# NeuroRegulation

The Official Journal of ISNR
INTERNATIONAL SOCIETY FOR NEUROREGULATION & RESEARCH

Volume 10, Number 2, 2023

# NeuroRegulation


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*NeuroRegulation* (ISSN: 2373-0587) is published quarterly by the International Society for Neuroregulation and Research (ISNR), 13876 SW 56th Street, PMB 311, Miami, FL 33175-6021, USA.



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

NeuroRegulation

ISNR INTERNATIONAL SOCIETY FOR NEUROREGULATION & RESEARCH

Volume 10, Number 2

2023

Contents

**RESEARCH PAPERS**



**PERSPECTIVES**

NeuroRegulation

ISNR INTERNATIONAL SOCIETY FOR NEUROREGULATION & RESEARCH

# Effects of Combined SMR Neurofeedback and Music Listening on Executive Function and Emotional Regulation in Hispanic/Latino Polydrug Users

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**Abstract**

**Background.** Substance use disorders (SUD) are a significant health problem affecting executive function. Neurofeedback training (NFB) allows subjects to voluntarily modulate brain activity, aiming to modify cognitive processes. Studies measuring neuropsychological processes and music have found significant changes in attention, memory, and speech, supporting the notion that music enhances brain functioning. In this study, we measured cognitive processes (decision-making and attention) and emotional regulation aspects in a sample of Puerto Ricans with SUD, before and after participating in NFB-assisted training sessions with or without music. **Method.** Forty-six residency program patients were assigned to NFB, NFB+Music, or a control group. NFB protocol included reinforcement training of low beta sensorimotor rhythm (SMR) and theta and high beta inhibition at Cz. **Results.** Data suggest favorable changes in decision-making, attention, inhibitory control, and emotional regulation in the NFB groups. No differences were found in behavioral, self-reported, and EEG data between NFB and NFB+Music. Statistically significant changes on SMR amplitude were observed in both experimental groups. Self-reports underpin participants' relaxation states during NFB sessions. **Discussion.** NFB training with and without music effectively optimizes executive function; however, NFB+Music seems to have a precise effect on emotion regulation, particularly in emotion expression.

***Keywords***: substance use disorder; EEG-neurofeedback; sensorimotor rhythm; SMR; music

**Citation**: Castillo-Reyes, I. J., & Cruz-Bermúdez N. D. (2023). Effects of combined SMR neurofeedback and music listening on executive function and emotional regulation in Hispanic/Latino polydrug users. *NeuroRegulation, 10*(2), 62–77. https://doi.org/10.15540/nr.10.2.62

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## Introduction

According to the U.S. Substance Abuse and Mental Health Services Administration, substance use disorders (SUD) are one of the most significant health and social problems, affecting 20.4 million people (SAMSHA, 2019). Particularly in Puerto Rico, one-fifth of the population is between 15 and 74 years old, with 9.2% suffering from an SUD (Administración de Servicios de Salud Mental y Contra la Adicción, 2009). It is known that impaired cognitive executive functions such as decision-making, working memory, attention, and inhibitory mechanisms are primary traits of SUD (Kozak et al., 2019; Noël et al., 2013). Neuroimaging studies have highlighted the dysfunctions of brain regions underlying these cognitive mechanisms in SUD (Li, Lu, et al., 2010; Noël et al., 2013). Dysregulation in motivational and affective circuits involving prefrontal cortices, amygdala, somatosensory cortex, and anterior cingulate cortex leads to impulsive behavior, poor evaluation of long-term consequences, and therefore to the occurrences of inadaptive behaviors (Bechara, 2005; Goldstein & Volkow, 2011; Koob & Volkow, 2016). These brain areas are associated not only with top-down processing (cognitive and behavioral monitoring) but with bottom-up (interoceptive) processing as well (Verdejo-Garcia et al., 2012).

Current SUD research suggests that approaches involving cognitive function strengthening might be appropriate for individuals or patients with high impulsivity levels, deficient decision-making skills, and poor executive functioning (Verdejo-Garcia, Garcia-Fernandez, et al., 2019). Moreover, the National Institute on Drug Abuse (NIDA) has supported the use of complementary strategies such as neurofeedback (NFB) to strengthen brain regions involved in executive function and inhibitory control in patients with addictive disorders (National Institute on Drug Abuse, 2010; Noël et al., 2013).

NFB training is a neuromodulation model in which individuals have access (through a brain–computer interface) to information about their neurological phenomena and are encouraged to self-regulate it through a basic principle of operant conditioning as well as through an experiential mental, perceptual, or conscious activity. In an electroencephalogram (EEG) NF setup, the individual receives real-time visual and/or audio information about their brain activity after achieving a certain state of neurological regulation. It can be used to uptrain or downtrain a rhythm or amplitude of a specific frequency or to normalize electrophysiological brain activity giving feedback according to how deviated the brain activity is from a normative database. During NFB training, not only are neuronal circuit ensembles modified but also the conscious psychophysiological activity involved with them.

## SMR Training on SUD Population

Sensorimotor rhythm (SMR) NFB training (12–15 Hz, or low beta) has shown effectiveness in counteracting cognitive and behavioral impairment associated with SUD (Sokhadze et al., 2014). SMR training was one of the first protocols used in the NFB field and tested within the animal model. Sterman et al. (1970) demonstrated that increasing the amplitudes at this frequency range made cats more resistant to the effects of a convulsive substance. Sterman (2010) also applied this protocol on human models showing significant reduction of seizures after SMR conditioning. Later on, Lubar and Lubar (1984) applied this protocol (SMR uptraining including theta down training) to children with attention-deficit disorders with hyperactivity, showing remarkable results on motor control and school performance. It is believed that SMR training produces greater integration of information in the cortex as it targets inhibitory mechanisms of thalami-cortical circuitry (Kaiser, 2008). This circuit regulates bottom-up mechanisms that reduce the interference of somatosensory information, enabling the cortex to process the information more effectively while relaxing the motor interferences (Gruzelier & Egner, 2005; Kober et al., 2015).

In the 2000s, SMR training protocol was added to the popularized Peniston and Kulkosky alpha-theta training protocol in a sample with mixed SUD by Scott et al. (2005). The authors believed that stabilizing attentional variables through SMR training would produce better outcomes after the alpha-theta training. As is known, ADHD and SUD are common comorbidities (Zulauf et al., 2014). Scott et al. (2005) reported decreasing depressive personality symptoms and anxiety, improvement of attentional variables, refining treatment adherence, and abstinence. Since that study, SMR NF training has been successfully employed on alcohol (Lackner et al., 2016), cocaine (Burkett et al., 2005; Horrell et al., 2010), crystal meth (Rostami & Dehghani-Arani, 2015), opioids (Cannon et al., 2008; Dehghani-Arani et al., 2010, 2013), mixed abusers (Keith et al., 2015), and general SUD with comorbid diagnosis (Fielenbach et al., 2018). These studies have generally reported beneficial changes of SMR NFB as a stand-alone or add-on intervention on cognitive executive functioning (i.e., attention), psychological symptomatology, addiction severity, quality of life, compulsive behavior, drug craving, and relief from withdrawal.

## Music Listening on Cognition and Behavior

Appreciation of music, particularly classical music, has been reported to produce an optimization of cognitive performance (Thompson et al., 2005). There are two types of interventions in the field of music therapy: receptive music therapy (RMT) and active music therapy (AMT; Li, Wang, et al., 2015). The RMT involves the listening of music provided by the therapist as a sung song or a musical production. The AMT consists of active participation in the musical creation, whether singing, playing an instrument, or improvising musically with body movements. Playing musical instruments requires the interaction of superior cognitive functions, and continuous practice produces complex changes in motor, auditory, and multimodal skills associated to functional and structural neuroplasticity (Schlaug et al., 2005).

Music stimulates multiple brain regions, particularly the brain stem, inferior colliculus, middle geniculate body, and the primary and secondary auditory cortices (Ragot et al., 2002). Neuroimaging studies show that music modulates metabolic brain activity in the amygdala, nucleus accumbens, hypothalamus, hippocampus, insula, cingulate cortex, and orbitofrontal cortex, all associated with

the regulation of emotions (Koelsch, 2014). Music listening as therapy, being a form of nonpharmacological intervention like NFB, positively modifies impulsivity, autonomic responses, memory, mood, and emotional regulation (Panksepp et al., 2012; Rickard et al., 2005). Therefore, the potential of music to produce changes in brain activity has implications for the development of neurological and psychiatric disorders interventions.

Music appreciation produces changes in basic socio-emotional feelings (socially constructed emotions) such as nostalgia, sadness, and tenderness. A series of theoretical studies have explored how music listening facilitates cognitive and affective self-regulation. For example, listening to music can be used to change, maintain, or reinforce affection, mood, and emotion (Chen et al., 2007) to unleash nostalgia and promote emotional regulation (Lonsdale & North, 2011; Van Goethem & Sloboda, 2011), to stimulate cognitive effects (Sloboda et al., 2016), as a meaningful tool for a social group (Maher et al., 2013), or as a tool promoting cognitive reassessment (Saarikallio & Erkkilä, 2007).

Few experimental studies have systematically measured the effect of listening to music on neuropsychological processes, particularly exploring its therapeutic effects in SUD populations. Researchers have found significant effects in executive-type cognitive processes such as sustained and focused attention, working memory, fluency of categorization and fluency of speech (Irish et al., 2006; Maclean et al., 2014; Mammarella et al., 2013; Särkämö et al., 2008; Thompson et al., 2005). Two studies revealed statistically significant results in variables related to mood (Baker et al., 2007; Särkämö et al., 2008). In four of these studies, investigators selected music from the Baroque period, particularly music by Vivaldi (Irish et al., 2006; Lake & Goldstein, 2011; Mammarella et al., 2013; Thompson et al., 2005) and the Jimmy Shand's Blue Polka piece (Maclean et al., 2014). In another study, authors used popular music (e.g., Foo Fighters, John Lennon, Elvis Presley) and found that music therapy sessions facilitate the experiencing of a moderate to high degree of positive emotions (Baker et al., 2007). The evidence supports the notion that incorporating passive listening of classical music to NFB training might enhance brain functional and cognition.

The primary objective of this study was to explore the effects of SMR NFB on executive functions such as sustained attention and decision-making on an SUD sample. The secondary objective was to test an SMR NFB protocol that included Baroque music listening during the NFB training on a SUD sample. Other outcome variables included were self-reported emotional and attentional regulation.

## Methods

This study was authorized by the University of Puerto Rico-Río Piedras' Institutional Review Board (protocol #145-038) and was conducted in accordance with the Declaration of Helsinki. The study complied with ethical standards for the protection of human participants in research, including an informed consent process.

### Study Design

The study design was based on a not blinded, randomized controlled trial with pre and post measurements.

### Participants

We recruited 59 adults by availability. Participants were receiving treatment for SUD in residential programs operated by nonprofit organizations in the metropolitan area of San Juan, Puerto Rico. These programs are supervised by the Mental Health and Addiction Services Administration (ASSMCA, in Spanish) of Puerto Rico's Health Department and provide rehabilitation services from a biopsychosocial perspective to adult men and women, including individual and group therapy based on a cognitive behavioral therapy (CBT) integrative model, occupational therapy, and spirituality (optional). The final sample was composed of 16 men and 27 women ($n$ = 46) between the ages of 21 and 50 years, most of them polydrug users (79%). Participants were randomly assigned to the NFB experimental group ($n$ = 14), NFB+Music experimental group ($n$ = 13), and control group ($n$ = 16, treatment as usual). There were not significant differences ($p$ > .05) in group composition (see Table 1 $\chi^2$ analysis). Participants who did not complete the first stage of treatment (detoxification and stabilization) and had a history of brain lesions were excluded. Patients with ongoing medication were included.

**Table 1**
*Sociodemographic*

| Variables | Group | | | | |
|---|---|---|---|---|---|
| | Control (%) (*n* = 16) | NFB (%) (*n* = 14) | NFB+Music (%) (*n* = 13) | $X^2$ | *p* |
| Sex | | | | 0.537 | .76 |
| Men | 7 (43.8) | 5 (35.7) | 4 (30.8) | | |
| Women | 9 (56.2) | 9 (64.3) | 9 (69.3) | | |
| Age | | | | 7.79 | .78 |
| 21–25 | 3 (18.8) | 5 (35.7) | 1 (7.7) | | |
| 26–30 | 3 (18.8) | 2 (14.3) | 3 (23.1) | | |
| 31–35 | 3 (18.8) | 2 (14.3) | 2 (15.4) | | |
| 36–40 | 2 (12.5) | 2 (14.3) | 4 (30.8) | | |
| 41+ | 5 (31.2) | 3 (21.4) | 3 (23.1) | | |
| Medication | | | | 1.39 | .49 |
| Yes | 11 (68.8) | 12 (85.7) | 9 (69.2) | | |
| No | 5 (31.2) | 2 (14.3) | 4 (30.8) | | |
| Drugs | | | | 20.14 | .06 |
| Cocaine (only) | 4 (25) | 0 (0) | 0 (0) | | |
| Meds (only) | 2 (12.5) | 0 (0) | 0 (0) | | |
| Marijuana (only) | 1 (6.2) | 2 (14.3) | 0 (0) | | |
| Alcohol and Cocaine | 0 (0) | 0 (0) | 1 (7.7) | | |
| Cocaine and Meds | 0 (0) | 0 (0) | 1 (7.7) | | |
| Meds and Marijuana | 1 (6.2) | 0 (0) | 0 (0) | | |
| Mixed substances (more than 2) | 8 (50) | 12 (85.7) | 11 (84.6) | | |
| Consumption time | | | | 8.26 | .082 |
| 1 year | 0 (0) | 3 (21.4) | 2 (15.4) | | |
| 3 years | 3 (18.8) | 0 (0) | 0 (0) | | |
| 5 years or more | 13 (81.2) | 11 (78.6) | 11 (84.6) | | |
| Reported psychiatric diagnosis | | | | 11.44 | .17 |
| Depression | 5 (31.2) | 8 (57.1) | 7 (53.8) | | |
| Bipolar | 4 (25) | 1 (7.1) | 0 (0) | | |
| Anxiety | 0 (0) | 1 (7.1) | 3 (23.1) | | |
| Attention deficit | 1 (6.2) | 1 (7.1) | 0 (0) | | |
| None | 6 (37.5) | 3 (21.4) | 3 (23.1) | | |

## Measurements

***NFB Equipment and Protocol***. SMR NFB training was provided using a BrainMaster Atlantis II amplifier and BrainAvatar software (version 4.0). We set a 60-Hz notch filter, sampling rate of 256 Hz, and 125 μv artifact threshold within BrainAvatar. Based on the 10–20 system, we used a monopolar electrode montage with an active electrode on Cz for the acquisition of SMR activity, with a reference electrode in the left ear lobe (A1) and a ground site on the right ear lobe (A2). Abrasive gel and conductive paste were used for electrode attachment. The electrode impedance was monitored across all sessions and kept under 5 kΩ. We used a standardized protocol for low beta reinforcement, called "Focus" on BrainAvatar software. The feedback was provided when the criteria of increasing the amplitude of SMR frequency (12–15 Hz), and inhibition of theta frequency (4–7 Hz) and high beta frequency (22–30 Hz) amplitudes were met. The protocol followed a schedule of seven blocks of 4 min in which the participant focused on "thermometers" showing each frequency amplitude. In the first block, the patient focused on inhibiting high beta; in the next two blocks on inhibiting theta, and in the next four blocks

on increasing SMR amplitude. Automatic threshold was selected. We used an external monitor and loudspeaker to provide audiovisual feedback and Baroque period music. In the NFB+Music group, the auditory feedback tone was in tune with the music selected in the key of D or G. Mind Media BV Zukor's Air game was the NFB game primarily used.

***Iowa Gambling Task (IGT)***. This computerized cognitive task measures the decision-making process as an element of executive function (Bechara et al., 2000; Damasio, 1996). The task consists of a set of cards from four different decks, with the purpose of maximizing money gain. Participants choose cards from the decks C and D since those two offer less immediate gains, but less long-term losses. By choosing cards of decks A and B, participants win more money in the short term, but eventually lose more (Bechara et al., 2000). This paradigm was executed from an open-source PEBL platform (Mueller, 2013), which is a faithful adaptation to the original test (Bechara et al., 1994). The computerized task was administered in Spanish, with a numerical classification of the groups of letters: A = 1, B = 2, C = 3, D = 4. The contingency with which the reward and penalties appear in this version are identical to those used in the original IGT.

***Sustained Attention to Response Task (SART)***. This Go/No-Go computerized task was used to measure executive function, particularly the ability to inhibit responses to infrequent and unpredictable stimuli during a quick, rhythmic period when frequent stimuli are responded to (Robertson et al., 1997). A modified version was administered in which stimuli (e.g., pictures of clock, book, umbrella) varied across all trials and were randomly presented at a 1.15-s rate. The task included 225 trials (each stimulus appeared 25 times) and each one fluctuated between 250 ms and 900 ms. Participants were instructed to respond by pressing the zero (0) key to each stimulus in the most accurate and possible way and to minimize errors by not responding to the "ball" stimuli. This task was executed on the E-prime platform (Psychology Software Tools, 2012).

***Emotion Regulation Questionnaire (ERQ)***. This 10-item scale measures the tendency of participants to regulate their emotions in two ways: cognitive reassessment of emotions and expressive suppression of emotions (Gross & John, 2003). The participants responded to each item using a 7-point Likert scale on intervals ranging from 1 (*strongly disagree*) to 7 (*very much in agreement*).

***Attention-Related Cognitive Errors Scale (ARCES)***. This 12-item scale explores daily mistakes that a person makes as a result of not paying enough attention to a task (Cheyne et al., 2006). Participants responded to each item in a 5-point Likert scale on intervals ranging from 1 (*never*) to 5 (*very often*).

***Mindful Attention Awareness Scale (MAAS)***. This 15-item scale measures the dispositional capacity of a person to be attentive and aware of the experience of the present moment in everyday life (Brown & Ryan, 2003). The respondents answered each item in a 6-point Likert scale on intervals ranging from 1 (*almost always*) to 6 (*almost never*).

## Procedure

Participants signed the inform consent to join the study and they completed a sociodemographic questionnaire and each of the scales (i.e., SART, ERQ, ARCES, MAAS). After randomization, the experimental groups (NFB and NFB+Music) received between 10 and 20 training sessions, 2 to 3 days a week for 4 to 8 weeks. The number of sessions was determined according to each participant's mastery level, availability, and desire to continue sessions based on his or her perceived quality of life improvement.

At the start of each training session, participants sat down with eyes open in a comfortable chair and were instructed to learn to control their brain activity. Muscle relaxation was encouraged throughout the sessions. The average of NFB sessions was 13.85 ($SD$ = 2.35) and each one lasted around 30 min. If a participant reported tiredness prior or during the NF session, a 15-min training was conducted. After the session, participants were given the opportunity to verbally report their experiences. Participants were reassessed with the previously mentioned scales and tasks after completing the training sessions.

## Analyses

Data were calculated and analyzed using SPSS (version 23, IBM) and Excel (Microsoft). IGT net scores were obtained by subtracting the number of favorable selections represented in the C + D cards, minus the number of advantageous selections represented in A + B cards, segmented in blocks of 20 trials. The following formula, (C + D) − (A + B), was calculated for each block selection from 1–20, 21–40, 41–61, 61–80, and 81–100. An ANOVA 3 X 5 (group X blocks) was used to identify possible interaction effects, group X blocks in the pretest, and then in the posttest. Then, an ANOVA 3 (group) x 2 (group X pre and post) was conducted to identify pre

and post changes for each block in relation to the groups. After the task completion, participants were asked to explain their task strategies.

SART performance was analyzed calculating the errors by omission (not responding to the stimuli: GO) and errors by commission (respond to the ball stimulus: NoGo), and reaction times. A mixed ANOVA was conducted to evaluate within-group and between-group changes for errors by omission and commission errors and reaction time for Go stimuli.

Reliability tests were evaluated for all self-report measurements using the pretest data. A mixed ANOVA was conducted to calculate within-between groups mean differences. A Pearson correlation coefficient was conducted to explore associations across self-report measurements.

SMR EEG amplitude grand mean were calculated for session #1, session #6, and session #11. Repeated-measures ANOVA were performed to compare SMR amplitude changes on experimental groups. A mixed ANOVA 3 X 2 was conducted to identify Time X Group interaction. A series of paired *t*-tests were conducted to compare between a pair of sessions. Descriptive analysis for all scores was also carried out.

## Results

### Effects on IGT

An ANOVA 3 (group) x 5 (blocks) on the net scores (C + D) − (A + B), using the correction for the degrees of freedom of Huynd-Feldt, did not reveal Group X Block interaction in the pretest, $F(8, 160) = 0.63$, $p = .74$, $\eta 2 = .031$. The net scores between the groups for the five blocks of cards did not differ in the pretest. However, using the Huynd-Feldt correction, the same analysis revealed a Group X Block interaction effect in the posttest, $F(5.91, 160) = 2.22$, $p = .04$, $\eta 2 = .10$. The finding revealed potential changes over time in the selection of the blocks among the groups.

The ANOVA 3 (group) x 2 (pre and post block) for evaluating the interaction of the effect of time for each block in relation to group, revealed no significant differences in the scores for the 1–20 selection block, $F(2, 40) = 0.037$, $p = .96$, $\eta 2 = .00$. The same was found for the 21–40 selection block, $F(2, 40) = 0.039$, $p = .96$, $\eta 2 = .00$; and the 41–60 selection block, $F(2, 40) = 1.22$, $p = .30$, $\eta 2 = .05$. However, we found significant differences in the scores for the 61–80 selection block, with a medium effect size, $F(2, 40) = 3.26$, $p = .04$, $\eta 2 = .14$. Time difference scores for each group in this block were the following: control group (pre: $M = -0.88$, $SD = 4.73$; post: $M = -0.25$, $SD = 4.49$), NFB (pre: $M = -2.29$, $SD = 4.21$; post: $M = 4.00$, $SD = 8.44$), and NFB+Music (pre: $M = -1.00$, $SD = 4.83$; post: $M = 4.62$, $SD = 8.57$).

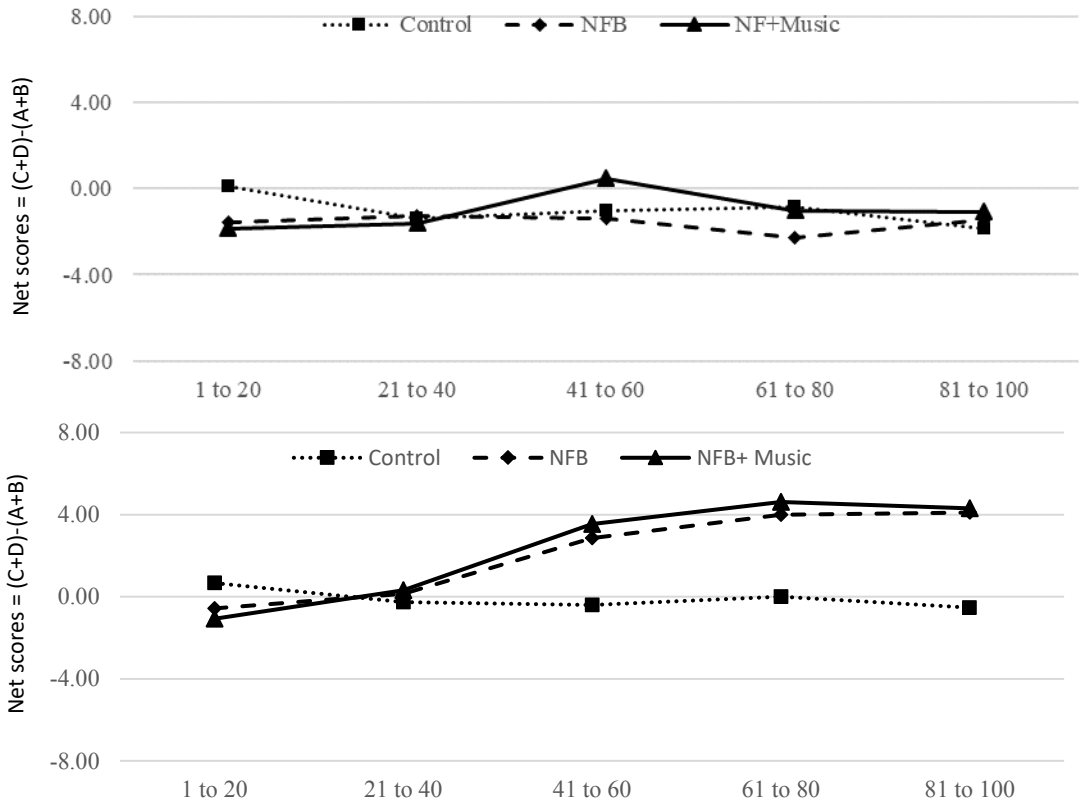
In the 81–100 selection block, we found no significant differences in the scores, but the effect size remained medium, $F(2, 40) = 2.55$, $p = .13$, $\eta 2 = .09$. Subsequent comparisons revealed no differences in scores between the experimental groups across all selection blocks.

Regarding the card selection strategy, most participants used a selection pattern intercalating choices between the set of cards in both the pretest and posttest. For example, a participant would select the set of cards in the order that they appeared on the screen or with a skipping strategy (i.e., selecting A + C, then B + D). In the pretest, only 16% of the sample could explain with precision the task and identified favorable versus unfavorable blocks of cards. However, despite constant losses, participants were inclined to continue selecting the disadvantageous cards because “they earned more money” with those.

A similar pattern was observed in the posttest. In the experimental groups, although the selection pattern showed a tendency to favorable card blocks, 63% of the participants could not describe conceptually which blocks of cards were more favorable and continued intercalating their choices despite the losses. However, 37% of the participants in the experimental groups ($n = 10$), described the task conceptually and were able to distinguish favorable from unfavorable blocks ($n = 6$ in NFB+Music, $n = 4$ in NFB). For the most part, they changed their course of selection toward favorable blocks of cards. Of those 10 participants, one participant who belonged to the NFB+Music group described the task conceptually accurately; however, the performance showed a tendency toward unfavorable cards in the posttest.

In the control group, 25% of the participants ($n = 4$) were able to identify the advantageous sets of cards from the unfavorable ones in the posttest. However, they did not change their card choices in the last blocks of the task.

