehensive validation studies specific to this software are lacking. This gap underscores the importance of conducting validation studies to ensure the reliability and accuracy of the TQ-7 software when used for research purposes. Such studies would enhance confidence in the software's ability to accurately process EEG data and filter artifacts, thereby improving the robustness and replicability of findings in future research using this tool.

Neurofeedback is a technique that still needs to be studied more rigorously; however, it shows potential to be an efficacious and nonpharmacological complementary treatment option for the intervention of affective disorders such as anxiety. When addressing research on neurofeedback within a specific population, as in the current study, it is essential to carefully consider the impact of external validity. The application of interventions like neurofeedback can be highly influenced by the specific characteristics of the studied population, such as age, health conditions, and specific brain patterns. Consequently, the challenge of generalizing the results to other populations becomes a significant concern. Individual nuances and inherent variabilities in different groups can limit the extension of findings, impairing the ability to extrapolate the benefits of the intervention beyond the studied research group. Therefore, reflection on external validity is crucial to understanding the extent to which the findings can be applied to other contexts and groups, providing a more comprehensive insight into the effectiveness of neurofeedback in different conditions.

Author Disclosure

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Effectiveness of Neurofeedback Training in Poststroke Cognitive Impairment

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Abstract

Introduction. Poststroke cognitive impairment (PSCI), characterized by cognitive deficits occurring up to 3 months after stroke, poses a substantial burden because this condition can persist and get worse over time. There has been no recommended conventional cognitive rehabilitation method that has a significant effect on cognitive improvement. Neurofeedback training (NFT) based on quantitative electroencephalogram (qEEG), emerges as a promising intervention for PSCI. However, research remains limited, necessitating further investigation into its effectiveness and clinical utility. **Methods**. This study assesses the efficacy of NFT in eight PSCI patients over 10 sessions (30 min/session) across 2 weeks with protocol based on qEEG for each patient. **Results**. Significant improvements were observed in total MoCA-Ina scores (mean increase of 2.63 points), particularly in visuospatial/executive, naming, attention, language, delayed recall, and orientation domains. Wilcoxon test indicated a significant improvement (p = .019, effect size: −0, 828) post-NFT. Multivariate analysis revealed no confounding influence of demographic and clinical factors on cognitive improvement. **Conclusion**. These findings highlight NFT's potential as an adjunctive therapy in PSCI rehabilitation, warranting further investigation for efficacy of NFT in larger studies and explore its long-term effects on cognitive function and quality of life for PSCI patients.

Keywords: poststroke cognitive impairment; neurofeedback training; quantitative electroencephalogram; MoCA-Ina

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Introduction

Poststroke cognitive impairment (PSCI), defined as cognitive deficits occurring up to 3 months after stroke, with a minimum duration of 6 months, is unrelated to any other conditions or diseases such as metabolic, endocrine, vasculitis, or depression (Danovska et al., 2012). PSCI is also defined as all problems in cognitive function that occur following a stroke, irrespective of the (stroke) etiology (Rost et al., 2022). This condition can result from all types of strokes (ischemic stroke, intracerebral hemorrhage, or subarachnoid hemorrhage). While stroke patients may experience improvement in physical function over time, cognitive impairment can remain a cause of disability and dependency (Hernández & González-Gálvez, 2021). These impairments can significantly affect the patient's quality of life and rehabilitation process, adding a substantial burden to both families and society (Chen et al., 2015).

Until now there has been no recommended conventional cognitive rehabilitation method that has a significant effect on cognitive improvement. New cognitive rehabilitation strategies using human-computer interface have been studied and reported to offer promising new treatment. These methods modulate brain waves using neurofeedback training (NFT) based on quantitative electroencephalogram (qEEG; Kober et al., 2015). NFT is type of biofeedback therapy which aims to

adjust brain waves within specific ranges, and optimal brain wave adjustments can affect various functional aspects of the patient (Cho et al., 2015). In NFT, EEG activity and brain waves are provided as visual or auditory feedback to the patients, allowing them to consciously adjust their brain wave activities with some repetitive training session (one session/days) to reach targeted training thresholds (Renton et al., 2017). NFT relies on operant conditioning to stimulate brain neuroplasticity and normalize the abnormal brain waveform. Such training can accelerate functional reorganization in poststroke brain, indicating the significant potential value of NFT in cognitive rehabilitation (Hammond, 2006; Kleim & Jones, 2008).

Research by Kober et al. (2015) reported that stroke patients with cognitive deficits, such as memory impairment, experienced improvement post-NFT with sensorimotor rhythm (SMR) and upper alpha protocols. Similarly, Cho et al. (2015) reported similar result, showing that NFT effectively enhances concentration and visual perception in poststroke patients. Meta-analysis conducted by Jackson et al. (2023) shows that NFT have a promising effect in episodic memory improvement. Objectively, Jang et al. (2019) found that MCI patients who received NFT therapy experienced an improvement in Montreal Cognitive Assessment (MoCA) scores of 4.4 points after 8 therapies and 6.2 points after 16 sessions. Research conducted by Marlats et al. (2019) involving 20 patients with mild cognitive impairment who underwent NFT therapy with the SMR protocol for 30 sessions, 2–3 times a week, showed an increase in the MoCA score of 1.9 points. Unfortunately, studies related to the effectiveness of NFT as cognitive rehabilitation in stroke patients are limited to single case studies, and adequate studies regarding its effectiveness and clinical utility have not been widely conducted. This study represents the first research in Indonesia assessing cognitive function improvement through NFT with the improvement parameter of the Indonesian version of the MoCA (MoCA-Ina) mean scores.

Methods

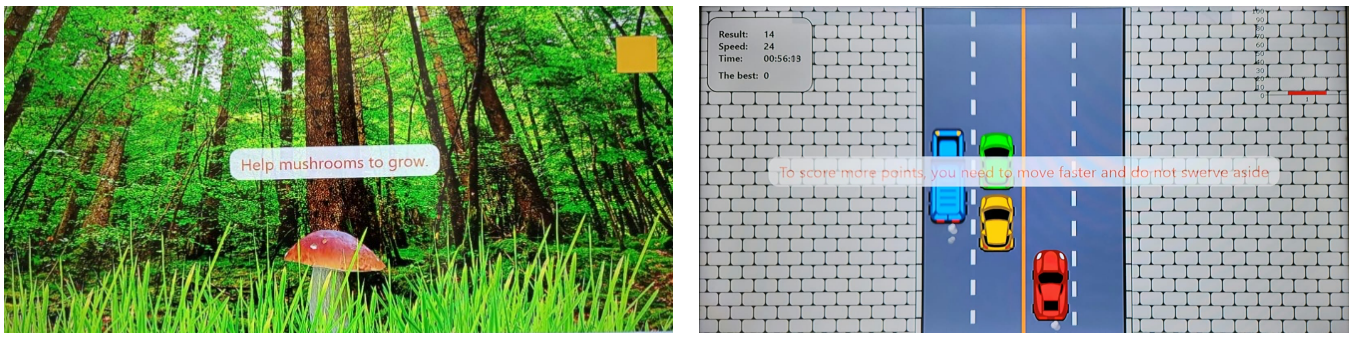
This study was a preexperimental design with one group pretest–posttest conducted at the Memory Clinic and Neurofeedback Clinic of Dr. Mohammad Hoesin Palembang Teaching Hospital from May to August 2023. The sample population consisted of patients diagnosed with PSCI based on comprehensive neurocognitive assessments (MMSE, MoCA-INA, *Clock Drawing Test* [CDT], *forward digit span, backward digit span,* CERAD, TMT A, TMT B, and *Clinical Dementia Rate* [CDR]) at the Memory Clinic, supervised and interpreted by a neurobehavior consultant, selected using consecutive sampling method. Inclusion criteria were patients aged ≥ 18 years with onset of cognitive impairment occurring ≥ 3 months poststroke, experiencing their first-time stroke, and having good vision and hearing function. Exclusion criteria were: patients with dementia, preexisting cognitive impairment before stroke (based on history taking and AD-8 test), psychiatric disorders such as depression, anxiety, aphasia, or concurrent neurological disorders (such as Parkinson's Disease, etc.), which can affect patients' cognitive function and cognitive test, and a history of medications affecting vigilance state. Dropout criteria included discontinuation of participation before study completion or death before completing the study.

Written informed consent was obtained from all participants before their inclusion and after getting the full explanation of the study procedures, risks, and benefits. The study protocol was approved by the Ethics Committee of Dr. Mohammad Hoesin Palembang Teaching Hospital (No. DP.04.03/D.XVIII.6.11/ETIK/55/2023). The researcher ensured patient confidentiality in accordance with applicable research ethics.

Patients first underwent a baseline assessment using the MoCA-Ina, followed by qEEG examination. Subsequently, they received NFT using Neurosoft-Neuron-Spectrum-61, consisting of 10 consecutive sessions over 2 weeks, with each session lasting 30 min. The treatment protocols used were based on initial qEEG results: three patients exhibiting low alpha wave activity received the alpha protocol, and five patients with low SMR wave activity received the SMR protocol.

In the alpha protocol, patients are asked to relax and focus on looking at the monitor containing images of mushrooms. Therapy is achieved if the size of the mushroom image increases compared to the initial size. In the SMR protocol the patient is asked to focus and concentrate on the monitor with several modalities such as racing a car or plane. If concentration is achieved, the patient's car will overtake other cars. Post-NFT, patients underwent a repeat assessment using the MoCA-Ina.

Figure 1. *Example of Visual Feedback (A) Alpha Protocol Therapy and (B) SMR Protocol Therapy*.



(A) (B)

Collected data were entered into SPSS version 22. Changes in mean MoCA-Ina scores and mean scores per cognitive domain were compared before and after therapy using paired simple *t*-tests for normally distributed data and Wilcoxon tests for nonnormally distributed data. The selected test has such shortcomings such as discards some information about the magnitude of differences between pairs. Furthermore, multivariate analysis was conducted to determine the influence of confounding variables on the change in mean MoCA-Ina scores. Significance was set at $p < .05$.

