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Aim and Scope

NeuroRegulation is a peer-reviewed journal providing an integrated, multidisciplinary perspective on clinically relevant research, treatment, and public policy for neurofeedback, neuroregulation, and neurotherapy. The journal reviews important findings in clinical neurotherapy, biofeedback, and electroencephalography for use in assessing baselines and outcomes of various procedures. The journal draws from expertise inside and outside of the International Society for Neuroregulation and Research to deliver material which integrates the diverse aspects of the field. Instructions for submissions and Author Guidelines can be found on the journal website (http://www.neuroregulation.org).

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RETRACTED ARTICLE: *EEG Signatures of Resilience Across Individuals With High and Low Anxiety*

Sahen Gupta[1] *and Jayasankara Reddy*[2]

[1]University of Portsmouth, School of Psychology, Sport & Health Sciences, Portsmouth, United Kingdom
[2]CHRIST (Deemed to be University), Department of Psychology, Bengaluru, India

Abstract

This is a retraction of the article *EEG Signatures of Resilience Across Individuals With High and Low Anxiety* originally published in Volume 12, Number 1, on March 24, 2025, page 12.

Citation: Gupta, S., & Reddy, J. (2026). RETRACTED ARTICLE: EEG signatures of resilience across individuals with high and low anxiety. *NeuroRegulation, 13*(2), 118. https://doi.org/10.15540/nr.13.2.118

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Rex L. Cannon, PhD, Currents, Knoxville, Tennessee, USA

Editorial Note

The Editor-in-Chief has retracted this article due to unresolved concerns regarding authorship. The article was originally published on March 24, 2025, in Volume 12, Number 1.

The online version of the article, with a watermark noting its retraction, is available at https://doi.org/10.15540/nr.12.1.12

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Efficacy of an Alpha Neurofeedback Training in the Treatment of Anxiety and Depression of a Group of Patients: A Pilot Study

Alexandra Glink[1,2,3], Maria Eugenia Gras[1,2], and Montserrat Planes[1,2]*

[1]University of Girona, Quality of Life Research Institute, Girona, Spain
[2]University of Girona, Department of Psychology, Girona, Spain
[3]Neuroon Clinic Psychology Center, Empuriabrava, Girona, Spain

Abstract

Background. Anxiety and depression are highly prevalent in the general population and primary care. While alpha rhythm (8–12 Hz) stimulation has been shown to reduce anxiety, its impact on broader emotional well-being, including depressive symptoms, is less studied. **Objective.** This exploratory study examined the effects of alpha neurofeedback training on anxiety and depression in adults. **Methods.** Fourteen female participants with anxiety and depressive symptoms were randomly assigned to an intervention group (n = 7) or a waitlist control group (n = 7). Psychological symptoms and alpha brainwave activity were assessed before and after the intervention. After the initial phase, the waitlist participants also received the training, forming a quasi-experimental design. **Results.** Ten sessions of alpha neurofeedback significantly reduced anxiety in both experimental and quasi-experimental phases. Depressive symptoms decreased notably only in the quasi-experimental phase, when all participants received the intervention. Alpha amplitude increased, and improvements in anxiety and depression were correlated, though not statistically significant. **Conclusions.** These preliminary findings suggest that alpha neurofeedback may be an effective nonpharmacological intervention to reduce anxiety and depression in adults. Results are exploratory, highlighting the need for larger, diverse samples and follow-up assessments to confirm the durability of effects.

Keywords: alpha; neurofeedback; anxiety; depression

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***Address correspondence to**: Dr. Alexandra Glink, Neuroon Clinic Psychology Center, C/Pla de Roses 15, E-17487 Empuriabrava, Girona, Spain. Email: alexandraglink@gmail.com

Edited by:
Rex L. Cannon, PhD, Currents, Knoxville, Tennessee, USA

Reviewed by:
Rex L. Cannon, PhD, Currents, Knoxville, Tennessee, USA
Randall Lyle, PhD, Mount Mercy University, Cedar Rapids, Iowa, USA

Introduction

Depression and anxiety disorders are among the most prevalent psychological conditions in both the general population and primary care settings. These highly disabling disorders result not only in substantial human suffering and loss of health but also in significant economic costs due to reduced productivity and healthcare burden (Demertzis & Craske, 2006; Kroenke et al., 2007). Given their strong association with morbidity and mortality (Kessler et al., 2007; Richards, 2011), early identification and effective treatment of both conditions are crucial.

In addition to traditional therapeutic approaches such as psychotherapy and pharmacotherapy, neurofeedback training has emerged as a promising complementary intervention for individuals diagnosed with anxiety and depression. These disorders are characterized by abnormal patterns of electrical activity within neural networks involved in emotion regulation and behavior (Menon, 2011).

Neurofeedback is a form of biofeedback that provides real-time information about cortical activity through electroencephalography (EEG). Using auditory or visual feedback, participants learn to voluntarily modulate specific EEG frequency components (Lubar, 1997). These components may

include individual brainwave frequencies, ratios between them, or measures of coherence. The ultimate goal of neurofeedback training is to enable individuals to optimize their brain activity, thereby promoting beneficial changes in emotional regulation, cognition, and behavior (Niv, 2013).

Early studies of neurofeedback focused on enhancing alpha activity in individuals with anxiety disorders, as increased alpha power has been associated with greater relaxation and reduced arousal (Hardt & Kamiya, 1978). Subsequent research has provided accumulating evidence supporting the efficacy of neurofeedback in the treatment of anxiety and depression. Reviews by Hammond (2006a, 2006b) and Moore (2000) summarized multiple studies demonstrating clinically significant improvements following neurofeedback interventions. Typically, protocols targeting parietal alpha enhancement are used for anxiety, whereas frontal alpha asymmetry training is commonly applied in the treatment of depression (Baehr et al., 2001; Choi et al., 2011).

In primary care, depressive and anxiety disorders frequently co-occur, and patients often present with somatic rather than psychological complaints, such as back pain, chest tightness, palpitations, sleep disturbances, appetite changes, or fatigue. This overlap underscores the urgent need to develop and evaluate new, effective, and noninvasive interventions targeting both disorders simultaneously.

The aim of the present study was to examine the effects of an alpha enhancement neurofeedback protocol—typically employed in the treatment of anxiety—on individuals presenting with both anxiety and depressive symptoms.

Materials and Methods

Participants

This study was conducted at a psychological center. Fifteen patients aged between 25 and 60 years with anxiety and/or depression were initially considered for participation. Only one male contacted the center to participate, and he was excluded to maintain intergroup similarity. After applying the exclusion criteria, 14 female participants (mean age = 37.85 years, *SD* = 11.07) were included in the analysis.

Ethics Statement

This exploratory study was conducted at a psychological center with adult participants who provided written informed consent prior to participation. Although the study did not receive formal approval from an Institutional Review Board (IRB), all procedures were performed under academic supervision and in accordance with the ethical standards of the Helsinki Declaration (World Medical Association, 1996). Participants were treated respectfully, their privacy was ensured, and data were collected and stored confidentially. The study represents preliminary, hypothesis-generating research in the field of neuroregulation.

Procedure

Written informed consent was obtained from all participants. A pro forma data sheet specifically designed to gather psychosocial information was used. Participants were divided into two groups by allocating consecutive patients alternately.

Anxiety and depression levels were initially assessed (Phase 1) using the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983). The HADS authors propose three cut points for each subscale (anxiety and depression): normal (0–7), doubtful disorder (8–10), and clinically relevant problem (≥ 11).

Initial alpha brainwave amplitude was measured and recorded. One group of seven participants (intervention group) received alpha neurofeedback training twice per week for 5 weeks. The other group served as a waitlist control and did not receive training during this period. In Phase 2, after the 5-week treatment period, anxiety, depression, and alpha amplitude were reassessed in both groups. In Phase 3, the waitlist control group received the same neurofeedback training as the intervention group and data were reassessed, resulting in a combined intervention group of 14 participants.

Electroencephalography

EEG data were collected at the P4 electrode (parietal cortex), using the International 10/20 electrode system. Gold cup electrodes were placed in a monopolar montage, with the ground electrode on the right ear and the reference electrode on the left ear. The scalp was prepared with NuPrep skin prep gel, and electrodes were adhered with Ten20 conductive paste (both from Weaver and Company, Aurora, CO).

Table 1
Distribution of Participants According to Group, Sociodemographic, and Clinical Variables

Sociodemographic Variables		Group	
		Intervention (*n* = 7)	Control (*n* = 7)
Gender	Male	0% (0)	0% (0)
	Female	100% (7)	100% (7)
Age	Between 25 and 60 years	100% (7)	100% (7)
Clinical Variables			
Anxiety or depression	Yes	100% (7)	100% (7)
	No	0% (0)	0% (0)
Symptoms	Muscular pain	42.9% (3)	14.3% (1)
	Insomnia	0% (0)	42.9% (3)
	Gastrointestinal discomfort	42.9% (3)	28.6% (2)
	Headache	14.3% (1)	14.3% (1)
Medication or substance that may influence the nervous system	Yes	0% (0)	0% (0)
	No	100% (7)	100% (7)

Note. Percentages and frequencies are presented by row.

Data were collected using the Nexus-10 MKII device and Biotrace+ software (Mind Media BV, Echt, NL) at a sampling rate of 256 Hz, ensuring skin impedance levels were below 10 kΩ. Raw data were processed using a Butterworth bandpass filter, and average peak-to-peak amplitudes (in μV) were calculated for the alpha frequency band (8–12 Hz). These amplitudes were used to guide neurofeedback training.

Neurofeedback

Participants underwent 10 sessions of alpha-enhancement neurofeedback over 5 weeks. Individual training sessions included two 15-min feedback screens (Smiley face and Waterfall). A threshold of 10 μV was set, with feedback screens pausing if alpha amplitude fell below this threshold. Positive reinforcement was provided when alpha amplitude exceeded the threshold. Mean alpha amplitude during training was monitored using a digital counter within the Biotrace+ software. A digital counter system within the Biotrace+ software was employed to determine the mean alpha amplitude that was occurring during training.

Statistical Analysis

All parametric statistical analyses were performed using SPSS, Version 14.0 for Windows. Due to the small sample size, nonparametric tests (Mann-Whitney, Wilcoxon, and Friedman) were used. For clarity, mean values of the variables are also reported.

Results

Anxiety and Depression Levels Pretreatment and Posttreatment

All participants were assessed using the HADS before and after neurofeedback training. Tables 2–5 present the mean scores and standard deviations for anxiety and depression subscales in both the experimental and quasi-experimental designs.

Table 2
Mean Scores and Standard Deviation (in Brackets) of the HADS Anxiety Subscale by Group, Before and After the Intervention, With Results of the Mann-Whitney U Test

Experimental Design	Pre *x* (*dt*)	Post *x* (*dt*)
Intervention group (*n* = 7)	11.29 (3.86)	7.43 (2.64)
Control group (*n* = 7)	12.00 (3.79)	12.23 (3.60)
Z (*p*)	−0.06 (.95)	2.20 (.03)

Table 3
Mean Scores and Standard Deviation (in Brackets) of the HADS Anxiety Subscale, Before and After the Intervention, With Results of the Wilcoxon T Test

Quasi-Experimental Design	Pre *x* (*dt*)	Post *x* (*dt*)
Intervention group (*n* = 14)	11.79 (3.62)	8.00 (2.75)
***Z* (*p*)**	−3.194 (.001)	

Table 4
Mean Scores and Standard Deviation (in Brackets) of the HADS Depression Subscale by Group, Before and After the Intervention, With Results of the Mann-Whitney U Test

Experimental Design	Pre *x* (*dt*)	Post *x* (*dt*)
Intervention group (*n* = 7)	9.57 (4.86)	6.14 (3.76)
Control group (*n* = 7)	9.29 (3.82)	9.57 (3.05)
Z (*p*)	−0.13 (.90)	−1.74 (.082)

Table 5
Mean Scores and Standard Deviation (in Brackets) of the HADS Depression Subscale, Before and After the Intervention, With Results of the Wilcoxon T Test

Quasi-Experimental Design	Pre *x* (*dt*)	Post *x* (*dt*)
Intervention group (*n* = 14)	9.57 (3.90)	7.07 (3.85)
***Z* (*p*)**	−2.840 (.005)	

The intervention group showed a significant reduction in anxiety levels compared to the control group after the neurofeedback training. When analyzing all 14 participants together, the decrease in anxiety remained statistically significant.

Regarding depression, no significant differences were observed between the intervention and control groups, although a notable reduction was evident. When considering all participants together, the reduction in depression reached statistical significance, albeit smaller than for anxiety.

Given these overall results, it was clinically relevant to examine individual changes in anxiety and depression (Tables 6 and 7).

Participants with normal anxiety did not show a reduction, whereas those with doubtful anxiety decreased by 40.89%, and participants with clinically relevant anxiety decreased by 29.05%.

Table 6
Mean Pre- and Posttest HADS Anxiety Scores and Percentage Change for Each Participant

Subject	Anxiety		% Change
	Pretest	Posttest	
1	10	4	−60.00%
2	9	6	−33.33%
3	17	11	−35.29%
4	9	7	−22.22%
5	9	6	−33.33%
6	12	11	−8.33%
7	13	10	−23.07%
8	13	10	−23.07%
9	14	9	−35.71%
10	17	10	−41.18%
11	5	5	0%
12	17	12	−29.41%
13	11	7	−36.36%
14	9	4	−55.56%
	Pretest x	Posttest x	% Change
	11.78	8.00	−32.09%

Table 7
Mean Pre- and Posttest HADS Depression Scores and Percentage Change for Each Participant

Subject	Depression		% Change
	Pretest	Posttest	
1	16	9	−43.75%
2	5	4	−20.00%
3	10	2	−80.00%
4	12	9	−25.00%
5	7	5	−28.57%
6	14	15	7.14%
7	15	13	−13.33%
8	9	10	11.11%
9	10	6	−40.00%
10	9	5	−44.44%
11	2	3	50.00%
12	11	9	−18.18%
13	7	5	−28.57%
14	7	4	−42.86%
	Pretest x	Posttest x	% Change
	9.57	7.07	−26.12%

Participants with normal depression decreased by 14%, those with doubtful depression decreased by 38.33%, and participants with clinically relevant depression decreased by 18.62%.

Alpha Amplitude Pretreatment and Posttreatment

Tables 8–10 display mean alpha amplitude before and after neurofeedback training.

Table 8

Mean Scores and Standard Deviation (in Brackets) of Alpha Amplitude at Baseline According by Group, Before and After the Intervention, With Results of the Mann-Whitney U Test

Experimental Design	Pre *x* (*dt*)	Post *x* (*dt*)
Intervention group (*n* = 7)	7.47 (1.09)	13.48 (6.04)
Control group (*n* = 7)	6.88 (1.80)	7.00 (1.76)
Z (*p*)	−0.32 (.75)	−3.00 (.003)

Table 9

Average Scores and Standard Deviation (in Brackets) of Alpha, Before and After the Intervention, With Results of the Wilcoxon T Test

Quasi-Experimental Design	Pre *x* (*dt*)	Post *x* (*dt*)
Intervention group (*n* = 14)	7.02 (1.38)	12.79 (4.62)
***Z* (*p*)**	−3.296 (.001)	

Table 10

Mean Pre- and Posttest Alpha Amplitude and Percentage Change for Each Participant

Subject	Alpha Amplitude		% Change
	Pretest	Posttest	
1	7.44	9.31	25.13%
2	4.89	9.29	89.97%
3	7.81	25.73	229.44%
4	7.24	12.57	73.61%
5	5.82	10.76	84.87%
6	4.32	8.22	90.27%
7	6.99	8.61	23.17%
8	7.17	10.60	47.83%
9	8.00	13.70	71.25%
10	8.14	15.28	87.71%
11	9.31	16.26	74.65%
12	5.90	12.55	112.71%
13	6.90	9.98	44.63%
14	8.37	16.18	93.30%
	Pretest x	Posttest x	% Change
	7.02	12.79	82.19%

Table 11
Spearman's Correlations Between Changes in Alpha Amplitude, Anxiety, and Depression

		Alpha-Anxiety Correlation r_s (p)	Alpha-Depression Correlation r_s (p)	Anxiety-Depression Correlation r_s (p)
Experimental Design	Intervention group (n = 7)	−0.073 (.877)	−0.148 (.751)	0.962 (.001)
Quasi-Experimental Design	Control group (n = 7)	−0.316 (.490)	−0.128 (.784)	−0.488 (.267)

Table 8 shows that while groups were similar at baseline, alpha amplitude significantly increased in the intervention group posttraining. These differences were confirmed in the quasi-experimental design, including the control group once they received training.

Overall, 64.28% of participants increased their alpha amplitude above 10 μV (mean pretest = 7.02 μV; mean posttest = 12.79 μV), representing an average increase of 82.19%. No systematic relationship was observed between initial alpha amplitude and percentage increase.

In the intervention group, the expected inverse relationship between alpha amplitude and anxiety/depression was observed, although correlations were not statistically significant. However, a strong, significant correlation between anxiety and depression improvements was found in the intervention group and quasi-experimental design, indicating that reductions in anxiety were closely linked to reductions in depression.

Discussion

This exploratory study suggests that 10 sessions (5 hr) of alpha neurofeedback training can increase alpha amplitude and reduce anxiety and depression symptoms in adult female participants. Both the experimental and quasi-experimental designs indicated statistically significant improvements after training, despite the small sample size.

These results are consistent with previous studies demonstrating alpha neurofeedback's ability to enhance alpha amplitude (Dempster & Vernon, 2009; Hardt & Kamiya, 1978; Zoefel et al., 2011). Research generally indicates that more training sessions yield better results, though a ceiling effect may occur after a certain number of sessions (Cho et al., 2008; Nowlis & Wortz, 1973).

From a clinical perspective, our results suggest that short-term alpha neurofeedback may effectively reduce anxiety. Participants with doubtful or clinically relevant anxiety demonstrated meaningful decreases in symptoms, consistent with early findings by Hardt and Kamiya (1976, 1978) and other studies (Hammond, 2006a, 2006b; Moore, 2000). Similarly, reductions in depression were observed, echoing findings from Linden et al. (2012) and Choi et al. (2011), who reported improvements in mood and executive function after neurofeedback training.

Correlation analyses indicated that larger increases in alpha amplitude tended to coincide with greater reductions in anxiety and depression, though these associations were small and nonsignificant. Notably, anxiety and depression improvements were strongly correlated, highlighting the intertwined nature of these symptoms.

Limitations and Future Directions

Given the exploratory nature of this study, results should be interpreted cautiously:

- (a) sample size and composition: only 14 female participants were included, limiting generalizability, particularly to males,
- (b) exploratory design: findings are preliminary and hypothesis-generating rather than confirmatory,
- (c) training duration: Although 5 hr of neurofeedback produced measurable effects, optimal session number and duration remain uncertain, and
- (d) follow-up data: long-term maintenance of changes was not assessed.

Future research should replicate these findings with larger, more diverse samples, systematically examine optimal training parameters, and include follow-up assessments to determine the durability of neurofeedback effects.

In conclusion, this exploratory study provides preliminary evidence that short-term alpha neurofeedback may increase alpha amplitude and reduce anxiety and depressive symptoms, supporting its potential clinical utility while highlighting the need for further research.

Author Declaration

The authors confirm that the study was conducted without any commercial or financial relationships that could be construed as potential conflicts of interest. No grants or external funding were received for this work. The authors used AI tools solely for limited grammatical and language editing. No AI was used in the creation of the manuscript's content, analysis, or conclusions, and the authors take full responsibility for the work.

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Effects of Raga Kirwani on EEG Microstates: An Inquiry of Brain Network Dynamics

Rupam Banerjee[1], Debashina Das[2], and Anwesha Chakrabarti[2]*

[1]West Bengal State University, Department of Psychology, Berunanpukhuria, Kolkata, West Bengal, India
[2]Sarojini Naidu College for Women, Department of Psychology, North Dumdum, Kolkata, West Bengal, India

Abstract

The raga system of Indian classical music has long been associated with emotional and cognitive regulations, but its effect on large-scale brain networks is still not adequately explored. This study sought to examine the impact of Raga Kirwani on resting-state brain dynamics using EEG microstate analysis. A within-subject approach was utilized with 10 healthy adult volunteers (*M* = 20.5 years, *SD* = 3.32). EEG data were acquired prior to and after a 5-min listening session of Raga Kirwani. Microstate characteristics, such as mean duration, occurrence, coverage, global explained variance (GEV), and transition probabilities, were obtained using the MICROSTATE toolbox in EEGLAB. Results indicated a decline in coverage of microstate B, reduced transition from C to B, and increased transition from C to D—a reduction in visual-spatial processing and an increase in executive activities. Although early, these findings offer basic evidence that Indian classical music may in fact function as a culturally ingrained instrument of mental alignment and control. Subsequent research with larger sample size and control is needed to expand upon these findings.

Keywords: Raga Kirwani; EEG; microstates; resting-state; Indian classical music; cognitive flexibility; DMN; music neuroscience

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***Address correspondence to**: Rupam Banerjee, 8/1, Shyamasreepally 3rd Lane, P.O. Nona Chandan Pukur, Barrackpore, Kolkata 700122, West Bengal, India. Email: rupambanerjee@sncwgs.ac.in

Edited by:
Rex L. Cannon, PhD, Currents, Knoxville, Tennessee, USA

Reviewed by:
Rex L. Cannon, PhD, Currents, Knoxville, Tennessee, USA
Randall Lyle, PhD, Mount Mercy University, Cedar Rapids, Iowa, USA

Introduction

Music is one of the most ancient and universal forms of human experience and expression that is capable of putting profound effects on cognition, emotion, and physiological processes. In the last few decades, with the advent of recent technologies, cognitive neuroscience has gradually focused understanding on how our brain reacts to music and its influence on mood (Blood & Zatore, 2001; Koelsch, 2010; Zentner et al., 2008), memory (Särkämö et al., 2008), attention (Meltzer et al., 2015; Treder et al., 2015; Xiao et al., 2024), and functional connectivity within and even across large-scale brain networks (Koelsch, 2014; Salimpoor et al., 2011). Despite the global variety of musical traditions and dispositions, the majority of them focused on western tonal systems, often neglecting the rich diversity of other global musical traditions (Cross, 2012; McDermott & Hauser, 2005).

Indian classical music is characterized by its deep and ancient intellectual foundations, intricate melody, and sophisticated and nonnatural rhythm. It has been historically linked to certain emotional, mental, and physiological conditions (Ubrangala et al., 2022). The central foundation to this system is the concept of raga, functioning as a melodic framework, that integrates sounds and melodies while also evoking certain moods and mental states, referred to as *rasa* (Clayton, 2000; Jairazbhoy, 1995). These ragas have shown unique cognitive and emotional impact and have been utilized with meditative practices and music therapy. Despite the increasing empirical focus on both the psychological and the physiological impact of ragas—especially concerning relaxation of anxiety, heart rate

regulations, and improvement in attention—a substantial gap still persists in our comprehension of their neurodynamic influence, particularly regarding intrinsic brain states during rest.

Raga Kirwani can be distinguished by its unique structure, forming a symmetric 7-note scale in both its ascent (arohana) and descent (avarohana). Specifically, with its notes being S–R–g–M–P–d–N–S′ (where *g* and *d* are lowered), it is very similar to the harmonic minor scale and has been conventionally linked to a self-reflective calm state. Although anecdotal and therapeutic applications of Kirwani have been recorded in traditional practices (Sharma et al., 2017; Ubrangala et al., 2022), its impact on the brain's intrinsic activity, particularly on the resting-state dynamics, has yet to be investigated.

Electroencephalography (EEG) microstate analysis provides an effective approach for investigating rapid dynamics of the resting-state activity of the brain. Microstates are transient, quasistable configurations of scalp potential topographies that endure for around 80–120 ms and have been believed to represent distinct global functional states of the brain (Michel & Koenig, 2018) and have also been referred to as the “the atom of thought” (Lehmann et al., 1998). A consensus has developed on four canonical microstates, designated A, B, C, and D (Koenig et al., 1999; Lehmann et al., 2005; Strik et al., 1997; Strelets et al., 2003; Kikuchi et al., 2011; Kindler et al., 2011), although studies have found other template maps to be useful too (Britz et al., 2010). These microstates are thought to be correlated with certain global functional networks:

- **Microstate A** – Auditory processing
- **Microstate B** – Visuo-spatial attention
- **Microstate C** – Default mode network (DMN)
- **Microstate D** – Executive control and salience network (Britz et al., 2010; Seitzman et al., 2017)

Alterations in the microstate parameters—specifically mean duration, occurrence frequency, coverage, and transition probabilities—have been associated with diverse mental states including alertness, meditation, mind wandering, and psychiatric disorders, such as schizophrenia and depression (Khanna et al., 2015; Michel & Koenig, 2018; Milz et al., 2016). Moreover, music has been demonstrated to influence EEG microstates. Previous research indicates that listening to emotionally charged or organized music can alter microstate characteristics in both skilled musicians and nonmusicians, suggesting that music may affect the brain’s plastic organization even during rest (Hill et al., 2017).

Despite all the advancements, the influence of Indian classical music—particularly Indian ragas—on EEG microstate dynamics has yet to be investigated. To our knowledge, this study is the first investigation into the impact of Raga Kirwani on EEG microstates in healthy persons. We recorded the resting-state EEG before and after a passive listening session with Raga Kirwani using a within-subject, pre–post methodology. We obtained the four canonical microstates and assessed the alterations in their temporal characteristics (length, occurrence and coverage), global explained variance (GEV), topographic consistency, and transition probabilities.

It was hypothesized that listening to Raga Kirwani would impact the dynamics of specific microstates, possibly indicating changes in attention, self-referential processing, and cognitive control. Considering Kirwani is conventional to meditative tranquility and introspective awareness, we expected a decrease in visuospatial and default mode activities (microstates B and C) and increase in auditory and salient network activity (microstates A and D).

This pilot study seeks to offer initial insights into how culturally rooted musical genres like the ragas may influence inherent brain processes and generate hypotheses for future studies in this niche area.

Methodology

Participants

Ten healthy adult participants (Mean age = 20.5 years, *SD* = 3.32) took part in the study. All of the participants were right-handed, with hearing sensitivity within normal limits, and did not report any diagnosed psychological or neurological disorder. None of them had received formal music training or had any knowledge regarding raga grammars. Informed consent was obtained from all individuals prior to participation.

Procedure

The study followed a within-subject pre–post design. Participants were seated in a sound attenuated lab and were instructed to keep their eyes closed and relax, and to inform the experimenter if they felt drowsy or might fall asleep. Three minutes of resting-state EEG were obtained, after which a 5-min instrumental excerpt of Raga Kirwani was

played through a stereo sound system at a comfortable volume. Finally, another 3 min of eyes-closed resting EEG data were recorded.

EEG Recording

EEG data was recorded using a medical grade 24-channel EEG system, with electrodes placed following the international 10–20 system. Signals were sampled at 256 Hz with impedance kept below 10 kΩ. The ground electrode was placed at the cheek and the reference electrode was attached to the left mastoid. Electro-oculographic (EOG) activity was recorded from additional electrodes placed above and below the eyes to monitor eye blink.

EEG Preprocessing

Data preprocessing was done using EEGLAB (Delorme & Makeig, 2004) in MATLAB following standard preprocessing protocol. Continuous resting-state EEG data were passed through 1 Hz highpass and 40 Hz lowpass filter and rereferenced to the average. Noisy data segments were first manually scanned and removed, and also cleaned utilizing artifact subspace reconstruction (ASR; Mullen et al., 2015; specifically, artifact-laden intervals were removed employing a burst criteria of 20 as advised by Chang et al., 2020). Bad channels were removed and interpolated if they (a) were flat for over 5 s, (b) exhibited more than three standard deviations of line noise compared to all other channels, or (c) correlated at less than 0.80 with adjacent channels. Independent component analysis (ICA) decomposition was done subsequently, and any remaining artifacts other than brain (e.g., muscle, eyes, heart, and signal noise) were removed. After careful consideration, 20 s of EEG data from each participant was finalized to be used for microstate analysis.

In EEG, or as in other signal processing methods, “garbage in = garbage out” is a phrase that researchers always adhere to. Thus, EEG data quality was of utmost importance to us and was rigorously screened and assessed; complete data from 5 out of an initial pool of 15 participants had to be removed for not passing the quality standard, resulting in the final pool of 10 participants.

Microstate Analysis

Microstate analysis was conducted using the MICROSTATE TOOLBOX (Poulsen et al., 2018) in EEGLAB. The data was segmented using the peaks from the Global Field Power (GFP), and the maps were clustered using a modified k-means clustering (Pascual-Marqui et al., 1995). A four-class solution (A–D) was selected to align with existing research. The last phase of microstate analysis, known as backfitting, was conducted on the preprocessed, spatially filtered data of each participant, yielding rich and comprehensive temporal information, individually for every participant. The mean maps and temporal plots of both the conditions were extracted for interpretation. The following microstate parameters were extracted:

1. Mean duration (ms): the average length of each microstate occurrence
2. Occurrence (Hz): the frequency of each microstate’s appearance per second
3. Coverage (% in time): the proportion of total time allocated to each of the microstate
4. Global explained variance (GEV): the amount of variance explained by each microstate class.
5. Transition probabilities: the probability of moving from one microstate to another

Statistical Analysis

All statistical analyses were performed using JAMOVI. Paired-comparison Wilcoxon Rank Test with rank biserial effect size was used to compare each microstate parameter between Rest 1 and Rest 2 conditions, controlling for FDR (Benjamini & Hochberg, 1995).

Ethical Declaration

This study was carried out in accordance with the ethical standard approved by the declaration of Helsinki. Ethical approval was obtained from the Internal Quality Assurance Cell (IQAC) of Sarojini Naidu College for Women and follows all ethical rules and guidelines to protect the identity of study participants. Individuals who took part were told they would be part of a study about Indian classical music, and they were also explained how the EEG would be administered in general. The people who took part in the experiment were also made very clear that they could leave right away if they felt any physical or mental pain. Before taking part, all volunteers were given a consent form where they gave written consent and were remunerated for their time.

Results

Microstate Temporal Parameters

Prior to the paired test, the descriptive statistics (Mean, *SD*, Skewness, Kurtosis, Shapiro-Wilk Test of Normality) were calculated which have been included below in Table 1.

Table 1
Descriptive Statistics

			Skewness		Kurtosis		Shapiro-Wilk	
	Mean	***SD***	**Skewness**	***SE***	**Kurtosis**	***SE***	***W***	***p***
TotalExpVar_Post	0.6793	0.06446	0.79629	0.717	0.9472	1.4	0.914	.346
TotalExpVar_Pre	0.6989	0.07612	0.08526	0.717	−1.4132	1.4	0.937	.554
TotalTime_Post	18.2608	0.36947	−0.20824	0.717	−1.9574	1.4	0.868	.118
TotalTime_Pre	18.4310	0.30929	−0.77132	0.717	0.3188	1.4	0.959	.790
Coverage_A_Post	30.2184	9.80493	−0.51444	0.717	−0.9390	1.4	0.920	.394
Coverage_A_Pre	27.3256	8.76498	0.29018	0.717	−1.2392	1.4	0.941	.596
Coverage_B_Post	19.3421	6.80554	−0.73612	0.717	0.6384	1.4	0.959	.790
Coverage_B_Pre	25.8501	8.37976	0.57846	0.717	−1.2817	1.4	0.897	.233
Coverage_C_Post	24.0232	8.30042	0.61245	0.717	−1.4110	1.4	0.862	.101
Coverage_C_Pre	26.4322	8.28414	0.52180	0.717	−0.2165	1.4	0.877	.145
Coverage_D_Post	27.3993	6.59225	1.94646	0.717	4.8014	1.4	0.749	.005
Coverage_D_Pre	19.7940	6.07969	0.41735	0.717	−0.5623	1.4	0.951	.700
DeltaTM_A→B_Post	−2.3450	18.89756	0.8209	0.717	0.8051	1.4	0.934	.523
DeltaTM_A→B_Pre	−2.1624	12.10113	−0.1919	0.717	−1.0712	1.4	0.942	.602
DeltaTM_A→C_Post	−4.5318	12.38031	0.6262	0.717	−0.7763	1.4	0.934	.517
DeltaTM_A→C_Pre	−8.2072	17.00817	−0.5791	0.717	−1.3977	1.4	0.890	.202
DeltaTM_A→D_Post	3.3214	12.71463	−1.7261	0.717	3.6362	1.4	0.831	.046
DeltaTM_A→D_Pre	8.7572	11.49947	0.5113	0.717	−1.4374	1.4	0.892	.207
DeltaTM_B→A_Post	1.2178	15.49359	−0.7045	0.717	−0.3319	1.4	0.933	.506
DeltaTM_B→A_Pre	−6.4780	13.53143	0.8708	0.717	−0.3678	1.4	0.899	.249
DeltaTM_B→C_Post	4.3856	19.82063	1.3737	0.717	1.0897	1.4	0.836	.052
DeltaTM_B→C_Pre	5.6810	9.61665	−0.8742	0.717	1.0531	1.4	0.951	.703
DeltaTM_B->D_Post	−8.6830	21.47835	−0.0313	0.717	−0.6383	1.4	0.977	.948
DeltaTM_B→D_Pre	−3.5866	20.43776	−0.8405	0.717	−0.6098	1.4	0.872	.130
DeltaTM_C→A_Post	9.6983	16.78708	−0.0122	0.717	1.5703	1.4	0.932	.504
DeltaTM_C→A_Pre	9.7430	12.46186	−0.0512	0.717	−0.3811	1.4	0.995	1.000
DeltaTM_C→B_Post	−14.9008	9.83953	0.5115	0.717	−1.8576	1.4	0.832	.047
DeltaTM_C→B_Pre	3.4866	18.38546	−0.1193	0.717	−1.0343	1.4	0.920	.394
DeltaTM_C→D_Post	2.4484	20.56274	−0.3426	0.717	0.4803	1.4	0.976	.941
DeltaTM_C→D_Pre	−20.0101	15.76679	−0.7811	0.717	0.8825	1.4	0.956	.758
DeltaTM_D→A_Post	−6.0860	15.31460	−0.8122	0.717	−0.3831	1.4	0.894	.220
DeltaTM_D→A_Pre	0.6416	20.94175	0.9077	0.717	1.3911	1.4	0.940	.580
DeltaTM_D→B_Post	2.2111	20.69236	−1.9507	0.717	4.6590	1.4	0.805	.023
DeltaTM_D→B_Pre	−8.4979	16.06718	−0.8021	0.717	−0.2705	1.4	0.921	.399
DeltaTM_D→C_Post	−4.1166	7.73106	−0.8466	0.717	0.8793	1.4	0.922	.408
DeltaTM_D→C_Pre	1.6457	19.28997	0.0874	0.717	−1.1650	1.4	0.963	.833

Table 2
Paired-Comparison Wilcoxon Rank Test With Rank Biserial Effect Size

		Wilcoxon (W)	*p*	Effect Size
TotalExpVar_Pre	TotalExpVar_Post	29	.496	0.2889
TotalExpVarPre_Pre	TotalExpVarPost_Pre	27	.652	0.2000
TotalTime_Pre	TotalTime_Post	29.5	.441	0.3111
TotalTime_Pre_Pre	TotalTime_Post_Pre	26	.721	0.1556
Coverage_A_Pre	Coverage_A_Post	15	.426	−0.3333
Coverage_A_Pre	Coverage_A_Post	25	.820	0.1111
Coverage_B_Pre	Coverage_B_Post	41	.027	0.8222
Coverage_B_Pre	Coverage_B_Post	31	.359	0.3778
Coverage_C_Pre	Coverage_C_Post	31	.359	0.3778
Coverage_C_Pre	Coverage_C_Post	27	.652	0.2000
Coverage_D_Pre	Coverage_D_Post	6	.055	−0.7333
Coverage_D_Pre	Coverage_D_Post	13	.301	−0.4222
DeltaTM_A→B_Pre	DeltaTM_A→B_Post	23	1.000	0.0222
DeltaTM_A→C_Pre	DeltaTM_A→C_Post	20	.820	−0.1111
DeltaTM_A→D_Pre	DeltaTM_A→D_Post	28	.570	0.2444
DeltaTM_B→A_Pre	DeltaTM_B→A_Post	15	.426	−0.3333
DeltaTM_B→C_Pre	DeltaTM_B→C_Post	28	.570	0.2444
DeltaTM_B→D_Pre	DeltaTM_B→D_Post	26	.734	0.1556
DeltaTM_C→A_Pre	DeltaTM_C→A_Post	22	1.000	−0.0222
DeltaTM_C→B_Pre	DeltaTM_C→B_Post	42	.020	0.8667
DeltaTM_C→D_Pre	DeltaTM_C→D_Post	5	.039	−0.7778
DeltaTM_D→A_Pre	DeltaTM_D→A_Post	26	.734	0.1556
DeltaTM_D→B_Pre	DeltaTM_D→B_Post	7	.074	−0.6889
DeltaTM_D→C_Pre	DeltaTM_D→C_Post	30	.426	0.3333

Note. The *p*-values reported are FDR-adjusted (Benjamini–Hochberg).

