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Prefrontal tDCS for Smoking Cessation: Focus on the Number of Sessions and Motivation to Quit

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Abstract

Neuromodulation through transcranial direct current stimulation (tDCS) has a *B* recommendation for the treatment of addiction according to therapeutic evidence guidance. We present an intervention, with randomization and placebo, to test the effectiveness of 10 tDCS sessions, without other treatment, spaced over 2 weeks, on tobacco consumption and craving, in 26 healthy smokers. The influence of motivation to quit, self-perceived efficacy, and previous physical dependence was assessed. Active dorsolateral prefrontal cortex (DLPFC, cathode F3/anode F4) tDCS (20 min at 2 mA) was compared to sham through pre–post design with 1-month follow-up. Data analysis included AUCg formulas, ANOVA's and linear regressions. The experimental group showed significantly less consumption than sham during intervention (p = .02, d = .95) but not at follow-up, as well as a significant decrease in craving (p = .04, η^2 = .15). The most prominent predictors of effectiveness were the number of cigarettes regularly smoked (B = 4.27, p = .001) and self-reported motivation to quit (B = −6.48, p = .05). In sum, tDCS helps to reduce tobacco consumption and craving, but its benefits are not maintained over time. It would be necessary to increase the number of sessions and control motivation and the level of previous consumption.

Keywords: tDCS; smoking; craving; motivation; sham

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Smoking is a leading preventable cause of disease and death, causing over 8 million deaths annually, including 1.3 million nonsmokers who are exposed to second-hand smoke (World Health Organization [WHO], 2023). Tobacco use disorder (TUD) is a chronic disorder characterized by compulsive tobacco-seeking and a loss of control over its use (5th ed.; DSM-5; Appendix A; American Psychiatric Association [APA], 2013). Noninvasive brain stimulation (NIBS) methods, such as transcranial direct current stimulation (tDCS), can target addiction neurocircuitry network and may help treat TUD and other substance use disorders (SUDs; (Mehta et al., 2024). NIBS targeting a central node of the addiction network as the dorsolateral prefrontal cortex (DLPFC) could improve the control of impulsive and risky behavior, allowing more functional decisions related to smoking. This could be possible since reward-based motivation is thought to be processed in the left DLPFC, while self-control is processed in the right DLPFC; so, many of the actual protocols seek to balance both sides (Balconi et al., 2014; Fecteau et al., 2014). In consonance with this, tDCS has shown evidence of being likely effective (level B) in treating SUDs by modulating DLPFC (cathode on left frontal, anode on right) according to therapeutic evidence guidance from Lefaucheur et al. (2017) and Fregni et al. (2021).

Recent meta-analyses have focused on tobacco consumption and craving. Kang et al. (2019) analyzed 12 studies and found significant improvements in cue-induced craving and smoking

rates with tDCS. Another meta-analysis by Chen et al. (2020) included eight studies and demonstrated significant benefits of tDCS on craving, showing decreased craving and improved quality of life compared to a placebo group. Mehta et al. (2024) reviewed 11 studies on tDCS in TUD (*n* = 448 participants including controls) showing positive outcomes (in tobacco craving and/or consumption) in seven studies, mainly with right anodal DLPFC stimulation and multisession tDCS protocols. However, the overall effect size was moderate though still considered clinically relevant (Hedge's *g* of .50) and nonsignificant due to high variability among studies. Chan et al. (2024) examined 13 studies (327 participants receiving active tDCS and 284 sham) and found a modest reduction in craving with tDCS, but variability in study conditions affected significance. Overall, while tDCS shows potential for treating TUD, more research is needed to clarify which variables influence treatment outcomes. The meta-analysis by Mehta et al. (2024) examined multisession tDCS protocols, with most applying five sessions of active tDCS (Boggio et al., 2009; Fecteau et al., 2014; Müller et al., 2021; Smith et al., 2015). Two studies found no effects on consumption or craving, while the other two showed positive effects, with one showing effects up to 4 days after stimulation ended. Other clinical trials with interventions of only three sessions showed either no results for smoking cessation (Falcone et al., 2018) or a temporary reduction in consumption with no long-term effects (Alghamdi et al., 2019). A study by Perri and Perrotta (2021) applied five sessions and found a reduction in craving but not in consumption. These inconclusive results suggest that more than 3–5 sessions may be necessary for reliable tDCS outcomes. Additionally, while psychological factors such as motivation and self-efficacy are crucial for smoking cessation, little research has explored their influence on tDCS outcomes. These are important to address given neuroimaging work showing the state of DLPFC is different depending on subjective motivation and resolve to stop addictive behavior (Silvanto & Pascual-Leone, 2008). Most studies also did not measure the long-term effects of tDCS beyond a few days. In sum, more research is needed to understand the interaction between nicotine addiction and tDCS and to develop an optimal treatment strategy.

Our general aim is to study the effects of repeated tDCS sessions on smoking consumption pattern and tobacco craving in people with TUD, through an improved design (a longitudinal randomized placebo-controlled trial) which will include the effect of the neurostimulation at the time of the intervention and after a follow-up of a month. In addition, we wanted to analyze the influence of certain psychophysiological variables on the tDCS outcome regarding tobacco consumption. Finally, with the additional aim to obtain more descriptive information about the subjective reception of the stimulation, we recorded all sensations after the application of tDCS and evaluated their influence on the outcome.

Method

Participants

From an initial pool of 67 individuals, 26 adults aged 23–69 participated in the study, including 14 women and 12 men equally randomly divided between experimental and placebo groups (each *n* = 13). Participants were recruited via email following promotions with posters and social media ads. All met DSM-5 criteria for TUD and had smoked for at least a year. Safety measures excluded those who were pregnant; had significant clinical, psychiatric, or neurological illnesses (such as epilepsy or traumatic brain injury); had metallic brain or skull implants, a history of stroke with cerebral stent placement or in carotid arteries, dermatological sensitivities, or pacemakers. The design standardized participants' physical dependence, motivation to quit smoking, and perceived self-efficacy. The flowchart for the selection of the participants according to CONSORT guidelines (Schulz et al., 2010) can be consulted in Figure 1. Descriptive data for demographical and all other variables of interest can be consulted in Table 1.

Materials

TDCS Apparatus. The study used the Brain Premier E1 tDCS device for neuromodulation, approved by the European Union for medical use and equipped with safety features. The device can provide a current output of 0.5 to 2 mA for 20 or 30 min, depending on the settings. For safety, stimulation starts with a gradual current increase over 30 s (ramp in) and decreases similarly before the session ends (ramp out). The study used round sponge electrodes measuring 1.5 in. in diameter.

Psychometric Measures. The psychometric assessment instruments used in this protocol were as follows: (a) a smoking interview (adapted from Becoña, 1994): this is a semi-structured interview to ascertain sociodemographic data, smoking history and current tobacco use; (b) a self-recording weekly template (from Monday to Sunday) which facilitates the recording of the total number of cigarettes smoked each day; (c) a visual analog scale for

Figure 1. *Flowchart for the Selection of the Participants According to CONSORT Guidelines.*

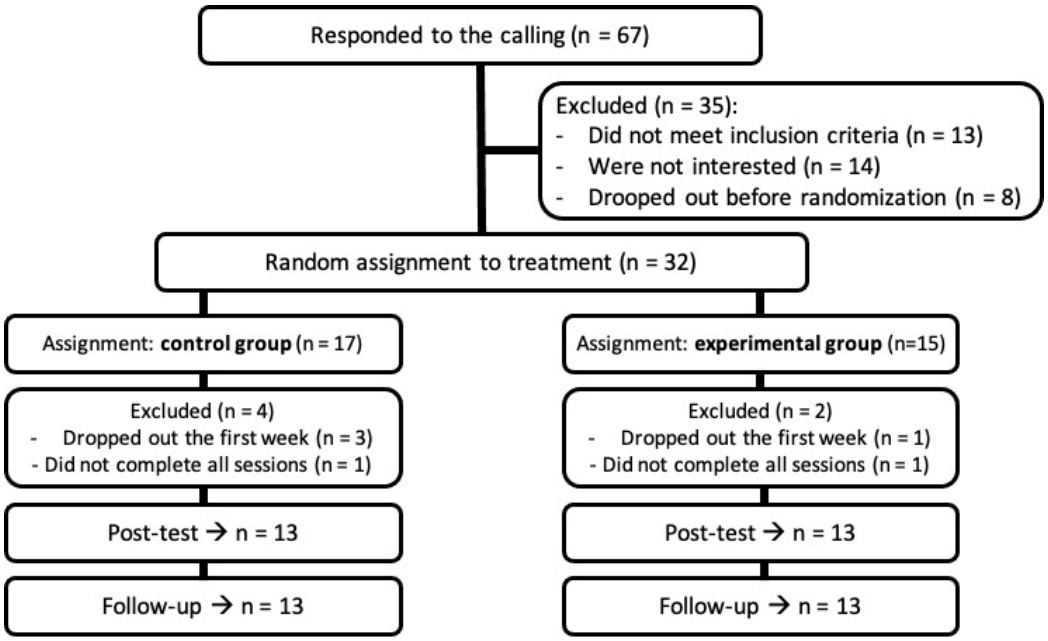


Table 1
Descriptive Data for Demographical and All Other Variables

	ACTIVE tDCS Mean (*SD*)	SHAM tDCS Mean (*SD*)	*t*, *p*
Gender	7 W & 6 M	7 W & 6 M	
Age	46 (13.08)	42.15 (11.16)	$t < 1$ n.s.
Years of Smoking	22.15 (13.70)	21.7 (10.28)	$t < 1$ n.s.
No. Cigarettes a Day	13.53 (4.09)	13.46 (4.74)	$t < 1$ n.s.
Physical Dependence	5.23 (1.96)	4.53 (2.56)	$t < 1$ n.s.
Motivation	7.46 (1.26)	7.69 (1.60)	$t < 1$ n.s.
Autoefficacy	5.38 (2.32)	6.46 (1.33)	t(gl 24) = 1.44, p = .08

Note. Descriptive data in means and standard deviations (*SD*) for demographic and other variables of interest at baseline, separated for the active tDCS group and the sham tDCS group. W = women, M = men.

craving (VAS-C), that measures the desire to smoke, where 0 corresponds to the total absence of desire and 10 to the maximum; (d) the Richmond Test (Richmond et al., 1993) to evaluate the motivation to quit smoking, which consists of four items with two or three response alternatives and classifies motivation as low (0–6 points), medium (7–9 points) and high (10 points); (e) the Fagerström Test of Nicotine Dependence (FTDN; Heatherton et al., 1991) to evaluate the physical dependence of smoking, which consists of six items with two or four response alternatives whose score ranges between 0 and 10, where it is considered a high degree of nicotine dependence from 6 or more points, although low scores do not necessarily indicate a low degree of dependence; (f) a visual analog scale for the perceived autoefficacy (VAS-EFI) to quit the smoking habit, where 0 corresponds to zero perceived efficacy and 10 is the maximum; and finally, (g) the tDCS-Related Feelings Questionnaire (Antal et al., 2017), a questionnaire that assesses the patient's possible sensations of distress after the application of tDCS, according to four degrees of intensity. Please note that some of the dependent

measures were taken in a slightly different time of the entire experiment, according to the design detailed below.

Design and Procedure

The study was a longitudinal randomized placebo-controlled trial with participants divided equally between a control group (sham tDCS) and an experimental group (active tDCS). Three phases were evaluated: a baseline phase, an intervention phase, and a follow-up 1 month after intervention ended. Participants who responded to the call were invited to an initial interview to obtain general and nonspecific information about their habit, check inclusion criteria, receive information about the study, and sign consent documents where appropriate. During the following week, the selected participants completed the self-recording weekly template for daily cigarette consumption (baseline: seven measurements preintervention phase). Immediately after this, the participants attended a second interview, in which most of the above-listed psychometric measures were collected (smoking interview, Fagerström test, Richmond test, VAS-EFI scale). From this moment, the intervention phase started and lasted for 2 weeks. Participants received a total of 10 tDCS sessions at 2 mA for 20 min, one session at the same time every working day for 2 weeks (see details of the protocol below). For the placebo condition, the same protocol was applied, but the tDCS device was disconnected (see details for the protocol below). During this intervention phase, we took two types of measures: on the one hand, the number of smoked cigarettes, which was recorded every day during the 2nd week of intervention (seven measurements, on-intervention phase); on the other hand, the level of craving, which was recorded with the VAS-C scale along the 2 weeks of intervention (three measures each week, six measures in total). Right after the completion of this intervention phase, the participants fulfilled the Antal test to explore sensations after the tDCS. The follow-up phase occurred 1 month after intervention and involved recording cigarette consumption over a week (seven measures) and assessing craving levels and the psychometric measures of physical dependence, motivation, and perceived self-efficacy again (note that, while these follow-up measures were recorded, they were not included in the statistical analyses for the current study aims and objectives).

TDCS Protocol

The study involved placing electrodes over the DLPFC following the international 10–20 system of Jasper, with the anode on the right frontal (F4) and the cathode on the left frontal (F3). The electrodes (of 6 cm diameter) were soaked in a 0.9% sodium chloride saline solution and positioned on the scalp after the area was cleaned with 96% alcohol. Participants received 10 sessions of tDCS at 2 mA for 20 min each, one session per day (Monday to Friday) for 2 weeks. For the placebo group, the same protocol was followed, but the tDCS device was turned off. To match the somatosensory effects of tDCS, we used a saline solution with a small amount of capsaicin (0.75 mg/g cream, Viñas laboratories) to simulate the slight itching or burning sensation of tDCS (capsaicin is a cream indicated for the relief of moderate to severe pain in painful diabetic neuropathy, and it causes a slight sensation of itching or burning on the skin). During neurostimulation, participants sat comfortably in a chair and listened to relaxing music through earphones. At the end of the tDCS protocol, all participants, whether in the sham or active groups, completed the Antal questionnaire (2017) to assess sensations and possible side effects of the intervention.

Ethics

All participants were provided with information about the study and signed several consent forms, including the Informed Consent Document, Confidentiality Commitment, tDCS Protocol Consent, and Informed Consent for the Use of Clinical Data. The Human Research Ethics Committee of our university approved the project (H1549015474557), ensuring it adhered to the fundamental principles of the Declaration of Helsinki and the Council of Europe Convention on Human Rights. The study also complied with legal and ethical standards in biomedical research and bioethical data protection as established by local legislation. The research was conducted in accordance with the ethical and legal standards in force, including the Declaration of Helsinki. The raw data collected for the study have been deposited in an open repository according to the DORA and CoARA agreements, and can be consulted in https://doi.org/10.5281/zenodo.10960954.

Statistical Analysis

Statistical analyses were performed using SPSS statistical software version 28.0.1.1. Descriptive statistics were calculated for all variables, and Spearman ρ correlations were conducted to explore relationships among demographic and psychometric variables at baseline. To assess cigarette consumption, a single representative measure was calculated for each phase (baseline, intervention, and follow-up). For this purpose, the area under the

curve with respect to the ground (AUCg) was calculated as a dependent measure according to the formula of Pruessner et al. (2003) for each phase. Such measure has been previously applied mainly for the analyses of hormonal response, especially cortisol (Fekedulegn et al., 2007) but also for behavioral variables related to addiction (Amlung et al., 2015), and it is useful to analyze data sets comprised of repeated measurements over time where the researcher wants to explore whether any changes occurred (Rodriguez, 2023). Thus, all posterior analyses for smoking behavior were based on this measure. Mean differences were tested using repeated-measures ANOVA. Normality was assessed with the Shapiro-Wilk test, and sphericity with Mauchly's test. Adjustments were made using the Greenhouse-Geisser correction when necessary. Post-hoc comparisons used robust *t*-tests with bootstrapping (n = 1,000) or comparisons with estimated marginal means difference and Bonferroni corrections. Effect sizes were reported using η^2 or Cohen's *d*. For craving, six raw scores were analyzed during the 2 weeks of tDCS using repeated-measures ANOVA with the same assumptions and post-hoc tests. Backward stepwise regression analyses were performed to assess the influence of baseline psychometric variables and the intervention on immediate and 1-month smoking outcomes. Data are reported in means and standard deviations (*SD*) or 95% confidence intervals when relevant.

Results

Descriptive Data and Relations Among Baseline Variables

Table 1 provides descriptive data for the sample, divided by groups. At the beginning of the trial, there were no significant differences between the groups in terms of mean age, years of smoking, number of cigarettes smoked per day, physical dependence, motivation to quit smoking, and perceived self-efficacy (though the placebo group had a slightly higher mean for this last variable). Spearman's ρ revealed significant correlations among some variables. Age was positively correlated with years of smoking (ρ = .66, p = .001), but not with the number of cigarettes smoked per day. Additionally, the number of cigarettes smoked per day was positively related to physical dependence (ρ = .50, p = .008). Finally, the initial motivation to quit smoking was positively related to perceived self-efficacy (ρ = .59, p = .001). No other significant relationships were observed at baseline.

Cigarette Consumption

The study aimed to evaluate whether daily tobacco consumption was reduced in the active tDCS group compared to the placebo group. Figure 2 displays daily cigarette consumption for each experimental phase, showing similar baseline consumption between groups. During the intervention phase, active tDCS caused a significant reduction in daily cigarette consumption, followed by a partial rebound during follow-up after the end of the intervention. To analyze the data, an AUCg was calculated for each phase and group. A repeated-measures ANOVA with Greenhouse-Geisser correction showed no significant main effect of the group (F < 1), but there was a significant main effect of the time of intervention, F(1, 62; 38, 9) = 47.49, p = .001, η^2 = .66. Most interesting, the interaction between the time and group, F(1, 62; 38, 9) = 16.61, p = .001, η^2 = .40, was significant, as shown in Figure 3. Post-hoc analysis using independent samples *t*-tests with bootstrapping revealed a significant difference between groups during the intervention phase, t(24) = 2.43, p = .02, d Cohen = .95, with the active tDCS group (Mean = 36.07; *SD* = 28.17) showing a greater reduction in cigarette consumption compared to the sham tDCS group (Mean = 61.80; *SD* = 25.74). No significant differences were found between groups at baseline (active tDCS: Mean = 84.11; *SD* = 25.70 vs. sham tDCS: Mean = 74.65; *SD* = 30.80) or follow-up (active tDCS: Mean = 54.88; *SD* = 34.93 vs. sham tDCS: Mean = 69.96; *SD* = 28.44). Further analysis of each group's data with estimated marginal means differences and Bonferroni corrections showed that the active tDCS group had significantly different means across all phases: baseline to intervention (I-J = 48.03; p = .001), intervention to follow-up (I-J = 18.80; p = .001), and baseline to follow-up (I-J = 29.23; p = .001) indicating a reduction in cigarette consumption during intervention and a partial increase during follow-up, although they did not recover the same level of consumption as in the baseline, maintaining a significantly lower level. In contrast, the sham tDCS group showed a different mean from baseline to intervention (I-J = 12.8; p = .04), and from intervention to follow-up (I-J = 8.15; p = .05) but no significant difference between baseline and follow-up, indicating some reduction during intervention but an increase back to baseline levels during follow-up.

Craving

The study's second objective was to evaluate whether craving for tobacco consumption decreased during intervention and whether there were differences between groups. A repeated-measures

ANOVA showed a significant main effect for the factor "group," $F(1, 24) = 4.51$, $p = .04$, $\eta^2 = .15$, due to a higher overall level of craving in the control group (Mean = 6.87; 95% IC [6.15, 7.59]) compared with the active tDCS group (Mean = 5.82; 95% IC [5.09, 6.54]). The ANOVA also revealed a significant main effect, $F(5, 120) = 9.29$, $p = .001$, $\eta^2 = .27$, for the factor "time" (six measures obtained across 2 weeks) that was nuanced by a significant interaction between the time and the group, $F(5, 120) = 7.58$, $p = .001$, $\eta^2 = .24$. Post-hoc analyses with separate ANOVAs for each group found no significant differences among the six measures for the control group, $F(5, 60) = 1.87$, $p = .11$. In contrast, the active tDCS group showed a significant effect of "time," $F(5, 60) = 11.04$, $p = .001$, $\eta^2 = .47$. In the active tDCS group, estimated marginal means difference with Bonferroni corrections showed a significant decrease in craving from the initial measure (Monday of the 1st week of intervention) to later points in the intervention phase. Significant decreases were observed when comparing the initial craving to timepoint 4 (Monday of the 2nd week: I-J = 2.15; $p = .01$), as well as timepoint 4 to 5 (I-J = 2.15; $p = .009$) and to 6 (end of intervention, Friday of the 2nd week; I-J = 2.84; $p = .002$). Comparisons among measures taken during the 2nd week of intervention did not reach statistical significance.

Regression Analysis on Smoking Behavior

The study explored the influence of initial baseline measures (age, years of smoking, number of cigarettes smoked per day, physical dependence, motivation to quit smoking, and perceived self-efficacy) along with tDCS intervention (active or sham) on smoking consumption. Backward stepwise regression analyses were performed on the AUCgINTERVENTION (outcome during the 2nd week of intervention) and AUCgFOLLOW-UP (outcome after a month) dependent variables. For the AUCgINTERVENTION outcome, the best-fitting significant mode, $F(5, 20) = 9.65$; $p = .001$; $R^2 = .63$, included intervention, age, number cigarettes smoked per day, and motivation to quit smoking.

Figure 2. *Number of Smoked Cigarettes a Day During Each Phase of the Trial, Separated for Each Group.*

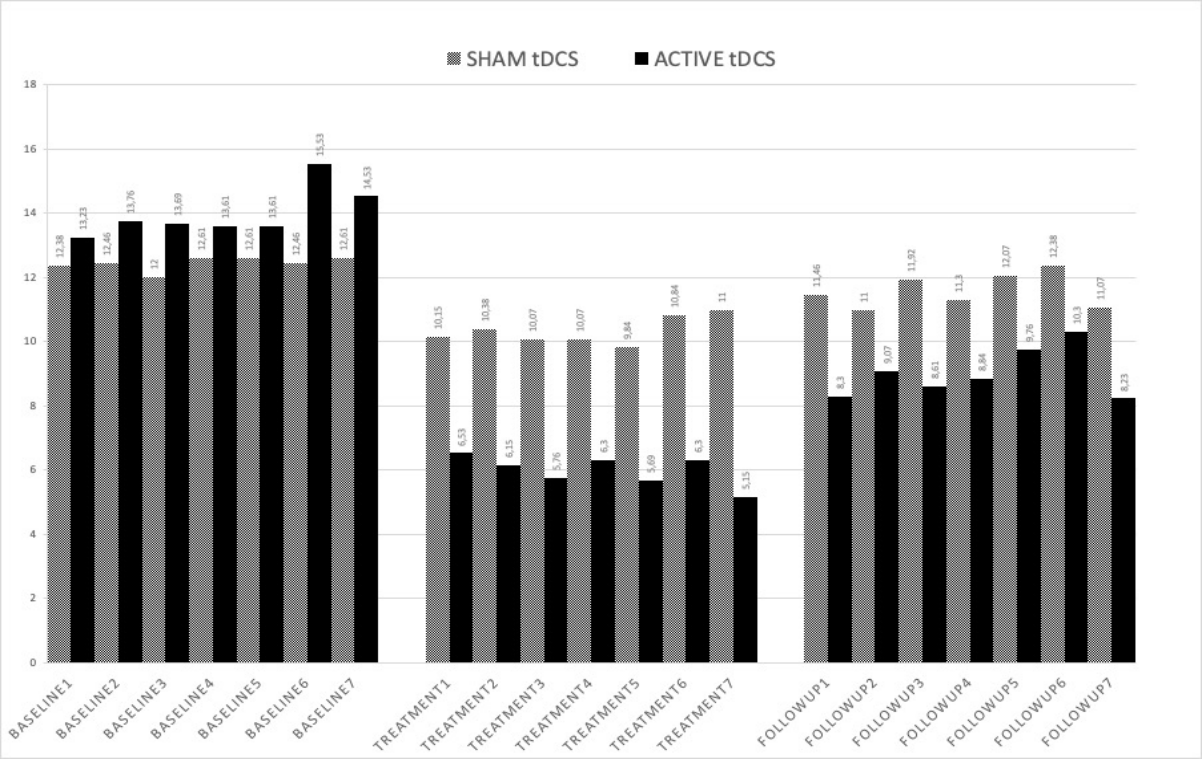
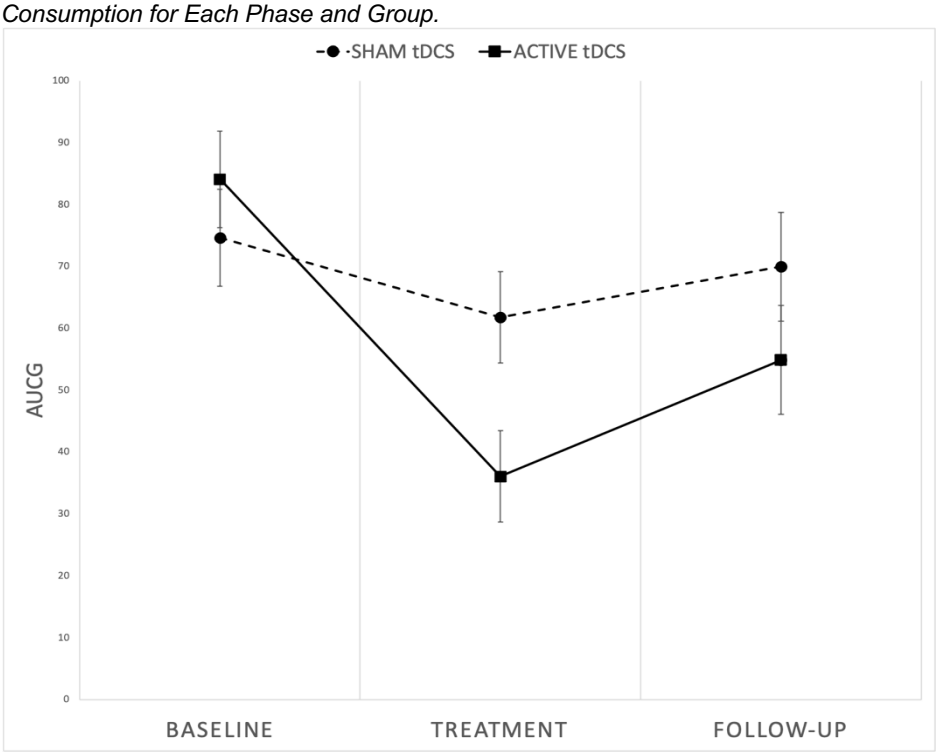
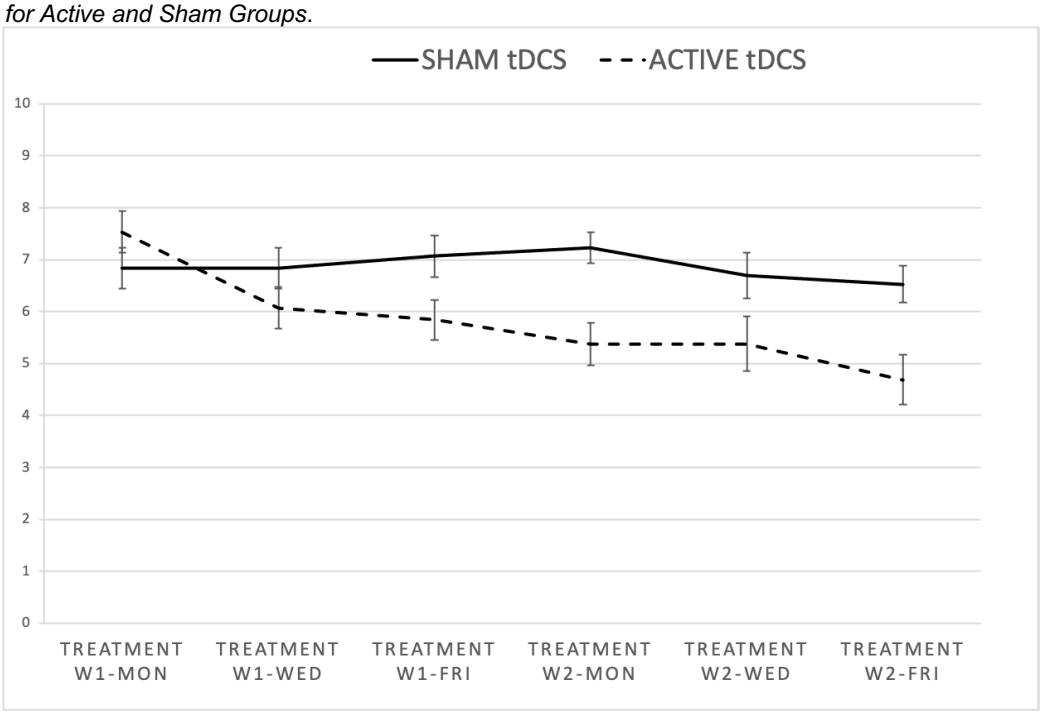


Figure 3. *Mean AUCg (Area Under the Curve From the Ground) Regarding Cigarette Consumption for Each Phase and Group.*



Note. Comparison between groups was significant just for the intervention (see text).

Figure 4. *Evolution for Craving Experience Along the 2 Weeks of tDCS Intervention, Separated for Active and Sham Groups*.



Note. There were some statistical differences only in the evolution of the active tDCS group (see text). Bars: standard error of the mean.

The stronger predictors were for number of cigarettes smoked per day (B = 4.27, t = 5.15, p = .001) and the intervention itself (B = −27.49, t = −3.62, p = .002). Motivation to quit smoking (B = −6.48, t = −2.06, p = .05) and age (B = 0.661, t = 2.08, p = .05) were also modestly significant predictors. Regarding the AUCgFOLLOW-UP outcome, the best-fitting significant model, $F(4, 21) = 8.28$, p = .001, R^2 = .53, included the intervention, age, number of cigarettes smoked per day and years of smoking as predictors. In this case, the number of cigarettes smoked per day (B = 5.74, t = 5.35, p = .001) was the most significant predictor, with intervention (B = −20.36, t = 2.31, p = .03) and age (B = 1.39, t = 2.44, p = .02) also being significant predictors.

Sensations After the tDCS

In both groups, most participants reported sensations just below the electrode (84.6% in the active group and 92.3% in the control group). A higher percentage of the control group (84.6%) experienced discomfort from the beginning compared to the active group (76.9%). However, for the active group, discomfort mostly persisted until the end (92.3%) compared to the control group (76.9%). Despite these differences, the discomfort did not affect more than half of the sample (53.8% in the active group and 61.5% in the control group) or affected them very little (46.1% in the active group and 38.4% in the control group). Proportions were similar between groups, and t-tests showed no significant differences in controlled variables such as itching, pain, burning, heat, metallic taste, fatigue, and dizziness. These results indicate the absence of significant differences between the two groups regarding neuromodulation sensations in our design using capsaicin.

Discussion

The study aimed to test the efficacy of DLPFC tDCS for treating tobacco consumption and craving during the intervention and after a 1-month follow-up. The findings revealed a significant reduction in self-reported daily tobacco consumption in the experimental group compared to the sham control group during the tDCS intervention, which consisted of 10 repeated sessions over 2 weeks at 20 min each and 2 mA. While the sham group also reduced their consumption, thus probing a certain placebo effect in the mechanism of the technique, the active tDCS group experienced a significantly greater reduction. However, this positive outcome was not sustained over time, as both groups experienced some rebound in smoking after a month. However, note that such rebound was not the same for both groups, since the experimental group recovered their addiction, but they did not do so at the baseline level, while the placebo group did return to their initial level of tobacco consumption. On the other hand, and regarding the craving experimented during the neuromodulation, we found it progressively decreasing along the 2 weeks of intervention only for the active tDCS group. When comparing the results to similar studies with multisession protocols, there were both similarities and differences. For instance, in the study of Verveer et al. (2020), participants received six tDCS sessions in 1 week (twice a day), and found the number of smoked cigarettes a day progressively decreased up to 1 week after the last tDCS session, though in both sham and active conditions and with no additional benefits for the active tDCS for the consumption neither for craving. Other studies, such as Hajloo et al. (2019), reported positive results for both cigarette consumption and craving, even after a month, with a protocol involving 10 sessions over 5 weeks. On the other hand, Mondino et al. (2018) applied 10 sessions on 5 consecutive days (twice a day) and found active tDCS significantly reduced craving but with no differences with sham tDCS in the number of smoked cigarettes during the intervention or after a month. Maybe a decisive factor is, apart from the number of sessions, the timing at which the sessions are delivered. It appears from the published studies the efficacy might be greater when the sessions are more spread over time. For instance, Ghorbani Behnam et al. (2019) applied 20 sessions over 4 or 12 weeks and found that the longer duration led to the highest abstinence rate (25.7%) at 6 months. Overall, the findings suggest the need for a minimum of 10 sessions, spaced out over time, to achieve stable benefits. Our study's design included 2 weeks of stimulation, but measured tobacco consumption during the 2nd week, with the intention of accumulating some neuromodulation prior to the assessment of the result. Anyway, it seems that 10 sessions may not have been sufficient for lasting effects, in line with the findings of Mondino et al. (2018) and Verveer et al. (2020). Longer duration protocols, such as Ghorbani Behnam et al. (2019), may lead to more sustained benefits even after 6 months. This raise the interesting possibility that aside from the potential biological effects of the tDCS, the psychological factors associated with an intervention which is sustained over many weeks might be critical to disrupt the addiction-sustaining habits.

The study also aimed to assess the influence of certain variables on the outcome of the tDCS intervention. Apart from the intervention itself, the number of cigarettes smoked per day was the best predictor of success both during intervention and in maintaining abstinence after a month. This suggests that the tDCS technique may be more effective for light smokers (around 10 cigarettes per day). Interestingly, motivation to quit smoking was also an important predictor of success during intervention, supporting the findings of Vitor de Souza Brangioni et al. (2018), who observed that tDCS coupled with high motivation significantly reduced cigarette consumption up to 4 weeks postintervention. Similarly, Fecteau et al. (2014) found benefits from five tDCS sessions in participants who wanted to quit smoking, and Verveer et al. (2020) suggested that the lack of positive results in their study might be partly due to participants' low motivation to quit smoking. Motivation appears to be a critical factor for immediate success in reducing or quitting smoking. As we commented in the introduction, neurostimulation can have state-dependent effects, thus pointing to a "motivated DLPF cortex" more prone to control addictive behavior. However, in this study, motivation did not influence the outcome after a month. Instead, age emerged as a significant predictor for maintaining abstinence, with older participants showing better restraint in consumption after a month (note that the study included participants up to around 60 years old). Factors such as years of smoking, physical dependence, and perceived self-efficacy to quit smoking were not strong predictors of outcome, at least as measured in this study.