Results

In this study, eight participants meeting inclusion criteria and having no exclusion criteria were enrolled. All subjects completed the study protocol without any reported adverse effects of NFT. The baseline characteristics of the participants are presented in Table 1.

Based on the distribution characteristic data, most patients were under the age of 65 (75%), predominantly male (62.5%), with the highest level of education being high school (50%). Eight patients (75%) had lesions in the subcortical area, and the time since stroke, until the diagnosis of PSCI was established, was mostly over 6 months, accounting for 62.5%.

Table 1
Distribution of Characteristics of Poststroke Cognitive Impairment Patients

Variable	Frequency (*n*)	Percentage (%)
Age		
≤ 65 years	6	75%
> 65 years	2	25%
Gender		
Male	5	62.5%
Female	3	37.5%
Education Level		
Informal education/no schooling	0	0%
Elementary school	1	12.5%
Junior high school	1	12.5%
Senior high school	4	50%
College/university	2	25%

Table 1
Distribution of Characteristics of Poststroke Cognitive Impairment Patients

Variable	Frequency (*n*)	Percentage (%)
Lesion Location		
Cortical	2	25%
Subcortical	6	75%
Both	0	0%
Time Since Stroke		
≤ 6 months	3	37.5%
> 6 months	5	62.5%
Modified ranking scale (mRS)		
mRS 0	1	12.5%
mRS 1	2	25%
mRS 2	2	25%
mRS 3	1	12.5%
mRS 4	2	25%
mRS 5	0	0%

In Table 2, the results of the MoCA-Ina examination are presented. The baseline mean MoCA-Ina score was 14.75 ± 8.464, with a maximum score of 25 and a minimum score of 5. In each domain of the MoCA-Ina, the mean scores were as follows: 2.63 ± 1.847 for the visuospatial/executive domain, 1.75 ± 1.389 for the naming domain, 3.25 ± 2.121 for the attention domain, 1.13 ± 0.835 for the language domain, 0.88 ± 0.991 for the abstraction domain, 0.75 ± 0.886 for the delayed recall domain, and 4 ± 1.773 for orientation. Based on these data, the abstraction and delayed recall domains were the most affected, with four out of eight patients scoring 0 during the test.

Table 2
Baseline Scores of MoCa-Ina Total and Per Domain

	Mean Score	± *SD*
Moca-Ina Total	14.75	8.464
Visuospatial/Executive	2.63	1.847
Naming	1.75	1.389
Attention	3.25	2.121
Language	1.13	0.835
Abstraction	0.88	0.991
Delayed Recall	0.75	0.886
Orientation	4.00	1.773

Bivariate analysis in Table 3 and 4 reveals a comparison of MoCA-Ina scores before and after NFT intervention. Most patients showed improvement with an increase in MoCA-Ina scores, with only one patient experiencing a decrease of 1 point in MoCA-Ina score after completing NFT. There was an average improvement of 2.63 points in MoCA-Ina scores with a *p*-value of .019 ($p < .05$) (effect size: −0, 828), indicating that NFT therapy leads to an improvement in average MoCA-Ina scores. Education level also influenced MoCA-Ina scores, where those with less than 12 years of education had 1 point added to their total MoCA-Ina score. Analysis of improvement in pre and post values based on adjustments to MoCA-Ina scores was also conducted, and based on the Wilcoxon test, statistically significant results were obtained ($p = .019$), indicating no significant difference in improvement between baseline MoCA-Ina scores and those adjusted for education.

Table 3
Comparison of Mean MoCA-Ina Score Before and After NFT

	Neurofeedback Training		
	Before	After	*p*-value
Mean score of Moca-Ina	14.75 ± 8.464	17.38 ± 9.606	.019

Note. *p*-value using Wilcoxon test.

Table 4
Comparison of Mean MoCA-Ina Score Per Cognitive Domain Before and After NFT

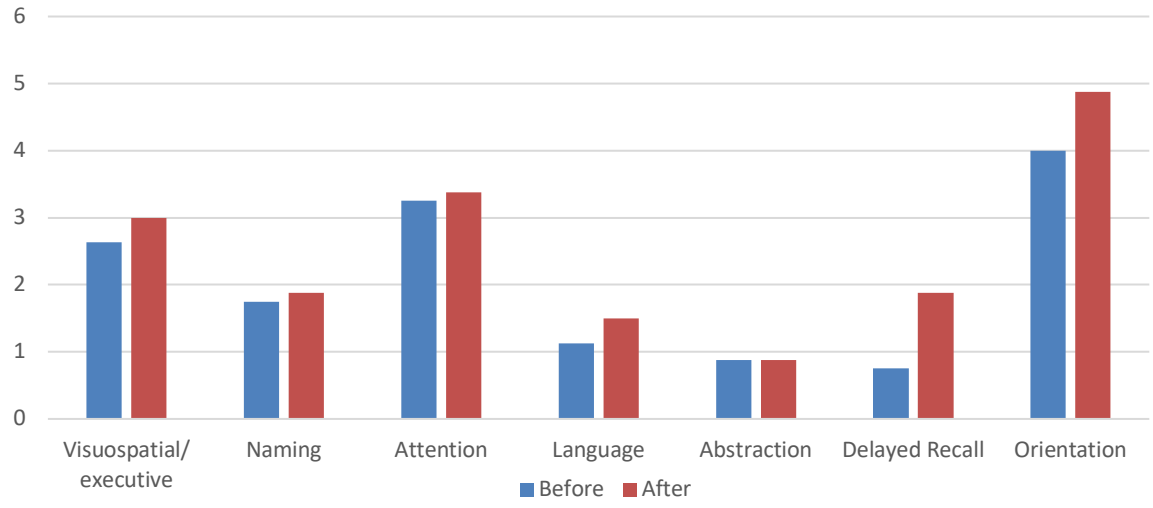
Cognitive Domain	Neurofeedback Training		
	Before	After	*p*-value
Visuospatial/Executive	2.63 ± 1.847	3.0 ± 2.070	.476[a]
Naming	1.75 ± 1.389	1.88 ± 1.356	.564[b]
Attention	3.25 ± 2.121	3.38 ± 2.134	.685[a]
Language	1.13 ± 0.835	1.5 ± 1.069	.197[a]
Abstraction	0.88 ± 0.991	0.88 ± 0.991	1.00[b]
Delayed Recall	0.75 ± 0.886	1.88 ± 1.959	.071[b]
Orientation	4.00 ± 1.773	4.88 ± 1.642	.131[b]

[a]Paired sample *t*-test; [b]Wilcoxon test

Upon analysis of cognitive domains, an increase in scores was observed in all domains except abstraction. Based on domain-specific analysis, it was found that after receiving 10 sessions of NFT, patients experienced improvement in MoCA-Ina scores with increases in visuospatial/executive function by 0.37 points, naming by 0.13 points, attention by 0.13 points, language by 0.37 points, delayed recall by 1.13 points, and orientation by 0.88 points. Statistical analysis was then performed to assess improvement using a one-sample paired *t*-test for the visuospatial/executive, attention, and language domains, and Wilcoxon test for naming, abstraction, delayed recall, and orientation domains. In each domain, no statistically significant differences were found ($p > .05$). This may be due to the small range of values per MoCA-Ina domain so that they do not show significant differences.

Multivariate analysis was conducted to examine the influence of confounding factors such as age, gender, educational level, lesion location, and time since stroke on the improvement of MoCA-Ina scores after receiving NFT. Patients were considered to have improved if there was an increase in MoCA-Ina score of greater than 2 points from baseline, and based on this criterion, six out of a total of eight samples (75%) showed improvement. According to the multivariate analysis, none of these variables were found to significantly affect the improvement of patient's MoCA-Ina scores ($p > .05$), as outlined in Figure 2.

Figure 2. *Comparison of Mean MoCA-Ina Scores Per Cognitive Domain Before and After NFT*.



Discussion

The finding of this study indicates that the use of NFT as an adjunct therapy in patients suffering from PSCIs can enhance overall cognitive function. There was significant improvement in mean MoCA-Ina score by 2.63 points (p = .019) following 10 sessions NFT intervention with tailored protocols based on qEEG. This result is in line with a previous study which reported that improvement in MoCA-Ina score occurs with an increase of ≥ 2 points (Zuo et al., 2022). Based on this finding, NFT can be a cognitive rehabilitation therapy modality that has benefits compared to other traditional modalities.

Several other studies also corroborate similar findings; for instance, Jang et al. (2019) reported that patients with MCI undergoing NFT experienced improvements in MoCA scores by 4.4 points after eight sessions and 6.2 points after 16 sessions. Additionally, improvements were noted in the complex memory domain, cognitive flexibility, attention, reaction time, and executive function (Jang et al., 2019). Similarly, Marlats et al. (2019) demonstrated a 1.9-point increase in MoCA scores (p < .012) along with enhanced alpha and theta waves in qEEG examination following NFT. Instead of MoCA-Ina, various other neurocognitive assessment parameters such as MMSE, Benton Visual Retention Test (BVRT), and Color Trails Test (CTT-1, CTT-2) have been extensively used concerning cognitive function improvement post-NFT (Jang et al., 2019; Marlats et al., 2019; Mroczkowska et al., 2014; Surmeli et al., 2016; Zuo et al., 2022). Unfortunately, there are still few studies regarding improvement of cognitive function using NFT in groups of patients diagnosed with PSCI, making this initial research one of the most useful studies.

NFT exhibits positive effects on memory enhancement and triggers neuronal plasticity in chronic stroke patients. This highlights NFT as a feasible alternative cognitive rehabilitation therapy that directly influences brain electrical activity. However, it is imperative to note that NFT outcomes may vary and are influenced by factors such as brain structural variances, interindividual differences in neuropsychological and psychological factors, as well as cognitive strategies used (Lecomte & Juhel, 2011).

Kober et al.'s 2015 study using SMR (12–15Hz) and upper alpha/UA (10–12 Hz) protocols found that SMR protocol enhances long-term memory function, visuospatial abilities, short-term memory, and learning efficiency, whereas UA protocol improves long-term memory, short-term memory, and working memory (Kleih-Dahms & Botrel, 2023; Kober et al., 2017). Furthermore, Cho et al. (2015) conducted a study on poststroke patients with cognitive impairments using beta-SMR protocol in 13 patients, with five 30-min sessions per week for 6 weeks, revealing improvements in visual discrimination, visual memory, and spatial relations (Cho et al., 2015).