The coverage of microstate B showed a significant reduction after listening to Raga Kirwani (W = 41, p = .027, r = 0.82). No significant change was observed in the coverage of microstates A, C, and D. While delta transition from microstate C to B was reduced in Rest 2 condition compared to Rest 1 (W = 42, p = .020, r = 0.87), delta transition from C to D increased (W = 5, p = .039, r = 0.78).

Global Explained Variance (GEV)

Analysis of GEV showed no significant difference across the microstates between Rest 1 and Rest 2 conditions suggesting that the overall stability and explanatory power of the microstate maps remained relatively stable between both the conditions.

Figure 1. *4-class Topography Maps of Rest 1 Condition (Percentage Representing Global Explained Variance of each Microstate).*

Figure 2. *4-class Topography Maps of Rest 2 Condition (Percentage Representing Global Explained Variance of each Microstate).*

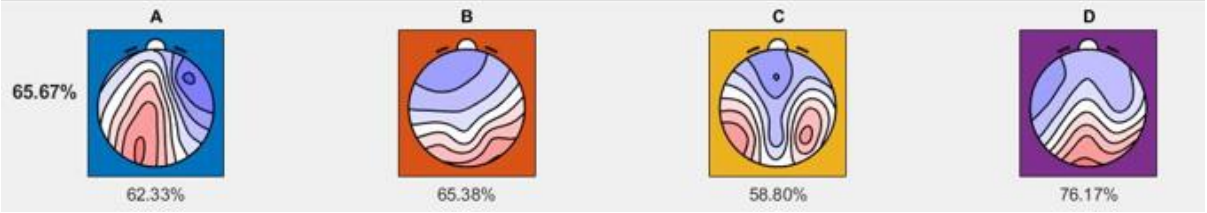


Figure 3. *Transition Matrix of Rest 1.*

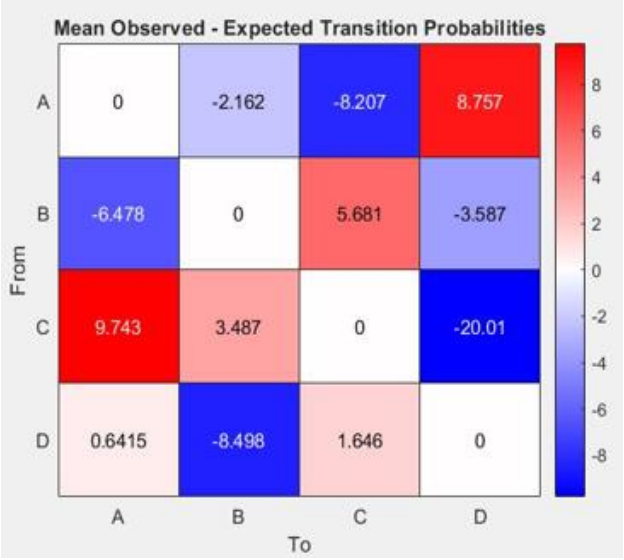
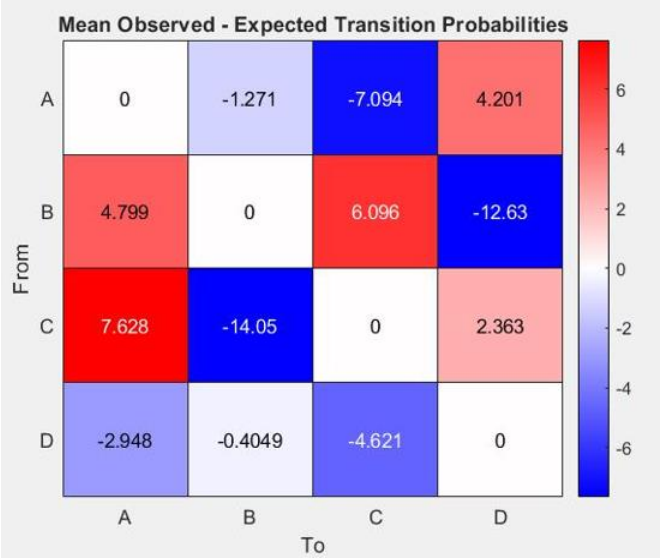


Figure 4. *Transition Matrix of Rest 2.*



Discussion

This study aimed to examine the effects of passive listening to Raga Kirwani, a traditional Carnatic raga, on resting-state brain dynamics by EEG Microstate Analysis. As far as we are aware, this is the first study that investigates the impact of this raga on microstate dynamics. The finding indicates three notable effects: (a) reduction in coverage of microstate B, (b) reduction in transition from microstate C to B, and (c) increased transition from microstate C to D.

Reduced Coverage and Return to Microstate B: Reduction in Visual-Spatial Processing

Microstate B has been generally associated with visual-spatial attention—activation in the parietal and occipital networks (Britz et al., 2010; Michel & Koenig, 2018). The observed reduction of its coverage following an exposure to Raga Kirwani indicates a transition from externally oriented visual processing. This corresponds to the subjective attributes of Kirwani, often described as meditative, introspective and emotionally soothing. This decrease in the visual microstate may correlate to diminished extrinsic awareness thereby promoting a more inward directedness of mental energy. This finding is in line with research indicating a similar reduced microstate B activity, in response to mindfulness meditation and other introspective techniques (Milz et al., 2016; Zanesco et al., 2021). Reduced return to microstate B from C further compliments the above finding, suggesting that following Kirwani's auditory input, the brain would be less inclined to revert back to visual sensory processing after self-reflection.

Increased Transition From C to D: Flexible Executive Switching

The increased transition from microstate C to D is especially noteworthy due to the fact that microstate C is often connected to the default mode network (DMN) and the self-referential processing, whereas microstate D indicates activation of the dorsal attention and salience network, associated with cognitive regulation and attentional reorientation (Michel & Koenig, 2018; Seitzman et al., 2017). This rise in C to D transition may signify improved flexibility and dynamic switching between the introspective (DMN) and executive control networks (Hao et al., 2025). Consequently, listening to Raga Kirwani may improve the adaptive connection between self-focused and goal-directed states, perhaps aiding control of emotions or cognitive rebalancing.

Cultural and Theoretical Implication

Raga Kirwani, traditionally linked to introspection, self-reflection, and emotional depth seems to influence both sensory and control-related neural states, even with just a 3-min passive listening session, indicating that Indian classical music may serve as a cognitive tool for mental alignment. This study adds to a growing body of work bridging Indian music with cognitive neuroscience, emphasizing the impact of culturally rooted, freely, and universally available music on brain activity.

Conclusion

Listening to Raga Kirwani produced significant and quantifiable alterations in EEG microstate activity during rest. There was a decline in visual-attentional microstate coverage, a reduction in transitions to visual states, and an improvement in the shift towards executive control modes. These findings indicate a transition from externally influenced processing to a more balanced and reflective brain condition, providing first evidence for the application of Indian classical music as a means of mental and emotional control.

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Authors' Declarations

The authors declare no conflict of interest related to this research. No funding was received for this study. All content of this manuscript is original and was developed by the authors. No generative AI tools were used to write the scientific content, analyses, or interpretations. AI-assisted tools (Research Rabbit and Perplexity) were used to support the literature search and review process only. Grammarly and QuillBot were used for language refinement and alignment with academic writing standards. The authors remain fully responsible for the accuracy, integrity, originality, and ethical compliance of the manuscript. The EEG data used in the study will be available from the corresponding author upon reasonable request, in accordance with ethical guidelines.

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The Effect of Different Techniques of Repetitive Transcranial Magnetic Stimulation on Parkinsonian Tremor

Doaa A. Mekkawy, Christine Ragaie, Hanan Amer, Hala ElHabashy, Hatem Shehata, and Mohammad Edrees Mohammad*

Faculty of Medicine, Cairo University, Cairo, Egypt

Abstract

Background. Tremor in Parkinson's disease (PD) is usually a disabling symptom that doesn't adequately respond to medications. Recently, the European clinical guidelines recommended repetitive transcranial magnetic stimulation (rTMS) as a Grade-B recommendation for improving motor function in PD. **Objectives.** To study the effect of different rTMS protocols on PD tremor. **Methods.** 60 PD patients were divided randomly into three groups equally according to rTMS protocols received; they were divided into Group I (5 Hz), Group II (1 Hz), and Group III (sham). Sessions were applied daily for 2 weeks. All patients were subjected to clinical assessment using different assessment tools; tremor Unified Parkinson's Disease Rating Scale (UPDRS) as well as total UPDRS, tremor amplitude and frequency by EMG before sessions, after last session, and 1 month later. **Results.** Group I showed the most significant reduction in mean UPDRS (tremor and total) after the last session and 1 month later ($p < .001$). Group I had the highest reduction in mean tremor amplitude and frequency by EMG after the last session and 1 month later ($p < .001$; $p < .05$, respectively). **Conclusion.** 5 Hz rTMS protocol was the most effective in improving PD tremor.

Keywords: Parkinson's disease; tremor; rTMS; UPDRS; EMG

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***Address correspondence to**: Christine Ragaie Fam, No 70 Street 108, El Maadi, Cairo, Egypt. Email: christinragaie@gmail.com

Edited by:
Rex L. Cannon, PhD, Currents, Knoxville, Tennessee, USA

Reviewed by:
Rex L. Cannon, PhD, Currents, Knoxville, Tennessee, USA
Mark S. Jones, DMin, University of Texas at San Antonio, San Antonio, Texas, USA

Introduction

Parkinson's disease (PD) is the second most common age-related neurodegenerative disorder after Alzheimer's disease. It is characterized clinically by resting tremor, rigidity, bradykinesia, and postural instability (Emamzadeh & Surguchov, 2018).

Tremor occurs in approximately 75% of PD patients. The pathophysiology of tremor has been linked to the combined actions of both the basal ganglia and the cerebello-thalamo-cortical circuit (Helmich, 2018). Tremor can be the predominant and most troublesome motor symptom, and poor response to dopaminergic agents is common (Abusrair et al., 2022).

It is well known from animal experiments that repetitive stimulation at the synaptic level can enhance or reduce synaptic transmission, a phenomenon known as long-term potentiation (LTP) or long-term depression (LTD). Transcranial magnetic stimulation (TMS) indirectly activates synapses so repeated pulses of TMS (i.e., rTMS) can theoretically activate the same set of synaptic connections multiple times and therefore replicate the situation seen in animal experiments (Di Lazzaro et al., 2018).

In 2020, the latest European clinical guidelines recommended rTMS over the primary motor cortex (M1) as a Grade-B recommendation for improving motor function in PD (Lefaucheur et al., 2020; Zhang et al., 2022).

High- and low-frequency rTMS have been shown to have different effects: enhance motor cortex excitability or briefly depress cortical excitability (Li et al., 2022).

In this study, we aimed to assess the effect of different rTMS techniques (5 Hz, 1 Hz, sham) on Parkinson's disease tremor.

Methods

A single-blind interventional controlled study was conducted on 60 patients with idiopathic PD, tremor dominant type which characterized by prominent tremor of one or more limbs with a relative lack of significant rigidity and bradykinesia. They were recruited from Kasr Al Ainy movement disorders clinic from October 2022 to November 2023. The diagnosis was made according to the UK PD Society Brain Bank Criteria (Hughes et al., 1992). Their ages ranged from 50 to 75 years. They were divided into three groups using simple random sampling method. This study was approved by the Research of Ethics Committee (REC) faculty of medicine Cairo University code: MD-357-2022. Written consent was obtained from all participants prior sharing in the study and was documented.

Group 1 (GI) received high-frequency (5 Hz) rTMS. Group 2 (GII) received low-frequency (1 Hz) rTMS. Group 3 (GIII) received sham rTMS, which is the control group. All groups received rTMS daily for 2 weeks using figure-of-eight coil applied to the primary motor area (M1). A repetitive transcranial magnetic stimulator (MagStim Rapid magnetic stimulator 2, Magstim company, White Land, Wales and UK), model S/N 2534, connected with a figure-of-eight coil with a diameter of 70 mm, was used in our sessions.

Group I (5 Hz)

Patients received rTMS to the primary motor area (M1; of 5 Hz frequency, 80% of resting motor threshold [RMT], 24 trains of 50 stimuli [train duration: 10 s separated by a 10-s pause]) delivered for a total of 1,200 pulses, daily for 2 weeks (six sessions; Lefaucheur et al., 2020).

Group II (1 Hz)

Patients received rTMS to the primary motor area (M1; of 1 Hz frequency, 80% of RMT for a total of 600 pulses, daily for 2 weeks (six sessions; Lefaucheur et al., 2020).

Group III (Sham)

Patients received sham rTMS stimulation to the primary motor area M1 daily for 2 weeks (six sessions; Lefaucheur et al., 2020).

Hot Spot Determination (Best Site)

Slightly changing the placement of the coil over the motor cortex (M1, which has been contralateral to the more affected upper limb). The position of figure-of-eight coil was adjusted at the beginning of each session to find the best scalp position (motor hot spot). M1 in general was 0–2 cm lateral to the vertex, tangentially to the subject's head surface, with the handle pointing posteriorly and positioned at 45° with respect to midsagittal axis to find the optimal scalp position to elicit motor responses in the contralateral thumb (motor hot spot; González-García et al., 2011).

Calculation of the Resting Motor Threshold (RMT)

RMT is defined as the lowest stimulus intensity that produced a minimal motor-evoked response and a visible abduction of the thumb contralateral to the stimulated hemisphere through contraction of the abductor pollicis brevis muscle (APB), about 50 μV in at least 5 of 10 trials at rest (González-García et al., 2011).

Sham Group

The control group got sham stimulation by turning the coil 90° from the scalp over the same area (M1) and the same intensity and protocol as real rTMS. This technique produced sound like active stimulation and some somatic sensations with negligible direct cortical sequalae (Benninger et al., 2012; Klirova et al., 2013).

Patients were kept on the same dopaminergic medications for a month prior to commencement rTMS sessions, during sessions, and for a month after the end of sessions. Exclusionary criteria were medications nonadherence, severe cognitive impairment (MMSE < 18), seizure disorders, presence of metallic head and/or neck implants, previous-skull surgeries and traumas, and recent forearm fracture (within 3 months).

All patients were subjected to history taking, medical and neurological examination, MMSE test (Folstein et al., 1975), PD assessment by Unified Parkinson's Disease Rating Scale (UPDRS; Goetz et al., 2008) and Modified Hoehn-Yahr staging (H&Y staging; Goetz et al., 2004).

Clinical assessment for tremor was done by tremor examination score of UPDRS Part III, from point 3.15a to 3.18 with total maximum score of 40. That included examination for postural tremor, kinetic tremor, resting tremor, presence of jaw or lip tremor, and constancy of tremor.

Further objective tool for tremor assessment was carried out using surface electromyography (EMG) to detect the amplitude and frequency of the tremor by Neuropack MEB9200 4-channels apparatus. The frequency and amplitude of a patient's tremor were recorded when the hand was in the sitting position at rest (put relaxed hand on thighs). The recording lasted for 30 s (Milanov, 2000).

Tremor frequency, or the number of oscillations per second, is measured in cycles per second (Hz). If the number of sampled points (N) is over a period in seconds (T), then the sampling rate is N/T (Hess et al., 2012). Tremor amplitude was measured peak to peak for each oscillation, and the mean value was considered (Hess et al., 2012). EMG measurements were done at three intervals: before sessions, after the last session, and 1 month from the last session (Rogasch et al., 2013).

All these measurements were done during off state (after overnight withdrawal of dopaminergic drugs) to avoid masking of tremor by medications effect (Dileone et al., 2017).

All patients were asked to report any side effects during sessions as seizures, dizziness, headache, etc.

Statistical Analysis

Data was coded and entered using the statistical package for the Social Sciences (SPSS) version 28 (IBM Corp., Armonk, NY, USA). Data was summarized using mean, standard deviation, median, minimum and maximum for quantitative variables, and frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Comparisons between groups were done using analysis of variance (ANOVA) with multiple comparisons post hoc test in normally distributed quantitative variables while nonparametric Kruskal-Wallis test and Mann-Whitney test were used for non-normally distributed quantitative variables (Chan, 2003a; Chan, 2003b; Chan, 2004).

Results

Clinical Characteristics of the Studied Groups

The general clinical characteristics of the three groups of the current cohort are shown in Table 1.

Mean Reduction in Different Clinical and Investigational Parameters Between Studied Groups

GI received rTMS with frequency of 5 Hz showed the best reduction in total and tremor UPDRS scores reflecting improvement in the disease generally.

Table 1
General Clinical Characteristics of the Studied Groups

Variables		**GI (5 Hz)** *n* = 20	**GII (1 Hz)** *n* = 20	**GIII (Sham)** *n* = 20
Age		59.80 ± 5.77	59.90 ± 6.34	63.10 ± 7.52
Gender	Male	14 (70%)	14 (70%)	16 (80%)
	Female	6 (30%)	6 (30%)	4 (20%)
Disease duration (years)		4.20 ± 3.44	5.90 ± 4.55	4.45 ± 5.53
Smoking		6 (30%)	6 (30%)	4 (20%)
Positive family history of Parkinson's disease		2 (10%)	4 (20%)	3 (15%)
Modified H&Y Scale before sessions		2.25 ± 0.6	1.98 ± 0.5	1.95 ± 0.79
Total UPDRS score before sessions		85.6 ± 31.51	59.35 ± 27.07	64.15 ± 37.32
Tremors UPDRS score before sessions		24 ± 6.95	22.75 ± 7.77	20.60 ± 8.40

They also showed the best reduction regarding tremor frequency and amplitude assessed by EMG.

GII submitted to rTMS with frequency of 1 Hz; it showed only improvement in tremor UPDRS scores after 1 month from last session with no effect on total UPDRS scores and tremor UPDRS after last session, as well as on tremor amplitude and frequency Tables 2, 3, and 4.

Table 2
Comparison of Mean Reduction in Different Clinical and Investigational Parameters Between Studied Groups

Variables	**Assessment after**	**GI (5 Hz)** Mean reduction ± *SD*	**GII (1 Hz)** Mean reduction ± *SD*	**GIII (sham)** Mean reduction ± *SD*	***p-value***
Total UPDRS scores	**Last rTMS session**	34.90 ± 15.99	10.55 ± 8.85	9.80 ± 7.24	**< .001**
	1 month later	27.80 ± 18.73	5.60 ± 4.98	1.65 ± 9.13	**< .001**
Tremors UPDRS	**Last rTMS session**	9.25 ± 3.77	5.35 ± 2.37	3.90 ± 2.14	**< .001**
	1 month later	6.20 ± 3.50	4.40 ± 1.07	−0.50 ± 2.20	**< .001**
Tremors amplitude by EMG (µv)	**Last rTMS session**	188.75 ± 179.96	24.45 ± 26.23	20.45 ± 25.63	**> .001**
	1 month later	169.55 ± 159.39	18.20 ± 34.48	−12.75 ± 74.93	**> .001**
***Tremors frequency by EMG* (/sec)**	**Last rTMS session**	1.25 ± 2.38	0.30 ± 0.57	0.05 ± 1.88	**.036**
	1 month later	0.65 ± 2.32	0.05 ± 0.60	−0.55 ± 2.42	**.028**

*p-value < .05 is considered significant. ** p-value < .01 is considered highly significant. *** p-value < .001 is considered very highly significant.

Table 3
Post Hoc Pairwise Comparison of Reduction in Different Clinical and Investigational Parameters Between Studied Groups

Variables	**Assessment after**	**GI (5 Hz) vs. GII (1 Hz)** *p*-value	**GI (5 Hz) vs. GIII (sham)** *p*-value	**GII (1 Hz) vs. GIII (sham)** *p*-value
Total UPDRS scores	**Last rTMS session**	**< .001**	**< .001**	.720
	1 month later	**< .001**	**< .001**	.544
Tremors UPDRS	**Last rTMS session**	**< .001**	**< .001**	.602
	1 month later	**< .001**	**< .001**	**.003**
Tremors amplitude by EMG (µv)	**Last rTMS session**	**< .001**	**< .001**	1.000
	1 month later	**.002**	**< .001**	.790
***Tremors frequency by EMG* (/sec)**	**Last rTMS session**	**.036**	**.035**	1.000
	1 month later	.870	**.028**	.373

*p-value < .05 is considered significant. ** p-value < .01 is considered highly significant. *** p-value < .001 is considered very highly significant.

Table 4
Comparison of Side Effects of rTMS Between the Groups

Variables		Group I (5 Hz)		Group II (1 Hz)		Group III (sham)		*p*-value
		Count	%	Count	%	Count	%	
Side effects of rTMS	**None**	16	80.0%	15	75.0%	18	90.0%	
	Headache	3	15.0%	3	15.0%	1	5.0%	
	Dizziness	1	5.0%	1	5.0%	0	0.0%	.722
	Numbness	0	0.0%	1	5.0%	0	0.0%	
	Neck pain	0	0.0%	0	0.0%	1	5.0%	

*p-value < .05 is considered significant. ** p-value < .01 is considered highly significant. *** p-value < .001 is considered very highly significant. ****Transient insignificant side effects mainly in the form of headache and dizziness (not leading to drop out) were reported among those receiving rTMS regarding the frequency (5 Hz, 1 Hz).

Discussion

PD is associated with tremor in 75% of cases that are disabling and resistant to therapy (Abusrair et al., 2022). To our knowledge, few studies investigated the role of rTMS in the management of PD tremor here in Egypt.

This study showed marvelous improvement in PD patients on rTMS as an add-on therapy regarding all Parkinsonian symptoms, especially motor ones. However, this improvement is transient, lasting for 1 month after the last session, meaning that these sessions need to be repeated. This improvement was noted across different evaluation metrics.

On total UPDRS score, only a significant reduction was seen after last session and 1 month later in Group I, meaning that both Group II and III have a placebo effect, which agrees with many studies done, like that of Goetz et al. (2000) and Okabe et al. (2003).

Regarding tremor score of UPDRS, which is a more specific scale for assessment of PD tremor, the effect of rTMS in Group II appeared 1 month after the last session, which was less in comparison to Group I that appeared significantly from last session as well as later. In this study, we proved that low-frequency rTMS has an effect superior to sham, which disagrees with previous studies, like that of Goetz et al. (2000) and Okabe et al. (2003) who showed that both have similar placebo effect.

The meta-analytic study done by Kim et al. (2019) showed that both high- and low-frequency rTMS on M1 have the potential to enhance PD patient's motor function, albeit with high frequency rTMS being more efficacious in mitigating motor symptoms and demonstrating a longer-term positive impact through long-term potentiation (LTP), often induced by high-frequency repetitive stimulations.

Several studies (Lefaucheur et al., 2020; Yang et al., 2018) have shown that the main causes of motor symptoms in Parkinson's disease are reduced neural reserve and automaticity due to malfunctioning basal ganglia. By directly enhancing cortical excitability, high-frequency rTMS augments the activity of the striatum and modulates inhibitory impulses within the globus pallidus interna. These mechanisms rectify basal ganglia dysfunction through the cortico-basal ganglia-thalamo-cortical circuit, resulting in improved motor function.

Another hypothetical explanation could be that high-frequency rTMS might directly activate dopaminergic neurons in the striatum, supplying endogenous dopamine as proven by a prior study conducted by Khedr et al. (2006, 2019) who reported that serum dopamine levels were significantly elevated after six daily sessions of high-frequency rTMS. Also, Strafella et al. (2003) found that high-frequency rTMS on motor cortex (M1) increases endogenous dopamine release in the ipsilateral dorsal striatum by using positron emission tomography (PET).

Regarding the same issue, in a large meta-analysis by Li et al. (2022) rTMS has been proven to be an effective treatment for motor symptoms of PD, and multisession high-frequency stimulation on bilateral M1 could be an optimal stimulation protocol. They found that high-frequency rTMS on M1 and supplementary motor cortex (SMA) has beneficial effects on limb function, tremor, and akinesia symptoms in PD patients, and low-frequency rTMS on SMA could relieve levodopa-induced dyskinesias symptoms (LID) by its inhibitory effect.

Moreover, in this study the significant reduction of total UPDRS in Group I over Group II and sham group, denoted that high-frequency protocol also could improve nonmotor symptoms of PD, even over M1 stimulation.

This finding is in agreement with Makkos et al. (2016), who found that the active treated group had significant improvement in nonmotor symptoms and health-related quality of life.

These results were explained by Lefaucheur (2019), as the repeated magnetic pulses can not only alter excitability at the site of stimulation but also influence brain regions anatomically connected to the stimulation site, which provide profound influence on the characteristics of brain circuitry. Indeed, recent meta-analysis studies recommended high-frequency rTMS over dorsolateral prefrontal cortex (DLPFC) as the best protocol for improving nonmotor PD symptoms (Lefaucheur et al., 2020; Zhang et al., 2022).

About the effects of rTMS on PD tremor that weren't sufficiently studied yet, the current study showed significant reduction in resting tremor amplitude and frequency with high frequency after last rTMS session and 1 month later.

The following results agree with Spagnolo et al. (2021) who evaluated the safety and efficacy of high-frequency rTMS with H-coil in PD management. They found that tremor scores revealed a mean decrease in the high-frequency group, while approximately no effect was detected in the sham group at the end of treatment measurement.

A study conducted by Siebner et al. (2000) found a slight decrease in tremor amplitude after a single session of 5 Hz rTMS over M1 in comparison to sham group in which assessment was done after 1 hr from rTMS session.

Indeed, a recent study by Qi et al. (2023) studied the effect of 1 Hz rTMS in comparison to sham and revealed no statistically significant difference in tremor frequency and amplitude by EMG after sessions among patients who received low-frequency rTMS and sham patients.

Conversely, a meta-analysis conducted by Zhu et al. (2015) determined that low-frequency rTMS demonstrated greater efficacy compared to sham stimulation for motor symptoms in PD tremor. Furthermore, they suggested that both high-frequency and low-frequency rTMS had beneficial effects on motor functions in PD patients. Additionally, they found that low-frequency rTMS exhibited higher safety in clinical practice compared to high-frequency rTMS.

The study assessed the adverse effects among three groups and found no significant differences. The transient and clinically insignificant side effects did not lead to dropouts. Headache was the most common side effect across all groups.

These findings agree with Kaur et al. (2019) and Vabalaite et al. (2021) who found that headache is the most common adverse effect of rTMS; however, they found it more in patients who received higher frequency rTMS. Lerner et al. (2019) explained headache from rTMS as it could be the direct stimulation of superficial nerves and muscles which depend on coil position or the increased cerebral blood flow as a response to stimulation, or both.

Conclusion

In view of the outcome of the current study, it could be concluded that 5 Hz rTMS protocol over M1 was more effective than 1 Hz rTMS protocol and sham rTMS, regarding the improvement in tremors UPDRS as well as total UPDRS scores and also improvement resting tremors frequency and amplitude in Parkinson's disease.

Limitation and Implication for Future Research

The current study highlighted the vital role of high-frequency rTMS as an add-on therapy in the management of all PD symptoms (motor, nonmotor) including tremor. This interventional study was conducted on an adequate number of patients which give reliability to the obtained results. However, more multicenter studies are needed and further studies with more prolonged time investigating nonmotor symptoms in detail after using rTMS to improve quality of life of PD patients.

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Author Disclosures

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involved in ethical publication and affirm that this work is consistent with those guidelines.

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Diagnostic Yield of Brain Imaging in Headache Patients With Intact Neurological Examination

*Omar A. Mahmood and Ali S. Yahya Al-Shakerji**

University of Mosul/College of Medicine, Mosul, Nineveh, Iraq

Abstract

Background. Many patients presenting with headache complaints are often concerned about the possibility of serious underlying conditions and request brain imaging to rule out ominous pathology. However, brain imaging is costly and carries potential risks for both patients and the healthcare system. **Objective.** This study aims to evaluate the diagnostic value of brain imaging for patients with headaches and intact neurological examination and to identify additional risk factors associated with abnormal imaging results. **Methods.** A retrospective cohort analysis was conducted on 185 patients with primary complaints of headache and normal neurological examinations, assessed at a general neurology clinic over a 4-year period. **Results.** Pathological findings on imaging studies were observed in 9.7% of cases, while 16.2% showed findings of uncertain significance. Patients with pathological or uncertain significance (US) findings are significantly older compared to those with normal results (p = .002 and p < .001, respectively). Male sex is associated with a higher likelihood of US findings (p = .03). Nonthrobbing headaches and the presence of red flags in patient history are linked to pathological findings (p = .001 and p = .002, respectively). The presumption of a secondary headache syndrome before ordering imaging is strongly associated with abnormal imaging results (p < .001 for pathological findings and p < .024 for US findings). **Conclusion.** The decision to perform brain imaging in patients with normal neurological examinations should be individualized based on patient demographics and the presence of nonthrobbing headaches or red flags in the clinical history. A lower threshold for imaging is recommended when secondary headache is suspected.

Keywords: brain imaging; pathological findings; uncertain significance; red flags; incidental findings

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***Address correspondence to**: Ali S. Yahya Al-Shakerji, College of Medicine, University of Mosul, Al Majmoaa Street, Mosul 41002, Iraq. Email: ali.sameer@uomosul.edu.iq

Edited by:
Rex L. Cannon, PhD, Currents, Knoxville, Tennessee, USA

Reviewed by:
Rex L. Cannon, PhD, Currents, Knoxville, Tennessee, USA
Tanju Surmeli, MD, Living Health Center for Research and Education, Sisli, Istanbul, Turkey

Introduction

Headache is a prevalent neurological disorder affecting people of all ages, with a higher incidence in women (Ahmed, 2012). It is one of the most common medical complaints that makes people seek medical advice. It has a lifetime prevalence of 99% and is one of the most common human afflictions (Silberstein & Lipton, 1996). Primary headaches, including migraine, tension-type, and cluster headaches, account for approximately 98% of cases. In contrast, secondary headaches require urgent attention due to potential life-threatening causes like tumors, infections, vessel abnormalities, or changes in brain pressure (Ahmed, 2012; Kelly et al., 2018).

The third edition of International Headache Criteria (IHCD-3) guides the classification of headache types (Langdon & DiSabella, 2017). Many headache syndromes are diagnosed according to clinical criteria rather than brain imaging findings or other investigations. Brain imaging is sometimes needed to exclude ominous diagnoses or support other differential diagnoses. Current guidelines discourage routine diagnostic tests in the absence of red flags, and the patient has no focal neurological deficit (Kelly et al., 2018). Brain tumors, though uncommon, can cause headaches and warrant investigation if red flags are present (Kirby & Purdy, 2014). Proper diagnosis and management of headaches are crucial for improving patients' quality of life and reducing healthcare costs (Ahmed, 2012).