**Figure 1.** *IGT Pretest (Above) Versus Posttest (Below) Net-Scores by Blocks of Trials*.




## Effects on SART

Omission errors analysis in the SART showed that, although an improvement was shown in the experimental groups, there was no significant effect between Time X Group interaction, $F(2,40) = 2.19$, $p = .12$, $\eta 2 = .09$. Analysis of commission errors revealed a significant difference with a large effect size on the Time X Group interaction, $F(2, 40) = 6.19$, $p = .00$, $\eta 2 = .236$. This result suggests that the participants of the experimental groups NFB (pre: $M = 27.85$, $SD = 14.28$; post: $M = 18.50$, $SD = 18.50$) and NFB+Music (pre: $M = 17.46$, $SD = 10.72$; post: $M = 10.30$, $SD = 5.89$) were more efficiently inhibited to the NoGo stimulus compared to control (pre: $M = 23.00$, $SD = 16.33$; post: $M = 22.75$, $SD = 15.87$). Reaction time analysis revealed no significant effect on the Time X Group interaction, $F(2, 79) = .311$, $p = .73$, $n2 = .01$.

**Table 2**
*SART Omission Errors, Commission Errors, and Reaction Time for GO Stimulus Averages*

| Groups | Omission Errors | | Comission Errors* | | Reaction time GO | |
|---|---|---|---|---|---|---|
| | Pre (*SD*) | Post (*SD*) | Pre (*SD*) | Post (*SD*) | Pre (*SD*) | Post (*SD*) |
| Control | 23.00 (16.33) | 22.75 (15.87) | 12.63 (5.32) | 13.44 (4.45) | 398.42 (62.39) | 378.53 (58.62) |
| NFB | 27.36 (14.28) | 18.50 (15.14) | 15.21 (5.70) | 10.93 (5.99) | 388.22 (70.31) | 370.29 (54.41) |
| NFB+Music | 17.46 (10.72) | 10.31 (5.89) | 14.54 (5.57) | 8.38 (3.92) | 378.79 (40.45) | 376.20 (66.35) |

**Note.** * < .01

### Effects on ARCES

ARCES reliability analysis revealed an *α* value of 0.869, proving to be a reliable instrument to assess the SUD population. A mixed ANOVA showed no significant main effect of the group variable on the ARCES scores, $F(2, 40) = 2.02$, $p = .146$, $\eta 2 = .09$. However, a significant effect and a large effect size were found between Time X Group interaction, $F(2, 40) = 15.76$, $p = .000$, $\eta 2 = .44$. Time difference scores for each group were the following: control group (pre: $M = 40.19$, $SD = 9.36$; post: $M = 40.31$, $SD = 9.99$), NFB (pre: $M = 44.50$, $SD = 12.69$; post: $M = 27.57$, $SD = 12.67$), NFB+Music (pre: $M = 45.38$, $SD = 16.14$; post: $M = 20.77$, $SD = 5.51$). These findings suggest that participants in the experimental groups improved their scores over time, after SMR NFB.

### Effects on MASS

MASS reliability analysis revealed an *α* value of 0.819, proving to be a reliable instrument to assess the SUD population. A mixed ANOVA analysis showed no significant main effect of the group variable on the MASS scores, $F(2, 40) = 2.67$, $p = .81$, $n2 = .11$. However, significant difference with a large effect size was found between Time X Group interaction, $F(2, 40) = 13.22$, $p = .00$, $\eta 2 = .398$. Time difference scores for each group were the following: control (pre: $M = 52.31$, $SD = 12.46$; post: $M = 53.50$, $SD = 14.39$), NFB (pre: $M = 43.86$, $SD = 18.01$; post: $M = 67.36$, $SD = 18.95$), NFB+Music (pre: $M = 50.69$, $SD = 16.52$; post: $M = 77.15$, $SD = 6.17$). These findings suggest that participants in the experimental groups significantly improved their scores over time, after training with SMR NFB.

### Effects on ERQ

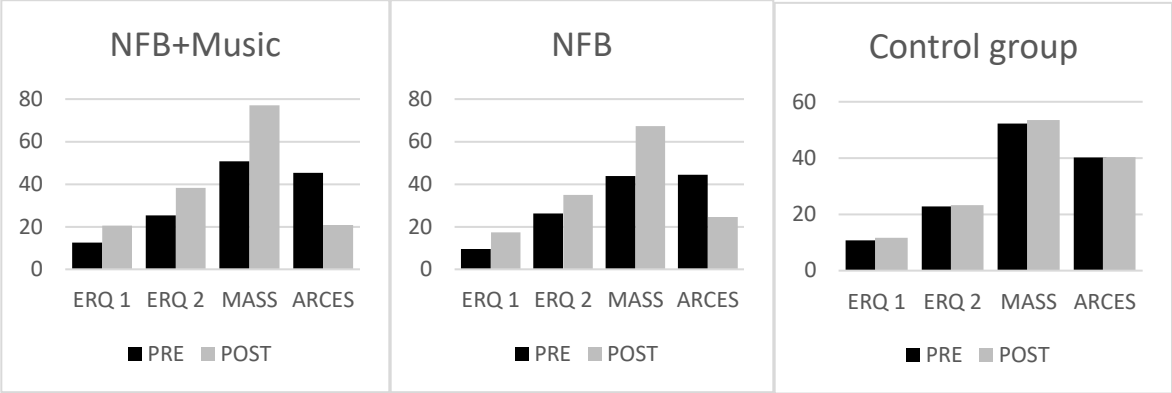
Reliability analyzes for the ERQ initially revealed little reliability for the Emotional Suppression subscale ($\alpha = 0.65$) in this population. Leaving the subscale item #2 out of the analysis (i.e., “I keep my emotions to myself”), it reached an *α* value of 0.731. Therefore, score analyzes in this subscale were made after eliminating item #2. In this scale, the Likert scale values were inverted; the value of 7 represents a positive value (i.e., emotional expression) and lower values represent a negative value (i.e., no emotional expression). The Cognitive Evaluation subscale obtained an initial *α* value of 0.719 and the Likert scale values were not inverted during analysis.

***Cognitive Reappraisal Subscale***. A mixed ANOVA showed a significant main effect of the group variable with a large effect size, $F(2, 40) = 6.92$, $p = .003$, $\eta 2 = .25$. In addition, a significant difference with a large effect size was found on Time X Group interaction, $F(2, 40) = 6.41$, $p = .004$, $\eta 2 = .24$. Multiple comparisons from the Bonferroni method showed significant differences in the posttest in the control group ($M = 23.31$, $SD = 9.33$) compared to the NFB group ($p < .05$; $M = 34.93$, $SD = 6.86$) and NFB+Music group ($p < 0.01$; $M = 38.31$, $SD = 4.07$). The NFB groups without Music and NFB+Music did not differ significantly ($p > .05$).

The scores for each group as a function of time are as follows: control (pre: $M = 22.81$, $SD = 9.56$; post: $M = 23.31$, $SD = 9.33$), NFB without Music (pre: $M = 26.29$, $SD = 8.90$; post: $M = 34.93$, $SD = 6.86$), NFB+Music (pre: $M = 25.38$, $SD = 9.39$; post: $M = 38.31$, $SD = 4.07$).

***Expression Suppression Subscale***. A mixed ANOVA showed a significant main effect of the group variable and a large effect size on the subscale of Emotion Expressive Suppression, $F(2, 40) = 6.38$, $p = .004$, $\eta 2 = .24$. However, no significant interaction effect was found for Time X Group, although a large effect size was obtained, $F(2, 40) = 3.21$, $p = .051$, $\eta 2 = .13$. Multiple comparisons from the Bonferroni method showed significant differences in the control group ($M = 11.62$, $SD = 7.20$) compared to the NFB group ($p < .05$; $M = 17.14$, $SD = 7.32$, $p = .02$) and NFB+Music group ($p < .05$; $M = 20.53$, $SD = 4.92$, $p = .00$) in the posttest. The NFB and NFB+Music groups did not differ significantly ($p > .05$). Scores for each group as a function of time were as follows: control (pre: $M = 14.88$, $SD = 5.63$; post: $M = 11.63$, $SD = 7.20$), NFB (pre: $M = 16.36$, $SD = 4.65$; post: $M = 17.14$, $SD = 7.32$), and NFB+Music (pre: $M = 14.46$, $SD = 5.63$; post: $M = 20.53$, $SD = 4.92$).

**Figure 2.** *Pre Versus Post Self-report Measurements Review.*




**Note.** ERQ 1: Cognitive Reappraisal subscale. ERQ 2: Suppressive Expression subscale.

## Effects on the EEG

Significant changes and large effect size were observed on the main effect of time (average values on training sessions #1, #6, and #11) on the SMR mean amplitude for the experimental groups, $F(2, 50) = 11.38$, $p = .00$, $\eta 2 = .31$. Paired *t*-test for a pair of sessions revealed no significant differences from session #1 to session #6, but significant differences from session #6 to session #11, $t(26, N = 27) = -4.86$, $p = .00$, $d = .38$; and from session #1 to session #11, $t(26, N = 27) = -2.90$, $p = .00$, $d = .27$. The average values for each training sessions were as follows: session #1 ($M = 5.44$, $SD = 1.64$), session #6 ($M = 5.25$, $SD = 1.48$), and session #11 ($M = 5.86$, $SD = 1.67$). No interaction effect was found on Time X Group, $F(2, 50) = .312$, $p = .73$, $\eta 2 = .01$. Averages for the groups were the following: session #1, NFB group ($M = 5.13$, $SD = 1.64$) and NFB+Music ($M = 5.77$, $SD = 1.39$); session #6, NFB group ($M = 4.95$, $SD = 1.63$) and NFB+Music ($M = 5.57$, $SD = 1.28$); session #11, NFB group ($M = 5.64$, $SD = 1.89$) and NFB+Music ($M = 6.09$, $SD = 1.44$). Figures 3 and 4 illustrate the results of changes in SMR amplitude in microvolts ($\mu$V).

**Figure 3.** *SMR ($\mu$V) Average Amplitude for the Experimental Groups.*

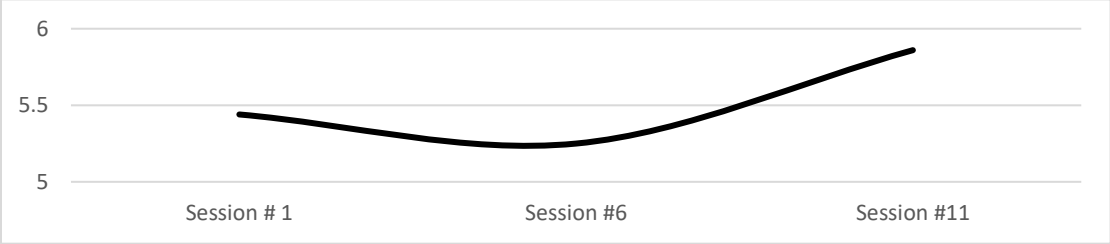
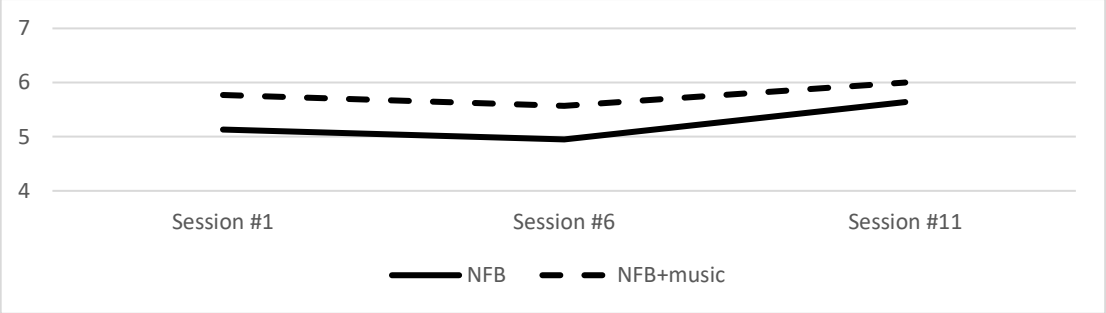


**Figure 4.** *SMR (μV) Amplitude NFB Versus NFB+Music.*




## Discussion

We measured the effects of combined SMR NFB and music on executive functions in individuals with SUD. To the best of our knowledge, this is the first study testing assisted NFB training with "music" on a Puerto Rican SUD sample. Additionally, this study used a control group and cognitive tasks as assessment tools to specifically measure executive function. Here we discuss relevant results and highlight peculiarities of the training procedure. We also identify challenges, limitations, and recommendations for future research.

### Effects of NFB and Music on IGT

IGT pretest results confirmed previous findings within the SUD population (Bechara & Damasio, 2002). These individuals typically do not achieve adequate performance in this cognitive task. According to Martínez-Selva et al. (2006), this phenomenon may be due to different factors: (a) preference for high-risk options; (b) inability to evaluate and distinguish favorable from unfavorable letters; (c) hypersensitivity to reward; (d) insensitivity to punishment; (e) problems with executive function (e.g., working memory); (f) low attentional performance; and (g) problems with impulse control. According to Bechara (2005), a myopia occurs over the future consequences of the decision, possibly due to dysfunctional connectivity in neural networks involved in the integration of bottom-up interoceptive signaling in decision-making processes (e.g., prefrontal cortex, amygdala, somatosensory regions, insula). The usual decisional behavior in individuals with SUD begins with an increased tendency to select card blocks in the middle, toward favorable cards, and then resume a decisional pattern for unfavorable cards (Bechara & Damasio, 2002). Bechara and Damasio (2002) have linked this decisional pattern to the lack of generation of anticipatory autonomic signals (i.e., somatic markers) that direct the decision based on previous experience. The results of our study suggest that NFB can potentially optimize interoception by modifying the SMR frequency generated by brain areas involved in this process.

The activity of SMR has been linked to the promotion of inhibitory mechanisms on the thalamo-cortical loop, which reduces motor interference, allowing optimization of cognitive processing and enabling the improvement of interoception, perception of the body, or body awareness (Egner & Gruzelier, 2004; Noël et al., 2013). Interoception refers to processes by which the bodily states (or somatic states) are transmitted back to the brain, giving rise to the awareness of the internal state and motivating the behavioral responses for homeostatic internal state (Verdejo-Garcia, Clark, et al., 2012). SMR NFB might promote the acquisition of somatic states (corporal and affective sensations) and more adaptive responses as we observed in the posttest. This regeneration of somatic states might suggest the regulation of autonomous bottom-up signals originating from the amygdala, which are involved in objective-oriented cognitive processes and the willpower to resist drugs (Bechara, 2005). It is in this sense that Noël et al. (2013) have recommended technologies and interventions of biofeedback and meditation as compatible methods to optimize interoception.

The optimization of decision-making through SMR NFB is evident in both experimental groups when compared to control, particularly at the penultimate block (61–80). Nonetheless, it is important to note that the averages did not approach what is considered an optimal task performance in the posttest. Bechara (2003) considers a good performance equivalent to a net-score close to 10 in individuals without SUD or brain lesions. In this study, participants reached a net-score close to 4 in the last blocks of the IGT in the posttest. The statistical significance between the groups

decreased in the last block (81–100), which suggest that maybe a higher number of training sessions are needed for this score become close to 10.

The changes on IGT performance after training might be also associated with variations in the execution strategy and aspects of working memory (Bagneux et al., 2013). Deficits in working memory decrease the chances of selecting favorable cards and lower individuals' capacity to identified favorable cards. However, in the posttest, the experimental groups simultaneously changed their selection course to more favorable card blocks as they conceptually figured out the task. Although working memory was not a variable considered in this study, results suggest possible neurocognitive changes in this function. The link between SMR training and changes in short-term visual memory in both clinical and healthy populations has also been studied previously (Kober et al., 2015). We suggest the use of objective measures and the implementation of NFB for optimizing memory-related variables.

### Effects of NFB on Attentional Variables

Previous studies have shown that SMR NFB training induces less commission and omission errors, better attention, and impulse control in Go/NoGo tasks in SUD population (Kaiser & Othmer, 2000; Keith et al., 2015; Scott et al., 2005) This type of training protocol has been shown to have an effect in fronto-striatal circuits (bilateral caudate and left black substance) during tasks that involve executive cognitive functions such as attention (Keith et al., 2015). This is important because this circuit also plays a central role in decision-making in people with SUD (Keith et al., 2015; Keramati & Gutkin, 2013). In the present study, significant differences were only found in commission errors analyses which demonstrates the effectiveness of SMR NFB training to enhance inhibitory mechanisms that enable impulse control (Kaiser & Othmer, 2000). However, not significant changes were found on reaction times and omission errors. Greater inhibition in the NFB+Music group was found, although the reaction times didn't change. The NFB group showed better reaction times than the NFB+Music group. Although the control group also showed remarkable improvements on reaction times, this improvement was not related to a better task performance.

### NFB and Emotional Regulation

Considering the link between decision-making and emotion (Bechara, 2005), training with NFB (with or without music) in this study proved to be effective in generating changes in cognitive appraisal and expressive suppression of emotions. A novel result of our study is that NFB+Music induced changes related to emotional regulation, particularly in the expressive suppression domain. Accordingly, the presence of music during NFB training promoted the expression of emotions, which is consistent with previous research evaluating the effects of music on mood, emotion, and affectivity (Baker et al., 2007; Koelsch, 2014; Lundqvist et al., 2009; Panksepp & Bernatzky, 2002; Rickard et al., 2005). Given that the suppression of feelings might be an obstacle to addiction recovery (Baker et al., 2007), listening to music as a therapeutic element could help the person to approach and express feelings during the rehabilitation process.

In terms of cognitive appraisal, the results reveal that, at the end of the training, participants of both experimental groups were able to link the changes in thought with subsequent changes in emotion (e.g., item #8: "when I want to feel a more positive emotion, I change the way I am thinking about the situation"). Additionally, we found better cognitive appraisal over negative emotions (e.g., item #5: "when I find myself in a stressful situation, I make myself think about it in a way that helps me maintain the calm").

### Effects on the SMR Amplitude

The inhibition of theta and high beta frequencies, combined with a reinforcement of SMR frequency has proved effective on executive function processes in clinical or healthy samples (Arns et al., 2014). Although the results in this study do not show significant changes in the SMR frequency, it does obtain a large effect size, which makes the magnitude of the change relevant in both experimental groups. The findings in this study show an initial tendency to decrease the SMR wave amplitude in the first sessions (approximately in sessions #5 and #6) and then a tendency to increase. These findings are consistent with previous studies in clinical and healthy populations, such as the study by Arns et al. (2014). In this study, the authors trained adult patients with ADHD, using the SMR amplitude as one of their protocols. Interestingly, the authors found significant training effects of this frequency and an increase in the density of the sleep spindles concurrently with the decrease in the delay of sleep onset. This suggests that the mechanisms by which SMR training operates and its effects at the level of cognitive processing are mediated by variables associated with sleep variation. In other words, a decrease in the delay of the onset of sleep (ergo better quality of sleep) has particular effects on cognitive processing. SMR NFB may act as a moderating factor in

improving cognitive processing, through the optimization of the circadian rhythm.

In this study, approximately 65% of the participants in the experimental groups were able to increase the SMR amplitude through the sessions. Arns et al., (2014) argued that the SMR NFB protocol is not about increasing the EEG amplitude in a specific frequency range, but about regulating the activity within a functional network (reticulo-talamocortical network), increasing the long-term potentiation which increases the synaptic sensitivity and the likelihood of future activations in that network. Based on this view, the researchers argued that the important thing in this protocol is that the participant learns to modulate the frequency amplitude either by decreasing it or increasing it, not necessarily increasing units in amplitude for each session; both strategies result in the increase in the density of the sleep spindles.

## Process Evaluation

One of the aspects verbalized most spontaneously during training sessions in this study was the continuous description of changes in sleep patterns by the participants. Previous research has linked the common presence of sleep disorders in populations with SUD, a phenomenon also associated with the high relapse rate (Mahfoud et al., 2009). Several participants of this study expressed suffering from insomnia, frequent sleep interruptions, and difficulty falling asleep, among other manifestations. Research has revealed the effect of SMR training on circadian modulation in patients suffering from insomnia and ADHD (Arns et al., 2014; Cortoos et al., 2010). Although this was not considered as a variable in this study, most of the participants in the experimental groups perceived an immediate effect of SMR training on the quality of their sleep through the sessions. Ninety percent of the participants expressed that their sleep, each time after the sessions, seemed to be interrupted less at night. They described their sleep as deep and with a high frequency of lucid dreams.

Interestingly, the content of dreams in this population involved some interaction with the drug (e.g., buying and consuming the drug, even smelling the drug). A participant expressed his concern about his perception of an increase frequency of lucid dreams in which he sensuously experienced the consumption of the drug. This caused concern to the participant and to other participants who subsequently experienced the same. Although this phenomenon has been investigated very little, with more or less discrepancy, the literature reveals that the frequency of lucid dreams that involve consumption of the substance are very common and are indicators of recovery (Colace, 2006; Flowers & Zweben, 1998). Future research should address circadian rhythm variations as an effect of training with SMR NFB in this population.

It has been seen that SMR training has an effect in inducing a feeling of calmness and tiredness (Gruzelier, 2014). Almost all participants who were on medication expressed their intended to lower the dose of their medications because they felt calmer. Particularly the participants in the NFB+Music group, who rated the music as soothing and peaceful, which could assist in the maintenance of relaxation states in this group. The calming effect was sometimes confused with a lethargic or drowsy feeling. It was very common to identify this particular sensation and sleep during the first sessions, manifestations that have also been observed in other studies (Keith et al., 2015). These sensations showed some kind of initial adjustment to the trainings. Once a couple of initial sessions were held and participants learned to inhibit theta, they felt more resilient, managing to maintain a very stable attentional state during the sessions. Although this was the norm, two participants had to start with 10-min sessions and gradually increase the time during the next sessions, because they were not able to maintain a considerable state of alertness for more than 20 min. Most of the participants expressed a good level of mastery approximately at session #8.

## Limitations

In the present study, although we tried to control different factors in the training process, the "novelty effect" and the hypermotivation of the participants could have increased observed effects. Due to the high costs of the technology and the time involved in carrying out the training, it was also not feasible to use a placebo group where training with virtual simulation of the EEG would be carried out. The diffusion of the intervention to the control group by the participants in the experimental groups caused deception feelings twice. In these cases, the participants were reoriented about the information contained in the informed consent they had signed. The presence of a placebo group, instead of a control group without training with NFB, could have lessened the feeling of disappointment of these participants in the control group.

This type of strategy has been widely debated in the NFB area in recent years (Fovet et al., 2017). Divergent opinions have questioned how ethical it is to have a subject trying to regulate physiological

signals produced by a simulation, which can produce unsuspected results. In addition, it is difficult to produce a realistic simulation, for example, like the feedback of the detection of muscular movement that a normal system would offer you. In that sense, the experimental simulation condition could act as a normal training condition while the subject is being taught to try to be still and regulate. It is more desirable to explore the specific electrophysiological mechanisms in which the NFB could produce neuronal plasticity.

With respect to the amount of the sample and characteristics of the population, although the sample used in this study was considerable with respect to the number of participants available in the residency programs, a more robust study would require a larger population sample.

With respect to the analysis, in this study there is no glimpse of quantitative and qualitative data triangulation with first-person reports during the sessions. A subsequent publication should address in more detail the linkage of the neurophysiological changes with the content of the mental strategy the participants used to regulate their brain activity. Validating the neurophysiological changes with verbal self-reports or interviews would contribute more precisely to the application of the neurophenomenology project proposed by Varela (1996).

### Recommendations

The use of a group with placebo training (e.g., with simulation of training or "sham NFB") could have strengthened the current design, generated more experimental control, and mitigated the "novelty effect" produced by the use of this technology. Future studies should consider the incorporation of a placebo group to control the effects of random factors, so that the benefits of NFB training can be seen more clearly. However, the realization of this type of study should seek a realistic simulation, the use of specific neurophysiological measures to explore neuroplasticity such as pre- and post-qEEG map reports and mitigate unsuspected effects that could cause induced self-regulation with signals that are not specific to the subject.

The inclusion of larger samples and the use of longitudinal designs (follow-ups) are necessary to increase the level of validity of the results in future investigations. The incorporation of qEEG measures, before and after training, would strengthen the observation of possible changes in brain activity in specific brain areas. With respect to the training protocol, individualized sLORETA *Z*-score training should be considered. The implementation of a tailored protocol, instead of a standard protocol for all participants, contributes to obtaining greater specificity by evaluating the effects of training based on individual differences.

Future studies might incorporate autonomic monitoring in the IGT performance and during the NFB protocol in order to evaluate possible changes in the re/generation of autonomic signaling (e.g., skin conductance). Similarly, the inclusion of this measure during training would provide information on physiological and affective changes in real time while the subject tries to self-regulate.

## Conclusion

As other authors have suggested, no treatment or therapy program cures a disease by itself (Gossop et al., 2002). Considering the complexity of the dimensions of SUD, it is needed to articulate the therapies and treatments within a biopsychosocial scope. The results of this study suggest that brain entrainment with or without music, can potentially optimize executive functions (decision-making and inhibitory control) as well as aspects related to emotional regulation in SUD population. Certainly, the SMR NFB should be considered as a paradigm to be integrated with other clinical methods (such as pharmacology and psychological therapy) to mitigate the harmful effect of drugs from a neuropsychological perspective. Future studies should investigate and replicate these findings in more controlled studies with larger samples.

### Acknowledgement

The authors gratefully acknowledge the support from the Biostatistics, Epidemiology & Research Design Core from The Hispanic Alliance for Clinical and Translational Research (Alliance, NIGMS Award Number U54GM133807).

### Author Declaration

The authors declare no conflicts of interest with respect to the research, authorship, and publication of this study. There is no financial interest or benefit that has arisen from this research.

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**Received:** April 20, 2023
**Accepted:** May 29, 2023
**Published:** June 29, 2023

NeuroRegulation

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# Association Between Heart Rate Variability and Executive Function Performance: A Cross-Sectional Study in Adult Population

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**Abstract**

The present study aimed at investigating the association between short-term heart rate variability and executive function performance in two groups of the adult population, that is, young adults and middle-aged adults. The influence of physical activity on heart rate variability and executive performance was also analyzed. A cross-sectional study was conducted on 143 adults; 65 middle-aged adults and 78 young adults. Each participant's heart rate variability was recorded during the ideal state, during the executive function task and recovery state. The executive function tests included the Delayed Matching of Sample (DMS), Spatial Working Memory (SWM) and Multitasking Test (MTT) on the Cambridge Neuropsychological Test Automated Battery (CANTAB). Physical activity levels were reported through IPAQ. Results revealed resting HRV indicator, RMSSD was able to predict correct scores in DMS, error rates in SWM, and reaction latencies in MTT in the adult population, and adults with high HRV performed better in the tests. Middle-aged adults demonstrated high sympathetic activity at rest, and reactivity of HRV was seen maximum during the MTT task. Young adults showed higher sympathetic activation to imposed demands of multitasking. Physical activity was able to predict executive scores and resting HRV. HRV was found to be associated with executive function performance in the adult population.