This study shows a positive influence of NFT on increasing the mean MoCA-Ina scores, although these results did not achieve statistical significance when analyzed separately for each cognitive domain. This is in contrast to previous studies where improvements were predominantly observed in memory and executive function. This variance may be attributed to the limited sample size and the limitations of the MoCA-Ina instrument, which assesses delayed memory exclusively without specifically examining working memory and long-term memory. Conversely, many other studies combine various neuropsychological tests to evaluate overall cognitive function improvement.

Although statistically may not be significant, from a subjective impression, patients who have undergone NFT tend to report significant improvements in concentration, attention, and memory, even in patients who do not show improvement in overall scores. Most studies indicate that NFT has the potential to enhance cognitive function. However, not all studies find statistically significant improvements in all aspects of cognitive function. Sociodemographic and clinical factors did not have significant influence on the improvement of Moca-Ina scores. Based on theory, younger age, higher level of education, and earlier initiation of therapy are usually associated with more meaningful improvements. However, this study did not find any significant relationship, possibly due to the relatively small sample size and mostly having at least a high school education and younger age (< 65 years). Sociodemographic data shows that patients with lower education (under senior high school) have lower mean baseline MoCA-Ina scores, which is in line with the hypothesis of "cognitive reserve" usually associated with higher educational levels. Thus, it can be concluded that NFT in this study, consistent with other research, is a beneficial therapy for improving cognitive function in patients with PSCI.

The aim of NFB is to enable the subject to become aware of particular patterns of cortical activity that are associated with more optimal behavior or state (Lecomte & Juhel, 2011). NFT therapy can induce

changes in brain electrical activity that synergize with cognitive function improvement through the patient's ability to modulate their brain electrical activity independently. Increased alpha waves are associated with improvement in working memory function and short-term memory. Alpha waves also play a role in inhibiting irrelevant or interfering processes, facilitating attention and memory processes through the suppression of distracting stimuli. Thus, it can be concluded that NFT can accelerate functional improvement and even improve patient functionality that cannot be achieved with other therapies. NFT primarily affects cognitive and personality improvement (Hammond, 2006; Kober et al., 2015). This can be a consideration and recommendation for neurologists in implementing the use of NFT as a cognitive rehabilitation therapy modality in addition to other modalities in poststroke patients. The NFT protocol was tailored based on qEEG abnormality (e.g., alpha, beta, theta, or SMR).

In NFT, EEG activity and brain waves are provided as visual or auditory feedback to the patient so that the patient can consciously adjust their brain wave activity to reach the targeted training threshold (Renton et al., 2017). NFT relies on operant conditioning to stimulate neuroplasticity (Hammond, 2006; Kleim & Jones, 2008). Additionally, NFT can also suppress excessive slow-wave activity typically found in stroke patients.

This study has several limitations. First, the small sample size can be attributed to several factors: difficulty in scheduling patients for 10 sessions of NFT, particularly since many patients come from rural areas; a majority of participants being diagnosed with poststroke dementia rather than mild cognitive impairment; and a limited number of visits by first-time stroke patients after 3 months of onset due to the hospital's role as a tertiary referral center. Second, the outcome was based solely on the patient's clinical condition without using other objective parameters, such as qEEG changes, which could provide more comprehensive insights into alterations in the brain wave spectrum. Third, the short follow-up period where the assessment was only carried out after 10 sessions over 2 weeks of NFT intervention so that the long-term effect of NFT was unknown. We suggest future research to address the limitations identified in this current study with a larger scale and longer follow-up period to assess the long-term effectiveness of NFT in PSCI rehabilitation.

Conclusion

NFT has shown efficacy in improving cognitive function among individuals with PSCI, as indicated by MoCA-Ina scores. Importantly, these improvements were not influenced by sociodemographic and clinical factors, suggesting that NFT may be considered as an adjunctive therapy to aid cognitive function recovery.

Author Disclosure

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Application of Transcutaneous Electrical Nerve Stimulation (TENS) in Stroke Rehabilitation: An Umbrella Review

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Abstract

Background. Given that stroke is one of the most important causes of long-term disability, it is essential to adopt efficient rehabilitation techniques to maximize functional recovery. Transcutaneous electrical nerve stimulation (TENS) has become a viable treatment option for stroke recovery in recent years. **Method**. A systematic search was conducted in several databases and complemented by manual searches of reference lists. Study selection criteria included systematic reviews, with or without meta-analyses, that assessed the effects of TENS on poststroke rehabilitation. The quality of the studies was assessed using the JBI assessment tool. **Results**. According to 34 systematic reviews, TENS is applied in several settings in poststroke rehabilitation, including motor dysfunction, urinary and fecal dysfunction, spasticity, and pain management, and has shown promising results in these areas. However, the absence of standardized guidelines makes it challenging to determine the optimal TENS parameters for specific poststroke rehabilitation goals. **Conclusion**. The application of TENS in poststroke rehabilitation has shown potential benefits. While these potential benefits are promising, it is important to note that the effectiveness of TENS may vary among individuals, and further research is needed to understand its optimal application and long-term effects.

Keywords: transcutaneous electric nerve stimulation (TENS); stroke; rehabilitation; systematic review

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Introduction

Stroke is one of the primary causes of permanent disability and impairment all over the world (Katan & Luft, 2018). In recent years, due to the declining stroke mortality rate, along with population growth and aging, there has been an increase in the number of people living with the consequences of this condition (Donkor, 2018). Hence, rehabilitation plays a crucial role in the recovery and overall outcomes of stroke patients (Hatem et al., 2016).

One noninvasive method that has gained popularity is transcutaneous electrical nerve stimulation (TENS), which involves the application of electrical currents through the skin to stimulate peripheral nerves. Though its most prevalent usage is for pain management, TENS is increasingly being employed in rehabilitation for various purposes (Tahmasbi,

Ghaderpanah, et al., 2023). For instance, several studies have suggested its beneficial effect on enhancing fecal or urinary function (Tahmasbi, Hosseini, et al., 2023; Tahmasbi, Mosaddeghi-Heris, et al., 2023; Tahmasbi et al., 2024).

In poststroke settings, the application of TENS has gained attention as a potential approach for rehabilitative purposes, offering noninvasive electrical stimulation to modulate neural pathways and promote recovery (In et al., 2021). For instance, stroke survivors often experience chronic pain, muscle stiffness, and discomfort. Different studies have suggested that TENS can help alleviate pain by stimulating the nerves and blocking pain signals to the brain (Li et al., 2023; Zhou et al., 2018). In addition, TENS has shown beneficial effects on regaining functional abilities, including muscle strength and balance, in stroke survivors (Cho et al., 2013; Jung et al., 2017).

However, the existing body of evidence on the effects of TENS in stroke rehabilitation is scattered across various systematic reviews (SR[s]) and meta-analyses (MA[s]), making it challenging to derive conclusive findings. An umbrella review, which systematically evaluates and synthesizes the findings of multiple SRs, can provide a comprehensive overview of the available evidence and offer valuable insights into the effectiveness of an intervention (Beheshti et al., 2023). Hence, this study aims to assess the current evidence on the use of TENS for stroke rehabilitation, providing a consolidated analysis of the existing SRs in this field.

Method

Registration and Ethics of Approval Statement

Upon registration of the study protocol with PROSPERO, an international prospective register of systematic reviews, a SR was carried out (reference number: CRD42023449886). The Preferred Reporting Items for Systematic Reviews (PRISMA) criteria have been followed in the presentation of the study's results (Page et al., 2021). The Ethical Committee of Tabriz University of Medical Sciences approved the current study (Code: IR.TBZMED.REC.1402.706). The protocol of the current study was registered in the Research Center for Evidence-based Medicine, Iranian EBM Centre: A JBI Centre of Excellence, Faculty of Medicine, Tabriz University of Medical Sciences (Code: 72647).

Review Question

The following research question was developed prior to designing the search strategy: "What evidence is available through the current SRs on the effects of TENS for the rehabilitation of stroke?"

Searching the Literature

As shown in Table 1, we created the search strategy in accordance with PICOS recommendations:

- P – population (stroke survivors aged ≥18 years),
- I – intervention (TENS),
- C – comparison (conventional rehabilitation, sham control, etc.),
- O – outcome (valid and reliable outcomes related to poststroke rehabilitation), and
- S – study design (SR, with and without MA).

Table 1

Different Key Terms Used in Designing the Search Strategy

Population	Intervention	Study design
Stroke	Transcutaneous electrical nerve stimulation	Systematic review
Cerebrovascular accident	Transcutaneous electrostimulation	Meta-analysis
Cerebrovascular apoplexy	Transcutaneous neuromodulation	
Brain Vascular accident	Transcutaneous nerve stimulation	
Brain infarction	Electrostimulation	
CVA	Electrical stimulation	
	Neuromodulation	
	TENS	

Note. The *OR* Boolean operator was used between the terms in each column, while *AND* was used to combine the columns.

From the beginning to August 1, 2023, a search of the literature was conducted in English through the following electronic bibliographic databases: MEDLINE (via PubMed), Scopus, Web of Science, Cochrane Library, and PEDro. Two independent reviewers conducted the search (S. E., F. T.). The full search strategies are available in the Appendix. To find research that might not have been found by

the database search, the reference lists of all pertinent publications were also manually searched. For additional research, the search results were imported into the EndNote X20 citation management software, and duplicates were automatically removed.

Study Selection and Eligibility Criteria

SRs, with or without MAs, on interventional or observational human populations that assessed the effects of TENS (via different protocols) on poststroke rehabilitation were included. We excluded studies with at least one of the following criteria: studies other than SR, not reporting the effects of the desired intervention, and the absence of English available full text. Moreover, we excluded articles that did not report quantitative data.