Brain magnetic resonance imaging (MRI) in headache patients has limited diagnostic value, with significant findings detected in only 4.9%–8.86% of cases (Jang et al., 2019; Yüksel et al., 2022). However, certain factors increase the likelihood of significant findings, including age over 65, acute onset of headache, and the presence of red flag in clinical history (Kaur et al., 2019; Yüksel et al., 2022). Common incidental findings include white matter abnormalities, arachnoid cysts, and enlarged perivascular spaces (Gurkas et al., 2017; Toker et al., 2023). Neuroimaging in such conditions is frequently requested for medicolegal documentation or reassurance, rather than based on clinical necessity, as its yield in patients with normal neurological examinations is equivalent to that of the general asymptomatic population (Mullally & Hall, 2018). Nevertheless, MRI remains a valuable tool for ruling out secondary causes of headaches (Jang et al., 2019). Given its limited diagnostic utility in the absence of concerning features, neuroimaging should be reserved for headache patients who present with red flags (Jang et al., 2019; Kaur et al., 2019). The MRI is the modality of choice for the brain tissue as it gives more detailed information, and there is no risk of radiation exposure (Kamtchum-Tatuene et al., 2020).

On the other hand, neuroimaging in headache patients may detect nonsignificant findings. Those findings may be incidental and unrelated to headache complaints or normal variants that can present in many normal people, leading to more consultations and more investigations to prove their nonrelevance or nonsignificance (Graf et al., 2010; Moodley & I Bhigjee, 2022). The detection of these incidental findings can increase stress and obsession about having a threatening disease and raise another dilemma about proving their significance or nonsignificance. For this reason, sometimes doing imaging studies in such conditions can do more harm than benefit, increasing healthcare costs and extending the waiting queues. The current guidelines recommend against routine neuroimaging in patients with normal neurological examinations; individual assessment is crucial (Kamtchum-Tatuene et al., 2020; Young et al., 2018).

This study aims to detect the frequency of abnormal neuroimaging in headache patients with normal neurological examination and to identify risk factors for abnormal findings using subgroup analysis.

Materials and Methods

Methods

This study is a retrospective cohort analysis conducted at a general neurology clinic in Mosul, Nineveh, Iraq. It included patients who presented with headache as their primary complaint and had a normal neurological examination. The data were extracted from electronic medical records spanning from October 2019 to January 2025.

Inclusion Criteria

Patients aged 4 years and older were eligible for inclusion if they presented with a chief complaint of headache, had no focal neurological deficits on examination, and underwent neuroimaging (MRI or computed tomography [CT]) following clinical evaluation.

Exclusion Criteria

Patients were excluded if they met any of the following conditions:

a) Headache was a secondary or accompanying symptom rather than the primary complaint.
b) Presence of a focal neurological sign or meningeal irritation on examination.
c) Neuroimaging was not performed.
d) Medical record was incomplete or lacked essential diagnostic or demographic data.

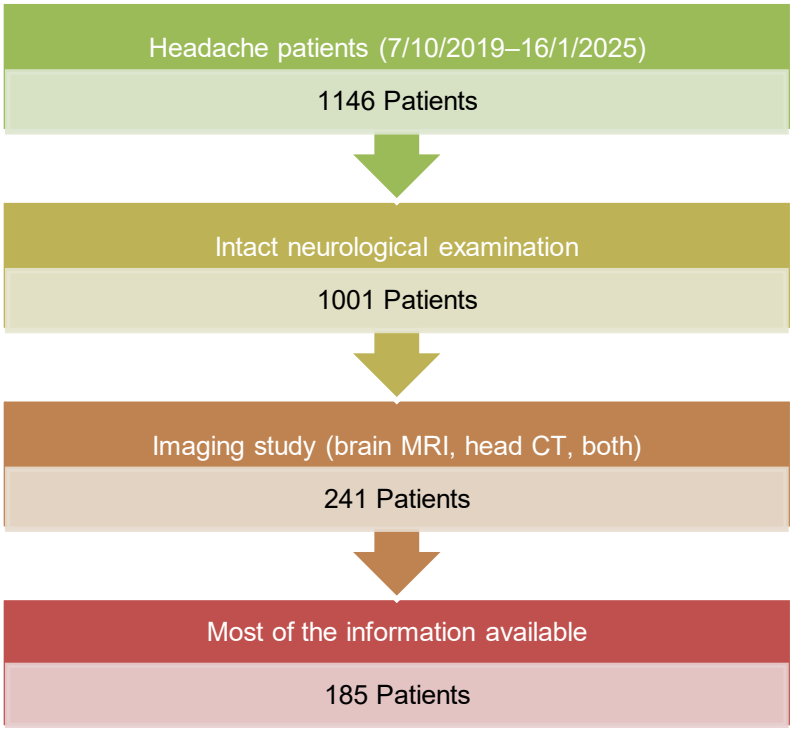
See Figure 1 for a detailed flowchart of patient selection.

The primary objective of the study was to evaluate the diagnostic yield of neuroimaging in patients presenting with headache and a normal neurological examination. The secondary objective was to identify clinical and demographic risk factors associated with abnormal imaging findings through subgroup analysis.

Ethical Approval

All participants involved in this study provided informed consent prior to their participation. The study was approved by the Mosul medical college ethics committee (Ref. No. UOM/COM/MREC/23-24/JUL9) and participants were fully informed about the purpose, procedures, and potential risks associated with their involvement.

Figure 1. *Flow Chart of Patients Gathering.*



Data Collection

Patient records were retrieved using Microsoft Access 2010, the digital medical record system utilized in the neurology clinic. Data were filtered using predefined criteria on the main interface to identify eligible cases. A total of 185 patients met the inclusion criteria and were enrolled in the study.

The collected data included patient demographics (age, sex), duration of headache (categorized into three groups: acute [days], subacute [months], and chronic [years]; Gonzalez-Martinez et al., 2024), history of present illness, presence of red flag symptoms, and relevant past medical, surgical, drug, social, and family histories. All patients underwent general and neurological examinations, the findings of which were documented.

Details of investigations, including neuroimaging studies (MRI or CT of the brain), and final clinical diagnoses were entered into Microsoft Excel 2010 for analysis.

Neuroimaging findings were classified into three categories:

a) ***Normal.*** No significant abnormalities reported by the radiologist or observed by the neurologist upon review.

b) ***Pathological.*** Findings deemed relevant to the patient's headache and requiring specific medical or surgical intervention.

c) ***Findings of US.*** Imaging abnormalities that may or may not be related to the headache and do not necessitate immediate or specific treatment (white spots of brain [Longstreth et al., 1996], arachnoid cyst [Al-Holou et al., 2013] and brain atrophy [Sargent & Lawson, 1980]).

Data Analysis

Data were analyzed using IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY, USA). Categorical variables were assessed using Chi-square tests applied to 2×2 and 3×3 contingency tables. A *p*-value of <.05 was considered statistically significant for 2×2 comparisons, while a Bonferroni-corrected *p*-value threshold of <.0056 was applied for 3×3 comparisons to account for multiple testing.

For continuous variables, one-way analysis of variance (ANOVA) was used to compare means among groups, following verification of normal distribution using the Kolmogorov–Smirnov and Shapiro–Wilk tests. Post hoc analysis was conducted using the Tukey Honest Significant Difference (HSD) test when appropriate.

The manuscript was prepared in accordance with the CONSORT (Consolidated Standards of Reporting Trials) guidelines (Moher et al., 2010).

Results

A total of 185 consecutive patients presenting with headache as their primary complaint and exhibiting normal neurological examinations were evaluated and included in the study (Figure 1). Among the cohort, 34.1% were male.

The duration of headache symptoms was categorized chronologically (Table 1):

- Acute (days): 38.9%
- Subacute (months): 20.0%
- Chronic (years): 41.1%

Red flag features in the clinical history (Table 2) were identified in 37.7% of patients. Additionally, 27% of patients exhibited instability in vital signs during examination (e.g., abnormal blood pressure, fever, or abnormal pulse), while 5% had abnormal general physical examination findings (e.g., anemia, jaundice, etc.).

Neuroimaging was ordered based on the presence of red flags or per patient request to alleviate anxiety. MRI was the preferred imaging modality, performed in 71.4% of cases, compared to 30.8% who underwent head CT. Some patients underwent both.

Patients with pathological imaging findings and those with findings of uncertain significance were significantly older than patients with normal imaging results (p = .002 and p < .001, respectively; Table 4).

A nonthrobbing headache quality and the presence of red flags in the history were both strongly associated with pathological imaging findings (p = .001 and p = .002, respectively).

Presumptive diagnosis of a secondary headache syndrome was significantly associated with both pathological findings and findings of US (p < .001 and p = .024, respectively). Additionally, male sex was significantly associated with the presence of findings of US (p = .03).

No statistically significant associations were found between imaging findings and either vital sign instability or abnormal general examination findings (p > .05 in all cases; Table 5).

Table 1
Frequency of Categorical Data

Variable	Frequency	Percentage
Sex (Male)	63	34.1%
Duration		
Days	72	38.9%
Months	37	20.0%
Years	76	41.1%
Red flags (Yes)	69	37.3%
Stability (No)	49	26.5%
General examination (abnormal)	10	5.4%
Type of imaging		
MRI	128	69.2%
CT	53	28.6%
Both	4	2.2%
Diagnosis (presumed secondary)	27	14.6%
Imaging finding		
Normal	137	74.1%
Findings of uncertain significance	30	16.2%
Pathological	18	9.7%

Table 2
Red Flags in History

1. Childhood-onset	15. Dysphasia
2. Old age >65 years	16. Numb chin
3. Acute in onset	17. Fever
4. Postcoital	18. Weight loss
5. Thunderclap in character	19. Flu-like illness
6. Cluster in character	20. Post-COVID-19
7. Loss of consciousness	21. No response to treatment
8. Forgetfulness	22. Changing character
9. Facial numbness	23. History of familial dyslipidemia
10. Facial weakness	24. History of benign intracranial hypertension
11. Facial pain	25. History of breast cancer
12. Deafness or tinnitus	26. History of chronic kidney disease
13. Sided numbness	27. History of recent trauma to head
14. Sided weakness	28. History of hypertensive crisis

Table 3
Pathological Findings and Findings of Uncertain Significance (US) in Headache Cohort

Pathological findings	No.	Findings of US	No.
1. Ischemic infarctions	8	1. White spots of the brain	25
2. Intracerebral hemorrhage	2	2. Brain atrophy	3
3. Cerebellopontine angle ependymoma	1	3. Arachnoid cyst	2
4. Maxillary sinusitis, pan sinusitis	2		
5. Parasagittal lesion (AVM or tumor)	2		
6. Internal carotid artery aneurysm	1		
7. CSF leakage from anterior cranial fossa to Right nasal sinus	1		
8. Linear skull fracture	1		

Table 4
Association Between Age and Imaging Findings Using One-Way ANOVA Test

	(I) Findings	Mean Age (Year)	*SD*	(J) Findings	Sig.(I–J)
Tukey* HSD	Normal	37.5	15.8	Findings of US	**< .001**
				Pathological	**.002**
	Findings of US	58.7	16.3	Normal	**< .000**
				Pathological	.239
	Pathological	51.1	14.2	Normal	**.002**
				Findings of US	.239

* = Tukey HSD test is used for post hoc multiple comparisons after assuring normal distribution of data (Kolmogorov–Smirnov and Shapiro–Wilk).

Table 5
Relation Between Clinicodemographic Features and Imaging Findings Using Chi-Square Tests 2x2 Table

Clinical & demographic features		Imaging findings		
		Normal	**Pathological**	**Findings of US**
Sex	Male	40	8	15
	Female	97	10	15
	OR	Ref.	1.9	2.4
	95%CI		0.71–5.3	1.08–5.4
	p-value		.19	**.03**
Headache characteristics	Throbbing	85	4	15
	Nonthrobbing	52	14	15
	OR	Ref.	5.8	1.6
	95%CI		1.8–18.7	0.7–3.6
	p-value		**.001**	.22
Red flags	No	90	5	21
	Yes	47	13	9
	OR	Ref.	4.9	0.82
	95% CI		1.7–14.8	0.39–1.9
	p-value		**.002**	.65
General examination	Normal	131	17	26
	Abnormal	5	1	4
	OR	Ref.	1.5	4
	95% CI		0.17–13.9	1–16
	p-value		.53*	.06*
Vital signs	Stable	92	12	19
	Unstable	33	6	10
	OR	Ref.	1.3	1.47
	95%CI		0.48–4.01	0.62–3.5
	p-value		.57*	.38
Preliminary diagnosis	Presumed 1º	122	9	22
	Presumed 2º	15	9	18
	OR		8.1	2.9
	95%CI		2.8–23.67	1.12–7.81
	p-value		**<.001***	**.037***

OR = odd ratio, CI = confidence interval, Ref. = Reference, 1º = primary headache, 2º = secondary headache, * = Fisher-exact test is used.

When evaluating the relationship between imaging findings and either the duration of illness (acute, subacute, chronic) or type of imaging modality (MRI, CT, or both) using 3×3 contingency tables, no statistically significant associations were detected after Bonferroni correction (Table 6).

Table 6

Relation Between Durations of Illnesses and Imaging Modalities From One Perspective and Imaging Findings From Another Perspective Using 3x3 Contingency Table Chi-Square Test

		Imaging findings		
		Normal (*p*-value)*	**Pathological (*p*-value)**	**Finding of US (*p*-value)**
Durations	**Days**	45 (.08)	12 (.18)	15 (.74)
	Months	31 (.69)	3 (.1)	3 (.69)
	Years	61 (.63)	3 (.3)	12 (1)
Imaging modality	**Brain** MRI**	89 (.35)	11 (.96)	28 (.04)
	Head CT	45 (.35)	6 (.99)	2 (.08)
	Both	3 (1)	1 (.91)	0 (.94)

* All *p*-values are not significant (significant *p* value after Bonferroni correction ≤ .0056). ** MRI = magnetic resonance imaging, CT = computed tomography.

Discussion

In Iraq, the diagnostic yield of neuroimaging in patients presenting with headache and a normal neurological examination has not been clearly established. In the present study, pathological findings were identified in 9.7% of patients, while findings of US were observed in 16.2%. These results are consistent with previous studies by Kamtchun-Tatuene et al. (2020) and Moodley & I Bhigjee (2022), which reported similar frequencies of abnormal imaging findings in comparable patient populations.

Clinically significant findings—defined as abnormalities that could potentially alter treatment decisions—were identified in approximately 10% of patients in our cohort. This proportion aligns with findings reported by Jang et al. (8.86%; 2019) and Kamtchun-Tatuene et al. (17.5%; 2020). However, these results contrast with those of Sempere et al. (2005), who reported a markedly lower prevalence of significant intracranial abnormalities (0.9%) in a cohort of patients with nonacute headaches. The observed discrepancies may be attributed to differences in study design, inclusion criteria, and the potential for missed cases in cohorts with less stringent data collection methods.

The white spots of the brain are more prevalent in migraineurs, tension-type headache, and middle-age patients, but their relation to headache is not clearly understood (Honningsvåg et al., 2018; Schramm et al., 2024). On the other hand, arachnoid cysts are often asymptomatic but larger cysts may cause headache, seizure or focal neurological deficit (Cherian et al., 2014). Brain atrophy has been also linked to headache, especially in migraineurs, by unknown mechanism (Devianne et al., 2022). We have assumed “finding of uncertain significance (US)” for these constellations that have been previously reported as “incidental findings” or “findings that do not change treatment plans” (Moodley & I Bhigjee, 2022).

Patients with pathological findings (51.1 years ± 14.2) and findings of US (58.7 years ± 16.3) are considerably older than those with normal findings (37.5 years ± 15.8). Kim et al. (2020) recognized that age ≥50 years at headache onset was related to incidental findings, while age ≥40 years was linked to pathological results. Similarly, Lemmens et al. (2021) emphasized that headache onset after age 50 should be considered a clinical warning sign.

A noteworthy finding in this cohort is the significant association between male sex and the presence of findings of uncertain significance. Khalid and Salih (2024) also demonstrated a higher rate of abnormal MRI findings among male patients compared to females. These studies emphasize the importance of sociodemographic factors in selecting headache patients for imaging techniques.

The relationship between headache duration and imaging abnormalities is complex. While some studies indicate that abnormal imaging findings increase with age and are more common in males, they appear largely independent of symptom duration (Sun & Cao, 2011). In pediatric populations, however, headache duration of less than 6 months has been linked to abnormal imaging (Medina et al., 1997), while other studies found that chronic headaches are more likely to yield abnormal findings (Rai, 2016). In our study, no significant association

was found between symptom duration and imaging abnormalities.

The throbbing quality of headache, often characteristic of migraine (Hernandez et al., 2024), was inversely associated with pathological imaging findings in this cohort. Specifically, nonthrobbing headaches were significantly more frequent among patients with pathological imaging but not among those with US findings. These findings underscore the need for further investigation into the pathophysiological relevance of headache quality in differentiating primary from secondary headache syndromes.

The utility of red flag symptoms in selecting patients for imaging remains controversial. While some authors argue that three or more red flags are necessary to predict abnormal imaging (Manoyana et al., 2022; Sobri et al., 2003), others report low diagnostic yield even in their presence (Tsze et al., 2019; Young et al., 2018). In our cohort, red flags were significantly associated with abnormal imaging findings, supporting their value in clinical decision-making.

Notably, abnormalities in general physical examination (e.g., pallor, jaundice, cyanosis) and vital sign instability (e.g., hypertension, fever, irregular pulse) were not predictive of abnormal imaging outcomes. Although hypertensive encephalopathy has been linked to cytotoxic edema on imaging, this is likely due to loss of cerebral autoregulation rather than ischemia (Schwartz et al., 1992). To our knowledge, this aspect remains underreported in the literature and merits further investigation.

Comparative studies on imaging modalities in headache patients show mixed results. CT is superior for detecting bony lesions, skull base pathology, and acute hemorrhages, whereas MRI provides better resolution for parenchymal abnormalities (Agarwal & Kanekar, 2022; Lemmens et al., 2021; McCullagh et al., 2022). In our study, no statistically significant advantage was observed for either MRI or CT—or their combination—in detecting clinically relevant abnormalities in an outpatient setting. Therefore, imaging choice should be guided by specific clinical features, suspected pathology, and urgency of assessment.

The strength of this study lies in the use of a digital medical database to minimize interpretive bias and the application of robust inclusion and exclusion criteria. Subgroup analysis provided valuable insights into underexplored aspects of headache imaging. However, several limitations must be acknowledged. The single-center design may limit generalizability, and referral bias may have led to an overestimation of abnormal findings, as many excluded patients with presumed benign headaches did not undergo imaging. Additionally, the retrospective nature of the study limits control over confounding variables and introduces record bias.

To the best of our knowledge, this is the first Iraqi cohort study to evaluate the frequency and nature of abnormal imaging findings in headache patients with normal neurological examinations, and to identify associated demographic and clinical predictors.

Conclusion

The decision to perform neuroimaging in headache patients with a normal neurological examination should be individualized, taking into account demographic characteristics, headache features, and clinical history. As an alternative or complement, neuroregulation and neuromodulation techniques, including neurofeedback and noninvasive stimulation, may offer more targeted and cost-effective strategies for managing this population. The presence of red flag symptoms, older age, and nonthrobbing headache quality were all associated with a higher likelihood of abnormal imaging. Male sex was linked to findings of uncertain significance. Importantly, physical exam abnormalities and vital sign instability were not predictive of imaging abnormalities.

Careful application of clinical guidelines and judicious use of imaging may reduce unnecessary investigations, lower healthcare costs, and shorten waiting times. Further prospective, multicenter studies with longer follow-up periods are warranted to better understand the clinical significance of incidental imaging findings and to refine the predictive value of specific headache features.

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Mapping Protocols and Evidence on Combined EEG Neurofeedback and Meditation: A Systematic Review

Juan P. Aristizabal[1,2], Vivian de Moura Dayrell[1], Alexandre Correia Pedra[2], Letícia Silva Madonado Cunha[1], Olivia Morgan Lapenta[3], and Wânia Cristina de Souza[2]*

[1]Federal University of Pará, Basic Psychological Processes Department, Belém, Pará, Brazil
[2]University of Brasília, Basic Psychological Processes Department, Brasília, Brazil
[3]University of Minho, Psychological Neuroscience Lab, School of Psychology, Braga, Portugal

Abstract

Background. The combination of meditation and EEG neurofeedback has gained attention as a nonpharmacological approach for emotion regulation, stress reduction, and cognitive enhancement. **Methods.** This systematic review, registered in PROSPERO (CRD42024554716) and conducted in accordance with PRISMA guidelines, aimed to map methodologies, protocols, and evidence on these combined interventions. Experimental or quasi-experimental empirical studies involving human participants across ages and contexts, published between 2015 and 2025, were included. Searches across six databases yielded 356 records; 45 met eligibility criteria. **Results.** Studies showed substantial methodological heterogeneity, with a predominance of randomized clinical trials (44%) and within-subject designs (33%). Focused attention and mindfulness meditations and auditory feedback prevailed; wearable devices were used in 35 studies. Intervention dose varied widely, from 1 to 50+ sessions, ranging from 1.5 to 80 min long. Primary outcomes consistently showed reductions in stress, anxiety, depression, and fatigue, alongside gains in well-being, attention, and resilience. Neurophysiological findings included increases in alpha and theta power. **Conclusions.** Combining meditation with EEG neurofeedback is a promising strategy, but the lack of protocol standardization, small sample sizes, and limited blinding reduce evidence robustness. Future research with rigorous methodology is needed to establish clinical efficacy and guide interventions.

Keywords: neurofeedback; meditation; mindfulness; electroencephalography; brain-computer interface

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***Address correspondence to**: Juan Aristizabal, PhD student, Behavioral Sciences, Psychology Institute. University of Brasília. Av. Parque Aguas Claras, Lote 25, Brasília, Brazil. Email: juparistizabalga@gmail.com

Edited by:
Rex L. Cannon, PhD, Currents, Knoxville, Tennessee, USA

Reviewed by:
Rex L. Cannon, PhD, Currents, Knoxville, Tennessee, USA
Tanya Morosoli, MSc: 1) Clínica de Neuropsicología Diagnóstica y Terapéutica, Mexico City, Mexico; 2) PPCR, ECPE, Harvard T. H. Chan School of Public Health, Boston, Massachusetts, USA

Background

Meditation encompasses a broad set of practices aimed at enhancing physiological, behavioral, and cognitive self-regulation by inducing specific attentional states (Davidson & Goleman, 1977; Shapiro & Giber, 1978). Rooted in Buddhist and yogic traditions, it has been reframed by contemporary science as a technique capable of producing psychosomatic effects and promoting psychological well-being (Brandmeyer & Delorme, 2018; Fincham et al., 2023). Empirical studies associate meditation with reductions in stress- and anxiety-related symptoms (Brandmeyer & Delorme, 2018; Shapiro & Giber, 1978) and with improved cognitive functioning (Basso et al., 2019; Lodha & Gupta, 2022). Although modalities vary, such as concentrative practice and mindfulness, they share two core components: deliberate attention orienting and cognitive-emotional self-regulation (Goleman, 1988).

Meditation is increasingly recognized for its potential to induce measurable neurophysiological changes. Regular practice can alter the autonomic nervous system, increasing heart rate variability (HRV; Y.-H.

Lee et al., 2022), lowering cortisol (Aguilar-Raab et al., 2021), and regulating skin-conductance reactivity (Boxmeyer et al., 2023), indices commonly associated with reduced stress and anxiety. Electroencephalogram (EEG) studies also reveal consistent changes, mostly including increased alpha and theta activity which are linked to relaxation and sustained attention, respectively (Cahn & Polich, 2006). These findings suggest that meditation not only shapes cognitive-emotional states but also modulates brain activity in ways that can be measured and potentially trained.

Building on this principle of neurophysiological self-regulation, EEG neurofeedback is an expanding field at the interface of applied neuroscience and clinical psychology that provides a brain self-regulation technique based on real-time monitoring of cortical electrical activity (Bielas & Michalczyk, 2021; Cantor, 2009; Hampson et al., 2020). Registered neural signals are processed and delivered as visual and/or auditory feedback, enabling individuals to learn how to voluntarily modify their brain-activity patterns (Hammond, 2011). This approach has been widely studied as a therapeutic tool for attention-deficit/hyperactivity disorder (ADHD; Arns et al., 2020; Butnik, 2005; Van Doren et al., 2019), anxiety (Aristizabal et al., 2024; Chen et al., 2021; Christian et al., 2024), and depression (Patil et al., 2023; Takamura et al., 2020; S.-Y. Wang et al., 2019), as well as in performance optimization contexts (Faller et al., 2019; Mikicin et al., 2015).

Neurofeedback and meditation have been examined in isolation and in combination as nonpharmacological interventions to enhance psychological well-being and emotion regulation (Brandmeyer & Delorme, 2013; Tarrant, 2020). However, there is still a gap in the literature regarding how their integration has been explored and how to optimize such protocols. In fact, studies show substantial methodological heterogeneity, complicating comparability, limiting generalizability, and hindering evidence-based guidelines development.

Given this context, this systematic review aims to critically map the existing evidence, not only to identify trends and gaps, but also to inform more consistent and replicable future investigations. Therefore, we examine studies combining meditation and neurofeedback as interventions across different human conditions, focusing on methodological designs, implemented protocols, and clinical and nonclinical contexts. In addition to synthesizing reported outcomes, the review provides a critical appraisal of the risk of bias in the included studies.

Method

This systematic review was preregistered in PROSPERO (https://www.crd.york.ac.uk/PROSPERO/view/CRD42024554716; accessed June 4, 2024) under CRD42024554716 and conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2021).

Search Strategy

The search was performed in six databases (EBSCO, PubMed, Web of Science, LILACS-BVS, *Periódicos* CAPES, and Scopus), using descriptors covering multiple denominations of the techniques. Key terms included *neurofeedback*, *EEG biofeedback*, *neural biofeedback*, *brain-computer interface* (BCI), *wearable devices*, *meditation*, *meditative state*, *mindfulness*, *relaxation*, *imagery*, and *breath focus meditation*. Terms were combined using the following Boolean expression: ("Neurofeedback" OR "EEG biofeedback" OR "biofeedback neural" OR "Brain Computer Interface" OR "BCI" OR "wearable devices") AND ("meditation" OR "meditative state" OR "mindfulness" OR "relaxation" OR "imagery" OR "breath focus meditation").

Selection Criteria and Process

Eligible studies were empirical with experimental or quasi-experimental designs evaluating combined neurofeedback and meditation interventions. Studies had to manipulate the variables of interest and report outcomes in mental health, cognition, behavior, or well-being using validated instruments. Articles published from 2015 to 2025 in English, Portuguese, or Spanish with human participants of any age and gender were eligible.

Exclusion criteria included theoretical papers, systematic reviews, meta-analyses; studies involving animals; and studies of other interventions (e.g., biofeedback, pharmacotherapy, psychotherapy) without a clear separation of effects attributable solely to neurofeedback and meditation. Titles and abstracts were screened independently by the two first authors; disagreements were resolved by a third reviewer. In the second stage, each full text was read by at least two researchers, with collective discussion for final inclusion.

Data Extraction and Analysis

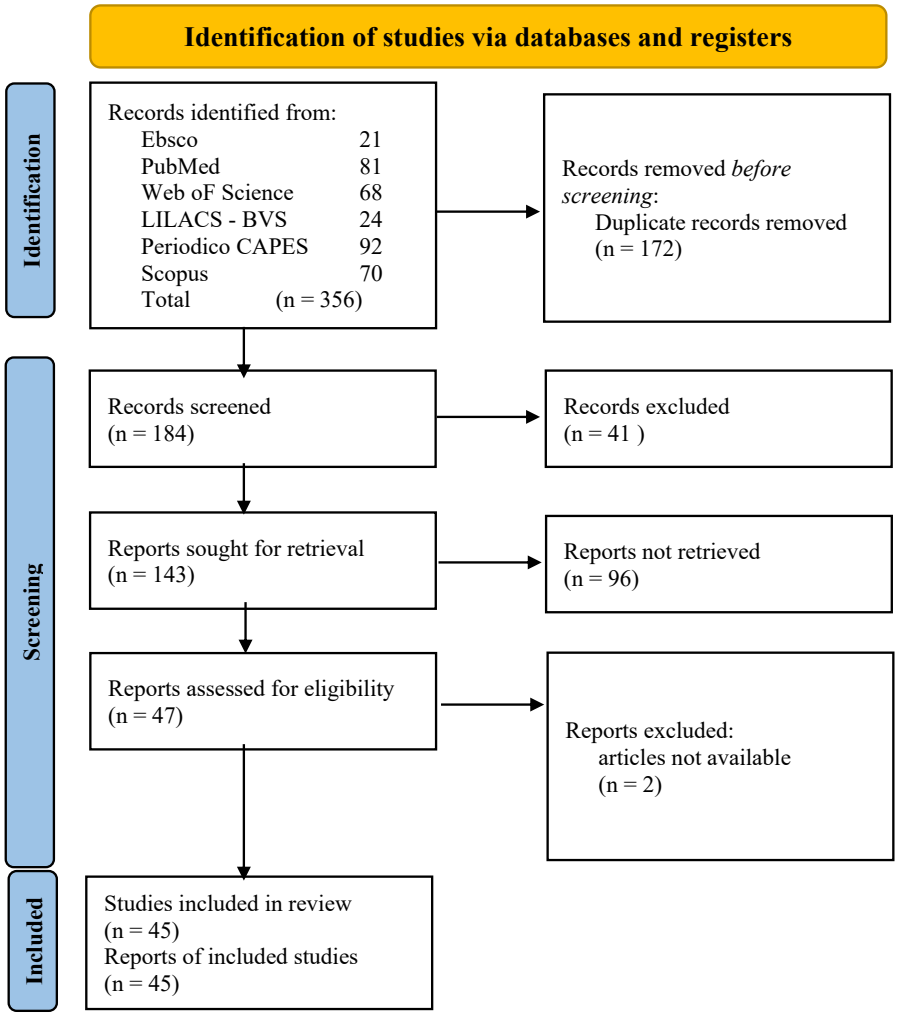
Data were extracted independently by the first four authors and organized in Microsoft Excel 2019 to present, clearly and systematically, methodological characteristics and intervention protocol details, following the PICOS strategy (Population, Intervention, Comparator, Outcomes, Study design), as recommended by the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins et al., 2022) and the PRISMA checklist (Page et al., 2021).

Key information targeted herein included methodological characteristics and intervention protocol specifics (please see Tables 3 and 5, respectively, in the Results section). Outcome-based analyses within each of these dimensions were subsequently conducted, generating graphs and descriptive statistics (means, percentages, trends, distribution patterns) to provide an integrated view of the current literature. Additionally, a risk-of-bias assessment was conducted for the included studies (please see Table 6 and Figure 7 in the Results section).

Results

The initial search identified 356 records; after screening and exclusions, 47 studies remained for eligibility assessment. Two lacked full-text availability, resulting in 45 studies included in the review. Figure 1 displays the flow diagram for the search, screening, and exclusion process according to the predefined criteria.

Figure 1. *Flowchart Study Selection.*



After the selection stage, the first four authors independently read the articles in full and extracted relevant data. The collected information was organized into two main tables (Tables 3 and 5).

General Characteristics

The analyzed data show a gradual increase is evident over 2015–2024, with a more pronounced rise from 2019 onward, as can be seen in Figure 2.

Moreover, Figure 3 and Table 1 present the geographic distribution of publications, with the United States accounting for 17 of 45 studies, underscoring its leading role in the field. The analysis identifies both high-producing countries and underrepresented regions, such as Latin America, where a notable gap indicates opportunities for local development and implementation of the interventions.

Figure 2. *Selected Publications by Year.*

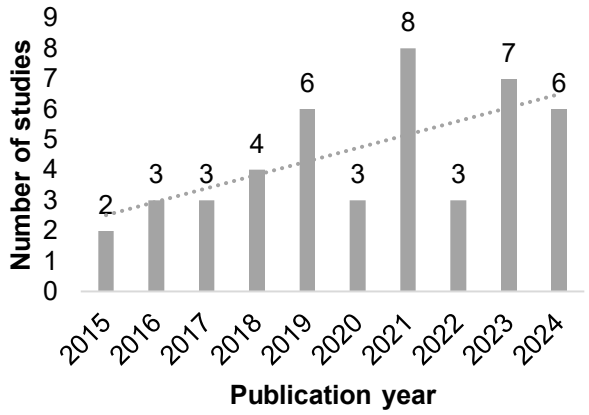


Figure 3. *Geographical Distribution of Studies*.