***Keywords***: executive function; neuropsychological tests; heart rate variability; autonomic function; aging; middle-aged

**Citation**: Sharma, N., & Shenoy, S. (2023). Association between heart rate variability and executive function performance: A cross-sectional study in adult population. *NeuroRegulation, 10*(2), 78–93. https://doi.org/10.15540/nr.10.2.78

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## Introduction

An individual's ability to engage in goal-directed behavior using creative problem-solving, behavior modification in response to environmental changes, the generation of strategies for complex actions, and the capacity to suppress prepotent behavioral and emotional responses are referred to collectively as executive function (EF; Suchy, 2009; Suchy, 2015; Williams et al., 2019).

EF is controlled by frontal lobes and related brain networks. The area of the prefrontal lobe, in particular, the dorsolateral prefrontal cortex (DLPFC) and the cingulate cortex (e.g., the anterior cingulate) have been related to the cognitive aspects of EF (Raaz, 2000; Reuter-Lorenz, 2000).

The autonomic nervous system (ANS) is responsible for regulating visceral functions through the sympathetic and parasympathetic branches which act antagonistically to preserve a dynamic equilibrium of vital functions. In the cardiovascular system this nonstationary balance results in the fluctuation between intervals of consecutive heartbeats, which is heart rate variability (HRV; Xhyheri et al., 2012). HRV is a marker of cardiac autonomic function and involves the interaction of activity from the sympathetic nervous system (SNS) and parasympathetic nervous system (PNS; Frewen et al., 2013). ANS function is also controlled by

cortical circuits located in the prefrontal cortex, the anterior cingulate gyrus, the orbitofrontal cortex, and the amygdala (Critchley, 2009; Parasuraman & Jiang, 2012).

The prefrontal cortex (PFC), which is most frequently active during tasks that require EF, is also involved in the modulation of autonomic activity. Studies on both humans and nonhuman animals have established that a network of higher brain regions that connect directly and indirectly to autonomic motor circuits influence heart regulation by the SNS and PNS (Ter Horst & Postema, 1997). The resting measures of HRV reflect the interaction of these higher and lower mechanisms, or the effectiveness of central-peripheral neural feedback (Thayer & Lane, 2000).

Individual differences in resting HRV can be used to predict cognitive performance in tasks challenging PFC (Thayer et al., 2009). A systematic review highlighted the influence of HRV, as a physiological correlate for ANS, on cognitive functions like global cognition, memory, language, attention, visuospatial skills, and processing speed, as well as EF. However, it was emphasized that a lack of understanding still exists regarding the association between EF and HRV; hence, more research was required (Forte et al., 2019).

Literature has shown a correlation between cognitive function and HRV (Forte et al., 2019; Grässler, Hökelmann, et al., 2020). Studies have been conducted investigating age-related effects on cardiac autonomic control by HRV in two spectrums of age; that is, young adults (in the age range of 18 to 30 years) and older adults (in the age range of 51 to 75 years) at resting state, during cognitive tasks, and in a recovery period after the cognitive testing (Capuana et al., 2012; Grässler, Dordevic, et al., 2021; Schapkin et al., 2012). However, the middle ages (adults in the age range of 40 to 60 years) is largely an unexplored age group where deterioration in both EF (Ferguson et al., 2021) as well as HRV (Britton, Shipley, et al., 2007) is observed.

Due to inconsistent findings regarding the middle-aged population in the existing literature (Britton, Singh-Manoux, et al., 2008; Kimhy et al., 2013; Mathewson et al., 2010; Zeki Al Hazzouri et al., 2018), there is a need to establish the relationship between autonomic function and EF abilities. The present study was planned with aim of determining the relationship between HRV and EF abilities in the middle-aged population. As many studies have confirmed the influence of HRV on EF abilities in young adults (Canabarro et al., 2017; Hansen et al., 2003; Luque-Casado et al., 2016), young adults were also examined in the study for comparison.

In order to make predictions regarding parasympathetic activity, all aspects of cardiac vagal control adaptability need to be integrated (i.e., resting, reactivity, and recovery HRV in response to cognitive tasks). Reactivity represents the transition between a resting state and a cognitive task (Laborde et al., 2018). As a result, many researchers have tried to analyze the changes in HRV with the varying mental workload. However, in all of the studies only a few aspects of EF were investigated, like attentional biases towards affective or highly salient information (Mathewson et al., 2010), attention (Duschek et al., 2009), working memory, and sustained attention (Hansen et al., 2003; Luque-Casado et al., 2016). These studies found HRV sensitive to task demands of different cognitive domains. But this research mostly focused on a single aspect of EF through a limited neuropsychological test. In the present study, Cambridge Neuropsychological Test Automated Battery (CANTAB), a fair neuropsychological validated and reliable computerized test battery was used to assess cognitive function (Green et al., 2019; Robbins et al., 1994). Some of the extensive subsets of CANTAB which allow measuring various cognitive domains tests for EF were employed.

The present study aimed to identify if resting HRV parameters were able to predict EF task scores. Also, we planned to investigate the effects of age group and condition (resting state, during the cognitive tasks, and in a recovery phase after the cognitive testing) on cardiac autonomic control. For this purpose, the HRV of young (YA) and middle-aged adults (MA) were recorded before, during, and after three different EF tests: Delayed Matching of Sample (DMS) for measuring short-term memory, Spatial Working Memory (SWM) for measuring visuospatial working memory, and Multitasking Test (MTT). Since physical activity levels are known to influence HRV levels (Melo et al., 2005), the physical activity levels of individuals were also taken into consideration and their influence on autonomic parameters and EF task was also analyzed.

As per previous findings, it was hypothesized that individuals with high resting parasympathetic activity would have better EF performance (Colzato et al., 2018; Frewen et al., 2013; Hansen et al., 2003; Stenfors et al., 2016). As HRV declines with increasing age, we expected lower resting HRV in MA compared to YA (Abhishekh et al., 2013).

Interpretation of HRV during cognitive tasks and HRV reactivity is more challenging compared to the interpretation of HRV obtained at resting state as it depends on the task difficulty (Laborde et al., 2018). We assumed lower EF capacities in MA compared to YA, and thus a higher mental workload for MA compared to YA resulting in more sympathetic activation with respect to the high cognitive load (Mathewson et al., 2010). We also expected individuals with high physical activity levels will influence their HRV levels (Melo et al., 2005).

## Methodology

### Participants

One hundred forty-eight adults, 67 MA and 81 YA from Guru Nanak Dev University, voluntarily took part in the study. Advertisements posted on notice boards throughout the administrative and academic blocks invited volunteers for the study from those who were either studying, working, or living on the university campus. The inclusion criteria for recruiting the subjects were as follows: (a) participants in the age group of 40 to 60 years were included in the MA group; (b) participants in the age group of 21 to 30 years were included in the YA group; (c) participants who had completed formal education up to class 12; (d) participants who were able to understand the English language; (e) participants who scored above 26 on the Mini-Mental State Examination (MMSE); and (f) participants who were willing to volunteer for the study.

Subjects were excluded under the following criteria: (a) obesity [body mass index (BMI) > 30 kg/m2], (b) any known case of neurological and psychiatric diseases, (c) any terminal disease, or (d) alcohol abuse or dependence in the last 2 years.

Participants maintained a regular sleep cycle a day before the study and refrained from consuming stimulating substances or engaging in strenuous physical activity on the study day in order to participate. The experiment received the University Ethics Committee's approval and adhered to the moral guidelines outlined in the Declaration of Helsinki. Before the experiment began, participants read and signed an informed consent declaration. Additionally, they were made aware of their freedom to withdraw from the study at any point.

### Apparatus: Measurement of Executive Function With CANTAB

All participants were seated at a comfortable seat height and handed the CANTAB iPad (Cambridge Cognition, 2006) to carry out the EF test by placing responses on the touch screen. Each test began with practice items at a basic level.

***1. Delayed Matching of Sample (DMS)*** assesses both simultaneous and short-term visual memory. It is a four-choice recognition test of abstract patterns that share color or pattern with distractors. The outcome variables were (a) the percentage of total correct responses, which measures the total number of trials in which a correct selection was made in the subject's first response (DMSTC); (b) the percentage of correct responses (all delays), which reports the percentage of correct responses when the target and the distractors were presented after the stimulus had been hidden, with delays of 0 ms, 4000 ms, and 12000 ms (DMSTCAD); (c) the mean latency between the presentation of the response stimuli options and the subject selecting the correct box on their first attempt in simultaneous and all delays trials (DMSML); (d) the mean latency between the presentation of the response stimuli options and the subject selecting the correct box on trials containing a delay between target and response stimuli presentation (DMSMLAD); (e) the mean latency between the presentation of the response stimuli options and the subject selecting the correct box on their first attempt for trials containing a simultaneous presentation of target and response stimuli (DMSMLS); (f) the mean latency between the presentation of the response stimuli options and the subject selecting the correct box on their first attempt for trials containing a 12-s delay (DMSML12); and (g) the probability of an error occurring when the previous trial was responded to incorrectly (DMSPEGC).

***2. Spatial Working Memory (SWM)*** is a self-ordered search test that assesses nonverbal working memory. Participants were asked to search through several colored boxes presented on the screen to find yellow tokens hidden inside. Each box contained only one token per trial. With each stage, the number of colored boxes kept on increasing. Searching a box more than once during a sequence resulted in within errors, and returning to an emptied box resulted in between errors. A double error could be categorized as both a within and a between error. The key outcome variables included (a) the total number of times a box is selected that is certain not to contain a token and therefore should not have been visited by the subject (i.e., between errors + within errors − double errors), calculated across all assessed 4-, 6-, and 8-token trials (SWMTE); (b) the number of times the subject incorrectly revisits a box in which a token has previously been found,

calculated across all assessed 4-, 6-, and 8-token trials (SWMBE); (c) the number of times a box is selected that is certain not to contain a token and therefore should not have been visited by the subject in trials with 12 tokens (SWMTE12); (d) the number of times the subject revisits a box in which a token has previously been found in trials with 12 tokens (SWMBE12); (e) the strategy score for the 6-box stage of the task only, calculated based on the number of times a subject begins a new search pattern from the same box they started with previously (SWMS6); and (f) the strategy score calculated across assessed trials with 6 tokens or more (SWMSX).

***3. Multitasking Test (MTT)*** measures the participant's ability to use multiple sources of potentially conflicting information to guide behavior and to ignore task-irrelevant information, posing a Stroop-like effect. An arrow was presented on either the left or right side of the screen, indicating the side of the arrow, or the arrow can also point either left or right, indicating the direction of the arrow. A cue was given at the top of the screen before each trial to suggest whether the participant should press the direction of the arrow (in the first set of trials), followed by the side of the arrow (in the second set of trials) using two response pads located on the left and right sides of the bottom of the screen during the single task stage. In the multitask stage, the participant had to respond based on the cue presented at the top of the screen, which could either be the side of the arrow or the direction of the arrow. As the complexity of the task grew in contrast to a single task, the multitasking task imposed a higher cognitive demand. Furthermore, in the multitasking stage, some of the task trials exhibited congruent stimuli (e.g., the arrow on the left side is pointing to the left side of the screen) or incongruent stimuli (e.g., the arrow on the left side is pointing on the right side of the screen). The cognitive demands on incongruent trials were higher than on congruent ones. The major outcomes of this task were (a) the number of trials for which the outcome was a correct response (MTTC); (b) the mean latency of response calculated across all correct trials (MTTML); (c) the mean latency of response in assessed blocks in which both side and direction rules were used (MTTMLMT); (d) the mean latency of response in assessed blocks in which a single, either direction or side, rule was used (MTTMLST); (e) the mean latency of response in congruent trails on all assessed blocks (MTTMLC); (f) the mean latency of response in incongruent trials on all assessed blocks (MTTLNOM); (g) the difference between mean latency of response on the trails that were congruent versus the trails that were incongruent (MTTICOST); and (h) the difference between mean latency of response during assessed blocks in which both rules were used versus assessed blocks in which single rules were used (MTTMTCM).

### IPAQ questionnaire

The 27-item long-form IPAQ was used to measure domain-specific physical activity for each intensity group, including physical activity at work, home, during transit, during leisure, and for the duration of inactive hours. Adults from the Indian Subcontinent have also demonstrated modest construct validity and test–retest reliability for items of the modified IPAQ-LF (Wani & Nabi, 2020).

### Measurement of Heart Rate Variability

Participants were fitted with an EQ02 (Equivital EQ02, Hidalgo, U.K), a wearable Lycra sensor belt with a fitted pocket for a Bluetooth device measuring multiple physiological parameters such as heart rate, HRV, respiratory rate mean, ECG, and chest expansion mean. A polar wristwatch was also worn by the participants for measuring the saturation of oxygen (Sp02) levels. Data acquisition and postprocessing of the recorded data were conducted using the LabChart software. The processed data was further analyzed in another software, the Kubios HRV software (v.3.0.0, HRV analysis, University of Eastern Finland). It includes a modified algorithm for detecting QRS as well as tools for noise reduction, trend removal, and analysis sample selection (Brennan et al., 2001).

HRV indices obtained included mean RR interval, root mean square of the successive differences (RMSSD), standard deviations of RR intervals (SDNN index), and PNS index that evaluated the activity of the PNS. HRV indices for sympathetic activity included mean HR, SNS index, and stress index (SI) were the referred parameters. The PNS index computed in Kubios HRV software is based on Mean RR, RMSSD, and HF power; and the SNS index is based on the mean heart rate, SI, and LF power (Cakir et al., 2019). SI in the Kubios software is computed by calculating the square root of Baevskey's stress index formula. This formula was developed using a histogram based on the 50 ms interval mapping of the RR intervals to calculate the stress levels (Baevsky & Chernikova, 2017).

### Procedure

Participants were asked to sit down comfortably on a chair with closed eyes after the EQ02 wearable device to measure HRV was strapped on. A resting HRV was measured for a duration of 5 min. The

seated participants were then handed the CANTAB iPad to carry out the EF test by placing responses on a touch screen. Simultaneously, HRV data was recorded while each participant performed EF tests (DMS, SWM, and MTT). Further, recovery data of HRV for a span of 5 min was recorded, once all the EF tests were completed. At the beginning of each EF task, all the participants had a familiarization period. They received verbal video graphic instructions and, after that, each task incorporated a demonstration before the beginning of the task. The sequence of the cognitive task was kept random to avoid any bias in the performance of the tests.

The time duration of the start and end of each task was noted for further analysis of HRV. During the experiment, the participants were seated in a well-illuminated room and isolated from external noise. Comfortable temperature (17.9 ± 0.5 ˚C) and relative humidity (64.9 ± 6.75%) values were maintained throughout the experimental session.

### Statistical Analysis

A priori power analysis was conducted before the study (G*power), which estimated that the minimal sample size needed was 130 participants (effect size = 0.15, $\alpha$ err prob = 0.05, power 1−$\beta$ err prob = 0.90). Five participants were excluded during the time of analysis including two YA and two MA due to incomplete experimental procedure (four participants) and a data outlier (one participant).

HRV parameters were non-normally distributed, namely SDNN, RMSSD, and SI; therefore, they were converted into logarithmic values (lnRMSSD, lnSDNN, and lnSI, respectively). Pearson analysis and linear regression were used to investigate the possible correlations and interdependence with EF test scores as the outcome variable and resting HRV parameters as the predictor variable. EF scores were compared amongst participants with high HRV versus low HRV using a *t*-test. An independent *t*-test was also applied for the comparison of HRV indices according to age at rest, during EF tests, and during recovery. In order to analyze changes in HRV across each EF test and with its increasing complexity from the resting state, a repeated measure ANOVA analysis was performed. Therefore, recorded HRV data was taken at different time points (i.e., during resting state, during DMS, during SWM, during MTT-single task, during MTT-multitask task, and during recovery). A mixed model ANOVA design was performed to analyze interactions of independent variables in the study (i.e., age, the difficulty of task, and gender) on the dependent variable of HRV. A regression analysis was also applied to investigate EF test scores and HRV indices as the outcome variable and physical activity levels (IPAQ METS) as the predictor variable.

## Results

Out of 148 participants, 143 were suitable for analysis. Table 1 shows their descriptive characteristics.

**Table 1**
*Descriptive Statistics of the Population (N = 143)*

| | |
|---|---|
| Age group (years) | Middle aged adults (n = 65, mean age = 45.5 ± 5.3 years)<br>Young adults (n = 78, mean age = 24.1 ± 2.1 years) |
| Gender | Males (n = 69, mean age = 37.4 ± 13.2 years)<br>Females (n = 74, mean age = 33.2 ± 12.1 years) |
| IPAQ METS (MET/week) | Mean: 4813.8 ± 232.8<br>Minimum: 677<br>Maximum: 12552 |

### Relationship of EF Scores With Resting HRV

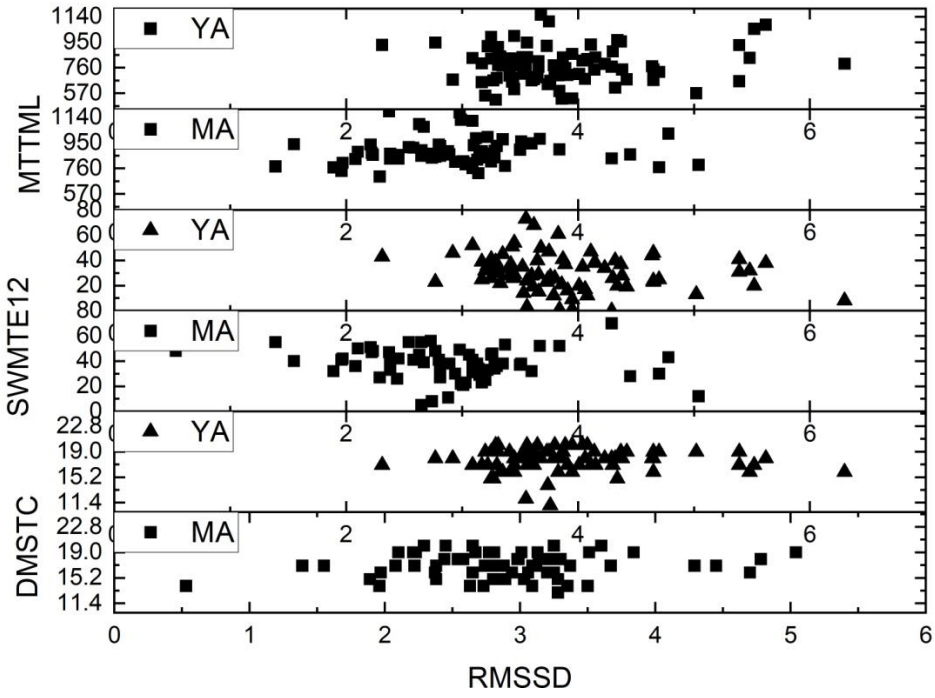
As multicollinearity was found in the parasympathetic indicators of HRV, we chose to represent only lnRMSSD. Logarithmic values of RMSSD were able to predict key parameters in EF tests. In the DMS task, regression trends were found in DMS correct score at $R^2$ = 0.03, $F(1,142)$ = 3.54, $p$ = .06. In the SWM task, SWM total errors at the 12-token stage at $R^2$ = 0.001, $F(1,142)$ = 13.16, $p$ < .001; and SWM between errors at the 12-token stage at $R^2$ = 0.001, $F(1,142)$ = 14.53, $p$ < .001. In the MTT task, overall reaction latency at $R^2$ = 0.007, $F(1,142)$ = 6.14, $p$ < .05; reaction latency during multitask at $R^2$ = 0.001, $F(1,142)$ = 9.39, $p$ < .05; reaction latency during the congruent task at $R^2$ = 0.006, $F(1,142)$ = 6.5, $p$ < .05; reaction latency during the incongruent task at $R^2$ = 0.011, $F(1,142)$ = 5.29, $p$ < .05 and multitasking cost at $R^2$ = 0.009, $F(1,142)$ = 5.78, $p$ < .05 (refer to Table 2, Figure 1).

**Table 2**
*Regression Analysis of Resting LnRMSSD as Predictor Variable (N = 143)*

| Outcome measure | Correlation Coefficient *R* | *p* value | Adjusted $R^2$ | Degree of freedoms | *F* stats | *p* value |
|---|---|---|---|---|---|---|
| DMS | | | | | | |
| DMSTC | 0.15 | .03* | 0.018 | (1,142) | 3.54 | .06* |
| DMSML | −0.07 | .21 | −0.002 | (1,142) | 0.67 | .41 |
| DMSMLAD | −0.06 | .21 | −0.003 | (1,142) | 0.61 | .43 |
| DMSMLS | −0.05 | .24 | −0.004 | (1,142) | 0.48 | .49 |
| DMSPEGC | −0.11 | .08 | 0.007 | (1,142) | 1.944 | .16 |
| SWM | | | | | | |
| SWMTE468 | −0.11 | .11 | 0.004 | (1,142) | 1.57 | .21 |
| SWMBE468 | −0.09 | .11 | 0.003 | (1,142) | 1.40 | .23 |
| SWMTE12 | −0.29 | .001** | 0.079 | (1,142) | 13.16 | .001** |
| SWMBE12 | −0.31 | .001** | 0.087 | (1,142) | 14.53 | .001** |
| SWMS | −0.07 | .18 | −0.001 | (1,142) | 0.79 | .37 |
| SWMSX | −0.10 | .11 | 0.003 | (1,142) | 1.48 | .22 |
| MTT | | | | | | |
| MTTC | 0.06 | .23 | −0.003 | (1,142) | 0.55 | .45 |
| MTTML | −0.20 | .007* | 0.035 | (1,142) | 6.14 | .014* |
| MTTMLMT | −0.25 | .001* | 0.050 | (1,142) | 9.39 | .003* |
| MTTMLST | −0.12 | .07 | 0.008 | (1,142) | 2.12 | .14 |
| MTTMLC | −0.21 | .006* | 0.037 | (1,142) | 6.50 | .012* |
| MTTLNOM | −0.19 | .011* | 0.029 | (1,142) | 5.29 | .023* |
| MTTICOST | 0.04 | .30 | −0.005 | (1,142) | 0.27 | .60 |
| MTTMTCM | −0.19 | .009* | 0.033 | (1,142) | 5.78 | .017* |

**Note.** Refer to Methodology section for explanation of acronyms; *$p < .05$; ** $p < .001$.

**Figure 1.** *Scatter Plot Demonstrating Key Parameters of EF Tests in Relation to Resting lnRMSSD Levels in YA And MA.*




Since lnRMSSD was able to predict EF scores, its median value was calculated to classify the population into high HRV versus low HRV group, and EF scores were compared similarly to a previous study (Hansen et al., 2003). A median value of 3.37 was obtained; the high HRV group was comprised of 67 individuals (8 MA, 59 YA), and the low HRV group was comprised of 76 individuals (57 MA, 19 YA). In comparison, it was found that the high HRV group performed significantly well in all EF tasks with more correct scores (DMSTC, $t$ = 2.1, $p$ < .05), lesser errors (SWMTE12, $t$ = −2.69, $p$ < .05; SWMBE12, $t$ = −3.24, $p$ < .05), and faster processing speed during the tasks (MTTML, $t$ = −3.88, $p$ < .001, MTTMLMT, $t$ = −4.35, $p$ < .001; MTTMLST, $t$ = −2.74, $p$ < .05; MTTMLC, $t$ = −3.81, $p$ < .001; MTTMLNOM, $t$ = −3.76, $p$ < .001 and MTTMTCM, $t$ = −2.52, $p$ < .05) in comparison to their counterparts with low HRV (refer to Table 3).

**Table 3**
*Comparison of EF Scores Between High HRV and Low HRV Adults*

| EF test parameters | High HRV ($n$ = 67) | Low HRV ($n$ = 76) | $t$ value | $p$ value |
|---|---|---|---|---|
| DMS | | | | |
| DMSTC | 17.6 ± 1.7 | 17.1 ± 1.8 | 2.1 | .037* |
| SWM | | | | |
| SWMTE12 | 30.4 ± 16.2 | 36.7 ± 10.7 | −2.69 | .008* |
| SWMBE12 | 27.6 ± 14.9 | 34.7 ± 10.3 | −3.24 | .002* |

**Table 3**
*Comparison of EF Scores Between High HRV and Low HRV Adults*

| EF test parameters | High HRV (*n* = 67) | Low HRV (*n* = 76) | *t* value | *p* value |
|---|---|---|---|---|
| MTT | | | | |
| MTTC | 151.2 ± 14.4 | 147.3 ± 18.5 | 1.39 | .16 |
| MTTML | 784.7 ± 134.1 | 868.5 ± 1622.6 | −3.88 | .001** |
| MTTMLMT | 876.2 ± 146.6 | 984.7 ± 150.9 | −4.35 | .001** |
| MTTMLST | 693.5 ± 139.2 | 754.6 ± 125.3 | −2.74 | .007* |
| MTTMLC | 762.8 ± 138.8 | 847.3 ± 123.8 | −3.81 | .001** |
| MTTLNOM | 806.6 ± 133.1 | 889.9 ± 131 | −3.76 | .001** |
| MTTMTCM | 182.7 ± 99.1 | 230.1 ± 126.4 | −2.52 | .013* |

**Note.** Mean, standard deviation, and *t*-test values of the high HRV and low HRV group; *$p$ < .05; ** $p$ < .001. Refer to Methodology section for explanation of acronyms.

### Changes in HRV During the EF Tests

The sympathetic activity was significantly high (lnSI, $t$ = 8.81, $p$ < .001; SNS index, $t$ = 4.71, $p$ < .001), and parasympathetic activity was significantly low in MA at resting (lnSDNN, $t$ = −7.41, $p$ < .001; lnRMSSD, $t$ = −7.97, $p$ < .001; PNS index, $t$ = −3.79, $p$ < .001) in comparison to YA. During EF tasks, sympathetic activity was raised in both groups but was higher in MA in comparison to YA, with the highest peak seen during MTT multitask. Significantly early recovery was observed in YA in comparison to MA with higher parasympathetic indicators (lnSDNN, $t$ = −5.93, $p$ < .001; lnRMSSD, $t$ = −6.96, $p$ < .001; PNS index, $t$ = −3.80, $p$ < .001).

As MTT multitask was found to be the most challenging task across the EF test, differences in percentage change of HRV parameters (resting value of HRV parameter − the value of HRV parameter during MTT multitask / resting value of HRV parameter) were also investigated. Mann Whitney U test was used for the comparison of percentage differences between MA and YA. It was found that the percentage change in stress index was significantly higher in YA in comparison to MA (refer to Table 4).