All titles and abstracts found by the literature search were separately examined by two reviewers (S. E., F. T.). They next collected the full texts of all potentially relevant research and assessed each one's eligibility. Reviewers discussed differences of opinion in this respect and, if necessary, sought resolution from a third reviewer (S. M.).

Data Extraction

In pairs, reviewers (S. E., F. T.) extracted data independently from the included SRs. Discussions or, if required, a third reviewer adjudication were used to settle disagreements (S. M.). They gathered data on the bibliography, quality assessment, interventions, outcomes, adverse events, and overall findings using a pretested data extraction form.

Quality Assessment

Two impartial reviewers assessed the quality of all the included SRs using the JBI assessment tool (S. E., A. R. M.). Eleven items on this checklist help direct the evaluation of SRs (Aromataris et al., 2015). If there were 0–1, 2–3, or more than 3 no/unclear responses, the SRs were classified as high, moderate, or low quality, accordingly. Differences of opinion were settled by discussion and, when needed, by referring to the third reviewer (S. G.).

Results

Study Selection

The literature searches led to the identification of 853 citations. However, after screening the title and abstract, 55 full-text published articles were selected for full assessment. Out of these, 21 were excluded and 34 studies were finalized for review. Figure 1 shows the flow diagram of the selection process for this umbrella review.

Overall Characteristics of the studies

All of the included studies were SRs, 18 out of 34 also conducted MA, and 3 out of 34 applied network MA (Ahmed et al., 2022; Fang et al., 2023; Xue et al., 2022). SRs were published from 2001 (Price & Pandyan, 2001) to 2023 (Fang et al., 2023; Perpetuini et al., 2023; Wang et al., 2023) and originated from all over the world. Different variations of TENS protocols and techniques were applied across studies, including transcutaneous vagal nerve stimulation (tVNS), which delivers electrical impulses to the auricular branch of the vagus nerve through the skin on the outer ear (Ahmed et al., 2022; Ramos-Castaneda et al., 2022; Wang et al., 2023; Xie et al., 2021; Yan et al., 2022; Zhao et al., 2022), and transcutaneous tibial nerve stimulation (tTNS), which involves the application of electrical stimulation to the tibial branch of the sciatic nerve through the skin on the lower limb (Ali et al., 2022; Gross et al., 2016). Regarding the safety profile, none of the studies reported any major events. Mild skin irritation (Mills & Dossa, 2016; Xie et al., 2021; Yan et al., 2022; Zhao et al., 2022), nausea and vomiting (Xie et al., 2021; Yan et al., 2022), and mild pain were reported by SRs (Xie et al., 2021; Yan et al., 2022). Table 2 provides a summary of the included studies. The results of the TENS application on different poststroke conditions are reported categorically in the following paragraphs.

TENS and Motor Rehabilitation

The majority of the included SRs (21/34) investigated the application of TENS for poststroke motor rehabilitation. Some of the earlier studies, like Pomerory et al. (2006) and Robbins et al. (2006) reported that not enough evidence is available to demonstrate TENS's usefulness in helping stroke patients recover their motor skills. However, in more recent publications, the evidence for the efficacy of TENS has grown substantially, which will be addressed in the following paragraphs.

Ahmed et al. (2022) reviewed different electric neurostimulation techniques, including tVNS. According to their results, tVNS effectively improves upper limb motor function. The efficacy of tVNS for motor rehabilitation was further confirmed by Ramos-Castaneda et al. (2022), Wang et al. (2023), Xie et al. (2021), Xue et al. (2022), Yan et al. (2022), and Zhao et al. (2022).

Figure 1. *PRISMA 2020 Flow Diagram for New Systematic Reviews Which Included Searches of Databases, Registers, and Other Sources*.

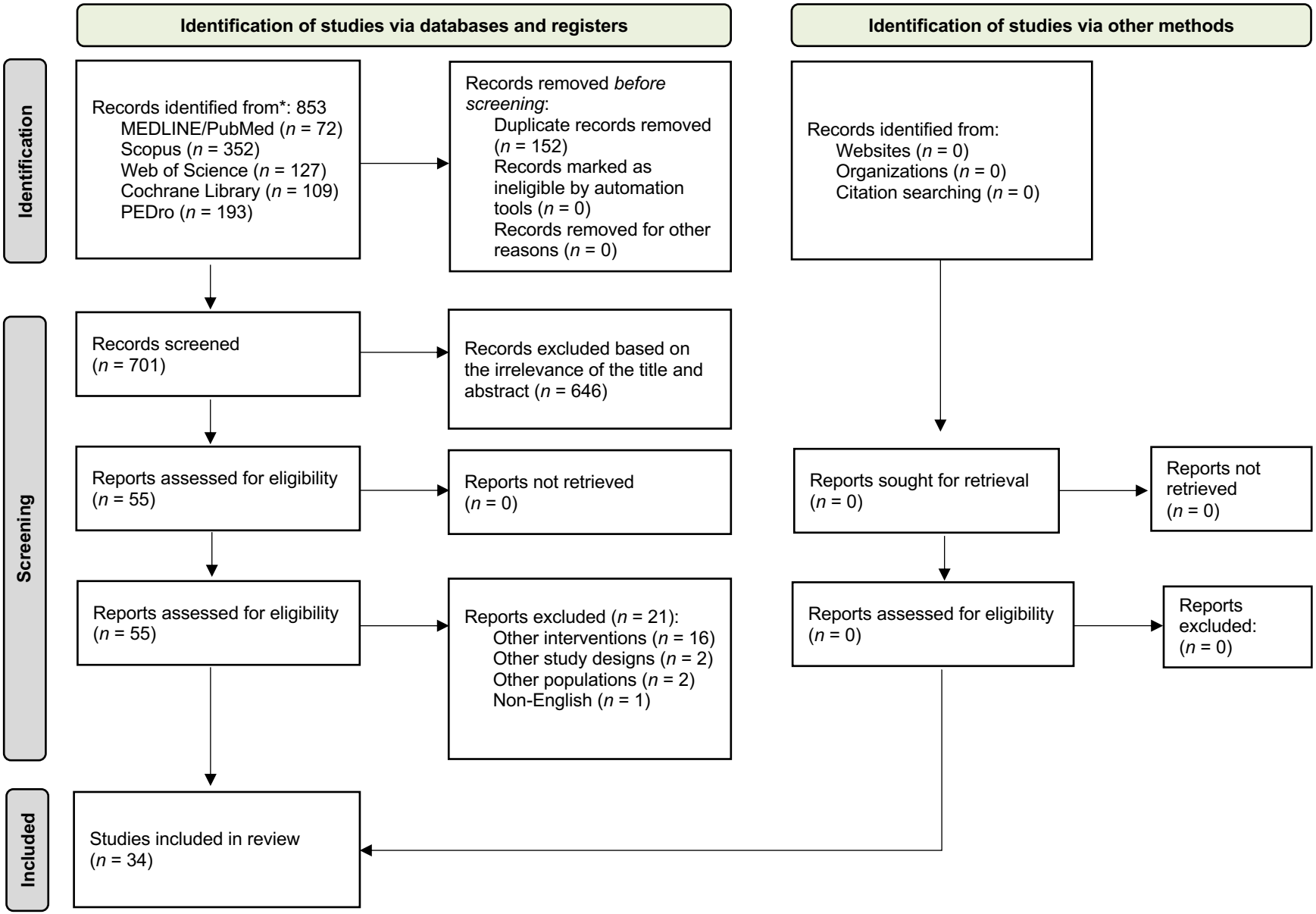

Table 2

General and Methodological Characteristics of Included SRs

Author, Year	Origin	Design	Journal	Searched Databases	Type of Intervention	Included Studies	Quality Appraisal	Grade	AE	Overall Results
Motor Function										
Ahmed et al., 2022	Turkey	SR + network MA	Neuromodulation: Technology at the Neural Interface	PubMed, WoS, Cochrane, and Google Scholar	Electrical neurostimulation, including tVNS	Total: 38 RCTs, tVNS: 2	The Cochrane RoB assessment tool	No	-	Analysis showed that tVNS is the most effective treatment for enhancing upper limb motor function and performance in daily living activities.
Fang et al., 2023	China	SR + network MA	PLoS ONE	CNKI, VIP Database for Chinese Technical Periodicals, WAN FANG Database, Chinese biomedical literature service system (SinoMed), PubMed, WoS, Embase, and Cochrane Library	Electrical stimulation including TENS and TEAS	Total: 33 trials, TENS: 6, TEAS: 4	The Cochrane RoB assessment tool	Yes	-	Compared to traditional TENS, TEAS in conjunction with acupuncture locations shown a higher potential for therapy.
Grant et al., 2018	Australia	SR + MA	Topics in Stroke Rehabilitation	MEDLINE, CINAHL, Embase, PEDro and OTseeker	Somatosensory stimulation	Total: 15 RCTs, TENS: 4	PEDro scale	Yes	-	Low-quality evidence from four trials suggested that sensory electrical stimulation, including TENS, did not significantly improve upper limb activity compared to placebo. Additionally, moderate-quality evidence from three trials showed that sensory electrical stimulation did not lead to significant improvements in motor impairment.
Laufer & Elboim-Gabyzon, 2011	Israel	SR	Neurorehabilitation and Neural Repair	PubMed, EMBASE, CINHAL, ISI Science Citation Index, Cochrane library, Cochrane Stroke Group Trials Register, Hooked on Evidence, and the PEDro database	TENS	Total: 15 clinical trials	PEDro scale	No	None	When combined with active training, TENS may help improve certain elements of motor recovery after a stroke.