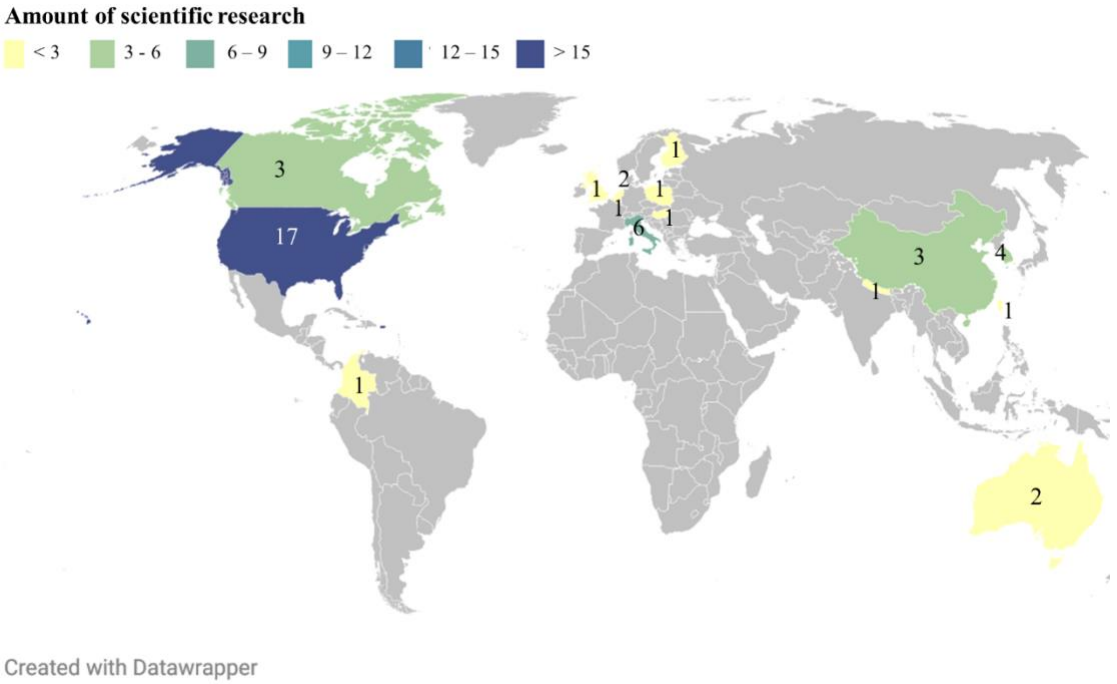


Table 1
Studies' Distribution Worldwide

Country	Amount of Scientific Research
United States of America	17
Italy	6
South Korea	4
Canada	3
China	3
Australia	2
Netherlands	2
Belgium	1
Colombia	1
Finland	1
Hungary	1
Nepal	1
Poland	1
Taiwan	1
United Kingdom	1

Regarding sample size and age, the mean sample size of the selected studies was 39.6 participants with substantial variability (*SD* = 28.6), indicating wide differences across studies. This range spans from case reports, such as Tarrant and Cope (2018) with firefighters, to larger samples, such as P. Wang et al. (2023) with 120 participants. Such heterogeneity reflects diverse methodological approaches, from exploratory and pilot studies to more structured clinical trials. Further, there was a predominance of female participants, averaging 60.1% (*SD* = 22.7). Summary of sample size, age and sex can be seen in Table 2.

Table 2
Population Characteristics

	N	**% Female**	**Mean Age (Years)**
Mean (*SD*)	39.6 (28.6)	60.1 (22.7)	34.3 (14.2)

In turn, the mean participant age was 34.3 years (*SD* = 14.2), indicating that young and middle-aged adults were the primary target population. Figure 4 depicts the distribution of mean-age intervals. A predominance of studies enrolled participants aged 20–30 years (*n* = 14). Only one study included children aged 0–10 years (Vekety et al., 2022) and another included older adults aged 70–80 years (P. Wang et al., 2023), highlighting a gap in the application of these interventions to extreme age ranges.

Notably, seven studies did not explicitly report mean age (Antle et al., 2018; Balconi et al., 2017; Choi et al., 2024; Martinez & Zhao, 2018; McMahon et al., 2021; Mikicin et al., 2015; Nieto-Vallejo et al., 2021), and six did not report gender (Balconi et al., 2017; Chen et al., 2021; Crivelli, Fronda, & Balconi, 2019; Crivelli, Fronda, Venturella, et al., 2019b; Hawley et al., 2021; Nieto-Vallejo et al., 2021). This omission constitutes a relevant methodological limitation, as the absence of these basic data hampers assessment of sample representativeness and the generalizability of results.

Finally, based on clinical and functional similarities, the investigated conditions were grouped into seven broad categories, synthesizing the diversity of therapeutic goals and application contexts of the interventions.

As can be seen in Figure 5, a predominance of research focuses on anxiety, mood, and stress disorders, represented in 19 of the 45 articles analyzed. This category ranges from isolated manifestations of anxiety or stress, as in Balconi et al. (2019), to complex constellations of symptoms, including burnout, depression, emotional exhaustion, and resilience, as in the study conducted by Ghosh et al. (2023). The emphasis on these clinical presentations underscores their relevance to contemporary mental health and points to the therapeutic potential of combining the techniques as strategies for regulating affect and psychophysiological stress.

The second most frequent category concerns cognitive performance and attentional regulation, covered in eight studies. These investigations examine interventions aimed at enhancing executive functions such as attentional control (Hunkin et al., 2021a; Vekety et al., 2022), impulsivity (van der Schoot et al., 2024), and performance on specific cognitive tasks, including working memory and reaction time (Brandmeyer & Delorme, 2020).

Figure 4. *Mean Ages Distribution.*

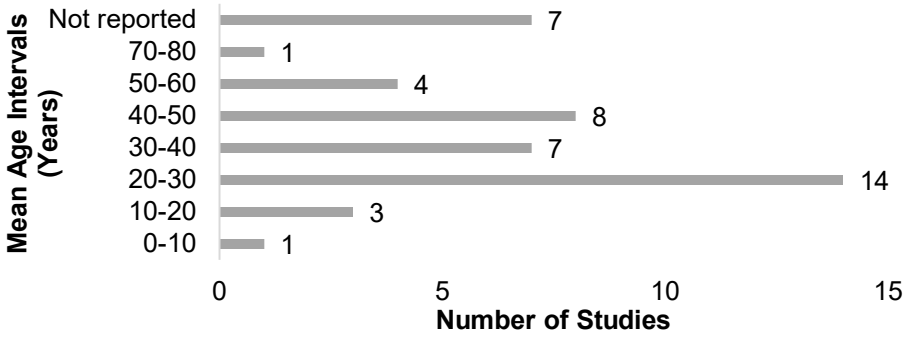


Figure 5. *Distribution of Conditions by Category.*

The presence of this category indicates interest in applications that increase performance in healthy populations or in high cognitive-demand settings.

Other less represented yet relevant categories include specific neurological and medical conditions, such as multiple sclerosis (Motolese et al., 2023), cancer (Millstine et al., 2019; Rolbiecki et al., 2023), atrial fibrillation (He et al., 2023), and poststroke sequelae (P. Wang et al., 2023), as well as traumatic brain injury (Polich et al., 2020). Additional studies addressed specific psychiatric disorders, including obsessive-compulsive disorder (Hawley et al., 2021), posttraumatic stress disorder (Choi et al., 2024; Schuurmans et al., 2021), and substance use disorders (Chiu et al., 2024).

Furthermore, interventions focused on the effects of the techniques on meditative states and mindfulness experiences were identified. These studies evaluated participants' ability to attain meditative states (Hunkin et al., 2021b; Sas & Chopra, 2015), the depth of these states (Kosunen et al., 2016), and the development of skills related to mindfulness and relaxation (Salminen et al., 2024; van Lutterveld et al., 2017). Unlike investigations centered on specific conditions such as anxiety or depression, these works primarily examined how combined use of the techniques facilitated induction of meditative states and improved meditation quality.

This thematic diversity demonstrates the breadth of contexts in which neurofeedback and meditation are applied, while also reinforcing clinical and methodological heterogeneity across studies that should be considered when interpreting results.

Methodological Characteristics

Table 3 synthesizes the methodological characteristics, accompanied by figures and summary analyses.

Table 3
Methodological Characteristics of the Included Studies

	Participants' Characteristics					Study Design			
Authors (Year)	***N***	**% Female**	**Population Type**	**Mean Age (*SD*)**	**Condition**	**Study Design**	**Control Condition**	**Randomization**	**Blinding**
Acabchuk et al. (2021)	53	73.10	Healthy university students, novice meditators	20.52 (2.76)	Depression, anxiety, stress	RCT	AC	Yes	No
Antle et al. (2018)	21	100	Girls in poverty with trauma history	5–11*	Anxiety and attention	Mixed-methods field experiment with control and repeated measures	PC (waitlist)	Yes	No
Balconi et al. (2017)	40	NR	University students	NR	Mild to moderate stress	RCT	AC	Yes	No
Balconi et al. (2019)	55	69	Healthy university adults	23.2 (1.8)	Mild stress	RCT with pre/post measures	AC	Yes	No
Bhayee et al. (2016)	26	46	Adults with moderate/high stress	Exp: 33.3 (4.7) Control: 32.0 (4.9)	Stress	RCT with repeated measures	AC	Yes	Allocation blinding
Brandmeyer & Delorme (2020)	24	50	Young healthy adults	25 (3)	Cognitive enhancement (working memory, reaction time)	Double-blind sham-controlled RCT	Sham control group	Yes, and counterbalanced	Double-blind
Chen et al. (2021)	34	NR	Adults with/without anxiety symptoms	Anxious: 37 (7.61) Healthy: 24.4 (1.49)	Anxiety	Mixed design: between-subjects (control) and within-subjects (repeated measures)	Condition comparison	NA	No
Chiu et al. (2024)	110	18.20	Adults with substance use disorder (SUD)	37.77	Substance use disorder (SUD)	Multicenter quasi-experimental within-subjects	Pre/post	No	No
Choi et al. (2024)	58	86.20	Adults with trauma history	18–45*	Posttraumatic stress disorder (PTSD)	RCT	PC (waitlist)	Yes	Data analysts
Christian et al. (2024)	5	40	High-achieving adolescents with anxiety	16.4 (0.55)	Anxiety and high performance	Single-case design (A-B-A), within-subjects, with follow-up	A1, B1, A2	NA	No

Table 3

Methodological Characteristics of the Included Studies

	Participants' Characteristics				Study Design				
Authors (Year)	***N***	**% Female**	**Population Type**	**Mean Age (*SD*)**	**Condition**	**Study Design**	**Control Condition**	**Randomization**	**Blinding**
Crivelli, Fronda, & Balconi (2019)	50	NR	Healthy adults, athletes/non-athletes	22.94 (2.22)	Attention, perceived stress, anxiety, psychological well-being	Three-group experimental design (athletic, non-athletic, AC) with pre/post evaluation	AC	Yes	No
Crivelli, Fronda, Venturella, et al. (2019a)	16	50	Executive professionals	44.38 (6.22)	Stress management and neurocognitive efficiency	Quasi-experimental within-subjects	Pre/post	No	No
Crivelli, Fronda, Venturella, et al. (2019b)	40	NR	Adults with mild stress	23.47 (2.33)	Mild stress symptoms	RCT	AC	Yes	No
Dunham et al. (2019)	Exp 57 Ctrl 191	80.7	Trauma center healthcare providers	36.5 (11.8)	Stress, emotional exhaustion, burnout risk	Non-randomized quasi-experimental	PC	No	No
Ghosh et al. (2023)	40	85	Pandemic frontline healthcare workers	41.3 (11.0)	Stress, burnout, depression, resilience, cognition	Pilot quasi-experimental within-subjects	Pre/post	No	No
Gu & Frasson (2017)	6	33	Healthy adults	29.67 (4.84)	Mild symptoms of stress, anxiety, and depression	Quasi-experimental within-subjects	Pre/post	NA	No
Hawley et al. (2021)	71	NR	Adults with OCD	26 (4.61)	OCD	RCT	PC (waitlist)	Yes	Data analysts
He et al. (2023)	80	39	Patients with atrial fibrillation	59 (11)	Atrial fibrillation (post ablation)	RCT	AC	Yes	Data analysts
Hunkin et al. (2021a)	35	58.82	Healthy university students	22.66 (7.35)	Mindfulness state and meditative experience	Within-subjects crossover experimental design	Condition comparison	Condition	No

Table 3
Methodological Characteristics of the Included Studies

Participants' Characteristics					Study Design				
Authors (Year)	***N***	**% Female**	**Population Type**	**Mean Age (*SD*)**	**Condition**	**Study Design**	**Control Condition**	**Randomization**	**Blinding**
Hunkin et al. (2021b)	68	59	Healthy adults	22.66 (7.35)	Attention regulation and cognition	Observational study (within- and between-subjects analysis)	Condition comparison	NA	No
Hwang et al. (2017)	24	75	University students	Male: 23.32 Female: 22.22	Psychological /emotional well-being and psychosocial flourishing	RCT	PC + AC	Yes	No
Kosunen et al. (2016)	43	60	Healthy university students	28.7	Meditative depth and presence	2×2 factorial within-subjects repeated measures design	Condition comparison and pre/post	Yes	No
E. Lee et al. (2024)	38	68.40	Adults with stress, depression, and/or sleep disorders	49.1 (12.15)	Stress, depression, sleep disorders	RCT	AC	Yes	Double-blind
Martinez & Zhao (2018)	19	58	Adolescents with disciplinary issues	NR	School disciplinary difficulties	Matched quasi-experimental	PC	No	No
McMahon et al. (2021)	5	40	Students with mild/moderate intellectual and developmental disabilities (IDD)	18–25*	Cognitive/adaptive deficits (IDD)	Single-case design (A-B-A-B), within-subjects	A1, B1, A2, B2	NA	No
Mikicin et al. (2015)	35	42.86	Healthy semi-professional university athletes	18–25*	High sports performance	Quasi-experimental	PC	NR	No
Millstine et al. (2019)	28	100	Women with recent breast cancer diagnosis	55.85 (10.8?)	Breast cancer (stress, fatigue, quality of life)	RCT with follow-up	PC	Yes	No

Table 3
Methodological Characteristics of the Included Studies

Participants' Characteristics					Study Design				
Authors (Year)	***N***	**% Female**	**Population Type**	**Mean Age (*SD*)**	**Condition**	**Study Design**	**Control Condition**	**Randomization**	**Blinding**
Min et al. (2023)	92	90	Adults with high stress	38.67 (10,82)	Stress	RCT with three parallel arms	AC + PC	Yes	No
Motolese et al. (2023)	27	69	Adults with multiple sclerosis	46.1 (8.7)	Multiple sclerosis: mood, cognition, QoL, fatigue	Quasi-experimental within-subjects	Pre/post	No	No
Nieto-Vallejo et al. (2021)	9	NR	Young healthy adults	20–35*	Attention and relaxation	Quasi-experimental within-subjects	Pre/post	No	No
P. Wang et al. (2023)	120	23.3	Stroke patients with hemiplegia	77.7 (7.44)	Poststroke hemiplegia	RCT	AC	Yes	Data analysts
Polich et al. (2020)	20	85	Adults with mild/moderate traumatic brain injury (TBI)	45.4 (3.0)	Chronic mood /cognitive symptoms post-TBI	Pilot RCT	AC	Yes	No
Rolbiecki et al. (2023)	15	53	Adults with cancer	52.4 (11.8)	Cancer-related pain and anxiety	Exploratory single-group quasi-experimental mixed-methods	Pre/post	No	No
Salminen et al. (2024)	43	60.50	Healthy university adults	28.7 (age range 20–48)	Meditative state, concentration, relaxation	Within-subjects mixed factorial design	AC + PC	Condition	No
Sas & Chopra (2015)	16	62.50	Healthy adults, novice /experienced meditators	41 (age range 20–60)	Mindfulness state and meditative experience	Quasi-experimental mixed design (within-subjects: control/monaural /binaural; between-subjects: expertise level)	Condition comparison and pre/post	Yes	No
Schuurmans et al. (2021)	77	40.30	Institutionalized adolescents	15.25 (1.79)	Posttraumatic stress disorder (PTSD)	RCT	AC	Yes	No
Smarinsky et al. (2023)	13	62	High school students with anxiety	17.1 (0.61)	Anxiety and introspection	Quasi-experimental time-series within-subjects	Pre/post	NA	No

Table 3

Methodological Characteristics of the Included Studies

Participants' Characteristics					Study Design				
Authors (Year)	***N***	**% Female**	**Population Type**	**Mean Age (*SD*)**	**Condition**	**Study Design**	**Control Condition**	**Randomization**	**Blinding**
Soriano et al. (2024)	31	81	Healthy adults	23.16 (age range 18–30)	*Alpha* power self-regulation	Within-subjects experimental design	Condition comparison and pre/post	Yes, and counterbalanced	Condition blinded
Svetlov et al. (2019)	S1: 99 S2: 46	77	University and general population	18–72*	Stress	S1: Within-subjects RCT; S2: Between-subjects RCT	S1: Condition comparison S2: AC	Yes	No
Tarrant & Cope (2018)	4	0	Firefighters	39.5 (5.6)	Mood and gamma patterns	Within-subject case study	Pre/post	No	No
Tarrant et al. (2022)	100	91	COVID-19 frontline healthcare workers	Control: 40.9 (13.9) Exp: 42.6 (14.4)	Positive/negative mood states	Between-subjects RCT with repeated measures (pre/post)	AC	No	No
van der Schoot et al. (2024)	8	75	Forensic outpatients with impulse control issues	40.88 (12.28)	Impulse control	Pilot quasi-experimental within-subject mixed-methods	Pre/post	NA	No
van Lutterveld et al. (2017)	32	34	Healthy adults, novice /experienced meditators	Novices: 51 (14) Expert: 53 (12)	Meditative state, concentration, relaxation	Double-blind randomized within-subjects experiment with feedback manipulation	Condition comparison and pre/post	Yes	Double-blind
Vekety et al. (2022)	31	51	Elementary school children	9.92 (4.35)	Attention	Pilot RCT	PC	Yes	No
Viczko et al. (2021)	41	68.29	Adults with moderate /severe anxiety or depression	35.4 (11.6)	Anxiety and depression	RCT	AC	Yes	Participant allocation

Note. AC = active control; PC = passive control; NR = not reported; NA = not applicable; RCT = randomized controlled trial; OCD = obsessive-compulsive disorder. *Age-range reported when mean age and standard error are not available in the original paper.

Firstly, the selected studies were classified into six broad categories and their percentage distribution presented in Figure 6.

The data indicate that randomized controlled trials (RCTs) were the most frequent design, representing 44% (*n* = 20) of the total sample. Within-subject designs were the second most common, accounting for 24% (*n* = 11). This design is particularly useful in exploratory studies or when participant selection is constrained by specific clinical conditions such as cancer (Rolbiecki et al., 2023), multiple sclerosis (Motolese et al., 2023), or substance use disorders (Chiu et al., 2024).

Quasi-experimental designs ranked third, comprising 18% of studies (*n* = 8). These studies assigned participants to conditions without random assignment.

The remaining categories were less represented and deviated and often adopted more individualized or integrative approaches, differing from traditional group-based experimental designs. Although less prevalent, these formats provide valuable contributions, particularly for exploring complex contexts, generating hypotheses, or deepening understanding of specific phenomena. For example, the case studies by Christian et al. (2024) and McMahon et al. (2021), which used an A–B–A design, enabled detailed analysis of interventions in individual cases. In this type of experimental design, an initial baseline phase (A) is followed by an intervention phase (B) and then a return to the baseline (A) without intervention. This sequence allows researchers to observe changes in the target behavior during and after the intervention, strengthening causal inferences by showing whether effects disappear or reappear when the intervention is withdrawn. Mixed-methods studies, such as those by Antle et al. (2018) and Rolbiecki et al. (2023), integrated quantitative and qualitative data, broadening understanding of both effects and processes involved. Finally, observational studies also yielded important descriptive evidence, exemplified by Hunkin et al. (2021b), which applied an observational design with within- and between-subjects analyses.

Furthermore, control strategies, randomization, and blinding were assessed and are summarized in Table 4.

Figure 6. *General Categories of Study Designs.*

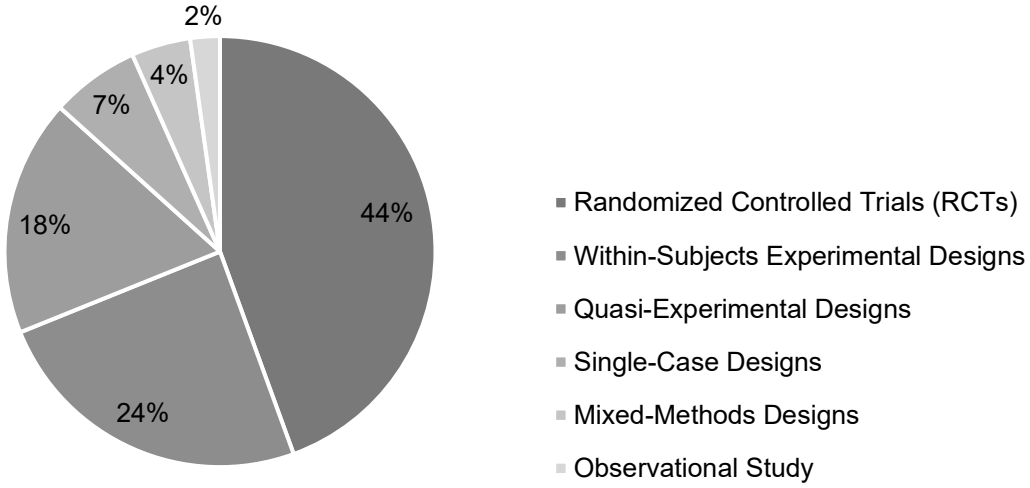


Table 4
Control Strategy, Randomization, and Blinding

Control Strategy	Number of Studies	Percentage
Active control	14	31.11%
Passive control	8	17.78%
Pre/post measures (within-subjects)	10	22.22%
Condition comparison	9	20.00%
Sham/placebo control	1	2.22%
Active + Passive control	3	6.67%
Randomization	**Number of Studies**	**Percentage**
Yes (randomized)	27	60%
No (not randomized)	10	22%
Not applicable	7	16%
Not reported/unclear	1	2%
Blinding	**Number of Studies**	**Percentage**
No blinding	35	77.78%
Blinded data analysts	4	8.89%
Double-blind	3	6.67%
Allocation blinding	2	4.44%
Condition blinding	1	2.22%

Building on these methodological features, we next detail the neurofeedback protocols implemented and the outcomes reported across studies. Table 5 provides a summary of key intervention features across the included studies, including equipment type, feedback modalities, neurofeedback protocols, meditation approaches, session number and duration, assessment strategies, and outcomes, which are subsequently described in detail.

The interventions were characterized primarily by the use of wearable devices to deliver neurofeedback, reported in 35 of the 45 included studies (78%). Their widespread adoption likely reflects accessibility, portability, and ease of use (Peake et al., 2018), which facilitate deployment in settings with lower technical demands and for practical, low-cost protocols. Only 10 studies employed conventional EEG equipment, typically used in laboratory or clinical contexts (Sharma & Meena, 2024).

As regards to feedback, most studies (60%) used auditory feedback, usually delivered either as simple sounds, such as pure tones, or as more complex soundscapes modulated in real time by the user's brain activity. Modulation occurred continuously, for example through gradual volume changes, or discontinuously, characterized by the presence or complete absence of the auditory stimulus. For example, the Muse Headband uses bird vocalizations to signal calm and focus, as well as modulated ambient sounds (e.g., ocean waves) that soften as the user attains greater relaxation.

Second most used was visual feedback, employed in 27% of studies. In this modality, visual stimuli varied either continuously or discretely. In continuous feedback, parameters such as screen brightness or object size were adjusted in real time, increasing or decreasing with participant performance. In discrete feedback, information was delivered at specific events; for example, a video paused or advanced depending on whether the training target was being met. In Tarrant et al. (2022), using the BrainLink Lite EEG, a luminous dragonfly signaled relaxation or focus, while the virtual environment adapted under distraction, stress, or anxiety. Finally, among the included studies, only Nieto-Vallejo et al. (2021) employed olfactory stimuli. The unimodal or multimodal sensory feedback modalities employed in the analyzed studies is depicted in Figure 7.

Table 5
Characteristics of the Interventions

Authors (Year)	Type of Feedback	NF Protocol	Location	Number of Sessions	Duration (min)	Meditation Type	Significant Results	Nonsignificant Results
Acabchuk et al. (2021)	Auditory	Proprietary alg.	AF7/8, TP9/10, Fpz	28 s (7×/week for 4 weeks)	10	FA on breath and bodily sensations	↓ DASS-21; ↑ MINDSENS (both groups), $p < .0001$	No significant EEG modulation (Muse); ↓ Calm time (App group)
Antle et al. (2018)	Visual	Alpha/theta ratio ↑ Beta	FP1	24 s (3–4×/week for 6 weeks)	15	FA on breath and bodily sensations	↑ Relaxation, attention during gameplay; ↑ Calm, attention (experimental > control, post test)	No pre-test differences in calm or attention
Balconi et al. (2017)	Auditory	Proprietary alg.	AF7/8, TP9/10, Fpz	28 s (estimated: 7×/week for 4 weeks)	10	FA on breath	↓ PSS (16%); ↑ focus (↑ N2 ERP); ↑ relaxation (↑ alpha/beta); ↑ subjective well-being	No effects in control group
Balconi et al. (2019)	Auditory	Proprietary alg.	AF7/8, TP9/10, Fpz	28 s/daily	10–20	FA on breath	↓ Perceived stress, anxiety, fatigue; ↑ vigor, HRV (rest & Stroop)	No change in HR, HRV (eyes closed), or mood (tension, anger, depression, confusion)
Bhayee et al. (2016)	Auditory	Proprietary alg.	AF7/8, TP9/10, Fpz	Minimum of 32 s	10	FA	↓ Stroop RT, somatization (BSI); ↑ calmness, body awareness	No significant effects in depression /anxiety (BSI), affect (PANAS), QoL (WHOQOL), Mindfulness (FMI), attention (d2, Digit Span), personality (BFI)
Brandmeyer & Delorme (2020)	Visual	↑ Theta (FMθ)	Fpz, Fz, F7/8, Cz, P7/8, and Oz	8 s over 2 weeks	30	FA on breath	↑ FMθ; ↓ RT (N-back); ↑ gamma; sustained effects	No effects in SART, local–global tasks, sham group
Chen et al. (2021)	Visual	Frontal alpha asymmetry	FP1/2, F7/8, F3/4	1 s with 3 experimental conditions	18	Mindfulness	↑ Alpha/theta/gamma after mindfulness-NFB in anxiety patients ($p < .05$)	Healthy controls also ↑ Alpha/theta /gamma, but nonsignificant

Table 5
Characteristics of the Interventions

Authors (Year)	Type of Feedback	NF Protocol	Location	Number of Sessions	Duration (min)	Meditation Type	Significant Results	Nonsignificant Results
Chiu et al. (2024)	NR	↑ Beta and SMR	Not specified	12 mindfulness + 12 NF s (total: 24)	NF 50 Mindfulness 60	Mindfulness-based relapse prevention therapy	↓ Addiction, anxiety (BAI), depression (BDI); ↑ QoL (multiple domains), $p < .01$	WHOQOL physical domain improvement non-significant ($p = .509$)
Choi et al. (2024)	Auditory	↑ Alpha	Not specified (uses two-channel EEG headset)	≥12 s (≥3× /week for 4 weeks)	50	Not specified; described as meditation with alpha wave and binaural beat feedback	↑ Psychological well-being, emotional stability; ↓ symptoms (SCL-47-R), $p < .01$	↓ PTSD (PDS) and anti-stress index (left) not significant ($p > .05$)
Christian et al. (2024)	Auditory	Proprietary alg.	AF7/8, TP9/10, Fpz	A1: 9 (baseline), B: 15 (intervention, A2: 9 (post)	5	FA on breath	60% reported ↓ anxiety at follow-up; stronger effects in low-income and minority participants	Isolated ↑ or stable anxiety in 2 participants; no sustained effect
Crivelli, Fronda, & Balconi (2019)	Auditory	Proprietary alg.	AF7/8, TP9/10, Fpz	14 s (1×/day for 2 weeks)	10–20	FA on breath	↓ Stress (PSS), RT, false responses; ↑ non-judgment (FFMQ), N2 amplitude	No effects in other FFMQ domains, STAI, cognitive tasks
Crivelli, Fronda, Venturella, et al. (2019a)	Auditory	Proprietary alg.	Inion, T3/4	14 s	10–20	FA on breath	↓ Stress, anxiety, anger, fatigue, RT; ↑ HRV, alpha-beta ratio, alpha blocking (frontal/parietal)	No significant cognitive /electrophysiological modulation
Crivelli, Fronda, Venturella, et al. (2019b)	Auditory	Proprietary alg.	AF7/8, TP9/10, Fpz	28 s	10–20	FA on breath	↓ Complex RT; ↑ alpha/beta ratio, alpha blocking, N2 (Fz, Cz)	ERP (Pz), cognitive tasks: $p > .05$

Table 5
Characteristics of the Interventions

Authors (Year)	Type of Feedback	NF Protocol	Location	Number of Sessions	Duration (min)	Meditation Type	Significant Results	Nonsignificant Results
Dunham et al. (2019)	Visual	Bispectral index: ↑ 11–20 Hz intermediate ↓ 30–47 Hz high	Frontal /temporal	8 s over 4 days	12	Mindfulness focused on expanded attention, conscious relaxation, and peripheral visual awareness	↓ Bispectral Index; ↑ relaxation, well-being (77% improved)	23% no improvement; smaller change in positive affect vs. nonstress scores
Ghosh et al. (2023)	Auditory	Proprietary alg.	AF7/8, TP9/10, Fpz	23.8 s on average	5.8 (2.2)	FA on breath and bodily sensations	↓ Stress, burnout; ↑ resilience, cognitive performance, QoL, $p < .01$	No effects in feature match, grammatical reasoning
Gu & Frasson (2017)	Visual	Proprietary alg.	AF3/4, F7/8, F3/4, FC5/6, T7/8, P7/8, O1/2	8 s	15	Sophrology (self-training in physical and mental relaxation)	↓ HADS-Anxiety/depression, time to relaxation; ↑ meditation score	TItR unchanged in low-threshold group
Hawley et al. (2021)	Auditory	Proprietary alg.	AF7/8, TP9/10, Fpz	56 s (1×/day for 8 weeks)	20	FA on breath and bodily sensations	↓ YBOCS; ↑ Alpha, Beta, non-reactivity (FFMQ); Alpha/Beta correlated with ↓ symptoms	No significant change in delta and theta bands
He et al. (2023)	Auditory and visual	Proprietary alg.	Frontal	Single session in a cardiac catheterization lab	35	Guided mindfulness (including body scan and visualization)	↓ Pain, anxiety, fatigue, opioid use ($p < .01$)	No effects in HR, BP, SpO_2, medication use
Hunkin et al. (2021a)	Auditory	Proprietary alg.	AF7/8, TP9/10, Fpz	Single lab session (with and without feedback) + 14 days home practice	10	FA on breath	↑ Mindfulness, mind wandering, ↑ perceived control (home practice)	↓ Calm/relaxation; feedback aversive to some participants ($p < .01$)

Table 5
Characteristics of the Interventions

Authors (Year)	Type of Feedback	NF Protocol	Location	Number of Sessions	Duration (min)	Meditation Type	Significant Results	Nonsignificant Results
Hunkin et al. (2021b)	Auditory	Proprietary alg.	AF7/8, TP9/10, Fpz	14 s home-based for 29 participants	10	FA on breath	Muse recoveries predicted ↓ mind wandering; explained variance in mindfulness/attention	Mind wandering differences (experienced vs. novice meditators); ICCs low (mind wandering = .27; recoveries = .17)
Hwang et al. (2017)	Visual	↑ Alpha and theta; ↓ Beta	Fp1/2	10 s	30–45	FA meditation and visualization	↑ FS, SPANE-N; large effect for SPANE-P (NFB group)	SPANE-P NS (mPPT); small control group effect
Kosunen et al. (2016)	Visual	↑ Alpha and theta	F3/4, C3/4, P3/4	1 s with 6 different conditions	10 x Cond.	FA on breath and bodily sensations	↑ Relaxation, presence, meditation depth; ↓ boredom (VR + NFB)	MEDEQ (e.g., relaxation, transpersonal states): NS
E. Lee et al. (2024)	Auditory	↑ Theta and alpha; ↓ High beta	Fp1/2	28 s (2×/day for 2 weeks)	12	Mindfulness: breath-focused and relaxation-based	↓ Stress, state anxiety, depression, insomnia; ↑ satisfaction (experimental group)	No intergroup qEEG or biomarker (BDNF, cortisol, ACTH, IL-6, TNF-α) differences
Martinez & Zhao (2018)	Auditory	Proprietary alg.	AF7/8, TP9/10, Fpz	20 s (1×/week from Oct 2016 to Mar 2017)	3	FA on breath	↓ Disciplinary referrals; ↑ Muse scores	↑ Control group disciplinary referrals
McMahon et al. (2021)	Auditory	Proprietary alg.	AF7/8, TP9/10, Fpz	20 s (10 with NF, 10 without)	5	FA on breath	↑ Mindfulness, attention to breath, affect (post session); high acceptability	No consistent Mindfulness/ attention (*n* = 2) /affect changes (*n* = 1)
Mikicin et al. (2015)	Auditory and visual	↑ SMR and Beta1 ↓ Theta and Beta2	C3/4	20 s over 4 months	30	Autogenic relaxation with green light and 7–13 Hz sound stimulation	↑ Alpha and beta1 (eyes closed), Kraepelin performance; ↓ RT	SMR and oscillation index NS
Millstine et al. (2019)	Auditory	Proprietary alg.	AF7/8, TP9/10, Fpz	Median of 29 s (range: 0–116)	≥3	FA on breath	↓ Emotional fatigue, stress; ↑ vigor, emotional well-being ($p < .01$)	No between-group differences