Participants in the study reported no significant side effects from tDCS, and no one withdrew due to discomfort during intervention. The most common sensations related to tDCS were mild burning, itching, and heat under the electrode, consistent with previous research. A systematic review by Matsumoto and Ugawa (2017) confirmed that the most common side effects from tDCS are mild skin-related issues that dissipate after electrode removal. The placebo strategy used in the study (using physiological saline solution with a small amount of capsaicin 0.75 mg/g cream) proved effective, as there were no significant differences in sensations between the active and sham groups. This strategy helped ensure that the participants' experiences during the study were similar regardless of the intervention group.

The study's results should be interpreted cautiously due to the small sample size and the fact that there were no objective measures such as expired CO_2, although, on the other hand, efforts were made to maintain homogeneity and a well-designed experiment. Several indicators were used to assess the therapeutic effects of tDCS as a smoking cessation treatment, such as self-recording, craving, and motivation to quit smoking. A follow-up measure was also included to evaluate the evolution of tDCS effects. The study's results partially align with previous research on tDCS for nicotine dependence, which found improvements in tobacco consumption habits following tDCS neuromodulation of DLPFC, especially when a minimum of 10 sessions is applied, preferably spread over time. This may be due to the modulation of cognitive control circuits involved in decision-making, self-control, and craving regulation, which promote executive function and enhance control over impulsive behaviors motivated by nicotine reward (Kang et al., 2019). In conclusion, tDCS targeting the DLPFC (anode F4 and cathode F3) at 2 mA for 10 sessions over 2 weeks significantly reduces self-reported tobacco consumption and craving. However, the effects are not stable, suggesting that extending the tDCS protocol beyond 10 sessions could enhance long-term outcomes.

Author Disclosure

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Neurofeedback for Alcohol Use Disorder: Implications for Single-Case Research Design and Examining Craving Desire

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Abstract

Substance use disorder (SUD) and alcohol use disorder (AUD) persist as a significant concern in the United States despite increasing treatment options. Effective interventions to reduce cravings and prevent relapse are still sought after. During the pandemic, drinking behaviors and cravings exacerbated among individuals with AUD. Neurofeedback shows documented promise in addressing AUD, yet studies often lack comprehensive data on craving. In this quantitative study, participants with AUD received 12 neurofeedback sessions using the Peniston protocol as inspiration for session designs. Four research questions guided the study, examining pre–post qEEGs; pre, post, and follow-up AUDIT scores; and neurofeedback sessions data. The study also tracked changes in self-reported craving levels over time. Hypotheses predict improvement in post-qEEGs, posttreatment craving scores, and neurofeedback session averages following each neurofeedback session. The discussion will focus on the implications for neurofeedback for AUD, cravings, and single-case research designs.

Keywords: neurofeedback; single-case research design; alcohol use disorder

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Alcohol use disorder (AUD) presents a significant and pervasive challenge in the United States (Edwards et al., 2015). Defined in the *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; *DSM-5*) as "a problematic pattern of alcohol use leading to clinically significant impairment or distress" (American Psychiatric Association [APA], 2013, p. 490), it stands as a valid target for intervention (Dehghani-Arani et al., 2013). Recognizing the importance of addressing ambivalence towards sobriety, the added criteria of "craving" in the *DSM-5* underscores its significance. Additionally, Schlauch et al. (2019) strongly encourages researchers to measure craving over time versus pre–post measurements.

Many treatment options exist for those with AUD; however, an alternative modality is the brain-based intervention known as neurofeedback or EEG-biofeedback (Demos, 2019). Neurofeedback has emerged as a promising approach in addressing addiction symptoms (Dehghani-Arani et al., 2013; Dousset et al., 2020; Shepard, 2015; Sokhadze et al., 2008) with recent calls for more robust studies that may include refined or innovative methodologies to further understand its efficacy (Omejc et al., 2019). Thus, this paper entails quantitative electroencephalogram (qEEG) data while also demonstrating innovative methodologies and analyses of neurofeedback session-to-session data and craving data, which will ideally inform clinicians with valuable insights and present future research options. Further, the methodical approach of single-case research designs (SCRDs) using neurofeedback data for SUD/AUD may offer insights into session-to-session brain wave patterns over

time, along with measured self-report craving desires.

Methods

La Vaque et al. (2002) acknowledge the importance of adhering to best practices in neurofeedback methodologies and studies. For this study, the recommendation of interest is encouraging researchers to incorporate multiple observations (La Vaque et al., 2002). Integrating multiple observations into research studies encompasses various methodologies, including SCRDs, which are also referred to as time series designs and allow participants to serve as their baseline (Kazdin, 2021). Key characteristics of SCRDs include (a) repeated dependent variable measures; (b) measurement across time; and (c) designation of the "case" as an individual, organization, or other type of group (Kazdin, 2021; Lobo et al., 2017). Researchers employing SCRD can also use multiple baselines (where participants start the intervention at different times), reversal designs, and multiple treatment designs based on their desired data results and research objectives. For instance, the A phase serves as the baseline with repeated measures but no intervention, while the B phase incorporates the intervention with the same repeated measurements as the A phase. The fundamental aim is to evaluate whether an intervention has any effect on the independent variable.

Given that variations of SCRDs offer diverse strengths for assessing intervention effects, the literature underscores the importance of researchers exercising caution when analyzing their data. A similar mindset may also prove beneficial for neurofeedback researchers and clinicians, given the significant disparities and complexities in subjects' individual life experiences, physiological development, and underlying brain patterns. Hence, the present study's research questions include the SCRD-based questions and additional questions comparing participants' pre- and post-qEEG data, and their pre–post and follow-up data using the Alcohol Use Disorders Identification Test (AUDIT; Saunders et al., 1993). The research questions guiding this study were as follows:

1. Is there a change in a participant's *z*-scores from pre- to postneurofeedback intervention of normative database comparison qEEG data?
2. Is there a change over time during the neurofeedback treatment sessions in participants' alcohol craving thoughts as measured by the Craving Desire scale (CDS; Ciraulo et al., 2013)?
3. Is there a change over time in neurofeedback session-to-session data for participants' mean magnitude of their respective brain wave frequencies in band 1, band 2, and band 3?
4. Is there a change over time in participants' alcohol use according to the pre, post, and follow-up scores of the AUDIT (Saunders et al., 1993)?

Clinicians

The present study engaged student clinicians, comprising master's level students in clinical mental health from a nationally accredited program approved by the Council for Accreditation of Counseling and Related Education Programs (CACREP). These students had previously fulfilled the didactic coursework requirements for neurofeedback set by the Biofeedback Certification International Alliance (BCIA) and were supervised by a certified and licensed supervisor during data collection and the administration of neurofeedback sessions. Furthermore, volunteer clinicians with neurofeedback training, such as faculty or alumni, were also involved in the study.

Measures

Demographic Questionnaire. The demographic questionnaire included gender, age, ethnicity, family alcohol use, family drug alcohol use, and a current list of medications. Additionally, the form contained questions about the participant's age of first alcohol use, any diagnosis of a mental health disorder, the state of their liver, and if they felt motivated for neurofeedback treatment.

CDS. Researchers Kavanagh et al. (2013) suggest that although a researcher may ask a single question of "Are you craving right now?" for the repeated dependent variable, that internal consistency may improve with an assessment that includes more than a single question. Hence, the postneurofeedback session, self-report measurement for craving in this study was the CDS (Ciraulo et al., 2013). The CDS, developed by Ciraulo et al. (2013), consists of three items assessing the current desire for alcohol. These items are "I do want a drink right now," "I crave a drink right now," and "I have a desire for a drink right now." Responses are rated on a 7-point Likert scale ranging from "very strongly agree" to "very strongly disagree." Ciraulo et al. (2013) specifically designed the CDS for use in AUD studies and for repeated postintervention measurements. The CDS minimum

score is a 3 with the maximum being a 21. Participants were asked after every session to self-report their craving level. All participants reported their CDS scores at 16 time points. Two were completed prior to neurofeedback treatment, 12 were completed after every neurofeedback session, and the last two were collected around 1–3 weeks poststudy. For the purpose of the study and exploring craving change, we computed the CDS scores into Phase A and Phase B.

AUDIT: Self-Report Version. AUDIT (Saunders et al., 1993) serves as an assessment tool to gauge whether an individual's alcohol consumption poses harm. Developed by the World Health Organization through collaboration among six countries, the AUDIT aims to screen drinking behavior and related issues (Saunders et al., 1993). Comprising 10 items, the questionnaire utilizes a range of responses for items 1–8, spanning from 0 to 4 to indicate the frequency of alcohol consumption (0 = *Never*, 1 = *Monthly or less*, 2 = *Two to four times a month*, 3 = *Two to three times a week*, 4 = *Four or more times a week*). A sample question is "How often do you have a drink containing alcohol?" Questions 9 and 10 employ a 3-point Likert scale (1 = *No*, 2 = *Yes*, *but not in the last year*, 3 = *Yes, during the last year*), with an example item being “Have you or someone else been injured as a result of your drinking?” The questionnaire’s structure allocates items 1–3 for assessing alcohol consumption, items 4–6 for alcohol dependence, and items 7–10 for alcohol-related issues. A score of 8 or more for males (7 or more for females) indicates harmful alcohol use (Saunders et al., 1993), while a score of 20 or more suggests alcohol dependence. The maximum score achievable on the questionnaire is 40 (Saunders et al., 1993). Internal consistency of the AUDIT, as demonstrated among 1,888 individuals, yielded mean values of 0.93 for drinking behavior and 0.81 for adverse psychological reactions (Saunders et al., 1993). Validity was assessed through comparison with known alcohol users and nondrinkers. Among alcohol users, 99% scored 8 or higher, with 98% scoring 10 or more. Conversely, only three nondrinkers (0.5%) scored 8 or more.

Instrumentation

Quantitative Electroencephalography. Before commencing neurofeedback treatment, a qEEG was conducted to analyze an individual’s baseline brainwave patterns and pinpoint areas for potential improvement through conditioning. It was recommended that clients refrain from consuming nonessential substances for at least 24 hr prior to the qEEG recording, unless instructed otherwise by a medical professional. Any medically prescribed substances were taken into consideration during the interpretation of the qEEG results. Medications were also considered for the development of treatment protocols as well as the Peniston protocol and the Scott-Kaiser modification (Dousset et al., 2020; Peniston & Kulkosky, 1989, 1990; Scott & Kaiser, 1998).

The 19-channel qEEG recordings were obtained using one of two systems: (a) the BrainMaster Discovery 24 high-impedance amplifier with NeuroGuide software (BrainMaster Technologies, Inc., Bedford, OH) or (b) the Mitsar BT 201 high-impedance amplifier with WinEEG software (Mitsar Co. Ltd., St. Petersburg, Russia). Recordings were conducted in both eyes-closed and eyes-open conditions, utilizing appropriately sized Electro-Caps (Electro-Cap International, Inc., Eaton, OH) fitted according to manufacturer guidelines, along with ear-clip leads. Electrode preparation procedures were carried out to ensure impedance levels remained at or below 5K ohms (Jones, 2015).

Neurofeedback. During the neurofeedback sessions, clinicians employed the BrainMaster Atlantis two-channel amplifiers (BrainMaster Technologies, Inc., Bedford, OH) along with BioExplorer software (Cyberevolution, Inc., Seattle, WA). Electrode site preparation involved cleaning the site, ground, and reference locations with rubbing alcohol and gently abrading them using PDI sterile alcohol prep pads and Nuprep skin prep gel. Gold-plated electrodes were then affixed to the clients using 10-20 conductive paste. Impedance measurements were carefully taken to ensure that interelectrode impedance remained below 5K ohms (Jones, 2015).

Participants

The specific characteristics and inclusion criteria encompassed individuals diagnosed with AUD who were aged 18 years or older. Exclusion criteria comprised active psychosis, current intoxication, advanced liver cirrhosis, and failure to meet the inclusion criteria. Participants were not restricted based on race, gender, ethnicity, or any other demographic variable. Prior to participant recruitment, the study obtained approval from the Institutional Review Board. Recruitment of participants involved reaching out to local counselors working with AUD clients, as well as outpatient facilities, through the distribution of flyers and emails. Additionally, social media platforms were utilized for recruitment purposes. Upon

expressing interest and contacting the Principal Investigator, potential participants received an email containing detailed study information and the Informed Consent document. All neurofeedback services were provided to participants free of charge, and they also received a nominal payment for their participation.

Data Analysis

For the pre–post qEEG data, we first de-identified participant data. Utilizing WinEEG, initial qEEG data underwent frequency domain analysis utilizing the fast fourier transform (FFT) technique as per Beauchamp (1973) and Congedo and Lubar (2003). WinEEG software facilitated this analysis by computing FFT and subsequently determining absolute power, relative power, and mean frequency for each electrode placement on the scalp (Congedo & Lubar, 2003). Next, using NeuroGuide software, participant data is compared with that of healthy individuals from the Lifespan Normative database, enabling clinicians to identify deviations from the norm which are typically expressed in *z*-scores. We also used NeuroGuide for artifacting all participants' qEEG data for EC and EO conditions. The common qEEG montage of LE = linked ears and AVE = average reference was applied. Data reports consist of AVE absolute power *z*-scores.

AUDIT scores consisted of collecting pre (around the initial qEEG), post (during the post qEEG), and follow-up (Qualtrics) measurements for each participant. Simple change score computations were calculated using *Statistical Package for the Social Sciences (SPSS) software version 26* (SPSS, 2019). The AUDIT scores function as the participants' self-report data. Self-report data is highly suggested by Wigton and Krigbaum (2015) to collect and compare with physiological data. The AUDIT pre, post, and follow-up data for all participants is reported in a single chart.

For the SCRD analyses, we initially inputted data into Excel to generate graphical representations depicting the participants' data alongside resulting trend lines. Subsequently, our analysis utilized the nonoverlap of all pairs (NAP) method pioneered by Parker and Vannest (2009). Unlike methods reliant on trend lines or averages, NAP is commonly employed in SCRD and favored in AB Phase designs. While some researchers have criticized NAP analysis for its perceived inability to distinguish between phases (Manolov & Solanas, 2018), it is pertinent to note that in neurofeedback sessions, participants continuously receive the intervention rather than distinct treatment and no-treatment phases. NAP scores are derived by comparing all data points across the two phases (Fielenbach et al., 2019). In our study, Phase A encompasses the initial defined group of neurofeedback sessions, while Phase B comprises the final or successive defined group of sessions. The resulting NAP scores yield effect sizes categorized as follows: 0.00–0.65 indicating a weak effect, 0.66–0.92 suggesting a medium effect, and 0.93–1.0 denoting a large effect (Parker & Vannest, 2009).

To enhance the robustness of the NAP findings, we employed simulation modeling analysis (SMA), a software program provided by Clinical Research Solutions (2021), which is freely downloadable and designed for SCRD involving fewer than 30 time points (Borckardt, 2006). This software enables the control of autocorrelation, assessment of session data slopes and trend lines, and conducts a 5,000-simulation test to identify the most fitting trend line or the most correlated model. The analysis offers five distinct models: (a) Model 1 proposes an increase in outcome measure during Phase A followed by a decrease in Phase B; (b) Model 2 suggests a stable Phase A followed by an increase in Phase B; (c) Model 3 indicates an increase in Phase A followed by stabilization during Phase B; (d) Model 4 proposes a continuous increase from Phase A into Phase B; and (e) Model 5 reveals an increase in Phase A, an immediate decrease, and a subsequent increase in Phase B.

SMA provided valuable insights into participants' neurofeedback session data, allowing for the prediction of subtle changes within the data and offering potential trajectories of participant response had the intervention been continued by clinicians.

Participant 1

Participant 1 (P1) reported having family members with drug and alcohol issues. P1 also stated he began drinking at age 15, identified as a Caucasian male, and when he began the study was 55 years old. P1 was taking doctor-prescribed medication for blood pressure, and an anti-depressant, an Antabuse (i.e., a medication that causes adverse effects with alcohol consumption). P1 reported he was motivated for neurofeedback treatment. Clinicians conducting neurofeedback sessions informed us of P1's elevated anxiety states during his first few sessions.

QEEG Findings. Analyzing P1's initial and final scores (Table 1), it is evident that there was a decrease in theta activity (4–8 Hz) across both EC

and EO conditions. Moreover, there was a significant reduction in higher beta activity, particularly notable in the EC condition. Additionally, in other channels observing EC beta activity (such as Fz, Cz, F3, and P3), initial pre *z*-scores mostly ranged from $z \geq 2.00$. Following the intervention, post scores for these channels exhibited a consistent trend toward the mean with $z \geq 1.00$. P1's individual protocol included downtraining 4–8 Hz, increasing 8–10 Hz, and downtraining 20–25 Hz at Pz with EC.

CDS. P1's mean values across different phases were as follows: Phase A (M = 10.6), Phase B (M = 7.6), and overall (M = 9.2). P1's test for level change yielded $R = -0.43$, $p = .20$; while the test for slope change showed $R = -0.27$, $p = .44$, indicating a decreasing slope vector during both Phase A and Phase B (Figure 1). To further examine the change in trend, we utilized the simple moving average (SMA) descriptive output for ordinary least squares (OLS), revealing an OLS Slope of $m = -0.45$, b = 13.03, 95% CI [7.88, 11.13]. Subsequently, we employed the SMA function of bootstrapped autocorrelation for OLS using the residuals of the fitted model, resulting in N = 16, lag-1 = −0.12, $p = .42$. Additionally, for Phase A, the values were n = 8, lag-1 = −0.48, $p = .09$; and for Phase B, n = 8, lag-1 = 0.003, $p = .30$. Results displayed in Figure 1.

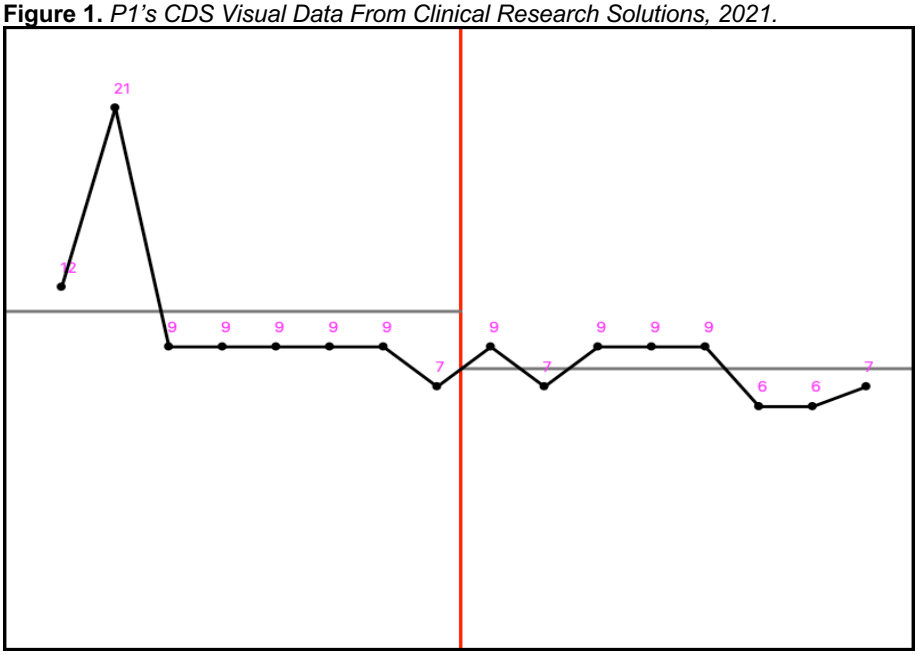
Table 1

Pre/Post qEEG Z-Score Data for P1

	EC Pre	EC Post	EO Pre	EO Post
4–8 Hz	0.89	0.09	0.75	0.17
8–10 Hz	0.57	−0.45	0.15	−0.31
20–25 Hz	4.41	1.54	4.81	2.06

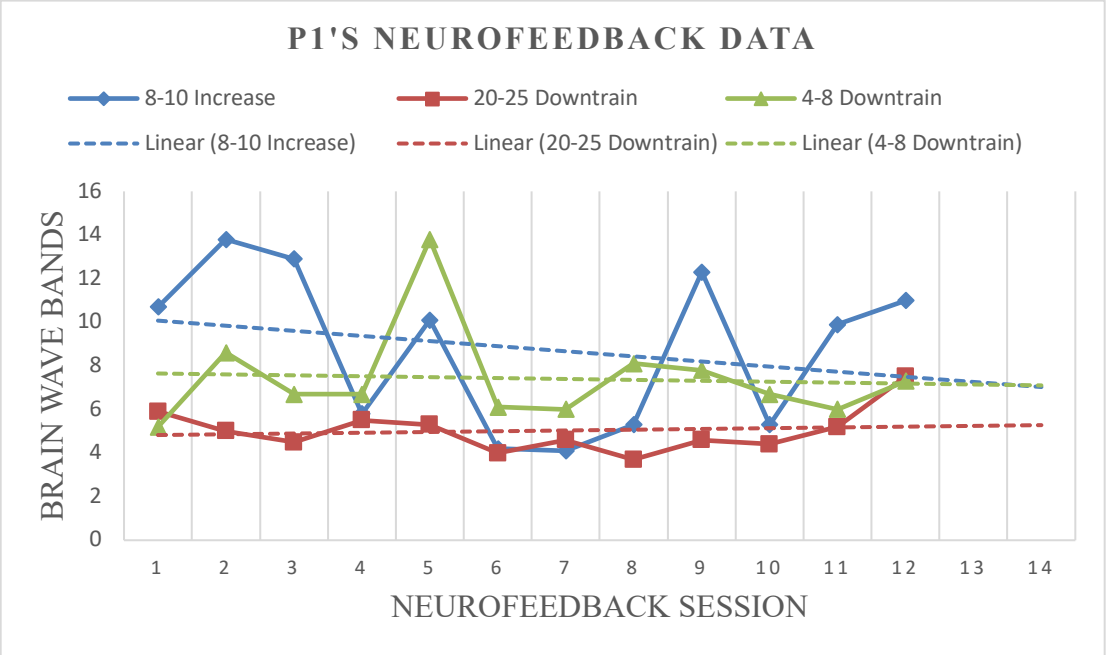
Note. EC = eyes closed; EO = eyes open.

Figure 1. *P1's CDS Visual Data From Clinical Research Solutions, 2021.*



Neurofeedback Session Data. Upon reviewing the visual representation of P1's data (Figure 2), it becomes apparent that the trend lines for both the 8–10 Hz and 20–25 Hz bands are moving in the opposite direction to the desired outcome. However, there is a slight decrease observed in the 4–8 Hz band, suggesting a potential trend toward achieving the protocol goal. This graphical representation serves as the SCRD visual analysis. 12 neurofeedback sessions were categorized into Phase A (n = 6) and Phase B (n = 6) for the analysis of NAP scores. These scores are instrumental in determining the effect size. P1's visual for neurofeedback data are in Figure 2 and the NAP results are detailed in Table 2.

Figure 2. *P1's Visual of Neurofeedback Data.*



According to his NAP scores, P1's data did not reveal any medium or large effects. Additionally, we used the SMA to further examine any unseen or minute changes. In P1's 4–8 Hz band, the SMA models indicated no significant change, with all partial correlations falling within the weak range (i.e., 0.1 to 0.3). Conversely, the 8–10 Hz band exhibited the most favorable fit with Model 1 (R = −0.65, p = .04), signifying a decrease in the outcome measure during Phase A followed by an increase in Phase B, aligning well with the established protocol. Similarly, the change effects observed in P1's 20–25 Hz band were best represented by Model 1 (R = −0.6, p = .03).

Table 2

Nonoverlap of All Pairs Statistical Outcomes for P1

	S	Pairs	NAP	VARs	*z*	*p*	90% CI
4–8 Hz	−2	36	0.472	156	−0.16	.873	[−0.626, 0.515]
8–10 Hz	−12	36	0.333	156	−0.96	.337	[−0.904, 0.237]
20–25 Hz	−8	36	0.389	156	−0.64	.522	[−0.793, 0.349]

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

Participant 2

Participant 2 (P2) self-identified as a 28-year-old Latino male in his Qualtrics demographic form. He indicated that someone in his family struggled with alcohol and drug abuse. P2 disclosed that his own struggle with alcohol began in 2014 at the age of 21. He reported not taking any medications and denied being diagnosed with a mental health disorder. His highest level of education was a college degree, and he expressed satisfaction with his level of social support. P2 expressed motivation for AUD treatment. Clinicians noted his exceptional commitment to neurofeedback sessions and punctuality in keeping his appointments. Throughout the neurofeedback interventions, P2 appeared externally content. Additionally, he was concurrently attending outpatient treatment, which ceased around his ninth neurofeedback session.

QEEG Findings. We artifacted data for both EC and EO conditions. Based on P2's pre- and postscores (see Table 3), there was an increase in the 4–8 Hz band and the 18–25 Hz band, contrary to the intended inhibition and decrease settings for his protocol. However, there was an increase in the 12–15 Hz band from pre to post in both EC and EO conditions. P2's neurofeedback protocol was inhibiting 4–8 Hz, increasing 12–15 Hz, and downtraining 18–25 Hz at Cz with EO.

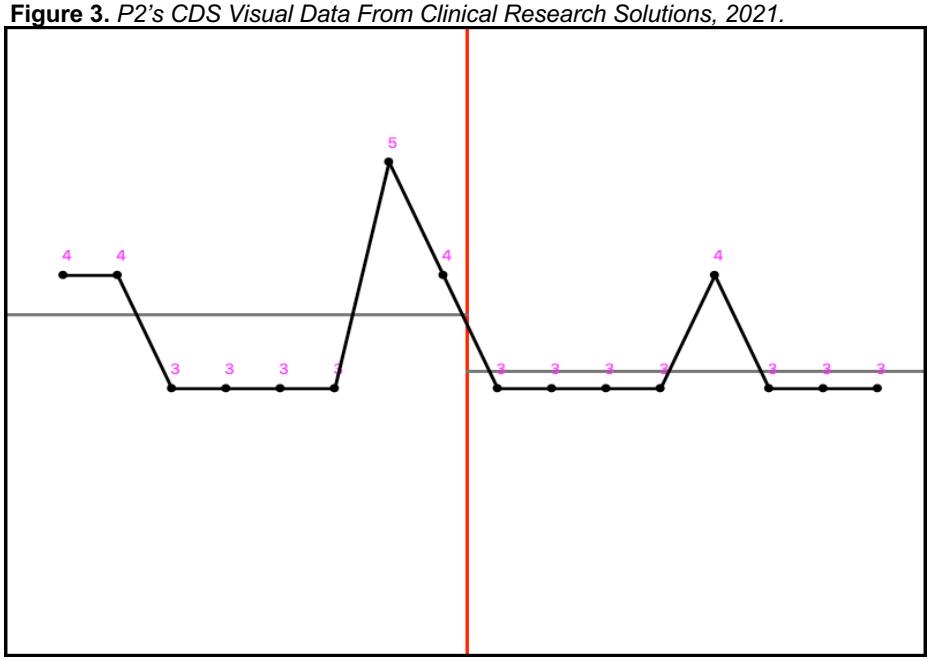
Table 3
Pre/Post qEEG Z-Score Data for P2

	EC Pre	EC Post	EO Pre	EO Post
4–8 Hz	0.66	2.07	0.03	1.01
12–15 Hz	0.96	1.64	0.57	1.20
18–25 Hz	1.98	2.45	1.71	2.89

Note. EC = eyes closed; EO = eyes open.

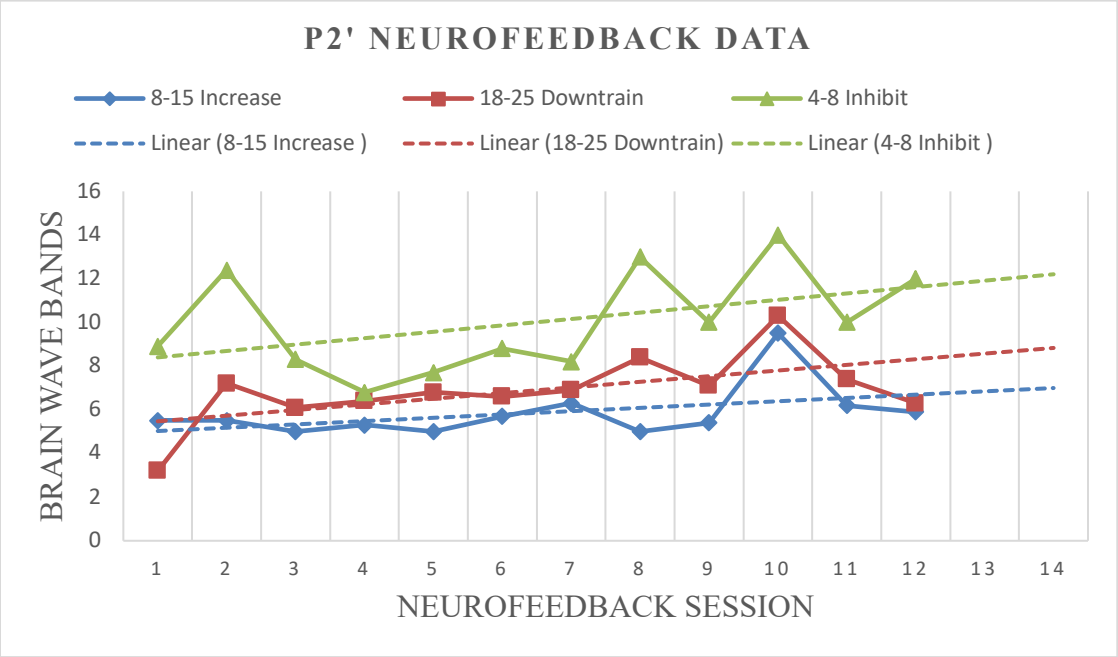
CDS. The mean scores for P2's phases (see Figure 3) were as follows: Phase A (M = 3.6) and Phase B (M = 3.1). The combined mean for both phases was (M = 3.4), which represents the equivalent of level change. Autocorrelation was programmed into all data points for both phases at .183 for lag-1. P2's test for level change yielded R = −0.42, p = .17. The test for slope change resulted in (R = .09, p = .77). For the OLS analysis, the OLS Slope resulted in m = −0.04, b = 3.7, 95% CI [3.13, 3.69]. Additionally, the bootstrapped autocorrelation was utilized for OLS with the residuals of the fitted OLS model, yielding results of N = 16, lag-1 = .15, p = .19. Phase-specific results indicated autocorrelation for Phase A (n = 8, lag-1 = .16, p = .17) and Phase B (n = 8, lag-1 = −.19, p = .35). Running the raw data and removing phase effects for the bootstrapped autocorrelation models revealed no significant effects.

Figure 3. *P2's CDS Visual Data From Clinical Research Solutions, 2021.*



Neurofeedback Session Data. While not the primary focus of his protocol, P2's 4–8 Hz band exhibited an increase rather than the desired inhibition of the wave. However, the 8–15 Hz band showed an increase according to the visual trend line. Given the proximity of these bands and their shared use of the 8 Hz data, some of the observed increase in the 8–15 Hz band may be influencing the 4–8 Hz data. This could potentially account for part of the increase in the 4–8 Hz band. Despite clinicians' emphasis on reducing the 18–25 Hz band, the trend line indicates the opposite effect. Figure 4 provides a visual representation of this analysis.

Figure 4. *P2's Visual of Neurofeedback Data.*



To reiterate, NAP scores ranging from .00 to .65 indicate a weak effect, .66 to .92 suggest a medium effect, and .93 to 1.0 signify a large effect. P2's data exhibited medium NAP score effects across all three brain wave bands (see Table 4). However, none of the *p* scores were significant, although the 18–25 Hz band approached significance, albeit in the opposite trend desired (i.e., increasing instead of decreasing). Furthermore, we analyzed the data using SMA and assessed the fit of five models. P2's 4–8 Hz band trend was best represented by Model 2, indicating a stable Phase A and an increase during Phase B (R = 0.56, p = .07). While P2's 8–15 Hz band did not yield significant findings in the SMA models, it also aligned well with Model 2 (R = 0.46, p = .16), partially supporting his desired trend. Conversely, the change effects for P2's 18–25 Hz band were best captured by Model 3 (R = 0.65, p = .03), demonstrating significance. Model 3 suggests an increase during Phase A followed by a stable or leveling-out Phase B, possibly indicating P2's initial achievement of his protocol goal followed by maintenance of that goal.

Table 4
Nonoverlap of All Pairs Statistical Outcomes for P2

	S	Pairs	NAP	VARs	*z*	*p*	90% CI
4–8 Hz	22	36	0.806	156	1.76	.078	[0.040, > 1]
8–15 Hz	20	36	0.778	156	1.60	.109	[−0.015, > 1]
18–25 Hz	24	36	0.833	156	1.92	.055	[0.096, > 1]

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

Participant 3

Participant 3 (P3) completed the demographic form indicating male gender, 57 years of age, and Latino ethnicity. He mentioned no familial history of alcohol or drug addiction. P3 recognized his initial alcohol-related issue at 17 years old. His current medication regimen included naltrexone, Seroquel, a blood pressure medication, and an antidepressant, prescribed for anxiety. His highest level of education is a master's degree. P3 expressed contentment

with his social support network and exhibited readiness for AUD treatment. During interactions, P3 displayed signs of anxiety through fidgeting, sweating, and body tension. Clinicians observed his restlessness during neurofeedback sessions, occasionally accompanied by yawning and drowsiness. Clinicians offered short breaks to this client. P3 took a 1-week hiatus from neurofeedback sessions due to a work-related commitment.

QEEG Findings. For P3, we used manual artifacting for both EC and EO conditions due to participant movement and tension. The individualized neurofeedback protocol for P3 was downtraining 4–10 Hz, increasing 12–15 Hz, and downtraining 25–30 Hz at Fz with EO. P3's outcomes revealed slight alterations in both the 4–10 Hz and 25–30 Hz bands (see Table 5). Notably, the latter exhibited a favorable shift towards the mean. In the 12–15 Hz band, there was a decrease during EC sessions but an increase during EO sessions. Consequently, the increase in the EO 12–15 Hz band was in accordance with the protocol and deemed beneficial.