Table 2

General and Methodological Characteristics of Included SRs

Author, Year	Origin	Design	Journal	Searched Databases	Type of Intervention	Included Studies	Quality Appraisal	Grade	AE	Overall Results
I.-H. Lin et al., 2019	Taiwan	SR	Archives of Physical Medicine and Rehabilitation	PubMed	Rehabilitative treatments including TENS	Total: 178, TENS: 2	PEDro scale	No	-	There was insufficient data to prove that experimental therapies were better than traditional rehabilitation.
Perpetuini et al., 2023	Italy	SR	Bioengineering	PubMed/MEDLINE, WoS, and Scopus	Electrosuit, using TENS	12 RCTs	None	No	-	Improvements in motor function and a decrease in spasticity have been observed to be positively correlated with the length and dose of the garment therapy.
Pomeroy et al., 2006	United Kingdom	SR	Cochrane Library	Cochrane Stroke Group Trials Register, CENTRAL, MEDLINE, EMBASE, CINAHL, AMED - Allied and Complementary Medicine Database, PEDro, REHABDATA and the ISI Science Citation Index	ES, including TENS	Total: 24 RCTs, TENS: 3	The Cochrane RoB assessment tool	No	-	At present, there are insufficient robust data to inform clinical use of electrostimulation for neuromuscular retraining.
Ramos-Castaneda et al., 2022	Colombia	SR + MA	Frontiers in Neurology	MEDLINE, CENTRAL, EBSCO and LILACS	VNS	Total: 8, TENS: 4	The Cochrane RoB assessment tool	No	None	VNS, combined with physical rehabilitation, improves upper limb motor function in stroke patients.
Sharififar et al., 2018	USA	SR + MA	Annals of Physical and Rehabilitation Medicine	MEDLINE via PubMed and the Cochrane Central Register of Controlled Trials	ES: TENS or peripheral electromyography triggered sensory stimulation, or acupuncture producing sensory effects without motor recruitment, in conjunction with routine rehabilitation	Total: 11, TENS: 3	PEDro scale	No	-	Electrical sensory input can contribute to routine rehabilitation to improve early poststroke lower-extremity impairment and late motor function, with no change in spasticity. Prolonged periods of sensory stimulation such as TENS combined with activity can have beneficial effects on impairment and function after stroke.

Table 2
General and Methodological Characteristics of Included SRs

Author, Year	Origin	Design	Journal	Searched Databases	Type of Intervention	Included Studies	Quality Appraisal	Grade	AE	Overall Results
Wang et al., 2023	China	SR + MA	Frontiers in Neurology	PubMed, Wanfang, Scopus, China Science and Technology Journal Database, EmbaseWoS, China Biology Medicine Disc, Cochrane Library, and China National Knowledge Infrastructure	VNS (taVNS, invasive VNS)	Total: 10, taVNS: 6	The Cochrane RoB assessment tool	Yes	There was no significant difference between the experimental and control groups in the incidence of AEs or serous AEs.	VNS is an effective and safe treatment for upper extremity motor dysfunction after a stroke.
Xie et al., 2021	China	SR + MA	Medicine	PUBMED, MEDLINE, EMBASE, Cochrane Library, WoS, CNKI, and Wan Fang Database	VNS (tVNS and invasive)	Total: 6 tVNS: 3	The Cochrane RoB assessment tool	No	In 3 tVNS trials, one reported skin redness, one mild nausea and vomiting; mild pain in the left ear and the last, no AE.	VNS resulted in improvement of motor function in patients after ischemic stroke, especially in the sub-chronic stage. Moreover, compared with implanted VNS, transcutaneous VNS exhibited greater efficacy in poststroke patients. Based on this meta-analysis, VNS could be a feasible and safe therapy for upper limb motor impairment.
Xue et al., 2022	China	SR + network MA	Journal of Clinical Medicine	MEDLINE, Embase, Cochrane Library and ClinicalTrials.gov	Different neurostimulation techniques, including TENS	Total: 88 RCTs, TENS: 8 tVNS: 1	The Cochrane RoB assessment tool	Yes	Almost none	Significant efficacy for improving the upper limb function after stroke with minimum AEs.
Yan et al., 2022	China	SR	Neuropsychiatric Disease and Treatment	PubMed, Embase, Cochrane Library, CNKI, Wanfang Database, and China Science and Technology Journal Database (VIP)	tVNS	4	The Cochrane RoB assessment tool	No	Two studies reported AE. One patient had redness of the skin at the electrode contact point; 28 one patient had mild nausea and vomiting, and one patient had pain in the left ear.	tVNS combined with rehabilitation training showed some improvement in upper limb motor dysfunction in poststroke patients.

Table 2

General and Methodological Characteristics of Included SRs

Author, Year	Origin	Design	Journal	Searched Databases	Type of Intervention	Included Studies	Quality Appraisal	Grade	AE	Overall Results
Zhao et al., 2022	China	SR + MA	International Journal of Rehabilitation Research	MEDLINE, WoS,Embase, CENTRAL and PEDro	VNS (transcutaneous and invasive)	Total: 5 tVNS: 2	PEDro scale	No	One study regarding tVNS did not report AEs, while one study reported that one patient in the tVNS group developed skin redness at the point of contact of the auricular skin with electrodes.	When used in conjunction with therapy, VNS can help stroke patients regain function in their upper limbs.
Aries et al., 2022	United Kingdom	SR	Brain Sciences	AgeLine, AMED, CINAHL PLUS, EMBASE, EMCARE MEDLINE, PEDro, PsycARTICLES, PsycINFO, SPORTDiscus and WoS, CENTRAL	Various types of somatosensory stimulation including TENS	Total: 16 RCTs, TENS: 6	The Cochrane RoB assessment tool	No	-	This study does not provide a comprehensive conclusion regarding the effects of TENS; however, it concludes that sensory stimulation might benefit the rehabilitation of stroke patients based on heterogeneous studies.
S. Lin et al., 2018	China	SR + MA	Journal of Rehabilitation Medicine	PubMed, Embase, WoS, EBSCO, and Cochrane Library	TENS	7 RCTs	The Jadad Scale	No	-	TENS had no effect on dynamic balance but is linked to a considerable reduction in spasticity, an increase in walking speed, and static balance.
Robbins et al., 2006	Canada	SR + MA	Archives of Physical Medicine and Rehabilitation	Medline, EMBASE, CINHAL, and PubMed	Functional and Transcutaneous electric stimulation	Total: 21, TENS: 3	Downs and Black checklist	No	-	Insufficient data was available to draw firm conclusions about TENS's efficacy.
Shankaranarayana et al., 2021	India	SR	Gait & Posture	MEDLINE, CINAHL, Cochrane Library, ProQuest, and Citation Indexes, WoS and Scopus	Gait training interventions	Total: 12, TENS: 1	PEDro scale	No	None	According to one trial, no significant difference between TENS and task-based program.

Table 2
General and Methodological Characteristics of Included SRs

Author, Year	Origin	Design	Journal	Searched Databases	Type of Intervention	Included Studies	Quality Appraisal	Grade	AE	Overall Results
Kwong et al., 2018	China	SR + MA	Clinical Rehabilitation	CINAHL, ClinicalTrials.gov, the Cochrane Central Register of Controlled Trials, EMBASE, MEDLINE, PEDro, PubMed and WoS	TENS	Total: 11	PEDro scale	No	None	For stroke survivors, TENS is useful in improving walking ability and decreasing plantar flexor spasticity.
Mijic et al., 2022	Germany	SR	Frontiers in Neurology	Pubmed/MEDLINE, Scopus, ScienceDirect, WoS/Clarivate, Cochrane Library, PEDro, and ClinicalTrials.gov	Peripheral electrical stimulation including TENS	Total: 10, TENS: 3	ROBINS-I for observational studies, NIH tool for pre-post studies without a control group	Yes	-	The shift in the amplitude and latency of somatosensory evoked potentials may suggest that PES have a predictive influence on sensory reconfiguration.
Urinary/Fecal Dysfunction										
Bapir et al., 2022	Unclear	SR + MA	The Archives of Italian Urology and Andrology	PubMed, EMBASE	Different treatments for neurogenic bladder with different etiologies, including TENS for stroke	Total: 62 RCTs, TENS/stroke: 4	The Cochrane RoB assessment tool	Yes	-	TENS reduced symptom scores, increased urodynamic results (maximum cystometry volume, flow rate, and pressure of the detrusor at the end of the filling phase), and improved voiding diary metrics (daily micturition, nocturia, urgent urination, and urge UI).
Cruz et al., 2022	Australia	SR + MA	International journal of stroke	MEDLINE, EMBASE, CINAHL, PEDro, and CENTRAL	Non-implanted electrical stimulation, including TENS	Total: 10 trials, TENS: 5, electroacupuncture: 5	PEDro scale	No	-	Combining research indicates that frequent and early electrical stimulation therapy is likely more beneficial than fake or no therapy at all.
Gross et al., 2016	Switzerland	SR + MA	European Urology	Embase, Medline, CENTRAL, and Health Technology Assessment Database	TENS (including TTNS)	Total: 22 (2 RCTs, 14 prospective cohorts, five retrospective case series, one case report); Stroke: mentioned in four studies	The Cochrane RoB assessment tool for RCTs, self-defined criteria for non-RCTs	No	One patient did not tolerate stimulation and stimulation had to be stopped. No other AEs were reported.	The excellent AE profile and good effects on bladder diary and urodynamic measures suggest that TENS may be a safe and effective treatment for NLUTD.