Table 5
Characteristics of the Interventions

Authors (Year)	Type of Feedback	NF Protocol	Location	Number of Sessions	Duration (min)	Meditation Type	Significant Results	Nonsignificant Results
Min et al. (2023)	Auditory	↑ Alpha /beta ratio (≥ 2.775)	FP1/2	28 s (2×/day for 4 weeks)	30	Mindfulness meditation with awareness training, abdominal breathing, and body scan	↓ Stress, depression, insomnia, emotional labor; ↑ resilience, relaxation index (NFB group)	No improvement in K-MAAS, KOSS, or PSS
Motolese et al. (2023)	Auditory	Proprietary alg.	AF7/8, TP9/10, Fpz	56 s (7×/week for 8 weeks)	30–45	FA on breath and bodily sensations	↓ RRS; ↑ Digit Span; ↓ beta power (scalp-wide)	HADS, SF-12, PSS, VAS, GSE, MFIS: NS
Nieto-Vallejo et al. (2021)	Visual, auditory, and olfactory	Proprietary alg. Attention /relaxation score (0–100); freq. not detailed	1 (single frontal sensor (Neurosky headset)	4 s (1 without feedback + 3 with different sensory feedbacks)	10	Trataka (open-eyed meditation focusing on an object)	↑ Attention (78%), relaxation (44.4%), subjective well-being (mood)	Olfactory stimulus ↓ relaxation (88.9%) and attention (66.6%)
P. Wang et al. (2023)	Visual and motor	ERD via motor imagery detection; freq. not specified	Primary motor and premotor area	40 s (5×/week for 8 weeks)	20 (BCI) + 80 weekly mindfulness	Mindfulness-based stress reduction	↑ Motor function, daily activity, mindfulness, sleep quality, QoL ($p < .001$)	MBI NS at 3-month
Polich et al. (2020)	Auditory	Proprietary alg.	AF7/8, TP9/10, Fpz	Up to 42 s (1×/day for 6 weeks)	12	FA on breath	↓ NSI, anxiety (BAI), depression (BDI-II); ↑ well-being (combined practice)	No cognitive performance or Calm% improvement
Rolbiecki et al. (2023)	Visual	Proprietary alg.	BrainLink device: prefrontal	1 s	22	Mindfulness	↓ Pain, fatigue; trend for anxiety and depression	↓ Anxiety ($p = .13$), depression ($p = .56$); sleepiness, nausea, shortness of breath, appetite NS
Salminen et al. (2024)	Visual	↑ Theta and alpha	F3/4, C3/4, P3/4	6 consecutive s	10	FA with external focal point and body scan	↑ Meditation depth (HMD + NFB); ↑ theta, gamma ($p < .05$)	No alpha modulation (NFB); presence unchanged (body scan vs. focal)

Table 5
Characteristics of the Interventions

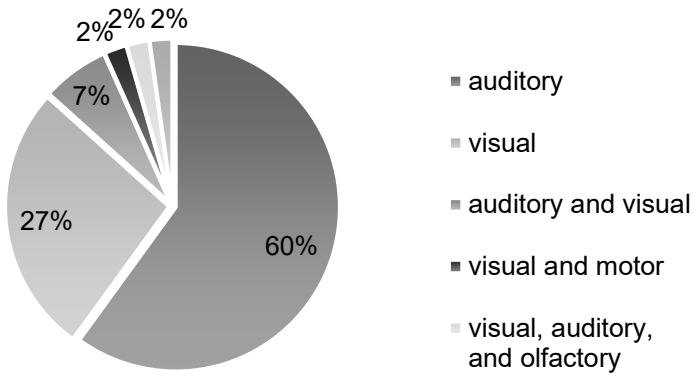
Authors (Year)	Type of Feedback	NF Protocol	Location	Number of Sessions	Duration (min)	Meditation Type	Significant Results	Nonsignificant Results
Sas & Chopra (2015)	Auditory	Proprietary alg.	AF3/4, F3/4, FC5/6, F7/8, T7/8, P7/8, O1/2	3 consecutive s (control, monaural, binaural)	10	Mindfulness with emphasis on attention self-regulation	↑ Meditation depth, benefit for beginners, subjective quietness duration; binaural more effective than monaural ($p < .05$)	Main effect of expertise on subjective rating; no interaction in self-assessment
Schuurmans et al. (2021)	Auditory	Proprietary alg.	AF7/8, TP9/10, Fpz	12 s	15–20	FA on breath	↓ Traumatic stress (CRIES-13), anxiety (SCAS), cortisol; ↑ Mindfulness (CAMM)	HR/cortisol unchanged (session 1)
Smarinsky et al. (2023)	Auditory	Proprietary alg.	AF7/8, TP9/10, Fpz	33 s (3×/week for 11 weeks)	5	FA on breath	↑ Correlation self-report & NFB (intervention/post); gender × introspection interaction	SR–NFB correlation NS ($r = −0.02$); no male introspection
Soriano et al. (2024)	Auditory	↑/↓ Alpha	Global analysis with 19 electrodes; emphasis on O1, O2, T5, T6 (greater power)	1 s with 4 training blocks (2 ↑ and 2 ↓ training)	6 x block	FA	↑ Alpha (up-training); ↓ Alpha (downtraining), $p < .05$	No significant differences in subjective reports or resting state transfer effect (pre/post × condition)
Svetlov et al. (2019)	Auditory	Proprietary alg.	AF7/8, TP9/10, Fpz	1 s (2 conditions)	7 x Cond.	FA on breath	↑ HRV, Calm%; ↓ EDA, effort perception (Calm%)	HRV, EDA, sAA, Calm% NS (Muse-assisted vs. unassisted)
Tarrant & Cope (2018)	Auditory and visual	Frontal gamma asymmetry	AF7/8	1 s	4–5	Open Heart meditation: gratitude or cultivation of positive emotions	↑ Left frontal gamma asymmetry, possitive affect PANAS, and STCI; ↓ negative mood	One participant ↓ left asymmetry (shifted to right); ↓ joviality (STCI); no change in negative mood
Tarrant et al. (2022)	Visual	↓ High beta	FP1/2	1 s	5	Progressive body-scan/relaxation mindfulness meditation	↑ Happiness, calm; ↓ confusion, fatigue, depression, tension, anger (experimental and control)	↓ Vigor (experimental); no changes in happiness, calm, fatigue (control)

Table 5
Characteristics of the Interventions

Authors (Year)	Type of Feedback	NF Protocol	Location	Number of Sessions	Duration (min)	Meditation Type	Significant Results	Nonsignificant Results
van der Schoot et al. (2024)	Auditory	Proprietary alg.	AF7/8, TP9/10, Fpz	8 s (2×/week for 4 weeks)	6	FA on breath and bodily sensations	↓ Impulsivity, aggression, tension; "↑ relaxation, body awareness, inhibitory control, Muse Calm%	AVL-AV anger, MOAS: no aggression reduction
van Lutterveld et al. (2017)	Visual	↑/↓ Low gamma– (condition-based)	PCC	1 s with multiple experimental combinations	1.5–7 (total ~45 per participant)	Effortless awareness-based meditation	94% linked ↓ PCC to effortless awareness; ↑ volitional signal control ($p < .001$)	No voluntary PCC control; no EO/EC difference
Vekety et al. (2022)	Auditory	Proprietary alg.	AF7/8, TP9/10, Fpz	8 s	1–4	FA on breath	↑ Stroop accuracy, alpha and theta (rest), calm states; ↓ errors (Hearts/Flowers)	Theta and alpha (EC) and Stroop RT: NS
Viczko et al. (2021)	Visual	Frontal gamma asymmetry	AF7/8	1 s	5	Compassion meditation (Open Heart)	↑ Happiness, calm, alpha and beta (frontal, midline, parietal), engagement; ↓ tension, depression	No significant group differences; ↓ frontal gamma in both (↑ trend in experimental only); vigilance changes not significant ($p = .096$)

Note. NR = not reported; MINDSENS = Mindfulness Sensitivity Index; DASS-21 = Depression, Anxiety and Stress Scale – 21 Items; PSS = Perceived Stress Scale; ERP = event-related potential; HRV = heart rate variability; Stroop RT = Stroop Task Reaction Time; BSI = brief symptom inventory; PANAS = positive and negative affect schedule; WHOQOL-BREF = World Health Organization Quality of Life – Brief; FMI = Freiburg Mindfulness Inventory; d2 = d2 Test of Attention; BFI = Big Five Inventory; FMθ = frontal midline theta; RT = reaction time; SART = sustained attention to response task; BAI = Beck Anxiety Inventory; BDI = Beck Depression Inventory; QoL = quality of life; PDS = Posttraumatic Diagnostic Scale; SCL-47-R = Symptom Checklist-47 Revised; STAI = State-Trait Anxiety Inventory; FFMQ = Five Facet Mindfulness Questionnaire; HADS = Hospital Anxiety and Depression Scale; TItR = time interval to relaxation; YBOCS = Yale-Brown Obsessive Compulsive Scale; HR = heart rate; BP = blood pressure; SpO_2 = oxygen saturation; ICCs = intraclass correlation coefficients; FS = Flourishing Scale; SPANE-N/P = Scale of Positive and Negative Experience – Negative/Positive Affect Subscale; mPPT = modified positive psychotherapy; MEDEQ = Meditation Depth Questionnaire; BDNF = brain-derived neurotrophic factor; ACTH = adrenocorticotropic hormone; IL-6 = Interleukin-6; TNF-α = Tumor Necrosis Factor Alpha; K-MAAS = Korean version of the Mindful Attention Awareness Scale; KOSS = Korean Occupational Stress Scale; RRS = Ruminative Response Scale; SF-12 = 12-Item Short Form Health Survey; VAS = Visual Analogue Scale; GSE = General Self-Efficacy Scale; MFIS = Modified Fatigue Impact Scale; MBI = Modified Barthel Index; CRIES-13 = Children's Revised Impact of Event Scale – 13 items; SCAS = Spence Children's Anxiety Scale; CAMM = Child and Adolescent Mindfulness Measure; EDA = electrodermal activity; STCI = State-Trait Cheerfulness Inventory; MOAS = Modified Overt Aggression Scale; AVL-AV = Aggression Questionnaire – Agressievragenlijst – Short Version; FA = focus attention meditation; Proprietary alg. = proprietary, undisclosed algorithm in wearable devices.

Figure 7. *Feedback Modalities Distribution.*



Concerning the EEG-based oscillations targeted or generating the feedback across the included studies, the most frequently trained frequency ranges comprised the theta band (4–7.5 Hz), the alpha band (8–12 Hz), the sensorimotor rhythm (SMR, 12–15 Hz), and the beta band (13–30 Hz). These frequency ranges served as the basis for both single- and multiband training protocols. In addition to single-band approaches (18%), an equivalent proportion of studies (18%) employed combined training of multiple bands, a common clinical and research practice aimed at achieving broader neuromodulatory effects.

Approximately 20% of the studies implemented combined protocols that trained alpha and theta concurrently, a configuration often selected due to its association with relaxation and internal attention (Dobrakowski et al., 2020). For instance, Salminen et al. (2024) applied a protocol that simultaneously increased alpha and theta activity, which was associated with enhanced deep relaxation and introspection. Similarly, E. Lee et al. (2024) adopted a protocol that increased alpha and theta power while inhibiting high beta activity (21–30 Hz), aiming to reduce cortical hyperactivity—a phenomenon frequently linked to anxiety, stress, and mental agitation (Lin et al., 2021). In contrast to these multiband designs, other studies focused on the modulation of a single oscillatory band to examine more specific neural mechanisms. For example, Choi et al. (2024) and Soriano et al. (2024) investigated isolated modulation of alpha activity, whereas Brandmeyer and Delorme (2020) targeted frontal midline theta.

SMR and beta protocols were identified in 11% of studies, particularly in applications related to attention and performance enhancement. Mikicin et al. (2015), for example, applied SMR- and beta-based training to optimize cognitive and physical performance in athletes, while Gadea et al. (2020) reported improvements in sustained attention, reductions in anxiety, and benefits for sleep quality.

Notably, A large majority of the analyzed studies (78%) used wearable devices with proprietary algorithms, such as Muse, Emotiv, and other commercial headsets. These systems provide feedback based on automated classifications of mental states (e.g., attention, relaxation, meditation) without explicitly reporting the brain frequencies involved in signal processing. This lack of transparency regarding the targeted frequency bands limits comparability across studies and obscures understanding of the underlying neural mechanisms being trained.

Alongside the neurofeedback parameters, the included studies also varied in the meditation practices implemented, with a majority focusing on breath-focused attention practices (62%), either in isolation or combined with awareness of bodily sensations. Some of these protocols also incorporated guided imagery (Hwang et al., 2017) or fixation on external points (Salminen et al., 2024).

Mindfulness-based practices were also highly represented (22%), generally defined as cultivating nonreactive awareness of the present moment. (Zhang et al., 2021). Within this category, interventions frequently drew upon standardized clinical frameworks, including mindfulness-based stress reduction (MBSR; P. Wang et al., 2023) and mindfulness-based relapse prevention (MBRP) for relapse prevention (Chiu et al., 2024). The body scan technique was another recurring component

across multiple studies. (He et al., 2023; Salminen et al., 2024; Tarrant et al., 2022).

Less common but theoretically relevant approaches together accounted for 11% of the protocols. Among them were compassion-based meditations, such as Open Heart meditation (Tarrant & Cope, 2018; Viczko et al., 2021), as well as specific traditional techniques like Trataka (Nieto-Vallejo et al., 2021), and Sophrology (Gu & Frasson, 2017).

Across the included studies, both the number and duration of neurofeedback and meditation sessions varied substantially. On average, intervention protocols comprised 16.5 sessions, with a mean session duration of 17.9 min. Protocols range was wide, extending from single-session protocols to programs comprising more than 50 sessions. Session durations also show heterogeneity, varying from 1.5 to 80 min. As illustrated in Figure 8, single-session protocols were the most common (*n* = 13). Longer interventions were less frequent, with only two studies reporting between 30 and 40 sessions: Bhayee et al. (2016), which implemented a minimum of 32 sessions, and Smarinsky et al. (2023), which applied 33 sessions. Four studies reported more than 40 sessions, namely Hawley et al. (2021) and Motolese et al. (2023), both with 56 sessions; P. Wang et al. (2023) with 40 sessions; and Polich et al. (2020) with 42 sessions. Notably, among these longer interventions, the only study that did not employ home-based wearable devices was P. Wang et al. (2023). All other studies in this group allowed participants to complete sessions within their own environments using wearable devices.

Figure 9 illustrates the distribution of sessions lengths across studies. The majority of protocols employed short sessions within 1–10 min (*n* = 15) and 10–20 min (*n* = 18) range. These data indicate a predominant trend toward short-duration protocols in the literature.

To evaluate the effects of these combined meditation and neurofeedback interventions, the included studies employed a range of assessment instruments encompassing psychological, cognitive, physiological, and qualitative measures.

A clear predominance of standardized psychometric measures targeting stress, anxiety, depression, and mindfulness was identified. Frequently used scales included the Perceived Stress Scale (PSS; Cohen et al., 1983), State–Trait Anxiety Inventory (STAI; Spielberger et al., 1983), Beck Depression Inventory (BDI; Beck et al., 1988), Beck Anxiety Inventory (BAI; Beck et al., 1988) and Five Facet Mindfulness Questionnaire (FFMQ; Baer et al., 2006), indicating primary evaluation goals centered on reducing psychological distress and enhancing emotional self-regulation.

Many studies incorporated complementary measures of attention, cognitive performance, and physiological variables, including the Stroop Task (Stroop, 1935), Digit Span (Wechsler, 2008), and the Continuous Performance Test (Conners, 1995). Additional neurophysiological assessments included heart rate variability (HRV) and electroencephalography (EEG), in traditional EEG, quantitative EEG (qEEG), and standardized low-resolution electromagnetic tomography (sLORETA) modalities.

Figure 8. *Session Counts of Included Studies.*

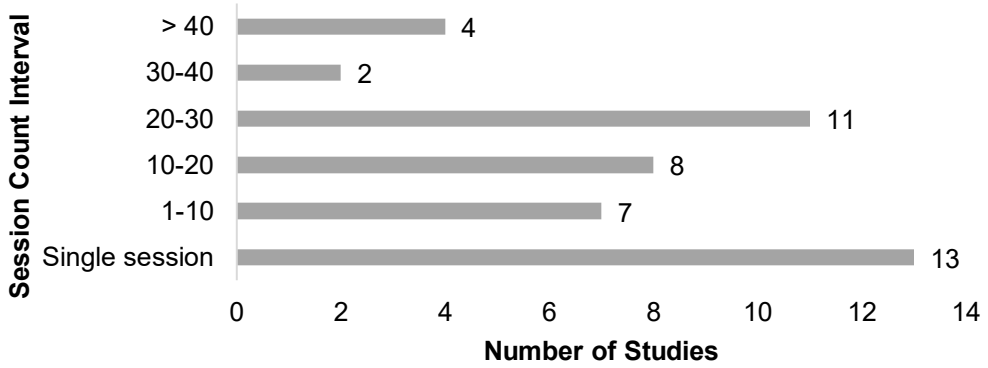
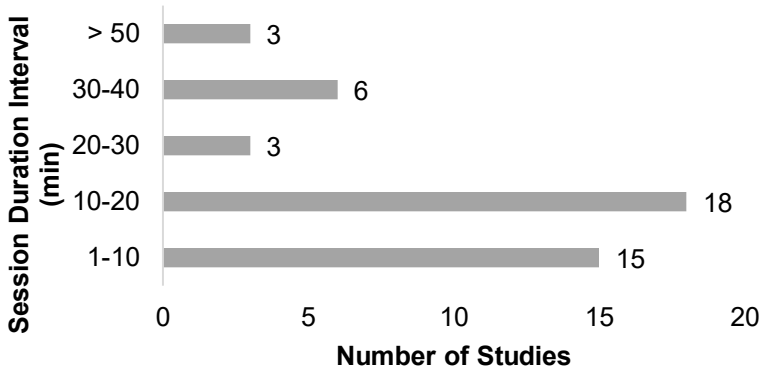


Figure 9. *Session Duration of Included Studies.*



Qualitative instruments such as interviews, diaries, and observations were used to capture subjective experience. For example, Antle et al. (2018) applied mixed methods to examine combined techniques among girls living in poverty and with trauma histories.

Most studies using wearable neurofeedback devices employed them for both intervention and outcome assessment. The Muse headset (InteraXon Inc.) was most frequent (*n* = 23), with metrics such as percent calm (%Calm) used as indicators of meditation or neurofeedback effects (Acabchuk et al., 2021; Balconi et al., 2019; Bhayee et al., 2016). Muse represented only one option, alongside devices with proprietary parameters and algorithms, including Neuroharmony M (Neuroharmony Ltda., Brazil) used by Choi et al. (2024), Emotiv EPOC (Emotiv Inc., San Francisco, CA, USA) used by Gu & Frasson (2017), and MindWave (NeuroSky Inc., San Jose, CA, USA) used by Nieto-Vallejo et al. (2021). Despite advantages of portability, accessibility, and easy integration in clinical and home settings, these devices raise methodological and epistemological concerns due to algorithmic opacity and limited specification and control of electrophysiological parameters (Acabchuk et al., 2021).

Only 10 studies conducted EEG analyses with traditional high-density systems using 32, 64, or 128 channels (Brandmeyer & Delorme, 2020; Chen et al., 2021; Soriano et al., 2024; van Lutterveld et al., 2017), which allow rigorous control of variables such as impedance, signal-extraction parameters, and filtering (Sharma & Meena, 2024). These capabilities exceed the simplified metrics of wearables devices and support more robust inferences about neurobiological mechanisms underlying the interventions (Cahn & Polich, 2006).

Taken together, these methodological choices reveal an emphasis on psychometric and neurophysiological assessments aimed at capturing both subjective and objective indicators of the effects of meditation combined to neurofeedback. However, the diversity of instruments and analytical approaches complicates direct comparisons across studies.

To provide an overview of the general findings across the 45 studies included in this systematic review, and to contextualize how these measures translate into empirical evidence, we present below a synthesis of the main results observed, together with illustrative examples drawn from a selection of representative studies. The summarized outcomes were organized into three categories, specifically, according to emotional–mood, cognitive, and meditative domains.

The emotional and mood outcomes include anxiety, fatigue, depression, somatic symptoms, and emotional reactivity. The cognitive outcomes focus on attention, memory, and executive functions. The indicators of the meditative domain include quality, depth, and engagement of practice. These categories synthesize most findings; comprehensive details for all included articles can be consulted in Table 5.

As noted in Figure 5, among the 45 studies included, 19 primarily assessed emotional and mood outcomes. Overall, combined techniques showed potential to improve these domains, although effects varied according to the protocol and participant

profile. For illustration, some representative studies are described below.

Consistent with Acabchuk et al. (2021), both the Muse (n = 25) and app-only (n = 27) groups showed significant improvements in mental health (DASS-21; d = 0.78 and 0.74, p < .001) and mindfulness (MINDSENS; d = 0.83, p < .001). EEG measures ("bird count" and "percent time calm") showed no change in the Muse group but decreased in the App group (bird count: d = −0.60, p < .001; percent time calm: d = −0.36, p < .01). EEG scores were strongly intercorrelated (r = 0.90, p < .01) but unrelated to mindfulness or mental health. Similarly, Bhayee et al. (2016) reported that neurofeedback-assisted mindfulness training (N-tsMT) led to specific improvements compared to the control group, including faster Stroop reaction times (Z = 3.29, p < .001, r = 0.65) and reduced somatic symptoms on the BSI (Z = 2.81, p = .004, r = 0.55), although no significant changes were detected in depression or anxiety factors. Attention gains correlated with symptom reductions, $r(24)$ = 0.44, p = .024; and higher neuroticism predicted greater improvement, $r(11)$ = −0.70, p = .007. The N-tsMT group also reported feeling calmer, $t(36)$ = 2.16, p = .04; and greater body awareness, $t(36)$ = 2.03, p < .05.

Chen et al. (2021) found that clinical status influenced participants' responses to the frontal alpha asymmetry protocol. After the intervention, a significant increase in mean power of alpha, theta, and gamma waves was observed across all participants. For anxious subjects, the results were $F(1, 338) = 127.65$, $p = 2.50 \times 10^{-25}$ (alpha); $F(1, 338) = 110.84$, $p = 1.31 \times 10^{-22}$ (theta); and $F(1, 338) = 633.73$, $p = 1.66 \times 10^{-79}$ (gamma). For healthy subjects, the corresponding values were $F(1, 338) = 9.93$, $p = 0.0017$; $F(1, 338) = 9.78$, $p = 0.0019$; and $F(1, 338) = 77.13$, $p = 8.13 \times 10^{-17}$, respectively. In the randomized controlled trial by E. Lee et al. (2024), the experimental group showed a significant reduction in stress (PSS: M = 25.85, SD = 4.97 to M = 19.40, SD = 4.56; p < .001), while the control group changed from M = 24.22, SD = 5.17 to M = 21.22, SD = 4.60 (p = .037 between groups). State anxiety decreased more in the experimental group (M = 11.95, SD = 10.46 vs. M = 6.50, SD = 7.69; p = .078). Both groups improved in depression, insomnia, trait anxiety, sleep quality, and quality of life (p < .05), with no significant between-group differences. No significant changes were observed in physiological indicators, and only the alpha band in qEEG showed a significant effect ($\chi^2 = 10.64$, p = .031).

In the study by Viczko et al. (2021), both experimental and control groups showed an increase in positive mood and a reduction in negative mood, with significant effects for happiness (p < .001), calmness (p < .001), depression (p < .001), tension (p < .001), and fatigue (p = .013). EEG analysis revealed increased frontal alpha activity (p = .008) and decreased gamma activity (p = .029), as well as elevated alpha and beta power in midline and parietal regions (p < .01).

Several studies focused on cognitive functions, exploring combined techniques to enhance attention, working memory, and cognitive regulation. In general, the evidence suggests beneficial but variable effects across cognitive domains. To illustrate these tendencies, a few examples are presented below. Results generally indicated improvements in cognitive performance and neurophysiological modulation, although not all domains showed significant effects. In Brandmeyer and Delorme (2020), the neurofeedback group showed a significant increase in FMθ power (44.62 dB) compared to the control group (44.35 dB), with a significant session correlation (r^2 = 0.49, p = .05) that became stronger after excluding nonresponders (r^2 = 0.85, p = .001). Significant effects were observed in the FMθ (3.5–6.5 Hz), low alpha (9–10 Hz), and beta (12–18 Hz) bands (p < .05). In the n-back task, the neurofeedback group demonstrated faster reaction times and increased gamma power over frontal midline and left temporoparietal regions (p < .01), effects not observed in the control group. Additionally, the association between neurofeedback and reduced mind-wandering was highlighted by Hunkin et al. (2021b), who found that the "Muse mind-wandering index" showed high internal consistency (Cronbach's α = 0.95) and was sensitive to attentional lapses within participants during the breath-counting task, with significant differences between correct, incorrect, and reset counts (miscounts: B = 2.84, p = .003; resets: B = 4.73, p < .001; δW = 0.56). Across participants, mean "Muse mind-wandering" was negatively correlated with the proportion of correct counts (r = −0.50, p = .002) and positively correlated with resets (r = 0.47, p = .004). The association with self-reported mind-wandering was minimal (rw = .01; rb = .11).

In elementary school children, Vekety et al. (2022) observed that the mindfulness + NF group showed significant differences in executive functions and brain activity compared to the control group. Specifically, improvements were observed in Stroop task accuracy, $F(1, 21) = 5.43$, p < .05; reductions in

errors on the Hearts and Flowers task, $F(1, 23) = 5.35$, $p < .05$; and increased theta and alpha power during eyes-open resting-state conditions with theta: $F(1, 18) = 7.09$, $p < .05$; and alpha: $F(1, 18) = 5.80$, $p < .05$). A positive correlation was found between changes in theta activity and reaction time ($r = 0.54$, $p = .03$). Additionally, there was a linear increase in calm/focused brain states, $F(1, 14) = 5.67$, $p = .03$; and in recovery from mind-wandering episodes, $F(1, 14) = 52.07$, $p < .001$.

Studies examining effects on meditation quality generally indicated potential to enhance attentional states, meditative depth, and neural pattern regulation, albeit with some limitations. To illustrate these general trends, selected studies are summarized below. Hunkin et al. (2021a) found that neurofeedback during the breath-counting meditation task was associated with greater attentional focus and reduced mind-wandering. Specifically, auditory feedback was associated with a 15% higher rate of correct breath counts ($RR = 1.15$, $p = .056$), a 41% lower rate of count resets ($RR = 0.59$, $p < .001$), and a 4.15-unit reduction in device-measured mind-wandering ($d = −0.22$, $p = .006$), with no significant correlation observed for recovery measures ($d = −0.11$, $p = .270$). Auditory feedback was also correlated with reduced subjective reports of calmness ($d = −0.83$, $p = .008$) and sleepiness ($d = −0.49$, $p = .016$).

Kosunen et al. (2016) observed that the combined use of a head-mounted display (HMD) and neurofeedback resulted in higher scores for relaxation, meditative depth, and sense of presence compared to the control condition (screen without feedback). In the Meditation Depth Questionnaire (MEDEQ), significant differences were observed for the factors Hindrances ($p < .01$), Relaxation ($p < .05$), Personal Self ($p < .01$), Transpersonal Qualities ($p < .01$), and Transpersonal Self ($p < .05$). No statistically significant differences were found between the HMD condition with and without neurofeedback ($p > .05$). In the same direction, Salminen et al. (2024) found that use of the HMD resulted in a significantly higher sense of presence compared to the computer screen ($p < .001$), and the neurofeedback condition further increased this effect ($p = .011$). Meditation depth was greater when using the HMD ($p < .001$). Frontal theta (4–6 Hz) power was higher with neurofeedback on than off ($p = .048$), while no significant differences were found for whole-head alpha (8–13 Hz) activity. Gamma (30–45 Hz) activity was significantly higher during HMD use ($p < .001$) and with neurofeedback activated ($p = .001$). The point-focus meditation condition elicited greater frontal theta activation ($p = .004$), whereas the body-scan meditation condition produced higher whole-head gamma activity ($p = .005$).

Soriano et al. (2024) revealed a significant main effect of training condition on absolute alpha power (8–14 Hz), $F(1, 30) = 10.49$, $p < .001$, $\eta^2 = 0.001$, with higher alpha power during the upregulation condition ($M = 4.14 \times 10^6$ μV², $SD = 2.25 \times 10^5$) compared to the downregulation condition ($M = 3.96 \times 10^6$ μV², $SD = 2.32 \times 10^5$). Regardless of training type (up- or downregulation), a general posttraining decrease in alpha power was observed (pre: $M = 4.63 \times 10^6$ μV²; post: $M = 4.17 \times 10^6$ μV²), $F(1, 30) = 6.70$, $p = .01$. These findings, together with the broader set of studies included in the review, suggest consistent yet context-dependent effects of combined mindfulness and neurofeedback interventions, with the full set of results detailed in Table 5.

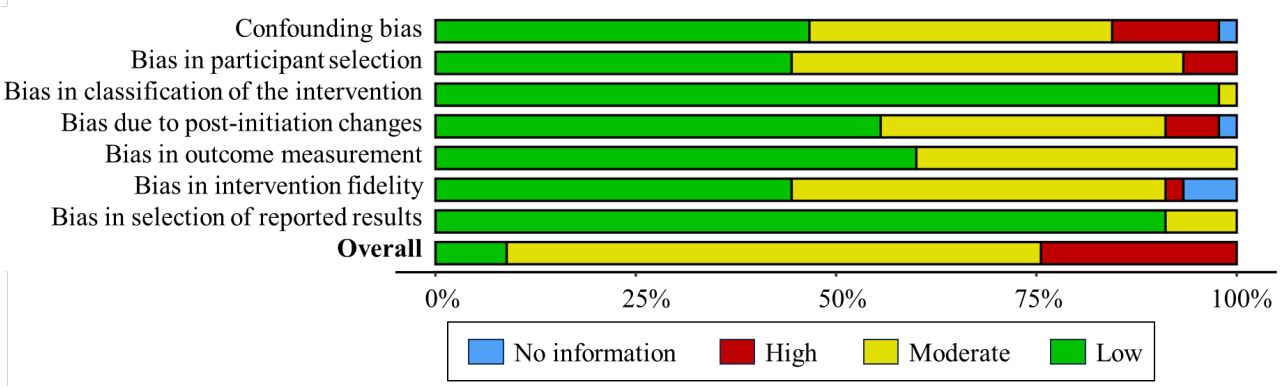
Risk of Bias

Risk of bias was assessed in accordance with PRISMA (Page et al., 2021) and guided by the Cochrane Handbook chapter “Assessing risk of bias in a nonrandomized study” (Sterne & Higgins, 2023). The first four authors independently evaluated the risk of bias across seven domains: (D1) bias due to confounding; (D2) bias in participant selection; (D3) bias in classification of the intervention/exposure; (D4) bias due to post initiation changes; (D5) bias in outcome measurement; (D6) bias in intervention fidelity; and (D7) bias in selection of reported results.

To facilitate visualization, the risk of bias across the seven assessed domains is summarized in Figure 10. The figure presents ratings for each domain as low risk (green), moderate risk (yellow), high risk (red), or no information available (blue). Visualizations were generated using the Risk-of-Bias VISualization tool (robvis; McGuinness & Higgins, 2021). Any discrepancies were resolved by consensus following discussion among the authors.

For bias in classification of the intervention (D3), most studies provided detailed descriptions of procedures and techniques, ensuring clear intervention characterization. With rare exceptions, protocols were explicitly reported, supporting comprehension and replicability (Bhayee et al., 2016; Brandmeyer & Delorme, 2020; Ghosh et al., 2023). Similarly, for bias in selection of reported results (D7), studies generally reported prespecified outcomes, with no clear indications of practices such as p-hacking, thereby maintaining transparency and

Figure 10. *Summary of Risk of Bias.*



integrity in reporting (E. Lee et al., 2024; Schuurmans et al., 2021).

By contrast, bias in selection of participants (D2) emerged as a critical issue. In some studies, inclusion and exclusion criteria were not clearly defined (Kosunen et al., 2016; Salminen et al., 2024), and convenience sampling frequently prevailed without robust justification, thereby limiting external validity (Smarinsky et al., 2023; Tarrant & Cope, 2018). A similar pattern was observed for bias due to confounding (D1), where key limitations included incomplete information on clinical history (Antle et al., 2018; Bhayee et al., 2016; Mikicin et al., 2015) and prior meditation experience (Smarinsky et al., 2023; Vekety et al., 2022; P. Wang et al., 2023), both fundamental to interpretation and generalization.

For bias in outcome measurement (D5), the principal weakness was the absence of blinded assessment procedures. As previously noted (Table 4), only 10 of 45 studies implemented any blinding, potentially compromising measurement objectivity. Additionally, the recurrent use of wearable devices as the primary evaluation method may introduce inaccuracies in quantifying observed effects.

Finally, for bias related to intervention fidelity (D6), there was limited standardization and insufficient monitoring of practice quality (Polich et al., 2020; Rolbiecki et al., 2023; van der Schoot et al., 2024). The predominance of home-based interventions using wearable devices, while increasing participant autonomy, introduces confounding variables outside experimental control. Some studies employed follow-up strategies, such as logging sessions via device-integrated apps; nonetheless, gaps persisted in controlling the practice environment. Scarce information on provider training or qualifications in technique delivery may also directly affect intervention consistency and efficacy (Soriano et al., 2024; Svetlov et al., 2019; Vekety et al., 2022; Viczko et al., 2021).

Discussion

This systematic review provides a comprehensive overview of the current literature on combining meditative practices and neurofeedback. Overall, the field is expanding but remains methodologically immature. A major challenge remains the marked heterogeneity in designs, protocols, and measurement instruments, which compromises comparability across studies and hinders the consolidation of robust empirical evidence.

Across the reviewed literature, several convergent themes emerge, such as methodological limitations, thematic focus, diversity of meditation types and neurofeedback protocols, and the observed spectrum of effects. Rather than treating these as separate blocks, the following synthesis integrates them to highlight cross-cutting patterns and research gaps.

Methodological and Sampling Constraints

A recurring challenge is the predominance of studies conducted in high income countries in the Northern Hemisphere, which restricts external validity and overlooks cultural variation that shapes both meditation practice (Buric et al., 2022) and response to neurofeedback (Wood & Kober, 2018). This pattern exemplifies the critique of Western, Educated, Industrialized, Rich, Democratic (WEIRD) samples described by Henrich et al. (2010). The scarcity of research in Latin American contexts is particularly critical, as social inequality, cultural

diversity, and heterogeneous economic conditions decisively influence adherence and protocol effectiveness (Migeot et al., 2024; Nagy et al., 2022). Progress in this matter requires not only greater international collaboration but also the cultural adaptation of both intervention and assessment methods.