**Table 4**
*Difference in Percentage Change in HRV Indices in MA and YA*

| % Change | MA (*n* = 65) | YA (*n* = 78) | *p* value |
|---|---|---|---|
| lnSDNN | 0.015 ± 0.52 | 0.074 ± 0.19 | .72 |
| lnRMSSD | −0.078 ± 0.9 | 0.075 ± 0.17 | .98 |
| SI | −0.04 ± 0.16 | −0.17 ± 0.39 | .01* |
| PNS index | −0.34 ± 2.18 | 0.17 ± 2.84 | .30 |
| SNS index | −0.41 ± 1.7 | 0.17 ± 5.74 | .67 |

The repeated-measures ANOVA with the within-participants factors of EF tasks showed statistical significance reached in all HRV indices namely in RR interval, $F(1,141) = 29.9$, $p$ < .001, $\eta$ *partial*$^2$ = 0.17; mean HR, $F(1,141) = 21.9$, $p$ < .001, $\eta$ *partial*$^2$ = 0.13; lnSDNN, $F(1,141) = 9.12$, $p$ < .001, $\eta$ *partial*$^2$ = 0.06; lnRMSSD interval, $F(1,141) = 5.82$, $p$ < .001, $\eta$ *partial*$^2$ = 0.04; lnStress index, $F(1,141) = 18.5$, $p$ < .001, $\eta$ *partial*$^2$ = 0.11; PNS index, $F(1,141) = 15.53$, $p$ < .001, $\eta$ *partial*$^2$ = 0.09; SNS index, $F(1,141) = 27.2$, $p$ < .001, $\eta$ *partial*$^2$ = 0.16. All parasympathetic indexes showed the lowest values

in the MTT Multitask, all $p \leq .01$. All sympathetic indexes showed the highest values in the MTT Multitask, $p < .005$. The between-subject effects, as per age group, revealed significantly different HRV indices in response to the same EF tasks, lnSDNN, $F(1,141) = 78.9$, $p < .001$, $\eta\ partial^2 = 0.35$; lnRMSSD interval, $F(1,141) = 67.3$, $p < .001$, $\eta$ partial$^2 = 0.32$; lnStress index, $F(1,141) = 97.9$, $p < .001$, $\eta\ partial^2 = 0.41$; PNS index, $F(1,141) = 12.38$, $p < .001$, $\eta\ partial^2 = 0.8$; SNS index, $F(1,141) = 22.4$, $p < .001$, $\eta\ partial^2 = 0.13$. Parameters indicating sympathetic activity were found to be higher and parameters indicating parasympathetic activity were lower in MA in response to EF tasks (Refer to Table 5 and Figure 2).

**Table 5**
*Repeated Measure ANOVA Analysis*

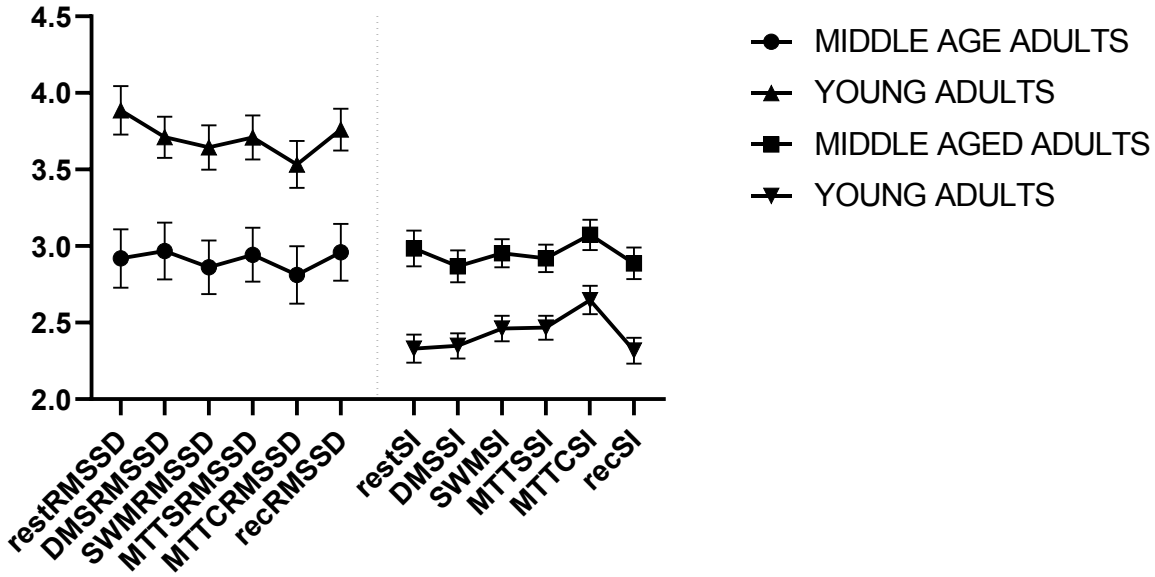
| HRV indices | Within subject's effect | Between subject's effect | Pair wise significance |
|---|---|---|---|
| RR interval | 29.91; (1,141); 0.001*; 17.5% | 2.23; (1,141); 0.13; 1% | Level 1 vs. Level 2<br>Level 1 vs. Level 3<br>Level 1 vs. Level 4<br>Level 1 vs. Level 5<br>Level 2 vs. Level 6<br>Level 3 vs. Level 5<br>Level 3 vs. Level 6<br>Level 4 vs. Level 5<br>Level 4 vs. Level 6<br>Level 5 vs. Level 6 |
| Mean HR | 21.91; (1,141); 0.001*; 13.5% | 1.43; (1,141); 0.23; 1% | Level 1 vs. Level 2<br>Level 1 vs. Level 5<br>Level 2 vs. Level 6<br>Level 3 vs. Level 5<br>Level 3 vs. Level 6<br>Level 4 vs. Level 5<br>Level 4 vs. Level 6<br>Level 5 vs. Level 6 |
| lnSDNN | 9.12; (1,141); 0.001*; 6.1% | 78.9; (1,141); 0.001*; 35% | Level 1 vs. Level 5<br>Level 2 vs. Level 5<br>Level 3 vs. Level 5<br>Level 4 vs. Level 5<br>Level 4 vs. Level 6<br>Level 5 vs. Level 6 |
| lnRMSSD | 5.82; (1,141); 0.001*; 4% | 67.37; (1,141); 0.001*; 32% | Level 1 vs. Level 5<br>Level 2 vs. Level 5<br>Level 4 vs. Level 5<br>Level 5 vs. Level 6 |

**Table 5**
*Repeated Measure ANOVA Analysis*

| HRV indices | Within subject's effect | Between subject's effect | Pair wise significance |
|---|---|---|---|
| lnSI | 18.59; (1,141); 0.001*; 11% | 97.96; (1,141); 0.001*; 41% | Level 1 vs. Level 5<br>Level 2 vs. Level 3<br>Level 2 vs. Level 4<br>Level 2 vs. Level 5<br>Level 3 vs. Level 5<br>Level 3 vs. Level 6<br>Level 4 vs. Level 5<br>Level 4 vs. Level 6<br>Level 5 vs. Level 6 |
| PNS INDEX | 15.53; (1,141); 0.001*; 9.9% | 12.38; (1,141); 0.001*; 8.1% | Level 1 vs. Level 2<br>Level 1 vs. Level 3<br>Level 1 vs. Level 4<br>Level 1 vs. Level 5<br>Level 2 vs. Level 6<br>Level 3 vs. Level 4<br>Level 3 vs. Level 6<br>Level 4 vs. Level 5<br>Level 5 vs. Level 6 |
| SNS INDEX | 27.23; (1,141); 0.001*; 16.2% | 22.44; (1,141); 0.001*; 13.7% | Level 1 vs. Level 5<br>Level 2 vs. Level 5<br>Level 2 vs. Level 6<br>Level 3 vs. Level 5<br>Level 3 vs. Level 6<br>Level 4 vs. Level 5<br>Level 4 vs. Level 6<br>Level 5 vs. Level 6 |

**Note.** Level 1: Resting; Level 2: DMS; Level 3: SWM; Level 4: MTT single task; Level 5: MTT multitask; Level 6: Recovery.

**Figure 2.** *Parasympathetic and Sympathetic Parameter Changes Across EF Tests.*




**Note.** Within subject difference in lnRMSSD values at $F(1,141) = 5.82$, 0.001* and between subject effects at $F(1,141) = 67.37$, 0.001*. Within subject difference in stress index at $F(1,141) = 18.59$, 0.001* and between subject effects at $F(1,141) = 97.96$, 0.001*.

Mixed model design ANOVA was applied to analyze changes in HRV with respect to age (MA and YA), the difficulty of condition (MTT single task and MTT multitask), and gender. It was found that lRMSSD was significantly low ($F = 75.3$, $p < .001$) and stress index was significantly high ($F = 90.2$, $p < .001$) in MA in comparison to YA with the MTT task. Parasympathetic activity indicated by lRMSSD and sympathetic activity indicated by Stress index were also inversely changed as the complexity of the task increased ($F = 4.01$, $p < .05$; $F = 14.2$, $p < .001$ respectively). It is interesting to note that gender differences were also visible where high parasympathetic activation in females during the MTT task ($F = 9.02$, $p < .05$).

### Association of Physical Activity Levels With EF and HRV

Physical activity levels were able to predict DMS correct score at $R^2 = 0.029$, $F(1,142) = 4.25$, $p = .04$ and MTT correct score at $R^2 = 0.021$, $F(1,142) = 3.09$, $p < .001$, however not in SWM task. In relation to resting HRV parameters, physical activity levels were correlated with mean RR, $r = 0.14$, $p = .04$ and mean HR, $r = -0.15$, $p = .03$. A correlation was also found with recovery HRV parameters, with mean RR, $r = 0.21$, $p = .004$ and mean HR, $r = -0.24$, $p = .002$. Regression analysis revealed physical activity levels predicted recovery HRV parameters namely mean RR at $R^2 = 0.048$, $F(1,142) = 7.04$, $p = .009$ and mean HR at $R^2 = 0.06$, $F(1,142) = 9.05$, $p = .003$.

## Discussion

The present study investigated the relationship between the autonomic function via short-term HRV assessment and executive performance via the administration of a neuropsychological test battery, CANTAB in MA and YA. In order to meet the broader aim, the study was further classified into three objectives: (a) association of EF task scores with resting HRV parameters; (b) analyzing HRV reactivity in response to three different EF tests: DMS for measuring short-term memory, SWM for measuring visuospatial working memory, and MTT; and (c) determining the role of physical activity in influencing autonomic function and EF of the adult population. In the forthcoming sections, we discuss each objective separately.

### Association of EF Task Scores With Resting HRV Parameters

It was found that individuals with higher resting parasympathetic indicator (i.e., RMSSD in the adult population) had better EF in comparison to their counterparts with lower parasympathetic tone. Individuals with lnRMSSD values ranging from 0.53

to 3.37 were considered lower parasympathetic activity, and those with higher values ranging above 3.37 to 6.3 were considered high parasympathetic activity. DMS correct score was higher, SWM errors, and reaction latencies during the MTT task were lower, indicating better EF performance in individuals with higher resting lRMSSD, a major indicator of parasympathetic activity. Our findings are supported by previous literature where higher RMSSD, a reflection of the vagal tone (Shaffer & Ginsberg, 2017), has been found to be associated with better cognitive performance (Hansen et al., 2003; Stenfors et al., 2016).

Studies have been conducted to find the relationship between HRV and memory functionality (Frewen et al., 2013; Gillie et al., 2014; Shah et al., 2011; Zeki Al Hazzouri et al., 2014). Although these studies have focused on long-term memory (Gillie et al., 2014) or verbal memory (Frewen et al., 2013; Shah et al., 2011). In the present study, the DMS task was used as a task which is specifically designed to challenge short-term memory at various levels of the task; spontaneously, immediate recall, at a 4-s delay after the abstract pattern is shown, and finally at a 12-s delay. We found that subjects with high HRV demonstrated better performance in short-term memory task with more correct scores at all levels tested.

The relationship between HRV and working memory, though investigated previously, has used different tasks by Hansen et al. (2003) and Frewen et al. (2013), with differing results in both. Hansen et al. (2003) showed an association of high HRV with correct responses in numerical-based working memory task, whereas Frewen et al. (2013) found no association in global cognitive function, comprising visuospatial function as one of the components. Our study differs from the previous studies in the fact that this is the first study to analyze the visuospatial component of working memory through SWM task. The task required the individual to search for hidden yellow tokens through several colored boxes, with the yellow token appearing in all the boxes once during the task, with the chances of committing an error increasing with each ascending stage (4-, 6-, 8-, and 12-token stage). It is intriguing to note that individuals with high HRV were able to demonstrate high visuospatial working memory in the advanced stage of the task (at the 12-token stage) with lesser errors in comparison to their counterparts with low HRV. Thus, it seems that the influence of HRV on measures of SWM may depend on the perception of the task difficulty with visuospatial tasks and numerical tasks requiring more composure for task performance.

During the performance of the MTT task, a computerized version of the spatial Stroop task (Sahakian et al., 1988), lower reaction latencies were exhibited by individuals with high HRV. A similar finding was reported by Mathewson et al. (2010), suggesting vagal cardiac control was associated with faster response times for a group of 81 healthy adults aged 17–55 performing pictorial Stroop task. Another cohort study conducted on middle-aged adults (CARDIA) demonstrated a significant correlation between higher quartile SDNN and improved EF and processing speed (Zeki Al Hazzouri et al., 2017). Mahinrad et al. (2016) found that individuals with lower HRV performed worse and saw a greater loss in processing speed, independent of cardiovascular risk factors and comorbidities, as part of the Prospective Study of Pravastatin in the Elderly at Risk.

Our findings propose that a higher resting parasympathetic state can ensure better EF performance even in MA despite the deteriorating effect of age seen previously (Hughes et al., 2018; Singh-Manoux et al., 2012). This notion can be validated by the results demonstrating 8 MA in the high HRV group performed significantly better in EF tasks in comparison to the low HRV group which also comprised 19 YA along with 57 MA. Conversely, studies have suggested that cardiovascular risk factors found in early to middle adulthood are associated with poor cognitive performance in midlife (Anstey et al., 2014; Yaffe et al., 2014). Therefore, it can be perceived that maintaining a high parasympathetic state during MA not only lowers the risk of cardiovascular morbidity and mortality but also contributes to better executive performance. Indulging in activities like physical activity and meditation can benefit middle-aged adults in achieving higher vagal tone and consequently improved executive functioning.

### HRV Reactivity in Response to EF Tests

Resting HRV in MA was found to be significantly poor in comparison to YA, proving our hypothesis. It is well established that a decrease in parasympathetic regulation over heart rate poses as a primary mechanism due to which age-related decline in autonomic function is seen (De Meersman & Stein, 2007; Umetani et al., 1998; Zhang, 2007). However, changes in sympathetic activity with age remain unclear (Byrne et al., 1996; Grässler, Dordevic, et al., 2021; Umetani et al., 1998). In the present study stress index, an indicator of

sympathetic activity, was found to be significantly higher in MA than in YA. The population of middle-aged individuals included in our study was mostly educated working class; hence, it is a possibility that they were in stress due to their jobs. Job stress has been linked to dementia and cognitive performance as well as CV risk factors and cardiovascular disease (Fishta & Backé, 2015; Jarczok et al., 2013, Theorell et al., 2016). Also, it has been discovered that midlife job stress is a strong predictor of cognitive performance (Andel et al., 2011; Stenfors et al., 2016).

An increase in sympathetic indicators (mean HR, stress index, and SNS) reflected autonomic responsiveness to the demands posed by the EF tests in both groups. These results are in coherence with the neurovisceral integration model proposed by Thayer et al. (2009) which state that both the EF and ANS indexed by HRV are under prefrontal cortical activity; hence, a sympathetic hyperactivation, with consequent prefrontal hypoactivation, would facilitate the disinhibition of the central nucleus of the amygdala (i.e., an adaptive response); the amygdala would promote a decrease in HRV and an increase in heart rate as shown in our study, with decreased HRV as the cognitive demands imposed by EF task increases.

Amongst the EF tests, HRV was the most reactive during the MTT task. Previous findings support performance-related reductions found in autonomic responsiveness in classic color Stroop paradigms (Boutcher & Boutcher, 2006; Delaney & Brodie, 2000; Wright et al., 2007) and pictorial strop task (Mathewson et al., 2010). However, a contradictory finding also exists (Hoshikawa & Yamamoto, 1997). This indicates that HRV does index some forms of executive effort, perhaps those that require assessing a rapid series of discrete stimuli while processing and responding in a speeded manner with a relatively high density of responses (Thayer et al., 2009), as in the case of MTT task in the present study. The remaining EF tests, DMS, and SWM were not a time-based task; therefore, the sympathetic activation was seen but not to higher extents. Byrd et al. (2015) proposed that slower, self-paced cognitive tasks involving multistep responses may require a form of executive functioning not indexed by HRV, which were the task characteristics of DMS and SWM in our study. This infers that HRV suppression is sensitive to a specific form of attentional control requiring vigilance to a rapid change course of stimuli not under the participant's control rather than a largely stationary stimulus where responding is under the participant's control.

MTT task was further classified into MTT single task and MTT multitask and, interestingly, within the task sympathetic activation was higher in response multitask stage in comparison to the single task stage. As task demands alter, HRV is significantly variable and responsive to cognitive processing (Luque-Casado et al., 2016). A novel finding of our study indicated females had better parasympathetic control as the difficulty of task increased in MTT. It is well established that females exhibit a higher vagal and a lower sympathetic modulation than men at resting levels (Agelink et al., 2001; Voss et al., 2015). However, demonstrating higher parasympathetic activity during the MTT task suggests that females were under less stress in handling multitasking stimuli in comparison to males. This maiden finding indicates further research on gender differences during executive performance focusing on all the domains.

It was fascinating to note that even though MTT multitask posed acute mental stress in both of the groups of the population, the percentage change in stress index levels of YA was higher (17%) in comparison to MA (4%). These results affirm the findings of Thayer et al. (2009), suggesting sympathetic activation in response to imposed cognitive demands. The lower percentage change in MA also gives an impression of the poor autonomic flexibility in them in response to higher demands.

### Role of Physical Activity in Influencing HRV and Executive Function

Adults with high levels of physical activity demonstrated higher HRV at resting and recovery HRV consistent with the previous literature (Albinet et al., 2010, 2016; Hansen et al., 2003). Association was also found between high levels of physical activity and DMS as well as MTT correct score. Physical activity is known to have a significant positive impact on cognitive function, and in particular EF (Daly et al., 2015; Liu-Ambrose et al., 2010). Since middle-aged population are at risk of declining EF and autonomic dysregulation as a function of age, poor autonomic function may develop due to stress (Dishman et al., 2000), depressive symptoms (Nahshoni et al., 2004), cardiovascular disease risk factors (Yaffe et al., 2014) such as type-2 diabetes (Carnethon et al., 2008), and hypertension (Singh et al., 1998), acting as a precursor to decline in EF abilities in later stages of life. Physical activity can be characterized as having a cardioprotective and brain-protective

role in accordance with previous literature (Albinet, Boucard, et al., 2010), and its adoption in middle age is highly recommended.

Limitations of the study include that the cross-sectional design of the study could not allow causal inferences in the longer stages of life between age-related change in autonomic cardiac adjustments and EF tests performance. The population of middle-aged adults included in the study were at clerical or academic posts in the university; hence, we did not anticipate the stress levels of the individuals which could be one of the limitations. Future studies are recommended to include scales to measure stress in the case of working adults.

In summary, the present study showed individuals with high HRV at rest perform well in executive performance, even in middle age. HRV reactivity was highest during the multitasking task in comparison to short-term memory and visuospatial memory abilities. Although middle-aged adults had high sympathetic activity at rest, young adults demonstrated higher sympathetic activation to imposed demands of multitasking and better task performance in comparison to the middle-aged with poor autonomic flexibility. High levels of physical activity might play a role in influencing HRV and consequently EF.

## Acknowledgements

The authors acknowledge the funding for the neuropsychological test battery used in the study under the NCSSR scheme of the Ministry of Youth Affairs and Sports, GOI.

## Author Declaration

The authors declare no conflict of interests. There is no funding to report.

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**Received:** April 24, 2023
**Accepted:** May 29, 2023
**Published:** June 29, 2023

NeuroRegulation

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# Brain Connectivity, Acute Post-Concussion Symptoms, and Cognition in Adults With Concussion: A Quantitative Electroencephalography Study

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**Abstract**

Mild traumatic brain injury (mTBI) accounts for 80–90% of all TBI. Post-mTBI symptoms are measured using the Post-Concussion Symptom Scale (PCSS); however, symptom heterogeneity limits specificity. Better understanding of the neuropathophysiology underlying post-concussion symptoms could enhance diagnostic accuracy. We explored the association between network connectivity, PCSS and neuropsychological functioning within 7 days post-mTBI. We hypothesized that network dysregulation would (a) correlate positively with PCSS scores and (b) correlate negatively with cognitive performance; and that (c) cognitive performance would correlate negatively with PCSS scores. Network activity was measured in 19 participants aged 21 to 65, following a medically diagnosed mTBI. Quantitative electroencephalography (qEEG) measured default mode, salience, and frontoparietal networks, while cognition was measured via neuropsychological assessment. Hypothesis (a) was not supported. Of the cognitive domains, support was only found for an association between network dysfunction and immediate memory. There was no association between neuropsychological performance and PCSS scores. PCSS scores were not a sensitive indicator of neuropsychological status and did not reflect the status of underlying brain network regulation. This study provides preliminary evidence for immediate memory as an indicator of altered network connectivity in acute mTBI. Evaluating neurophysiological and cognitive impacts of mTBI may improve understanding of individual recovery needs.

***Keywords***: default mode network; salience network; frontoparietal network; post-concussion symptoms; quantitative electroencephalography

**Citation**: Buhagiar, F., Fitzgerald, M., Hellewell, S. C., Bell, J., Moore, S., Gozt, A. K., Thorne, J., Thomas, E., Celenza, A., Xu, D., Robinson, S., Cowen, G., Bynevelt, M., Fatovich, D. M., & Pestell, C. F. (2023). Brain connectivity, acute post-concussion symptoms, and cognition in adults with concussion: A quantitative electroencephalography study. *NeuroRegulation, 10*(2), 94–117. https://doi.org/10.15540/nr.10.2.94

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## Introduction

An estimated 99 to 275 out of 100,000 (incidence) Australians suffer a traumatic brain injury (TBI; James et al., 2019; Pozzato et al., 2019). On a global level, incidence rates range from 331 to 412 per 100,000 (James et al., 2019). Mild traumatic brain injury (mTBI) makes up 80–90% of all traumatic brain injuries (Gardner & Yaffe, 2015; Jungfer, 2017), with an incidence of mTBI in people aged 16 to 59 years reported to be 302 per 100,000 person-years (Skandsen et al., 2019). The terms concussion and mTBI are often used interchangeably (Patricios et al., 2023). While some suggest that concussion is a less severe type of mTBI, others do not differentiate between the two terms (Mayer, Quinn, et al., 2017). The position statement on concussion in sport by the American Medical Society for Sports Medicine (Harmon et al., 2019) described concussion as a "traumatically induced transient disturbance of brain function that involved a complex pathophysiological process." Importantly, mTBI can result in diffuse axonal injury and disruption of the long white matter tracts, which connect various regions within brain networks resulting in alterations in function (Bai et al., 2022). The types of events resulting in mTBI include sports injuries, cycling accidents, assaults, falls, and motor vehicle accidents (Jagnoor & Cameron, 2014; Langer et al., 2020). The different mechanisms of injury have common biomechanical forces including linear and rotational acceleration (Rowson et al., 2016), with rotational forces being more likely to cause diffuse axonal injury (Gennarelli, 1971; Zhang et al., 2006). Individuals with diffuse axonal injury are three times more likely to have unfavorable outcome, than those with focal brain injuries (van Eijck et al., 2018).

Symptoms experienced following mTBI include anxiety/mood, cognitive, headache/migraines, vestibular, ocular, and fatigue (Harmon et al., 2019). While symptoms in adults last 2 weeks on average, up to 50% experience persistent post-concussion symptoms (PPCS) beyond the expected 2-week timeframe [17–19 (L. J. Carroll et al., 2014; de Freitas Cardoso et al., 2019; McInnes et al., 2017; Rivara & Graham, 2014)]. Studies have reported that 50% of participants experienced cognitive dysfunction at 3 months postinjury (Theadom et al., 2016), with deficits in executive function, working memory, and memory recall seen up to 24 months post-mTBI (Bai et al., 2022; Bedard et al., 2020; E. L. Carroll et al., 2020; de Freitas Cardoso et al., 2019). Individuals with higher PPCS scores display poorer cognitive performance compared to those with lower PPCS scores (Custer et al., 2016). A complex array of pre- and postinjury biopsychosocial factors influence an individual's post-concussion experience, such as personality characteristics, preexisting psychological disorders, and individual coping strategies (Young, 2020). Postinjury interventions such as rest versus exercise have also been debated (Allen, 2022; Liotta, 2021), with emerging research suggesting that physical activity modulates brain network activity and overall brain health (Dorsman et al., 2020; McFadden et al., 2013; Schmitt et al., 2019).

### Network Connectivity

As the knowledge of mTBI pathophysiology develops, there is an emerging understanding that the post-mTBI phenomena are best reframed as a disorder of dysfunctional brain networks (Hayes et al., 2016; Iverson, 2019). In fact, altered network connectivity within the brain has been linked to cognitive function and overall symptom severity following mTBI (Bai et al., 2022; D'Souza et al., 2020), making it a potentially contributing neurophysiological factor to the PPCS phenomenon. Post-concussion symptoms have been associated with altered activity within the salience network (SN), the default mode network (DMN), and the frontoparietal network (FPN) following mTBI (Bonnelle, Leech, et al., 2011; Ham et al., 2014; Han et al., 2016; Jilka et al., 2014; Mayer, Mannell, et al., 2011; Messé et al., 2013; Sharp, Beckmann, et al., 2011; Shumskaya et al., 2012; Sours et al., 2015; Sponheim et al., 2011; Stevens et al., 2012; Tang et al., 2011; Zhou, Lui, et al., 2014; Zhou, Milham, et al., 2012). The DMN plays a central role in focusing our thoughts internally, being inhibited when shifting attention externally, and the network is active at rest (Hayes et al., 2016). Hence, understanding network connectivity post-mTBI may inform the brain–behavior relationship and help with contextualizing symptoms.

### Measuring Network Function

Functional magnetic resonance imaging (fMRI) and diffusion weighted imaging (DWI) are typically used to measure brain network function in a research setting (Mortaheb et al., 2021; Pavlovic et al., 2019). Both these methods are costly and highly technical, limiting accessibility to functional neurophysiological assessment for the general population. Quantitative electroencephalography (qEEG) is a cheaper, less invasive, more portable, and accessible neuroimaging option, offering better temporal resolution than fMRI. Brain biomarkers detected using qEEG such as coherence, amplitude, and power, have been correlated with MRI findings in

TBI, stroke and tumor populations, demonstrating its potential utility as a measure of brain function (Thatcher, Biver, et al., 1998a, 1998b; Thatcher, North, et al., 2001). In mTBI, coherence, phase, and amplitude asymmetry measures using qEEG differentiated controls from mTBI with 95% accuracy (Thatcher, North, et al., 2001). Additionally, this increased brain dysfunction was associated with reduced cognitive performance on measures of verbal comprehension, visuospatial processing, processing speed, object naming, word fluency, inhibition/switching, and visual and verbal memory recall in a sample of mild to severe TBI participants (Thatcher, North, et al., 2001). Decreased coordination of neural functioning within the frontal regions on qEEG have also been observed following blast-related mTBI (Sponheim et al., 2011).