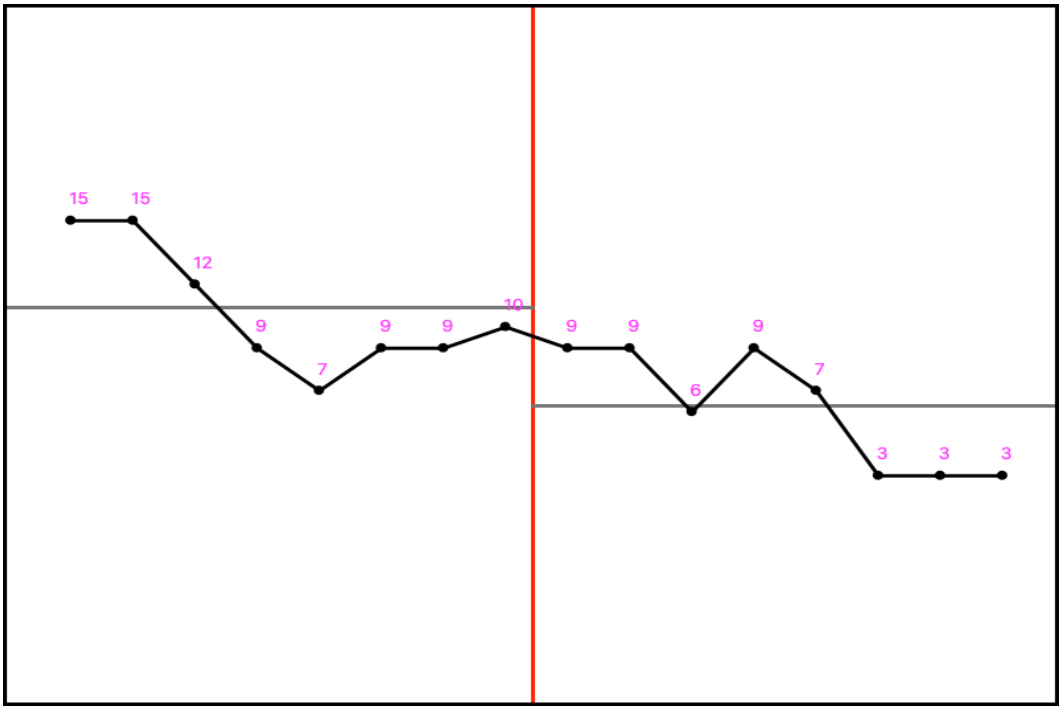
CDS. P3's phase (see Figure 5) means were calculated as follows: Phase A (M = 10.8) and Phase B (M = 6.1). The overall mean across all phases with a sample size of 16 was (M = 8.4). Utilizing the SMA and conducting tests for level change, P3's data yielded R = −0.65, p = .18. Additionally, the test for slope change resulted in R = 0.03, p = .95. In the ordinary least squares (OLS) analysis, the descriptive analysis function was employed to determine the OLS Slope, resulting in m = −0.99, b = 10.57, 95% CI [4.25, 7.86]. The OLS analysis indicated significant results for the entire sample (N = 16, lag-1 = .43, p = .02), as well as for Phase A (n = 8, lag-1 = .47, p = .01), but not for Phase B (n = 8, lag-1 = −.23, p = .38).

Table 5
Pre/Post qEEG Z-Score Data for P3

	EC Pre	EC Post	EO Pre	EO Post
4–10 Hz	0.28	0.79	−0.22	0.61
12–15 Hz	2.00	1.00	0.08	1.38
25–30 Hz	−0.58	−0.29	−0.63	−0.10

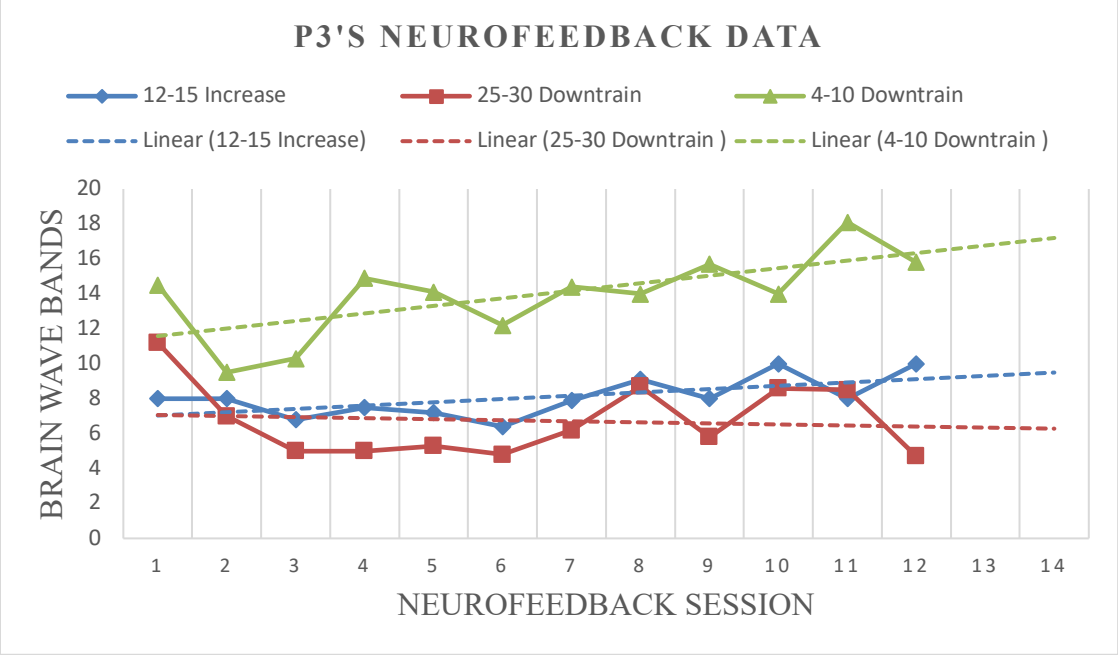
Note. EC = eyes closed; EO = eyes open.

Figure 5. *P3's CDS Visual Data From Clinical Research Solutions, 2021.*



Neurofeedback Session Data. Following P3's protocol, the visual representation (see Figure 6) of his training bands (12–15 Hz and 25–30 Hz) suggests a slight positive trend in the desired direction. However, the 4–10 Hz band does not exhibit a visual trend in the desired direction. It's plausible that artifacts, such as altered data due to P3's movements during sessions, could influence his data, particularly in the higher band range or alter the 25–30 Hz band. Nonetheless, there is a visual decrease in his 25–30 Hz band, aligning with protocol objectives. To delve deeper into the analysis, we utilized the NAP scores derived from P3's resulting brain bands. The NAP scores, presented in Table 6 are utilized to determine effect size.

Figure 6. *P3's Visual of Neurofeedback Data.*



Based on the NAP scores, all of P3's brain wave bands exhibited a medium effect. Notably, the 12–15 Hz band showed a significant change in the desired direction for his personalized protocol, approaching a large effect size. Further analysis involved examining P3's brain wave bands using the SMA. For the 4–10 Hz band, Model 4 yielded the best fit (R = 0.66, p = .07), indicating a progressive increase throughout both Phase A and Phase B, aligning with the observed trend. P3's 12–15 Hz band demonstrated optimal fit with Model 2 (R = 0.74, p = .02), depicting stability during Phase A followed by an increase during Phase B, in accordance with his protocol. Lastly, P3's 25–30 Hz band aligned most closely with Model 5 (R = −0.52, p = .09), illustrating a decrease during Phase A, followed by an immediate increase and subsequent decrease during Phase B.

Table 6

Nonoverlap of All Pairs Statistical Outcomes for P3

	S	Pairs	NAP	VARs	*z*	*p*	90% CI
4–8 Hz	20	36	0.778	156	1.60	.109	[−0.015, > 1]
12–15 Hz	28	36	0.889	156	2.24	.025	[0.207, > 1]
25–30 Hz	10	36	0.639	156	0.80	.423	[−0.293, > 1]

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

Participant 4

Participant 4 (P4) completed the demographic form, identifying herself as female, 59 years old, and of white ethnicity. P4 disclosed a family history of alcohol abuse but not drug abuse, with her first experience of alcohol abuse dating back to the age of 8. She reported being prescribed medication for thyroid gland issues, panic attacks and/or sleep (benzodiazepine), blood pressure, heartburn, and anti-nausea. Additionally, P4 acknowledged a diagnosis of anxiety and held a degree in accounting as her highest level of education. P4 expressed feeling "very satisfied" with her social support and exhibited motivation for AUD treatment. Clinicians noted P4's mild anxiety during most sessions, along with her perception that time passed quickly at the end of each neurofeedback session. Despite this, P4 generally maintained a content demeanor and consistently attended all scheduled sessions, displaying dedication according to clinicians' observations.

QEEG Findings. Manual artifacting was used for P4's EC pre data due to muscle tension with the remaining data being ran through automatic artifacting. Her protocol involved inhibiting 4–7 Hz, increasing 9–11 Hz, and inhibiting 25–30 Hz, specifically at the Oz site. However, P4's data presented an additional challenge as the neurofeedback program did not encompass training at the Oz site. Given that Oz is situated between O1 and O2, an additional step was necessary to incorporate data from both sites. This involved combining and averaging the data from O1 and O2 locations. In P4's 4–7 Hz band, there was a slight increase rather than the desired inhibition. Both her EC and EO data in the 9–11 Hz band showed a minor increase, consistent with her protocol. However, in the 25–30 Hz band, P4's data showed an approximate 1 standard deviation increase during EC, contrary to her protocol. Conversely, during EO, her 25–30 Hz band decreased by approximately 2 standard deviations, aligning with her protocol (see Table 7).

Table 7

Pre/Post qEEG Z-Score Data for P4

	EC Pre	EC Post	EO Pre	EO Post
4–7 Hz	1.09	1.51	0.01	0.68
9–11 Hz	0.16	0.18	0.18	0.49
25–30 Hz	0.95	2.40	4.38	2.29

Note. EC = eyes closed; EO = eyes open.

CDS. Like with every participant, neurofeedback clinicians prompted P4 to evaluate her current craving level. P4 consistently expressed how her recent outpatient program and neurofeedback had greatly reduced her craving thoughts. In each of the 16 data points, P4 consistently rated her cravings at the lowest level of 3. Consequently, we opted not to analyze her CDS data, as it would simply show a flat line graphically.

Neurofeedback Session Data. The visual trend lines (see Figure 7) for all P4's data pose challenges for visual analysis. To restate, P4's protocol involved inhibiting brainwave bands within the range of 25–30 Hz and 4–7 Hz. P4's bands being inhibited is somewhat reflected in the visual charts. Ideally, P4's 9–11 Hz band should show an increase over time, but the trend in the visual data is unclear.

None of P4's NAP scores (see Table 8) revealed a notable effect or significant change. P4's 4-7Hz band exhibited the strongest fit with Model 3 (R = −0.36, p = .17), albeit the correlation was weak. Similarly, P4's 9–11 Hz band, also displaying a weak correlation, demonstrated the closest fit with Model 1 (R = −0.31, p = .27), indicating a decrease in Phase A followed by an increase in Phase B. While this change is minor, the upturn in Phase B corresponds with the desired trend for P4's protocol. Conversely, the 25–30 Hz band did not exhibit a significant effect or change, aligning most closely with Model 1 (R = −0.32, p = .19).

Participant 5

The fifth participant (P5) identified as a 54-year-old male of white ethnicity. P5 noted that no one in his family had struggled with alcohol or drug abuse. He disclosed beginning alcohol use at the age of 15 and currently takes medications for blood pressure, cholesterol, blood thinning, depression, and naltrexone. While P5 hasn't received a formal diagnosis for a mental health disorder, he expressed grappling with feelings of depression and anxiety. Despite accumulating university credits, P5 did not complete his degree. He indicated feeling "satisfied" with his current level of social support. P5 demonstrated charisma and enthusiasm for neurofeedback sessions. However, due to his local job commitments, he faced challenges attending certain session times, leading to fluctuations in mood influenced by work stress. Additionally, P5 recently completed an outpatient program.

Figure 7. *P4's Visual of Neurofeedback Data*.

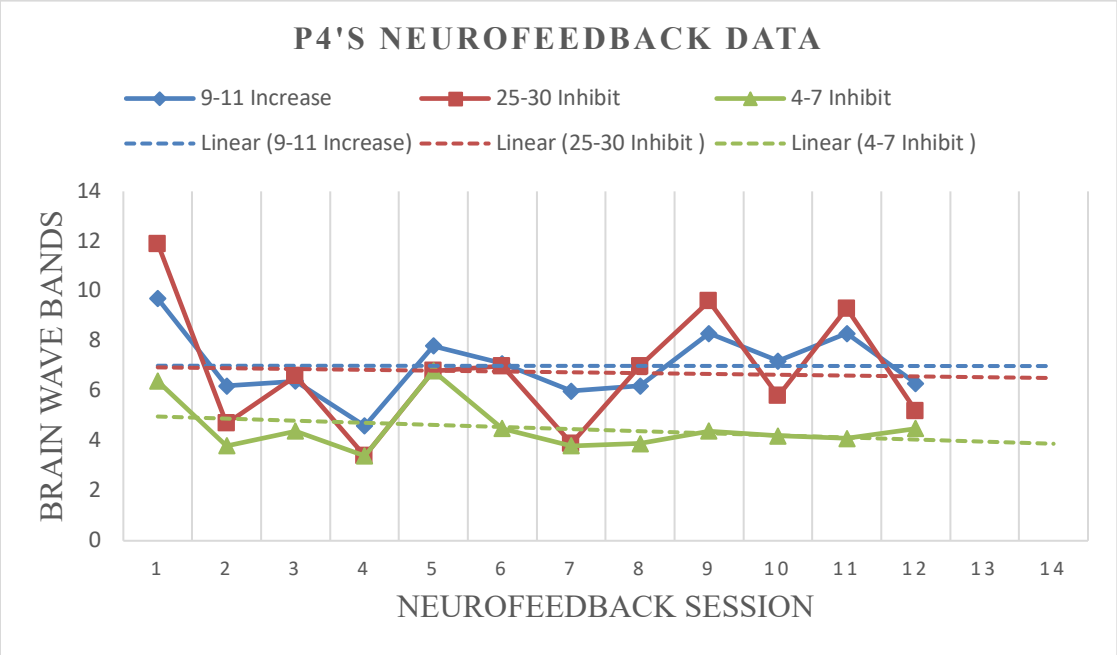


Table 8

Nonoverlap of All Pairs Statistical Outcomes for P4

	S	Pairs	NAP	VARs	*z*	*p*	90% CI
4–7 Hz	−9	36	0.375	156	−0.72	.471	[−0.821, 0.321]
9–11 Hz	1	36	0.514	156	0.08	.936	[−0.543, 0.599]
25–30 Hz	3	36	0.542	156	0.81	.810	[−0.487, 0.654]

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

QEEG Findings. We employed automatic artifacting for all P5's qEEG data, except for his post-EO data (see Table 9). Due to muscle tension issues, we opted for manual artifacting in this instance. P5's personalized neurofeedback protocol involved EO with the site location set at Cz, targeting the decrease of 4–10 Hz, increase of 12–15 Hz, and decrease of 20–30 Hz. Below are P5's *z*-scores. Reviewing P5's qEEG data, it appears he managed to marginally reduce his 4–10 Hz band during both EO and EC conditions, as well as his EC 20–30 Hz band. However, there was no significant change observed in his 12–15 Hz band. Notably, P5's pre- and post-qEEG data exhibited *z*-scores that did not raise any concerns and remained consistent with the norm.

CDS. P5's averages indicate Phase A (*M* = 6.13) and Phase B (*M* = 3), with a total mean of (*M* = 4.56) across all 16 sessions, reflecting changes in levels (see Figure 8). Furthermore, P5's test for level change yielded *R* = −0.72, *p* = .07, while the test for slope change resulted in *R* = −0.42, *p* = .35. Descriptive statistics for P5's data using OLS showed a slope of m = -0.39 and an intercept of b = 7.9, with a 95% confidence interval of [3.56, 5.69]. Bootstrapped autocorrelation for OLS utilizing the residuals revealed *N* = 16 with lag-1 = .17, *p* = .16. Phase results with the OLS residuals indicated a significant lag-1 of −0.71, *p* = .01 for Phase A (*n* = 8) and lag-1 of .00, *p* = .0001 for Phase B (*n* = 8). Thus, the overall OLS line showed no significance, both phase levels displayed a significant change.

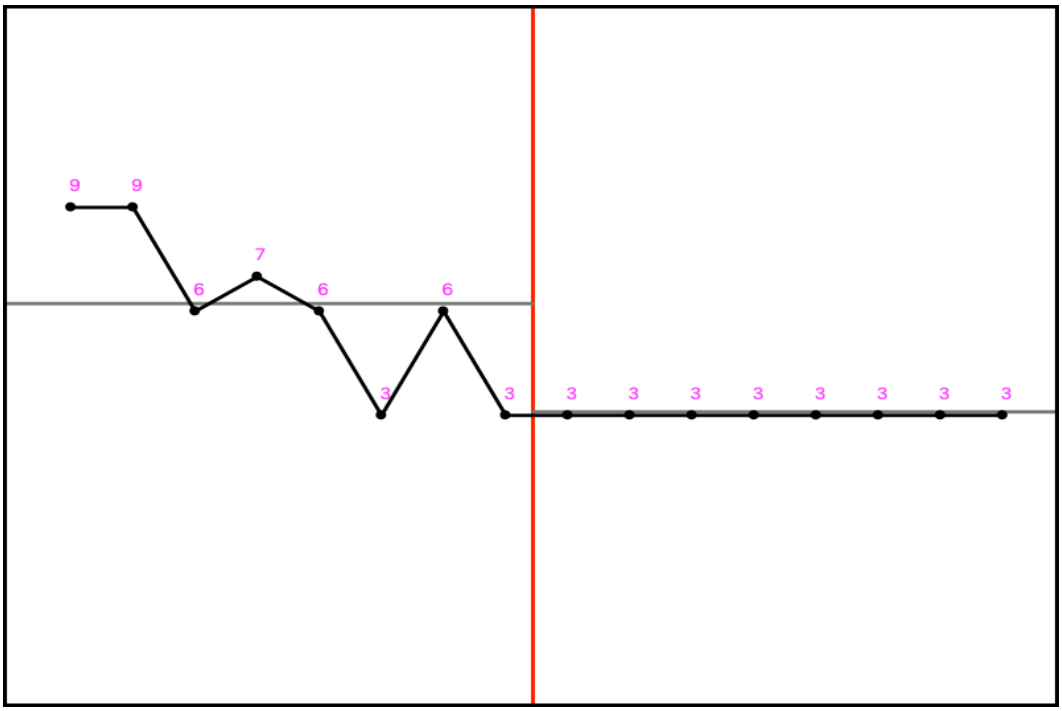
Table 9
Pre/Post qEEG Z-Score Data for P5

	EC Pre	EC Post	EO Pre	EO Post
4–10 Hz	0.72	0.23	0.22	−0.005
12–15 Hz	0.07	−0.08	0.07	0.06
20–30 Hz	0.28	−0.10	0.09	0.82

Note. EC = eyes closed; EO = eyes open.

Neurofeedback Session Data. From a visual standpoint, P5's data reveals coherent trend lines (see Figure 9). Following P5's protocol, the trend lines depicting the increase in 12–15 Hz and decrease in 20–30 Hz frequencies seem to show a positive trajectory. Throughout the sessions, P5 exhibited occasional jaw tension and minor movements. Table 10 presents an analysis of his session data using NAP scores for further examination.

Figure 8. *P5's CDS Visual Data from Clinical Research Solutions, 2021.*



P5's NAP scores for the 4–10 Hz and 20–30 Hz frequency bands showed weak or minimal effects, lacking significant values. Although the 12–15 Hz band displayed a medium NAP score aligning with the intended protocol trend, the associated p-value did not reach significance. Moving forward, we delved into analyzing P5's neurofeedback session data using SMA modeling. Notably, the 4–10 Hz band demonstrated the strongest fit with SMA Model 3 (R = 0.57, p = .04), characterized by an increase in Phase A followed by stabilization in Phase B. Similarly, P5's 12–15 Hz band data showed the closest fit with Model 3 (R = 0.40, p = .06). Conversely, his 20-30Hz band data aligned with Model 4 (R = −0.32, p = .18), suggesting a preferred decrease throughout the sessions.

AUDIT Results

All participants' AUDIT pre-post and follow-up data were composed into a single graph which is displayed below in Figure 10. Pre-time point data was collected during the participants' qEEG session, post was collected following their final neurofeedback session, and follow-up was collected 3–4 weeks after the neurofeedback sessions had concluded.

Figure 9. *P5's Visual of Neurofeedback Data*.

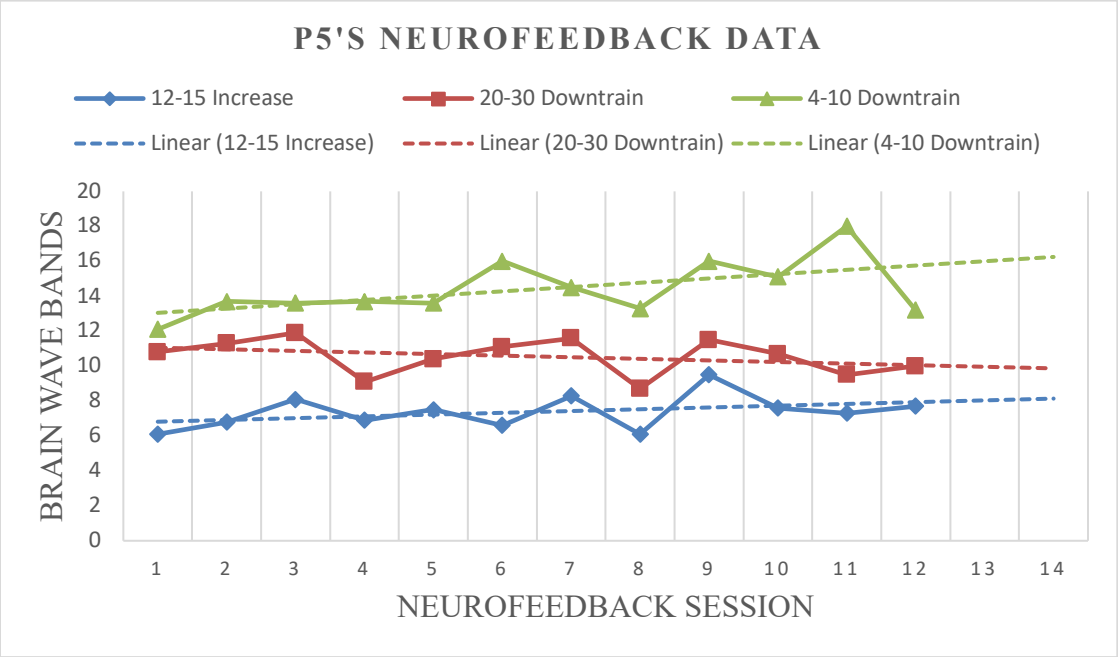


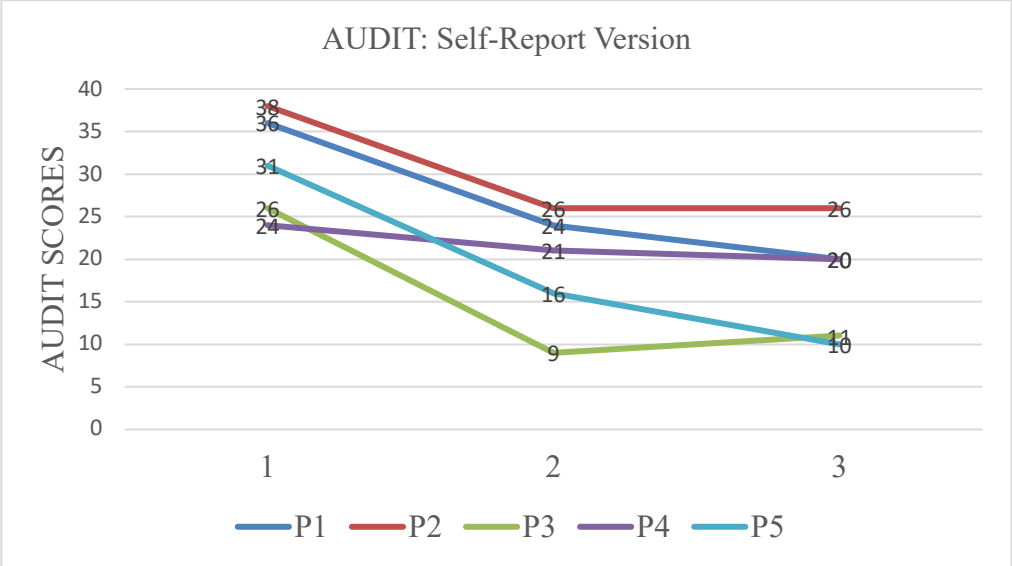
Table 10

Nonoverlap of All Pairs Statistical Outcomes for P5

	S	Pairs	NAP	VARs	*z*	*p*	90% CI
4–10 Hz	11	36	0.653	156	0.88	.379	[−0.265, 0.876]
12–15 Hz	17	36	0.736	156	1.36	.174	[−0.099, > 1]
20–30 Hz	−8	36	0.389	156	−0.64	.522	[−0.793, 0.349]

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

Figure 10. *Participants' Self-Report AUDIT Scores (Pre, Post, Follow-Up).*



Discussion

The main objective of this study was to investigate the efficacy of neurofeedback in curbing cravings and enhancing self-regulation through a combination of self-report evaluations and physiological measurements. Comparing pre and post qEEG data across participants revealed diverse outcomes. P1 experienced a desirable slight decrease in theta (4–8 Hz) activity and an undesirable decrease in alpha (8–10 Hz). However, P1 also exhibited a significant decrease in his beta (20–25 Hz) EC/EO conditions by 2 standard deviations. P2 achieved notable success in elevating his sensorimotor rhythm (SMR) by approximately 1 standard deviation. Similarly, P3 demonstrated effective results by enhancing their EO SMR by about 1 standard deviation. P4 managed to marginally increase alpha (9–11 Hz) and decrease EO beta (25–30 Hz), aligning with their prescribed protocol. P5 succeeded in slightly reducing theta (4–10 Hz) and EC beta (20–30 Hz).

Considering participants' neurofeedback sessions, outcomes also exhibited a spectrum of variability. Each participant was administered tailored neurofeedback protocols. While certain individuals displayed subtle shifts aligning with intended objectives, others evidenced notable changes characterized by moderate to substantial protocol goals. Furthermore, certain participants evinced indications of prospective enhancement in neurophysiological regulation contingent upon sustained participation in neurofeedback sessions. For neurofeedback session data, we employed SCRD methodology which enabled us to scrutinize individual transformations over the course of neurofeedback treatment comprehensively. This approach facilitated a nuanced understanding of shifts by analyzing data points from diverse vantage views. For example, P5's visual analysis exhibited promising trends, demonstrating alignment with his protocol. Notably, SMA revealed for his SMR (12–15 Hz) band a best fit with Model 3 (R = 0.40, p = .06), suggesting a Phase A increase followed by a stable Phase B, consistent with the prescribed protocol and but potentially indicating a learning plateau. Furthermore, P5's 20–30 Hz band demonstrated a consistent decrease across sessions, aligning well with Model 4 (R = −0.32, p = .18). Without supplementary analyses or the application of SCRD, discerning these subtleties might have proven challenging.

The CDS served as a pertinent instrument for self-reported assessment of craving intensity. Three out of four participants conveyed a discernible attenuation in alcohol cravings, a phenomenon persisting beyond the cessation of neurofeedback session. Conversely, P1's data indicated a marginal escalation in craving intensity during the concluding phase of the assessment. Subsequent scrutiny of pre, post, and follow-up evaluations employing the AUDIT unveiled that four out of five participants registered either diminished or static scores, indicative of a protracted reduction in overall alcohol consumption. Despite the diversity observed in participants' qEEG data and neurofeedback session outcomes, it was their self-reports of craving and alcohol use that yielded more illuminating insights.

Limitations and Implications for Research

The neurofeedback sessions took place in an academic environment rather than in a dedicated research facility. It is pertinent to note potential factors such as variations in session administration by students, including differences in threshold settings and varying levels of proficiency in neurofeedback techniques. While efforts were made to monitor sessions for electrode pops and other potential artifacts, it's important to acknowledge that session averages remained uncorrected for artifacts, which could potentially distort data. Additionally, many participants had either completed or had a few remaining outpatient addiction treatment sessions prior to their involvement in the current study.

The utilization of SCRD in the context of neurofeedback session data constitutes a novel methodological approach, meriting the attention from future scholars. Researchers may find it advantageous to either emulate the format employed in this study or explore alternative SCRD methodologies and analytical techniques. A notable attribute of SCRD methodologies lies in their capacity to discern subtle fluctuations in participant data across temporal dimensions (Lenz, 2015), thereby furnishing neurofeedback practitioners with valuable insights into requisite protocol modifications or instances of reaching learning plateaus. This tailored examination of individual physiological responses to interventions holds considerable potential for enriching the efficacy of neurofeedback services, particularly for professionals within counseling or psychological domains who seek to ascertain meaningful indices of client progress.

Conclusion

Our study explored neurofeedback for AUD using pre and post qEEGs, pre/post/follow-up AUDIT scores, and assessing craving desire over time. Five participants completed the study, with outcomes resulting in varied changes in their qEEG and neurofeedback session averages. We also utilized SCRD methods and analyses for recognizing individualized protocols and examining discrete complexities and trends in neurofeedback session averages. Repeated assessment of the CDS and AUDIT scores displayed promising results through self-reports of reduction in craving desire and alcohol use.

Author Declaration

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The Impact of Exercise, Diet, and Meditation on Cognitive Function, Prefrontal Hemodynamics, Functional Connectivity, and Biochemical Parameters

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Abstract

Exercise, diet, and meditation enhance physical wellness and psychological well-being, commonly boosting productivity. However, their specific effects remain limited. This study assessed these methods using cognitive changes, prefrontal cortex blood flow, brain connectivity, key blood parameters, and daily self-assessments of 46 middle-aged Indo-Europeans (22 women) engaged in intermittent fasting, cardio-strength training, or daily meditation for 8 weeks. The meditation group showed significant improvement in executive function, with an increase in task-switching reaction time (255.22 ± 317.20 ms) and enhanced heart rate variability. There was a significant decrease in creatinine concentration (5.04 ± 0.89 g/dL) and an increase in zinc concentration. The diet group experienced a significant decrease in brain oxygenation (−2.48 ± 2.50 of TSI) and an increase in leptin levels (2.15 ± 0.04 g/dL). Over 60 min of daily physical activity correlated with quicker responses. All groups demonstrated improved attention compared to controls, with decreased inhibition latency (meditation: 12.97 ± 41.99 ms, diet: 9.90 ± 49.07 ms, exercise: 16.38 ± 49.07 ms). Meditation and exercise groups showed reduced connectivity across six frequency bands. Serotonin levels dropped notably in the diet group (99.02 ± 7.04 g/dL). After 2 months, exercise and meditation showed greater benefits than diet or controls.

Keywords: electroencephalography; functional near-infrared spectroscopy; functional connectivity; cognitive functions; meditation; diet

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Introduction

Work productivity significantly impacts quality of life and well-being. It is influenced by various factors including chronic diseases, depression, infectious diseases, and conditions such as chronic pain, chronic fatigue, and shift work (Okdeh et al., 2023; Picard & McEwen, 2014). However, the precise effect of daily habits on human performance and physiology remains incompletely understood (Harrington, 2001; Yetton et al., 2019).

With increasing confidence, exercise, diet, and meditation are recognized as simple yet effective methods for enhancing well-being and achieving a healthy, productive life (Arya et al., 2018; Borchardt & Zoccola, 2018; Mattson et al., 2017; Reimers et al., 2018). However, there is still no overarching evidence demonstrating conclusively that these activities improve cognitive function or brain performance due to incomplete understanding of their underlying mechanisms (Chiesa et al., 2011; Kuczmarski et al., 2014; Northey et al., 2018).

The measurable physiological markers of work productivity and performance remain difficult to find, though they are believed to be cunningly connected to cognitive functioning. Previous research indicates that cognitive complexity, stress, and uncertainty directly impact task performance and can indirectly influence overall productivity and occupational safety (Jahncke et al., 2011; Kikkawa et al., 2023; La Torre et al., 2019; Reganova et al., 2023; Woods & Dekker, 2000). Given the physiology of cognitive functions, neurotransmitters are considered potential candidates for estimating cognitive performance as they play critical roles in cognitive functioning (Garcia-Esparcia et al., 2018; Volk et al., 2015). However, it's important to note that neurotransmitters produced in the neural system may not always be accurately reflected in blood serum or cerebrospinal fluid (CSF) levels, which may not fully represent neural status (Bak et al., 2006).

On the other hand, numerous widely measured biochemical blood markers have been proven to be connected to the level of cognitive functioning (Jensen et al., 2015; Popiołek et al., 2020). Biochemistry blood test data used to be limited to clinical applications, but in the last decade, it has been routinely used in many professional settings as a physiological monitoring tool, for example, to define aging markers (Engelfriet et al., 2013). Such an approach provides relevant information including identification of inflammation processes, as well as the levels of macronutrients and vitamins, oxidative stress, and energy deficiency. Regular blood tests can be used to monitor personal efficacy or analyze the efficacy of various interventions, such as physical exercise, nutritional strategies, mental training, etc. One of the main challenges in using biomarker data is the wide interindividual variability. There is also a lack of longitudinal observations of biomarkers on certain populations. Therefore, external influences (e.g., seasonal) can also affect the data. With the help of the profiling and monitoring approach, biochemical blood marker measurement combined with contextual personalized data has the potential to improve the quality of life of the general population, enhance and partially test the application of 4P healthcare principles (i.e., predictive, preventive, personalized, participative) in daily life, and collect information for further fundamental and practical studies on human health and telemedicine.