Table 2

General and Methodological Characteristics of Included SRs

Author, Year	Origin	Design	Journal	Searched Databases	Type of Intervention	Included Studies	Quality Appraisal	Grade	AE	Overall Results
Ali et al., 2022	Nigeria	SR + MA	Therapeutic Advances in Chronic Disease	Cochrane library, EMBASE, MEDLINE, PEDro, Scopus, and WoS	Intravaginal electrical stimulation, TENS, neuromuscular electrical stimulation, TTNS, pelvic floor muscle training, and behavioral therapy	Total: 14, TENS/Stroke: 2	PEDro scale	Yes	-	According to meta-analyses, electrical stimulation can help stroke and multiple sclerosis patients with their urgency symptoms.
Thomas et al., 2019	United Kingdom	SR + MA	Cochrane Library	Cochrane Incontinence and Cochrane Stroke Specialized Registers, which contain trials identified CENTRAL, MEDLINE, MEDLINE In-Process, MEDLINE Epub Ahead of Print, CINAHL, ClinicalTrials.gov, WHO ICTRP	Different rehabilitative approaches, including TENS and TTNS	Total: 20 trials, TENS: 3 TTNS: 2	The Cochrane RoB assessment tool	Yes	TTNS-related side effects, such as slight skin irritation and ankle cramps in 1 trial	Physical treatment with TENS may reduce the mean frequency of incontinent episodes during a 24-hr period, based on two trials reporting three comparisons. ability.
Spasticity										
Fernández-Tenorio et al., 2019	Spain	SR	Neurología	PubMed, PEDro, and Cochrane databases	TENS	Total: 10, Stroke: 6	PEDro scale	No	None	Because TENS has no AEs, is inexpensive, and is simple to use, it is suggested as a possible therapy for spasticity.
Garcia & Vargas, 2019	Brazil	SR	Journal of Musculoskeletal and Neuronal Interactions	Scopus, PubMed, BVS, Google Scholar and BASE databases	Somatosensory electrical stimulation including TENS	Total: 10 TENS/Stroke: 7	None	No	-	Mostly positive effects from application of TENS were reported for improving spasticity and reflex responses.
Mahmood et al., 2019	India	SR + MA	Archives of Physical Medicine and Rehabilitation	PubMed, PEDro, CINAHL, WoS, CENTRAL, and EMBASE	TENS	15; 10 RCTs and 5 non-RCTs	The Cochrane RoB assessment tool	No	None	Compared to placebo TENS, TENS in conjunction with other physical therapy treatments was more successful in decreasing lower limb spasticity.

Table 2

General and Methodological Characteristics of Included SRs

Author, Year	Origin	Design	Journal	Searched Databases	Type of Intervention	Included Studies	Quality Appraisal	Grade	AE	Overall Results
Marcolino et al., 2020	Brazil	SR + MA	Disability and Rehabilitation	MEDLINE, Cochrane Library, EMBASE and Physiotherapy Evidence Database	TENS alone or as additional therapy	10 RCTs	The Cochrane RoB assessment tool	No	None	TENS can provide additional reduction in chronic poststroke spasticity, mainly as additional therapy to physical interventions.
Mills & Dossa, 2016	Canada	SR	American Journal of Physical Medicine & Rehabilitation	MEDLINE, EMBASE, and Cochrane Central Register of Controlled Trials.	TENS	Total: 14 RCTs, Stroke: 7	PEDro scale	No	Transient mild skin irritation with erythema that resolved spontaneously.	Better responses in outcome measures were seen when TENS was used in combination with active vs. as a single therapeutic modality.
Pain										
Chen et al., 2016	Taiwan	SR	The Journal of Physical Therapy Science	Academic Search Premier; CINAHL Plus with full text Medline Proquest; Medline Ovid SP; ProQuest Health and Medical Complete; Pubmed; Science Direct online; Scopus; The Cochrane Library; and WoS	Non-invasive physical modalities including TENS	Total: 16, TENS: 1	Evidence Classification Scheme for Therapeutic Interventions	No	-	One study found that when 15 patients were given high-frequency (traditional) and low-frequency (acupuncture-like) TENS treatments, one-third of them had a brief increase in pain.
de Sire et al., 2022	Italy	SR + MA	Annals of Physical and Rehabilitation Medicine	PubMed, Scopus, and WoS	Different rehabilitative techniques including TENS	Total: 12, TENS: 1	PEDro scale, The Cochrane RoB assessment tool	No	-	For patients with hemiplegic shoulder pain, adding segmental neuromyotherapy to conventional treatment improves arm function overall and relieves pain.
Price & Pandyan, 2001	United Kingdom	SR	Clinical Rehabilitation	Cochrane Stroke Review Group trials register and undertake further searches of Medline, Embase and CINAHL	ES, including TENS	Total: 4, TENS: 3	Self-defined checklist	No	None	There seem to be advantages for passive humeral lateral rotation, although the data from RCTs so far neither supports nor contradicts the idea that ES around the shoulder following a stroke affects ratings of pain.

Table 2

General and Methodological Characteristics of Included SRs

Author, Year	Origin	Design	Journal	Searched Databases	Type of Intervention	Included Studies	Quality Appraisal	Grade	AE	Overall Results
Other Condition(s)										
Lisa et al., 2013	Belgium	SR	NeuroRehabilitation	PubMed, WoS, and PEDro	Different rehabilitative techniques including TENS	Total: 15 RCTs, TENS: 1	9-item Delphi list	No	-	TENS is an effective method for reducing unilateral neglect syndrome.

AE = Adverse Event; CENTRAL = Cochrane Central Register of Controlled Trials; CINAHL = Cumulative Index to Nursing & Allied Health Literature; CNKI = China National Knowledge Infrastructure; ES = Electrostimulation; MA = Meta-analysis; NIH = National Institutes of Health; PEDro = Physiotherapy Evidence Database; RCT = Randomized controlled trial; RoB = Risk of bias; SR = Systematic review; taVNS = Transcutaneous auricular vagus nerve stimulation; TEAS = Transcutaneous electrical acupoint stimulation; TENS = Transcutaneous electrical nerve stimulation; TTNS = Transcutaneous tibial nerve stimulation; tVNS = Transcutaneous vagus nerve stimulation; VNS = Vagus nerve stimulation; WoS = Web of Science

The goal of Grant et al.'s (2018) study was to ascertain if somatosensory stimulation might improve upper limb motor performance following a stroke. According to their included trials, an overall improvement following TENS was reported. For instance, in one of their included trials, patients were told to wear a wristwatch-like device called a ReliefBand, which uses surface electrodes to give biphasic square-wave electrical stimulation at a frequency of 31 Hz for 2 hr per day, right before motor training (dos Santos-Fontes et al., 2013).

Further, the I.-H. Lin et al. (2019) study suggested that while electrical stimulation was found to be effective in enhancing motor recovery poststroke, its superiority over conventional rehabilitation was not supported by strong evidence.

The Fang et al. (2023) study investigated and compared five commonly used electrical stimulation techniques for treating stroke patients with lower limb impairment through a network meta-analysis. According to their results, transcutaneous electrical acupuncture stimulation (TEAS), which delivers electrical impulses to certain acupuncture points, showed more therapeutic promise compared to traditional TENS (Fang et al., 2023).

The application of TENS in combination with other rehabilitative methods was also investigated. According to Sharififar et al. (2018) SR, electrical sensory inputs, such as TENS, combined with routine therapy can improve lower-extremity impairment in the early poststroke period and motor function in the long term. However, it did not have a significant impact on spasticity. Further, according to Laufer and Elboim-Gabyzon's (2011) research, TENS sensory stimulation can help improve certain parts of motor recovery after a stroke, especially when combined with active training.

Most recently, Perpetuini et al. (2023) conducted a SR of the effectiveness of the Exopulse Mollii Suit (EMS), a wearable device that delivers electrical stimulation transcutaneously, in neurological disorders like stroke. Their results showed that this device can improve motor functions and reduce spasticity. The duration and dose of the treatment, which are dependent on the patient's health and the objectives of the treatment, have been linked to these effects. Patients also reported a feeling of well-being in the afflicted limb during the electrical stimulation (Perpetuini et al., 2023).

The purpose of Aries et al.'s (2022) SR was to assess how well somatosensory stimulation of the feet and lower limbs can improve walking and balance following a stroke. The interventions included in the review involved different sensory stimulation, such as customized insoles, taping, and electrical stimulation, among others. TENS was investigated through six studies, all of which reported positive effects.

S. Lin et al. (2018) reported improved walking speed, static balance, and reductions in spasticity following TENS supplementation. However, the dynamic balance was unaffected by the treatment.

In Shankaranarayana et al. (2021), only one of the included studies contributed to the effects of TENS on poststroke gait. In this trial, three groups of participants were recruited to test TENS and a task-based program which concentrated on motor learning that occurs upon the completion of meaningful tasks like bodyweight support treadmill training. Group 1 was the only group to get task-based instruction. In addition to task-based training, Groups 2 and 3 had TENS for 30 and 60 min, respectively. The findings demonstrated that there was no discernible difference in each group's performances from one another (Shankaranarayana et al., 2021).

TENS increased walking capacity measured by gait speed or the Timed Up and Go Test, according to Kwong et al. (2018) SR. Additionally, TENS helped stroke survivors with their paretic plantar flexor spasticity. The duration of TENS sessions had an impact on its effectiveness. Research with 60-min sessions demonstrated an increase in walking capacity, but trials with shorter sessions (20 or 30 min) did not demonstrate a statistically significant benefit (Kwong et al., 2018).

Lastly, Mijic et al. (2022) examined the role of peripheral electrical stimulation (PES), including TENS, in poststroke patients. The review showed that there is insufficient data to support the use of somatosensory evoked potentials as a predictor to gauge a stroke patient's likelihood of rehabilitation. The research did, however, find a relationship between alterations in the components of somatosensory evoked potentials and various measures of sensory and motor function. There is a favorable connection and association between evaluations of motor function and PES that induce a voluntary contraction for a certain activity or task. This implies that alterations in the amplitude and latency of somatosensory evoked potentials may indicate a predictive influence of PES on sensory reconfiguration (Mijic et al., 2022).

TENS and Urinary/Fecal Dysfunction

Five SRs investigated the use of TENS for poststroke urinary dysfunction (Ali et al., 2022; Bapir et al., 2022; Cruz et al., 2022; Gross et al., 2016; Thomas et al., 2019) and one for fecal dysfunction (Cruz et al., 2022). In Bapir et al. (2022) SR, when it comes to reducing the frequency of nocturia episodes in patients with overactive bladder (OAB) symptoms linked to neurological illnesses, such as stroke, TENS was found to be more effective compared to its sham-control. Cruz et al. (2022) SR reported that TENS significantly improves urinary continence when started within 3 months of a stroke. However, when TENS was initiated more than 3 months after stroke, the effect size was medium. This indicates that the timing of TENS treatment may influence its effectiveness in reducing urinary dysfunction in stroke patients (Cruz et al., 2022). The effect of nonimplanted electrical stimulation on poststroke fecal incontinence was the subject of only one of their included studies, which found that the TENS group's improvement was noticeably higher than that of the controls (Cruz et al., 2022).