Hence, altered qEEG measures like phase, coherence, and amplitude asymmetry (current source density [CSD]) within specific brain regions (e.g., the frontal lobe) have shown diagnostic and prognostic utility in mTBI (Haneef et al., 2013; Thatcher, North, et al., 2001). While phase difference (PD) refers to the temporal synchrony of electrical activation between two brain areas, indicating the data transfer efficiency within a neuron cluster (Fell & Axmacher, 2011; Rabinovich et al., 2012), coherence refers to the degree of EEG frequency correlation between two electrodes, reflecting the activity similarity in the underlying brain areas, quantifying the level of connectivity between the areas of interest (Haneef et al., 2013). Lagged coherence (LC) addresses the impact of volume conduction present with instantaneous coherence (IC; Milz et al., 2014). Although qEEG has been validated as a functional measure for mTBI, its utility for measuring network function post-mTBI remains limited, with one study demonstrating that functional connections detected by qEEG were comparable with DWI findings in mTBI (Sponheim et al., 2011). Research has demonstrated that the integration of brain function occurs at a global level via networks of neurons rather than within a single localized area (Luria, 1973; Mesulam, 2000), highlighting the importance of assessing the brain's global and integrated functions within distinct networks rather than individualized areas of function. Considering that mTBI results in stretching and shearing of the axonal and vascular structures, including disruption of white matter tracts (McKee & Daneshvar, 2015; Mito et al., 2022; Narayana, 2017; Pavlovic et al., 2019), measuring network activity post-mTBI is important to determine whether global, higher order, integrated brain functioning has been impacted.

## Quantifying Post-Concussion Sequelae

Post-mTBI symptoms are often measured using a questionnaire such as the Post-Concussion Symptom Scale (PCSS; Lovell et al., 2006). While the PCSS is a valid and reliable measure (Lovell et al., 2006; McLeod & Leach, 2012), the heterogeneity of post-mTBI symptoms offers limited specificity for diagnostic purposes. For example, 45% of a very large sample ($n$ = 11,759) drawn from the general population met the criteria for PPCS in one European study (Voormolen et al., 2019). While the cognitive status of the individuals was not specified, the level of education varied from primary school to college or university level education. Improving our understanding of the neurophysiology underlying post-concussion symptoms is one way to enhance diagnostic specificity, by considering not only clinical presentation or symptom ratings but also an individual's neurophysiological status. The pathophysiology of mTBI has been described as a complex interaction of events caused by both primary and secondary damage, resulting in structural as well as functional changes (Masel & DeWitt, 2010; Young, 2020). Primary damage refers to damage that has occurred at the time of injury, while secondary damage refers to pathophysiology evolving days or even months postinjury (Pavlovic et al., 2019). In fact, changes in brain activity have been observed after mTBI, even when the clinical symptoms have resolved, suggesting that the absence of symptoms is not synonymous with recovery (Barr et al., 2012; McCrea et al., 2010; Prichep et al., 2013).

The present study aimed to measure the association between brain network connectivity, acute PCSS scores, and cognition (processing speed, inhibition/switching, immediate memory, visuospatial/constructional, language, attention, and delayed memory) in Australian adults within 7 days after mTBI. It was hypothesized that network dysregulation (DMN, SN, and FPN) would be (a) positively correlated with acute PCSS scores and (b) negatively correlated with cognitive performance as measured on neuropsychological tests. Additionally, it was hypothesized that (c) cognitive performance would be negatively correlated with PCSS scores. To the best of our knowledge, this study is the first to investigate the utility of measuring network function using qEEG in the acute stages post-mTBI and as such, serves as an initial pilot study of this novel approach in an mTBI sample.

## Materials and Methods

### Participants

Participants were drawn from the larger ongoing CREST study (Gozt et al., 2021), where all Phase II participants with qEEG and neuropsychological data available at the time of this study were selected for inclusion. Ethics approval was provided by the Human Research Ethics committees of St. John of God Health Care (#1628), Curtin University (HRE2019-0209), Royal Perth Hospital (#RGS0000003024), and Ramsay Health Care (#2009). Participants had received a medical diagnosis of concussion (< 24 hr posttraumatic amnesia, < 30 min loss of consciousness; Gumm et al., 2011) and were assessed within 7 days of injury ($M$ = 4.22, $SD$ = 1.26). Data were collected from 19 participants (10 females), aged between 21 and 65 years with an average of 13.5 years of education. Participation was voluntary, and participants were remunerated for parking costs if applicable. Written informed consent to participate in the study was obtained from all participants.

### Procedure

Participants were recruited from several emergency departments, medical and allied health practitioners, as well as sporting clubs and self-referral across Perth, Western Australia. All participants were required to have a medical diagnosis of concussion. A phone interview (Phase I) was conducted with all participants, and those who met eligibility criteria were invited to attend a face-to-face assessment (Phase II) within 7 days of injury. Phase II inclusion criteria included participants being willing and able to attend the Curtin University and Perron Institute for Neurological and Translational Sciences research tenancies located at the Ralph and Patricia Sarich Neuroscience Research Institute within 7 days of injury, and Sir Charles Gardiner Hospital for MRI within 9 days of injury (a leeway of an additional 2 days was required for the fMRI component, due to the hospital-based MRI scanner having limited availability in the context of a global COVID-19 pandemic). Inclusion criteria for Phase I and exclusion criteria for Phase I and Phase II are details in Gozt et al. (2021).

The Phase II assessment was 2.5 to 3 hr in duration and included qEEG, blood analysis, neuropsychological assessment, exercise tolerance testing, as well as vestibular/oculomotor testing. Eligible participants also had a brain MRI scan within 9 days following their mTBI. This study focused only on the qEEG and components of the neuropsychological measures at Phase II; more details regarding participant recruitment and assessment procedures for the wider CREST study are available in Gozt et al. (2021). Data from other outcomes will be presented at a later date.

### Materials

Connectivity within the DMN, SN, and FPN was measured using resting-state qEEG. EEG recording (resting-state, eyes-closed condition) was acquired via a 19-channel Electro-cap (Electro-cap International Inc., n.d.) and a MITSAR-EEG-BT amplifier (Mitsar, Ltd., n.d.). Quantitative analysis was performed via NeuroGuide and NeuroNavigator software (Applied Neuroscience, Inc., 2023), which have been previously validated in an mTBI population (Rapp et al., 2015; Thatcher, North, et al., 2001). Scalp recording of the EEG signals was conducted using a 19-channel Electro-cap with standardized 10–20 placement, which was fitted for size according to head circumference. Preparation for each electrode included parting of the hair and insertion of Electro-Gel electroconductive gel. A linked-ears montage was used to record activity from all 19 electrodes, using a sampling rate of 500 Hz, with impedance < 10 kΩ and a low pass filter of 50 Hz. Both eyes-open and eyes-closed data were obtained in a resting state, recording 5 min for each condition, with an eye mask used for the eyes-closed condition, to reduce eye-movement artefact. A minimum of 1 min of artifact-free data from the eyes-closed recording was selected via NeuroGuide software, which also accounted for drowsiness. Low resolution electromagnetic tomography analysis (LORETA) via the NeuroNavigator software, was used for source localization to detect altered network activity. NeuroNavigator has been described as a

> 3-Dimensional Electrical Neuroimaging tool [that] uses a real-MRI with 12,270 voxels; the Boundary Element Method (to compute the inverse solution to avoid the errors inherent in the use of a spherical head model, allowing for more accurate source localization at depths); and swLORETA (standardized weighted LORETA; adjusts for source space inhomogeneity and provides accurate estimates of source gradients from the upper to the lower cortical layers). (Applied Neuroscience Inc., 2023)

Research has supported the use of sLORETA to localize brain activity changes to fMRI (Cannon et al., 2011; Kerasidis & Simmons, 2021; Vitacco et al., 2002). Participants' activity was quantified in deviation from the normal ($z$ score), by comparison

to a sex and age-matched normative database (*N* = 727; information about the normative database is available in Thatcher, Walker, et al., 2003). The component Brodmann areas (BA; Brodmann, 1909) for all three networks were automatically selected by the software program (DMN: bilateral BA 2, 7, 10, 11, 19, 29, 30, 31, 35, 39, 40; SN: bilateral BA 8, 9, 10, 13, 22, 23, 24, 25, 29, 30, 31, 32, 33; FPN: bilateral BA 1, 2, 3, 5, 7, 8, 9, 10, 39, 40, 45, 46). For clarification, the Brodmann areas were a topical reference of the software's source localization, the network nodes were not selected based on predetermined Brodmann areas, but rather the Brodmann area was provided as a reference point for the localization of the network.

The level of network function was denoted by *z* scores (i.e., the amount of activity in standard deviations as compared to a normative database), for a spectrum of frequencies ranging from 1 to 30 Hz. Measures included CSD for individual Brodmann areas as well as IC, LC, and PD to represent the degree of connectivity between Brodmann area pairs, within the networks of interest. CSD was measured in microamperes squared per cycle/second, while IC and LC were measured as correlation coefficients, with numbers approaching 1 representing higher similarity (coherence) between the signals. PD was estimated by calculating the instantaneous PD between time series and ranged from 0 to ±180 degrees. The measures of coherence, phase, and CSD were found to differentiate between mTBI and controls in previous research (Thatcher, North, et al., 2001); hence, a correlation with PCSS scores was expected on all four measures. Five separate measures were calculated for each network, including the peak *z* score, mean *z* score, *z* score variance, total number of *z* scores above ±1.96, and the percentage of *z* scores above ±1.96. Activity ranging between *z* scores of 0 and ±1.96 was considered normal, while *z* scores greater than ±1.96 were considered significantly altered (deviated from the norm). With regards to the five levels of each measure (peak *z*, mean *z*, *z* variance, number of *z* scores above ±1.96, percentage of *z* scores above ±1.96), peak *z* score was used as per previous literature (Ims, 2019). The remaining measures were used to capture several elements of the network dysregulation (if present). Based on the standard normal curve cut-off for significant deviation from the normal, 1.96 was selected. We intended to capture not only how many areas were dysregulated, but also what percentage of the network they equate to (as not all networks had the same number of sites). The focus of the present study was on dysregulated activity, regardless of whether it was hypoactive (negative *z* score) or hyperactive (positive *z* score). A topographical representation of network dysregulation can be seen in Figure 1, where the degree of dysregulated activity is represented by colors on a spectrum of *z* scores.

### Post-Concussion Symptoms (PCS)

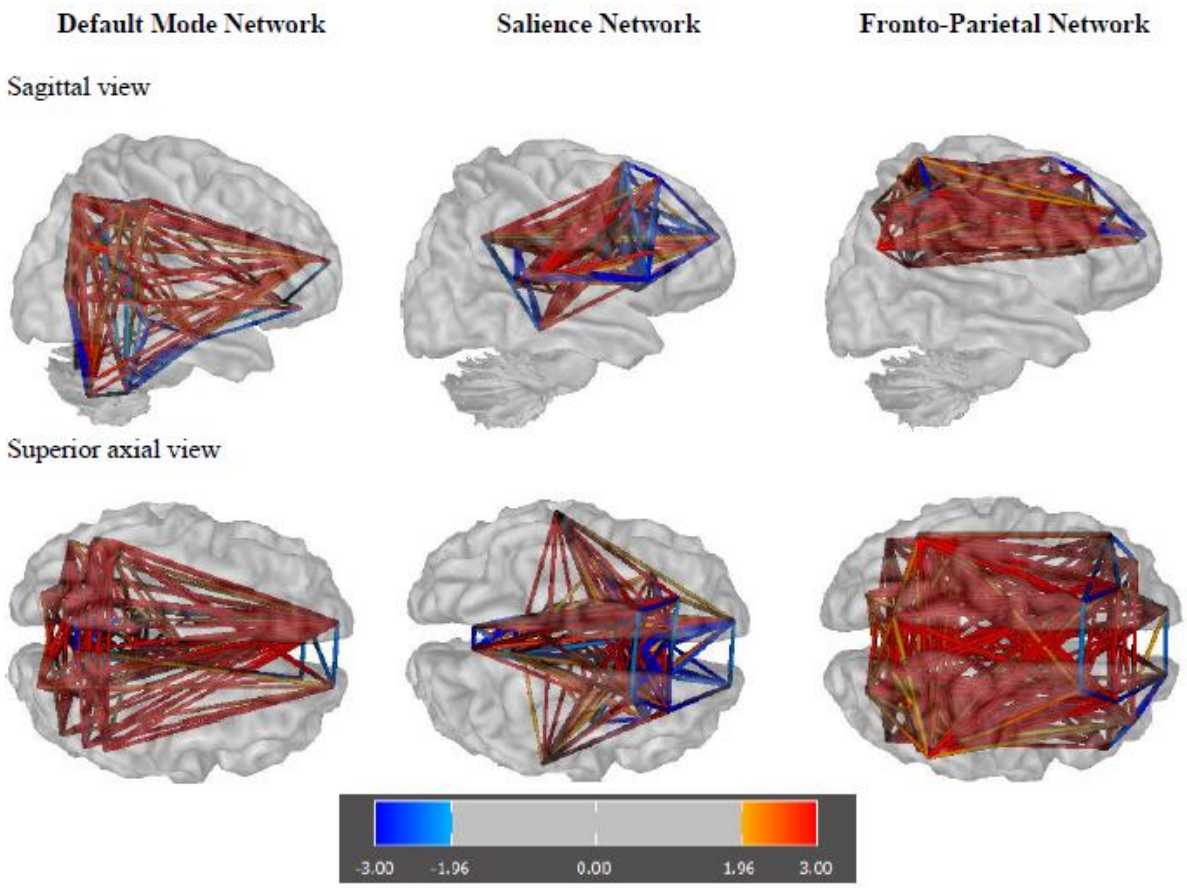
The PCSS (Lovell et al., 2006) consists of 22 self-report items used to assess symptom severity after concussion. Symptoms were rated on a Likert scale from 0 (*none*) to 6 (*severe*), where higher PCSS total symptom scores indicated an increased symptom burden. The cognitive, physical, affective, and sleep symptom domains were also analyzed using a factor structure established in a concussed adult sample (Merritt et al., 2017). The test–retest reliability of the PCSS measured as part of the ImPACT (Immediate Post-Concussion Assessment and Cognitive Testing) neuropsychological battery was 0.81 (Schatz & Ferris, 2013).

### Cognitive Function

***Processing Speed and Inhibition/Switching***. The Trail Making Test (TMT) part A and B (Reitan & Wolfson, 1985) were used. TMT-A required participants to sequentially connect numbers on a page, while TMT-B required a similar sequential procedure while switching between numbers and letters (e.g., 1-A, 2-B, etc.). The raw scores (time to complete the task) were converted to *z* scores using the normative sample detailed in Tombaugh (Tombaugh, 2004) for data analysis, where a higher positive *z* score indicated faster task completion. Test-retest reliability was found to be adequate (0.70) for TMT-A and TMT-B (Levine et al., 2004), and predictive validity for psychosocial outcomes following head injury was also noted (Colantonio et al., 2000).

***Overall Neuropsychological Function***. The Repeatable Battery for the Assessment of Neuropsychological Status Update (RBANS) (Randolph, 2012) was used. It was selected due to its utility in assessing a broad range of relevant cognitive domains that have been identified to be impacted following mTBI, while remaining brief to administer.

**Figure 1**. *Topographical Representation of Dysregulated Network Connectivity, in NeuroNavigator.*




**Note.** The occipital lobe is located on the left side of all images. Individual lines represent altered connectivity within a network. The degree of deviation from the norm is indicated by the color scale on the *z* score color spectrum. These images represent partial networks only, since normal (or unaltered) connections are not depicted. Data displayed above is from a single participant with mTBI.

Moreover, it provided an embedded measure of effort which was determined to be an important factor in mTBI research (Young, 2020). The RBANS consisted of five subscales including immediate memory, visuospatial/constructional, language, attention, and delayed memory. An index score was obtained for each of the subscales, and these were summed up to give a composite total score. Higher scores indicated better cognitive function. The RBANS total index score was found to have high specificity (0.94) and sensitivity (0.82) in a traumatic brain injury sample (McKay et al., 2008).

***Effort***. The Rey 15-Item Test (FIT; Rey, 1964) was used to measure performance validity. Participants were asked to recall 15 items. One point was awarded for each correct item (maximum = 15 points), where scores of 9 or higher demonstrated adequate effort. The FIT has been found to have a specificity of 85% (Reznek, 2005). Additionally, the RBANS effort index was calculated as described in Silverberg et al. (2007).

## Design and Statistical Analysis

An observational cross-sectional study design was used. For the first hypothesis, the dependent variable was network function with three levels: DMN, SN, and FPN. For each network the functional connectivity was characterized by five measures including peak *z* score, mean *z* score, *z* score variance, total number of *z* scores above ±1.96, and the percentage of *z* scores above ±1.96 across IC, LC, and PD. The independent variable was PCSS score with five levels, total score and four symptom domain scores: cognitive, physical, affective, and sleep. Pearson product moment correlation and Spearman's rank-order correlation were used to

measure the correlation between brain dysregulation and PCSS scores.

For the second hypothesis, the dependent variable was network function with three levels as described for the first hypothesis. The independent variables included six cognitive index scores from the RBANS (total index score, immediate memory, visuospatial/constructional, language, attention, and delayed memory), as well as the *z* scores for TMT-A and TMT-B. Spearman's rank-order correlation were used to measure the correlation between brain network function and cognitive function.

For the third hypothesis, the dependent variables included six cognitive index scores from the RBANS (total index score, immediate memory, visuospatial/constructional, language, attention, and delayed memory), as well as the *z* scores for TMT-A and TMT-B. The independent variable was PCSS score with five levels, total score and four symptom domain scores: cognitive, physical, affective, and sleep. Pearson product moment correlation and Spearman's rank-order correlation were used to measure the correlation between cognitive function and PCSS scores.

The Benjamini-Hochberg method was used to correct for multiple comparisons as described in the relevant results sections below.

## Results

### Network Connectivity and Post-Concussion Symptoms

To test the hypothesis that network (DMN, SN, FPN) dysregulation (as measured by qEEG) would be positively correlated with PCSS scores in the acute post-concussion phase, analyses were conducted on 19 participants. Of the 60 network function variables, 6 were normally distributed; however, the assumptions of linearity and homoscedasticity were not met, so nonparametric analysis was conducted on all measures. Eighty-four outliers were detected (> 3 standard deviations from the mean) and winsorized (Field, 2013).

### Demographic Characteristics

Table 1 shows the descriptive statistics for demographic variables including concussion injury characteristics, medical, and health history. Of note, none of the participants had a history of epilepsy/seizure disorder or non-migraine-type headaches, 47.4% were taking at least one medication (asthma medication, *n* = 4; antidepressants, *n* = 2; antihypertensives, *n* = 1; hormone therapy, *n* = 2; paracetamol, *n* = 1; melatonin, *n* = 1; thyroxine, *n* = 2; hair loss medication, *n* = 1; dexamphetamines, *n* = 1), and 89.5% of participants exercised regularly (2.88 days per week on average). Only one participant had legal involvement relating to their concussion. Of the 19 participants, 63.2% had a sport-related injury and 57.9% sustained additional physical injuries at the time of their concussion. While only 21.1% reported experiencing loss of consciousness ranging from 3 s to 10 min (31.6% were unsure), 57.9% experienced posttraumatic amnesia (ranging from < 5 min to > 120 min). Just over half the participants (52.6%) had one or more previous concussions, and 26.3% reported they were under the influence of alcohol at the time of injury.

### Network Connectivity and Post-Concussion Symptoms

To assess the size and direction of the linear relationship between brain network dysregulation and PCSS, a Spearman's rank-order correlation was conducted for all network connectivity measures as listed in Table 2. No significant correlations were found between network dysregulation and total PCSS score.

### Network Connectivity and Post-Concussion Symptom Domains

To further explore the relationship between brain network dysregulation and PCSS symptom domains (cognitive, physical, affective, sleep), Spearman's rank-order correlation was conducted for all network connectivity measures as listed in Table 3. After one outlier was detected and winsorized (Field, 2013), only the cognitive symptom domain was normally distributed. Since the assumptions of linearity and homoscedasticity were not met, nonparametric analyses were conducted for all variables. A significant correlation was found between the SN and the PCSS affective symptom domain; however, this correlation did not remain significant after Benjamini-Hochberg correction for multiple comparisons.

### Network Connectivity and Cognitive Function

To test the hypothesis that altered network connectivity would be associated with cognitive performance (measured by a neuropsychological battery) in the acute post-concussion phase, Spearman's rank order correlation was conducted. Three outliers were detected within the cognitive variables and winsorized (Field, 2013), being three or more standard deviations away from the mean. Assumption testing revealed that the variables which were normally distributed did not meet the

assumptions of linearity or homoscedasticity, so nonparametric analyses were used. Table 4 shows that DMN and FPN connectivity as well as DMN, SN and FPN CSD were significantly correlated with the RBANS immediate memory index. There was also a significant correlation between DMN and SN network connectivity and the TMT-A; however, this did not remain significant after correcting for multiple comparisons using the Benjamini-Hochberg method.

**Table 1**

*Descriptive Statistics for Demographic Variables and Injury Characteristics*

| | *% (n)* | *M* | *SD* |
|---|---|---|---|
| Age (years) | 100 (19) | 34.26 | 12.45 |
| Education (years) | 100 (19) | 13.47 | 2.20 |
| Sex | | | |
| Male | 47 (9) | | |
| Female | 53 (10) | | |
| Time Since Concussion Injury (days) | 100 (19) | 4.22 | 1.26 |
| Exercise Days Per Week | 100 (19) | 2.88 | 0.93 |
| Number of Alcohol Drinks at Time of Injury | 100 (19) | 3.50 | 2.45 |
| | Yes | No | Unsure |
| | % *(n)* | % *(n)* | % *(n)* |
| Mechanism of Injury (Sport-related) | 63.2 (12) | 36.8 (7) | |
| Loss of Consciousness (< 30 min) | 21.1 (4) | 47.7 (9) | 31.6 (6) |
| Posttraumatic Amnesia (< 24 hr) | 57.9 (11) | 42.1 (8) | |
| Alcohol at Time of Injury | 26.3 (5) | 73.7 (14) | |
| Other Injuries at Time of Concussion | 57.9 (11) | 42.1 (8) | |
| Previous Concussions | 52.6 (10) | 47.4 (9) | |
| Epilepsy/Seizure Disorder | | 100 (19) | |
| Migraine | 21.1 (4) | 78.9 (15) | |
| Other Headaches | | 100 (19) | |
| Mental Health Disorder | 31.6 (6) | 68.4 (13) | |
| Sleep Disorder | 10.5 (2) | 89.5 (17) | |
| Learning Disorder | 15.8 (3) | 84.2 (16) | |
| Regular Exercise | 89.5 (17) | 10.5 (2) | |
| Medications | 47.4 (9) | 52.6 (10) | |
| Legal Involvement | 5.3 (1) | 94.7 (18) | |

**Note.** The participants listed in the No category for Loss of Consciousness ($n$ = 9) did not experience loss of consciousness. Overall, participants who reported > 30 min of loss of consciousness and > 24 hr of posttraumatic amnesia were excluded from the study.