One potential blood parameter for assessing cognitive performance is creatinine. Previous studies have indicated that higher serum creatinine levels are associated with better overall cognitive performance, short-term working memory, and episodic memory, as well as associative learning in middle-aged men (Hakala et al., 2022). Additionally, other research suggests that creatinine supplementation in food may also improve short-term memory, intelligence, and reasoning (Avgerinos et al., 2018). Uric acid's antioxidant properties can have beneficial effects, especially in the context of neurodegenerative diseases. Recent research indicates that uric acid may provide neuroprotective effects in Alzheimer's disease and Parkinson's dementia. Hypouricemia is considered a risk factor for accelerated disease progression and may serve as a potential marker of malnutrition. Conversely, elevated serum uric acid levels may have a detrimental impact on the course of vascular dementia (Tana et al., 2018). Zinc plays a critical role in the nervous system (Bhatnagar & Taneja, 2001), functioning as a neurotransmitter and second messenger. It takes part in regulating hippocampal long-term potentiation, enhancing neuronal survival, and facilitating learning and memory processes (Choi et al., 2020). Various neurotransmitters offer valuable insights into cognitive function. For example, decreased extracellular levels of 5-HT (serotonin receptors) have been linked to impaired memory consolidation (Cowen & Sherwood, 2013). Furthermore, the significance of noradrenaline in numerous cognitive processes, such as vigilance, attention, learning, and memory, is well established (Holland et al., 2021). Dopamine receptors in the prefrontal cortex control three key aspects of

cognitive control—gating, maintaining, and relaying (Pillon et al., 2003). Leptin, the prototypical adipokine, expresses receptors across the cortex and various other brain regions. While predominantly investigated for its involvement in regulating energy intake and expenditure, leptin plays a pivotal role in numerous neurocognitive processes. It interacts with a range of hormones and neurotransmitters to fulfill these functions (Farr et al., 2015). Indeed, leptin influences hippocampal-dependent learning and memory, and more recently leptin has been shown to have antidepressant properties (Harvey, 2007).

The research data provides a diverse set of methods for improving cognitive performance, including physical and cognitive exercise (Moniruzzaman et al., 2020), mindfulness practices (Cifu et al., 2018), and intermittent fasting (Ooi et al., 2020). These interventions have demonstrated effects on both cognitive performance and biochemical blood parameters. For instance, recent studies have shown that physical fitness levels are associated with performance in attention, memory, spatial imagery, reaction speed, and executive functions such as cognitive flexibility and inhibition control (Chang et al., 2012; Pontifex et al., 2012). Moreover, a high testosterone-to-cortisol ratio suggests greater anabolic drive and has been strongly associated with positive training and performance outcomes (Pedlar et al., 2019), while low iron status compromises the erythropoietic effects of altitude linked to endurance performance (Garvican-Lewis et al., 2018). Recent studies indicate that physical activity and exercise play a significant role in preventing and mitigating symptoms of depression (Agbangla et al., 2023; Danielsen et al., 2023; Jacinto et al., 2023; Josefsson et al., 2014; Rosenbaum et al., 2014; Sachs et al., 2023; Schuch et al., 2016) and may have antidepressant effects in individuals with neural system-related conditions (Adamson et al., 2015).

Several studies suggest that regular physical exercise enhances daily performance by promoting better stress adaptation, reducing anxiety (Knöchel et al., 2012), and fostering the development of social skills (Erickson et al., 2011), memory (Winter et al., 2007), and creative thinking (Oppezzo & Schwartz, 2014). These observed effects are believed to be associated with exercise-induced neuronal adaptations and the interplay of monoamines (Acworth et al., 1986; Guillouzo & Guguen-Guillouzo, 1986). Additionally, another study revealed a significant improvement in cognitive flexibility among participants undergoing aerobic training for 10 weeks, with no significant changes observed in attention and mental speed (Masley et al., 2009). Moreover, aerobic exercises positively influence the connectivity of the default brain and executive control networks, as well as synchronize brain regions associated with reward and attention (Voss, Erickson, et al., 2010; Voss, Prakash, et al., 2010; Weng et al., 2017). Conversely, research investigating the effects of exercise on motor coordination in adults is relatively limited compared to aerobic exercise's impact on cognitive functions. One notable study demonstrated that motor coordination training yielded better results in reducing task-switching costs compared to cardiovascular training (Johann et al., 2016).

The effects of dietary restrictions on cognitive function have been extensively studied in recent years; however, the findings have not consistently demonstrated a clear pattern (Dias et al., 2020). The lack of consistency can be explained by variations in experimental protocols, leading to contrasting cognitive outcomes. For instance, in one study, it was reported that ketone-fed rats exhibited a 38% faster completion rate in an 8-arm radial maze test compared to those on other diets and made more correct decisions before errors occurred (Murray et al., 2016). Conversely, another study found that ketone-fed rats experienced severe impairments in visual-spatial memory and decreased brain growth (Zhao et al., 2004). In experiments with mice subjected to intermittent fasting, improved learning and memory capacities were observed based on Barnes maze and fear conditioning assessments, along with a thicker CA1 pyramidal cell layer, when compared to mice with unrestricted access to a regular diet (control mice; Li et al., 2013). Additionally, older adults with mild cognitive impairments who regularly practiced intermittent fasting showed better cognitive scores and displayed a reversal in cognitive function improvements over a 36-month period (Ooi et al., 2020). However, a separate pilot study in humans reported a decrease in cognitive function, as assessed by the Montreal Cognitive Assessment, and short-term memory in the intermittent fasting group (Christensen, 1974). Despite the indirect effects of intermittent fasting on neuroplasticity and neuroprotective functions for both animals and humans having been detected, few studies have investigated changes in specific patterns of activation and functional connectivity within brain networks (Mattson et al., 2018; Murphy et al., 2014).

Systematic reviews of various types of meditation have reported preliminary positive effects on

cognitive functions, including attention, memory, executive function, processing speed, and general cognition (Chiesa & Serretti, 2009; Dharmawardene et al., 2016; Gard et al., 2014; Goyal et al., 2014; Moore & Malinowski, 2009; Newberg et al., 2010). These beneficial effects are believed to be partially attributed to stress reduction. Additionally, longitudinal mind-body practices have been associated with gene expression changes related to inflammatory pathways and increased telomerase activity (Jacobs et al., 2011; Zhu et al., 2012).

Comparative analysis has revealed distinct differences in the functional connectivity of the brain between more experienced and less experienced meditators, as well as changes in connectivity patterns among novice meditators. Specifically, participants with greater meditation experience exhibited increased connectivity within attentional networks, as well as between attentional regions and medial frontal regions (Hasenkamp & Barsalou, 2012). During resting-state, meditators demonstrated greater resting-state functional connectivity (rs-FC) within the dorsal attention network (Froeliger et al., 2012).

To explore changes in metabolism during cognitive tests after exercise, functional near-infrared spectroscopy (fNIRS) is often employed. Comparing the activity of the prefrontal cortex during meditation using fNIRS suggests that oxygen consumption in the right prefrontal cortex is increased during meditation compared to the resting state (Deepeshwar et al., 2015). At the same time, the effect of regular meditation on brain activity while solving cognitive tasks has not been sufficiently studied.

The interpretation of the impact of these interventions is challenging due to several factors, including variations in the duration of interventions, participant demographics (age, gender, etc.), and the parameters measured. Although a growing body of evidence indicates a positive cognitive effect of the mentioned above practices, comparing their effects remains difficult due to differences in experimental designs. In our study, we sought to compare the effects of 8 weeks of regular physical exercise (either high-intensity interval training or strength training), intermittent fasting, and meditation on cognitive performance and physiology parameters.

Based on previous data, we formulated the following hypotheses:

1. Both meditation and exercise will enhance memory, attention, and cognitive flexibility while reducing biochemical markers of the stress.
2. During cognitive tests, we expect higher oxygenation levels in the right prefrontal cortex for meditators and in the left prefrontal cortex for the exercise group after 2 months of training.
3. Regular meditation might result in an increase in global connectivity, and exercise may lead to the redistribution of connectivity patterns.
4. Intermittent fasting could enhance cognitive performance through increased mitochondrial activity throughout the body.

By examining these interventions' effects on cognitive performance and physiological parameters, our study aims to contribute valuable insights into their potential benefits and mechanisms of action. Addressing these hypotheses will help bridge gaps in understanding the impact of these practices on cognition and overall well-being.

Materials and Methods

Participants

Sixty healthy, right-handed Indo-European adults aged 25 to 50 were recruited to participate in the study. They were randomly and evenly assigned to four different groups. However, at the start of the study, two participants from the diet group dropped out, and one requested to be transferred to another random group. Consequently, 46 participants (22 women, mean age 33.4 ± 7.7 years) completed the study: 14 in the meditation group, 8 in the diet group, 16 in the exercise group, and 8 in the control group.

Participants meeting the following criteria were included: (a) no prior regular practice of meditation, intermittent fasting, or exercise. Through interviews, it was confirmed that none had practiced intermittent fasting, attended meditation classes, or engaged in regular exercise over the past year. Moreover, none had participated in vipassana or held a degree in sports; (b) normal health as determined by routine clinical examination, with a BMI ranging from 18 to 25. Individuals on medication or dietary supplements and those with medical records of mental or cognitive disabilities were excluded from the study. Participants with infectious diseases during the 8-week study period were excluded from the analysis.

The study protocol and the nature of the experiments were explained to the subjects before obtaining signed informed consents. Each subject signed the consent form for routine medical monitoring, including the statement of agreement for the use of the results for scientific purposes. The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of I. M. Sechenov First Moscow State Medical University (protocol No. 28-19 on 18.11.2022).

Training Protocols

All activities lasted for 8 weeks. Daily throughout the study, participants reported their activity parameters in a telegram bot: sleep time, heart rate, total training duration, the number of steps, the time of the last meal, and a subjective assessment of well-being. The main goal of all groups was to follow the training program in a disciplined manner. The regularity of the exercise and meditation was checked by collecting heart rate samples from workouts and meditation sessions. The quality of the diet plan was assessed from the participants' daily reports.

Meditation (M). The participants in this group practiced twice a day, for 15–20 min in the morning and the evening. Each session included a warm-up exercise for the eyes, alternating breathing of the left and right nostrils (anuloma-viloma) for 5 min, and 22 long breaths with a focus on sensing their nostrils.

Intermittent Fasting (D). Participants in the diet group alternated 1 week of 8/16 intermittent fasting (16 hr of fasting every day) with 1 week of the low-carb diet between weeks of the cycle: Week 1 – 8/16 intermittent fasting, Week 2 – low carb diet, Week 3 – 8/16 intermittent fasting, and so on for 8 weeks in total. All participants received detailed verbal and written instructions on the diet plan and a list of recommended products.

Exercise (E). The exercise group members trained three times a week according to a prewritten program. The training included a 5–10 min warmup of cardio-aerobic exercises, 20 min of static-dynamic training, 10–15 min of cardio-aerobic training, and 10 min of stretching. Static-dynamic training consisted of strength training for the thigh, lower leg, abdomen, back, chest, shoulder and gluteal muscles. The complete training protocol, including the number of repetitions, can be found in the Appendix B.

Measurements

To comprehensively study the influence of trainings, we measured a diverse array of metrics, including four cognitive tests, tissue saturation indexes (TSI) obtained through fNIRS, EEG functional connectivity analysis, biochemical blood tests, recurring daily reaction time assessments, heart rate variability (HRV) parameters, daily step counts, and sleep efficiency measurements.

Cognitive Tests. All participants performed cognitive tasks with simultaneous measurements of brain activity with EEG and fNIRS taken twice: before the onset of the training process and immediately after (8 weeks after the first measurement). Each test lasted for about 30 min and included the following parts: 1 min resting state with eyes open, 1 min resting state with eyes closed, and four cognitive tests: Corsi test, Iowa gambling test (IGT), stop signal test (SSt), and task switching test (TSt; standard protocol tests from platform https://www.psytoolkit.org; Stoet, 2010, 2017). These tests were selected to check the performance of such cognitive domains as working memory/attention and executive function (Cullen et al., 2007). We did not consider the change in verbal memory, visual construction or abstract reasoning, based on other research (Kuczmarski et al., 2014; Northey et al., 2018) and because of the time limit for subjects sitting comfortably during the test. Based on the test results, we evaluated the following parameters: the maximum length of the memorized sequence and the rate of correct answers in the Corsi test for working memory, the percentage of selecting the low-risk variations in the Iowa gambling test, the cost of switching in the TSt and the inhibitory latency, the accuracy, and the time rate of correct answers in the SSt. The Corsi test included 10 presentations of sequences of up to 10 elements; SSt included 90, TSt 120, and IGT 100 stimulus presentations, respectively.

FNIRS. Measurements were conducted with NIRS4 brain and body spectrometer (Medical Computer Systems Ltd., Moscow, Russia) using two 4-channel arrays of optodes (one light source/emitter and four detectors in each device) covering the frontal and prefrontal area. Each device was square-shaped, with a diagonal length of 5 cm. At the vertices of the square there were detectors and a source in the center. The device was installed in such a way that the diagonal of the first square fell on the positions F6 and Fp2, and the diagonal of the second square fell on the positions F5 and Fp1. Near-infrared light was used at two wavelengths (770 and 850 nm). Changes in the concentration of oxygenated (O2Hb)

and deoxygenated hemoglobin (HHb) were recorded continuously throughout the task with NIRSSensLSL Software. Signals obtained from the eight NIRS channels were acquired with a sampling rate of 10 Hz. The raw optical density signals were converted to hemoglobin concentration changes (in mmol/mm) using the modified Beer–Lambert law in MATLAB (adapted NIRS to HbH, HbO, TSI Brainstorm functions). TSI is defined as a ratio between oxygenated and total hemoglobin:

$$HbT = HHb + HbO$$
$$TSI = \frac{HbO}{HbT} * 100\%$$

The hemodynamic values corresponding to each cognitive test were calculated as the difference between the TSI averaged over eight sensors and the time of the test, and TSI averaged over eight sensors and 1 min with open eyes and no task.

Electroencephalography (EEG). To study functional connectivity, we considered the EEG internode coherence. The coherence of two signals depends on their phase difference. Maximum coherence occurs when the phase difference is fixed between two signals. The coherence is zero (or near to zero) if the phase difference between two signals is random during time. Coherence is considered as:

$$coh_{ij}^2(w) = \frac{E\left[C_{ij}^2(w)\right]}{E[C_{ii}(w)] * E\left[C_{jj}(w)\right]}$$

where $C_{ij}(w)$ is Fourier transform of the cross-correlation between EEG nodes (node i, and node j) and $C_{ii}(w)$ is co-spectrum. Coherence was calculated in 10-s overlapping windows in the frequency domain, and then the coherences of all epochs were averaged over time.

All EEG signals were recorded with a NeuroPlay-8Cap (ltd. Neuro-assistive technologies; Moscow, Russia) using 8 surface electrodes (F3, F4, C3, C4, P3, P4, O1, O2) mounted on a cap following the International 10–20 positioning system. The ground and reference electrode was A2. There were dry electrodes, the electrode impedance was kept less than 100 kΩ. This impedance is acceptable for dry electrode systems (Higashi et al., 2017; Shad et al., 2020). All data were digitized in continuous recording mode (125 Hz sampling rate). The data was preprocessed via scipy toolbox for python. The zero mean EEG data of each subject is preprocessed using a band pass filter in 0.5–48 Hz for removing the artifacts. The signal was divided into 1-s epochs, and all epochs in which the signal amplitude exceeded 100 μV were excluded. When the subjects were familiarized with the test conditions, the EEG was not recorded. EEG recording for analysis was carried out continuously throughout the test from the moment the start button was pressed until the end of the test. The division of the signal into epochs was carried out only for the purpose of clearing the signal. For further signal processing, spectral bands were used: delta (0.5–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), beta1 (12–18 Hz), beta2 (18–30 Hz), and gamma (30–48 Hz). The relative spectral power was considered as the proportion of the power in a given band to the entire spectrum. Frontal characteristics were calculated using electrodes F3, F4, C3, and C4. Interhemispheric connectivity was considered as the average connectivity between pairs of electrodes C3-C4, P3-P4, C3-P4, and C4-P3. Sagittal connectivity was considered as the average connectivity between pairs of electrodes F3-O1, F4-O2, F3-O2, and F4-O1.

Physiological Metrics: Blood Tests, HRV, Activity, Sleep. All participants used triaxial accelerometers to measure motion. The obtained data was used to estimate physical activity, sedentariness, and sleep quality. For consistency of the obtained results, HRV metrics were measured with the help of Welltory (https://welltory.com), an application which uses photoplethysmography and electrocardiogram measurements taken with BLE heart rate monitors like Polar, Apple Watch, Fitbit, and mobile phone's camera. In this study, we collected physical activity levels including daily step count, active time, and sedentary time. Fitbit automatically deems the period of time active when a physical activity of at least three metabolic equivalents are performed. Sleep-related information is generated, including total time in bed, total sleep time, and awake time. Sleep efficiency was calculated as the combination of sleep duration and subjective fatigue feeling. Heart rate and HRV were measured every day at the same time of the day (in the morning or the evening).

A Telegram chatbot was used to send reminders to the participants and to collect daily productivity data. Only the data from the users who filled in more than 80% of the questionnaires was analyzed (n = 45). Most of the missed measurements were observed during the weekends (45% of missed questionnaires). Productivity was subjectively assessed by the participants themselves. Reaction time was measured based on the results of online

test completions (https://humanbenchmark.com/tests/reactiontime).

Blood samples were collected in the morning from the antecubital vein into the clot activator tubes on Week 1 and Week 8. The investigable parameters were creatinine, uric acid, ALT zinc, testosterone, homocysteine, adrenaline, noradrenaline, serotonin, leptin, and dopamine. To eliminate interassay variance, all samples were analyzed in the same laboratory using the same methods.

Statistical Analysis. The obtained data were analyzed for normality of distribution using the Shapiro-Wilk's test. Since not all studied parameters appeared to be normally distributed, we utilized the nonparametric (Vickers, 2005) Wilcoxon's test to compare the groups. Comparable values were in the form of differences between values at the end of the experiment (after 8 weeks of training) and at the beginning. To assess changes in cognitive test scores, TSI of fNIRS, and rhythmic characteristics and parameters of EEG functional connectivity, we employed a one-way ANOVA test. Post hoc Tukey criteria were applied for multiple test correction. The relationship between the values of various biochemical parameters and daily measurements was examined using the Pearson correlation coefficient. The values are presented as mean ± *SD*, with a *p*-value less than .05 considered statistically significant. All statistical analyses were conducted using the scipy.stats package in Python.

Additionally, a priori and post hoc analysis were performed using the G*Power 3.1.9.7 software (Faul et al., 2007). Considering four groups with two repeated measures, a large effect size, an alpha error probability of .05, and a high power ($1 - \beta > 0.85$), the required sample size for both ANOVA (repeated measures) and Wilcoxon's test was determined to be 40 participants. With an alpha level of .05, the current sample size, and the effect size calculated for this study, we achieved adequate power ($1 - \beta > 0.8$) for most characteristics, except for a few noted in the results tables.

Results

Cognitive Tests

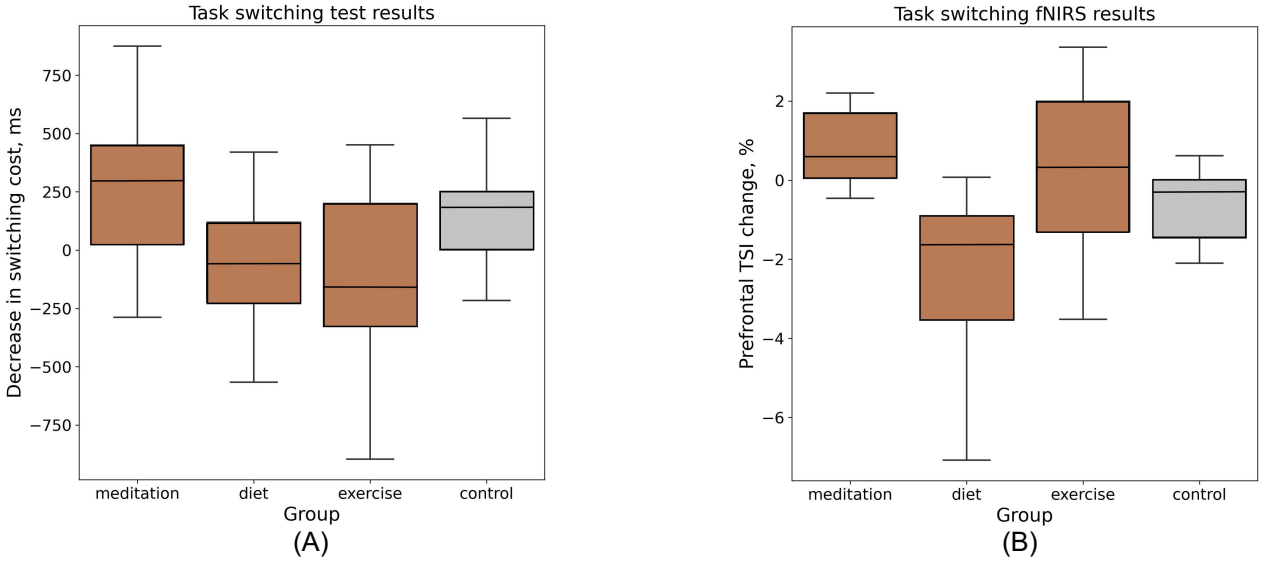
For all types of data described in the measurement section, we compared changes in results for different types of impacts (groups: M, D, E, C). No significant correlations were found between data of different types. There were no significant differences across four groups in changes in the Corsi working memory metrics and IGT decision-making. However, it was observed that the inhibitory latency was significantly improved for M, D, and E groups as compared to C (Appendix Table A1), according to the SSt. There were no differences between the groups in the accuracy and speed of reaction in SSt. In addition, the M had significantly improved the executive function after two months of training compared to the E and D groups (Appendix Table A2). The executive function was assessed via the cost of switching between tasks in TSt (Figure 1A).

Significant differences in 2-month changes in hemodynamics of the prefrontal cortex area, as indicated by fNIRS data, were observed in the TSt task: the M group showed significantly higher changes compared to both the D and E groups (see Appendix Table A2 and Figure 1B). Similarly, in the Corsi test, the M group showed more significant changes than the D group (see Appendix Table A3), and in the Iowa Gambling Test (IGT), the C group obtained higher changes compared to the D group (see Appendix Table A4). Thus, significant differences were only found for the TSt task in both test scores and changes in hemodynamics (see Figure 1B). Notably, 2 months of beginner meditation yielded better results for executive function and prefrontal cortex oxygenation during the TSt task compared to 2 months of intermittent fasting.

Electroencephalography

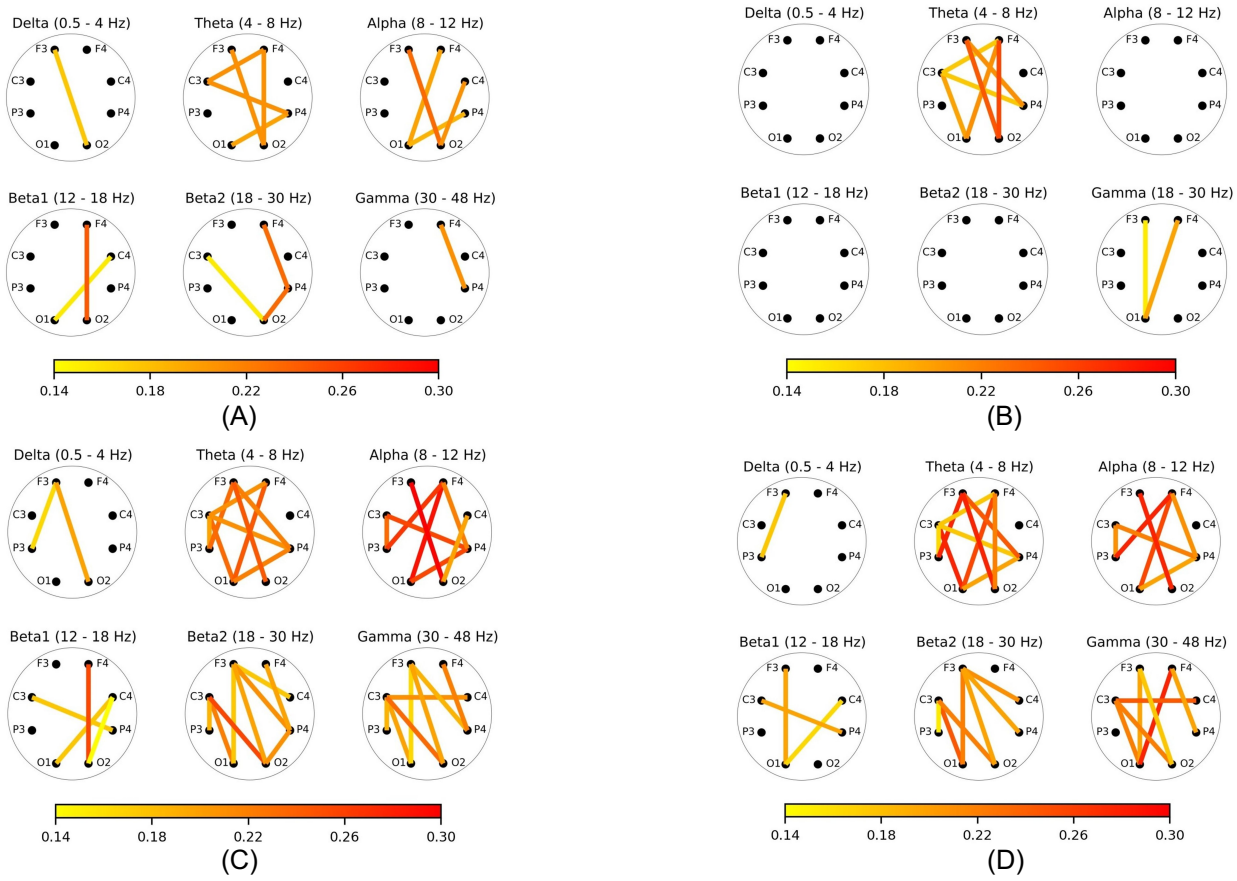
In the resting state with opened eyes no significant differences in absolute or relative spectral powers were found. However, there was a significant decrease in sagittal coherence for the meditator group compared to the diet (in theta and alpha bands) and control (in theta frequencies) groups. A significant decrease in coherence was also found for the E group: sagittal (theta, alpha), interhemispheric (theta, beta2), and left hemispheric (theta), in comparison to the D and C groups. In addition, the E group had a significant decrease in mean alpha, left and right hemispheric alpha coherence compared to the diet group, and a decrease in mean theta and left hemispheric beta1 compared to the control group (Appendix Table A5). A detailed comparison of rs-FC is depicted at Figure 2. Each part of the figure illustrates the significant differences in coherence changes for pairs of groups in the rs-FC between electrodes: (A) D-M groups, (B) C-M groups, (C) D-S groups, and (D) C-S groups.

Figure 1. *(A) TSt Results by Groups. (B) Changes in Prefrontal Hemodynamics During the Solution of the Task Switching Test by Groups.*



Note. (A) The vertical axis shows the decrease in switching cost in ms. Switching cost for M is significantly higher than for D and E groups. (B) The vertical axis shows the change in TSI in percent. Change in TSI for M and E is significantly higher than for D group.

Figure 2. *Significant Differences in Changes for Pairs of Groups in the rs-FC. (A) D-M Groups, (B) C-M Groups, (C) D-S Groups, (D) C-S Groups.*

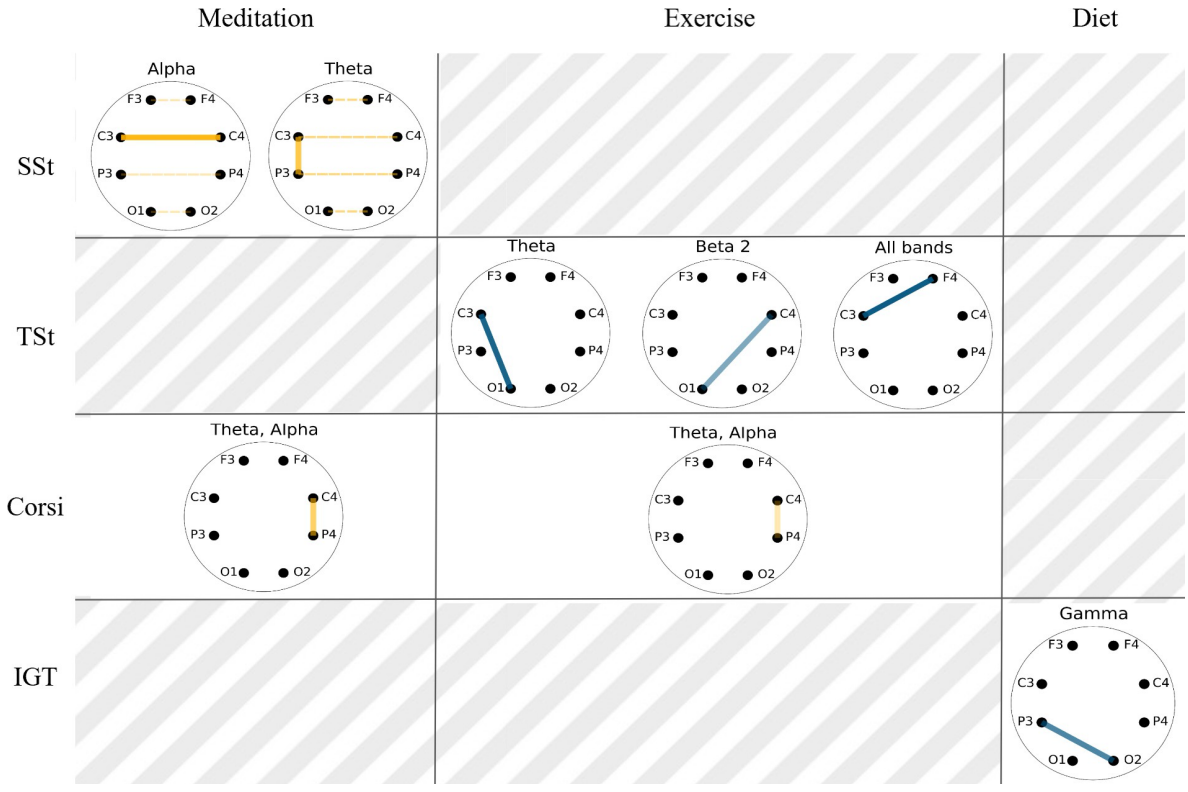


The pattern in FC during the test execution differs from the resting state. For M, compared with the E and C groups, interhemispheric coherence in theta and alpha significantly increased during SSt (Appendix Table A1). There was also a significant increase in the connectivity between electrodes C3 and C4 in theta and beta2 ranges in the meditation group compared to the E group during TSt (Appendix Table A2). Other single connectivity changes can be found in Appendix Tables A1–A4. Significant spectral changes were observed only for the Corsi test in the beta ranges (Appendix Table A3). All changes in comparison to the Control group are illustrated in Figure 3.

Biochemical Parameters

Creatinine concentration changed significantly in the meditation group and the difference was reckoned 5.04 ± 0.89 g/dl. Uric acid concentration also increased significantly in the meditation group and was 8.15 ± 1.62 g/dl, whereas in the other three groups it decreased and was 19.30 ± 6.29 g/dl and 19.37 ± 5.44 g/dl in the functional training group and the fasting group respectively. Notably, we also observed a significant decrease in uric acid level in the control group, which amounted to 18.71 ± 7.12. Testosterone level remained the same in all the observed groups. Leptin increased significantly in the fasting group to 2.15 ± 0.04 g/dl. Regardless of the intervention type, serotonin decreased significantly in all the groups. It must be noted that the most dramatic decrease of serotonin was observed in the fasting group and the difference was estimated as 99.02 ± 7.04 g/dl. The meditation group also demonstrated a significant increase in zinc blood concentration, while the fasting group had increased norepinephrine concentrations. However, as for the rest of the observed differences, statistical significance could not be established for any of the parameters before and after the study.

Figure 3. *Significant Differences in Changes of FC In Comparison to the Control While Solving Different Tests (Which is Represented by Different Rows and Different Columns Correspond to Training Type).*



Note. Blue lines mean negative values, yellow lines are positive. Transparency characterizes the absolute values of changes.

Daily Measurements

We observed a relationship between the intensity of training and reaction time in the exercise group. On days with high physical activity, participants reported fatigue more frequently compared to days with low physical activity (see Figure 4A). Furthermore, when comparing observed groups, we found a decrease in the number of daily steps in the fasting group compared to the control group (Figure 4B).

Sleep efficiency, defined as a function of sleep duration and subjective perception of fatigue reported by participants, correlated well in most participants. We noted a significant difference in sleep efficiency within the fasting group. Interestingly, participants with low sleep quality in this group did not report fatigue as expected.

We did not find significant changes in HRV parameters for the Diet or Exercise group. However, the values differed significantly in the meditation group when comparing values from the last week to the first, and moreover, after and before meditation (Figure 5).