Three methodological limitations stand out. First, the predominance of active controls, though informative, complicates the identification of specific versus nonspecific intervention effects (Kober et al., 2018). Second, blinding strategies are scarce: only 10 of 45 studies implemented any blinding, exposing results to expectation bias (Patel et al., 2020; Voigt et al., 2024). Third, placebo conditions are rarely used, with Brandmeyer and Delorme (2020) providing the only randomized double-blind trial with a sham condition. Studies combining active and sham conditions (e.g., Min et al., 2023) offer a more promising avenue, as they help to disentangle the contribution of each element.

Another critical issue is the mismatch between intervention length and the nature of the techniques. Given that both meditation (Basso et al., 2019; Brandmeyer et al., 2019) and neurofeedback (Domingos et al., 2021; Esteves et al., 2021) demand gradual training and sustained engagement, short or single-session protocols risk reducing ecological validity and underestimating the interventions' potential.

Thematic analysis indicated a concentration on anxiety, mood, and stress disorders, addressed in 19 of 45 articles. Within this category, studies range from daily stress to more complex conditions such as burnout and depression (Balconi et al., 2019; Ghosh et al., 2023). Other investigations examined cognitive performance and attention regulation, including executive functions such as attentional control, impulsivity, and working memory (Brandmeyer & Delorme, 2020; Hunkin et al., 2021b; van der Schoot et al., 2024; Vekety et al., 2022). Less frequently, research explored neurological conditions, specific psychiatric disorders, meditative states, adaptive needs, and sports performance (Choi et al., 2024; Kosunen et al., 2016; McMahon et al., 2021; Mikicin et al., 2015; Motolese et al., 2023). This diversity underscores the heterogeneity of applications in the field.

The variety of meditation practices further complicates synthesis, as they have distinct goals and specific neurophysiological effects. Focused attention practices typically increase alpha and beta activity, aiming to strengthen attentional regulation and cognitive control (Salminen et al., 2024; Zhang et al., 2021), while deeper or open-monitoring practices engage theta oscillations associated with relaxation and affective integration (Hwang et al., 2017; Tarrant et al., 2022). Likewise, mindfulness and body scan, which emphasize full awareness and interoceptive perception, display neurophysiological profiles that differ from compassion-based approaches such as Open Heart meditation or from visual practices such as Trataka (Gu & Frasson, 2017; Nieto-Vallejo et al., 2021; Viczko et al., 2021). Such diversity enriches the field but reinforces the need for clear conceptual distinctions and standardized outcome definitions to compare effects across modalities.

Similarly, neurofeedback protocols targeted distinct frequency bands, most often targeted theta 4–8 Hz, alpha 8–12 Hz, sensorimotor rhythm (SMR) 12–15 Hz, and beta 13–30 Hz because of their links to attention, emotional regulation, and self-regulation (Brandmeyer et al., 2019; Cahn & Polich, 2006; Dobrakowski et al., 2020). For example, protocols that increase alpha or theta aim to modulate relaxation or attentional focus (Choi et al., 2024; Soriano et al., 2024). In turn, combined approaches, such as increasing theta and reducing high beta, appear particularly effective for stress and mood modulation (E. Lee et al., 2024; Salminen et al., 2024); while SMR and beta training appear relevant to cognitive performance, emotional regulation, and sleep improvement (Chiu et al., 2024; Gadea et al., 2020; Mikicin et al., 2015).

A notable trend is the widespread use of commercial devices such as Muse and Emotiv (Chiu et al., 2024; Dobrakowski et al., 2020). Although these devices expand access to neurofeedback training and facilitate data collection in nonlaboratory settings, they raise concerns about transparency and scientific rigor (Acabchuk et al., 2021). Their proprietary architectures typically restrict access to raw EEG data and rely on closed-source algorithms that infer mental states such as relaxation or attention through internal classifications that are seldom disclosed. This opacity limits the reproducibility of findings and hinders precise interpretation of the underlying neurophysiological mechanisms (Flanagan & Saikia, 2023). In contrast, multichannel systems with full control of training parameters and complete metric access enable more accurate control of artifact removal, impedance levels and frequency-band targeting while also providing higher spatial resolution, supporting fine-

grained topographic and functional analyses of cortical activity (Sharma & Meena, 2024).

Importantly, neurofeedback protocol design should consider not only trained frequency bands but also be aligned with the meditation technique employed, ensuring that trained frequency bands correspond to the attentional, emotional, and interoceptive processes cultivated in practice. Thus, not merely combining meditation and neurofeedback but integrating them within a synergistic framework of self-regulation and awareness.

Observed Effects and Future Perspectives

Across studies, effects clustered around three outcome axes: emotional, cognitive, and meditative. Emotional outcomes were most consistent, showing reductions in anxiety, stress, and depression, especially in vulnerable populations (Acabchuk et al., 2021; Antle et al., 2018; Chen et al., 2021; E. Lee et al., 2024). Cognitive improvements included enhanced working memory, attention, and inhibitory control (Brandmeyer & Delorme, 2020; Hunkin et al., 2021b; Vekety et al., 2022), often accompanied by increases in frontal theta and gamma power. Meditative outcomes reflected deepened meditative experience associated with modulations in alpha, theta and beta bands (Hunkin et al., 2021a; Kosunen et al., 2016; Salminen et al., 2024).

The results indicate that the most consistent benefits were observed in emotional outcomes, particularly among participants with higher baseline vulnerability (Chen et al., 2021; E. Lee et al., 2024). Protocols that increased alpha and theta activity and reduced high beta were associated with decreases in stress, anxiety, depression, and insomnia, as well as higher satisfaction with the interventions (E. Lee et al., 2024). Nonetheless, the lack of intergroup changes in biomarkers and electrophysiological parameters suggests that improvements may have been primarily reflected in subjective and behavioral measures. This trend aligns with the general pattern observed across studies, in which emotional and self-reported indicators showed more stable improvement than physiological markers.

Across the reviewed literature, studies combining meditation and neurofeedback reported positive changes in emotional, cognitive, and neurophysiological variables, although effect sizes and consistency varied depending on protocol characteristics and participant profiles (Acabchuk et al., 2021; Bhayee et al., 2016; Brandmeyer & Delorme, 2020; Vekety et al., 2022; Viczko et al., 2021). Reductions in stress, anxiety, fatigue, and depression were accompanied by improvements in attention, executive functioning, and body awareness. EEG findings commonly showed increased alpha and theta activity, patterns related to relaxation and calmness, and decreases in gamma power, associated with alertness (Salminen et al., 2024; Viczko et al., 2021). Despite these convergences, results regarding physiological and mindfulness-related measures were not uniform, as indicated by the absence of transfer effects in some studies (Soriano et al., 2024). However, results varied according to task, context, and participant profile, limiting comparability and generalization of findings. Moreover, the scarcity of follow-up assessments and the limited evidence of transfer to everyday contexts further constrain the ecological validity of the observed effects.

Risk of bias assessment indicated modest progress in transparency of intervention and results, but persistent weaknesses in sampling, control conditions and blinding, reducing validity and objectivity. Low standardization and insufficient monitoring of interventions further compromise result consistency.

Final Considerations

To strengthen evidence quality, future studies should adopt randomized controlled trials with sham control (placebo) and blinding of participants and or assessors, accompanied by preregistration and a priori sample size estimation. Protocols must report, in verifiable detail, both the procedure and the neural target (e.g., alpha uptraining at the right parietal region P4), specify the feedback type, and describe artifact handling procedures, in accordance with the neurofeedback best practice checklist (Ros et al., 2020). Whenever possible, multichannel systems that allow access to raw EEG signals should be prioritized. When consumer devices are used, studies must rely on devices already validated against well-established laboratory equipment and clearly document the algorithms employed and the quality of the acquired signals. Only under these conditions can effects on underlying neurophysiological mechanisms be inferred with greater precision.

Studies should state the meditation modality employed (e.g., focused attention, open monitoring, compassion, or body scan) and align neurophysiological hypotheses with training objectives, since effects can vary substantially across techniques (Cahn & Polich, 2006).

Regarding samples and outcomes, larger multicenter studies incorporating geographic and cultural diversity are recommended, avoiding exclusive reliance on western, educated, urban populations. Cultural adaptation of materials should be ensured, along with detailed reporting of age, gender, and contextual variables. Outcomes should integrate emotional, cognitive, and meditation practice indicators together with neurophysiological markers. In addition, mediator and moderator analyses (e.g., adherence, motivation, prior experience) should be prespecified. Finally, longitudinal investigations with higher ecological applicability are needed to assess effect durability and transfer to everyday life.

Author Declaration

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Role of Therapeutic Currents on Hand Function in People with Stroke: A Systematic Review and Meta-Analysis

Shifa Fatima, Sarah Parveen, Chhavi Arora Sehgal, Majumi M. Noohu, and Muhammad Azharuddin*

Centre for Physiotherapy and Rehabilitation Sciences, Jamia Millia Islamia, New Delhi, India

Abstract

Proper upper limb (UL) function is very crucial for manual exploration and manipulation of the environment. Dexterity is affected after stroke and takes times to recover. Effective and economical treatment approaches are desired to overcome the numerous challenges associated with UL rehabilitation. This review aims at establishing the effectiveness of various therapeutic currents on hand function in individuals with stroke. A search was conducted in three databases for randomized controlled trials published from inception to November 2024. The methodological quality of the included studies was measured by the PEDro scale. Cochrane risk-of-bias tool for randomized trials (RoB 2) was used to assess the risk of bias. Meta-analysis was performed on the studies providing sufficient and complete data. The search identified 334 records from which 12 records met the eligibility criteria. The average PEDro score was 6.92. Majority of the trials presented with low risk of bias. Meta-analysis of functional electrical stimulation (FES) showed no significant effects of FES on dexterity (SMD = 2.03, $Z = 1.81$, $p = .07$). Meta-analysis of FES trials identified a small effect size which, while not significant, warrants further investigation. Large and more robust trials are needed with larger sample size to draw more definite conclusions.

Keywords: electric stimulation; stroke; upper extremity; hand function

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***Address correspondence to**: Sarah Parveen, Centre for Physiotherapy and Rehabilitation Sciences, Jamia Millia Islamia, New Delhi 110025, India. Email: sarahjmi880281@gmail.com

Edited by:
Rex L. Cannon, PhD, Currents, Knoxville, Tennessee, USA

Reviewed by:
Rex L. Cannon, PhD, Currents, Knoxville, Tennessee, USA
Genomary Krigbaum, PsyD, GK Wellness Consulting Services, Riverton, Wyoming, USA

Introduction

Stroke has been identified as the major cause of disability and the second leading cause of death in the world (Katan & Luft, 2018). Spasticity and weakness are primary motor impairments, and they offer serious problems to patient management (Li, 2017). In addition, people with stroke also present seizures (Kammersgaard & Olsen, 2005), emotional lability (Chohan et al., 2019), urinary incontinence (Patel et al., 2001), pain (Chohan et al., 2019), depression (Hackett et al., 2005), and cognitive impairment (Chohan et al., 2019). Stroke also has a major impact on mobility (Hankey, 2003). Motor deficits affecting the upper limb are persistent and disabling (Lai et al., 2002). After 6 months, only 50% of stroke survivors regain upper limb function (Kwakkel et al., 2003). The impairment is very bothersome as proper hand function is requisite for manual exploration and manipulation of the surrounding environment (Fischer et al., 2007).

The hand is a versatile element of the body. It can apply force and manipulate delicate items. It also plays a vital role in verbal communication and serves as a tactile interface that links the body to its environment. About 45% of all activities of daily living (ADL) performed during the day involve hand function (Lucareli et al., 2010). Independent figure movement—which is considered as the primary indicator of manual dexterity—takes time to recover following a stroke. Damage to cerebellum, subcortical structures, and sensory and motor areas of the brain leads to motor impairment, which in turn affects dexterity and coordination between arms, hands, and fingers (Pollock et al., 2014).

Effective and inexpensive approaches are desired which can focus on ecologically valid goal setting with increasing challenges. For the recovery of the upper limbs in chronic stroke patients, a range of different therapies has led to satisfactory results (Lang & Schieber, 2009). The available research emphasizes the need for interdisciplinary and multimodal approaches in the rehabilitation of the paretic hand (Hlustík & Mayer, 2006). Current rehabilitation emphasizes the centrally initiated mechanism of motor learning training defined as the acquisition or modification of movement through practice in addition to the peripherally initiated electrical stimulation to enhance excitability (Holden, 2005; Krakauer, 2006).

To date, research done to investigate the role of therapeutic current in stroke rehabilitation includes the effectiveness of functional electrical stimulation (FES) mobility, hand function, and foot drop (Akter et al., 2023; Dantas et al., 2023; Mijic et al., 2023); neuromuscular electrical stimulation (NMES) for functional connectivity (Crema et al., 2022; Guo et al., 2022; Yang et al., 2018); unilateral/bilateral transcutaneous electrical nerve stimulation (TENS) for upper limb motor recovery and mobility (Chen et al., 2022; Namsawang & Muanjai, 2022; Senarath et al., 2023); efficacy of transcranial direct current stimulation (tDCS) for dysphagia and upper limb motor function (Bengisu et al., 2024; Garrido et al., 2023); and repetitive transcranial magnetic stimulation (rTMS) for pain (Aydın et al., 2024; Du et al., 2019). In addition, NMES (Crema et al., 2022; Huang et al., 2021; Park, 2020), tDCS (Bolognini et al., 2020; Garrido et al., 2023; Morone et al., 2022), FES (Huang et al., 2021; Y.-S. Kim et al., 2023), and rTMS are several promising treatment options available for the rehabilitation of upper limbs in people with stroke. Systematic reviews and meta-analysis have been done investigating the effect of FES (Eraifej et al., 2017), noninvasive brain stimulation (Ahmed et al., 2023; Bai et al., 2019; Xie et al., 2023), and TENS (Mahmood et al., 2019). Yet, there is still lack of clarity on the effectiveness of different therapeutic currents on dexterity in people with stroke. Considering this knowledge gap, the present review aims to summarize the effect of various therapeutic currents on dexterity of people with stroke. This review also aimed to determine the short-term and long-term effectiveness of therapeutic currents on dexterity. It represents an important addition to the literature that focuses on the application of therapeutic currents on dexterity and will help in summarizing and understanding the different currents helpful in improving dexterity in people with stroke. The relative effectiveness of different currents must be known in order to choose an appropriate one. However, there is currently a dearth of thorough overview of studies in this field.

Methods

The protocol of this systematic review was registered in the International prospective register of systematic reviews (PROSPERO) via registration number CRD42021239673.

Eligibility Criteria

Studies were selected according to the eligibility criteria, which were based on the PICO (participant, intervention, comparator, and outcome) format. Studies other than randomized controlled trials (RCT) or in any other language than English were not included. Studies done on animals were excluded. Studies administering therapeutic currents (excluding brain stimulation, both invasive and noninvasive) to stroke patients aged more than or equal to 18 years in order to examine its effect on hand function were included. No restrictions were placed on the controls.

Information Sources

Electronic systematic searches of MEDLINE (accessed by PubMed), Web of Science (Web of Science Core Collection), and Scopus databases were conducted from inception to November 2024. This systematic review and meta-analysis was done following the standard Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement (Moher et al., 2009).

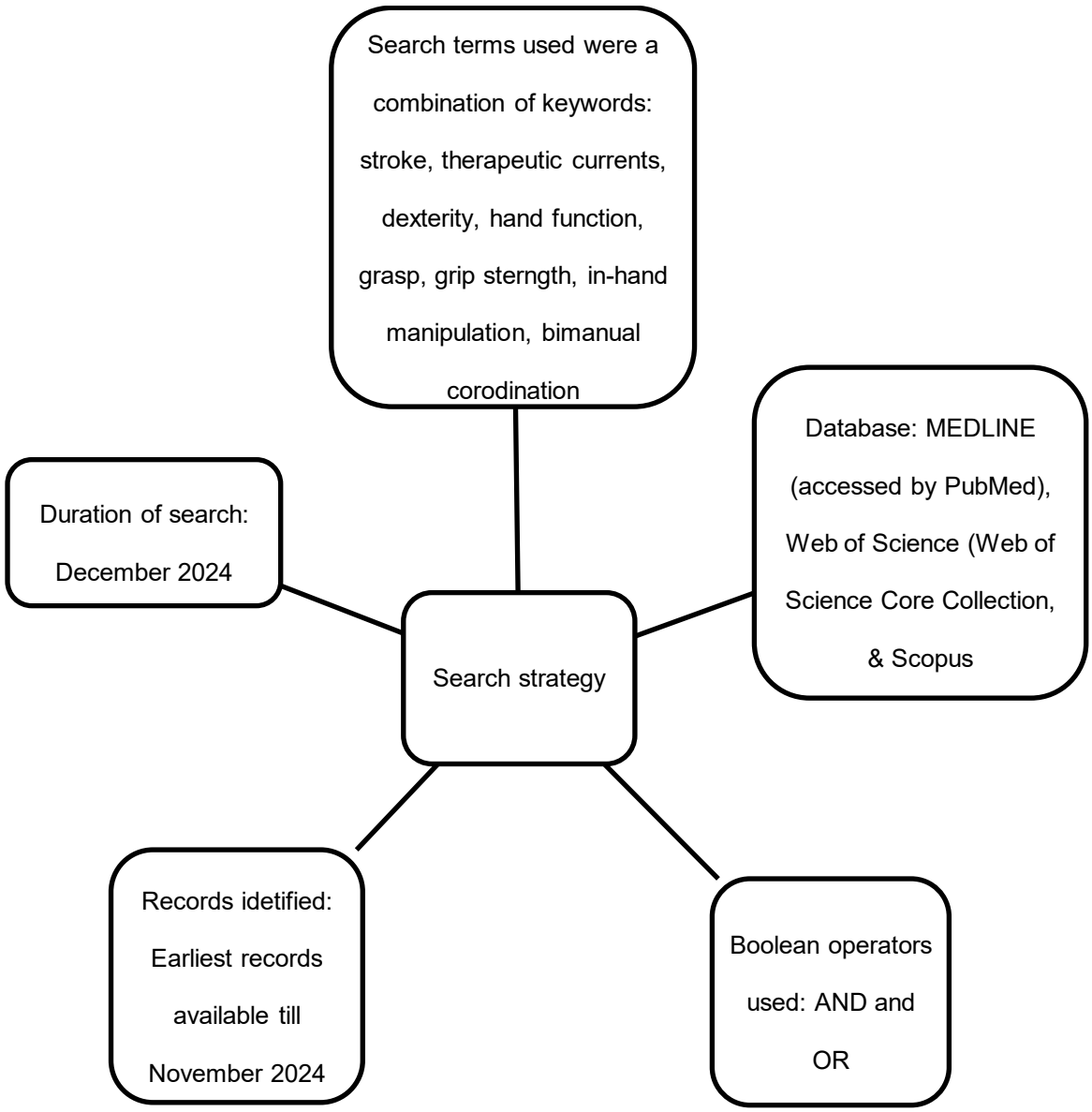
Search Strategy

One author (SP) performed the search in December 2024. A search strategy was developed that focused on the following key search terms: *stroke*, *therapeutic currents*, *dexterity*, *hand function*, *grasp*, *grip strength*, *in-hand manipulation*, and *bimanual coordination*. The keywords were combined with the Boolean operator AND and OR (Figure 1). Detailed search strategy can be seen in supplementary file attached.

Selection Process and Data Extraction

Data on the characteristics of trial author, year of publication, participants (age, gender, Brunnstrom stage), interventions (type, duration, etc.), outcome measures, and significant findings were extracted by two authors independently (SP and MA). Any disagreement was cleared by mutual consensus and unresolved disagreements were taken to the third author (MMN). In case of unclear of incomplete data in included studies, the author(s) of the study was contacted.

Figure 1. *A Schematic Presentation of Search Strategy.*



Quality Assessment of Trials

For assessing the methodological quality of all the retrieved evidence, the authors used an 11-point PEDro scale designed to rate the quality of randomized controlled trials (Verhagen et al., 1998). Each criterion was rated either *yes* (score = 1) or *no* (score = 0) to minimize the ambiguity in responses. The total score for the methodological quality of each included study was calculated by summing all the responses (maximum score = 10). Studies were then classified as poor (score of < 4), fair (score of 4 or 5), good (score of 6 to 8), and excellent (score of > 8) quality based on the total score obtained (de Morton, 2009). Trials were independently assessed for quality by two authors (CAS and SF). If there was any disagreement on any criterion, it was reassessed by each reviewer independently. Unresolved disagreements were identified and discussed in a consensus meeting. Any conflict that remained unresolved was then taken to a third reviewer (MMN), who was independent of the initial deliberations, and a final consensus was reached.

Risk of Bias Assessment

CAS and MA independently assessed risk of bias for included trials using the version 2 of the Cochrane risk-of-bias (RoB 2) assessment tool with the following domains: randomization process, deviations from the

intended intervention, missing outcome data, measurement of the outcome, and selection of the reported result. Each domain was categorized as either low, some concerns, or high (Sterne et al., 2019).

Data Synthesis and Analysis

Meta-analysis was performed for only those studies providing sufficient information on the outcome measure. The meta-analysis was performed using Cochrane Collaboration's Review Manager 5.4.1 software. Effect sizes were calculated as standardized mean differences (SMDs) using Hedge's *g*, the bias-adjusted version of Cohen's *d*, as implemented in RevMan 5.4.1. Heterogeneity between the studies was quantified using I2 test, which measures the percentage of the observed variability between effect estimates beyond chance. A value of I2 < 25% indicates low heterogeneity, 25–75% indicates moderate heterogeneity, and > 75% indicates high heterogeneity (Higgins et al., 2003).

Results

Out of the total of 334 records identified, 40 duplicates were removed. A total of 294 records went through the screening process by reading titles and abstracts by two authors (SF and SP). Twelve articles were found to be relevant based on the eligibility criteria (Figure 2).

Study Characteristics

All the studies included in this systematic review were RCT (*n* = 12). Trials included in the review were published from 2007 (Bhatt et al., 2007) to 2021 (Alwhaibi et al., 2021; Ambrosini et al., 2021; Sentandreu-Mañó et al., 2021). Included trials were conducted in various geographical areas including Taiwan (Lee et al., 2015), Korea (S.-H. Kim et al., 2016), Ohio (Knutson et al., 2016; Knutson et al., 2020), Spain (Sentandreu-Mañó et al., 2021), Brazil (Lourenção et al., 2008; Salazar et al., 2020), United States (Bhatt et al., 2007), Denmark (Ghaziani et al., 2018), France (Sattler et al., 2015), Saudi Arabia (Alwhaibi et al., 2021), and Italy (Ambrosini et al., 2021).

The included studies recruited 627 participants. The sample size ranged from 20 (Bhatt et al., 2007; S.-H. Kim et al., 2016; Sattler et al., 2015) to 102 (Ghaziani et al., 2018). A mixed ratio of both genders was observed. Studies included in this review used a variety of outcome measures to assess hand function which includes BBT (Box and Block test; Alwhaibi et al., 2021; Ambrosini et al., 2021; Bhatt et al., 2007; S.-H. Kim et al., 2016; Knutson et al., 2016; Knutson et al., 2020; Lee et al., 2015; Sentandreu-Mañó et al., 2021), functional magnetic resonance imaging (fMRI; Bhatt et al., 2007; S.-H. Kim et al., 2016), maximal voluntary grip force (Salazar et al., 2020), finger tracking test (Bhatt et al., 2007; S.-H. Kim et al., 2016), motor activity log (MAL; Ambrosini et al., 2021; Knutson et al., 2020), and Jebsen and Taylor Hand function test (JHFT; Bhatt et al., 2007; S.-H. Kim et al., 2016; Sattler et al., 2015; Table 1).

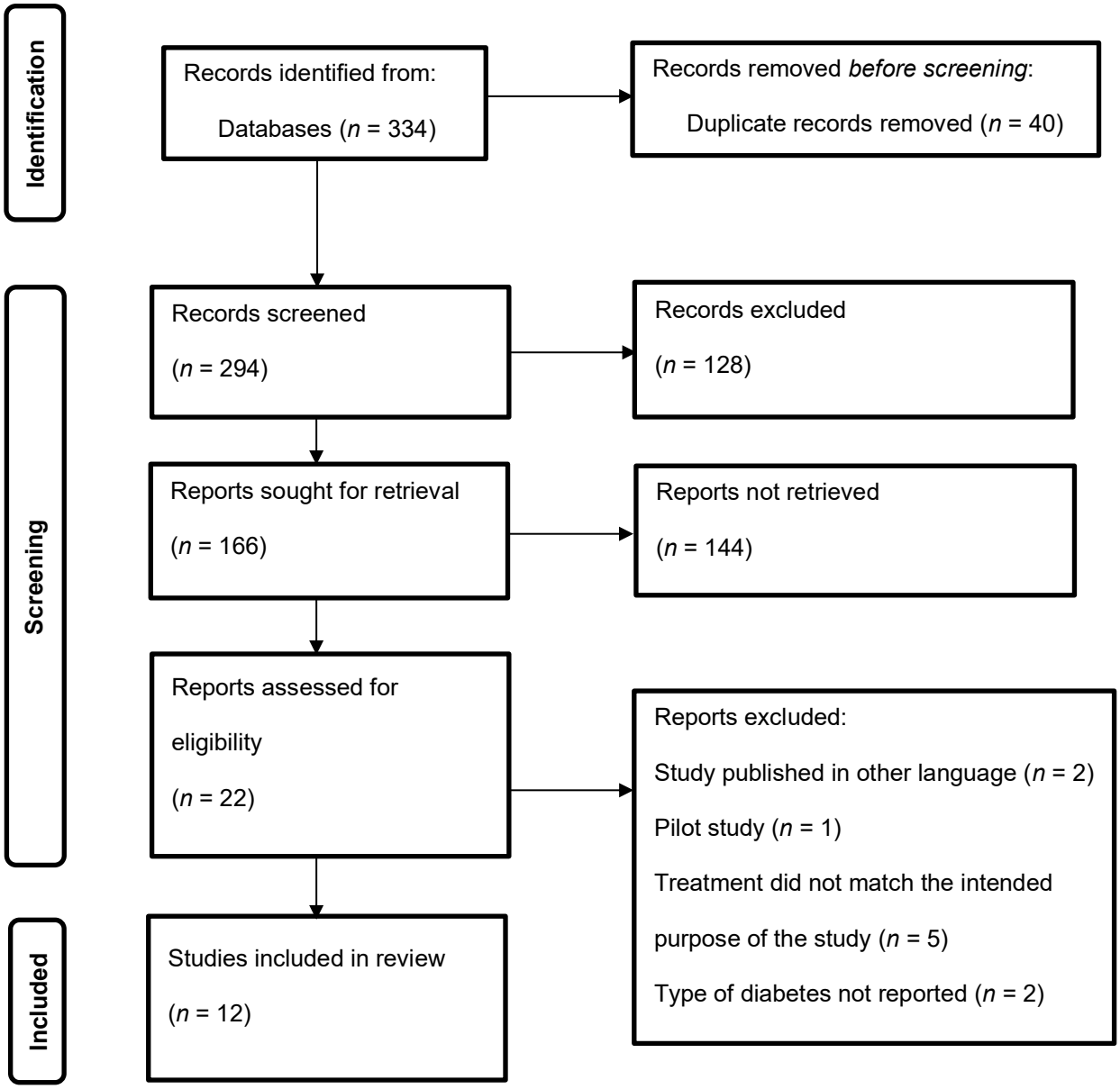
Different types of therapeutic currents either alone or in combination were used. Four trials administered FES (Ambrosini et al., 2021; Knutson et al., 2016; Knutson et al., 2020; Lourenção et al., 2008). One study used NMES (Sentandreu-Mañó et al., 2021), mirror therapy (MT) in addition to mesh glove (MG) afferent stimulation was given in trial (Lee et al., 2015) and one trial delivered electrical somatosensory stimulation (ESS; Ghaziani et al., 2018). One study administered electromyogram (EMG)-triggered NMES (S.-H. Kim et al., 2016), while another used EMG-triggered ES (Bhatt et al., 2007). One trial used TENS (Alwhaibi et al., 2021). Combination of tDCS and repetitive peripheral nerve stimulation (rPNS) was used in one trial (Sattler et al., 2015). One trial delivered concurrent bicephalic tDCS and FES (Salazar et al., 2020). The total number of sessions per week ranged from five consecutive daily sessions (Sattler et al., 2015) to 5 days per week 9 (S.-H. Kim et al., 2016; Lee et al., 2015; Table 1).

The therapeutic currents used in the included trials have varied parameters. The pulse width of the current used varied from 50 s (S.-H. Kim et al., 2016) to 300 ms (Salazar et al., 2020). Frequency of the current ranged from 5 Hz (Sattler et al., 2015) to 100 Hz (Alwhaibi et al., 2021). Duration of intervention varied from 13 min (Sattler et al., 2015) to 1.5 hr (Lee et al., 2015). The intensity of the current was at sensory threshold of paretic hand (Lee et al., 2015) or above the motor threshold (Ambrosini et al., 2021; Table 2).

Quality Assessment of the Trials

The average PEDro score was 6.92 (Table 3). Based on quality scoring, two studies were of fair quality (Knutson et al., 2020; Lourenção et al., 2008), seven studies were of good quality (Alwhaibi et al., 2021; Ambrosini et al., 2021; Bhatt et al., 2007; S.-H. Kim et al., 2016; Knutson et al., 2016; Lee et al., 2015; Sentandreu-Mañó et al., 2021) and three trials were of excellent quality (Ghaziani et al., 2018; Salazar et al., 2020; Sattler et al., 2015). All the included studies lack subject blinding except for one trial (S.-H. Kim et al., 2016). Therapist blinding was reported in only

Figure 2. *Flow Chart of Search Strategy, Retrieval of Articles, Exclusion, Inclusion, and Evidence Synthesis.*



three studies (Bhatt et al., 2007; Ghaziani et al., 2018; S.-H. Kim et al., 2016). Two trials did not report assessor blinding (Ambrosini et al., 2021; Lourenção et al., 2008). All the included trials had reported between-group differences and point measure and variability. Reporting of dropouts was not done in four studies (Alwhaibi et al., 2021; Knutson et al., 2020; Salazar et al., 2020; Sattler et al., 2015). Intention-to-treat analysis was observed in five studies (Bhatt et al., 2007; Ghaziani et al., 2018; S.-H. Kim et al., 2016; Salazar et al., 2020; Sattler et al., 2015).