**Table 2**

*Spearman's Rank-Order Correlation Between Network Connectivity and PCSS Scores, N = 19*

| Network Connectivity Measures | Descriptive Statistics | | Spearman's Correlation | |
|---|---|---|---|---|
| | *M* | *SD* | *r* | *p* |
| DMN IC Peak *Z* score | 4.81 | 1.89 | −0.060 | 0.808 |
| DMN IC Mean *Z* Score | 0.84 | 0.27 | 0.101 | 0.681 |
| DMN IC *Z* Score Variance Within Network | 0.40 | 0.22 | 0.075 | 0.759 |
| DMN IC Number of *Z* scores > 1.96 *SD* | 485.32 | 540.95 | 0.090 | 0.713 |
| DMN IC Percentage *Z* scores > 1.96 *SD* | 7.00 | 7.81 | 0.090 | 0.713 |
| SN IC Peak *Z* Score | 5.02 | 2.53 | −0.185 | 0.449 |
| SN IC Mean *Z* Score | 0.89 | 0.29 | −0.023 | 0.927 |
| SN IC *Z* Score Variance Within Network | 0.47 | 0.29 | −0.022 | 0.930 |
| SN IC Number of *Z* scores > 1.96 *SD* | 846.53 | 923.99 | −0.009 | 0.970 |
| SN IC Percentage *Z* scores > 1.96 *SD* | 8.68 | 9.48 | −0.009 | 0.970 |
| FPN IC Peak *Z* Score | 5.28 | 2.36 | 0.044 | 0.857 |
| FPN IC Mean *Z* Score | 0.83 | 0.24 | 0.146 | 0.550 |
| FPN IC *Z* Score Variance Within Network | 0.48 | 0.30 | 0.107 | 0.663 |
| FPN IC Number of *Z* scores > 1.96 *SD* | 594.11 | 592.77 | 0.102 | 0.679 |
| FPN IC Percentage *Z* scores > 1.96 *SD* | 7.18 | 7.16 | 0.102 | 0.679 |
| DMN LC Peak *Z* Score | 4.22 | 2.21 | −0.178 | 0.465 |
| DMN LC Mean *Z* Score | 0.73 | 0.19 | 0.166 | 0.497 |
| DMN LC *Z* Score Variance Within Network | 0.40 | 0.26 | −0.032 | 0.898 |
| DMN LC Number of *Z* scores > 1.96 *SD* | 349.63 | 349.11 | 0.070 | 0.775 |
| DMN LC Percentage *Z* scores > 1.96 *SD* | 5.05 | 5.04 | 0.070 | 0.775 |
| SN LC Peak *Z* score | 4.23 | 2.30 | −0.067 | 0.786 |
| SN LC Mean *Z* Score | 0.69 | 0.14 | 0.108 | 0.659 |
| SN LC *Z* Score Variance Within Network | 0.35 | 0.20 | −0.028 | 0.909 |
| SN LC Number of *Z* scores > 1.96 *SD* | 361.21 | 319.76 | 0.067 | 0.786 |
| SN LC Percentage *Z* scores > 1.96 *SD* | 3.70 | 3.28 | 0.067 | 0.786 |
| FPN LC Peak *Z* Score | 3.88 | 1.97 | −0.025 | 0.919 |
| FPN LC Mean *Z* Score | 0.68 | 0.16 | 0.063 | 0.798 |
| FPN LC *Z* Score Variance Within Network | 0.35 | 0.25 | 0.008 | 0.973 |
| FPN LC Number of *Z* scores > 1.96 *SD* | 293.21 | 291.49 | 0.078 | 0.752 |
| FPN LC Percentage *Z* scores > 1.96 *SD* | 3.54 | 3.52 | 0.078 | 0.752 |

**Table 2**

*Spearman's Rank-Order Correlation Between Network Connectivity and PCSS Scores, N = 19*

| Network Connectivity Measures | Descriptive Statistics | | Spearman's Correlation | |
|---|---|---|---|---|
| | *M* | *SD* | *r* | *p* |
| DMN PD Peak *Z* score | 5.04 | 2.82 | −0.172 | 0.482 |
| DMN PD Mean *Z* score | 0.84 | 0.38 | −0.047 | 0.848 |
| DMN PD *Z* Score Variance Within Network | 0.30 | 0.11 | −0.022 | 0.930 |
| DMN PD Number of *Z* scores > 1.96 *SD* | 574.68 | 829.51 | −0.074 | 0.763 |
| DMN PD Percentage *Z* scores > 1.96 *SD* | 3.19 | 2.35 | −0.038 | 0.878 |
| SN PD Peak *Z* score | 5.28 | 3.77 | −0.345 | 0.148 |
| SN PD Mean *Z* score | 0.75 | 0.20 | −0.224 | 0.357 |
| SN PD *Z* Score Variance Within Network | 0.30 | 0.12 | −0.216 | 0.375 |
| SN PD Number of *Z* scores > 1.96 *SD* | 361.53 | 291.44 | −0.217 | 0.372 |
| SN PD Percentage *Z* scores > 1.96 *SD* | 3.71 | 2.99 | −0.217 | 0.372 |
| FPN PD Peak *Z* Score | 5.11 | 2.17 | −0.088 | 0.721 |
| FPN PD Mean *Z* Score | 0.98 | 0.51 | −0.083 | 0.736 |
| FPN PD *Z* Score Variance Within Network | 0.40 | 0.17 | −0.071 | 0.771 |
| FPN PD Number of *Z* scores > 1.96 *SD* | 969.58 | 1187.48 | −0.119 | 0.628 |
| FPN PD Percentage *Z* scores > 1.96 *SD* | 11.71 | 14.34 | −0.119 | 0.628 |
| DMN CSD Peak *Z* score | 2.85 | 1.44 | −0.062 | 0.801 |
| DMN CSD Mean *Z* score | 1.22 | 0.88 | −0.209 | 0.390 |
| DMN CSD *Z* Score Variance Within Network | 0.37 | 0.29 | −0.210 | 0.389 |
| DMN CSD Number of *Z* scores > 1.96 *SD* | 127.11 | 200.44 | −0.173 | 0.478 |
| DMN CSD Percentage *Z* scores > 1.96 *SD* | 19.26 | 30.37 | −0.173 | 0.478 |
| SN CSD Peak *Z* score | 3.10 | 1.79 | −0.111 | 0.652 |
| SN CSD Mean *Z* score | 1.28 | 0.88 | −0.164 | 0.504 |
| SN CSD Mean *Z* Score Variance Within Network | 0.43 | 0.38 | −0.159 | 0.515 |
| SN CSD Number of *Z* scores > 1.96 *SD* | 171.95 | 258.94 | −0.182 | 0.456 |
| SN CSD Percentage *Z* scores > 1.96 *SD* | 20.47 | 30.83 | −0.182 | 0.456 |
| FPN CSD Peak *Z* score | 2.87 | 1.69 | −0.169 | 0.489 |
| FPN CSD Mean *Z* Score | 1.36 | 1.06 | −0.163 | 0.506 |
| FPN CSD *Z* Score Variance Within Network | 0.28 | 0.15 | −0.227 | 0.350 |
| FPN CSD Number of *Z* scores > 1.96 *SD* | 155.95 | 249.25 | −0.194 | 0.427 |
| FPN CSD Percentage *Z* scores > 1.96 *SD* | 21.66 | 34.62 | −0.194 | 0.427 |

**Note.** DMN = default mode network; SN = salience network; FPN = frontal-parietal network; IC = instantaneous coherence; LC = lagged coherence; PD = phase difference; CSD = current source density.

**Table 3**
*Spearman's Rank-Order Correlation Between Network Connectivity and PCSS Domains, N = 19*

| Network Connectivity Measures | Spearman's Correlation | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | PCSS Cognitive | | PCSS Physical | | PCSS Affective | | PCSS Sleep | |
| | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* |
| DMN IC Peak *Z* score | −0.279 | 0.247 | −0.050 | 0.839 | −0.113 | 0.646 | 0.023 | 0.926 |
| DMN IC Mean *Z* Score | −0.070 | 0.777 | −0.001 | 0.996 | −0.187 | 0.444 | 0.171 | 0.484 |
| DMN IC *Z* Score Variance Within Network | −0.103 | 0.676 | −0.059 | 0.812 | −0.111 | 0.651 | 0.170 | 0.488 |
| DMN IC Number of *Z* scores > 1.96 *SD* | −0.056 | 0.819 | −0.016 | 0.949 | −0.111 | 0.651 | 0.209 | 0.391 |
| DMN IC Percentage *Z* scores > 1.96 *SD* | −0.056 | 0.819 | −0.016 | 0.949 | −0.111 | 0.651 | 0.209 | 0.391 |
| SN IC Peak *Z* Score | −0.328 | 0.171 | −0.143 | 0.558 | −0.260 | 0.282 | −0.108 | 0.658 |
| SN IC Mean *Z* Score | −0.078 | 0.750 | 0.069 | 0.778 | −0.272 | 0.260 | 0.068 | 0.783 |
| SN IC *Z* Score Variance Within Network | −0.119 | 0.629 | 0.012 | 0.961 | −0.230 | 0.343 | 0.140 | 0.566 |
| SN IC Number of *Z* scores > 1.96 *SD* | −0.085 | 0.728 | 0.040 | 0.872 | −0.271 | 0.262 | 0.159 | 0.515 |
| SN IC Percentage *Z* scores > 1.96 *SD* | −0.085 | 0.728 | 0.040 | 0.872 | −0.271 | 0.262 | 0.159 | 0.515 |
| FPN IC Peak *Z* Score | −0.173 | 0.479 | 0.070 | 0.775 | −0.092 | 0.707 | 0.166 | 0.498 |
| FPN IC Mean *Z* Score | 0.055 | 0.824 | 0.140 | 0.567 | −0.071 | 0.774 | 0.167 | 0.494 |
| FPN IC *Z* Score Variance Within Network | −0.054 | 0.825 | −0.027 | 0.913 | −0.044 | 0.857 | 0.159 | 0.516 |
| FPN IC Number of *Z* scores > 1.96 *SD* | −0.034 | 0.889 | 0.013 | 0.958 | −0.089 | 0.718 | 0.127 | 0.606 |
| FPN IC Percentage *Z* scores > 1.96 *SD* | −0.034 | 0.889 | 0.013 | 0.958 | −0.089 | 0.718 | 0.127 | 0.606 |
| DMN LC Peak *Z* Score | −0.247 | 0.307 | −0.150 | 0.541 | 0.020 | 0.936 | −0.091 | 0.712 |
| DMN LC Mean *Z* Score | 0.036 | 0.883 | 0.074 | 0.764 | 0.254 | 0.294 | 0.245 | 0.312 |
| DMN LC *Z* Score Variance Within Network | −0.170 | 0.485 | −0.074 | 0.765 | 0.126 | 0.606 | 0.052 | 0.831 |
| DMN LC Number of *Z* scores > 1.96 *SD* | −0.083 | 0.736 | −0.083 | 0.736 | 0.161 | 0.509 | 0.136 | 0.579 |
| DMN LC Percentage *Z* scores > 1.96 *SD* | −0.083 | 0.736 | −0.083 | 0.736 | 0.161 | 0.509 | 0.136 | 0.579 |
| SN LC Peak *Z* score | −0.176 | 0.471 | −0.129 | 0.598 | 0.091 | 0.710 | −0.032 | 0.897 |
| SN LC Mean *Z* Score | −0.015 | 0.950 | −0.005 | 0.983 | 0.103 | 0.673 | 0.152 | 0.535 |
| SN LC *Z* Score Variance Within Network | −0.130 | 0.597 | −0.147 | 0.548 | 0.094 | 0.703 | −0.018 | 0.941 |
| SN LC Number of *Z* scores > 1.96 *SD* | −0.025 | 0.920 | −0.159 | 0.516 | 0.012 | 0.962 | 0.086 | 0.727 |
| SN LC Percentage *Z* scores > 1.96 *SD* | −0.025 | 0.920 | −0.159 | 0.516 | 0.012 | 0.962 | 0.086 | 0.727 |
| FPN LC Peak *Z* Score | −0.081 | 0.742 | −0.127 | 0.603 | 0.032 | 0.897 | −0.123 | 0.615 |
| FPN LC Mean *Z* Score | −0.036 | 0.885 | −0.075 | 0.759 | 0.128 | 0.603 | 0.043 | 0.862 |
| FPN LC *Z* Score Variance Within Network | −0.126 | 0.608 | −0.154 | 0.528 | 0.044 | 0.858 | −0.046 | 0.853 |
| FPN LC Number of *Z* scores > 1.96 *SD* | −0.053 | 0.831 | −0.160 | 0.512 | 0.103 | 0.674 | −0.003 | 0.990 |
| FPN LC Percentage *Z* scores > 1.96 *SD* | −0.053 | 0.831 | −0.160 | 0.512 | 0.103 | 0.674 | −0.003 | 0.990 |

**Table 3**
*Spearman's Rank-Order Correlation Between Network Connectivity and PCSS Domains, N = 19*

| Network Connectivity Measures | Spearman's Correlation | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | PCSS Cognitive | | PCSS Physical | | PCSS Affective | | PCSS Sleep | |
| | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* |
| DMN PD Peak *Z* score | −0.304 | 0.206 | −0.255 | 0.292 | −0.200 | 0.412 | −0.004 | 0.989 |
| DMN PD Mean *Z* score | −0.207 | 0.394 | −0.012 | 0.961 | −0.301 | 0.210 | 0.000 | 0.999 |
| DMN PD *Z* Score Variance Within Network | −0.180 | 0.461 | 0.032 | 0.895 | −0.263 | 0.276 | 0.069 | 0.780 |
| DMN PD Number of *Z* scores > 1.96 *SD* | −0.251 | 0.300 | −0.015 | 0.952 | −0.304 | 0.206 | 0.029 | 0.907 |
| DMN PD Percentage *Z* scores > 1.96 *SD* | −0.218 | 0.371 | 0.017 | 0.945 | −0.271 | 0.261 | 0.063 | 0.799 |
| SN PD Peak *Z* score | −0.396 | 0.093 | −0.245 | 0.312 | −0.378 | 0.111 | −0.186 | 0.446 |
| SN PD Mean *Z* score | −0.265 | 0.274 | −0.092 | 0.709 | **−0.500*** | **0.029** | −0.098 | 0.690 |
| SN PD *Z* Score Variance Within Network | −0.255 | 0.293 | −0.022 | 0.927 | **−0.465*** | **0.045** | −0.094 | 0.702 |
| SN PD Number of *Z* scores > 1.96 *SD* | −0.261 | 0.280 | −0.034 | 0.890 | −0.446 | 0.056 | −0.081 | 0.742 |
| SN PD Percentage *Z* scores > 1.96 *SD* | −0.261 | 0.280 | −0.034 | 0.890 | −0.446 | 0.056 | −0.081 | 0.742 |
| FPN PD Peak *Z* Score | −0.236 | 0.331 | −0.052 | 0.832 | −0.322 | 0.178 | 0.118 | 0.631 |
| FPN PD Mean *Z* Score | −0.149 | 0.543 | 0.045 | 0.856 | −0.402 | 0.088 | 0.044 | 0.858 |
| FPN PD *Z* Score Variance Within Network | −0.166 | 0.497 | −0.010 | 0.968 | −0.380 | 0.109 | 0.069 | 0.781 |
| FPN PD Number of *Z* scores > 1.96 *SD* | −0.212 | 0.384 | −0.065 | 0.792 | −0.392 | 0.097 | 0.055 | 0.823 |
| FPN PD Percentage *Z* scores > 1.96 *SD* | −0.212 | 0.384 | −0.065 | 0.792 | −0.392 | 0.097 | 0.055 | 0.823 |
| DMN CSD Peak *Z* score | −0.232 | 0.339 | −0.072 | 0.769 | −0.143 | 0.559 | 0.018 | 0.941 |
| DMN CSD Mean *Z* score | −0.359 | 0.131 | −0.313 | 0.191 | −0.132 | 0.590 | −0.110 | 0.653 |
| DMN CSD *Z* Score Variance Within Network | −0.348 | 0.144 | −0.265 | 0.273 | −0.119 | 0.628 | −0.172 | 0.481 |
| DMN CSD Number of *Z* scores > 1.96 *SD* | −0.323 | 0.177 | −0.226 | 0.353 | −0.176 | 0.471 | −0.069 | 0.778 |
| DMN CSD Percentage *Z* scores > 1.96 *SD* | −0.323 | 0.177 | −0.226 | 0.353 | −0.176 | 0.471 | −0.069 | 0.778 |
| SN CSD Peak *Z* score | −0.287 | 0.233 | −0.103 | 0.674 | −0.073 | 0.768 | −0.039 | 0.873 |
| SN CSD Mean *Z* score | −0.324 | 0.176 | −0.255 | 0.293 | −0.064 | 0.796 | −0.101 | 0.680 |
| SN CSD Mean *Z* Score Variance Within Network | −0.304 | 0.205 | −0.165 | 0.500 | −0.058 | 0.815 | −0.154 | 0.529 |
| SN CSD Number of *Z* scores > 1.96 *SD* | −0.349 | 0.143 | −0.175 | 0.474 | −0.120 | 0.626 | −0.091 | 0.712 |
| SN CSD Percentage *Z* scores > 1.96 *SD* | −0.349 | 0.143 | −0.175 | 0.474 | −0.120 | 0.626 | −0.091 | 0.712 |
| FPN CSD Peak *Z* score | −0.336 | 0.160 | −0.156 | 0.524 | −0.168 | 0.492 | −0.090 | 0.714 |
| FPN CSD Mean *Z* Score | −0.314 | 0.190 | −0.236 | 0.331 | −0.073 | 0.767 | −0.034 | 0.889 |
| FPN CSD *Z* Score Variance Within Network | −0.317 | 0.186 | −0.230 | 0.343 | −0.097 | 0.691 | −0.255 | 0.293 |
| FPN CSD Number of *Z* scores > 1.96 *SD* | −0.342 | 0.152 | −0.182 | 0.455 | −0.154 | 0.530 | −0.079 | 0.747 |
| FPN CSD Percentage *Z* scores > 1.96 *SD* | −0.342 | 0.152 | −0.182 | 0.455 | −0.154 | 0.530 | −0.079 | 0.747 |

**Note.** * = significant at $p = 0.05$; DMN = default mode network; SN = salience network; FPN = frontal-parietal network; IC = instantaneous coherence; LC = lagged coherence; PD = phase difference; CSD = current source density; PCSS = Post-Concussion Symptom Scale.

**Table 4**

*Spearman's Rank-Order Correlation Between Network Connectivity and Cognition, N = 19*

| Network Connectivity Measures | Spearman's Correlation | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | TMT-A | | TMT-B | | RBANS Total Index | | Immediate Memory Index | | Visuospatial Index | | Language Index | | Attention Index | | Delayed Memory Index | |
| | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* |
| DMN IC Peak *Z* score | 0.280 | 0.246 | 0.089 | 0.718 | 0.018 | 0.940 | −0.162 | 0.508 | 0.104 | 0.673 | 0.316 | 0.187 | 0.158 | 0.519 | 0.225 | 0.354 |
| DMN IC Mean *Z* Score | 0.286 | 0.234 | 0.198 | 0.417 | **−0.477*** | **0.039** | **−0.482*** | **0.036** | −0.204 | 0.402 | 0.168 | 0.492 | 0.074 | 0.764 | −0.352 | 0.139 |
| DMN IC *Z* Score Variance Within Network | 0.327 | 0.172 | 0.190 | 0.437 | −0.399 | 0.090 | **−0.457*** | **0.049** | −0.081 | 0.741 | 0.232 | 0.340 | 0.013 | 0.958 | −0.184 | 0.452 |
| DMN IC Number of *Z* scores > 1.96 *SD* | 0.336 | 0.159 | 0.238 | 0.327 | −0.448 | 0.054 | −0.455 | 0.050 | −0.061 | 0.803 | 0.236 | 0.331 | −0.084 | 0.731 | −0.193 | 0.428 |
| DMN IC Percentage *Z* scores > 1.96 *SD* | 0.336 | 0.159 | 0.238 | 0.327 | −0.448 | 0.054 | −0.455 | 0.050 | −0.061 | 0.803 | 0.236 | 0.331 | −0.084 | 0.731 | −0.193 | 0.428 |
| SN IC Peak *Z* Score | 0.392 | 0.097 | 0.163 | 0.504 | −0.146 | 0.551 | −0.298 | 0.216 | −0.083 | 0.735 | 0.353 | 0.138 | 0.257 | 0.288 | −0.04 | 0.872 |
| SN IC Mean *Z* Score | 0.332 | 0.165 | 0.338 | 0.157 | −0.453 | 0.051 | −0.298 | 0.216 | −0.188 | 0.442 | 0.110 | 0.653 | 0.047 | 0.849 | −0.181 | 0.457 |
| SN IC *Z* Score Variance Within Network | 0.403 | 0.087 | 0.288 | 0.232 | −0.379 | 0.110 | −0.237 | 0.329 | −0.109 | 0.656 | 0.127 | 0.604 | −0.051 | 0.835 | −0.016 | 0.948 |
| SN IC Number of *Z* scores > 1.96 *SD* | 0.427 | 0.068 | 0.346 | 0.147 | −0.443 | 0.058 | −0.259 | 0.284 | −0.166 | 0.496 | 0.096 | 0.696 | −0.046 | 0.850 | −0.118 | 0.631 |
| SN IC Percentage *Z* scores > 1.96 *SD* | 0.427 | 0.068 | 0.346 | 0.147 | −0.443 | 0.058 | −0.259 | 0.284 | −0.166 | 0.496 | 0.096 | 0.696 | −0.046 | 0.850 | −0.118 | 0.631 |
| FPN IC Peak *Z* Score | 0.251 | 0.300 | 0.185 | 0.448 | −0.140 | 0.568 | −0.326 | 0.174 | 0.101 | 0.681 | 0.326 | 0.173 | 0.067 | 0.785 | −0.003 | 0.991 |
| FPN IC Mean *Z* Score | 0.331 | 0.167 | 0.263 | 0.276 | −0.422 | 0.072 | **−0.482*** | **0.037** | −0.025 | 0.918 | 0.303 | 0.208 | 0.042 | 0.865 | −0.196 | 0.421 |
| FPN IC *Z* Score Variance Within Network | 0.272 | 0.260 | 0.127 | 0.606 | −0.342 | 0.152 | **−0.471*** | **0.042** | −0.029 | 0.907 | 0.279 | 0.248 | 0.021 | 0.931 | −0.122 | 0.619 |
| FPN IC Number of *Z* scores > 1.96 *SD* | 0.311 | 0.195 | 0.167 | 0.495 | −0.369 | 0.120 | **−0.487*** | **0.035** | −0.061 | 0.805 | 0.316 | 0.188 | 0.060 | 0.806 | −0.173 | 0.479 |
| FPN IC Percentage *Z* scores > 1.96 *SD* | 0.311 | 0.195 | 0.167 | 0.495 | −0.369 | 0.120 | **−0.487*** | **0.035** | −0.061 | 0.805 | 0.316 | 0.188 | 0.060 | 0.806 | −0.173 | 0.479 |
| DMN LC Peak *Z* Score | 0.443 | 0.057 | 0.370 | 0.119 | −0.049 | 0.841 | −0.068 | 0.782 | 0.142 | 0.561 | 0.315 | 0.190 | −0.178 | 0.466 | 0.303 | 0.208 |
| DMN LC Mean *Z* Score | 0.396 | 0.093 | 0.345 | 0.148 | −0.209 | 0.390 | −0.173 | 0.478 | −0.055 | 0.823 | 0.230 | 0.344 | −0.084 | 0.733 | 0.097 | 0.693 |
| DMN LC *Z* Score Variance Within Network | **0.460*** | **0.048** | 0.325 | 0.175 | −0.087 | 0.723 | −0.131 | 0.592 | 0.084 | 0.732 | 0.311 | 0.195 | −0.093 | 0.706 | 0.274 | 0.257 |
| DMN LC Number of *Z* scores > 1.96 *SD* | 0.343 | 0.151 | 0.223 | 0.358 | −0.194 | 0.427 | −0.110 | 0.655 | −0.008 | 0.974 | 0.214 | 0.378 | −0.127 | 0.604 | 0.199 | 0.414 |
| DMN LC Percentage *Z* scores > 1.96 *SD* | 0.343 | 0.151 | 0.223 | 0.358 | −0.194 | 0.427 | −0.110 | 0.655 | −0.008 | 0.974 | 0.214 | 0.378 | −0.127 | 0.604 | 0.199 | 0.414 |
| SN LC Peak *Z* score | 0.346 | 0.147 | 0.267 | 0.270 | 0.029 | 0.906 | −0.012 | 0.960 | 0.151 | 0.536 | 0.198 | 0.416 | −0.225 | 0.355 | 0.300 | 0.212 |
| SN LC Mean *Z* Score | **0.462*** | **0.046** | 0.422 | 0.072 | −0.131 | 0.594 | 0.033 | 0.893 | −0.169 | 0.489 | 0.276 | 0.252 | −0.087 | 0.724 | 0.110 | 0.654 |
| SN LC *Z* Score Variance Within Network | **0.492*** | **0.033** | 0.333 | 0.164 | −0.101 | 0.680 | −0.107 | 0.661 | −0.050 | 0.840 | 0.320 | 0.181 | −0.107 | 0.662 | 0.205 | 0.399 |
| SN LC Number of *Z* scores > 1.96 *SD* | 0.386 | 0.103 | 0.188 | 0.441 | −0.337 | 0.158 | −0.163 | 0.505 | −0.140 | 0.567 | 0.152 | 0.535 | −0.206 | 0.396 | 0.001 | 0.997 |
| SN LC Percentage *Z* scores > 1.96 *SD* | 0.386 | 0.103 | 0.188 | 0.441 | −0.337 | 0.158 | −0.163 | 0.505 | −0.140 | 0.567 | 0.152 | 0.535 | −0.206 | 0.396 | 0.001 | 0.997 |

**Table 4**

*Spearman's Rank-Order Correlation Between Network Connectivity and Cognition, N = 19*

| Network Connectivity Measures | Spearman's Correlation | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | TMT-A | | TMT-B | | RBANS Total Index | | Immediate Memory Index | | Visuospatial Index | | Language Index | | Attention Index | | Delayed Memory Index | |
| | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* |
| FPN LC Peak *Z* Score | 0.340 | 0.155 | 0.183 | 0.452 | −0.065 | 0.791 | −0.116 | 0.637 | 0.052 | 0.833 | 0.223 | 0.358 | −0.241 | 0.320 | 0.113 | 0.644 |
| FPN LC Mean *Z* Score | 0.416 | 0.076 | 0.442 | 0.058 | −0.006 | 0.980 | 0.075 | 0.761 | −0.115 | 0.639 | 0.204 | 0.402 | −0.156 | 0.523 | 0.146 | 0.552 |
| FPN LC *Z* Score Variance Within Network | 0.342 | 0.152 | 0.257 | 0.288 | −0.043 | 0.861 | −0.053 | 0.830 | 0.051 | 0.836 | 0.252 | 0.298 | −0.138 | 0.573 | 0.196 | 0.420 |
| FPN LC Number of *Z* scores > 1.96 *SD* | 0.291 | 0.227 | 0.242 | 0.319 | −0.112 | 0.649 | −0.087 | 0.722 | −0.032 | 0.895 | 0.198 | 0.417 | −0.143 | 0.560 | 0.136 | 0.579 |
| FPN LC Percentage *Z* scores > 1.96 *SD* | 0.291 | 0.227 | 0.242 | 0.319 | −0.112 | 0.649 | −0.087 | 0.722 | −0.032 | 0.895 | 0.198 | 0.417 | −0.143 | 0.560 | 0.136 | 0.579 |
| DMN PD Peak *Z* score | 0.239 | 0.324 | 0.35 | 0.141 | −0.303 | 0.207 | −0.319 | 0.183 | −0.156 | 0.525 | 0.353 | 0.138 | 0.061 | 0.803 | −0.165 | 0.499 |
| DMN PD Mean *Z* score | 0.214 | 0.379 | 0.158 | 0.519 | −0.386 | 0.102 | **−0.469*** | **0.043** | −0.218 | 0.369 | 0.140 | 0.567 | 0.253 | 0.296 | −0.396 | 0.093 |
| DMN PD *Z* Score Variance Within Network | 0.296 | 0.219 | 0.207 | 0.395 | −0.425 | 0.070 | **−0.500*** | **0.029** | −0.194 | 0.425 | 0.175 | 0.473 | 0.214 | 0.379 | −0.403 | 0.087 |
| DMN PD Number of *Z* scores > 1.96 *SD* | 0.320 | 0.182 | 0.229 | 0.345 | −0.366 | 0.124 | **−0.478*** | **0.038** | −0.165 | 0.499 | 0.213 | 0.380 | 0.208 | 0.392 | −0.351 | 0.141 |
| DMN PD Percentage *Z* scores > 1.96 *SD* | 0.318 | 0.185 | 0.203 | 0.405 | −0.368 | 0.121 | **−0.490*** | **0.033** | −0.164 | 0.501 | 0.208 | 0.394 | 0.204 | 0.403 | −0.366 | 0.124 |
| SN PD Peak *Z* score | **0.482*** | **0.037** | 0.424 | 0.071 | −0.176 | 0.472 | −0.236 | 0.331 | −0.028 | 0.908 | **0.481*** | **0.037** | 0.032 | 0.897 | 0.090 | 0.714 |
| SN PD Mean *Z* score | 0.447 | 0.055 | 0.298 | 0.215 | −0.397 | 0.092 | −0.254 | 0.294 | −0.344 | 0.149 | 0.132 | 0.590 | 0.142 | 0.562 | −0.276 | 0.252 |
| SN PD *Z* Score Variance Within Network | **0.528*** | **0.020** | 0.421 | 0.073 | −0.275 | 0.254 | −0.178 | 0.467 | −0.215 | 0.377 | 0.281 | 0.244 | 0.137 | 0.575 | −0.152 | 0.533 |
| SN PD Number of *Z* scores > 1.96 *SD* | **0.465*** | **0.045** | 0.369 | 0.120 | −0.354 | 0.137 | −0.221 | 0.363 | −0.231 | 0.341 | 0.160 | 0.513 | 0.120 | 0.625 | −0.175 | 0.473 |
| SN PD Percentage *Z* scores > 1.96 *SD* | **0.465*** | **0.045** | 0.369 | 0.120 | −0.354 | 0.137 | −0.221 | 0.363 | −0.231 | 0.341 | 0.160 | 0.513 | 0.120 | 0.625 | −0.175 | 0.473 |
| FPN PD Peak *Z* Score | 0.407 | 0.084 | 0.271 | 0.262 | −0.392 | 0.096 | −0.433 | 0.064 | −0.209 | 0.391 | 0.244 | 0.314 | 0.153 | 0.533 | −0.320 | 0.182 |
| FPN PD Mean *Z* Score | 0.453 | 0.052 | 0.365 | 0.125 | **−0.486*** | **0.035** | −0.410 | 0.081 | −0.307 | 0.201 | 0.219 | 0.368 | 0.184 | 0.450 | −0.396 | 0.093 |
| FPN PD *Z* Score Variance Within Network | 0.447 | 0.055 | 0.315 | 0.189 | **−0.500*** | **0.029** | −0.425 | 0.070 | −0.316 | 0.187 | 0.137 | 0.576 | 0.182 | 0.455 | −0.426 | 0.069 |
| FPN PD Number of *Z* scores > 1.96 *SD* | 0.453 | 0.052 | 0.337 | 0.159 | **−0.496*** | **0.031** | −0.424 | 0.070 | −0.310 | 0.196 | 0.178 | 0.465 | 0.133 | 0.587 | −0.403 | 0.087 |
| FPN PD Percentage *Z* scores > 1.96 *SD* | 0.453 | 0.052 | 0.337 | 0.159 | **−0.496*** | **0.031** | −0.424 | 0.070 | −0.310 | 0.196 | 0.178 | 0.465 | 0.133 | 0.587 | −0.403 | 0.087 |