Figure 4. *(A) Changes in Reaction Time After Training Session Depending on its Duration. (B) Average Number of Steps Per Day by Group.*

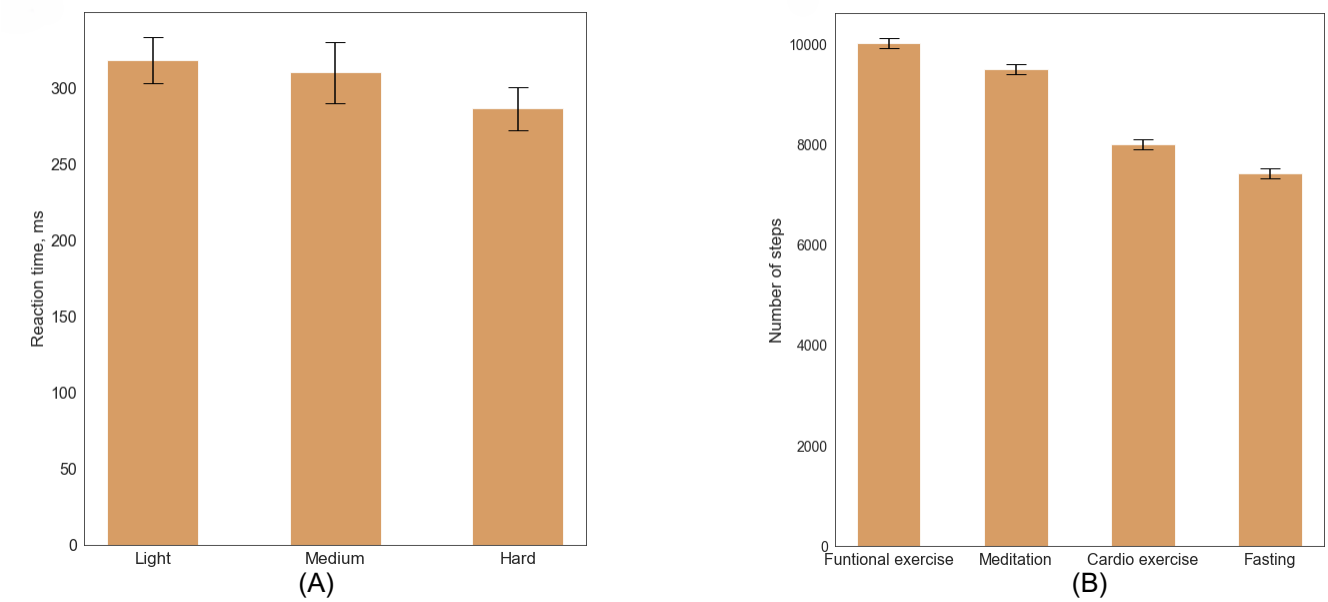
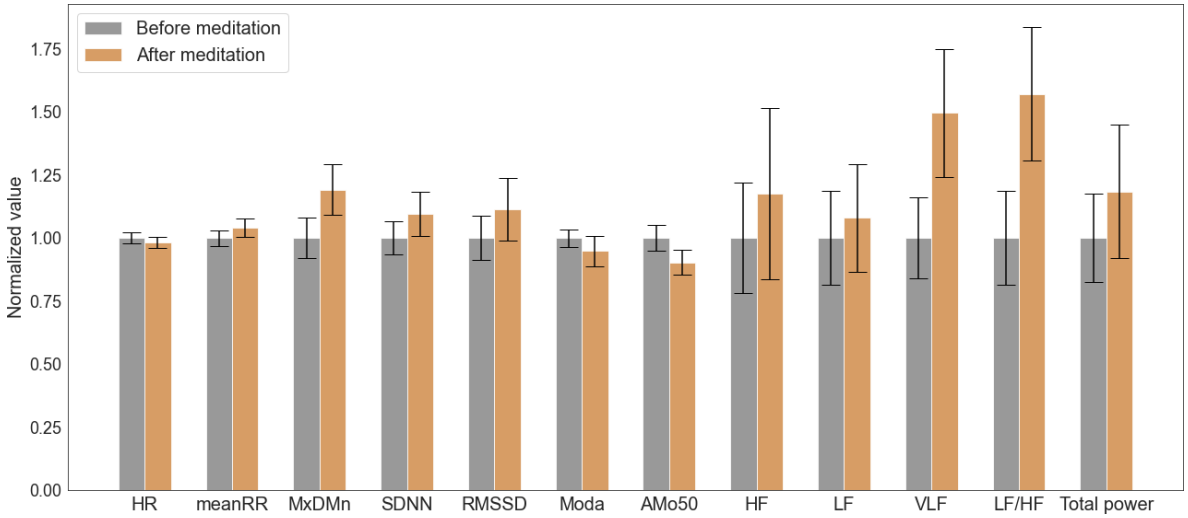


Figure 5. *Changes in HRV Parameters After Meditation Practice.*



Note. All values were normalized on the corresponding values before meditation.

Discussion

Our findings demonstrate that all types of the studied interventions, meditation, diet, and sports, positively affect the reduction of inhibitory latency equally in comparison with the control group, which is quite consistent with previous studies (Chang et al., 2012; Pontifex et al., 2012). We also reveal that different types of activity have different effects on cognitive function and patterns of brain activity. Specifically, we have shown that in order to increase the executive function, 2 months of meditation may be more effective than sports and diet for beginners. Based on the literature review, no similar comparison was carried out, although an increase in executive function was shown separately for meditation and sports (Gard et al., 2014; Moore & Malinowski, 2009; Newberg et al., 2010).

Other researchers have repeatedly noted the connection between cognitive load in solving intellectual tasks and an increase in oxygenation in the prefrontal cortex (Causse et al., 2017; Verner et al., 2013). Although the current study did not find direct correlations between these indicators, the intergroup changes are in good agreement with the above trend. For example, according to the TSt in the group of meditators compared to the diet group, the results of the test itself and the level of oxygenation of the prefrontal cortex are significantly higher.

Overall, we observed a decrease in prefrontal cortex oxygenation in the dietary group compared to the control group in IGT. There is also evidence that oxygenation for the diet group decreased compared with the meditation and exercise groups for the TSt and compared with the meditation group for the Corsi test. This could be explained by a more economical mode of activity of the whole organism under conditions of resource limitation. At the same time, the increase in oxygenation during problem solving in people who performed physical training is often explained by the general training of the cardiovascular system (Hötting et al., 2012), and for meditators—a conscious focus on brain activity (Miyashiro et al., 2021). We got little meaningful results for the diet group, partially because most of this group did not make it to the end of the study. Due to the low diet group size, only the high-impact results were recorded as significant.

Less expected results were obtained for changes in functional connectivity. When interpreting these results, we aim to be cautious. However, it is important to note that observed changes significantly depend on chosen metric. Additionally, the limitations arise from the fact that many of these metrics are based on correlation. In the current study we observed the decrease in coherence in the M and E groups compared to the C and D groups in a resting state. At the same time, there was an increase in functional connectivity in the meditation group compared with the control group (interhemispheric in the SSt, in the Corsi test on the right side) and compared with the diet group (in the left hemisphere in the IGT) and an increase in functional connectivity in the exercise group in comparison with the control group in the Corsi test. Meanwhile, these results are quite logical and may be accounted for the efficiency of the brain of meditators and the group of sports has increased: lower energy consumption in a resting state and higher synchronization in solving specific problems. The evidence from meditation research is more conclusive. For example, a decrease in functional connectivity during meditation has been shown for all frequency ranges for five different meditation traditions (Lehmann et al., 2012). It is well known that the activity of the default mode network in experienced meditators decreases in comparison with the beginners, with a higher connectivity of the executive network of the brain, according to fMRI data (Brewer et al., 2011).

At the same time, the data on the change in connectivity after several weeks of physical training are less clear-cut. For example, 12 weeks of walking showed an increase in functional connectivity in the PCC/precuneus for the elderly (Chirles et al., 2017). Similarly, 6-week Quadrato motor training in adults resulted in increased limbic and frontal-temporal connectivity in the alpha range with open eyes in a resting state (Lasaponara et al., 2017). At the same time, it was shown that gymnasts have a decrease in functional connectivity in the frontal-parietal and cingulo-opercular networks of attention control in a resting state. According to the authors, this decreased rs-FC might be due to the high intensity and amount of training suggesting a strong degree of automaticity leading to an increased neural efficiency (Dosenbach et al., 2007). Analyzing the studies on the effect of exercise on EEG data presented in the meta-review (Gramkow et al., 2020) showed that the final results are often contradictory, depending on the intervention and method of data processing. Perhaps such a difference in research results for meditation and sports can be explained by the fact that, regardless of the type of meditation, the practitioner often strives to control attention and stop the mind-wandering. While in physical activity the following processes can prevail: an increase in

power of the cardiovascular system, muscle growth, the increasing function of attention and thinking for playing sports, learning new movements, and redistributing the body's resources. Another interesting outcome of our results is that for an exercise group at rest, frontal-occipital connectivity decreases across all frequency ranges. Another work (Beaty et al., 2018) shows the correlation between connectivity and creativity. In this article, creative people have higher fronto-occipital connectivity than noncreative people. Hence, it can be assumed that exercise for beginners can negatively affect their creativity. Although, in our work, in contrast to the work of Beaty et al. (2018), EEG was used instead of fMRI. However, it is not always possible to extrapolate trends in functional connectivity obtained for the EEG to fMRI data and vice versa (Plis et al., 2011), since due to different operating frequency ranges, the trends may not comply or even be opposite (Danks & Plis, 2019).

The fasting group demonstrated a significant decrease in leptin blood concentration. The rapid (in 8 weeks) decrease in serum leptin levels during fasting may indicate that leptin release was regulated by factors other than changes in the body fat mass. The lack of leptin changes during fasting, when basal insulin and glucose levels were maintained at basal levels, suggested that insulin and/or glucose might play a role in leptin release regulation (Boden et al., 1996). In the study of intermittent fasting in adults with mild cognitive impairment, subjects exhibited significant increment in superoxide dismutase activity and reduction in body weight, levels of insulin, fasting blood glucose, malondialdehyde, C-reactive protein (CRP), and DNA damage (Ooi et al., 2020). On the other hand, we observed an increase in norepinephrine. Previous studies on neurotransmitter levels in rats showed that fasting regimes caused a significant increase of serotonin and norepinephrine. Additionally, fasting caused a significant decrease in aspartate aminotransferase (AST), urea, and creatinine, alongside a decrease in the weight of the body, liver, and stomach while causing a significant increase in phagocytic activity and phagocytic index (Shawky et al., 2015). The participants of the current study did not demonstrate significant changes in AST and creatinine, which can be connected to a mild diet plan.

In our study, we found a decreasing trend in urea level in all the groups, which can be explained by seasonal changes that were observed previously (Jacobs et al., 2011). Previous research also indicates that high serum uric acid may negatively influence vascular dementia. Contrarily, moderate levels of uric acid may have neuroprotector function (Tana et al., 2018). We assume that the dynamics of serum uric acid levels should be further monitored and possibly be a predictor of cognitive changes in response to daily routine changes. In our case, there was no significant change in epinephrine concentration in the fasting group, which can be found in patients with ketoacidosis (Christensen, 1974).

The participants in the fasting group demonstrated less consistency in their fatigue perception and sleep duration; there was no strong correlation between fatigue in the days after short sleep periods and sleep quality, as we observed in the other groups. It might be connected to the change in brain neuromediator concentration in blood serum (norepinephrine and serotonin). We assume that norepinephrine and serotonin serum levels can be considered as markers of human performance based on the current finding, and the combination of elevated levels of norepinephrine and decreased level of serotonin may lead to increased work productivity. Another reason for less subjective fatigue in participants might be connected to increased mitochondrial activity, which is observed during intermittent fasting (Lettieri-Barbato et al., 2018). The current finding also provides evidence for mitochondrial influence on mood and cognition (Picard & McEwen, 2014).

We found a significant increase in zinc blood serum concentration in the meditation group. A number of cross-sectional studies have investigated the association between physical activity and zinc status, while the obtained results remain contradictory. Some studies showed lower serum zinc concentration in athletes (Arikan et al., 2008), while other studies report no significant differences in zinc status between athletes and controls (Crespo et al., 1995; Nuviala et al., 1999). Still, there was no evidence reported on the influence of meditation and breathing techniques on zinc blood levels previously. The lack of conformity in the results may be driven by factors other than physical activity levels, for example, differences in dietary habits between the populations. In previous studies there are some evidence that during physical exercise the increase in plasma zinc levels might be the result of muscle leakage of zinc into the extracellular fluid following muscle damage (Noakes, 1987). Also, physical stress produced by exercise involves several neuroendocrine molecules that can interact with the metabolism (Sakata et al., 1991).

In the current study, we found a decrease of the creatinine's level in the meditation group. It is consistent with the previous results on the effect of yoga on creatinine blood level. Patients with chronic kidney disease, undergoing a yoga-training regime along with conventional treatment showed a significant reduction in blood urea and serum creatinine values over a period of 6 months. This can be attributed to the significantly beneficial impact of yoga on renal functions (Pandey et al., 2017). Our work demonstrates the positive effect that short meditations produce on creatinine levels.

Breathing techniques that were used in the daily meditation practices in our study stretch the lung tissue and produce inhibitory signals from the action of slowly adapting receptors and hyperpolarizing currents. These inhibitory signals coming from cardiorespiratory regions might influence the functions of the autonomic nervous system and are associated with resultant conditions characterized by reduced metabolism and parasympathetic dominance (Balaji et al., 2012). Previous studies confirmed that 30 min of daily yoga practice for 4 months showed a significant reduction in oxidative stress (malondialdehyde, protein oxidation, and phospholipase A2 activity) and an increase in antioxidant activity (superoxide dismutase and catalase activities) in patients with chronic kidney disease who were experiencing hemodialysis treatment (Gordon et al., 2013).

Daily observations of HRV levels in the meditation group demonstrated improvement in HRV parameters right after meditation. There was also a significant decrease in HRV levels in comparison to the other groups at the end of the 8th week of the study. However, we did not find any changes in neuromediator blood serum concentration. The correlation between subjective perception of fatigue and sleep duration remained unchanged throughout the study, while some of the recent studies on hemodialysis patients demonstrated that 12-week yoga intervention has proven to alter fatigue levels (Yurtkuran et al., 2007). The same study reported a significant reduction in creatinine, blood urea, alkaline phosphatase, and cholesterol along with significant improvement in erythrocyte and hematocrit count, which is consistent with our observations of creatinine and uric acid blood levels.

Changes in the concentration of uric acid and creatinine were registered in exercise groups which is consistent with previous studies (El Abed et al., 2011; Groussard et al., 2003; Hammouda et al., 2012). These findings are also consistent with previous observations showing that short aerobic exercise increases pro-oxidants more than anaerobic exercise (El Abed et al., 2019). We found that physical exercise led to better attention and reaction according to the daily tests and comparison of pre- and poststudy cognitive test results. It has been previously highlighted that physical exercise is related to improvement in reaction time (van de Water et al., 2017). Previous research also demonstrated that physical activity and exercise could support the development of cognitive functioning and specifically attention (Kao et al., 2017). For this reason, it could be considered that the practice of physical exercise and the development of physical condition could have an impact on reaction time, whether directly, through training of the capacity to respond to a given stimulus, or indirectly, through the impact it would have on cognitive functioning (Gentier et al., 2013).

The amount of daily physical activity has been related to reaction time. The participants who had more hours (more than 60 min a day) of physical activity showed a faster reaction. These results are congruent with previous research that had pointed out such associations (Okubo et al., 2017; Reigal et al., 2019). The significant differences in cognitive test results emphasize the importance of regular physical training for healthy adults. There was no correlation between fatigue and duration of exercise. While physical exercise therapy has been shown to increase HRV in healthy individuals (Dixon et al., 1992; Furlan et al., 1993; Pichot et al., 2005), we did not observe a significant long-term effect of exercise on HRV levels.

Conclusion

The significant results of the pilot study show specific correlations between changes in cognitive functions, patterns of brain activity, and physiological parameters with the type of activity. Specifically, physical activity may have a positive effect on cognitive functions, especially in tasks related to attention and reaction time. In addition, the longer the exercise session, the faster the reaction time. However, physical exercise can have a negative effect on creativity in those with the condition. Meditation can be considered an effective way to improve executive functions. Although exercise and meditation have more immediate and direct positive effects, diet may have long-term benefits for brain performance.

Insight into the various influences of these physical and mental practices may help tailor interventions

aimed at improving physiological and cognitive well-being. However, to make more accurate conclusions, it is necessary to conduct a series of studies on large samples, where different ages, sex, and types of activity will be widely represented, and also separate close-up studies for each area of activity, taking into account various mechanisms of influence on a person.

Author Declaration

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Appendix A

Table A1
Significant Differences in Changes for Different Interventions for the Stop Signal Test. SD – Standard Deviation

Test Results (Inhibitory Latency, ms) ± *SD*					
Meditation > Control	Meditation	Control	*p*-value	power	effect
	12.97 ± 41.99	−43.78 ± 57.39	.02	0.76*	1.11
Diet > Control	Diet	Control	*p*-value	power	effect
	9.90 ± 49.07	−43.78 ± 57.39	.02	0.61*	1.01
Sport > Control	Sport	Control	*p*-value	power	effect
	16.38 ± 49.07	−43.78 ± 57.39	.02	0.81	1.13
Functional Connectivity (Coherence) ± *SD*					
Meditation > Sport	Meditation	Sport	*p*-value	power	effect
Interhemispheric theta	0.125 ± 0.150	−0.055 ± 0.066	.03	0.76*	1.55
C3 P3 theta	0.173 ± 0.155	−0.096 ± 0.104	.01	0.93	2.04
Interhemispheric alpha	0.106 ± 0.118	−0.066 ± 0.064	.02	0.87	1.81
C4 C3 alpha	0.193 ± 0.137	−0.159 ± 0.160	.02	0.97	2.36
C3 P3 beta1	0.161 ± 0.180	−0.185 ± 0.118	.03	0.96	2.27
Interhemispheric all rhythms	0.089 ± 0.127	−0.079 ± 0.060	.05	0.82	1.69
C4 C3 all rhythms	0.149 ± 0.170	−0.144 ± 0.119	.02	0.92	2.00
Meditation > Control	Meditation	Control	*p*-value	power	effect
Interhemispheric theta	0.125 ± 0.150	−0.053 ± 0.082	.03	0.73*	1.47
C3 P3 theta	0.173 ± 0.155	−0.046 ± 0.121	.01	0.79*	1.57
Interhemispheric alpha	0.106 ± 0.118	−0.066 ± 0.077	.02	0.84	1.73
C4 C3 alpha	0.193 ± 0.137	−0.099 ± 0.133	.02	0.95	2.16
Interhemispheric all rhythms	0.089 ± 0.127	−0.089 ± 0.103	.05	0.76*	1.54
C4 C3 all rhythms	0.149 ± 0.170	−0.112 ± 0.157	.02	0.78*	1.60

* = Power size below 0.8.

Table A2
Significant Differences in Changes for Different Interventions for the Task Switching Test. SD – Standard Deviation

Test Results (Switching Cost, ms) ± *SD*					
Meditation > Diet	Meditation	Diet	*p*-value	power	effect
	255.22 ± 317.20	−72.89 ± 320.90	.03	0.71*	1.03
Meditation > Sport	Meditation	Sport	*p*-value	power	effect
	255.22 ± 317.20	−106.55 ± 386.17	.03	0.85	1.03
FNIRS (ΔTSI) ± *SD*					
Meditation > Diet	Meditation	Diet	*p*-value	power	effect
	0.38 ± 1.60	−2.48 ± 2.50	.04	0.84	1.36
Sport > Diet	Sport	Diet	*p*-value	power	effect
	0.22 ± 2.46	−2.48 ± 2.50	.04	0.68	1.10
Functional Connectivity (Coherence) ± *SD*					
Meditation > Sport	Meditation	Sport	*p*-value	power	effect
C3 O1 theta	0.064 ± 0.108	−0.140 ± 0.053	.02	0.99	2.40
C4 C3 theta	0.128 ± 0.207	−0.206 ± 0.152	.04	0.94	1.83
C4 O1 beta2	0.055 ± 0.063	−0.078 ± 0.066	.04	0.97	2.06
C4 C3 beta2	0.089 ± 0.156	−0.178 ± 0.066	.04	0.99	2.23
F4 C3 all rhythms	0.058 ± 0.069	−0.138 ± 0.078	.05	0.99	2.66
Control > Sport	Sport	Control	*p*-value	power	effect
C3 O1 theta	−0.140 ± 0.054	0.009 ± 0.101	.02	0.96	1.84
C4 O1 beta2	−0.078 ± 0.066	0.023 ± 0.063	.04	0.89	1.56
F4 C3 all rhythms	−0.138 ± 0.078	0.041 ± 0.122	.05	0.94	1.75

Table A3
Significant Differences in Changes for Different Interventions for the Corsi Test. SD – Standard Deviation

FNIRS (ΔTSI) ± *SD*					
Meditation > Diet	Meditation	Diet	*p*-value	power	effect
	1.39 ± 1.53	−1.98 ± 2.05	.03	0.95	1.86
Relative Power Spectrum Changes ± *SD*					
Meditation > Sport	Meditation	Sport	*p*-value	power	effect
Left hemisphere beta 1	0.028 ± 0.027	−0.070 ± 0.053	.04	0.99	2.33
Meditation < Sport	Meditation	Sport	*p*-value	power	effect
Frontal beta2	−0.050 ± 0.020	0.041 ± 0.058	.05	0.99	2.47
Meditation < Control	Meditation	Control	*p*-value	power	effect
Average beta2	−0.036 ± 0.026	0.071 ± 0.048	.02	0.99	2.77
Frontal beta2	−0.050 ± 0.020	0.125 ± 0.101	.05	0.99	2.40
Sport < Control	Sport	Control	*p*-value	power	effect
Average beta2	0.012 ± 0.037	0.071 ± 0.048	.02	0.78*	1.38
Functional Connectivity (Coherence) ± *SD*					
Meditation > Control	Meditation	Control	*p*-value	power	effect
P4 C4 theta	0.147 ± 0.187	−0.130 ± 0.122	.03	0.94	1.75
P4 C4 alpha	0.152 ± 0.187	−0.128 ± 0.132	.02	0.94	1.74
Sport > Control	Sport	Control	*p*-value	power	effect
P4 C4 theta	0.082 ± 0.078	−0.130 ± 0.122	.03	0.97	2.07
P4 C4 alpha	0.104 ± 0.051	−0.128 ± 0.132	.02	0.99	2.32

Table A4
Significant Differences in Changes for Different Interventions for the Iowa Gambling Test. SD – Standard Deviation.

FNIRS (ΔTSI) ± *SD*					
Control > Diet	Control	Diet	*p*-value	power	effect
	1.29 ± 3.42	−2.49 ± 2.93	.04	0.61*	1.19
Functional Connectivity (Coherence) ± *SD*					
Meditation > Diet	Meditation	Diet	*p*-value	power	effect
C3 P3 beta1	0.093 ± 0.104	−0.160 ± 0.136	.03	0.60*	2.09
O2 P3 gamma	0.086 ± 0.091	−0.100 ± 0.061	.03	0.99	2.40
Control > Diet	Diet	Control	*p*-value	power	effect
O2 P3 gamma	−0.100 ± 0.061	0.044 ± 0.068	.03	0.93	2.22

* = Power size below 0.8.

Table A5
Open Eyes Resting State. Significant Differences in Changes for Different Interventions for the Resting State With Open Eyes. SD – Standard Deviation

Functional Connectivity (Coherence) ± *SD*					
Meditation < Diet	Meditation	Diet	*p*-value	power	effect
Sagittal theta	−0.055 ± 0.116	0.136 ± 0.189	.002	0.66	1.21
Sagittal alpha	−0.023 ± 0.136	0.182 ± 0.175	.004	0.71	1.31
Meditation < Control	Meditation	Control	*p*-value	power	effect
Sagittal theta	−0.055 ± 0.116	0.168 ± 0.111	.002	0.97	1.96
Left hemisphere theta	0.0001 ± 0.117	0.130 ± 0.082	.003	0.74*	1.29
Sport < Diet	Sport	Diet	*p*-value	power	effect
Sagittal theta	−0.087 ± 0.066	0.136 ± 0.189	.002	0.84	1.58
Interhemispheric theta	−0.063 ± 0.062	0.098 ± 0.060	.020	0.99	2.63
Left hemisphere theta	−0.092 ± 0.051	0.105 ± 0.108	.003	0.98	2.33
Sagittal alpha	−0.093 ± 0.066	0.182 ± 0.175	.004	0.97	2.08
Average alpha	−0.063 ± 0.064	0.129 ± 0.142	.040	0.90	1.74
Left hemisphere alpha	−0.098 ± 0.093	0.135 ± 0.134	.040	0.96	2.02
Interhemispheric beta2	−0.086 ± 0.064	0.090 ± 0.121	.020	0.92	1.81
Sport < Control	Sport	Control	*p*-value	power	effect
Average theta	−0.055 ± 0.040	0.111 ± 0.079	.020	0.99	2.65
Sagittal theta	−0.087 ± 0.066	0.168 ± 0.111	.002	0.99	2.79
Interhemispheric theta	−0.063 ± 0.062	0.096 ± 0.086	.020	0.98	2.12
Left hemisphere theta	−0.092 ± 0.051	0.130 ± 0.082	.003	0.99	3.25
Sagittal alpha	−0.093 ± 0.066	0.144 ± 0.093	.004	0.99	2.93
Left hemisphere beta1	−0.055 ± 0.089	0.098 ± 0.072	.040	0.97	1.89
Interhemispheric beta2	−0.086 ± 0.064	0.100 ± 0.120	.020	0.97	1.93

* = Power size below 0.8.

Appendix B

The Exercise group alternated between the first type of program (on the first training day) and the second type (on the second training day) throughout the entire experimental period.

Program 1 (Main Section):

1. Latissimus dorsi (back muscles)
    - Wide-grip lat pulldown to the chest
    - Wide-grip lat pulldown behind the neck
    - Narrow reverse-grip lat pulldown with a shortened range of motion
    - Horizontal row on a machine

Series: Three sets of 30–40 s each; 30-s rest between sets.

2. Pectoral muscles (chest muscles)
    - Wide-grip push-ups
    - Barbell press on a bench or machine
    - Dumbbell Flyes

Series: Three sets of 30–40 s each; 30-s rest between sets.

3. Abdominal muscles (abs)
    - Torso curls with hands in front (slight elevation, shoulders not touching the floor)
    - Leg raises while lying on the back (45–80 degrees at the hip joint)
    - Bent leg raises in a combined machine (short range of motion)
    - Vertical leg raises while lying on the back, lifting the glutes off the floor: additional weights and machines can be used.
    - Curls with a slight twist and side leg raises
    - Torso curls while lying, knees bent and turned to one side (touching the floor)
    - Torso curls while lying, knees bent and turned to one side (touching the floor)

Series: Three sets of 30–40 s each; 30-s rest between sets.

4. Leg muscles (gluteal muscles)
    - Leg press (feet positioned high on the platform)
    - Extensions on an inclined bench
    - Squats in a Smith machine

Series: Three sets of 30–40 s each; 30-s rest between sets.

*Two sets in total.

Program 2 (Main Section):

1. Muscles of the front thigh
    - Forward lunges
    - Leg extensions on a machine
    - Knee raises while standing on one leg (using weights or resistance bands)
    - Leg raises (straight or slightly bent) while lying down (using weights or resistance bands)
    - Squats
    - Leg press
    - Half-lunge squats: 30–40 s per leg
    - Leg curls on a machine
    - Hip extensions (backward) while standing or lying down (using weights, resistance bands, crossover machine, or body weight)
    - Knee curls while standing or lying down (using weights, resistance bands, or body weight)
    - Pelvic paises with one leg support

Series: Three sets of 30–40 s; 30-s rest between sets.

2. Muscles of the back thigh
    - Leg curls on a machine
    - Hip extensions (backward) while standing or lying down (using weights, resistance bands, crossover machine, or body weight)
    - Knee curls while standing or lying down (using weights, resistance bands, or body weight)
    - Pelvic paises with one leg support

Series: Three sets of 30–40 s; 30-s rest between sets.

3. Muscles of the back calf
    - Calf raises with body weight or external weights (barbell, Smith machine)
    - Seated calf raises with external weights (barbell, dumbbells, etc.) or on a machine
    - Foot flexions on a machine

Series: Three sets of 30–40 s; 30-s rest between sets.

4. Abdominal muscles
    - Torso curls with hands in front (slight elevation, shoulders not touching the floor)
    - Leg raises while lying on the back (45–80 degrees at the hip joint)
    - Bent leg raises in a combined machine (short range of motion)
    - Vertical leg raises while lying on the back, lifting the glutes off the floor: additional weights and machines can be used.
    - Curls with a slight twist and side leg raises
    - Torso curls while lying, knees bent and turned to one side (touching the floor)
    - Torso curls while lying, knees bent and turned to one side (touching the floor)

Series: Three sets of 30–40 s; 30-s rest between sets.

*Two sets in total.

NeuroRegulation

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A Case Study Utilizing Virtual Reality to Reduce Behavioral Symptoms and Brainwave Activity Related to Anxiety

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Abstract

Of the mental health disorders, anxiety conditions maintain the highest base rate. The goal of this case study was to demonstrate the effectiveness of TRIPP VR, a virtual reality meditation application, utilizing a qEEG analysis program to recognize significant changes in brain wave patterns governing neuroelectrical impulses when compared to pretest results. Additional outcome measures included behavioral rating scales. A 13-year-old female demonstrating clinical signs of anxiety completed the required trials. Twenty-five sessions of meditation using TRIPP VR were administered to the participant over 8 weeks. Metrics used to demonstrate effectiveness included qEEG analysis and behavioral rating scales via a pre–post test design. Behavioral rating scales and qEEG analysis (which both use a normative population database) revealed marked decreases in the patient's negative affect and anxiety as well as a significant decrease in hiBeta (20–30 Hz) amplitudes. Significant physiological changes were also noted in regions of interest (ROI) proposed to correlate with anxiety, impulsivity, depression, and emotional inhibition. Of note, the patient remained "at risk" for anxiety. The current findings provide preliminary evidence which demonstrates the immersive potential of VR therapy to reduce symptoms of anxiety and possibly other psychological conditions. Limitations and the implications of these findings are discussed.

Keywords: qEEG; brain maps; virtual reality; VR therapy; TRIPP; anxiety; behavioral rating scales

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Introduction

Although standard treatment regimens have been established to treat anxiety, a variety of modalities continue to surface, particularly as technology advances. Methodologies for assessing gains in treatment are also numerous and include subjective report as well as quantifiable objective measures. Expansion of intervention modalities poses benefit for providers, their clients, and public health efforts. Cavallo et al. (2023) conducted a review of the scientific literature and found that over the past several years the application of virtual reality (VR) for mental health treatment has increased and is also supported by the American Psychiatric Association (APA, 2021). VR therapy is being promoted nationally and internationally for mental health conditions by companies such as Amelia Virtual Care (Gurr & Laitz, 2023) based upon clinical case studies that rely upon subjective outcome variables. In fact, EaseVRx recently received FDA approval for their VR treatment for patients 18 years or older diagnosed with chronic lower back pain (Food and Drug Administration [FDA], 2021).

Anxiety conditions are the most prevalent mental health disorders in the world, occurring cross-culturally and impacting 4% of the global population in 2019 (World Health Organization [WHO], 2023). Alongside gold standard interventions such as cognitive behavioral therapy and psychopharmacology, meditation is a recognized tool utilized in the treatment of generalized anxiety disorder, social anxiety disorder, and other

anxiety-related diagnoses (Goldin et al., 2015; Hoge et al., 2013). As technology-based approaches grow in accessibility and relevance, VR interventions for anxiety continue to garner research attention. Studies have demonstrated that VR meditation interventions can significantly improve anxiety levels, worry, negative mood, and quality of life (Berberyan et al., 2023; Lepilkina et al., 2023; Riches et al., 2023). Beyond meditation, other applications include biofeedback-related treatments, breathwork and exposure and response therapy (Donnelly et al., 2021). Though novel utilities and drawbacks remain under investigation, VR interventions for the treatment of anxiety exhibit numerous benefits for the anxious client.

Meditation interventions for anxiety are beneficial with or without VR components, illustrating the power of the practice (Navarro-Haro et al., 2019; Poetar et al., 2023). However, VR modalities have been shown to uniquely strengthen mental health treatment. The immersive nature of VR is often heralded as a major benefit of the tool, increasing a user's sense of presence and therefore engagement (Cavallo & Brubaker, 2024; Curran & Hollett, 2024; Goral et al., 2024; Navarro-Haro et al., 2017; Seabrook et al., 2020). This has implications for mental health treatment, as difficulty with "buy-in" and continued engagement can act as barriers to continuing treatment. One study examining a mindfulness-based intervention with and without an adjunctive VR module for those with generalized anxiety disorder demonstrated improved adherence to treatment for the VR condition (Navarro-Haro et al., 2019). Other studies have shown similar outcomes, citing reduced dropout rates for those receiving VR imagery versus standard imagery during relaxation (Malbos et al., 2022). Further, some findings support advantages of VR-based meditation interventions that surpass participant engagement and perceived presence. It has been shown that VR treatments can aid in producing physiological changes in healthy and anxious groups (Mazgelyté et al., 2021; Tarrant et al., 2018). Lastly, a growing number of studies highlight the superiority of VR based interventions as compared to conventional meditation and mindfulness (Kaplan-Rakowski et al., 2021; Ma et al., 2023).

Though a promising treatment modality, barriers to utilizing VR meditation interventions have also been explored. As compared to traditional anxiety interventions, the use of a VR console or device necessitates an additional element of consideration for treatment. Difficulty with portability has been identified as a challenge (Nicksic Sigmon et al., 2023). Additionally, though the immersive nature of VR tools has proven additive, it can also have adverse effects. In assessing motion sickness, some investigators have reported minimal impact on participants (Seabrook et al., 2020). However, simulator sickness has been shown to prevent engagement for others (Gao et al., 2024; Mimnaugh et al., 2023). Other barriers include weight of the VR device and perceived video quality (Seabrook et al., 2020). Further, optimal dosage for VR sessions remains unknown, affecting clinical implementation (Gao et al., 2024; Ma et al., 2023).

Alongside advancements in treatment fueled by technology, novel outcome methodologies have surfaced and continue to garner interest. Quantitative electroencephalography (qEEG) has demonstrated considerable potential for a variety of clinical applications, including epileptic screening and diagnosis, arrhythmia and stroke monitoring, and mood/anxiety disorders (Popa et al., 2020). Though exploration of the utility of qEEG has been plentiful, few studies have examined its suitability for VR interventions. To date, only one study has called the validity of qEEG data acquisition for VR users into question (Cavallo et al., 2023). Researchers tasked participants with staring at a neutral stimulus for a brief period both with and without a VR console; minimal differences in brainwave patterns were found between the two conditions, providing preliminary evidence of qEEG data obtained in conjunction with a VR platform. Barring this investigation, there is a dearth of knowledge surrounding the use of qEEG as an outcome variable for VR interventions. In one investigation that employed qEEG analysis for a VR mindfulness intervention in a sample of anxious participants, both VR and non-VR conditions experienced reduced anxiety; however, qEEG data aided in differentiating the groups, demonstrating a shift from higher to lower beta frequencies for those receiving the VR module (Tarrant et al., 2018). Additionally, traditional EEG analyses have been effectively employed for VR meditation interventions, evidencing comparable potential (Fu et al., 2021; Zhang et al., 2021).

The present study aims to examine the effectiveness of a VR meditation application (TRIPP VR) using several objective outcome measures including brainwave analysis. As efficacious anxiety treatment is pertinent to public health, it is vital to continue exploring methodologies for intervention and treatment progression. While VR meditation has shown promise in improving mood symptoms, level of engagement and quality of treatment, its utility for anxiety conditions and relevant physiological

impacts continue to warrant exploration. Existing research suggests that VR may produce physiological changes, but qEEG has rarely been used to assess VR interventions. This case study will be the first to explore the effectiveness of the TRIPP VR application for a participant with clinically significant anxiety, utilizing rating scales and qEEG analysis in an effort to underscore objectivity and further bolster the utility of specific qEEG analysis tools which pinpoint regions of interest (ROI). In light of available empirical evidence, it is hypothesized that the participant will experience decreases in anxiety, coupled with aligning shifts in electrical activity following the intervention, particularly in the amplitude reduction of beta frequencies.