Risk of Bias Assessment of the Trials

The assessment of risk of bias was depicted in Figure 3 and 4. The overall risk of bias varied across the included trials. Seven trials were judged to have had low overall risk of bias (Alwhaibi et al., 2021; Ambrosini et al., 2021; Ghaziani et al., 2018; Knutson et al., 2016; Lee et al., 2015; Salazar et al., 2020; Sentandreu- Mañó et al., 2021) and one trial reported high risk of bias (Lourenção et al., 2008). The remaining three trials were deemed to have had some concerns (Bhatt et al., 2007; S.-H. Kim et al., 2016; Knutson et al., 2020). Majority of trials

Table 1
Characteristics of the Included Trials

Trial	Sample size (*n*)	Gender (M/F)	Mean age (in years)	Onset of stroke	Outcome measures	Outcome measure tool	Findings
Alwhaibi et al. (2021)	40	19/21	52.5	≥ 6 months poststroke	Motor recovery; dexterity; brain activity	Fugl Meyer Assessment for upper extremity; BBT; quantitative EEG (qEEG)	TST combined with TENS acupoints proved better in improving brain plasticity
Ambrosini et al. (2021)	72	50/22	63.9	Participants were having first stroke; 2 weeks up to 9 months with major unilateral functional impairment	Arm and hand functions; arm motor impairment; manual dexterity; health-related quality of life	ARAT; Motricity Index; motor activity log; BBT; SS-QoL	Significant effects were observed in RETRAINER group in comparison to ACT on both ARAT and BBT; but not in SS-QoL
Bhatt et al. (2007)	20	11/9	66.31	Participants with poststroke duration of at least 6 months	Motor recovery; dexterity; hand functions; brain reorganization	Jebsen Taylor test; finger tracking test; BBT; fMRI	CM intervention more effective on brain reorganization than either intervention alone
Ghaziani et al. (2018)	102	53/49	71.5	Participants diagnosed with acute stroke confirmed by magnetic resonance imaging or CT scan	Manual dexterity; upper limb functions; hand grip strength; palmar, key, and tip pinch strength	BBT; UEFM; hand grip strength; perceptual threshold of touch; modified Rankin scale; palmer, key, and tip pinch strength	ESS protocol (both high-dose and low-dose) prior to arm training equally effective as arm training alone – all outcome measures
S.-H. Kim et al. (2016)	20	11/9	48.2	Participants having more than 6 months of stroke	Dexterity; pinch strength; muscle activity	Jebsen-Taylor test; finger tracking test; BBT; fMRI	EMG-stimulation + TOT more effective than EMG-stimulation alone for motor recovery (FMA) and dexterity (BBT) following arm-paresis poststroke
Knutson et al. (2016)	80	51/29	55.85	Participants enrolled in the study had onset of more than 6 months from hemorrhagic /ischemic stroke	Manual dexterity; upper limb impairment; activity measure (functional ability – upper extremity)	BBT; UEFM; AMAT	Significant group differences were observed in CCFES group than cNMES group on BBT (p = .045)

Table 1
Characteristics of the Included Trials

Trial	Sample size (*n*)	Gender (M/F)	Mean age (in years)	Onset of stroke	Outcome measures	Outcome measure tool	Findings
Knutson et al. (2020)	67	43/24	55	Participants had upper limb hemiparesis with moderate to severe hand impairment (within 2 years of first ischemic /hemorrhagic stroke).	Manual dexterity; upper extremity motor impairment; activity limitation	BBT; reachable workspace; SULCS; UEFM; AMAT; MAL	No significant group differences on BBT, SULCS, AMAT; arm and hand CCFES improved RW, UEFM more than hand CCFES
Lee et al. (2015)	48	34/14	52.74	Unilateral stroke with onset greater than 6 months and mild to moderate impairment (Fugl-Meyer Assessment for upper extremity)	Muscular properties (muscle tone and stiffness); sensorimotor functions (limb functions: motor, sensory changes, dexterity, ambulation); daily function	Myoton-3 myometer; Fugl Meyer Assessment for upper extremity, lower extremity; revised Nottingham sensory assessment; BBT; 10-meter walk test; FIM	MT + MG induced significant and distinctive effects on muscular properties, manual dexterity and daily function; no significant group differences seen in upper extremity function
Lourenção et al. (2008)	59	37/22	55.4	Participants were chronic ischemic hemiplegic patients (more than 6 months)	Hand function; manual dexterity index; joint ROM, elbow and wrist; spasticity, elbow and wrist		No significant difference between the groups in terms of manual dexterity index
Salazar et al. (2020)	30	15/15	60	Individuals with ischemic or hemorrhagic chronic stroke confirmed by head CT or MRI at least 6 months before recruitment	Motor performance measures; movement quality measures; handgrip strength; motor impairment	Reach-to-target kinematic analysis; Jamar hydraulic hand dynamometer, Fugl Meyer Assessment for upper extremity	Concurrent bicephalic tDCS and FES slightly improved reaching motor performance and handgrip force

Table 1
Characteristics of the Included Trials

Trial	Sample size (*n*)	Gender (M/F)	Mean age (in years)	Onset of stroke	Outcome measures	Outcome measure tool	Findings
Sattler et al. (2015)	20	14/6	67.6 ± 10	Single, unilateral hemispheric ischemic stroke within 4 weeks	Motor performance; transcranial magnetic stimulation cortical excitability	Jebsen and Taylor Hand Function Test (JHFT); Jamar hydraulic hand dynamometer; Fugl Meyer Assessment for upper extremity; Nine-hole Peg Test; Hand tapping test (9HPT); Motor Evoked Potential (MEP); resting and active motor thresholds (RMT, AMT), TMS	**Anodal tDCS + rPNS significantly improved hand motor function** (JHFT, p = .01); no significant differences in grip strength or Fugl-Meyer scores
Sentandreu-Mañó et al. (2021)	69	50Hz NMES: 13/7 30Hz NMES: 11/9 Control: 13/7	70.96	Poststroke spastic hemiparetic patients (poststroke period < 18 months) with clinical stability	Shoulder motor control; range of motion, resting angle; grip strength; pinch strength; muscle tone; manual dexterity; muscle electrical activity; activities of daily living	MESUPES-arm test; JAMAR finger goniometer; dynamometer; hydraulic pinch gauge; MAS; BBT; EMG - radial extensor and radial flexor - carpals; Barthel index	Both NMES protocols produced significant improvements in range of motion, grip and pinch strength, MAS, muscle electrical activity in extensors of wrist; no significant difference in BBT noted

Note. BBT= Box and Block test; MT= Mirror therapy; MG = Mesh gloves; FIM = Functional Independence Measure; NMES = Neuromuscular electrical stimulation; MESUPES=; MAS = Modified Ashworth Scale; EMG = Electromyography; SULCS = Stroke upper limb capacity scale; UEFM = Upper extremity Fugl-Meyer; AMAT = Arm motor abilities test; MAL = Motor activity log; CCFES = Contralaterally controlled functional electrical stimulation; RW = Reachable workspace; cNMES = cyclic Neuromuscular electrical stimulation; SS-QoL= Stroke Specific Quality of Life; ACT = Advanced conventional therapy; ARAT = Action research arm test; ESS = Electrical somatosensory stimulation; TOT= Task-oriented training; FMA = Fugl-Meyer Assessment; CT = computerized topography; CM = combination.

Table 2
Characteristics of the Intervention Used

Trial	Experimental	Device	Parameters used	Control
Alwhaibi et al. (2021)	TENS Acupoint + task-specific training (TST) - 18 sessions for 6 successive weeks, 3 sessions per week	Phyaction 785 (Uniphy B.V., Netherlands)	TENS Acupoint - 100 Hz, 0.2 ms, square pulses, 2–3x sensory threshold, 20 min	TST + sham electrical stimulation (80 min/session, 3 sessions/week, 6 weeks)
Ambrosini et al. (2021)	EMG triggered FES	RehamovePro, Hasomed GmbH	Pulse frequency: 25 Hz; width: 300 μs; intensity: subject specific above motor threshold	ACT: 90 min, three times a week for 9 weeks
Bhatt et al. (2007)	ES group - wrist and finger extensors	Neuromove NM900 (Stroke Recovery systems; Denver, CO, USA)	Asymmetrical, rectangular, biphasic, constant current; pulse width: 200 μs; frequency: 50 Hz; on-off time was 7.15 s	TR group: electro goniometer placed at metacarpophalangeal joint-index finger bilaterally (ten 1-hr sessions over 2–3 weeks)
Ghaziani et al. (2018)	ESS - high/low dose		High dose ESS: suprasensory ESS; mode: continuous; pulse width: 250 μs; frequency: 10 Hz; application time: 1 hr Low dose/placebo ESS: suprasensory ESS; mode: intermittent (active stimulation intervals of 3 s delivered in loops of 2.5 min); pulse width: 250 μs; frequency: 10 Hz; application time: 1 hr	Low dose ESS (1 hr) followed by usual arm training (15 min) Duration: 4 weeks poststroke
S.-H. Kim et al. (2016)	EMG-stimulation: wrist and finger extensors + TOT	81 (W)	Biphasic rectangular electrical impulses with pulse width of 50μs	EMG-stimulation: wrist and finger extensors for 20 min/day, 5 days/week for 4 weeks
Knutson et al. (2016)	Hand CCFES- finger and thumb extensor	-	Pulse frequency: 35 Hz; amplitude: 40 mA; modulated pulse duration: 0 to 250 μs	Arm+Hand cNMES: 60 min/session × 10 session/week = 10 hr/week
Knutson et al. (2020)	Arm+Hand CCFES: triceps and finger extensors Hand CCFES: finger extensors	-	Pulse frequency: 35 Hz; amplitude: 40/60 mA; width: 255 μs	cNMES: 60 min/session × 10 session/week = 10 hr/week

Table 2
Characteristics of the Intervention Used

Trial	Experimental	Device	Parameters used	Control
Lee et al. (2015)	MT+MG afferent stimulation	Mesh glove (anode) + sleeve electrode around elbow joint (cathode)	Stimulation frequency: 50 Hz; pulse duration: 300 μs; intensity: set at sensory threshold of paretic hand Application time: 30 min	MT followed by functional task training Duration: 1.5 hr/day, daily regimen, 5 days/week MT + sham stimulation Duration: 1.5 hr/day, 5 days/week for 4 weeks
Lourenção et al. (2008)	OT+FES + EMG-BFB	Quadrikron KC 170	-	OT+FES group (twice weekly session of OT+ FES)
Salazar et al. (2020)	tDCS plus FES along with conventional therapy (10 sessions of concurrent tDCS and FES - 30 min, five times a week for 2 weeks) FES - anterior deltoid, serratus anterior, triceps brachii and wrist extensor muscles of the paretic arm	tDCS - TCT neurostimulator (Research Version) FES (Dualpex-071 Quark Medical, Brazil)	tDCS - 2mA bi-cephalic tDCS with a relative current density of 0.08 mA/m^2, for 30 min FES - frequency = 40 Hz, pulse width = 300 ms; ON time (contraction) = 6 or 8 s; OFF time = 2× ON time.	Sham tDCS plus FES along with conventional therapy (30 min, five times a week for 2 weeks)
Sattler et al. (2015)	Anodal tDCS + rPNS (Radial Nerve Stimulation)	Magstim Eldith DC Stimulator Plus (tDCS), DIGITIMER DS7A (rPNS)	**tDCS:** Anodal over ipsilesional M1, 1.2 mA, 13 min/session, 5 days **rPNS:** 5 Hz, intensity below M-response threshold, 13 min/session. **Both stimulations applied simultaneously.**	**Sham tDCS + rPNS**, same protocol
Sentandreu-Mañó et al. (2021)	NMES -35Hz NMES -50Hz	Beac Medical IntelliSTIM BE 28-E	Stimulation frequency: 35 Hz/50 Hz (low frequency), symmetrical rectangular biphasic wave; pulse duration: 300 μs. C-R time: 5–25 s (first 2 weeks), 5–20 s (3rd week), 5–15 s (4th week), 5–10 s (5th–6th week), 5–5 s (7th–8th week) Application time: 20 min (first two sessions) followed by 30 min (for subsequent sessions)	Conventional treatment Duration: 60 min each session, 3 days/week for 8 weeks

Note. MT = Mirror therapy; MG = Mesh glove; NMES = Neuromuscular electrical stimulation; C-R = Contraction: Relaxation; CCFES = Contralaterally-controlled functional electrical stimulation; cNMES = cyclic neuromuscular electrical stimulation; ACT = Advanced conventional therapy; EMG = Electromyography; FES = Functional electrical stimulation; OT = Occupational therapy; EMG-BFB: Electromyography biofeedback; TR = Track training.

Table 3
Methodological Quality Assessment

Trial	Random allocation	Concealed allocation	Group similarity at baseline	Subject Blinding	Therapist Blinding	Assessor Blinding	Drop-outs < 15%	Intention to treat analysis	Between-group difference reported	Point measured and variability data	Total Score	Quality
Alwhaibi et al. (2021)	Yes	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes	7/10	Good
Ambrosini et al. (2021)	Yes	Yes	No	No	No	No	Yes	Yes	Yes	Yes	6/10	Good
Bhatt et al. (2007)	Yes	No	Yes	No	Yes	Yes	Yes	No	Yes	Yes	7/10	Good
Bruchez et al. (2016)	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	7/10	Good
Ghaziani et al. (2018)	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	9/10	Excellent
S.-H. Kim et al. (2016)	Yes	No	Yes	No	No	Yes	Yes	No	Yes	Yes	6/10	Good
Knutson et al. (2020)	Yes	No	Yes	No	No	Yes	No	No	Yes	Yes	5/10	Fair
Knutson et al. (2016)	Yes	Yes	No	No	No	Yes	Yes	No	Yes	Yes	6/10	Good
Lourenção et al. (2008)	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes	5/10	Fair
Salazar et al. (2020)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	9/10	Excellent
Sattler et al. (2015)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	9/10	Excellent
Sentandreu-Mañó et al. (2021)	Yes	No	Yes	No	No	Yes	Yes	No	Yes	Yes	7/10	Good

presented with low risk of bias arising from randomization process (Bhatt et al., 2007; Ghaziani et al., 2018; S.-H. Kim et al., 2016; Knutson et al., 2016; Lee et al., 2015; Salazar et al., 2020; Sattler et al., 2015; Sentandreu-Mañó et al., 2021). Four trials (Alwhaibi et al., 2021; Bhatt et al., 2007; S.-H. Kim et al., 2016; Sentandreu-Mañó et al., 2021) showed some concerns in the risk of bias due to the deviation from the intended intervention while one study (Lourenção et al., 2008) showed high risk. Two studies (Ambrosini et al., 2021; Knutson et al., 2016) reported some concerns in risk of bias due to missing outcome data and two trials (Bhatt et al., 2007; Lourenção et al., 2008) showed high risk. There was some concern in two studies (Bhatt et al., 2007; Sentandreu-Mañó et al., 2021) for measuring the outcome and high risk for one trial (Lourenção et al., 2008). In the selection of the reported result domain, two trials showed some concern (Alwhaibi et al., 2021; S.-H. Kim et al., 2016).

Figure 3

Risk of Bias Assessment of the Included Trials Using the RoB-2 (Intention-to-Treat Analysis)

Intention-to-Treat	Unique ID	Study ID	Experimental	Comparator	Outcome	Weight	D1	D2	D3	D4	D5	Overall
	5	Ambrosini et al. (2021)	RETRAINER + EMG − trigger	ACT	Dexterity	1	▲	●	▲	●	●	●
	7	Ghaziani et al. (2018)	High does ESS	Placebo	Dexterity	1	●	●	●	●	●	●
	10	Salazar et al. (2020)	tDCS + FES	Sham tDCS + FES	Motor Performance	1	●	●	●	●	●	●
	12	Sattler et al. (2015)	Anodal tDCS + rPNS	Sham tDCS +rPNS	Motor Performance	1	●	●	●	●	●	●

●	Low risk
▲	Some concerns
■	High risk

D1	Randomization process
D2	Deviations from the intended interventions
D3	Missing outcome data
D4	Measurement of the outcome
D5	Selection of the reported result

Figure 4

Risk of Bias Assessment of the Included Trials Using the RoB-2 (Per-Protocol Effect)

Per-protocol	Unique ID	Study ID	Experimental	Comparator	Outcome	Weight	D1	D2	D3	D4	D5	Overall
	1	Lee et al. (2015)	MT + MG afferent stim	MT + Sham	Dexterity	1						
	2	Sentandreu-Mañó et al. (2021)	NMES	Conventional therapy	Dexterity	1						
	3	Knutson et al. (2020)	CCFES	NMES	Dexterity	1						
	4	Knutson et al. (2016)	CCFES-Hand	cNMES	Dexterity	1						
	6	Bhatt et al. (2007)	ES + TR	ES/TR	Dexterity	1						
	8	S.-H. Kim et al. (2016)	EMG Stim + TOT	EMG-STIMSs	Dexterity	1						
	9	Lourenção et al. (2008)	OT + FES + EMG − BFB	OT + FS	Dexterity	1						
	11	Alwhaibi et al. (2021)	TENS Acupoint + TST	shamES + TST	Motor recovery, dexterity	1						

Low risk	
Some concerns	
High risk	

D1	Randomization process
D2	Deviations from the intended interventions
D3	Missing outcome data
D4	Measurement of the outcome
D5	Selection of the reported result

The Magnitude of Effect: The Result of Meta-Analysis

Seven studies (Ambrosini et al., 2021; Ghaziani et al., 2018; S.-H. Kim et al., 2016; Knutson et al., 2016; Knutson et al., 2020; Lee et al., 2015; Sentandreu-Mañó et al., 2021) were grouped to determine the effect on dexterity. There is moderate quality evidence suggesting a moderate effect (SMD = 0.85, 95% CI: −0.11, 1.81) favoring control/sham over therapeutic current. Heterogeneity was high (I2 = 94%). The one study with the largest treatment effect was Kim and colleagues (S.-H. Kim et al., 2016) at 0–4 weeks. Two trials (Alwhaibi et al., 2021; Sentandreu-Mañó et al., 2021) assessed the 5- to 8-week effects of therapeutic current versus control treatment. There is low-quality evidence suggesting a small effect (SMD = −0.09, 95% CI: −0.52, 0.35).

Three studies (Ambrosini et al., 2021; Knutson et al., 2016; Knutson et al., 2020) examined the 9- to 12-week effects of therapeutic current on dexterity and were meta-analyzed. The meta-analysis favored control treatment (SMD = 2.71, 95% CI: −0.57, 5.99). The heterogeneity was high (I2 = 98%; Figure 5).

Four studies (Ambrosini et al., 2021; Knutson et al., 2016; Knutson et al., 2020; Lee et al., 2015) involving 196 patients with stroke reported the effects of FES on dexterity. High heterogeneity was observed (I2 = 97%, $p < .00001$). The pooled analysis showed no significant difference between the FES and the control group (SMD = 2.03, $Z = 1.81$, $p = .07$; Figure 6).

Figure 5

Forest Plot Illustrating the Overall Effect of Therapeutic Current on Dexterity to Control Treatment in the Immediate to 12 Weeks Showing Low Effect Favoring Control Treatment

	Favors TC			Favors CT				Mean Difference	
Study or Subgroup	**Mean**	***SD***	**Total**	**Mean**	***SD***	**Total**	**Weight**	**IV, Random, 95% CI**	**Year**
1.1.1 0–4 Weeks									
Bhatt et al. (2007)	0	0	0	0	0	0		Not estimable	2007
Lee et al. (2015)	14.4	13.5	15	13.31	9.25	16	5.3%	1.09 [−7.11, 9.29]	2015
S.-H. Kim et al. (2016)	27.9	1.85	10	29.5	2.41	10	20.0%	−1.60 [−3.48, 0.28]	2016
Ghaziani et al. (2018)	19.2	15.2	53	19.9	16.2	49	8.1%	−0.70 [−6.81, 5.41]	2018
Subtotal (95% CI)			**78**			**75**	**33.3%**	**−1.40 [−3.16, 0.36]**	
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.45$, df = 2 ($P = .80$); $I^2 = 0\%$									
Test for overall effect: $Z = 1.56$ ($P = .12$)									
1.1.2 5–8 Weeks									
Sentandreu-Mañó et al. (2021)	11.62	9.89	21	12.2	12.95	20	6.6%	−0.58 [−7.66, 6.50]	2021
Sentandreu-Mañó et al. (2021)	10.75	9.51	21	12.2	12.95	20	6.7%	−1.45 [−8.43, 5.53]	2021
Alwhaibi et al. (2021)	20	12.3	20	38	22.1	20	3.2%	−18.00 [−29.08, −6.92]	2021
Subtotal (95% CI)			**62**			**60**	**16.5%**	**−5.69 [−14.85, 3.47]**	
Heterogeneity: $Tau^2 = 47.39$; $Chi^2 = 7.53$, df = 2 ($P = .02$); $I^2 = 73\%$									
Test for overall effect: $Z = 1.22$ ($P = .22$)									

Figure 5

Forest Plot Illustrating the Overall Effect of Therapeutic Current on Dexterity to Control Treatment in the Immediate to 12 Weeks Showing Low Effect Favoring Control Treatment

	Favors TC			Favors CT				Mean Difference	
Study or Subgroup	**Mean**	***SD***	**Total**	**Mean**	***SD***	**Total**	**Weight**	**IV, Random, 95% CI**	**Year**
1.1.3 9–12 Weeks									
Knutson et al. (2016)	4.6	0.61	32	1.8	0.31	40	23.5%	2.80 [2.57, 3.03]	2016
Knutson et al. (2020)	13.5	1.8	21	9.6	1.8	8	21.2%	3.90 [2.43, 5.37]	2020
Ambrosini et al. (2021)	61	15	32	58	18	32	5.4%	3.00 [−5.12, 11.12]	2021
Subtotal (95% CI)			**85**			**80**	**50.1%**	**2.88 [2.48, 3.28]**	
Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 2.11$, df = 2 ($P = .35$); $I^2 = 5\%$									
Test for overall effect: $Z = 14.07$ ($P < .00001$)									
Total (95% CI)			**225**			**215**	**100%**	**0.61 [−1.53, 2.76]**	
Heterogeneity: $Tau^2 = 5.06$; $Chi^2 = 40.12$, df = 8 ($P < .00001$); $I^2 = 80\%$									
Test for overall effect: $Z = 0.56$ ($P < .57$)									
Test for subgroup differences: $Chi^2 = 24.85$; df = 2 ($P < .00001$); $I^2 = 92\%$									

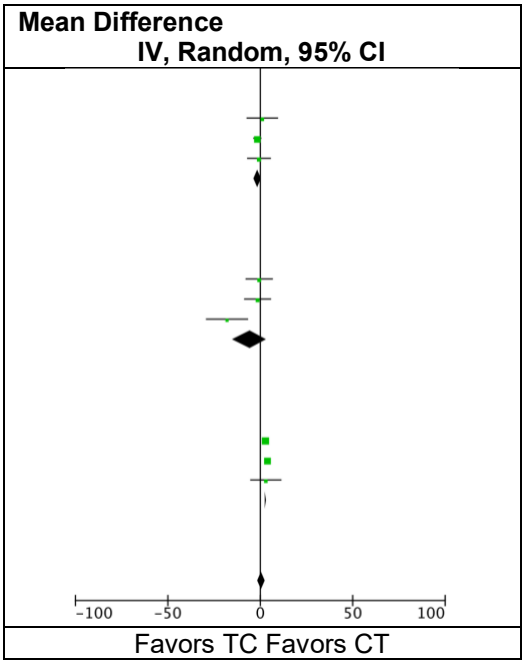
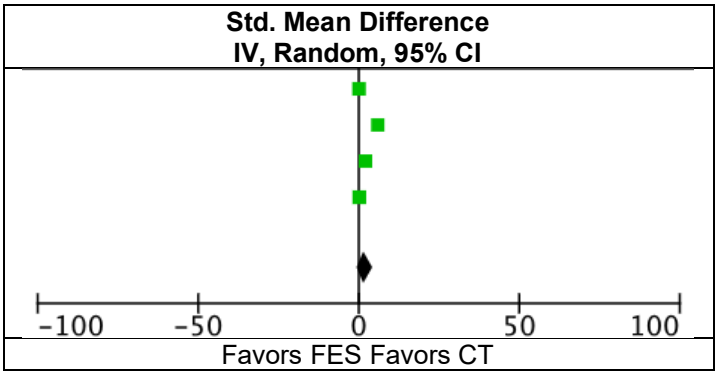


Figure 6

Result of the Meta-Analysis and Forest Plot for the Effect of FES on BBT

	Favors FES			Favors CT				Std. Mean Difference	
Study or Subgroup	**Mean**	***SD***	**Total**	**Mean**	***SD***	**Total**	**Weight**	**IV, Random, 95% CI**	**Year**
1.1.1 0–4 Weeks									
	14.4	13.5	15	13.31	9.25	16	25.3%	0.09 [−0.61, 0.80]	2015
	4.6	0.61	31	1.8	0.31	40	24.4%	5.93 [4.83, 7.03]	2016
	13.5	1.8	21	9.6	1.8	8	24.7%	2.11 [1.10, 3.11]	2020
	61	15	32	58	18	32	25.6%	0.18 [−0.31, 0.67]	2021
Subtotal (95% CI)			**100**			**96**	**100.0%**	**−2.03 [−0.17, 4.24]**	
Heterogeneity: $Tau^2 = 4.89$; $Chi^2 = 99.04$, df = 3 ($P < .00001$); $I^2 = 97\%$									
Test for overall effect: $Z = 1.81$ ($P = .07$)									

Note. FES functional electrical stimulation; BBT Box and Block test.



Discussion

This systematic review sought to summarize and evaluate the existing literature on various therapeutic currents to guide better clinical decision-making for clinicians and physical therapists working in stroke rehabilitation settings with people having dexterity impairment. According to the findings of the present review, therapeutic currents can be used alone or as an adjunct in order to improve the hand functions of the people with stroke; however, they failed to produce any long-term effects.

Two studies investigated the effect of contralaterally-controlled FES (CCFES) on stroke patients. Knutson and colleagues compared the effects of contralaterally controlled FES to cyclic NMES. CCFES is more effective in improving and facilitating motor recovery than NMES. This is because CCFES provides control of stimulation intensity in real-time, synchronized opening of hands, and practice of the task using stimulation (Knutson et al., 2016). Another trial evaluated the effect of adding contralaterally controlled triceps stimulation to hand CCFES by comparing the outcomes of participants receiving hand CCFES to those receiving Arm+Hand CCFES. They also compared the Arm+Hand to Arm+Hand cyclic NMES (cNMES), which stimulated simultaneous elbow extensors with preset timing and timing (i.e., stimulation was not controlled by the participant). After 12 weeks of intervention, it was observed that adding contralaterally controlled elbow extension to hand CCFES does not improve gains in hand dexterity (Knutson et al., 2020). CCFES has a mechanical advantage over cNMES like CCFES provides real-time patient-controlled intensity of stimulation to the paretic hand (i.e., intention-driven movement), synchronized opening of both hands, and stimulation-assisted task practice with the paretic hand (Knutson et al., 2016).

One trial investigated the effect of electromyographic biofeedback (EMG-BFB) in addition to occupational therapy (OT) and functional electrical stimulation on spasticity, range of motion, and upper extremity function. Ischemic stroke patients receiving

OT+FES+EMG-BFD showed greater improvement in upper extremity hand function than those who received only OT+FES indicating that EMG-BFD can be used as an adjunct to other treatment regimen (Lourenção et al., 2008). These findings might result from the fact that biofeedback training involves skilled repetitive movements and inhibition of unwanted activity of antagonistic muscles (Basmajian et al., 1975).

One study investigated the effect of early administration of ESS on arm functioning in people with stroke. The ESS was delivered for 1 hr along with 15 min of task-oriented arm training but was equally beneficial when arm training was given alone (Ghaziani et al., 2018). Bhatt and colleagues evaluated the combined effect of electrical stimulation plus motor learning-based tracking training on cortical reorganization and its relationship to functional recovery. After 2–3 weeks of intervention, ES along with motor learning was effective in cortical reorganization (Bhatt et al., 2007). Electrical stimulation is proposed to work through a sensorimotor coupling mechanism (Cauraugh et al., 2000). Increased proprioceptive signals from evoked movements are thought to bombard the somatosensory cortex, thereby increasing motor corticoneural excitability (Cauraugh et al., 2000). The increased motor cortical excitability facilitates greater voluntary activation of its neuronal networks leading to improved function (Wu et al., 2006).

One study compared the effect of two NMES protocols with different stimulation frequencies on upper limb impairment and upper limb function in older individuals with spastic hemiparesis after stroke. Both the NMES protocols were found to be effective in manual dexterity (Sentandreu-Mañó et al., 2021). The specific mechanisms underlying NMES intervention are complex and unclear, but findings suggest that improvement could be mediated by local and central effects. At the local level, reference has been made to changes in muscular strength, modification of viscoelastic characteristics, and increase of blood flow (de Kroon et al., 2004; Ring & Rosenthal, 2005) and at the central level, NMES was supposed to influence cortical plasticity (Chipchase et al., 2011; Quandt & Hummel, 2014). Low to moderate NMES frequencies were preferred when the function of the muscle is linked to sustained repetition of the fine motor movements (Vromans & Faghri, 2018).

One trial done by Lee and colleagues examined the combined effect of MT+MG on muscular properties, sensorimotor functions, and daily function in people with chronic stroke. The intervention was given for 1.5 hr per day for five days per week for a total of 4 weeks. It was observed that MT+MG was effective in improving muscular properties, manual dexterity, and daily function (Lee et al., 2015). MT in addition to MG stimulation decrease the stiffness of flexors of forearm and simultaneously increasing the tone of extensors, which leads to improvement in ability to grasp and release cubes (Keenan & Matzon, 2011). The sensory inputs from the MG stimulation and the visual inputs from the mirror facilitate neuroplastic changes in the sensorimotor cortex of the brain and enhance improvement in manual dexterity (Michielsen et al., 2011).

Two studies examined the combined effect of tDCS with and rPNS (Sattler et al., 2015) and FES (Salazar et al., 2020). Sattler and colleagues compared the effect of tDCS plus rPNS and rPNS with sham tDCS on the motor recovery using the JHFT. tDCS when added to rPNS may be helpful in improving motor hand recovery in the acute phase after stroke (Sattler et al., 2015). Another study compared the concurrent bicephalic tDCS and FES and sham tDCS and FES on handgrip force in chronic poststroke patients (Salazar et al., 2020).

One trial compared the effects of TENS acupoints and task-specific training (TST) and TST alone on cortical activity and the motor function of the affected UE in people with stroke. Both being equally effective, TST only or combined with TENS can be considered as an effective treatment strategy for improving motor function of hand in chronic stroke patients (Alwhaibi et al., 2021). TENS activates the fibers of small diameters arriving from the muscles (ergo receptors) which results in phasic muscle twitches. These receptors were responsible for the facilitation of proprioception and kinesthetic senses.

Two studies evaluated the effects of EMG-triggered stimulations on the upper extremity function (Ambrosini et al., 2021; S.-H. Kim et al., 2016). One trial investigated the effect of electromyogram-triggered neuromuscular stimulation (EMG-stim) in addition to task-oriented training (TOT) on muscle activation, motor recovery, and dexterity in people with chronic stroke. Following 4 weeks of intervention, EMG-stim in combination with TOT was found to be better than EMG-stim alone for the improvement in dexterity (S.-H. Kim et al., 2016). One study compared the effect of arm training supported by a RETRAINER with electromyograph-triggered functional electrical stimulation and advanced conventional therapy (ACT) on dexterity, arm function, strength, ADL, QoL in people with stroke. Following 9 weeks of training, it was observed that

hybrid robotic system, allowing to perform personalized, intensive, and task-oriented training, with enriched sensory feedback, was superior to ACT in improving arm functions and dexterity after stroke (Ambrosini et al., 2021). EMG-stimulation was confirmed to be an effective intervention that accelerates neurological recovery by increasing motor unit. Improved muscle performance may also provide positive effects on motor recovery and hand function after stroke (S.-H. Kim et al., 2016). These therapeutic effects of EMG-stimulation were further significantly improved when an adjunct intervention was added.

The stimulation parameters reported across the included studies—particularly frequencies between 20–50 Hz and pulse durations of 200–300 μs—are consistent with those commonly used in neurorehabilitation for motor recovery after stroke (de Kroon et al., 2004; Sheffler & Chae, 2007). Moderate-frequency stimulation is known to promote muscle contraction, enhance cortical excitability, and facilitate motor learning, especially when combined with voluntary movement or task-specific training (Bergquist et al., 2011; Rushton, 2003). The observed consistency of parameters across trials supports their clinical relevance. However, heterogeneity in session durations, total treatment periods, and stimulation modes (e.g., FES vs. NMES) may explain the variability in clinical outcomes, particularly in studies that did not observe long-term effects.

Seven studies were grouped for meta-analysis to determine the long-term effectiveness of therapeutic currents on dexterity versus control (Ambrosini et al., 2021; Ghaziani et al., 2018; S.-H. Kim et al., 2016; Knutson et al., 2016; Knutson et al., 2020; Lee et al., 2015; Sentandreu-Mañó et al., 2021). During the 9- to 12-week period, the meta-analysis suggests that there is moderate quality evidence that electrical stimulation was not effective in producing any positive effects in the long term. Due to the limited available literature, it was difficult to identify the mechanism behind the inability of therapeutic currents to produce long-lasting positive effects. This may, however, be attributed to factors such as short intervention duration, lack of structured follow-up, or absence of ongoing home-based practice. Some studies suggested that participants may not have adopted long-term behavioral or lifestyle changes supportive of motor function maintenance after the intervention phase, which could limit lasting gains.

This review identified several limitations within the included studies. First, the included trials used different outcome measures to assess dexterity, which might have led to the significant heterogeneity of the results. Second, the present review included a large number of studies in which current was as adjunct component of other intervention. The lack of common outcome measure was also identified as a limitation of the present review that restricted the number of outcomes included in the meta-analysis.
The main strength of the present review is that it provides an RCT update summary of the effects of various therapeutic currents on dexterity of people with stroke, while it implies prospective observations and a causal rationale. The findings imply that the improvement of the dexterity by therapeutic currents in people with stroke is practical and generalizable.

Conclusion

There is growing evidence base regarding trials investigating the effect of different therapeutic currents on upper extremity function in people with stroke. Synthesized data from trials examining the effect of FES showed small to moderate effect size for improving dexterity which, while not significant, warrants further investigation into the practical implications of these findings. In addition to this, therapeutic currents failed to bring any positive change in the long run. However, the application therapeutic currents have demonstrated its feasibility as a tool for the rehabilitation of upper limb function in people with stroke.

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NeuroRegulation

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Neurophysiological Effects of Traditionally-Prepared Kava Measured by EEG: A Pilot Case Study

Mitchell A. Head[1], Mahonri Owen[1], Apo Aporosa[2], Connor Flynn[3], Martin Atkins[1], and Helen Turner[3]*

[1]The University of Waikato, School of Engineering, Hamilton, New Zealand
[2]The University of Waikato, Te Wānanga Waiora Division of Health, Hamilton, New Zealand
[3]Chaminade University of Honolulu, School of Natural Sciences and Mathematics, Honolulu, Hawaii, USA

Abstract

Introduction. Kava (*Piper methysticum*) is a culturally significant Pacific keystone species traditionally consumed as a water-based beverage. Global demand has led to commodification and misrepresentation, with kava often diverging from traditional forms. Evidence on the physiological and therapeutic effects of traditionally prepared beverage kava remains limited, while conflation with nonkava products risks obscuring cultural meaning and safety. This study addresses these gaps. **Methods**. A pilot electroencephalography (EEG) study investigated neurophysiological effects of traditionally prepared kava in culturally authentic settings. Two experienced adult male users were observed over a 6-hr session. Resting-state EEG was recorded pre- and postconsumption with the EMOTIV Insight 5-channel EEG headset. **Results.** EEG findings showed divergent responses. One participant displayed increased alpha and theta activity consistent with relaxation, while the other showed elevated gamma power linked to cognitive focus. These differences may reflect individual habituation or cultural use. Results highlight the need for larger studies connecting EEG data with behavioral measures to explore the ethnopsychopharmacology of traditional kava. **Conclusion.** This pilot study provides preliminary evidence that traditionally prepared kava produces measurable neurophysiological effects aligned with its cultural role as a calming, relational substance. The study underscores the value of culturally grounded, rigorous research on kava.