**Table 4**

*Spearman's Rank-Order Correlation Between Network Connectivity and Cognition, N = 19*

| Network Connectivity Measures | Spearman's Correlation | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | TMT-A | | TMT-B | | RBANS Total Index | | Immediate Memory Index | | Visuospatial Index | | Language Index | | Attention Index | | Delayed Memory Index | |
| | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* |
| DMN CSD Peak *Z* score | 0.215 | 0.376 | 0.146 | 0.551 | −0.376 | 0.113 | **−0.595***** | **0.007** | −0.004 | 0.988 | 0.198 | 0.417 | −0.022 | 0.929 | −0.299 | 0.214 |
| DMN CSD Mean *Z* score | 0.162 | 0.506 | −0.143 | 0.560 | −0.336 | 0.159 | **−0.681***** | **0.001** | 0.062 | 0.801 | 0.195 | 0.423 | −0.037 | 0.880 | −0.239 | 0.325 |
| DMN CSD *Z* Score Variance Within Network | 0.147 | 0.548 | −0.042 | 0.865 | −0.346 | 0.147 | **−0.675***** | **0.002** | 0.108 | 0.660 | 0.259 | 0.284 | −0.053 | 0.829 | −0.176 | 0.471 |
| DMN CSD Number of *Z* scores > 1.96 *SD* | 0.174 | 0.475 | −0.058 | 0.815 | **−0.462*** | **0.047** | **−0.720***** | **0.001** | 0.086 | 0.727 | 0.084 | 0.731 | −0.100 | 0.682 | −0.319 | 0.183 |
| DMN CSD Percentage *Z* scores > 1.96 *SD* | 0.174 | 0.475 | −0.058 | 0.815 | **−0.462*** | **0.047** | **−0.720***** | **0.001** | 0.086 | 0.727 | 0.084 | 0.731 | −0.100 | 0.682 | −0.319 | 0.183 |
| SN CSD Peak *Z* score | 0.122 | 0.619 | 0.048 | 0.846 | −0.356 | 0.135 | **−0.659***** | **0.002** | 0.180 | 0.460 | 0.141 | 0.565 | −0.037 | 0.879 | −0.208 | 0.394 |
| SN CSD Mean *Z* score | 0.073 | 0.767 | −0.172 | 0.481 | −0.349 | 0.143 | **−0.734***** | **0.000** | 0.160 | 0.512 | 0.140 | 0.567 | −0.005 | 0.984 | −0.233 | 0.337 |
| SN CSD Mean *Z* Score Variance Within Network | 0.110 | 0.653 | 0.013 | 0.957 | −0.332 | 0.165 | **−0.641***** | **0.003** | 0.176 | 0.472 | 0.223 | 0.360 | −0.035 | 0.888 | −0.137 | 0.577 |
| SN CSD Number of *Z* scores > 1.96 *SD* | 0.150 | 0.540 | −0.011 | 0.966 | −0.340 | 0.154 | **−0.665***** | **0.002** | 0.230 | 0.343 | 0.190 | 0.436 | −0.117 | 0.633 | −0.200 | 0.413 |
| SN CSD Percentage *Z* scores > 1.96 *SD* | 0.150 | 0.540 | −0.011 | 0.966 | −0.340 | 0.154 | **−0.665***** | **0.002** | 0.230 | 0.343 | 0.190 | 0.436 | −0.117 | 0.633 | −0.200 | 0.413 |
| FPN CSD Peak *Z* score | 0.187 | 0.442 | 0.056 | 0.819 | −0.350 | 0.142 | **−0.654***** | **0.002** | 0.081 | 0.740 | 0.205 | 0.399 | 0.011 | 0.963 | −0.251 | 0.300 |
| FPN CSD Mean *Z* Score | 0.216 | 0.376 | −0.133 | 0.588 | −0.327 | 0.172 | **−0.696***** | **0.001** | 0.073 | 0.766 | 0.152 | 0.533 | 0.051 | 0.837 | −0.248 | 0.306 |
| FPN CSD *Z* Score Variance Within Network | 0.149 | 0.542 | −0.037 | 0.881 | −0.319 | 0.183 | **−0.666***** | **0.002** | 0.160 | 0.512 | 0.305 | 0.203 | −0.077 | 0.754 | −0.125 | 0.610 |
| FPN CSD Number of *Z* scores > 1.96 *SD* | 0.212 | 0.384 | −0.041 | 0.869 | −0.381 | 0.107 | **−0.672***** | **0.002** | 0.111 | 0.650 | 0.077 | 0.756 | −0.070 | 0.777 | −0.254 | 0.294 |
| FPN CSD Percentage *Z* scores > 1.96 *SD* | 0.212 | 0.384 | −0.041 | 0.869 | −0.381 | 0.107 | **−0.672***** | **0.002** | 0.111 | 0.650 | 0.077 | 0.756 | −0.070 | 0.777 | −0.254 | 0.294 |

**Note.** * = significant at $p = 0.05$; ** significant at the 0.01 level; *** = remained significant after Benjamini-Hochberg correction for multiple comparisons; DMN = default mode network; SN = salience network; FPN = frontal-parietal network; IC = instantaneous coherence; LC = lagged coherence; PD = phase difference; CSD = current source density; PCSS = Post-Concussion Symptom Scale; RBANS = The Repeatable Battery for the Assessment of Neuropsychological Status Update; TMT-A = Trail Making Test Part A; TMT-B = Trail Making Test Part B.

### Cognitive Function and Post-Concussion Symptoms

To test the hypothesis that higher PCSS scores are associated with reduced cognitive performance (measured by a neuropsychological battery) in the acute post-concussion phase, Pearson product-moment correlation analyses were conducted. Three outliers were detected and managed using winsorization, being three or more standard deviations away from the mean. Assumption testing revealed that the PCSS total score was not normally distributed according to the Shapiro-Wilk statistic ($p$ = 0.018); however, since skew and kurtosis were within ±1 (0.757 and −0.236, respectively), a $z$-test was used to assess for normality as described in Mishra et al. (2019). The values for zskew (1.44) and zkurtosis (−0.23) were within ±1.96, so normality was assumed. All other assumptions for Pearson's correlation were met.

Table 5 shows the descriptive statistics for the cognitive variables. All participants demonstrated adequate effort on cognitive testing as measured by their FIT scores ranging from 12 to 15, and their RBANS effort index scores being 3 or below. To assess the size and direction of the linear relationship between post-concussion symptoms and cognitive function, a Pearson's product-moment correlation was conducted (see Table 5 for results). No significant correlations were found between acute symptoms and cognitive function.

To further explore the relationship between cognitive function and PCSS domains, Spearman's rank-order correlation was conducted as listed in Table 6. While the PCSS cognitive domain was normally distributed, the assumptions of linearity and homoscedasticity were not met, so nonparametric analyses were conducted for all variables. No significant correlations were found between cognitive function and PCSS symptom domains.

## Discussion

To our knowledge, this study is the first to investigate the utility of measuring network function using qEEG in the acute stages post-mTBI and, as such, serves as an initial pilot study of this novel approach in an mTBI sample. The present study aimed to measure the association between brain network connectivity, acute PCSS scores, and cognition (processing speed, inhibition/switching, immediate memory, visuospatial/constructional, language, attention, and delayed memory) in Australian adults within 7 days after mTBI.

The hypotheses that network dysregulation would be positively correlated with PCSS total score and PCSS symptom domains were not supported. This finding was not in keeping with previous literature suggesting an association between altered brain network connectivity and post-concussion symptoms (D'Souza et al., 2020; Mortaheb et al., 2021; Ramage et al., 2022). DMN integrity is essential for cognition, and cingulum damage or decreased DMN connectivity as detected by diffusion tensor imaging (DTI) have been associated with sustained attention deficits following mTBI (Bonnelle, Leech, et al., 2011). Furthermore, reduced DMN connectivity, as measured by neurite orientation dispersion and density imaging (NODDI) and DTI, has been linked with increased symptoms 6 months post-mTBI (Palacios et al., 2020). Altered connections between the DMN and other networks such as the SN and FPN have also been seen on resting-state fMRI post-mTBI. The SN has a central role in shifting attention externally (Hayes et al., 2016), as well as modulating DMN activity (Sharp, Scott, et al., 2014). Impaired connectivity between the DMN and SN has been associated with reduced DMN inhibition during a task requiring external focus on fMRI, and this was linked with cognitive impairments post-TBI (Bonnelle, Ham, et al., 2012; Jilka et al., 2014). Altered connectivity between the DMN and SN may also be due to structural pathology within the SN as seen on fMRI (Hayes et al., 2016), and heightened connectivity within both networks has been associated with cognitive deficits in a DTI and NODDI study (Palacios et al., 2020). The FPN is central to various cognitive tasks including reasoning, working memory, set-shifting, attention, (Martínez et al., 2013; Niendam et al., 2012), and novel complex tasks (Chenot et al., 2021). Altered connectivity seen on fMRI within the FPN has been linked to heightened cognitive fatigue and reduced sustained effort during cognitive activities, 3 to 24 months post-mTBI (Ramage et al., 2022). Furthermore, a review of various functional neuroimaging techniques including fMRI and magnetoencephalography, found a reduced negative association between the FPN and DMN is commonly linked to PPCS (Mortaheb et al., 2021).

**Table 5**
*Pearson Product-Moment Correlations Between PCSS Score and Cognitive Function, N = 19*

| Cognitive Measure | Descriptives | | Pearson Correlation | |
|---|---|---|---|---|
| | *M* | *SD* | *r* | *p* |
| PCSS Total Score | 26.89 | 21.57 | | |
| TMT-A *Z* score | −0.20 | 1.07 | −0.139 | 0.285 |
| TMT-B *Z* score | −0.78 | 1.34 | −0.160 | 0.256 |
| RBANS total Index Score | 91.47 | 11.40 | −0.058 | 0.407 |
| Immediate Memory | 93.05 | 14.94 | 0.143 | 0.279 |
| Visuospatial/constructional | 95 | 17.11 | −0.110 | 0.328 |
| Language | 103.21 | 12.06 | −0.371 | 0.059 |
| Attention | 92.47 | 15.92 | −0.051 | 0.418 |
| Delayed Memory | 94.26 | 9.71 | 0.020 | 0.468 |

**Note.** TMT = Trail Making Test; RBANS = Repeatable Battery for the Assessment of Neuropsychological Status.

**Table 6**
*Spearman's Rank-Order Correlation Between Cognitive Function and PCSS Domains, N = 19*

| Cognitive Measures | Spearman's Correlation | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | PCSS Cognitive | | PCSS Physical | | PCSS Affective | | PCSS Sleep | |
| | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* |
| TMT-A | −0.279 | 0.248 | −0.118 | 0.632 | −0.356 | 0.134 | −0.131 | 0.594 |
| TMT-B | −0.114 | 0.643 | 0.056 | 0.820 | −0.138 | 0.572 | 0.100 | 0.685 |
| RBANS Total Index | −0.224 | 0.357 | −0.034 | 0.889 | 0.109 | 0.658 | −0.133 | 0.589 |
| Immediate Memory Index | −0.020 | 0.937 | −0.004 | 0.985 | 0.017 | 0.945 | 0.125 | 0.611 |
| Visuospatial Index | −0.217 | 0.372 | 0.214 | 0.379 | 0.088 | 0.721 | 0.078 | 0.752 |
| Language Index | −0.287 | 0.233 | −0.173 | 0.478 | −0.207 | 0.396 | −0.336 | 0.160 |
| Attention Index | 0.027 | 0.914 | 0.180 | 0.461 | 0.070 | 0.776 | −0.108 | 0.661 |
| Delayed Memory Index | −0.189 | 0.439 | 0.069 | 0.779 | 0.263 | 0.278 | 0.082 | 0.738 |

**Note.** PCSS = Post-Concussion Symptom Scale; RBANS = The Repeatable Battery for the Assessment of Neuropsychological Status Update; TMT-A = Trail Making Test Part A; TMT-B = Trail Making Test Part B.

One possible reason for these findings is that while qEEG has been previously used to measure brain function in mTBI (Rapp et al., 2015), the current study used a novel approach measuring whole networks rather than individual brain areas. The whole network approach may have "averaged out" the dysfunctional areas resulting in reduced detection of dysfunction. Another reason may be that 89% of participants exercised on average 3 days per week, and physical activity has been shown to modulate brain health (Dorsman et al., 2020; McFadden et al., 2013), so it is possible that their exercise level was protective against network dysregulation and cognitive deficits. Additionally, 47% of participants were taking medication, so it is possible that their brain activity and cognitive function was modulated by the medications, concealing the true effects of mTBI on their brain's connectivity. It is therefore recommended that

exercise and medication are accounted for in future research as potential confounding factors.

The hypothesis that network dysregulation would be negatively correlated with cognitive performance was partially supported. Network connectivity (DMN, FPN) and CSD (DMN, SN, FPN) were significantly correlated with immediate memory measures. This supports the findings in previous literature that brain dysfunction is correlated with cognitive dysfunction post-mTBI (Bonnelle, Ham, et al., 2012; Jilka et al., 2014; Thatcher, North, et al., 2001). While acknowledging the limitations of the current study, this finding may have significant implications for the clinical assessment of mTBI, considering that neuropsychological measures of immediate memory are relatively quick and easy to administer in a clinical setting, and may be an indicator of brain network dysfunction in the acute post-mTBI phase. Testing this hypothesis in a larger sample, with a more comprehensive cognitive assessment battery would improve its generalizability and may add to its utility in the clinical setting.

The hypotheses that cognitive performance would be negatively correlated with PCSS total score and PCSS symptom domains were not supported. This was not consistent with previous literature suggesting that individuals with higher symptom scores had inferior cognitive function compared to those with lower symptom scores (Custer et al., 2016); however, participants in the present study were older (minimum 21 years) than those who participated in the previous study (minimum 13 years) and this may be one reason for the different findings. It is also possible that our neuropsychological measures were not sensitive enough to detect mild dysfunction as is the case for most individuals in mTBI, hence, a more comprehensive cognitive battery is recommended for future research. Finally, the PCSS may be too sensitive to non-mTBI specific symptoms, highlighting the need to better understand the underlying factor structure of this commonly used measure.

Limitations of the current study include a small sample size and limited power. The age range was also large, and in conjunction with the small sample size, did not allow for stratification of age categories, to explore whether age-related effects were also impacting the findings. Specifically, the literature suggests that with advancing age, there is a reduction in within-network resting-state functional connectivity and an increase in functional connectivity across networks (Ferreira & Busatto, 2013; Kong et al., 2020). This is especially the case for the DMN and networks involved in higher order cognition (Andrews-Hanna et al., 2007; Chan et al., 2014; Damoiseaux et al., 2008) which may be considered to encompass all three networks analyzed in this study. Additionally, it is acknowledged that age-related cognitive decline may also have an impact on neuropsychological test performance, limiting the interpretation of cognitive deficits as purely mTBI-related in older age groups. While the nature of neuropsychological testing is somewhat protective against this effect due to the comparison of raw scores with age-matched normative databases, it remains possible that subclinical changes may already be occurring, regardless of the observed scores. Given the limited sample size, the heterogenous mechanisms of injury within the sample may be seen as a limitation, particularly since over half the participants had sports-related injuries. Nonetheless, considering mTBI is a heterogeneous condition, the fact that this sample encompasses that heterogeneity makes it more applicable to the general population than a single injury mechanism sample. There was also a lack of control group; however, this was countered by the fact that the brain network and cognitive measures for each participant were compared to a normative sample of typically developing adults. It is acknowledged that normative databases used in this study may not be completely representative of the current cohort given the anticipated impact of the COVID-19 pandemic on individuals and the community, resulting in an increased prevalence of stress, mental health challenges, and a changing society. Additionally, individuals with comorbid conditions were not separated for analysis purposes, which may have impacted the results due to overlapping or amplified effects. While the impact of multiple mTBI remains controversial (Young, 2020), it has been suggested that repeated mTBI may result in poorer outcomes (Mez et al., 2017). Considering 52.6% of participants in this study had one or more previous mTBI, it is worth noting that these participants may differ from participants who had a single injury, and hence, this factor may limit generalizability of the results. Having a larger sample size may provide a more convincing demonstration of the impact of multiple mTBI on functioning. Moreover, six participants stated they were unsure whether they experienced loss of consciousness which may result in misclassification of mTBI. However, participants received a medical diagnosis of mTBI prior to being accepted into the study, so that reduced the likelihood of misclassification. Additionally, it was anticipated that if participants experienced loss of consciousness

> 30 min, their LOC would have been observed by a third party or referrer and they would not have been referred to the study. Nonetheless, removing the ambiguity in future studies would be optimal.

The neuropsychological battery used was limited to a screening and repeatable battery which may not have been sensitive enough to detect mild cognitive deficits and it may not have covered all the relevant cognitive domains for post-mTBI. For example, executive functioning measures may be more sensitive to long tract changes since execution functioning requires higher order integrated functioning. It is recommended that future research considers a more comprehensive measure of executive function. It is possible that individuals who sought medical attention required to receive a diagnosis were more motivated for recovery and this may have influenced their symptom ratings and/or their engagement with early intervention or proactive recovery. Finally, confounding variables such as medical history and medication were identified but not accounted for as a variable in this analysis. Overall, there were a number of confounding variables in this study, and it is suggested that further research will be required to confirm the findings of this study relating to the relationships between network connectivity, PCSS scores, and cognition using a more focused methodology.

Future studies could replicate the study in a larger sample with multiple follow up time-points postinjury, to determine the natural history of these findings and their implications for the long term. Observing participant recovery in a longitudinal setting and identifying predictors of long-term outcomes (e.g., symptoms, quality of life) may improve our understanding of the clinical implications of network function and cognitive deficits, better informing decision-making in the acute setting and providing guidance for rehabilitation in a clinical context. Additionally, with a larger sample size it would be of interest to explore sex differences across variables such as PCSS scores, network function, alcohol use at time of injury, exercise levels (i.e., mild versus moderate and vigorous activity and exercise duration), education and whether being under the influence of alcohol at time of injury is associated with increased or worse posttraumatic amnesia. It would also be important to analyze participants with comorbid conditions separately to improve the generalizability of the findings. Lastly, the qEEG analysis techniques utilized in this study were somewhat novel. While previous literature established that coherence, phase, and CSD of specific 10–20 electrode sites differentiated between mTBI cases and controls (Thatcher, North, et al., 2001), to our knowledge these measures had not been explored previously in the context of network connectivity in the mTBI population. The measures selected (peak *z*, mean *z*, *z* variance, numbers of *z* scores above ±1.96, percentage of *z* scores above ±1.96) were also exploratory in nature, and were intended to represent the extent of network dysregulation from several perspectives, that is, not simply looking at the highest *z* score (or the extent of deviation at a single site) but also how many sites within the network were outside the expected range based on a normal curve interpretation using standard deviations. The study requires replication in a larger sample where further stratification of the sample to account for various potential confounding variables may be accounted for. Moreover, the dysregulation was not qualitatively assessed in this study (i.e., it was not determined whether the dysregulation was more prevalent in the slow or fast frequency bands). Adding this information in future research may improve the depth of interpretation of the findings and may also provide an opportunity to differentiate subtypes of PPCS-related dysfunction. For example, those who have comorbid conditions such as attention-deficit/hyperactivity disorder or depression may display a different pattern of dysregulation (e.g., more dysregulation is slow versus fast wave activity) compared to those without comorbid conditions. Further investigation into the utility of qEEG as a measure of network function in the mTBI population, particularly by exploring the association with resting-state fMRI findings, may add to the validity of this neurophysiological measure in the acute setting, enabling a more comprehensive assessment and hence a better understanding of mTBI.

In conclusion, this study demonstrated that in an adult sample with acute concussion, PCSS scores were not a sensitive indicator of neuropsychological status (as indicated by cognitive measures) and did not reflect the status of underlying brain network regulation. The current study also provides preliminary evidence for immediate memory task performance as an indicator of underlying altered network connectivity in acute mTBI. The results of this study bring into question the common practice of using self-report symptom ratings as an indicator of recovery (or injury severity). While this practice may be a useful method to track symptom change over time, and initial symptom burden may inform the recovery trajectory, the findings highlight the need for better development of more screening measures sensitive to mTBI, as well as further evaluating neurophysiological and cognitive impacts of

concussion in the acute post-concussion period. Improving our understanding may assist with selecting targeted interventions and facilitating a more comprehensive recovery post-mTBI including the considering of appropriate guidelines for returning to daily occupations such as sports, work, and school.

## Acknowledgement

This study would not have been possible without the wider Concussion Recovery Study (CREST) team members including Melissa Licari, Alexander Ring, Glenn Arendts, Ben Smedley, Sjinene Van Schalkwyk, Philip Brooks, John Iliff, Ashes Mukherjee, Stephen Honeybul, Shaun Markovic, and Anoek Van Houselt. Sincere thanks to the CREST participants for their contributions to our research.

## Author Declarations

Melinda Fitzgerald is the Chief Executive Officer of the charitable organization Connectivity—Traumatic Brain Injury Australia. Funding for this research project was provided by the Neurotrauma Research Program WA (NRP) and was funded by the State Government of Western Australia through the Department of Health. We thank the Perron Institute for Neurological and Translational Science for its support for this research through the award of a Perron Internal Grant. The funding agencies did not have any role in the planning, conduct or writing of this manuscript.

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**Received:** April 25, 2023
**Accepted:** May 28, 2023
**Published:** June 29, 2023

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# Neural Network Improvements Induced by REST Flotation in Chronic Lower Back Pain Patients: An Exploratory Investigation

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**Abstract**

Thalamocortical dysrhythmia is a shared hallmark of numerous neurodivergent conditions. Restricted environment stimulation therapy (REST) flotation causes desirable neural shifts in anxious or depressed populations towards classically defined healthy spectra. In this exploratory investigation, chronic lower back pain patients were randomly assigned to the experimental condition, six 1-hr REST flotation sessions, or the control condition, six 1-hr nap pod sessions. Participants underwent quantitative electroencephalograms (qEEG) before and after their six sessions. Chronic lower back pain patients were chosen because of the high prevalence of the disease condition and the known network changes that contribute to the transition of pain from acute to chronic. Results showed traditional qEEG pain-associated signatures shift to reflect more regulated, healthy activity across the pain and default mode networks in our experimental condition. Dysregulation in neural oscillations can be indicative of symptomology, and the changes observed in the experimental group reflect healthier activity in all frequency bands, while the control group showed no significant changes in any 1 Hz bin. These significant cross-spectral improvements show promise for REST flotation as a supplemental nonpharmacological treatment for chronic pain.

***Keywords***: qEEG; chronic lower back pain; REST flotation; neural networks; default mode network

**Citation**: McGaughey, T. A., Gregg, M. K., & Finomore, V. S. (2023). Neural network improvements induced by REST flotation in chronic lower back pain patients: An exploratory investigation. *NeuroRegulation, 10*(2), 118–133. https://doi.org/10.15540/nr.10.2.118

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## Introduction

Neural network alterations are a hallmark of disease states. In particular, thalamocortical dysregulations can be observed in neurodivergent populations such as Parkinson's disease, Alzheimer's disease (AD), chronic pain, and depression (Vanneste et al., 2018). The thalamocortical dysrhythmia model suggests that disturbances arise between the cortex and thalamus, impeding the flow of information. This disruption may impact cognition, movement, and sensation since higher-level cognitive functions are driven by the interactions between the thalamus and cortex.

Chronic lower back pain (CLBP) is one of the leading causes of disability worldwide, with over 550 million cases in 2019, and has one of the highest number of years lived with disabilities ratio of any disease (Chen et al., 2022). One of the critical shifts in the "chronification" of pain is the transition of pain from the motor cortex to other centers throughout the brain, such as the prefrontal cortex. Traditional interventions rely heavily on ameliorating patients' physical pain, which fails to encapsulate patient suffering as a whole. In addition, these deficits contribute to comorbidities such as anxiety, particularly kinesiophobia, and depression (Gore et al., 2012). This is keenly reflected in the representation across the quantitative electroencephalogram (qEEG) spectra as

dysregulations in the pain network and default mode network (DMN; Alshelh et al., 2018; Kisler et al., 2020).

A noninvasive method used to explore electrical brain activity, qEEG can be used during active states (listening to cues, watching stimuli, performing cognitive tasks), and rich data can also be collected during resting states. Resting-state qEEG rhythms can be indicative of states of arousal and informative of the cognitive processing and potential pathology (Babiloni et al., 2016; Koo et al., 2017; Lee et al., 2014; Trammell et al., 2017). Spectral qEEG data can be broken down by frequency bands which further elucidate various neurological mechanisms in neural networks. Dysregulated electrical activity impacts the function of networks and can indicate pathology (Cecchetti et al., 2021; Li, Pagnotta et al., 2015). This dysregulation can manifest differently by frequency band and by location or network (Gollan et al., 2014; Moon et al., 2018).