Further, the effectiveness and safety of TENS for treating neurogenic lower urinary tract dysfunction (NLUTD) in patients with underlying neurological illnesses, such as stroke, multiple sclerosis, and spinal cord injury, were examined in Gross et al. (2016) SR. The results of the review indicate that both acute and chronic TENS show promise in improving various aspects of NLUTD (Gross et al., 2016).

According to Ali et al.'s (2022) MA, electrical stimulation—including TENS—significantly reduces urge urine incontinence brought on by stroke.

A Cochrane review by Thomas et al. (2019) included two trials on the subject. In one of them, transcutaneous posterior tibial nerve stimulation (TPTNS) showed minimal or no impact on the number of participants who were continent after treatment or the number of incontinent episodes. In the other study, there was evidence of improvement in the group receiving TPTNS after 26 weeks.

TENS and Spasticity

Five SRs focused on the application of TENS in management of poststroke spasticity (Fernández-Tenorio et al., 2019; Garcia & Vargas, 2019; Mahmood et al., 2019; Marcolino et al., 2020; Mills & Dossa, 2016), and one SR mentioned spasticity as a secondary outcome. The results of the review suggest that because of its affordability, simplicity of use, and lack of side effects, TENS is regarded as an effective therapy for spasticity (Fernández-Tenorio et al., 2019). In the Garcia and Vargas (2019) SR, inconsistent results were reported by included trials; some suggesting an improvement in spasticity even after one session while there were reports of lack of efficacy.

TENS was more successful in decreasing lower limb spasticity when it was administered in conjunction with other physical therapy than when it was administered as sham stimulation, according to Mahmood et al. (2019) SR. Moreover, compared to other physical therapy therapies alone, TENS applied in addition to other treatments was more successful in lowering spasticity (Mahmood et al., 2019).

The findings of Marcolino et al. (2020) research showed that TENS, either used alone or as an additional therapy, is effective in reducing poststroke spasticity compared to placebo TENS. Their analysis showed statistically significant improvements in spasticity, particularly in the lower limbs.

Lastly, in the study by Kwong et al. (2018), as mentioned in the previous section, TENS was effective in reducing paretic plantar flexor spasticity in stroke survivors.

TENS and Pain

Three SRs investigated the effects of the TENS application on poststroke pain; including shoulder pain (de Sire et al., 2022; Price & Pandyan, 2001) and central pain (Chen et al., 2016).

In Chen et al. (2016) SR, only one study was found that examined the use of TENS as a noninvasive modality intervention for central poststroke pain (CPSP).

Price and Pandyan (2001) study focused on the efficacy of various forms of surface electrical stimulation in the prevention and treatment of shoulder pain after stroke, which found insufficient evidence to draw any conclusions.

A variety of rehabilitation techniques were studied in de Sire et al. (2022) SR, but only one trial looked at the effectiveness of TENS in addition to traditional therapy as opposed to conventional rehabilitation alone. In this trial, the study group was given 12 intramuscular and subcutaneous injections of 5 mL of 1% lidocaine solution into the tight band and trigger sites, close to the affected spinal region (paraspinal block), in addition to 20 min of local heat application and TENS to deltoid and supraspinatus

muscles (40 Hz, 11 mA) and 10 min of passive stretching of the affected shoulder three times per week for 4 weeks. Over the course of the 4-week treatment period, the intervention group outperformed the control group, which received the hospital's standard treatment regimen, in shoulder pain outcome measures (Ratmansky et al., 2012).

TENS and Other Condition(s)

In a SR by Lisa et al. (2013) TENS was mentioned as one of the treatment modalities that can reduce the symptoms of unilateral neglect in poststroke patients. This SR suggested that TENS, along with other interventions such as optokinetic stimulation, somatosensory electrostimulation, mirror therapy, and virtual reality training, can be effective in alleviating the symptoms of unilateral neglect (Lisa et al., 2013).

Risk of Bias Assessment

Based on the JBI quality evaluation checklist, 8 out of 34 studies were rated as high quality, 14 as moderate, and 12 as low quality. The included SRs' strongest domains were addressing the research question (33/34), adequate sources and resources of data (32/34), using proper method of quality assessment (31/34), and proper inclusion criteria (30/34). There were major concerns in domains of publication bias and providing guidance for policy and practice. The result of the assessment of risk of bias is presented in Table 3. For every individual outcome, we created "traffic light" charts of the domain-level evaluations.

Table 3

The Quality of the Included Systematic Reviews, Based on the JBI Checklist

	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Overall Quality
Ahmed et al., 2022	✅	✅	⚠️	✅	✅	⚠️	✅	✅	✅	✅	✅	Moderate
Ali et al., 2022	✅	✅	✅	✅	✅	✅	✅	✅	✅	✅	❌	High
Aries et al., 2022	✅	✅	❌	✅	✅	✅	✅	✅	❌	❌	❌	Low
Bapir et al., 2022	✅	✅	⚠️	✅	✅	✅	✅	✅	✅	❌	❌	Moderate
Chen et al., 2016	✅	❌	⚠️	✅	✅	⚠️	⚠️	❌	❌	❌	❌	Low
Cruz et al., 2022	✅	✅	✅	✅	✅	✅	✅	✅	❌	❌	✅	Moderate
de Sire et al., 2022	❌	✅	✅	✅	✅	✅	✅	✅	⚠️	✅	❌	Moderate
Fernández-Tenorio et al., 2019	✅	✅	⚠️	✅	✅	⚠️	⚠️	❌	❌	❌	✅	Low
Fang et al., 2023	✅	✅	✅	✅	✅	✅	✅	✅	✅	⚠️	⚠️	Moderate
Garcia & Vargas, 2019	✅	⚠️	✅	❌	❌	⚠️	❌	❌	❌	⚠️	❌	Low
Grant et al., 2018	✅	✅	✅	✅	✅	✅	✅	✅	❌	❌	❌	Moderate
Gross et al., 2016	✅	✅	⚠️	✅	❌	⚠️	✅	✅	❌	✅	✅	Low
Kwong et al., 2018	✅	✅	✅	✅	✅	✅	⚠️	✅	✅	✅	✅	High
Laufer & Elboim-Gabyzon, 2011	✅	✅	⚠️	✅	✅	✅	✅	✅	❌	✅	❌	Moderate
I.-H. Lin et al., 2019	✅	✅	⚠️	❌	✅	✅	⚠️	✅	❌	✅	❌	Low
S. Lin et al., 2018	✅	❌	❌	✅	✅	❌	❌	✅	NA	❌	❌	Low
Lisa et al., 2013	✅	✅	✅	✅	✅	❌	❌	✅	❌	✅	✅	Moderate
Mahmood et al., 2019	✅	✅	❌	✅	✅	❌	✅	✅	❌	✅	✅	Moderate
Marcolino et al., 2020	✅	✅	✅	✅	✅	✅	✅	✅	❌	✅	❌	Moderate
Mijic et al., 2022	✅	✅	⚠️	✅	✅	⚠️	❌	✅	✅	❌	❌	Low
Mills & Dossa, 2016	✅	✅	⚠️	✅	✅	✅	✅	✅	❌	❌	✅	Moderate
Perpetuini et al., 2023	✅	✅	⚠️	✅	❌	❌	❌	✅	❌	❌	✅	Low
Pomeroy et al., 2006	✅	✅	✅	✅	✅	✅	✅	✅	❌	✅	✅	High

Table 3
The Quality of the Included Systematic Reviews, Based on the JBI Checklist

	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Overall Quality
Price & Pandyan, 2001	✅	✅	⚠️	✅	✅	✅	✅	✅	NA	✅	✅	High
Ramos-Castaneda et al., 2022	✅	✅	⚠️	✅	✅	⚠️	✅	✅	NA	❌	✅	Moderate
Robbins et al., 2006	✅	✅	⚠️	✅	✅	✅	✅	❌	❌	❌	✅	Low
Shankaranara et al., 2021	✅	✅	✅	✅	✅	⚠️	✅	❌	❌	❌	✅	Low
Sharififar et al., 2018	✅	✅	⚠️	✅	✅	✅	✅	✅	❌	❌	✅	Moderate
Thomas et al., 2019	✅	✅	✅	✅	✅	✅	✅	✅	✅	✅	✅	High
Wang et al., 2023	✅	✅	⚠️	✅	✅	✅	✅	✅	✅	✅	✅	High
Xie et al., 2021	✅	✅	⚠️	✅	✅	✅	✅	✅	NA	❌	✅	Moderate
Xue et al., 2022	✅	❌	❌	✅	✅	⚠️	⚠️	✅	✅	✅	❌	Low
Yan et al., 2022	✅	✅	✅	✅	✅	✅	✅	✅	NA	❌	✅	High
Zhao et al., 2022	✅	✅	✅	✅	✅	✅	✅	✅	NA	❌	✅	High

✅ = Yes; ⚠️ = Unclear; ❌ = No; NA = Not Applicable.
Q1 = Is the review question clearly and explicitly stated?; Q2 = Were the inclusion criteria appropriate for the review question?; Q3 = Was the search strategy appropriate?; Q4 = Were the sources and resources used to search for studies adequate?; Q5 = Were the criteria for appraising studies appropriate?; Q6 = Was critical appraisal conducted by two or more reviewers independently?; Q7 = Were there methods to minimize errors in data extraction?; Q8 = Were the methods used to combine studies appropriate?; Q9 = Was the likelihood of publication bias assessed?; Q10 = Were recommendations for policy and/or practice supported by the reported data?; Q11 = Were the specific directives for new research appropriate?