Keywords: kava; naturalistic setting; EEG; brain activity; ethnopsychopharmacology

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***Address correspondence to**: Apo Aporosa, University of Waikato, Gate 1, Knighton Road, Hamilton 3240, New Zealand. Email: apo.aporosa@waikato.ac.nz

Edited by:
Rex L. Cannon, PhD, Currents, Knoxville, Tennessee, USA

Reviewed by:
Rex L. Cannon, PhD, Currents, Knoxville, Tennessee, USA
Randall Lyle, PhD, Mount Mercy University, Cedar Rapids, Iowa, USA

Introduction

Kava is often explained as the *Piper methysticum* plant and the drink made by straining the roots and basal stump through water. This explanation however overlooks kava's deep cultural significance throughout much of the Pacific and Pacific diaspora, shaped by over 2,000 years of traditional knowledge (Lebot et al., 1992). Kava is not simply a plant or drink; it is arguably the Pacific's most dominant cultural keystone species (Aporosa, 2019a). It embodies both cultural form and function inclusive of utensils such as a designated wooden bowl (*tanoa* or *kumere*) from which the kava is served into *bilo*/*ipu*/*apu*—half coconut shell cups—to attendees in hierarchical order seated on woven mats who engage in *talanoa*, or culturally guided discussion (Fa'avaei et al., 2016). That cultural form and function underpins a central role in *veiyaloni* or *vā*; the fostering of relational bonds through shared ancestry, cultural practices, and social experience enriched by spiritual and ceremonial exchange and linguistic expression (Aporosa & Fa'avae, 2021). Furthermore, kava is understood to possess *mana*, or spiritual power, enhancing its role in both ceremonial practice and less formal occasions underpinned by culturally informed behavior standards (Aporosa, 2019a). While traditional Pacific knowledge recognizes the term *kava* as both a verb and a noun (Aporosa, 2024) and integral to Pacific identity expression, kava is gaining traction among non-Pacific users. Increasing numbers are choosing

to reflect traditionally-influenced use systems as part of social connection (see Figure 1), with some of that use intentionally aimed at improving mental health (Aporosa et al., 2025).

Research reports that for many Pacific peoples, a typical kava use session is 6 hr in duration, with each drinker consuming 3.6 L (6.33 pints) of kava beverage, which can amount to more than 5,000 mg of kavalactones (KL, some of the active chemicals in kava) in a single sitting (Aporosa, 2014). Pharmacology explains that kava contains over 20 lactones, together with flavokavains and “diverse secondary metabolome[s]” (Bian et al., 2020; Cheung et al., 2022; Sarris et al., 2012). Despite publications asserting how KL work in the body and brain, Kautu and colleagues (2017) explain there are large knowledge gaps, including “modes of action … [and] the neurophysiological mechanisms associated with kavalactone metabolism” (p. 1, 5). This gap remains, with analytical chemists and biologists within our wider team undertaking work exploring these unknown factors specifically linked to traditionally influenced kava use.

Even at high consumption rates over many hours, users explain kava’s effects as subtle, lacking marked euphoria, inebriation, intoxication (Aporosa, 2019b; 2022), vestibular disturbance, or contributing to fall risk (Aporosa et al., 2022b). Professor of Medicine, Dr. Peter d’Abbs (1995), explains that kava does "not lead to violent behavior … not befuddle the mind … and can be used to stimulate 'clear-headed' discussions ..." (p. 169) Additionally, research is clear that frequent kava use does not lead to addiction (Aporosa, 2019b) and is statistically safer than paracetamol (Rasmussen, 2005), contributing to kavas regulation in several countries as “food” (Fink, 2024; New Zealand Government, 2015). The World Health Organization summarizes, "On balance, the weight-of-evidence from both a long history of use of kava beverage [therefore, kava as used and defined by Pacific traditional knowledge] and from the more recent research findings indicates that it is possible for kava beverage to be consumed with an acceptably low level of health risk." (Abbott, 2016, p. 26)

Figure 1. *Mixed Ethnicity Group Drinking Kava at Fale Talanoa, Four Shells Kava Lounge, Auckland, Aotearoa New Zealand (Photographer: Todd M. Henry, 2024).*

A search of academic databases shows hundreds of peer-reviewed published works reporting “clinical trials of kava.” Most of those works commence with a statement that often reflects the comments in the earlier paragraph explaining the cultural significance and traditional use practices of kava. For instance, “kava [inferring the traditional substance and associated use practices] … has demonstrated …” (Hu, 2024, p. 1516). Descriptions of this nature lead the reader to assume the clinical trials being reported utilized kava in the methodology. However, an inspection of those methodologies typically show that a product made from *Piper methysticum* (i.e., extracts, tinctures and pharmacologically manufactured pills and capsules) and not kava was used. Exemplifying this is Belcaro’s (2016) review of kava clinical trials. He reports that "[m]ost of these studies used a standardized WS 1490 Kava extract formulation, which is composed of 70% kavalactones” (p. 52). Sarris and colleagues’ (2011) review of clinical trials, which sought to understand kava efficacy and safety, reports that most studies used a pill or tablet containing extracted kavalactones administered at a dose of 300–600 mg per day. Similarly, Prescott and colleagues’ (1993) clinical trial assessing body sway initially appears to have utilized kava as opposed to a product made from, or containing, *Piper methysticum*. They explain mixing their kava “using a method that approximated traditional techniques” (p. 50). However, upon further reading, they report their kava was then diluted with orange juice, which does not conform with traditional practice or comply with the definition of kava. Additionally, the participants only consumed a small amount in comparison to typical traditionally influenced settings.

Conversely, Saletu and colleagues (1989) report the use of Kavain, a single kavalactone extracted and isolated from *Piper methysticum*, in a “double-blind, placebo-controlled EEG brain mapping study,” showing this particular lactone has “a significant effect on the human central nervous (CNS)” (p. 187). While this finding is interesting, it contributes little to our understanding of kava ethnopsychopharmacology, or the effects of kava on the brain when all constituents are consumed together with the elements of *set and setting* linked to culture and practice (Aporosa, 2022). Finally, it is common for findings from studies that used *Piper methysticum*-based nutraceuticals and extracts in the methodology to be “overlaid on kava as used in naturalistic traditionally influenced settings … incorrectly assuming effect correlation” (Aporosa, 2022, p. 22). This is not new, has been standard practice for over 30 years, and raises questions about academic rigor and the role of kava research in feeding kava mis- and disinformation.

Kava misinformation and misunderstanding is not limited to the research space. Adding to confusion are products made from, or containing, *Piper methysticum*. New commodification’s and appropriations such as extracts, high potency “shots,” gummies, and flavored pop-culture drinks containing *Piper methysticum* are advertised on social media platforms, routinely misrepresented and mismarketed as kava, reported as containing “noble kava extract” (in the case of a new line of gummy-lollies), or advertised as “premium kava” (according to a brand of flavored “kava seltzer”). Further adding to kava misinformation and increasing confusion is the rise of establishments in the United States called kava bars. Styled on cafés or alcohol bars, these commercial venues often serve beverages made from *Piper methysticum*, marketed as kava, yet prepared and consumed in ways that bear little resemblance to traditional Pacific practices. Price (2024) reports that over 80% of U.S. kava bars also offer kratom (*Mitragyna speciosa*; also see Xie & Milton, 2023), a Southeast Asian plant with addictive, opioid-like effects, either alongside or mixed into *Piper methysticum*-based drinks (Trepany, 2025; Upton, 2025, p. 80–81). This practice not only misrepresents kava but fundamentally alters its effects. Kim (2021) for instance states that kratom is added to *Piper methysticum* beverages in kava bars to give a “euphoric hit,” a change not manifested in naturalistic kava use (Aporosa et al., 2022a). Further, clinical addiction psychiatrist Dr. Cornelieu Stanciu warns that the mixing of kratom with *Piper methysticum* creates a unique synergistic action increasing the addition potential of kratom (quoted in Carney, 2024, 19 min 55 s).

In summary, hundreds of peer-reviewed studies have used methodological inputs that bear little to no resemblance to traditional kava yet make claims implying direct applicability to kava. This conflation (combined with the commodification, appropriation and kava bar practices explained above) creates a significant research gap and widespread misunderstanding about what kava actually is. Our work has two key goals. First, to educate research and commercial communities about what can and cannot be identified as kava, including when discussing and extrapolating therapeutic impacts or risks to kava users who experience traditional usage. Here we exemplify study design from a Pacific-centric position informed by our traditional knowledge systems and include methodological

statements that define kava for the purposes of this research. As Pacific "owners" of kava, we (Pacific members of our team) assert the term *kava* refers to far more than the plant or its chemical extracts. It reflects a deeply embedded cultural construct rooted in Pacific epistemologies, use-settings, and relational systems. Second, in this study and our wider research we seek to advance kava ethnopsychopharmacology that differentiates from prior studies that claim to use kava but, in practice, rely on commodification's and/or products containing *Piper methysticum*. We argue our research contributes to a more accurate scientific understanding of kava, one that aligns with cultural integrity, informs as to risks and benefits, and reinforces safety boundaries.

Methods

Definition of Kava for the Purposes of This Study

For this study, kava is defined not merely as the beverage produced by mixing the ground roots of *Piper methysticum* with water, nor as commercial derivatives such as extracts, capsules, or beverages containing *Piper methysticum*. These commercial forms vary in composition and safety profile and may include additives such as kratom (*Mitragyna speciosa*; Snowden , 2022; Xie & Milton, 2023). In alignment with Pacific traditional knowledge, kava is understood as a holistic cultural construct that extends beyond physical form to encompass ceremonial and relational contexts in which it is, including the practices of *talanoa*, a dialogic and relational mode of engagement that integrates physical, spiritual, ancestral, and communal dimensions consumed (Aporosa, 2019a, 2024; Lebot, 1992). The concept of *talanoa-vā* further emphasizes the spatial and temporal relationships maintained through trust, mutual understanding, and ongoing dialogue (Aporosa & Fa'avae, 2021, Fa'avae et al., 2016; Vaka et al., 2016). Accordingly, throughout this research, the term *kava* is used in its culturally grounded sense, reflecting its embeddedness in Pacific epistemologies and relational systems. Use of the term to refer solely to the plant, beverage, or its isolated chemical constituents is considered an oversimplification and misrepresentation of its traditional meaning.

Kava Preparation

The kava beverage used in the study was prepared by primary investigator AA, following the same "recipe" as that used in previous naturalistic kava use clinical trials (Aporosa et al., 2020, 2022a, 2022b). In total, 8 L (2.1 gallons) of kava was mixed using kava powder originating from Sagani in Northern Fiji. After mixing, the 8 L of kava was poured into a *kumete*. The room where the kava was consumed during the feasibility study was organized to reflect a *faikava* space, or a traditionally influenced kava use venue, inclusive of woven mats placed on the floor in which participants sat cross-legged, consumed kava, and engaged in *talanoa*. Complying with cultural protocol and spoken in the Fijian language to acknowledge those present together with the *mana* (sacred) of the kava space, AA measured and served 100 mL of kava from the *kumete* into *bilo* (coconut shell cups, also known as *ipu*). AA guided the kava consumption protocols throughout the session to ensure compliance with kava's holistic definition. Additionally, to maintain the naturalistic setting, AA invited colleagues and friends from the community to join the kava session. Invited individuals were served beverage kava from a separate batch to that of the two individuals taking part in the study.

Ethical Framework, Study Participants, and Human Subjects Waiver

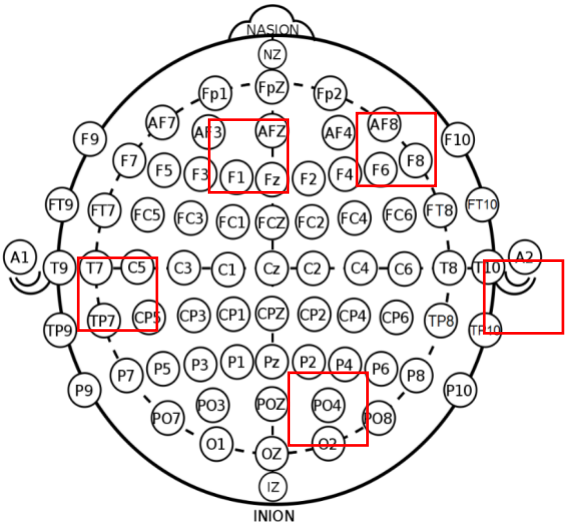
This study utilized the Pacific Post-development Methodological Framework (PPdMF), which combines the indigenous Fijian *vanua* research framework with *talanoa*, Pacific respect values and post-development theory to guide the use of Western-developed, -standardized, and -normed psychometric measures with Pacific people, in order to ensure equity and decolonize research practice (Aporosa et al., 2021). The PPDMF guided the collection of this data. The feasibility study involved only two participants: P1 and P2. Both participants are male as this is the dominant kava using gender and are regular kava consumers. Both participants are senior academic staff members at the University of Waikato, and therefore Article 5 of the Nuremberg principles, approving "self-experiments when an experiment … [is] not expected to do harm" (Hanley et al., 2019, p. 39), was employed and ethics approval was not sought. P1, of Fijian ancestry, has been the principal investigator on several kava studies attached to this project. He has over 40 years of experience in kava preparation and consumption and the related cultural aspects, including kava consumption protocols. P2 is Aotearoa born, of English (non-Pacific) ancestry, and has been drinking kava in naturalistic settings for over 15 years.

EEG Measurement Protocol

EEG signal acquisition was performed with the Emotiv Insight device, a 5-channel wireless EEG headset. The headset was primed and placed on each participant's head. Each electrode is placed on

the scalp according to the International 10–10 system, at five positions AF3, AF4, T7, T8, and Pz used in the study, shown below in Figure 2. The subjects were seated in a chair and closed their eyes for the duration of the test. The subjects were asked to clear their mind for 20 s. A base state EEG signal was acquired with the subject in this natural relaxed brain state. Once the optimum signal quality of 100% is attained (according to the Emotiv software) recording begins. If the signal quality drops below the threshold, the recording is deleted and repeated. An auditory cue was given to indicate to the subject that recording has begun. The recording lasts for 5 mins. Once the data has been recorded successfully there is a 2-s pause and the next recording begins. Upon acquisition, the EEG data was processed through a high-pass filter employing a Hanning window and converted to the frequency domain using a fast Fourier transform.

Figure 2. *Emotiv Insight 5-Channel Wireless EEG Headset Positions of Five Isolated Electrodes (AF3, AF4, T7, T8, and Pz) Used to Collect the Study Data. (Image: Saia et al., 2023, p. 11628).*



EEG Procedure

EEG acquisition occurred at two points during the feasibility study: prior to any kava consumption and post-kava consumption, 6 hr after the consumption of the first *bilo* of kava. The study's 6-hr duration was agreed upon to represent the period of a typical traditionally-influenced kava session. The study commenced at 10 a.m., with both participants welcomed and briefed on the procedure for the day by MO (the psychometrician). Once the baseline testing was complete, the participants were invited to take a seat on the mats and begin consuming kava. At this point, the other individuals taking part in the kava session were invited to enter the room. The participants consumed six 100 mL serves of kava per hour, replicating typical traditionally-influenced kava consumption volumes. This equated to the participants consuming one serve every 9.5 min, with AA using a stopwatch to alert when it was time to consume their next serve.

EEG Data Visualization

The schematic of electrode positions (presented in Figure 4) was generated in Python using the plot_glass_brain function from the nilearn neuroimaging library (v0.11.0; Nilearn contributors, 2024). A transparent glass brain template was plotted in the *z*-plane view, and key EEG electrode sites (AF3, AF4, T7, T8, Pz) were overlaid using MNI coordinates corresponding to the International 10–10 electrode placement system. Split semicircles indicating changes in bandpower amplitude were generated utilizing matplotlib (v3.10.0; Hunter, 2007).

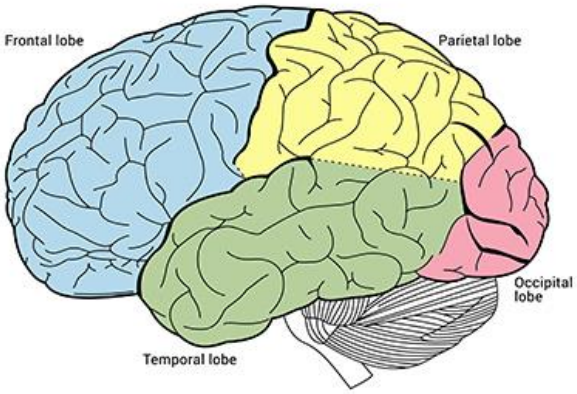
Results

Selection of EEG Placement and Target Brain Wave Activity Assessment

The feasibility study involved small-scale acquisition of EEG signals from five locations on the scalp of two participants. The study aimed to investigate whether there is an observable difference in brain state before and after kava consumption, specifically within a naturalistic kava use test setting. Figure 3 shows a schematic of the human brain, and we describe electrode placement in *Methods*. EEG electrodes were strategically positioned to acquire electrical brain activity data over the frontal lobe (electrodes in AF3 and AF4), parietal lobe (Pz), and temporal lobe (T7 and T8). The frontal lobe houses the frontal association cortex (prefrontal cortex and the motor-related areas excluding the primary motor cortex [see Figure 3]). The frontal association complex is involved in the planning of actions and movement (executive function) as well as abstract thought. The temporal lobe is responsible for processing sensory information and helps in recognising language and forming memories. The parietal lobe is responsible for sensory information, including touch, temperature, pressure and pain.

Of particular interest to this study is the EEG signal acquired from the above-mentioned lobes of the brain. This study targeted the following five frequency bands within the EEG signal. Theta θ (4–8 Hz), alpha α (8–12 Hz), low beta β (12–16 Hz),

Figure 3. *Brain Schematic.*



Note. Showing division of each of the hemispheres into four lobes: frontal, parietal, temporal and occipital (University of Queensland, 2024).

high beta β (16–25 Hz), and gamma γ (25–45 Hz). Alpha α waves connect conscious thinking and subconscious mind and are associated with calming and relaxation. Alpha waves in healthy, awake adults occur while resting with the eyes closed. They disappear during sleep and when there is concentration on a specific task. Alpha waves are maximal over the occipital region. Beta β waves replace alpha waves during attention to tasks or stimuli and are of higher frequency. They are common while concentrating, or when a person is under stress or experiencing psychological tension. If a patient opens their eyes or begins a mental activity, the alpha waves decrease to be replaced by beta waves all over the scalp. Low beta β waves are active in a waking state. They are involved in conscious thought and logical thinking and tend to have a stimulating effect. High beta β is associated with significant stress, anxiety, paranoia, high energy, and high arousal. Theta θ waves are involved in sleep or daydreaming. These waves tend to be more dominant in deeply relaxed or meditative states. Theta waves in normal adults may appear transiently during sleep. Gamma γ waves are important for learning, memory, and information processing. They are produced when intensely focused or actively engaged in solving a problem.

EEG Measurement Data

This preliminary study analyzed EEG to assess neurophysiological changes before and after kava consumption. Figure 4 provides a visual summary of the EEG data obtained from both participants. After kava consumption, Participant 1 showed a decrease in α and θ waves, while γ waves increase compared to baseline. Low and high β exhibit only minor changes and do not show a clear directional trend. After kava consumption, Participant 2 shows a notable increase in α waves and an increase in θ waves after kava consumption. Small increases also occur in both low and high β, while γ waves decrease relative to baseline. Table summaries of pre- and post-kava values for each electrode (AF3, AF4, T7, T8, and Pz) can be found in Appendix A. In brief, the largest shifts for both participants appear in the frontal (AF3, AF4) and temporal (T7, T8) electrode sites, with additional changes at the parietal site (Pz).

Discussion

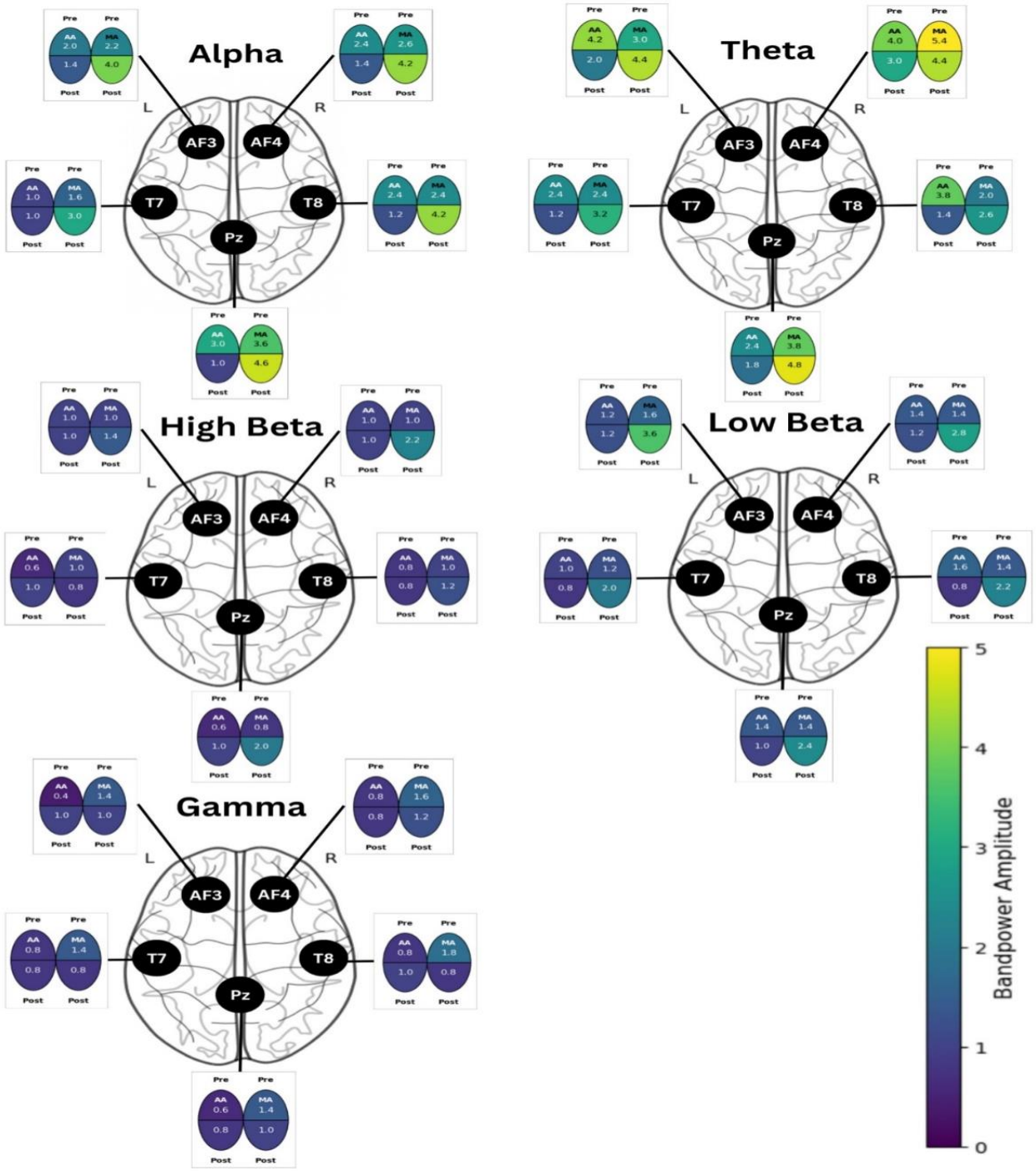
Neurophsyiological Activity Similarities and Contrasts Between Participants

Participants exhibited contrasting EEG responses following kava consumption, with each participant showing almost opposite effects. Participant 1 showed a decrease in α and θ waves while γ increased, indicating an active mind and heightened focus (Herrmann et al., 2005; Jensen et al., 2007). Reductions in α and θ may suggest a move away from relaxation and introspection toward greater attentional engagement, consistent with higher γ power being associated with integrative processing (Fries, 2001). Although low and high β showed minor shifts, they did not display a clear directional trend (Niedermeyer, 2011). In the case of Participant 2, there was a considerable increase in the presence of α waves, suggesting an enhanced connection between conscious and subconscious processes and a calmer, more relaxed state (Cahn & Polich, 2006). This was further supported by a noticeable increase in θ waves, which are often linked to sleep or daydreaming and are dominant when a person is deeply relaxed or meditative (Başar et al., 1999; Klimesch, 1999).

Participant 2 also displayed small increases in both low and high β, possibly reflecting mild cognitive stimulation, while γ decreased. A reduction in γ waves may imply diminished focused engagement or reduced information processing (Basar-Eroglu et al., 1996).

It is suggested that additional electrode-level examination be conducted, given that activity at AF3 and AF4—positioned above the frontal lobe—is associated with planning, decision making, and behavioral control (Fuster, 2017). For Participant 2, AF3 showed increases in most frequency bands except γ, while AF4 displayed decreases in γ and θ alongside increases in other bands, indicative of a

Figure 4. *Changes in EEG Bandpower Amplitude Across Five Frequency Bands (Alpha, Theta, High Beta, Low Beta, and Gamma) Before and After Kava Consumption.*



Note. Topographic head maps illustrate the location of key electrode sites (AF3, AF4, T7, T8, Pz), with surrounding oval plots showing pre- (upper) and post- (lower) kava mean bandpower amplitudes for each site in the two participants (P1, left and P2, right). The color scale represents normalized bandpower amplitude from 0 (purple) to 5 (yellow). Notable post-kava increases in alpha and theta bandpower are observed particularly in frontal and parietal regions, consistent with relaxation and sedative effects. High and low beta bands show reduced or unchanged activity, while gamma activity remains low across conditions. These spectral changes reflect a shift toward a calmer, less aroused neural state following kava intake.

relaxation-related profile. Conversely, Participant 1 presented decreased α and θ and increased γ at both AF3 and AF4, suggesting enhanced executive functioning and focus. Temporal (T7, T8) and parietal (Pz) sites also displayed shifts, though to varying extents (Kropotov, 2016).

We also considered these EEG findings in light of our published *Brain Gauge* study which reported kava use as having a statistically significant detrimentally effect on temporal order judgment (TOJ), a cognitive function associated with frontal–striatal circuits (Aporosa et al., 2022a). The heightened γ in Participant 1 could theoretically improve TOJ (Pöppel, 1997; van Wassenhove et al., 2007), whereas the lower γ in Participant 2 might hinder it. From a physiological perspective, the observed alterations in EEG band power could reflect underlying changes in cortical excitability and network connectivity. Increased α and θ power—as seen in Participant 2—are often associated with inhibitory neural processes and a state of relaxed introspection, potentially mediated by enhanced GABAergic activity (Başar et al., 1999; Klimesch, 1999). In contrast, the increased γ band activity observed in Participant 1 is typically linked with local cortical processing and integrative functions that support rapid information processing (Fries et al., 2001; Jensen et al., 2007), which may facilitate the precise temporal sequencing required for optimal TOJ performance (Pöppel, 1997; van Wassenhove et al., 2007). These divergent patterns underscore the possibility that individual differences, perhaps due to habitual kava use or cultural background, may modulate the balance between relaxation and cognitive alertness during kava consumption. Future studies that include behavioral assessments of TOJ alongside EEG measures would help clarify the neurophysiological mechanisms at play.

Implications of Participants' Contrasting EEG Measurements

Even within this small sample, the distinct EEG outcomes highlight the importance of individual variability and justify more extensive research. By demonstrating that both relaxation-oriented and focus-oriented neurophysiological profiles can emerge under kava consumption, these results emphasize the complexity of kava's ethnopharmacology. Larger studies with direct behavioral measures—such as TOJ tasks—are needed to confirm the extent to which these EEG patterns predict functional outcomes. Ultimately, exploring these mechanisms more deeply will not only clarify kava's effects on brain function but also support its culturally informed and safe application in traditional and contemporary contexts.

Individual differences that may underlie these divergent outcomes create the pressing need for wider, demographically stratified and fully historied study cohorts. Confounding effects of age, sex, genetics, metabolism and pharmcodynamics, health conditions, and kava use history (length, practice, habituation) will need to be assessed. Ultimately, application of exciting new techniques such as machine learning to data from an at-scale study could provide consumers and regulators with much-needed data on individual features associated with different outcomes of kava use. From a regulatory perspective, this type of data set on traditional kava use would then set a standard for the knowledge base, standing in contrast to abstracted and adulterated products containing *Piper methysticum* that, while market and presented as kava, has little in common with the Pacific cultural keystone species.

Implications for Kava Misinformation and Disinformation

This study develops and implements a proposed best practice for defining kava when used in research, and potentially in commercial settings. The traditional and naturalistic definition of kava used here is combined with the long-term goal of addressing research gaps on kava exposure that has fidelity to the traditional practice. Together, these have the potential to support a best practice benchmarking that (a) limits the definition (and claim) of kava to its Pacific-centric and culturally-authentic self, and (b) creates a way for consumers, practitioners, and regulators to clearly differentiate when they are presented with information on *Piper methysticum*-derived products that are not kava per se. There are significant implications here for wider societal understanding of kava outside the cultural and research communities.

For example, using the term *kava* to describe only the plant, its derivatives, or *Piper methysticum*-containing products and practices in many kava bars is a reductionist misrepresentation that not only distorts kavas traditional meaning but also misrepresents kava to customers. In the U.S., false advertising is considered a "deceptive trade practice" and, in some cases, counters regulations including the 2004 Federal Trade Commission Act. Similarly, Critchfield et al. (2023) observe that kratom's availability in venues called kava bars reinforces the mistaken idea that the two are similar. The FDA reports 36 deaths linked to kratom-

containing products (Gottlieb, 2018), and "has determined that kratom, when added to food, is an unsafe food additive," adding that "kratom is not lawfully marketed as a dietary supplement and cannot be lawfully added to conventional foods" (FDA, 2025). Kratom (unlike kava) is concerning in terms of health effects and addictive potential (Carney, 2024; Towers et al., 2026). Heaton (2025) warns that U.S. kava bars serving *Piper methysticum* beverages "laced with … kratom" has raised concern among Pacific kava advocates who fear that kava will be wrongly blamed for kratom-related harms. Vanuatu's Biosecurity Director, Tekon Timothy Tumukon (2024), has warned that U.S. establishments are misleading consumers by marketing kratom-kava blends as "fresh kava." He proposes that such products be rebranded to avoid confusion and to prevent another global ban on kava exports, referring to the *European Kava Ban* of the early 2000s in which nutraceuticals and products containing *Piper methysticum* were believed responsible for hepatotoxicity cases and several deaths (Showman et al., 2015). Kava-kratom confusion (misinformation [Peifer, 2024]) and deliberate conflation (disinformation [Lewis, 2024]) has extended to regulatory bodies, the media, and financial institutions. Tumukon's comment has merit, particularly as many commercial products containing *Piper methysticum* are advertised as kava, appropriate the safety profile of the traditionally prepared beverage in their advertising, and imply that this applies equally to their own formulations. Advertisements also highlight, or allude to, kava's cultural significance, calming and sleep-promoting properties, inaccurately suggesting correlation between kava and their commercial commodifications.

Conclusions

This study contributes to the nascent field of kava ethnopsychopharmacology by demonstrating that even within a small sample, individual variability in EEG responses is evident. Moving forward, it is essential to replicate these findings in larger cohorts and to incorporate direct behavioral assessments to validate the relationship between EEG dynamics and cognitive performance. Such efforts will not only deepen our understanding of the neurophysiological mechanisms underlying kava's effects but will also inform the safe and culturally relevant application of kava in both traditional and contemporary contexts.

There are cultural, academic, community, commercial, and regulatory stakeholders within the kava ecosystem, all of whom are negatively impacted by the aforementioned confusion and conflation of safe kava with commodified and appropriated products containing *Piper methysticum*—some of which include addictive kratom—that are inconsistent with traditional knowledge definitions of kava. We propose the establishment of a research definition, methodological framework, and evidence base that starts with traditional kava use and is supplemented by work on the abstracted and adulterated forms, rather than vice versa. This will bring increased clarity extending from culture to academia and radiating out into community, commerce, and society as a lens through which decision-making on kava at the personal and institutional level can be better informed.

By advancing research that centers on culturally defined kava and employs traditional preparation and use-settings, we seek to provide a clearer, more accurate understanding of kava's cognitive, neurological, and relational effects. Rigorous, culturally grounded research is essential, not only to safeguard kava's integrity and the communities that steward it but also to ensure that health claims and regulatory frameworks are informed by evidence that accurately reflects kava as it is known, used, and experienced in the Pacific—kava that is also increasing in popularity among non-Pacific peoples seeking to genuinely engage with both this cultural keystone species and its relational space.

Author Declarations

Funding was provided by Health Research Council of New Zealand Pacific Project Grant, 25/153, to SA. GB Sciences Research Award to HT. No artificial intelligence (AI) tools were used in the preparation of this manuscript. MO, MH, and CF are all casual kava drinkers. AA and MA are long-term kava drinkers. For AA, kava and the kava culture are also important aspects of his Fijian ancestry and cultural practice. HT is a member of the U.S. Scientific Advisory Board and has received prior research funding from GB Global Biopharma, a phytomedicine-focused company with an interest in medical marijuana and the therapeutic potential of *Piper spp*.

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Appendix A

Table A1

Table Values Reported as Normalized Arbitrary Units

Participant 1	Theta	Alpha	Low Beta	High Beta	Gamma
Pre					
AF3	4.2	2.0	1.2	1.0	0.4
T7	2.4	1.0	1.0	0.6	0.8
Pz	2.4	3.0	1.4	0.6	0.6
T8	3.8	2.4	1.6	0.8	0.8
AF4	4.0	2.4	1.4	1.0	0.8
Post					
AF3	2.0	1.4	1.2	1.0	1.0
T7	1.2	1.0	0.8	1.0	0.8
Pz	1.8	1.0	1.0	1.0	0.8
T8	1.4	1.2	0.8	0.8	1.0
AF4	3.0	1.4	1.2	1.0	0.8

Participant 2	Theta	Alpha	Low Beta	High Beta	Gamma
Pre					
AF3	3.0	2.2	1.6	1.0	1.4
T7	2.4	1.6	1.2	1.0	1.4
Pz	3.8	3.6	1.4	0.8	1.4
T8	2.0	2.4	1.4	1.0	1.8
AF4	5.4	2.6	1.4	1.0	1.6
Post					
AF3	4.4	4.0	3.6	1.4	1.0
T7	3.2	3.0	2.0	0.8	0.8
Pz	4.8	4.6	2.4	2.0	1.0
T8	2.6	4.2	2.2	1.2	0.8
AF4	4.4	4.2	2.8	2.2	1.2