Materials and Methods

Participants

The intervention was performed as a case study on a 13-year-old female showing clinically significant levels of anxiety. Since the participant was a minor, signed parental consent was received to provide the VR treatment and pre–post assessments from the participant's parents.

Equipment

The tools used to complete this case study were the TRIPP app, an Electro-Cap, and a VR headset. TRIPP is a VR app, available on the Meta Quest and other VR platforms, that was created to assist individuals in developing meditation skills and improving focus and a sense of calm through 8- to 12-min guided sessions, 3–5 times a week.

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

VR Headset. The VR headset used to complete the TRIPP app sessions was the Meta Quest 2 headset (formerly the Oculus). The headset includes two handheld controllers. The Meta Quest 2 is usually used for gaming and watching 360-degree VR videos with 20 pixels per degree visuals and a fast-switch LCD display spanning 1832 x 1920 pixels per eye with a 120 Hz refresh rate. The headset weighs 503 g and measures 224 x 450 mm.

Measures

The case study included baseline testing and postintervention testing. The pre–post testing involved measurements of qEEG brain mapping analysis and behavioral rating scales.

Behavioral Rating Scales

The rating scales utilized for the current case study included the Behavior Assessment System for Children (BASC-3) and the Millon Adolescent Clinical Inventory (MACI-II). The BASC-3 is a self-report rating scale which identifies areas where adolescents are in the at-risk and/or clinically significant range for behavior and emotional problems. This process is done through a clinical and adaptive *t*-score profile composed based on the patient's self-report. The report can also be completed by the patient's parent or teacher. The MACI-II is an additional social and behavior rating scale that interprets if there are mental health concerns utilizing age-based comparisons. The MACI-II displays the following primary analyses: (a) profile summary for personality patterns, (b) expressed areas of concern, and (c) clinical syndrome scores. These MACI-II scores are based on normative data presented according to percentile ranks with cut-off scores for interpretable or clinically significant levels of elevation. For the purposes of the current case study, only the clinical syndrome scales were analyzed since the other two types of primary scores produced by the MACI-II lend themselves toward clinical and subjective interpretation.

QEEG Brain Mapping Analysis

QEEG is a procedure that processes the recorded EEG electrical activity of the brain with multiple sensors through an amplifier connected to a computer. The obtained EEG is processed with various algorithms, such as the fast Fourier transform (FFT). Using statistical analysis, the metrics are compared to a normative database of reference values. Colorized brain maps are produced as a result of the analysis. QEEG information is used as a tool to interpret areas of brain dysregulation and function by various experts. Pre–post qEEGs allow for tracking of changes in brain function as a result of various interventions such as neurofeedback, exercise or medication. This case study design also employed BrainMaster's *Z*-Builder EEG analysis program to identify significant changes in an individual's qEEG based upon the hypothesis that traditional qEEG analysis approaches using normative comparisons appear to be less sensitive to changes in atypical population samples. BrainMaster's *Z*-Builder EEG analysis

program compares the individual to their own baseline qEEG analysis (Collura & Tarrant, 2020).

Procedure

The participant completed 25 sessions using the TRIPP VR app as a treatment protocol over an 8-week period with initial guidance provided by a technician. Prior to the first session, the participant completed two behavioral rating scales that were delivered and completed electronically on a secure server. During the first session, the participant received an initial qEEG assessment before using the VR TRIPP. Subsequently, during the initial session, the subject wore a VR headset for approximately 10–12 min while watching and participating in VR guided meditation videos. The VR videos are designed to regulate breathing with an immersive and interactive experience. The participant then took the VR equipment home for 8 weeks. Throughout those 8 weeks, they received weekly check-in emails. These emails included questions such as “how often do you remember to do your VR exercises?” and “do you have a specific time that you begin your sessions?” At the end of 8 weeks, the participant came back to the office to return the VR equipment and complete the post qEEG and the behavioral rating scales (BASC-3 and MACI-II). A subsequent parental rating form for the BASC-3 was completed by the same parent that completed the BASC-3 prior to the intervention phase.

Data Analysis

QEEG is produced through statistical analysis of the EEG; that is, conversion of the time domain EEG record (voltage plotted against time) to the frequency domain (amplitude or power plotted against frequency) using the FFT. The qEEG bands considered were delta (1–3 Hz), theta (4–8 Hz), alpha (8–12 Hz), beta (15–20 Hz), and high beta (20–30 Hz). In this study, raw EEG data were collected noninvasively from the participant’s scalp before their first session and after the 8 weeks using a BrainMaster Discovery 20-channel EEG (BrainMaster Technologies, Bedford, OH). Electrode caps were used to place recording electrodes over the 19 standard regions defined by the International 10/20 system referenced to linked ears: Fp1, Fp2, F3, F4, F7, F8, T3, T4, C3, C4, P3, P4, T5, T6, O1, O2, Fz, Cz, and Pz. All channels of EEG were acquired with 24-bit resolution at the sampling rate of 256 Hz. Automated artifacting using SARA was uniformly applied without exception in order to remove human error or bias in the analysis and selection of which data should be rejected. The NeuroGuide EEG and qEEG analysis system software (Applied Neuroscience, Inc., Largo, FL) was used for the signal processing of the qEEG. Quantitative data were presented using absolute power group means comparison between the pre–post intervention brain waves. Statistical analyses were also performed utilizing NeuroStat’s paired *t*-test for comparing the absolute power differences between the pre–post test results conditions across the 19 scalp locations acquired for each of the five previously mentioned frequency bandwidths. Finally, critical *p*-values for determining level of significance were reported for both the paired *t*-test and BrainMaster’s *Z*-Builder EEG analysis tool.

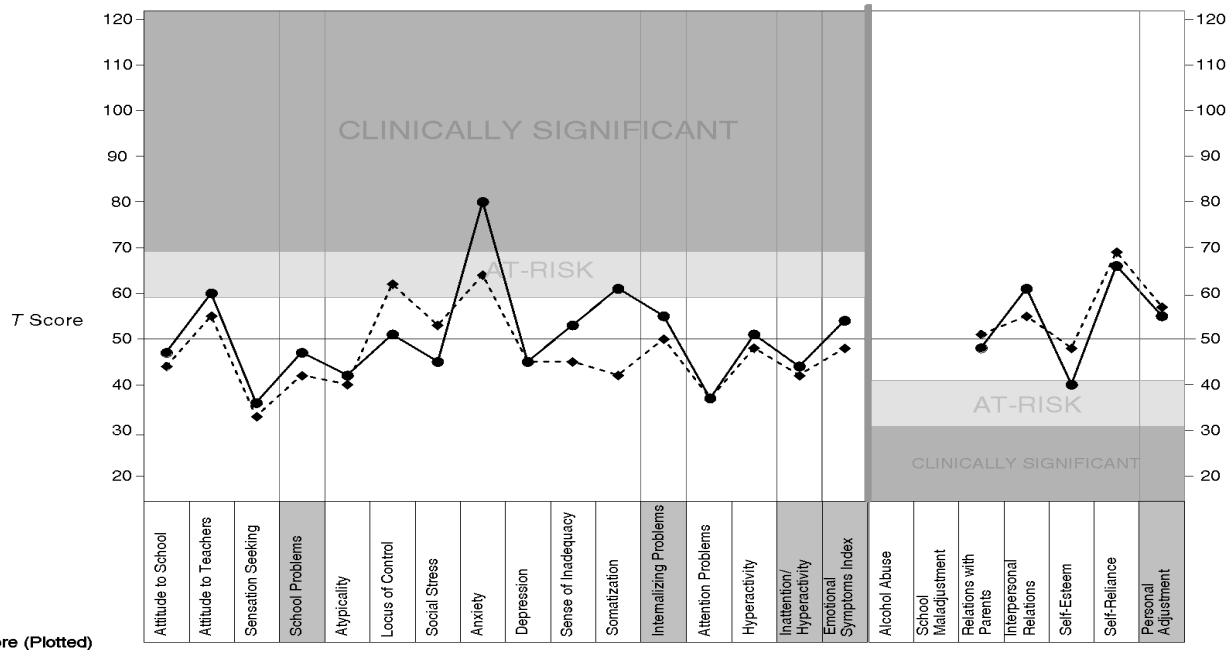
Results

The case study included one adolescent female participant who met criteria for a generalized anxiety disorder based upon prior psychological evaluation results. Overall, behavioral rating scales and qEEG analyses illustrated moderate decreases in the subject’s anxiety symptoms as measured by behavioral rating scales and electrical brain activity. An examination of each outcome measure is presented below.

Behavioral Rating Scales

BASC-3. The participant and their guardian completed the BASC-3 rating scale prior to and following the VR meditation intervention (Reynolds et al., 2015). The BASC-3 measures several areas related to the behavioral and emotional well-being of children and adolescents. Of note, one subscale directly measures anxiety, while others assess different areas of functioning such as depression, self-esteem, and tendencies to internalize. An assessment of adaptive functioning is also embedded in the measure. For clinical scales, *t*-scores below 60 are considered unremarkable; between 60–69 indicate *at-risk* or slightly elevated levels of concern and are associated with behaviors that should be monitored; and above 70 reflect *clinically significant* or markedly elevated concerns that require immediate attention. For adaptive scales, *t*-scores are interpreted inversely, where *t*-scores above 70 are considered *very high*, indicating complete mastery in a specific adaptive area; between 60-69 are *high*; between 41–59 are *average*; between 31–40 indicate *at-risk adaptive behaviors*; and those below 30 reflect *adaptive functioning that is clinically significant*. Figures 1 and 2 illustrate the pre–post *t*-score values for each of the domains and subdomains.

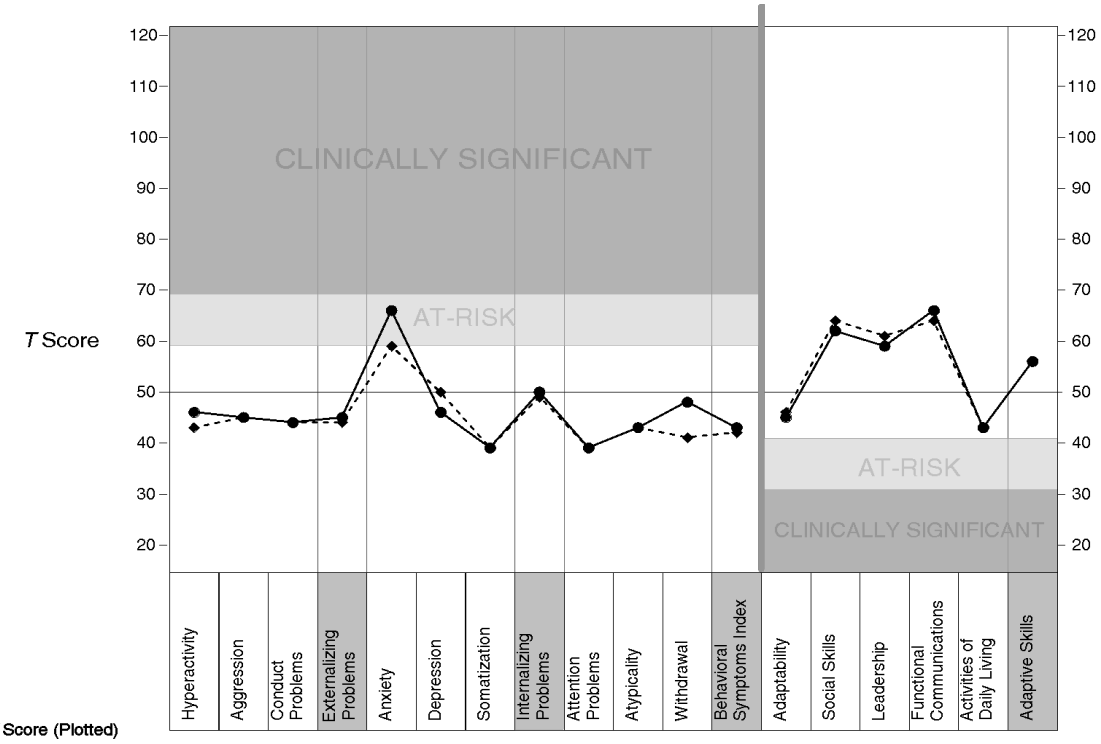
Figure 1. *Participant Self-Report for the BASC-3.*



T Score (Plotted)																							
Pre	47	60	36	47	42	51	45	80	45	53	61	55	37	51	44	54	--	--	48	61	40	66	55
Post	44	55	33	42	40	62	53	64	45	45	42	50	37	48	42	48	--	--	51	55	48	69	57

Note. -- indicates that the scale is not available for this form or the age at the time of the administration is not scorable for the norm group selected.

Figure 2. *Guardian Report for the BASC-3.*



T Score (Plotted)																		
Pre	48	45	44	45	66	46	39	50	39	43	48	43	45	62	59	66	43	56
Post	43	45	44	44	59	50	39	49	39	43	41	42	46	64	61	64	43	56

Perceptions of anxiety symptoms improved across raters. After the 8-week, 25-session intervention, the participant's self-rated anxiety decreased from a *t*-score of 80 (99th percentile) to 64 (90th percentile). Though anxiety remained a relevant behavioral area for monitoring, scores indicated notably decreased severity of symptoms such that the participant's *t*-score no longer fell in the clinically significant range according to a normative sample. Regarding guardian ratings, *t*-scores for anxiety decreased from 66 (92nd percentile rank) to 59 (84th percentile rank) such that the posttest *t*-value fell into the unremarkable or typical range. Additional changes were noted on the self-report form. The participant was no longer in the at-risk range for somatization, dropping from a *t*-score of 61 (86th percentile rank) to a *t*-score of 42 (15th percentile rank), representing typical levels of somatic complaints. Additionally, scores were in the at-risk range for self-esteem concerns prior to the module; self-ratings in this area improved similarly, with t-scores increasing from 40 (14th percentile rank) to 48 (32nd percentile rank). Of note, the participant's locus of control score evidenced an increase from a pretest *t*-score of 51 (64th percentile rank) to a posttest *t*-score of 62 (87th percentile rank), indicating mildly at-risk levels following the intervention.

MACI-II. The participant also completed the MACI-II (Millon et al., 2020). This rating scale is tailored to measure adolescent mental and behavioral health concerns. It contains several dozen scales in five clinically relevant domains. Among the areas measured are personality patterns, expressed concerns and clinical syndromes. Only the clinical syndrome scales were analyzed for the current study. Scores are presented as base rates (BR), which are set to reflect the prevalence rates of clinical syndrome criteria or classification. BR scores below 75 are *unremarkable*. Those between 75 and 85 are considered to be *present*, and scores above 85 are deemed *prominent and clinically significant*. Table 1 illustrates that prior to the intervention, the participant had a BR of 95 for anxious feelings,

Table 1

Pre vs. Post Self-Report for the MACI-II

Clinical Syndromes	Score PR	BR	Profile of BR Scores 0 60 75 85 115
Pretest			Present Prominent
Binge-Eating Patterns	58	60	
Substance-Abuse Proneness	30	0	
Delinquent Predisposition	9	0	
Anxious Feelings	76	95	
Depressive Affect	23	20	
Suicidal Tendency	21	0	
Disruptive Mood Dysregulation	22	20	
Post-Traumatic Stress	60	63	
Reality Distortions	23	9	

Clinical Syndromes	Score PR	BR	Profile of BR Scores 0 60 75 85 115
Posttest			Present Prominent
Binge-Eating Patterns	23	0	
Substance-Abuse Proneness	30	0	
Delinquent Predisposition	9	0	
Anxious Feelings	65	85	
Depressive Affect	6	0	
Suicidal Tendency	21	0	
Disruptive Mood Dysregulation	17	10	
Post-Traumatic Stress	45	45	
Reality Distortions	23	9	

which is considered prominent. Postintervention, the BR score for this subdomain was 75, eliminating the clinical relevance of this symptom. All other scales within the clinical syndrome profile were at nonclinical levels both before and after the intervention. Although nonclinical, a trend was evidenced posttreatment for decreased patterns of binge eating (a BR decline of 60 points), depressive affect and disruptive mood dysregulation (BR declines of 20 points), and posttraumatic stress (BR decline of 18 points).

QEEG Analysis

The 19 channels EEG recording had a duration of 6:03 min for eyes open and a duration of 6:02 min for eyes closed condition for raw EEG signals (see Figure 3). After applying SARA to automatically remove artifact, EEG recordings of 4:38 min for eyes open and 3:44 min for the eyes closed condition were produced and used for data analysis. Figure 4 presents qEEG analyses from the qEEG Pro report, which provides EEG Biomarkers based upon surface amplitude results and the agreement between the EEG results and the patients' symptoms. The red bars in Figure 4 reflect that the participant's symptom severity for anxiety remained unchanged. However, the relationship between the participant's brain activity deviations from a normative population and the participant's symptoms, as depicted by the green pie chart in Figure 4, revealed a 20% decrease in the deviant brain activity specific to anxiety and insomnia. The "high" color intensity depicted for anxiety and insomnia indicates a robust level of scientific support for the association between these biomarkers and the disorder (Keiser, 2018).

Figure 3. *Raw EEG Segment for Eyes Closed Condition.*

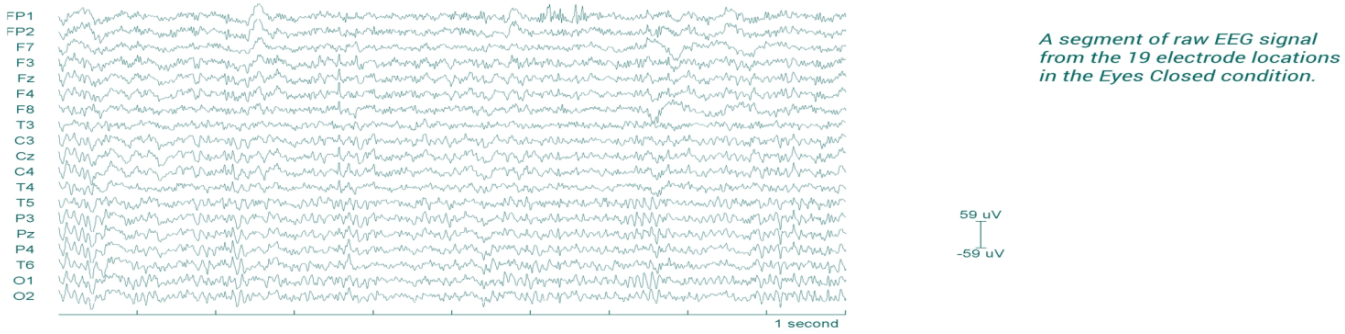
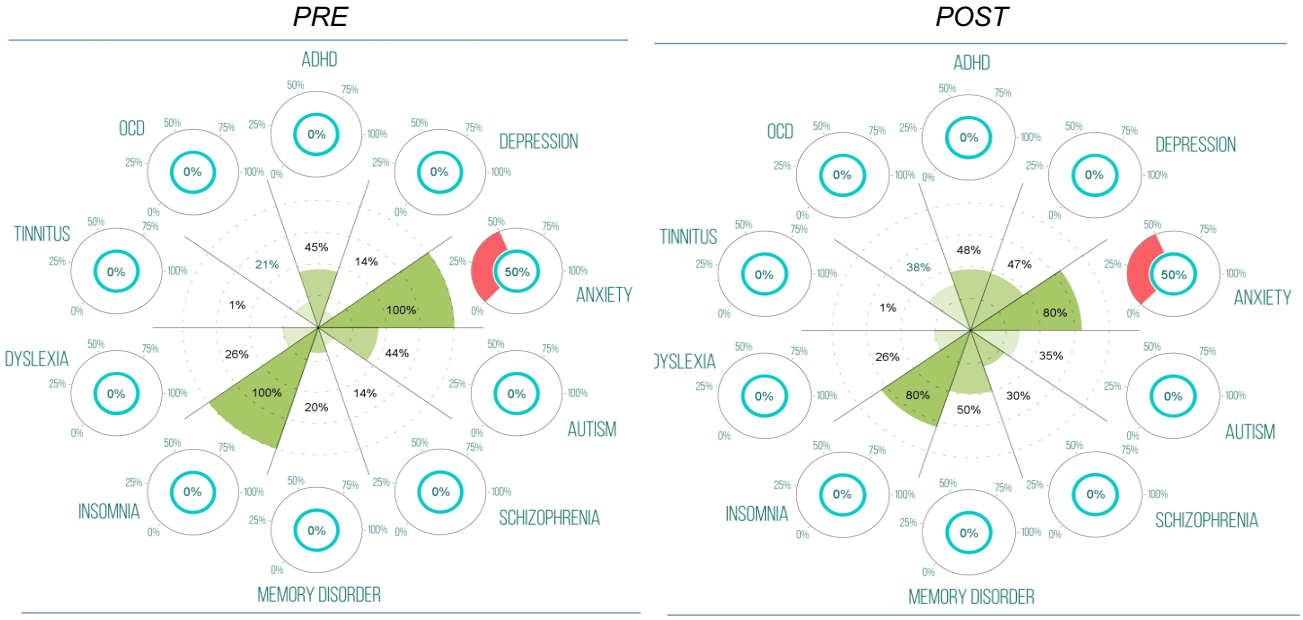
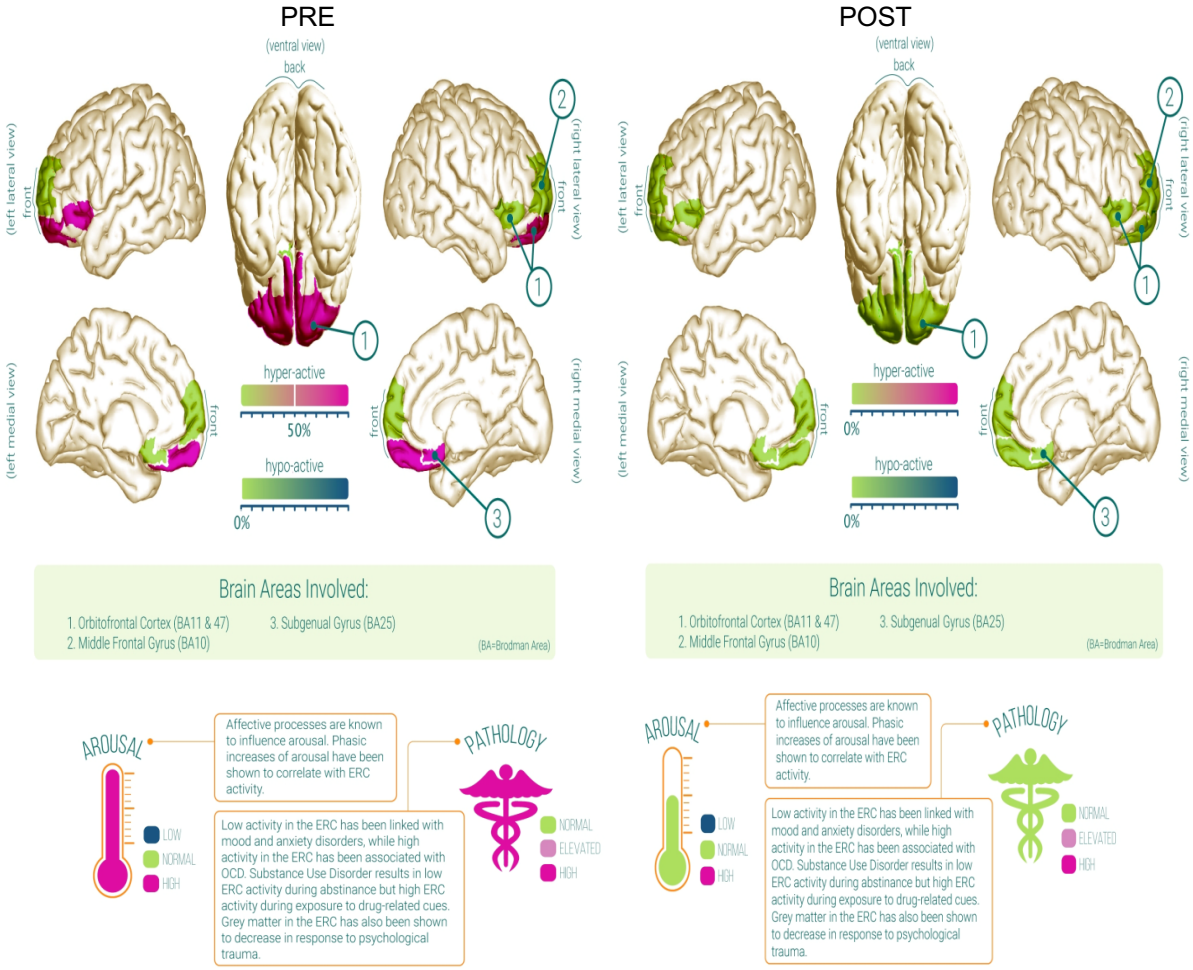


Figure 4. *EEG Biomarker Match Pre vs. Post.*



The qEEG Pro report also uses source localization techniques to determine the activity and connectivity of well-known "resting-state networks" based upon scientific literature (Keiser, 2018) that indicates the following networks represent functional units: the default mode network, the dorsal attention network, the emotion regulation cortex, the sensory motor cortex, the memory network, and the visual cortex. For the purposes of the current case study, only those networks which revealed abnormal arousal and pathology during the pre-test qEEG assessment are presented. Analysis of the results revealed only the emotion regulation cortex (ERC) to be implicated as all other networks failed to reveal abnormal brain activity levels both before and after the intervention. The ERC plays a role in emotion regulation, empathy, risk assessment, decision-making, and fear processing. The ERC also consists of the middle frontal gyrus, which is involved in emotional decision-making and the orbitofrontal gyrus, which is known for its role in the evaluation of emotional stimuli and the representation of the somewhat intangible concepts of personality or "cognitive style." The subgenual gyrus is also part of the ERC and plays a role in regulating emotion, endocrine function, and autonomic states associated with the neural processing of fear, reward, and stress. Figure 5 depicts a clinically significant improvement in the hyperactive connectivity levels in the orbitofrontal cortex and subgenual gyrus before (50%) and after (0%) hyperactive connectivity levels, resulting in brain activity specific to the ERC being restored from high arousal and pathology levels to normal levels. *Z*-score analysis (Table 2) revealed excessive hyperactivity in the prefrontal and frontal lobe due to significantly higher amplitude in the High Beta waves.

Figure 5. *Pre vs. Post Brain Activity in Resting-State Network: The Emotion Regulation Cortex.*



Z-Scores Analysis

The results of the generated brain maps from the normative database did show statistically significant changes. The *z*-score analysis of the absolute power metric was utilized for analysis where the colors depicted in the maps below (see Figure 6) indicate the amount of standard deviation represented as *z*-scores. Based upon clinical practice, clinically significant deviations are indicated with an absolute *z*-score value of two or greater. The brain maps presented in Figure 6 suggest that, prior to the intervention, this individual presented with excessive High Beta activity present in the frontal, parietal and occipital cortices due to excessive power in those regions. Postassessment of brain activity evidenced decreased High Beta activity in the frontal lobe by at least one standard deviation (*z*-score difference of 1 or greater). A *z*-score comparison (see Table 2) revealed significantly elevated power levels greater than two standard deviations from the normative database at the following locations in the High Beta frequency: Fp1 (*SD* = 2.2), Fp2 (*SD* = 2.2), F3 (*SD* = 2.3), Cz (*SD* = 2.2), C4 (*SD* = 2.3), T5 (*SD* = 2.3), P3 (*SD* = 2.6), Pz (*SD* = 2.8), P4 (*SD* = 2.8), and T6 (*SD* = 2.6). A postintervention *z*-score analysis (Table 2) revealed a decrease in power which represented typical power levels according to a normative database at the following locations in the High Beta frequency: Fp1 (*SD* = 1.2), Fp2 (*SD* = 1.2), F3 (*SD* = 1.4), and C4 (*SD* = 1.9).

Paired *T*-Test Analysis

Neuroguide's NeuroStat statistical software was utilized to provide an analysis of any significant intraindividual differences. This allows the analysis to measure improvement based upon the individual's unique EEG activity as opposed to a comparison against a normative database targeting significant differences represented by populations means only. Figure 7 presents the paired *t*-test data for the within-subject, single case design. *P*-values are presented both pictorially in the brain maps as well as numerically. The color legend located below the brain maps indicates that statistically significant brain activity differences ($p < .05$) existed post intervention in the following EEG frequency bands and brain regions: Delta (left frontal, $p = .006$; right frontal, $p = .009$; left central, $p = .001$; frontocentral, $p = .005$; parietal, $p < .04$), Theta (left frontoparietal = .002; right frontal parietal, $p = .000$; left frontal, $p = .000 - .01$; right frontal, $p = .000 - .001$; left central, $p = 0.000$; right central, $p < .04$; left temporal, $p < .02$; frontocentral, $p = .001$; central, $p = .002$), Alpha (left frontoparietal, $p = .001$; right frontoparietal, $p = .001$; left frontal, $p = .000 - .01$; right frontal, $p = .000 - .002$; left central, $p = .000$; left parietal, $p = .005$; right parietal, $p < .05$; left occipital, $p < .02$; right occipital, $p = .006$; left temporal, $p = .000 - .001$; frontocentral, $p = .001$; central, $p = .002$), Beta (left frontoparietal, $p = .000$; right frontoparietal, $p = .000$; left frontal, $p = .000$; right central, $p < .03$; right occipital, $p = .000$; left temporal, $p = .001$; right temporal, $p = -.001$), and High Beta (left frontoparietal, $p = .000$; right frontoparietal, $p = .000$; left frontal, $p = .000 - .001$; right frontal, $p = .001$; left temporal, $p = .000$; right temporal, $p = -.009$).