Discussion

TENS is a noninvasive peripheral nerve stimulation technique that involves the application of low-intensity electrical currents to the peripheral nerves through electrodes placed on the skin (Teoli et al., 2024). This technique has garnered significant attention in the field of stroke rehabilitation, mainly due to its potential to enhance motor and sensory recovery. The precise mechanisms by which TENS can be beneficial to stroke recovery are still unclear, even though there is an increasing number of published research in this area. Currently, several theoretical concepts are proposed in this regard. First, researchers have proposed that TENS can trigger the gate control hypothesis of pain modulation by stimulating peripheral nerves and activating A-beta fibers, which are large-diameter sensory fibers (Johnson, 2007). Second, TENS can provide sensory stimulation to the affected area, promoting neuroplasticity and cortical reorganization, hence, helping restore sensory input to the brain and facilitate the reorganization of neural networks (Bao et al., 2020). In addition, by activating weakened or paralyzed muscles, TENS may help prevent muscle atrophy and promote muscle strengthening (In et al., 2021). Neurochemical changes have also been attributed to TENS; as it has been suggested to modulate the release of various neurotransmitters such as endorphins, serotonin, and norepinephrine (Sluka & Walsh, 2003). These neurochemical changes may contribute to pain relief, mood enhancement, and modulation of neuronal excitability, which could have positive effects on stroke rehabilitation outcomes. Moreover, a recent in vitro study has suggested that by inhibiting neuronal oxidative stress and pyroptosis, TENS can enhance brain ischemic injury (Tan et al., 2023).

According to the results of our study, TENS offers several advantages as an intervention in stroke rehabilitation which are addressed thoroughly in the previous section. Further, it is noninvasive, and electrodes are placed on specific areas of the body, allowing for targeted stimulation without the need for incisions or implants. This noninvasive nature makes TENS a safe and well-tolerated option for individuals recovering from stroke.

However, it is worth noting that the quality of the evidence varied across the included SRs. While some reviews reported robust evidence supporting the efficacy of TENS in stroke rehabilitation, others

highlighted the need for higher quality studies and larger sample sizes to draw definitive conclusions. Standardization of outcome measures and protocols for TENS application would also contribute to better comparability and generalizability of the findings across studies.

Furthermore, even though there appears to be a lot of available data in favor of TENS usage in poststroke rehabilitation, the overall body of research is still relatively limited. Many studies have small sample sizes and varying methodologies. Some patients may experience significant pain reduction or improvements in motor function, while others may not respond as favorably. Factors such as the location and severity of the stroke, the presence of other medical conditions, and individual differences in pain perception or motor recovery potential can influence the response to TENS. Also, the absence of standardized guidelines and the uncertainty of its long-term effects make it challenging to determine the optimal TENS parameters for specific poststroke rehabilitation goals. The gaps in the current scientific literature identified in the current study can inspire and guide future research to build upon existing knowledge and address important unanswered questions.

Lastly, it should be considered that while TENS may be helpful in stroke recovery, it is crucial to take each patient's unique circumstances into account, including stroke severity, lesion location, and comorbidities, when determining the suitability and optimal parameters for TENS application. Personalized approaches to TENS intervention, tailored to individual patient needs, may yield better outcomes and the current literature is unable to provide sufficient data in this regard.

Strengths and Limitations

This study has several strengths and limitations that need to be noted. First, the findings were presented following the PRISMA guidelines, which provide a standardized framework to enhance credibility and transparency. Further, the study employed a comprehensive search strategy that adhered to the PICOs guidelines in multiple electronic bibliographic databases, in addition to the manual search. With no time restrictions in the search, included studies were published from 2001 to 2023, spanning over 2 decades. This extended study period enhances the likelihood of encompassing studies conducted at different time points, thereby contributing to a more comprehensive understanding of the topic.

This study was also subject to some limitations. First and foremost, some limitations are directly the results of an umbrella design. For instance, the quality of the umbrella review is dependent on the quality of the included systematic reviews. If the SRs themselves are of low quality or have methodological limitations, it can affect the overall reliability and validity of the umbrella review. Therefore, it is crucial to critically appraise the included SRs and consider their methodological rigor. In addition, depending on the selection criteria used in the umbrella review, there may be overlapping primary studies across the included systematic reviews. If the same primary studies are included in multiple SRs, it can potentially inflate the significance of those studies and result in an overestimation of the effect sizes or impacts of certain interventions or exposures.

Apart from the methodology, some limitations are associated with the target intervention. For instance, the included studies applied different variations of TENS protocols and techniques. This heterogeneity in TENS application makes it challenging to draw consistent conclusions or make direct comparisons between studies. In the context of urinary dysfunction, TENS was found to have a larger effect on improving urinary continence when initiated within 3 months after stroke compared to when initiated more than 3 months later. This indicates that the timing of TENS application may be an important factor to consider, but further research is needed to establish optimal timing and its impact on outcomes. Some areas, such as the effects of TENS on poststroke pain and balance/gait, had a limited number of included studies (three and four studies, respectively). These limitations highlight the need for more robust research in these areas to draw more definitive conclusions.

Conclusion

The results of this study point to a generally favorable trend in TENS's application for several facets of poststroke rehabilitation, including motor recovery, balance, urinary and fecal function, pain management, and spasticity. Nevertheless, the low to moderate quality SRs supports this conclusion. Future research should explore this intervention further through well-designed clinical trials to establish their optimal protocols, long-term effects, and treatment plans that are tailored to individual needs.

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Appendix

Search Strategies

PubMed

Search: ((((((((((((("Transcutaneous Electric Nerve Stimulation"[Mesh]) OR (Transcutaneous Electric Nerve Stimulation[Title/Abstract])) OR (Transcutaneous Electrical Nerve Stimulation[Title/Abstract])) OR (Transcutaneous Nerve Stimulation[Title/Abstract])) OR (Transcutaneous Electric Stimulation[Title/Abstract])) OR (TENS[Title/Abstract])) OR (electrostimulation[Title/Abstract])) OR (neuromodulation[Title/Abstract])) OR (transdermal electric nerve stimulation[Title/Abstract])) OR (transdermal electrical nerve stimulation[Title/Abstract])) OR (transdermal nerve stimulation[Title/Abstract])) OR (transdermal electric stimulation[Title/Abstract])) OR (Transcutaneous Neuromodulation Therapy[Title/Abstract])) OR (Nerve Stimulation, Transcutaneous[Title/Abstract])) AND ((((((((((((("Stroke"[Mesh] OR "Embolic Stroke"[Mesh] OR "Hemorrhagic Stroke"[Mesh] OR "Thrombotic Stroke"[Mesh] OR "Ischemic Stroke"[Mesh] OR "Stroke, Lacunar"[Mesh] OR "Brain Stem Infarctions"[Mesh] OR "Infarction, Middle Cerebral Artery"[Mesh] OR "Infarction, Anterior Cerebral Artery"[Mesh] OR "Anterior spinal artery stroke" [Supplementary Concept]) OR (stroke[Title/Abstract])) OR (embolic stroke[Title/Abstract])) OR (hemorrhagic stroke[Title/Abstract])) OR (thrombotic stroke[Title/Abstract])) OR (ischemic stroke[Title/Abstract])) OR (lacunar stroke[Title/Abstract])) OR (brain ischemia[Title/Abstract])) OR (brain infarction[Title/Abstract])) OR (brain attack[Title/Abstract])) OR (Cerebrovascular accident[Title/Abstract])) OR (CVA[Title/Abstract])) OR (intracerebral hemorrhage[Title/Abstract])) OR ((((("Ischemic Attack, Transient"[Mesh]) OR (Ischemic Attack, Transient[Title/Abstract])) OR (Transient Ischemic Attack[Title/Abstract])) OR (Transient Ischemic Stroke[Title/Abstract])))) Filters: Meta-Analysis, Systematic Review

Web of Science (WoS)

Transcutaneous electric nerve stimulation OR Transcutaneous electrical nerve stimulation OR Transcutaneous nerve stimulation OR Transcutaneous electric stimulation OR transdermal electric nerve stimulation OR transdermal electrical nerve stimulation OR transdermal nerve stimulation OR transdermal electric stimulation OR neuromodulation OR electrostimulation OR TENS (Topic) and Stroke OR cerebrovascular accident OR CVA OR ischemic stroke OR brain stroke OR cerebral stroke OR hemorrhagic stroke OR brain attack OR transient ischemic stroke OR TIA OR brain infarction OR cerebral infarction OR cerebrovascular infarction OR intracranial stroke OR intracranial hemorrhage (Topic) and systematic review OR meta-analysis OR review systematic OR metaanalysis OR meta analysis OR comprehensive review (All Fields)

COCHRANE

Search Name: STROKE + UMBRELLA
Date Run: 01/08/2023 05:46:20
Comment:

ID	Search	Hits
#1	systematic review OR meta-analysis OR review systematic OR metaanalysis OR meta analysis OR comprehensive review	69196
#2	Transcutaneous electric nerve stimulation OR Transcutaneous electrical nerve stimulation OR Transcutaneous nerve stimulation OR Transcutaneous electric stimulation OR transdermal electric nerve stimulation OR transdermal electrical nerve stimulation OR transdermal nerve stimulation OR transdermal electric stimulation OR neuromodulation OR electrostimulation OR TENS	10864
#3	Stroke OR cerebrovascular accident OR CVA OR ischemic stroke OR brain stroke OR cerebral stroke OR hemorrhagic stroke OR brain attack OR transient ischemic stroke OR TIA OR brain infarction OR cerebral infarction OR cerebrovascular infarction OR intracranial stroke OR intracranial hemorrhage	91257
#4	#1 AND #2 AND #3	152

Scopus

(TITLE-ABS-KEY ("Transcutaneous electric nerve stimulation" OR "Transcutaneous electrical nerve stimulation" OR "Transcutaneous nerve stimulation" OR "Transcutaneous electric stimulation" OR "transdermal electric nerve stimulation" OR "transdermal electrical nerve stimulation" OR "transdermal nerve stimulation" OR "transdermal electric stimulation" OR neuromodulation OR electrostimulation OR tens) AND TITLE-ABS-KEY (stroke OR "cerebrovascular accident" OR cva OR "ischemic stroke" OR "brain stroke" OR "cerebral stroke" OR "hemorrhagic stroke" OR "brain attack" OR "transient ischemic stroke" OR tia OR "brain infarction" OR "cerebral infarction" OR "cerebrovascular infarction" OR "intracranial stroke" OR "intracranial hemorrhage") AND TITLE-ABS-KEY ("systematic review" OR "meta-analysis" OR "review systematic" OR metaanalysis OR "meta analysis" OR "comprehensive review"))