Figure 6. *Pre vs. Post qEEG Absolute Power (uV Sq) Z-Score Values.*

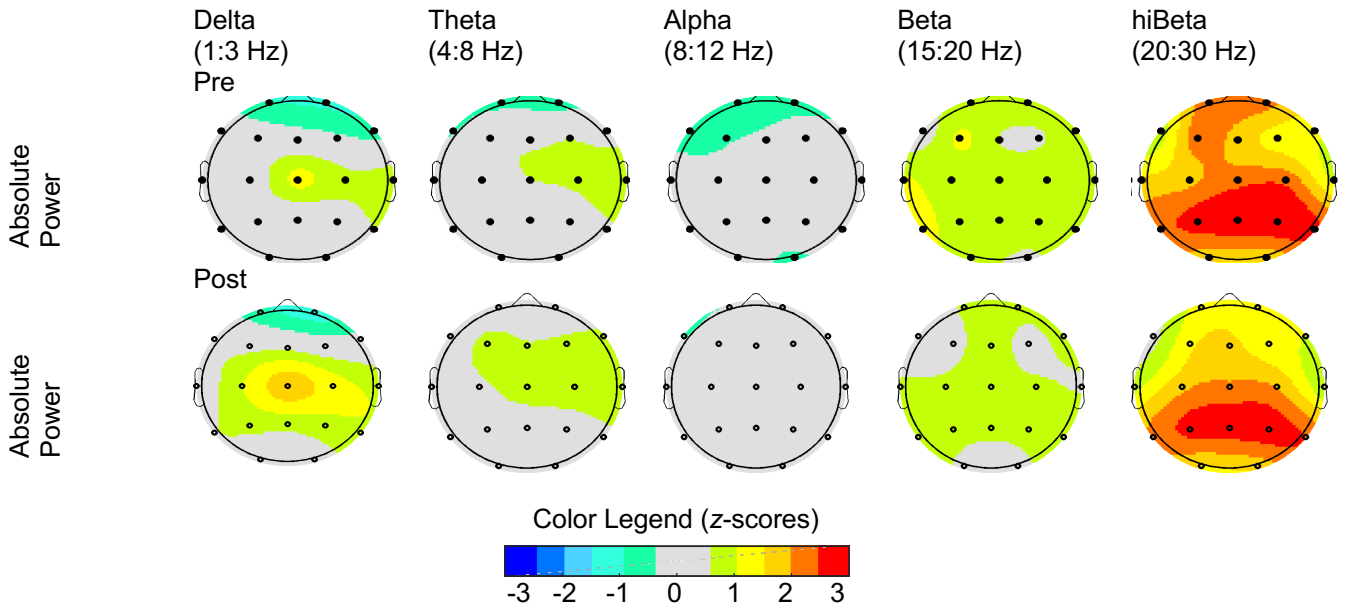
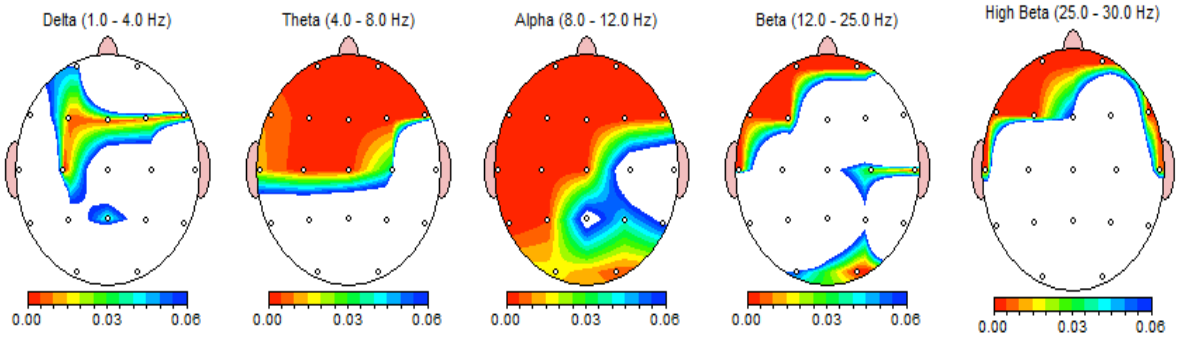


Table 2
Pre vs. Post Amplitude Z-Scores According to Location and EEG Frequencies

Pre	Absolute Power (uV^2)									
Ch	Delta	*Z*-Delta	Theta	*Z*-Theta	Alpha	*Z*-Alpha	Beta	*Z*-Beta	hiBeta	*Z*-hiBeta
FP1	26.7	−0.9	11.0	−0.6	7.9	−0.6	4.8	0.9	9.4	2.2
FP2	25.5	−1.1	10.9	−0.6	8.8	−0.5	5.1	0.9	9.6	2.2
F7	25.7	0.0	8.8	−0.4	5.9	−0.8	3.3	0.2	4.9	0.8
F3	27.7	0.0	20.4	0.4	12.6	−0.4	8.5	1.1	11.1	2.3
Fz	29.2	0.0	24.0	0.4	14.8	−0.3	6.5	0.5	7.9	1.7
F4	26.1	−0.2	21.9	0.5	14.8	−0.2	6.6	0.5	8.3	1.3
F8	19.0	−0.6	11.0	0.2	8.3	−0.3	4.6	0.9	6.2	1.2
T3	13.8	0.2	8.9	0.2	9.1	0.1	5.2	1.1	8.1	1.6
C3	24.5	0.2	18.0	0.1	18.0	−0.2	6.5	0.8	7.7	1.8
Cz	42.1	1.2	29.8	0.6	20.2	−0.3	7.9	1.0	9.4	2.2
C4	30.4	0.7	23.5	0.7	19.7	−0.1	7.8	1.0	9.7	2.3
T4	18.7	0.9	12.1	0.9	11.1	0.3	5.0	0.9	5.9	1.0
T5	20.4	0.3	14.7	0.3	24.4	0.0	8.0	1.2	9.5	2.3
P3	27.6	0.2	19.5	0.2	34.5	0.0	8.1	0.8	10.7	2.6
Pz	28.3	0.0	20.7	0.0	31.2	−0.3	8.7	0.9	11.1	2.8
P4	27.9	0.1	20.0	0.2	32.7	−0.1	8.4	0.8	12.1	2.8
T6	26.5	0.5	18.0	0.5	29.8	0.0	7.8	1.0	12.0	2.6
O1	26.4	0.0	17.9	0.1	54.3	−0.1	10.3	0.8	14.6	1.7
O2	26.5	0.0	18.6	0.1	41.2	−0.4	9.3	0.5	14.0	1.6
Post	Absolute Power (uV^2)									
Ch	Delta	Z-Delta	Theta	Z-Theta	Alpha	Z-Alpha	Beta	Z-Beta	hiBeta	Z-hiBeta
FP1	28.1	−0.8	14.4	0.1	9.5	−0.3	4.3	0.6	5.9	1.2
FP2	23.2	−1.3	13.2	−0.1	10.3	−0.2	4.5	0.7	6.3	1.2
F7	28.8	0.3	10.7	0.1	7.5	−0.4	3.0	0.0	4.1	0.4
F3	30.8	0.4	23.6	0.7	15.8	0.0	5.8	0.4	7.6	1.4
Fz	33.2	0.4	26.5	0.6	17.7	0.0	7.3	0.8	7.5	1.6
F4	29.0	0.1	23.9	0.7	17.5	0.1	6.3	0.4	7.8	1.2
F8	23.2	−0.2	13.5	0.7	11.6	0.3	4.3	0.7	5.8	1.0
T3	13.6	0.2	10.1	0.5	10.3	0.3	4.1	0.7	5.2	0.8
C3	32.3	1.0	20.9	0.4	24.5	0.3	6.2	0.7	7.7	1.8
Cz	51.8	1.8	34.4	0.9	26.1	0.1	6.9	0.7	8.7	2.1
C4	36.8	1.3	24.8	0.8	24.3	0.2	6.5	0.6	8.4	1.9
T4	18.6	0.9	11.0	0.7	12.7	0.5	4.1	0.5	4.8	0.6
T5	23.0	0.5	15.6	0.4	32.7	0.3	6.5	0.8	8.8	2.1
P3	33.6	0.6	20.1	0.2	43.4	0.3	7.5	0.7	10.5	2.6
Pz	37.3	0.7	22.2	0.2	40.4	0.1	7.5	0.6	10.4	2.7
P4	37.2	0.8	21.8	0.3	45.5	0.2	7.9	0.7	11.3	2.7
T6	31.8	0.9	18.3	0.5	39.2	0.3	7.6	0.9	11.2	2.4
O1	31.8	0.4	18.9	0.2	67.9	0.1	9.0	0.5	13.4	1.5
O2	32.4	0.4	20.4	0.3	64.4	0.0	9.0	0.4	14.5	1.7

Figure 7. *FFT Absolute Power Paired T-Test: Post Minus Pre Brain Maps.*



While Figure 7 simply indicates whether a significant change existed between pre vs. post-qEEG absolute power, Table 3 and Figure 8 below provide directional change indicators. Significant *p*-values presented in red font indicate a significant increase in amplitude/power in the indicated qEEG frequency bandwidths following the intervention. Conversely, significant *p*-values presented in blue font indicate a significant decrease in amplitude/power in the indicated qEEG frequency bandwidths following the intervention. The significant changes in amplitude from the post minus pre differences depicted in Figure 8 below indicate the magnitude of change in microvolts across the five qEEG frequency bandwidths. Based upon the brain maps displayed in Figure 8, the participant demonstrated increased power in frontal-central Delta up to 7.0 uV. Sq., frontal-central Theta up to 5.7 uV. Sq., central-parietal Alpha and occipital Alpha up to 10.8 uV. Sq., and right-central occipital Beta up to 12.0 uV. Sq. Conversely, the participant demonstrated decreased power in frontal High Beta and in left-temporal High Beta up to −2.3 uV.Sq. This indicates that the participant's overall brainwave power mean higher frequency shifted from the Beta/High Beta to higher Alpha mean frequency levels.

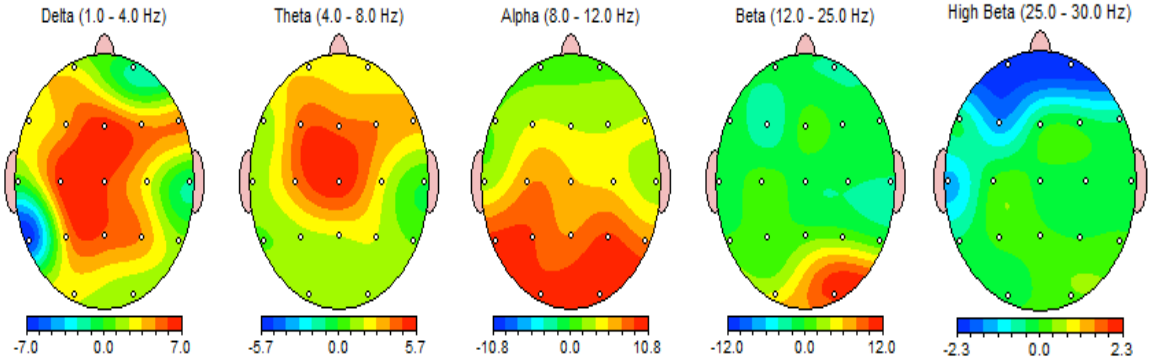
Table 3
FFT Absolute Power Paired T-Test: Post Minus Pre (P-Value)

	Delta	Theta	Alpha	Beta	High Beta
Intrahemispheric: Left					
FP1	0.050	0.002	0.001	0.000	0.000
F3	0.006	0.000	0.000	0.000	0.000
C3	0.001	0.000	0.000	0.221	0.643
P3	0.081	0.122	0.005	0.559	0.187
01	0.128	0.155	0.018	0.055	0.875
F7	0.113	0.010	0.000	0.004	0.000
T3	0.436	0.011	0.001	0.001	0.000
T5	0.869	0.121	0.000	0.928	0.292
Intrahemispheric: Right					
FP2	0.500	0.000	0.001	0.000	0.000
F4	0.009	0.001	0.002	0.224	0.300
C4	0.115	0.036	0.090	0.025	0.345
P4	0.081	0.119	0.041	0.071	0.613
02	0.298	0.178	0.006	0.000	0.208
F8	0.003	0.000	0.000	0.946	0.001
T4	0.643	0.830	0.116	0.000	0.009
T6	0.517	0.784	0.061	0.469	0.355

Table 3
FFT Absolute Power Paired T-Test: Post Minus Pre (P-Value)

	Delta	Theta	Alpha	Beta	High Beta
Intrahemispheric: Center					
Fz	0.005	0.001	0.000	0.259	0.067
Cz	0.116	0.000	0.002	0.073	0.339
Pz	0.036	0.130	0.071	0.178	0.269

Figure 8. *FFT Absolute Power Difference: Post Minus Pre (uV Sq).*



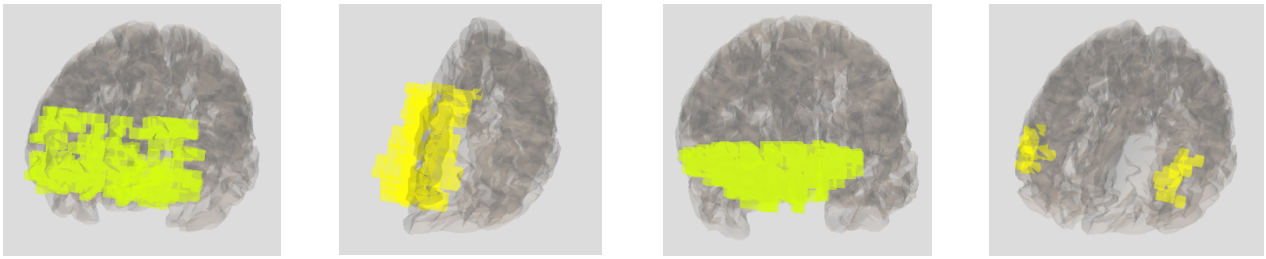
Z-Builder ROI

Finally, the *Z*-Builder tool compares specific Brodmann areas (BA) representing definitive regions of the cerebral cortex associated with specific sensory, motor, and higher cognitive functioning behaviors. The present *Z*-Builder analysis focused solely on the BA ROIs specific to biomarkers related to anxiety. The *Z*-builder analysis compares the individual to their own baseline qEEG. The BA ROI's selected for pre-post comparison were BAs 10, 11, 32, and 46. Because the *Z*-builder analysis program does not provide brain map comparisons of pre-post differences, Table 4 below provides *Z*-score values for ROIs for which a *Z*-score, or standard deviation, of ±0.7 or higher was obtained, as per the recommendations of the *Z*-Builder developer (Collura & Tarrant, 2020). Significant changes were evidenced in the Beta (12–25 Hz) and High Beta (25–30 Hz) wavebands. Many of the BA ROIs listed in Table 4 indicate a significant change postintervention with the greatest magnitude of change occurring in a reduction of High Beta in BA 10 (*SD* = −1.09), BA 11 (*SD* = −1.035), and BA 46 (*SD* = −1.005). Figure 9 provides a visual representation of the BA brain regions positively impacted along with the neuropsychological functions correlated with the specific BA.

Table 4
Z-Builder Specific BA ROI Analysis

ROI Name	Beta.LR	Hibeta.LR
Brodmann 10	−0.763	−1.09
Brodmann 11	−0.829	−1.035
Brodmann 32	−0.456	−0.831
Brodmann 46	−0.862	−1.005
Color Code for *Z*-value		
Z-score is >/= 0.70 − 0.99		
Z-score is >/= 1.00		

Figure 9. *Z-Builder.*



Brodmann 10 | Brodmann 11 | Brodmann 32 | Brodmann 46

Site	BA ROI	Function
Fpz	10, 11, 32	emotional inhibition, oversensitivity, impulsivity, motivation, and attention
Fp1	10, 11, 46	cognitive emotional valancing (lateral orbital frontal), irritability, intrusiveness, depression, social awareness (approach behaviors)
Fp2	10, 11, 46	emotional inhibition (lateral orbital frontal), impulsivity, tactlessness, mania, social awareness (avoidance behaviors)

Discussion

This case study set out to determine the efficacy of TRIPP VR, a VR meditation application, as measured by standardized behavioral rating scales and changes in physiological brainwave patterns. The findings from this investigation highlight several important considerations for the use of virtual and augmented reality technologies in anxiety treatment approaches and general mental health interventions.

As predicted, the case study demonstrated notable and significant decreases in the participant's anxiety levels, as evidenced by both behavioral rating scales and qEEG analysis. The reduction of the participant's anxiety symptoms supports the potential of TRIPP VR as a viable treatment approach for anxiety disorders. The immersive nature of VR meditation interventions may facilitate greater engagement and adherence to treatment, which can be a significant advantage over traditional modalities. In fact, the present case study yielded similar decreases in Beta activity while implementing VR-based training as evidenced in a prior study (Cavallo & Brubaker, 2024), which coined the term "beta shunting." Further research should continue to explore the theoretical implications that VR training minimizes and/or blocks out external distractions at a level that promotes lower beta frequencies, thus allowing the user to engage in a more immersive learning experience.

The fact that the participant remained in the at-risk range for anxiety suggests that while the intervention may be beneficial, TRIPP VR is not yet a standalone intervention and should be integrated with other therapeutic approaches for comprehensive treatment. Nonetheless, these findings, combined with the qEEG data revealing significant decreases in excessive frontal High Beta amplitude, indicate the potential for VR mindfulness training to result in brain state changes. When considering a recent randomized control study completed by Kral et al. (2022), which failed to replicate prior research findings suggesting structural brain changes (as assessed through fMRI) following traditional mindfulness interventions, the present case study findings suggests that mindfulness training delivered in a VR environment can result in a change in EEG brain activity. Furthermore, the paired combination of physiological and behavioral outcome measures employed in the current study provided a robust qualitative analysis, which yielded congruent and symbiotic levels of improvement in the participant's behavioral and physiological manifestations of anxiety. While the results of this case study are promising, they are also limited by the study's design. The single-case approach limits the generalizability of the findings. Additionally, the participant's age and development are not fully representative of the broader population with anxiety disorders. To establish the efficacy of TRIPP VR, larger-scale studies are necessary. Additionally, diversifying the participant sample and including a control condition are recommended to expand findings. Such studies should also explore longitudinal effects and the sustainability of the observed benefits.

The positive outcomes observed in this case study suggest that TRIPP VR, in combination with qEEG analysis, holds potential as an innovative tool for anxiety treatment. For clinicians, incorporating VR-based interventions could enhance the therapeutic treatment approaches and offer patients novel, engaging options. Additionally, the feasibility and convenience of VR technology make it an enticing option, particularly in settings with limited access to traditional therapies. The results also suggest that VR could be an effective and very practical tool for school counselors and psychologists to use in an educational setting to address test anxiety and general school-related anxiety. Exploring the integration of TRIPP VR with other therapeutic modalities, such as cognitive-behavioral therapy, could provide insights into optimal treatment combinations. Investigating the use of EEG analysis tools in conjunction with VR and augmented reality interventions could also further delineate the neurophysiological factors underlying anxiety reduction and expand the development of personalized treatment protocols. For example, in the current case study the participant successfully restored High Beta amplitude brainwave activity to typical levels in the frontal and prefrontal cortices following the VR intervention. However, according to a normative qEEG database, although the participant's High Beta amplitudes decreased slightly in the parietal and temporal lobes following the VR intervention, the amplitude levels continued to fall at or greater than two standard deviations above typical levels. From a clinical perspective, the combination of behavioral and physiological data suggests that the participant gained a better sense of cognitive and/or executive functioning control of their anxiety but might still struggle with autonomic sensory-motor manifestations of anxiety (i.e., twirling hair, picking at nails, verbal rumination, etc.). Therefore, while the VR training resulted in clinically significant improvements, a clinician might also build upon such success by introducing additional training modalities, such as biofeedback and/or neurofeedback, to target improvements in anxiety-related behaviors associated with High Beta amplitudes in the parietal and temporal lobes.

In conclusion, this case study provides preliminary evidence supporting the use of TRIPP VR as an effective tool for reducing anxiety. While further research is necessary, the integration of technological advancements in mental health treatment offers promising avenues for enhancing patient outcomes.

Author Disclosure

The authors declare that they have no conflicts of interest to disclose. Also, there are no financial interests related to this study that could be perceived as influencing the results or interpretation of the manuscript.

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KEYNOTE PRESENTATIONS

Attachment Shock: Brainstem Reactivity in Developmental Trauma Implications for Neurofeedback and Psychotherapy

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Neglect and abuse in childhood impact every major system in the developing brain and these impacts endure all too often across a lifetime. These enduring effects are now most frequently referred to as developmental trauma. Research strongly suggests that emotional neglect is the core issue in developmental trauma. Research from Lyons-Ruth, et al. has found a particular attachment dilemma, established by the age of 18 months, that predicts “borderline personality” and suicidality in late adolescence (I will explain why I use quotes here in the talk). Lanius et al. have provided the most insight to date on the effects of early childhood trauma. They have done extensive research on the differences between the brains of those who have endured early trauma and those who have not. We will look at many of these findings particularly as they implicate the role of the brainstem in developmental trauma.

The focus in psychotherapy and in neurofeedback has been almost exclusively on top-down, cortical control of subcortical drivers. As we will see, in trauma the driver is the brainstem, more specifically attachment shock that is retained in the brainstem. It is the brainstem that elicits the reactivity of the amygdala and that drives thought patterns in the cortex. Neurofeedback protocols are being developed to quiet reactivity in the brainstem; I will share these, but my primary goal is to encourage clinical neurofeedback practitioners and Q-based researchers to take up this pursuit of quieting the brainstem.

In my pursuit, I met Frank Corrigan, MD, the author of a new therapy called Deep Brain Reorienting and perhaps the world’s foremost expert on the brainstem. It is his contention that the shock of attachment rupture, as well as other traumatic shocks, are retained in the brainstem and, as long as they remain unprocessed, the person who has experienced them is at risk. Frank was a research psychiatrist at the NHS for many years, and he worked almost exclusively with severely traumatized patients. When I asked what motivated him to develop DBR, his response was direct and impassioned: “Too many people were dying.” His approach seems to facilitate a conversation between the patient and her brainstem. It is intriguing and the clinical outcomes, which I will show you, are robust. Presently several neurofeedback practitioners and researchers, myself among them, are meeting regularly with Dr. Corrigan and his coinvestigator, Jessica Christie-Sands, PhD, to see how we might enhance the synergy between neurofeedback and DBR for an even more effective treatment for those suffering with developmental trauma. This talk is your invitation into this very important conversation.

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Affectivism, Components of Emotion, and the Emotional Brain

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What is an emotion? What are its functions and brain substrates? How can we study and measure emotions and other affective phenomena? We will discuss the recently proposed notion of affectivism, the approach in which the inclusion of affective processes in models of mind, brain, and behavior not only explains affective phenomena but, critically, further enhances the power to explain cognition and behavior. This broad approach will be the basis of a discussion concerning the emotional brain and models of emotion. We will present a multicomponential definition of emotion: a particular event is first appraised by the individual according to their current concerns, values, and goals (or, more generally, motivational processes). Then, this elicitation process can trigger an emotional response in multiple components: autonomic physiology, action tendency, expression, and feeling. These processes modulate cognitive mechanisms such as attention, memory, learning, and decision-making. Several models of the emotional brain have been proposed and can be related to the major theories of emotion. For instance, affective neuroscience approaches have been used in reference to the basic emotion theory, to constructionist theories, and to appraisal theories. With respect to the emotional brain, most theories of emotion agree that many cerebral regions and networks are important for various emotional processes and that the amygdala is a key region of the emotional brain, but important debates exist with respect to its specific function. A particular focus of the presentation will review results suggesting that the amygdala is neither specific to the emotion of “fear” nor to the affective dimension of “arousal” but is rather a key region that subserves the appraisal of concern-relevance. We will discuss the idea that this amygdala-based mechanism is a key basis of appraisal effects both on the emotional response and on several cognitive mechanisms such as attention, learning, and memory.

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Towards a Road Map for Optimizing Neurofeedback Training Based on Research and Cognitive Neuroscience

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Neurofeedback is a complex learning paradigm that involves a number of neural and psychological learning processes. The dominant view is that neurofeedback learning is based on operant conditioning (Sherlin et al., 2011) and current theoretical work by myself and others has provided deeper analyses and mathematical foundations (Davelaar, 2018; Lubianiker et al., 2022). These advancements help in understanding the dynamics of neurofeedback learning, but they also highlight points of continued confusion shared among academics and clinicians. For example, asking the question of “how many sessions is optimal for learning?” might trigger answers based on clinical experience or estimates based on extrapolations

from research. Both approaches are valid but are conditionalized on the technical settings of the neurofeedback equipment (threshold choice, feedback type) and the individual characteristics of trainees. These considerations matter when planning research (Ros et al., 2020) or managing clients' expectations. Therefore, to provide a general answer to the main question, a number of preliminary questions need to be answered. Here lies the catch. In order to generalize, a large amount of data is needed that contains as many of the relevant parameters as possible, but in clinical practice and academic research, wild variations in parameter settings are rare or even impossible (if not unethical). Through collaborative research involving clinicians and academics (and equipment providers), there are ways to explore the large parameter space.

In this talk, I will argue in favor of closer connections between neurofeedback clinicians and academics, whilst acknowledging their different objectives and time constraints. I will start with an examination into the behaviorist foundations of neurofeedback, discussing the particular version of behaviorism, Thorndikean behaviorism, that is explicitly adopted by clinicians. This contrasts with the actual version, Tolmanian behaviorism, being used, as revealed implicitly by the neurofeedback practice of setting thresholds. I then continue with addressing the question space, which demonstrates an appetite from clinicians and academics to understand more about the mechanisms of neurofeedback learning, its relation with other bodily processes, and how this knowledge can be used in a practical sense. Finally, I will present some progress from our lab that have a direct translation into clinical practice without impeding on existing standards. I will close with some suggestions on how clinical practice could feed into research programs and vice versa, opening up a discussion on a mutually beneficial road map that can educate the next generation of neurofeedback clinicians and researchers.

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PLENARY SESSION PRESENTATIONS

Clinical Implications of the Bayesian Brain, the Autonomic Nervous System, and the Triple Network

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To reduce the inherent uncertainty in a changing environment, the brain evolved as a complex adaptive system. It functions as a predictive machine that aids in finding safety and satiation. When neither can be found, the brain seeks information in the internal and external environment to update its predictions. To optimally adapt to changing environments, the brain predicts what the next situation will be based on its intention and the context. It attempts to verify the accuracy of the prediction by using different senses. If no new information can be gained by the senses, the brain will resort to memory. Failure to update our predictive capacity may result in the overreliance on memory to solve life's challenges. This often results in psychopathology, especially when those memories distort current functioning.

The central autonomic network (CAN) impacts this maladaptive process through control of the sympathetic nervous system (SNS), the parasympathetic nervous system (PNS), and the enteric nervous system. Not simply the autonomic nervous system (ANS), the CAN is conceptualized as a combination of the ANS, endocrine, and immune systems. The SNS promotes a state of elevated activity known as fight or flight. The main goal of the SNS is to prepare the body for physical or goal directed activity. The PNS produces the rest and digest process that involves lowered heart rate and blood pressure. The main purpose of the PNS is to conserve energy and to regulate bodily functions such as digestion and elimination.

The control of the CAN is embedded in the central hubs of the triple network. These three networks include the self-representational default mode network, the behavioral relevance assessing salience network, and the goal-oriented central executive network. As such, neurofeedback training

of these regions has proved useful for depression, anxiety pain, addiction, and a host of other psychopathologies.

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See Your Brain, Train Your Mind, Change Your LIFE!

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While neuroscience and mental health professionals acknowledge the role of emotions in decision-making, application of this knowledge is hampered by the lack of a common language and a model that illustrates the potential neurological pathways. By better understanding the brain's decision-making process and the role of emotions in those decisions, we can begin to expose the moment-by-moment dynamics of human behaviors and the role played by precognitive thoughts. Armed with this knowledge, we may be able to help individuals recognize and reflect on decisions in a more logical manner.

This presentation will offer insights into how humans react to personal triggers in a conversation, thus, exposing underlying precognitive beliefs and related emotions that ultimately lead to our behaviors and decisions. We will highlight the protocols used to generate these modified event-related potentials with a focus on gamma frontal lobe asymmetry as well, exposing the asymmetry of Brodmann's areas 9 and 10 as primary emotional processing areas and Brodmann's areas 44 and 45 as secondary emotional processing resource. Changes in these Brodmann areas, as a participant processes a new stimulus, will be presented using quantitative analysis and will serve as validation of the resulting parallel sLORETA visual maps.

The ultimate takeaway from this presentation is the creation of a model that allows a client to see their thought and feelings (expanded self-awareness) and provide follow up training that leads to self-regulation. The power of seeing one's brain, in real time, cannot be over emphasized. These concrete images have transformative ability. During the presentation, we will show pre–post videos exposing the ability to calm their brain and, as a result, alter their behaviors.

Administering these protocols in real-world contexts, such as during coaching sessions, job interviews, and possibly even in psychotherapeutic milieus (given proper ethical constraints), are promising areas for additional study and promise to impact and potentially expose hidden decision-making mechanisms of the preconscious mind.

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Optimizing Photobiomodulation for Brain Health: Latest Advances in Parameter Settings

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Introduction. Photobiomodulation (PBM) harnesses light energy to achieve therapeutic outcomes, applying transcranial applications for brain health. Despite its potential, the PBM field, including transcranial PBM, relies heavily on outdated research, predominantly derived from cell culture and animal studies, with human clinical trials being relatively rare and heterogenous in methodology and protocols. Moreover, the market has many new PBM devices marketing with poorly supported claims, underscoring the urgent need for updated, evidence-based parameter settings and standardized reporting. This presentation aims to bridge this gap by unveiling novel discoveries that refine these parameters, thereby enhancing clinical outcomes. The knowledge gained from this presentation will benefit neurofeedback practitioners in the use of PBM to complement their practice.

Methods. The research discussed here employs a multifaceted approach mostly used in parts before in the literature, integrating Raman spectroscopy to examine protein and cellular structures, alongside methodologies measuring cellular electrical properties, advanced microscopy, functional magnetic resonance imaging (fMRI), electroencephalography (EEG), magnetic resonance spectroscopy (MRS), and computer modeling. This comprehensive suite enables us to systematically explore the efficacy of various PBM parameters—including laser/LED selection, wavelength, positioning, duration, pulse frequency, phase, coupling, and duty cycle—across proteins, cellular mechanisms, physiological responses, and clinical results. Our findings are extracted from both published literature and ongoing, unpublished studies, providing a robust foundation for our conclusions.

Results. We have identified critical parameters, notably pulse frequency, power density, and light-source positioning, that significantly impact treatment efficacy. For example, pulse frequencies of 10 Hz and 40 Hz exhibit distinct effects on brain function, offering promising avenues for treating conditions such as dementia, traumatic brain injuries, depression, and autism. Similarly, wavelengths of 810 nm and 1060/1070 nm demonstrate unique physiological impacts, and optimal power densities identified at approximately 100 mW/cm^2 for transcranial irradiation and 5–9 mW/cm^2 for intranasal application. Strategic positioning and skin contact during transcranial application further enhance these effects.

Conclusion. PBM stands out for its versatility and potential in brain health interventions. Through our research, we have observed how specific parameter settings can significantly boost PBM's effectiveness. These insights pave the way for more targeted, efficacious treatments, underscoring the importance of continuous research and the integration of new findings into clinical practice for optimal patient outcomes. Practitioners using PBM will benefit from the updated information presented here.

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EEG and the Search for the Buried Message: Application of Homomorphic Deconvolution, ICA, sLORETA, and Machine Learning

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We often think of the EEG as consisting of frequencies, generated by free-running oscillators. However, this belies the truth that the EEG is produced by a multitude of discrete events distributed in time. The classical evoked potential technique is a way of introducing these transients so that they can be measured as single events. The efforts to decompose the resting EEG have met with limited success due to the effects of volume conduction and the presence of many generators at once. The search for a "buried message" has long been deemed without merit, but this is due to the fact that the tools of the time (mathematics and computer processing) were not up to the task of detecting such signals.

This report describes a method that successfully deconvolves resting EEG sources into events and time points, revealing the underlying discrete time structure. By first applying independent components analysis (ICA) to remove the effects of volume conduction, and then using a frequency-domain deconvolution, it is possible to see the morphology of individual brain events and to reconstruct the exact time points at which they occur. The detailed time statistics of each component reveals the pattern of subcortical spiking that elicits each brain event. While the qEEG is like a "blender" that analyzes the entire record without regard to morphology, this method is more like a scalpel and tweezers, that manages to identify and take apart the constituent events.

In reading EEG, clinicians place high importance on the morphology of the waves and the exact timing, including effects that change across time. The qEEG does not reflect these aspects, as it insists on breaking the EEG into "frequency bands" that have predefined ranges, and it further analyzes the entire recording as one huge sample, albeit broken into segments ("epochs"). The method described here is based on first decomposing the signal into its apparent volume-conducted sources and further processing these components using frequency-domain averaging to produce an estimate of each event wave. The process further matches the signatures against the measured component, to determine the most likely times ("instants") for the occurrence of each event. These time-point series provide important statistical information regarding the point process that defines the occurrence of these brain events. If this point process is highly regular, then a prominent frequency band may emerge, as well as harmonics reflecting the energy at all frequencies. If it is less regular, the energy will be more smoothly spread across the range. Some often visible components are eye blinks, eye movement, EKG artifact, blood-volume pulse, and similar physiological yet not-brain sources. Remaining sources reflect the commonly recognizes sources (posterior alpha, midline theta, etc.), and show additional detail, e.g., multiple PDR sources, or complex temporal sources.

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App-Based Combined HRV and Frequency Harmonics Training: Quieting Through Both the Central and Autonomic Nervous System(s). Clinical Trial Results

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This plenary session will show in-depth data from the 2024 clinical trials of an integrated app pairing standard heart rate variability resonant frequency

training with both subthreshold delivery of specific sound/harmonic frequencies and above threshold delivery of "colored" sound (e.g., pink versus white, green, or brown sound). The intervention was specifically engineered to gain coaccess through both the central nervous system (via auditory mechanisms) and the autonomic nervous system (via breathwork) with the aim of quieting regions/wave frequencies of the brain associated with hyperarousal.

Participants included any individual over 16 years old, currently in treatment for active symptoms and/or diagnoses in the general classification of overarousal. This included poor stress tolerance, anxiety, anxious depression, anger outbursts, panic attacks, brain chatter, addiction/cravings, study/test anxiety, OCD, insomnia and their sequalae (e.g., nonrestorative sleep and fatigue), perseveration, argumentativeness, obsession, compulsion, cognitive rigidity (stubbornness), and eating disorders (and other practice of self-harm e.g., cutting), as well as hypervigilance (associated with trauma).

Results show significant alterations in theta, beta, gamma, and alpha bandwidths at both Fz and O1 (as per the 10/20 international system) associated with quieting. Subjective reporting of participants further aligned with statistical findings.

Discussion will also cover unexpected secondary findings which turned out to be main effects. Specifically, markers of mental efficiency also improved fueling hypotheses regarding the power of an intervention that can quiet without sedative effects.

Further discussion will differentiate universal effects versus gender-specific, condition/ailment-specific, environment-specific, and age-relative subeffects. Discussion will further cover therapeutic limitations and cautions as well as advantages including specific discussion of females (as per gender assigned at birth) and (sexual) trauma as well as gender neutral pedophiliac trauma; high stress/conflict exposure atmospheres and professions/professional stress tolerance, immune function, and toxin effects to name a few.

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Habit Formation and Automaticity: Psychoneurobiological Correlates of Gamma Activity

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Mental health management is an emerging public health crisis (Kohn et al., 2004; Singh et al. 2022), and mental health services are insufficient (Patel et al., 2009), necessitating new effective, affordable, and accessible interventions that lead to sustainable change. To further research interventions to address this crisis, the current work examines the science of habit formation and automaticity as a possible way to create sustainable change and the improvement of mental health by building in practices leading to the discontinuation of detrimental behavior and the growth of practices that improve mental health.

The present study used a unique psychoneurobiological approach, specifically looking at how habits and automaticity form using a whole person context in the hopes of contributing to how habit formation can be used in mental health interventions. While a sizeable body of literature on habit formation and automaticity looking at simple behaviors such as overall activity level and diet exists, few studies have investigated the complex behavior formation needed to instill new beneficial mental health habits. Additionally, limited research has looked at the neurophysiological or biological correlates of these mental processes and changes. Madhavan et al. (2015) proposed that, during active learning or recall, individuals exert more cognitive energy compared to information maintenance, resulting in heightened gamma activity. This new data demonstrates that gamma increases as learning is taking place then decreases once the behavior is learned (habituated), providing evidence of habit formation and automaticity and its nonlinear nature.

The current pilot study seeks to contribute to the field's developing knowledge of habit formation and automaticity as something that can be deliberately and mindfully learned, through a planned and guided approach over a specified time frame, to empower individuals to achieve lasting improvements in mental health challenges. Our research contributes practical strategies to improve interventions and achieve sustainable outcomes for the public health

emergency in mental health and build a more gestalt picture of the healing journey (Leaf et al., 2023).

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EEG in Depth: Seeing Psyche in Brainwaves

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This presentation is of my dissertation work and a chapter published in the 2023, *Introduction to QEEG and Neurofeedback*. A theoretical interpretation of an EEG-based psychophysiology. The exploration to unfold in the presentation is the linking of Sigmund Freud's and Carl Jung's respective models of the psyche with electroencephalographic phenomena, neuroanatomy, and neurodevelopmental findings. This union is a marriage between star-crossed lovers: Romeo, being the brain's electrical EEG patterns, from the family of objective, quantifiable and empirical physiology, and Juliet, as psychodynamic psychology, from a family of subjective, qualitative, and humanistic perspective. The progeny of these two camps is psychophysiology, which we will define as the interrelatedness of the third-person body/brain and the first-person mind/soul. These fields of neurology and psychology have historically been kept apart by the authorities of their respective academic and clinical circles. The loyalties of their respective camps have endowed their union with entanglement, rivalry, and disregard.

The thesis we embark on in this presentation is as follows: the EEG spectrum covers the gamut of consciousness, from the recesses of the deep and primal unconscious (delta), through the waters of the personal unconscious (theta), into states of flow, trance, and meditation (alpha/theta and alpha), bridged to the ego states (beta); in pursuit of the self-actualized individual (gamma). The psychodynamic model of the psyche contains these same elements, in the same order: collective unconscious, personal unconscious, the cusp of unconscious and conscious, and ego; all of which, when integrated, lead to the capital "S" Self, the actualized individual. This chapter serves to define how the brain and the mind marry, via a psychodynamic lens.

This talk is meant for an audience of mental health care practitioners who have ties to the field of psychology. It is not meant to be a reduction of the complexity and beauty of the empirical and neurological findings of EEG, but an interpretive lens, backed by tomes of research, into the deeper recessed of the human experience.

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Can Mind-Matter Interactions Be Influenced by Low Power PEMF and Heart Rate Variability?: A Pilot Study

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While psi-related abilities such as mind-matter interactions (psychokinesis; PK) are often considered controversial topics, there is a well-established literature exploring the empirical evidence for these experiences. The most extensive number of experiments on PK have focused on attempts to mentally influence output of electronic, binary-bit random event generators (REGs), referred to as micro-PK.

One of the most extensive and well-known efforts to experimentally study micro-PK using REGs was conducted by the Princeton Engineering Anomalies Research Lab (PEAR; Dobyns, 2015; Jahn & Dunne, 2011). Over the course of a 12-year period, this lab studied 91 volunteer participants, each making multiple attempts, resulting in nearly 2.5 million trials. The results clearly showed that trials involving mental influence deviated from mean chance expectation to a significant degree (Williams, 2021).

Other examinations of micro-PK effects have focused on the potential role of brain activity. For example, two studies have found a correlation between success on REG tasks and frontal lobe damage (Freedman et al., 2003; Freedman et al., 2018), leading the researchers to suggest that the frontal lobes, and in particular the left middle frontal region may act as a filter to inhibit mind-matter interactions (Freedman, 2018). Supporting this notion, a recent article published in Cortex, found a significant micro-PK effect following rTMS inhibition of the left medial middle frontal lobe (Freedman et al., 2024).

The current study sought to examine if the results above could be replicated with a low power PEMF device. Each participant engaged in three sessions/conditions, using counter-balanced methods along with heart rate variability recordings synchronized to the REG output. In each session, three microtesla coils (BrainMaster Technologies) were attached to the scalp in positions targeting either the left frontal lobe (Fp1, F3, and F7), the right frontal lobe (Fp2, F4, and F8), or the entire frontal lobe (F3, FZ, and F4; placebo condition). During the left and right conditions, the participant received 20 min of randomized stimulation between 3 and 5 Hz. During the second half of each session the participant completed a series of three REG runs, each consisting of 200 trials, attempting to increase the output of 1's rather than 0's. Following stimulation, each participant completed an additional two REG runs.

Data collection for this study is currently underway and will include approximately 12 participants. Data will be analyzed to test for condition, order, and time effects as well as any changes in HRV metrics related to REG success. Preliminary analyses suggest that the stimulation conditions result in more significant deviations (higher success) than the placebo condition, although there does not appear to be a significant difference between right or left hemisphere stimulation. The results will be discussed in relation to physiological mechanisms potentially related to mind-matter influence as well as implications for the argument that consciousness can influence structures outside of the physical body.

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Preliminary Evidence for Efficacy of 4-Channel Live *Z*-Score Neurofeedback Training Among Individuals With Posttraumatic Stress Disorder

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Individuals with traumatic experiences may develop symptoms of posttraumatic stress disorder (PTSD) along with comorbid conditions like anxiety and major depressive disorders (Brunello et al., 2001; Kessler et al., 2017). Past studies utilizing amplitude training and alpha-theta training have demonstrated the efficacy of neurofeedback (NF) in alleviating trauma-related symptoms (Peniston & Kulkosky, 1991; van der Kolk et al., 2016). Despite symptom reductions, these studies often lacked an explanation of how targeted electrode sites were functionally related to PTSD symptoms. A potential solution to this issue is live *z*-score NF training (LZT), a state-of-the-art NF method that normalizes brain activity through real-time comparison to an age- and sex-matched normative database (Thatcher, 2013). Therefore, we conducted the first study to assess the acceptability and potential efficacy of LZT for treating PTSD. After a diagnostic interview using the MINI neuropsychiatric interview (Sheehan et al., 1998), 14 PTSD patients (8 females; mean age = 21.06, *SD* = 2.18) underwent 10 quantitative electroencephalogram (qEEG)-guided LZT sessions and three assessment sessions at pre-, mid-, and posttreatment. Each assessment session included self-report measures of trauma-related symptoms, acceptability, and safety concerns, as well as a 10-min eyes-open and eyes-closed resting-state EEG recording. Training sessions, lasting 20 min each, involved participants watching a video of their choice. Repeated measures ANOVAs indicated significant improvements in the symptoms of PTSD, anxiety, insomnia, and emotion dysregulation. Additionally, a significant correlation was found between beta (13–30 Hz) power in the parietal region (P3 and P4) and self-reported PCL-5 scores. Although these results are promising, we found that the treatment effects, including changes in the pattern of the qEEG map, were not uniform across the participants, which needs further investigation. While these results require replication in larger samples with active control groups, the study provides evidence that LZT holds potential as an effective treatment for PTSD.

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The Depression Network: A Neuroimaging Case Study of Acute Stimulation

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Depression is an intense feeling of sadness, irritability, worthlessness, hopelessness, and an overall empty mood. The human brain depression network is a combination of the default mode network, task positive network, cognitive control network, salience network, reward network, and affective network. The common areas amongst these networks are the amygdala, thalamus, hippocampus, cingulate cortex, and prefrontal cortex. In clinical depression there is a general imbalance of the above networks. There is excessive activation of the default mode network, as well as increased activity in the medial prefrontal cortex, amygdala, and hippocampus. The neuroanatomical structure of depression shows structural and functional differences in the brain. The hippocampus and prefrontal cortex often show atrophy in depression. The cortical-thalamo-striatal network and cortical-thalamo-amygdalar network show overconnection. Within these networks there is too little projection from the amygdala to the striatum and too much projection from the amygdala to the nucleus accumbens. This single-case investigation of active stimulation of the depression network first conducted a 19-channel qEEG recording of a standardized eyes-open baseline of this human brain network and then presented to the participant a commonly depressive video recording. EEGs were then carefully artifacted and a dependent-groups *t*-test comparison of the depressive challenge minus the baseline was conducted. A comparison table of network output and three-dimensional, colored, and Brodmann-area labeled differences were then displayed showing the statistically significant brain regions activated by the depressive stimulus. Heightened activity from pre–post scan was noted in the lower right occipital lobe for this visual stimulus and in the upper left and right temporal lobes. There was a significant increase in activity during the intervention in the left temporal lobe, which could be due to depressive ruminations. There was also a decrease in activity from pre–post scan in the middle temporal lobe and the upper occipital lobe. There was also heightened activity in the left amygdala area from the pre- to postintervention scans. As reported in previous research, exaggerated amygdala activation has been noted in depression and sadness. It has also been previously established that the amygdala has a large involvement in emotional states and emotional stress. Discussion is presented highlighting the depression network brain regions activated by this acute stimulation and implications for neurofeedback treatment are offered.

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The Human Pain Network: A Neuroimaging Case Study of Acute Stimulation

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Pain is described as an unpleasant sensory and emotional experience that sends threatening signals to the brain. Pain can be separated into two categories:

- Acute: caused by noxious environmental stimuli which dissipates after a few minutes, lasting < 6 months
- Chronic: pain persisting beyond the healing process, lasting > 6 months

Pain processing and modulation begin at the nociceptors (sensory receptors for painful stimuli) and send signals throughout the peripheral (PNS) and central nervous systems (CNS). Then the brain processes the pain through various neurological areas such as the amygdala, thalamus, hippocampus, and habenula. Painful stimuli produce an increase in activity throughout the human brain

pain network. The Brodmann areas identified as most active during a pain-inducing event are the pain network, comprised of areas 1, 2, 3, 4, 5, 13, 24, 32, 33, including the periaqueductal gray (PAG), the thalamus (Th), the primary somatosensory cortex (S1), the posterior parietal cortex (PPC), the insular cortex, the amygdala (Amyg), the prefrontal cortex (PFC), the anterior cingulate cortex (ACC), and the supplementary motor area (SMA). Modulating these pain sensations are more frontal areas including the ventromedial prefrontal cortex (vmPFC), the orbitofrontal cortex (OFC), the S1, the insula, the nucleus accumbens (NAc), the dorsal prefrontal cortex (dPFC), rostral anterior cingulate cortex (rACC), the thalamus, the amygdala, the periaqueductal grey (PAG), and the rostral ventromedial medulla (RVM). Quite obviously, many brain areas are involved in the sensation, perception, and processing/modulation of pain.

This single-case investigation of acute active stimulation of the human pain network first conducted a 19-channel EEG recording of a standardized eyes-open and eyes-closed baseline and then presented to the participant a commonly used, moderately pain-inducing stimulus, the cold pressor test of the right hand submersed in a bucket of ice water. EEG activity was recorded during this pain challenge in both eyes-opened and eyes-closed conditions. EEGs were then carefully artifacted and a dependent-groups *t*-test comparison of the acute pain challenge minus each respective baseline condition was conducted, exploring primarily connectivity (coherence) measures. A comparison table of network output and three-dimensional, colored, and Brodmann-area labeled differences were then displayed showing the statistically significant brain regions activated by the pain stimulus for each condition.

Results revealed that the eyes-open intervention produced significant hypocoherence connectivity between left Brodmann areas 1 and 4, S1, and primary motor cortex, respectively. The eyes-closed intervention resulted in hypocoherence in Brodmann area 1 only. Higher cortical activity was shown in the eyes-closed intervention when compared with the eyes-open intervention. Both interventions revealed that the prefrontal cortex, amygdala, thalamus, and habenula were highly active during the experience of acute pain.

These results suggest that 19-channel swLORETA deep-brain neurotherapy targeted at reduced prefrontal cortical, amygdala, thalamic, and habenula activity could offer a reduced perception of pain, even for chronic pain conditions. Certainly, more research is indicated on a group basis, but these single-case results are suggestive of potential treatment pathways to be pursued in further group studies.

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The Effectiveness of Neurofeedback for Refugees and Asylum Seekers With Trauma Symptoms: A Pilot Study

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The primary goal of the research is to assess the effectiveness of a neurofeedback protocol for refugees and asylum seekers with trauma symptoms. A growing amount of evidence supports the effectiveness of neurofeedback in reducing mental disorder symptoms (Micoulaud-Franchi et al, 2021; Russo et al., 2022). Neurofeedback is a noninvasive treatment that instructs individuals on

ways to control their brain functions by measuring brainwaves and sending audio or video feedback (Marzbani et al., 2016). Because it does not require talk therapy, neurofeedback holds the potential to serve refugees and asylum-seeking clients despite language barriers. Improving access to evidence-based mental health care treatment is critical, particularly as 31% of refugees experience posttraumatic stress disorder (PTSD), which is significantly higher than the general population (Blackmore et al., 2020). However, the efficiency of neurofeedback in treating PTSD symptoms for refugee clients is under-researched. Askovic and colleagues (2020) published one known study on this topic; however, their study utilized an average of 27 neurofeedback sessions. Not all refugees or asylum seekers have the social capital or resources to afford those treatments or participate for this duration of treatment. Thus, evidence to support the effectiveness of affordable and brief neurofeedback treatment for refugees or asylum seekers with trauma symptoms is necessary for mental health professionals and clients to make an informed decision about the treatments.

This project serves as a pilot project to design an optimal neurofeedback protocol for refugees to alleviate trauma symptoms. We hypothesize that the trauma symptoms of refugees and asylum seekers who receive 10 neurofeedback sessions will be significantly decreased over time. We recruited 10 participants who identify themselves as refugees or asylum seekers and provided 10 neurofeedback sessions to each refugee client, primarily using the 4-channel *Z*-score Dynamix protocol. Measurement tools include the Posttraumatic Stress Disorder Checklist for DSM-5 (PCL-5) before and after their sessions each time. Results will indicate the decrease of the PCL-5 scores over time, suggesting the neurofeedback as an intervention to serve refugees and asylum-seeking clients with traumatic symptoms.

The significance of this study lies in its potential to provide evidence for the effectiveness of neurofeedback as a treatment for trauma symptoms in refugees, a group that often faces barriers to accessing traditional talk therapy due to language and cultural differences. By demonstrating the feasibility of a brief and affordable neurofeedback protocol, this research aims to inform mental health professionals and clients about viable treatment options, ultimately contributing to the advancement of mental health care for refugees. The findings from this study are expected to have implications for clinical practice and literature in neurofeedback.

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Effects of Interactive Brain Neurotherapy Based on fMRI-EEG-Neurofeedback on Structural Connectivity of Motor Cortex Networks in Stroke Patients

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Introduction. Structural connectivity is an indicator of the anatomical connectivity of brain regions and is analyzed by processing diffusion-weighted magnetic resonance imaging (DW-MRI). The method allows the visualization of the conductive pathways of white matter and investigation according to diffusion parameters. Neurofeedback (NFB) based on hemodynamic (fMRI) and EEG signals of the selected area of the of the cortex was used to assess effects of intervention in stroke.

Materials and Methods. Study recruited 14 patients (58 ± 7.5 years) with paresis in the upper extremity with less than 6 months poststroke. The patients underwent neurorehabilitation and were divided into two groups: NFB group (*N* = 7) and control (standard of care only, *N* = 7) groups. Treatment in the NFB group was complemented by six fMRI-EEG-NFB sessions. Before (T1), after the course (T2) of treatment, and 6 months later (T3), test sessions were conducted using DW-MRI. Anisotropy was analyzed in the ipsilesional and contralesional

hemispheres, and corpus callosum. The DW-MR-tractography analysis was carried out in the above areas and all pathways passing through these areas. Among the diffusion parameters there were analyzed fractional, kurtosis fractional and quantitative anisotropies; average diffusion capacity; and axial and radial diffusion coefficients. Depression of any of the anisotropy indices characterizes the processes of demyelination and loss of axons in the pathways; an increase, on the contrary, reflects tracts densification and an increase in the structural connections.

Results. All patients had changes of their structural connectivity in both hemispheres. During the pre–post period (T1-T2) in both groups the fibers of the ipsilateral tracts showed increased axial and decreased diffusion, and tended to loosen connectivity in the contralateral areas as indexed by decrease in kurtosis fractional anisotropy. The groups differed in changes in the corpus callosum connections. For the fMRI-EEG-NFB group, the fibers loosened in the projection of the premotor cortex showed increase in the radial diffusion and had consolidation in the projection of the primary motor cortex featured by decrease in the axial diffusion; whereas in the control group, there were noted the opposite effects. Six months later (T2-T3), both groups showed densification of fibers in a form of increased axial, radial, and middle diffusion coefficients, while the processes of demyelination and axon loss were still observed along the corticospinal tract in a form of decreased kurtosis anisotropy. There was a lower dynamic of axon loss ipsilaterally in the NFB group as compared to the control group. In the corpus callosum projection of the premotor cortex, the fibers showed increased fractional and quantitative anisotropies, and the same tendency was found in the projection of the primary motor cortex characterized by increased fractional anisotropy.

Conclusions. Structural changes in stroke are occurring in both hemispheres, stimulating the long-term reorganization of the pathways. Complementing neurorehabilitation with neurotherapy based on fMRI-EEG-NFB as compared to standard of care neurorehabilitation resulted in a more pronounced decrease in the dynamics of axon loss along with their densification on the lesion side and an increase in interhemispheric structural connections. Acknowledgement: Supported by RFBR grant 20-015-00385.

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Single-Case Research Design: Exploring PTSD Protocols for Neurofeedback at a University Clinic

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Neurofeedback has emerged as a promising treatment for PTSD, with its roots tracing back to Peniston and Kulkosky's pioneering study in 1991 on alpha–theta neurofeedback for Vietnam veterans. Building on this foundation, Gapen et al. conducted a pilot study in 2016, revealing encouraging outcomes for chronic PTSD patients. Subsequent research by van der Kolk et al. in the same year further validated these findings through a randomized, waitlist-controlled study, demonstrating statistically significant results. These developments signal a potential shift in both the treatment and conceptualization of mental health disorders and PTSD.

Considering the complexity of PTSD and individual experiences, we aim to explore individual participant changes within their neurofeedback session data. While traditionally employed in educational research,

the methodology of single-case research designs (SCRDs) has garnered increasing interest across various disciplines in the past decade (Ganz & Ayres, 2018). Researchers turn to SCRDs when faced with numerous intervention data points and a desire to assess individual changes. Key characteristics of SCRDs include repeated measurement of the dependent variable over time, allowing for a nuanced understanding of the impact of interventions on individuals, organizations, businesses, or other groups (Kazdin, 2021). Our research questions are:

(a) Is there a change over time in participants' mean magnitude (i.e., band 1, band 2, and band 3 in BioExplorer) of their neurofeedback session-to-session data, based on their corresponding brain wave frequencies?, and
(b) How does participants' 1st neurofeedback intervention period (Phase B) compare to their 2nd neurofeedback intervention period (Phase C)?

Phase B is participants' first university semester of neurofeedback sessions and Phase C is their second intervention period. Our data will consist of retrospective neurofeedback data collected at a university clinic by student clinicians. We will be utilizing five to six participants receiving neurofeedback for PTSD and their corresponding session data. Our analysis will consist of nonoverlap of all pairs (NAP) which is not reliant on trend lines or means (Parker & Vannest, 2009) and simulation modeling analysis (SMA), a software program that considers autocorrelation, testing slope, and line trends of the neurofeedback session data and runs 5,000 simulation tests that determine the best fit model (i.e., trend line).

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Analysis of Runner's High Through Quantitative Electroencephalography and Computer-Brain Interface

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Runners' high is a short feeling of euphoria or bliss that occurs after running or physical exercise. These effects are typically felt after at least 45 min of running; however, it is not clear if its effect is enhanced with more strenuous running or longer times. In this study, the effects of runners' high will be examined and analyzed through quantitative electroencephalography, which entails both EEG recordings and further analysis by brain-mapping software. This study is currently ongoing, and will take approximately 6 weeks, divided into nine total sessions. Participants will first be recorded by a 19-channel EEG for an eyes-open and eyes-closed baseline. During the following interventions, participants will run various, set times then be recorded by EEG for 20 min directly after their runs. Before the interventions begin, participants will be given a questionnaire to assess their running capabilities, which will be used to create a running pace that they will follow during the runs. Participants will all run at a pace that allows them to exert effort in each run, but not too much to cause excess fatigue. The route that participants will run is going to be held constant, with the only thing changing being the time that they will run for. The participants will engage in the following runs as an intervention, where they will do one of these runs per week: a 15-min run, a 45-min run, two 55-min runs, a 75-min run, a 90-min run, then a final 60-min run. As said before, runner's high only takes effect after 45 min, however the 15-min run is in place to serve as a sort of extra baseline test. The runs following the 45-min runs will be used to measure any increasing effects of runner's high based on increased effort, and the final 60-min run is in place to examine if the effects of runners high dissipate as the runner becomes more adapted to longer runs. The EEG data will then be transformed into a three-dimensional view of the brain through low resolution electromagnetic tomography (LORETA), then a post minus preintervention *t*-test will be performed to analyze the results. The results will be analyzed based on the comparison of current source

density (CSD). CSD is a method to estimate the location, intensity, and direction of brain activity and their connections, and any hypercoherence or hypocoherence will be analyzed. As runner's high is involved with feelings of sedation and anxiolysis, it is expected that the results will yield hypocoherence, specifically in areas such as the prefrontal cortex, the amygdala, thalamus, hippocampus, supplementary motor area, premotor area, primary motor cortex, the cerebellum, the ventral tegmental area, and the striatum.

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ISF Neurofeedback as an Adjuvant Treatment for Adults With Generalized Anxiety Disorders: A Randomized Controlled Pilot Study

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Anxiety disorders are among the most prevalent neuropsychiatric disorders in the world. Within that category, generalized anxiety disorder (GAD) is one of the most common disorders having a more significant functional impact (Giacobe & Flint, 2018). GAD is a disorder characterized by its chronicity, exacerbated anxiety, and a difficulty to regulating it underlying a feeling of uneasiness which impairs the health and quality of life of those suffering this condition (APA, 2013). A better understanding of the neurophysiological processes associated with anxiety has raised an increased interest for interventions that influence the brain's electrical regulation. Neurofeedback (NFB), a therapeutic intervention that involves a brain computer interface allowing to monitor and modulate real-time electroencephalographic (EEG) parameters is a method that has shown promising evidence in the treatment of diverse mood disorders (Abdian et al., 2021; Batail et al., 2019; Chen & Lin, 2020; Ribas et al., 2018). Recently, NFB prospective studies have also explored the regulation of the infra-slow brain's electrical signals (below 0.1 Hz). Previous studies have shown a regulation of autonomic nervous system (ANS) physiological measures suggesting that ISF NFB may influence brain networks involved with the ANS balance (Bekker et al., 2021; Leong et al., 2018; Perez et al., 2022). However, research on infra-slow fluctuations (ISF) NFB is still limited, and additional evidence is needed. The goal of the present study was to assess the adjuvant benefit of ISF NFB compared to group-based mindfulness for GAD in adults. The study was carried out with 22 participants and the groups were randomly assigned. Therefore, the experimental group received ISF NFB plus mindfulness-based stress reduction (MBSR), whereas the control group received MBRS alone. GAD-7, a validated scale to assess the severity of GAD symptoms and qEEG, the quantitative and normative analysis of the EEG were administered before and after the treatment. Our results indicate that neurofeedback with MBRS has a statistically significant greater effect on the reduction of GAD symptomatology in adults compared with MBRS alone. Psychophysiological findings are still being analyzed.

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Can Machine Intelligence Automation Assist in the Inspection of Clinical EEGs?

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We are teaching the computer how to “look at” an EEG and compare it with a large sample of others, to see how it compares. It is not “normative” in that it is compared with clinical samples, not “normals.” The purpose of our system is to prescreen EEGs that have not yet been inspected or artifacted, to determine how well they fit into a “typical” type of recording. This report can provide a heads-up of what to look for when proceeding to look at the EEG for purposes of clinical referral or to prepare the recording for qEEG analysis. This is therefore, a “pre-Q” or even a “pre-pre-Q.”

It gives you a heads-up of what the EEG is like, if you had looked at hundreds of them and knew what to look for, including having seen plenty of abnormal EEGs. You would do this before a qEEG analysis, to have an idea of what you might see. And, yes, it uses independent components analysis (ICA) to remove eye artifact, and it uses methods that are human-instructed (by our team) machine learning, not entirely artificial intelligence, to know what to do. This is not AI.

AI consists of methods where a computer attempts to learn to classify and respond to different information, by being presented with a vast amount of material, which it sorts through, and creates rules and so on. It may be guided or unguided, and can achieve remarkable capabilities (see, for example, the Score system1 which accurately detects and described important EEG features from preinspected EEG recordings). This is not qEEG.

QEEG consists of processing EEG recordings to produce metrics useful in the interpretation of the frequencies and connectivity revealed in the EEG. QEEG requires that recordings be carefully inspected and artifacted, and that the age be noted when submitting the data to analysis. This is machine intelligence.

We equip the computer with a program that is designed to use digital signal processing in order to simulate what a doctor does when they do a visual inspection of an EEG. We pick the rules and do not allow the machine to make decisions about which metrics or derived computations are used. We define a set of reasonably informed metrics motivated by the concepts of the posterior dominant rhythms, amplitude foci and magnitudes, time course of various metrics, and so on. We then present the program with a number of EEGs (currently in the hundreds) and allow it to compute the population statistics of the input samples. In this regard it is similar to qEEG.

We do not select EEGs other than the fact that they were submitted and reported on by a board-certified clinical neurophysiologist/qEEG diplomate, in consultation with one or two board-certified qEEG diplomates. The purpose of the doctor’s report is to comment on the quality of the EEG submitted and make any relevant clinical observations regarding severe abnormalities or EEG quality problems.

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Resting-State Electroencephalography Complexity is Associated With Oral Ketamine Treatment Response: A Bayesian Analysis of Lempel-Ziv Complexity and Multiscale Entropy

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Subanesthetic doses of ketamine are a promising novel treatment for reducing symptoms of suicidality (Can et al., 2021; Ionescu et al., 2019; McIntyre et al., 2020); however, the evidence for prognostic biomarkers is sparse. Recently, measures of complexity, including Lempel-Ziv Complexity (LZC) and multiscale entropy (MSE), have been implicated in ketamine's therapeutic action (Murphy et al., 2023; Schartner et al., 2017). Moreover, these nonlinear indices of brain dynamics are associated with treatment response to both antidepressants and transcranial magnetic stimulation (Jaworska et al. 2017; Lebiecka et al., 2018; Méndez et al., 2012). We evaluated electroencephalogram (EEG)-derived LZC and MSE differences between responders and nonresponders to oral ketamine treatment (Can et al., 2021), hypothesizing that treatment responders would have higher neural complexity at baseline compared to nonresponders and that this would be attenuated posttreatment. Additionally, we predicted elevated complexity in the eyes open compared to the eyes-open condition, as observed in previous studies (Lord & Allen, 2023; Yang et al., 2023). Thirty-one participants (mean age = 45.64, *SD* = 13.95; 54% female) received six single, weekly (titrated) doses of oral racemic ketamine (0.5–3 mg/kg) and underwent EEG scans at baseline (week 0), posttreatment (week 6), and follow up (week 10). Resting-state (eyes closed and open) recordings were processed in EEGLAB, and complexity metrics were extracted using the Neurokit2 package. Participants were designated responders or nonresponders by clinical response (Beck suicide scale [BSS] score reduction of ≥ 50% from baseline to the respective timepoint or score ≤ 6) and then compared in terms of complexity across task types and time. Employing a Bayesian mixed effects model with timepoint, task, and response status as fixed effects and by-participant random effects (random intercepts and slopes). As hypothesized, there was evidence for a main effect of task for LZC, with higher eyes-open compared to eyes-closed values across timepoints and response status. Similarly, higher MSE values were observed in the eyes-open condition for scales 1–4, with the opposite observed from scales 6–10. Averaged over channels (global level), responders displayed elevated eyes-open baseline complexity (LZC and MSE scales 1–4) compared to nonresponders, with these values decreased at posttreatment (6 weeks) and follow-up (10 weeks) in responders only. Exploratory Bayesian analyses revealed the elevated baseline eyes-open LZC in oral ketamine responders was not reflective of a global increase in entropy, rather it was spatially localized to the left frontal lobe (electrodes F1, AF3, FC1, and F3). This is the first evidence showing EEG-complexity metrics may be sensitive biomarkers for evaluating and predicting oral-ketamine treatment response and highlights the left prefrontal cortex as a key region implicated in response among individuals living with chronic suicidality and depression.

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Cognitive and Behavioral Traits Enhancement in AD Patients: A Substantial Impact of Binaural Beats Stimulation on Theta and Alpha Bands

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Alzheimer's disease (AD), a common neurological ailment, is characterized by a gradual decline of mental acuity resulting in dementia and adverse impact on an individual's behavioral performance, making AD patients incapable of performing normal daily tasks and activities independently. Currently, AD has afflicted about 50 million individuals worldwide. This research explored binaural beat stimulation's (BBS) potential for facilitating and enhancing AD patients' behavioral and neurological aspects, which were validated through analysis of brain's functional connections. There were 25 AD patients, who volunteered to participate in this study and receive 12 days of stimulation. These patients were divided into those who received BBS and others who received standard auditory stimulation (SAS). This study involved the employment of blessed dementia scale, Mini-Mental State Examination, and depression anxiety stress scale for a comprehensive behavioral analysis. The neural data was acquired through EEG. The neurological analysis was conducted by means of determining imaginary coherence, functional connectivity, and graph theory. The paired *t*-tests ($p < .05$) compared both groups' pre- and posttreatment outcomes. Findings of this study revealed that significantly improved ($p < .05$) results in the BBS group were observed for all behavioral scales. Coincidentally, functional connectivity results exhibited striking changes in AD post-ICH in the theta, alpha, and gamma bands. Specifically, in the theta band there was considerable increase in strong inter- and intraregional connectivity with occipital, parietal, and temporal brain regions being dominant, indicating a strong positive effect of BB on AD patients' working memory. Concurrently, the neurological analysis through graph theory also indicated a significant increase in cluster coefficient along with local efficiency in the theta and alpha band. These above-mentioned results of BBS group signify the efficacy of BB stimulation as a nonpharmacological intervention for the neurocognitive enhancement of individuals afflicted with AD, contributing to improvement in such patients' overall health.

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Addiction and Identity: Personality Insights and Experience Cultivate Difficult Perceptual Mechanisms in Populations of Inmates With Substance Abuse Problems

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Introduction. Understanding the intricate relationship between self-perception and experience, as underscored by Freud's psychoanalytic theory and Skinner's behaviorism, is crucial in exploring how adverse childhood experiences profoundly influence the development of substance use disorders (SUD) and associated psychopathology as well as their patterns in the

human brain (Barch et al., 2018; Cannon et al., 2008; Hawes & Allen, 2023; Lensch et al., 2021; Paulino et al., 2024).

Methods. This observational data consists of 111 individuals (40 female) with mean age 37.26, *SD* = 9.47. Participants completed initial screening and informed consent prior to neurofeedback training. Participants completed the self-perception and experiential schemata assessment (SPESA) and the personality assessment inventory (PAI; Morey, Lutz, FL) prior to LORETA neurofeedback procedures.

Results. Significant inverse correlations were found on most scales of the PAI with the total score on the SPESA. The results suggest an important relationship between negative experiences and experiences of psychopathology. Certain patterns of experience are present in this population with 64.5% reporting at least one prior treatment for SUD; 39.6% report a prior psychiatric diagnosis in childhood; 58.6% report violence was common in the home; 77.5% report alcohol and drugs were used in the home and 59.5% report abuse in the developmental periods. Linear regression results show the SPESA total score shows a predictive relationship: R^2 = .64, adjusted R^2 = .50, $F(31, 79)$ = 4.57, p = .000. The scales on the PAI identifying affective components of anxiety, traumatic stress, phobias, negative relationships, and antisocial behavior patterns were significant.

Discussion. The basic neural mechanisms of patterning behaviors and perceptions of past experiences and their influences on social, executive, and emotional processes are paramount when working with clients in any population. Additionally, the neural mechanisms of self-regulation are poorly understood; however, neurofeedback and neuromodulation data contribute to our understanding of these mechanisms and the potential to influence learning using neurofeedback or neuromodulation procedures (Downar et al., 2024; Fielenbach et al., 2017; Gabrielsen et al., 2022; Holland & Holbert, 2022). The data obtained in this study demonstrate significant correlations between the self, its experiences, and perceptions with psychological experiences in a heterogeneous population of inmates with substance use disorders. The importance of influencing currents and activity within the brain may represent the best potential toward integrative functioning relative to operant efficiency and improved self-regulatory mechanisms.

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ERP Neuromarkers of PTSD Associated With Hawaii Red Hill Toxic Jet Fuel Exposure

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The jet fuel leak from the Hawaii Red Hill Underground Fuel Storage Facility began in November 2021 and created an ongoing public health crisis impacting hundreds of thousands of O'ahu residents. The health effects of jet fuel exposure have been shown to impact many aspects of human physiology including immune, gastrointestinal, cardiovascular, integumentary, and nervous systems. Scalp resting-state electroencephalogram (rsEEG) and event-related

potentials (ERPs) have been shown to be useful in the assessment of brain functioning in the context of toxic encephalopathy, epilepsy, anxiety, depression, OCD, ADD/ADHD, and posttraumatic stress disorder (PTSD). In this case series, rsEEG and ERP data of 31 subjects with self-reported cognitive and/or neurological changes following HRH were analyzed. Subjects completed at least 10 min of eyes open, 10 min of eyes closed, and 22 min of task EEG recording using a standardized cued Go-NoGo visual continuous performance task (VCPT) from the HBImed methodology for calculation of ERPs. Slowed alpha, unstable vigilance, focal and generalized slowing, and excessive beta activity were noted in the rsEEG across various symptom presentations. ERP group analysis of a subset of subjects (N = 18) constrained by age (18–50 years) showed two statistically significant (p < .01) differences when compared to a database of healthy controls (N = 200). The action suppression ERP component is generated in the supplementary motor cortex to inhibit a prepared action and was reduced in amplitude in the study group. The visual P1/N1/P2 ERP component complex is generated in the primary and secondary visual areas and reflects the process of visual object categorization and is modulated by the activation of the amygdala via the thalamus. This component was reduced in latency and increased in amplitude in the study group. Group comparisons were conducted by joint diagonalization of covariance matrices. These findings are consistent with the diagnosis of PTSD. Limitations of this study including subject sample bias are discussed. Possible reasons for PTSD diagnosis are discussed, including lack of medical care access, institutional disregard, displacement, loss of life, denial of care, and fear of retaliation.

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QEEG-Guided sLORETA Neurofeedback Effects on Event-Related Potentials and Cognitive Performance in a 7-Year-Old Moderate Concussion Patient: A Case Study

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A concussion can induce brain electrical activity alterations, detectable as anomalies on an electroencephalogram (EEG). These alterations typically signify disruptions in the brain's normal communication pathways, impacting various cognitive functions. Consequently, individuals may experience impairments in attention, memory, and executive functions. Additionally, behavioral manifestations of concussions often include increased irritability, fatigue, and difficulties in academic or social interactions.

The use of standardized low-resolution electromagnetic tomography analysis z-score neurofeedback (sLZNFB) represents a promising approach for targeting network disruptions in deep cortical regions. This study aimed to investigate the effects of sLZNFB on brain electrophysiology and cognitive performance in a 7-year-old girl who suffered from a moderate Grade II concussion while riding her bicycle without a helmet at the age of 6. The patient exhibited deficits in attention, processing speed, and memory.

The study used a pre-experimental design with pre–post comparison. To this end, LZNFB was applied to affected brain areas for 20 sessions. Baseline and posttreatment measurements were made on qEEG metrics, whole-brain event-related potentials (oddball and visual paradigms), attention, memory, executive function, reaction time, and cognitive flexibility. Clinical improvements were found in variables related to processing speed after 16 sessions of sLZNFB on computerized tasks. Significant changes in the eyes-closed resting-state z-score maps were found in lateral/central Delta frequency and connectivity variables in all frequencies in the eye-closed condition. An

increased inhibition of the Alpha Mu rhythm in the eyes-open condition was also observed. Event-related potentials on oddball auditory and visual tasks showed greater organization, significant changes in early components (N1 and N2), and less P300 latency. In addition, parents reported significant improvements in mood and reading throughout the sessions.

These findings suggest the potential effectiveness of LZNFB on cognitive performance improvement among pediatric concussion patients. Further studies with a larger number of patients and control groups may be required to evaluate the full potential of this type of training in concussion patients.

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