Restricted environment stimulation therapy (REST), achieved through sensory deprivation, is seen in the literature as early as the 1950s, with an uptick in rigorous clinical investigations in the last 10 years. Not only has REST flotation shown promise in reducing anxiety and depression (Jonsson & Kjellgren, 2016), but recent work by Al Zoubi et al. (2021) shows alteration in the DMN in healthy patients (Al Zoubi et al., 2021). In brief, Al Zoubi et al. (2021) saw significant changes in the following Broadman Areas (BA) as determined by the published MRI Montreal Neuroscience Imaging Atlas coordinates; 1, 4, 13, 17, 37, and 39 (Al Zoubi et al., 2021). Since REST flotation has the ability to improve neural networks, we inferred that REST flotation might be beneficial for counteracting the network alterations that contribute to the development of chronic pain. The working theory for REST flotation is that reduced sensory input may help to reset networks and alleviate pain. Therefore, our research question asks: does REST flotation alter neural network changes in CLBP patients?

## Methods

All study-related procedures were approved by the West Virginia University (WVU) Institutional Review Board (AAHRPP Accredited). This substudy is part of a larger clinical trial (NCT05260918). Participants were recruited from the WVU Center for Integrated Pain Management and were enrolled from January to December of 2022. Flyers with general study information were hung in exam rooms and distributed to patients with a primary diagnosis of back pain. Interested participants completed the intake survey via QR code through Qualtrics (Qualtrics, 2023). Research personnel reviewed questionnaire responses, and individuals who met the inclusion criteria were invited to visit WVU's Rockefeller Neuroscience Institute (RNI). In brief, inclusion criteria for the study included (a) MRI compatibility, (b) right-handedness, (c) consistent medications for at least the previous 30 days, (d) chronic back pain (as defined below), (e) 18–65 years of age, (f) naïve to mindfulness intervention, and (g) the ability to enter and exit a bathtub without assistance. After a brief tour, interested participants completed the written informed consent process, which included participants going over the consent form with a trained member of the research team, being afforded the opportunity to ask any questions they may have had, and being given time to review all study-related materials prior to signing the consent form. After informed consent was obtained, participants were assigned a unique study code, which was then used to identify all study-related materials. Participants were then randomly assigned to the experimental REST flotation group or the control nap pod group. There was limited access to the master study index, which is the only index linking participants with their study code.

A total of 16 participants were enrolled, and after performing manual and statistical artificing, 10 participants' records were included in the final analyses. An additional participant was then excluded after self-reported extreme life stressors required psychiatric intervention. Therefore, the subsequent analyses are based on $N = 9$. General participant demographics are noted in Table 1.

Inclusion criteria required patients to have CLBP, defined as consistent musculoskeletal back pain that has a moderate-to-severe impact on the patient's life for at least the last 12 weeks. Participant medications are noted below, psychiatric and allergy medications were most prevalent [Supplement 1]. Medication effects were mitigated by using the Laplacian montage in all qEEG analyses.

### Float Tank

REST is often achieved through the use of sensory deprivation tanks. For this investigation, we used two Deluxe Quest Floatation Suite tanks (Superior Float Tanks, n.d.). Each tank measures 238 cm in length by 198 cm in width by 224 cm in height and contains approximately 3800 L salt water with 680 kg of Epsom salt dissolved in 37° C water yielding a specific gravity of 1.30 kg/m$^3$.

**Table 1**
*Participant Demographics by Group*

| | Mean Age (Years) | Mean Weight (Kg) | Height (cm) | M/F | Caucasian | African American | Asian |
|---|---|---|---|---|---|---|---|
| Float | 39.5 ± 13.9 | 80.1 ± 18.3 | 174 ± 13.8 | 2/4 | 67% | 11.5% | 11.5% |
| Nap | 26 ± 2 | 104.5 ± 15.9 | 177.8 ± 13.2 | 2/1 | 100% | 0% | 0% |

The float tanks are thoroughly insulated to prevent light and sound pollution. Participants engaged in six biweekly float sessions, with each session lasting 1 hr and, though encouraged to float with the tank lights and music off, they were given the option to activate them at any time from inside the tanks for comfort. Participants also had the ability to signal research staff via intercom or push-button if required.

### Nap Pod

The control condition for this investigation was the MetroNaps EnergyPod nap pod (MetroNaps, n.d.). Participants in this condition engaged in a similar number of sessions as the float condition. The nap pod is located in a dark, quiet room without windows. There was a motion-activated dim red light for participant safety if they needed to exit the pod for any reason. Participants also had the ability to signal research staff via intercom or push-button if required.

### qEEG Recording

The qEEG was recorded using the CGX Quick-20m, an FDA-cleared wireless headset (Cognionics, n.d.). The system uses dry electrodes recorded from 19 scalp locations consistent with the International 10–20 system (FP1, FP2, F3, F4, Fz, F7, F8, C3, C4, T3, T4, T5, T6, P3, P4, Pz, O1, and O2) and references A1 and A2 (linked-ear montage). The Fp1 and Fp2 electrodes were placed carefully approximately 1 cm above the eyebrows, in line with the participant's pupils. The remaining electrodes were then stretched over the scalp. The cap is designed to reliably align with most head shapes and sizes while maintaining the integrity of the standard 10–20 system. qEEG data were collected in an awake resting state, eyes-closed condition at baseline, and again following treatment.

The qEEG was digitally recorded at 500 samples per second using NeuroGuide software (Version 3.2.7; Applied Neuroscience Inc., n.d.). A 1-Hz high-pass and 40-Hz low-pass filter were applied along with a 60-Hz notch filter to mitigate electrical artifacts. Artifact removal was performed using the NeuroGuide artifact rejection toolbox. Data was then remontaged to Laplacian and visually examined for any further artifacts (EMG, eye movement, electrode pop), which were removed manually. Though Laplacian helps to mitigate the effects of medicine as it sets the global field effects to zero, the impact on the qEEG cannot be entirely ruled out. A list of pharmaceuticals the participants took is listed in S1. Records containing at least 60 s of artifact-free data were included in the analyses. Each maintained a split-half reliability of 0.95 or higher or a test–retest value of 0.93 or higher. Finally, the records were analyzed using NeuroGuide's NaviStat software package for group comparisons using both absolute power and *z*-scored normative comparisons. The NeuroGuide Lifespan database is comprised of 727 normal individuals aged 2–82 years (Thatcher, 2008). Participants were screened prior to inclusion. Those with any history of abnormal prenatal, perinatal, or postnatal development, history of central nervous system diseases, disorders of consciousness, febrile or psychogenic convulsions, and any abnormal deviation in mental or physical development were excluded.

While EEG is recognized for temporal resolution, it lacks the spatial capabilities of other neuroimaging techniques. However, advancements have been made in source localization in EEG over the past 2 decades. Palmero-Soler improved upon the previously used sLORETA method that uses a spherical model of 6200 MRI voxels. This improvement, swLORETA or weighted sLORETA, uses a realistic head model with the boundary element method (BEM) to analyze 12,700 5-mm voxels of current source density allowing for improved source localization of subcortical structures. The centermost voxel of the BA is used to define the region of interest (ROI; Palmero-Soler et al., 2007).

NeuroGuide's NaviStat software includes groups of BAs to correlate with functional networks. Based on Navistat's definition, the pain network is defined as the somatosensory network with the inclusion of several key pain ROIs like the thalamus, amygdala,

and habenula (BA 1, 2, 3, 4, 5, 13a, 24, 32, 33, Thalamus, Habenula, and the Amygdala). Navistat defines the Default Mode Network as BA 2, 7, 10, 11, 19, 29, 30, 31, 35, 39, 40, Cerebellum Crus 1, Cerebellum Crus 2, and Cerebellum 9. See S4 (Pain) and S5 (DMN) for the Talairach coordinates of the centermost voxel of each BA ROI in the networks of interest. A paired *t*-test was used to observe changes between baseline and post-float session interventions using absolute power and *z*-scored comparison.

### Statistical Analysis

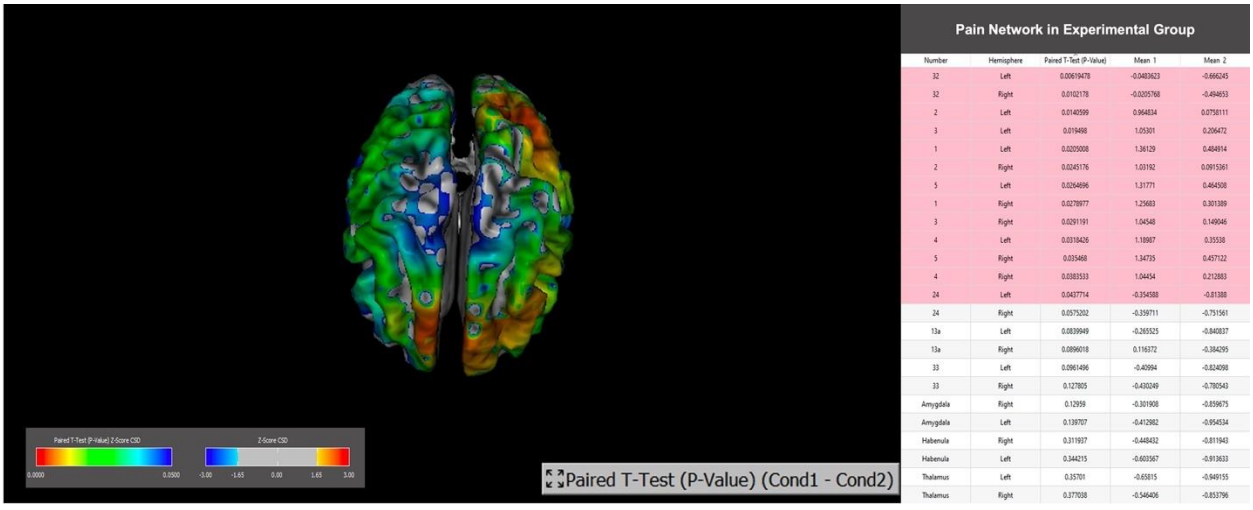
Group level differences were calculated via paired *t*-test by network-defined ROIs across the frequency spectra using NeuroNavigator's NaviStat default statical package. Each *t*-test was informed by the power of the centermost voxel in each ROI according to the schema that follows. For each ROI, there were three *t*-tests (Experimental Baseline vs. Experimental Follow-Up, Control Baseline vs. Control Follow-Up, and Control Baseline vs. Experimental Baseline). However, there were only two overlapping *t*-tests with the same data input (Baseline Control vs. Baseline Experimental and Baseline vs. Follow). Therefore, a Bonferroni correction was used to correct for multiple comparisons. An initial alpha value of 0.90 was selected since these data are preliminary results based on a small sample size. After the Bonferroni correction, a *p*-value of .05 for each ROI indicates statistical significance. There is no need to correct for multiple comparisons across ROIs since each ROI has a unique set of data.

## Results

### Differences Between Groups

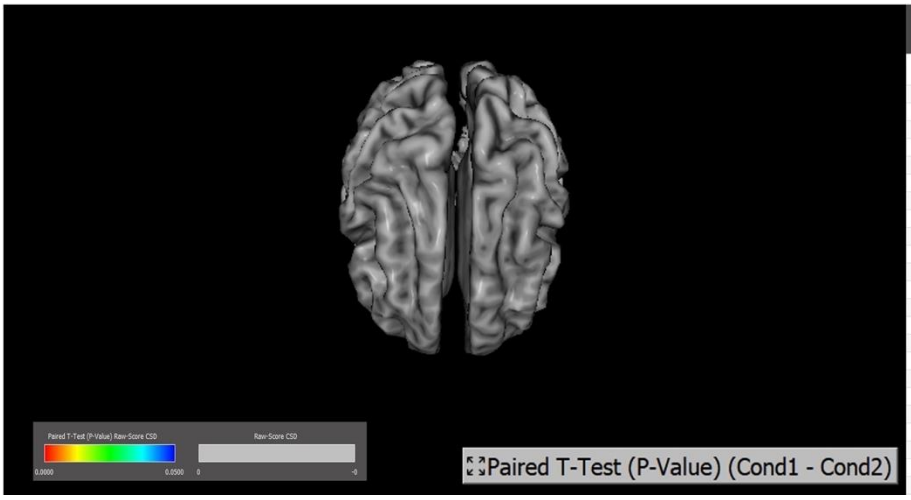
There are no significant differences between the nap and float groups at baseline via an independent two-tailed *t*-test. A paired samples *t*-test showed significant changes in the pain network in the REST flotation experimental group over time in all but six 1-Hz frequency bins out of the 30 Hz analyzed. No significant differences were observed in the nap control group paired sample *t*-test over time. An example showing significance observed in the pain network at 21 Hz in the REST floatation group (Figure 1) compared to the control group (Figure 2) is shown below. In Figure 1, there are 12 significant changes in the pain network over time for the experimental group, with no significant improvements in the control group. It is also important to note that these surface renderings represent a 1-Hz bin. Figure 5 shows the total number of significant changes across the network of interest, and the significant changes by exact ROI by hertz are shown in the supplement.

**Figure 1.** *Group Level Surface Rendering of 21 Hz of Significant Changes Across the Pain Network in the Float Condition.*




**Note.** Highlighted regions in the chart represent statically significant changes.

**Figure 2.** *Group Level Surface Rendering of 21 Hz of Significant of Significant Changes Across the Pain Network in the Control Condition.*

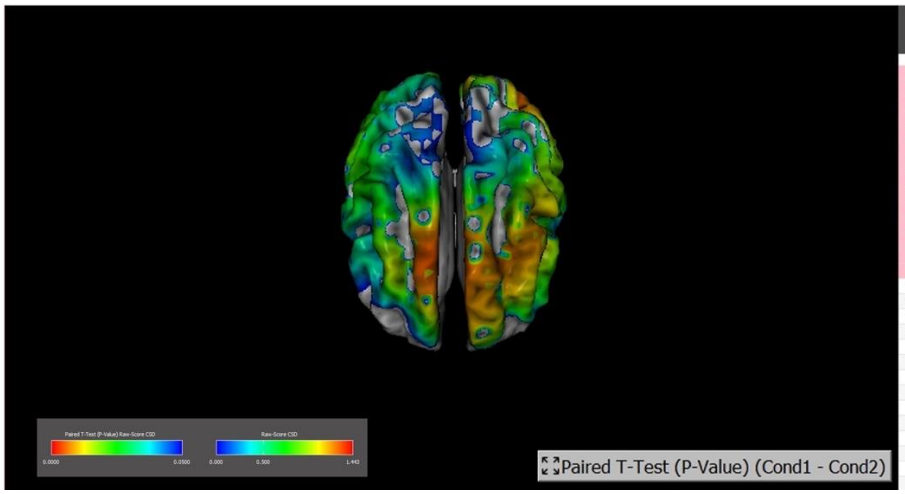



**Pain Network in Control Group**

| Number | Hemisphere | Paired T-Test (P-Value) | Mean 1 | Mean 2 |
|---|---|---|---|---|
| 1 | Left | 0.357104 | 1.22859 | 0.922162 |
| 1 | Right | 0.29295 | 1.25787 | 0.941373 |
| 13a | Left | 0.451261 | -0.317539 | -0.43459 |
| 13a | Right | 0.686714 | -0.434703 | -0.365246 |
| 2 | Left | 0.310851 | 0.715996 | 0.47853 |
| 2 | Right | 0.25367 | 0.990752 | 0.700352 |
| 24 | Left | 0.239883 | -0.253391 | -0.0877079 |
| 24 | Right | 0.263387 | -0.331521 | -0.0871223 |
| 3 | Left | 0.338147 | 0.94969 | 0.688831 |
| 3 | Right | 0.296423 | 1.12477 | 0.844976 |
| 32 | Left | 0.310023 | -0.0686319 | -0.042557 |
| 32 | Right | 0.314853 | -0.256732 | -0.0829705 |
| 33 | Left | 0.232084 | -0.256507 | -0.0745008 |
| 33 | Right | 0.255565 | -0.326801 | -0.061626 |
| 4 | Left | 0.305097 | 1.17809 | 0.901643 |
| 4 | Right | 0.369709 | 1.22644 | 1.00504 |
| Thalamus | Left | 0.822361 | -0.267783 | -0.304792 |
| Thalamus | Right | 0.883945 | -0.277589 | -0.250663 |
| 5 | Left | 0.309333 | 1.31863 | 1.02229 |
| 5 | Right | 0.28565 | 1.43917 | 1.1126 |
| Habenula | Left | 0.633481 | -0.0256242 | -0.131484 |
| Habenula | Right | 0.693874 | -0.0543672 | -0.144479 |
| Amygdala | Left | 0.76502 | -0.262365 | -0.341453 |
| Amygdala | Right | 0.997236 | -0.469476 | -0.468506 |

The same method was used to observe changes in the DMN in both experimental and control conditions. The paired samples *t*-test showed significant changes in the DMN in the REST floatation experimental group in all but three 1-Hz frequency bins out of the 30 Hz analyzed. Again, no significant changes were observed in the control group paired samples *t*-test over time. An example showing significance observed in the DMN at 4 Hz in the REST floatation group (Figure 3) compared to the control group (Figure 4) over time is shown below.

**Figure 3.** *Group Level Surface Rendering of Significant Changes to the DMN at 4 Hz via a Paired Samples T-Test in the Float Condition.*

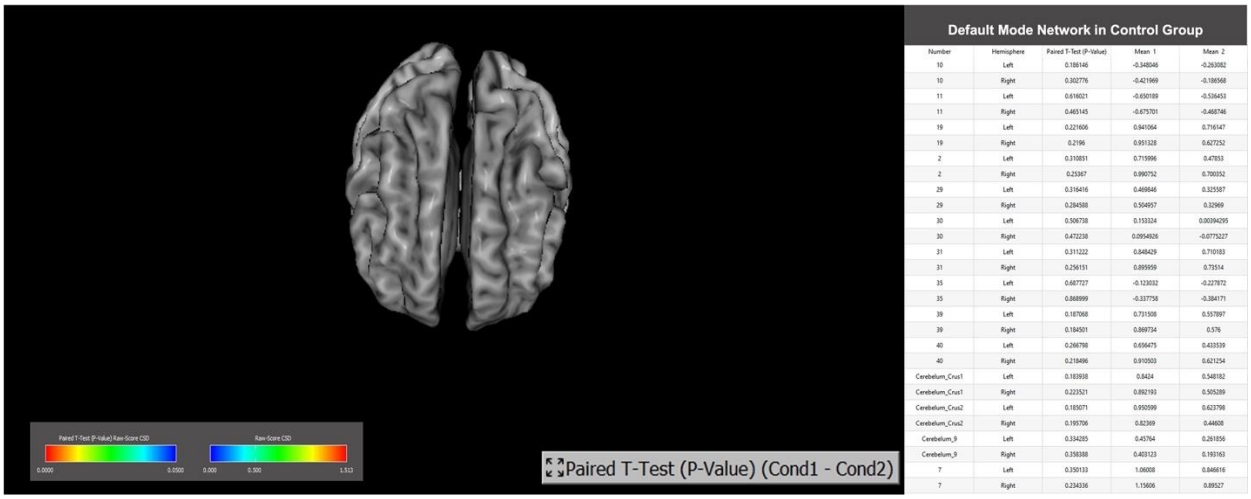



**Default Mode Network in Experimental Group**

| Number | Hemisphere | Paired T-Test (P-Value) | Mean 1 | Mean 2 |
|---|---|---|---|---|
| 7 | Left | 0.00656557 | 1.189 | 0.374269 |
| 40 | Left | 0.0111456 | 0.974962 | 0.0712733 |
| 39 | Left | 0.0117183 | 0.900198 | 0.00700807 |
| 2 | Left | 0.0140599 | 0.964834 | 0.0758111 |
| 10 | Left | 0.0222561 | -0.0874014 | -0.633314 |
| 40 | Right | 0.0236166 | 1.08459 | 0.11521 |
| 31 | Left | 0.0236704 | 0.549356 | -0.115003 |
| 2 | Right | 0.0245176 | 1.03192 | 0.0915861 |
| 7 | Right | 0.0280681 | 1.15583 | 0.286057 |
| 19 | Left | 0.0305319 | 0.57824 | -0.165881 |
| 39 | Right | 0.0312625 | 1.07401 | 0.130969 |
| 31 | Right | 0.037773 | 0.54697 | -0.136305 |
| 10 | Right | 0.0419732 | 0.0151415 | -0.474456 |
| 19 | Right | 0.0474049 | 0.799368 | -0.0713547 |
| Cerebellum_Crus1 | Right | 0.0643134 | 0.701406 | -0.204936 |
| Cerebellum_Crus2 | Right | 0.094722 | 0.481262 | -0.366229 |
| Cerebellum_Crus1 | Left | 0.115054 | 0.257546 | -0.447196 |
| Cerebellum_Crus2 | Left | 0.12288 | 0.289003 | -0.380477 |
| 11 | Right | 0.139073 | -0.361467 | -0.728496 |
| 35 | Left | 0.140514 | -0.356783 | -0.931252 |
| 35 | Right | 0.149802 | -0.283688 | -0.843479 |
| 29 | Right | 0.163467 | -0.0779028 | -0.54222 |
| Cerebellum_9 | Right | 0.166758 | -0.0447452 | -0.689977 |
| 29 | Left | 0.174493 | -0.222314 | -0.601054 |
| Cerebellum_9 | Left | 0.178416 | -0.12361 | -0.711418 |
| 30 | Right | 0.211809 | -0.25188 | -0.742828 |
| 11 | Left | 0.238615 | -0.595859 | -0.934597 |
| 30 | Left | 0.251465 | -0.458725 | -0.866465 |

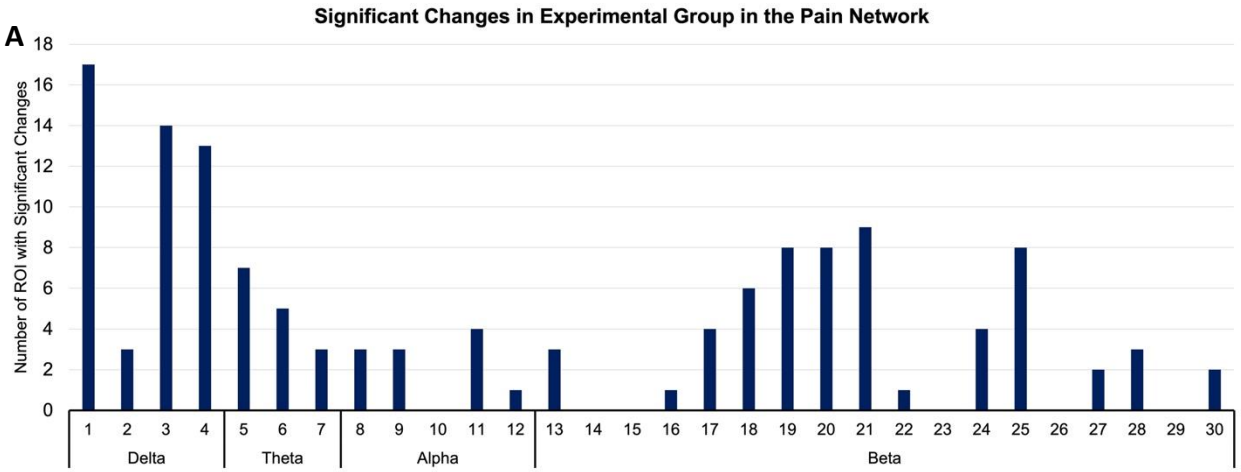
**Note.** The highlighted rows in the chart indicate statistically significant changes over time.

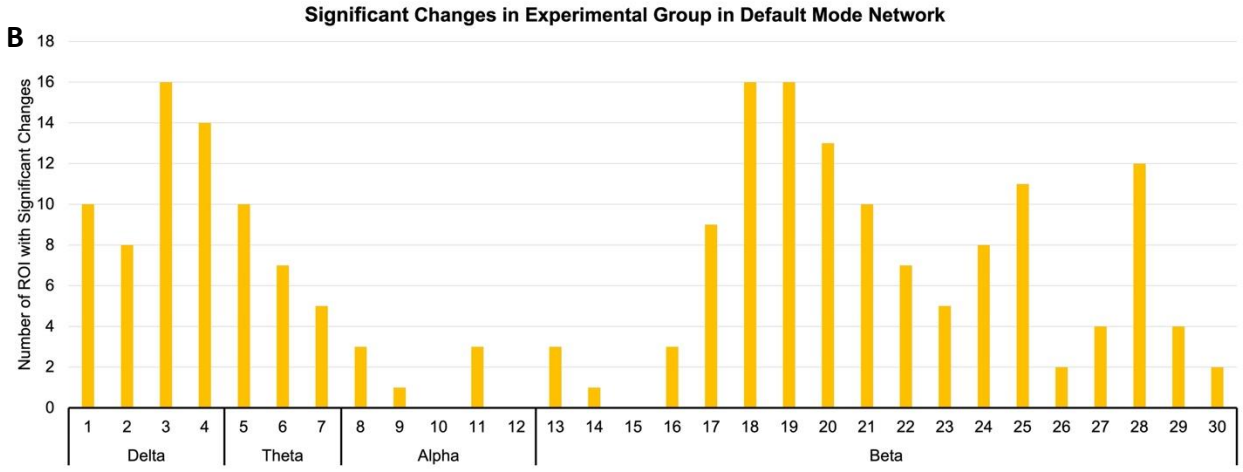
**Figure 4.** *Group Level Surface Rendering of Significant Changes to the DMN at 4 Hz via a Paired Samples T-Test in the Control Condition.*




No significant changes were seen in the control group over time in either network's 1-Hz frequency bins. The NaviStat surface renderings provide group changes in 1-Hz bins. Since all frequency bands (1–30 Hz) were included in the scope of this paper, the number of significant changes per ROI by 1-Hz bin were plotted (Figure 5) to display the significance observed in each frequency band. The bars represent changes in both Pain (5A) and DMN (5B) networks in the experimental group over time. For reference, the pain network is comprised of 24 ROIs, and the DMN is comprised of 28 ROIs. No significant changes were seen in the control group over time.

**Figure 5.** *Significant Changes by Frequency in Pain Network (A) and Default Mode Network (B) in 1-Hz Bins.*






## Discussion

The mechanism behind REST flotation is still unclear. REST flotation significantly reduces auditory, visual, and thermal or tactile stimulation. This reduction in stimuli may help the brain reset itself by allowing the DMN to reign supreme.

Shifts in spectral power can be indicative of functional and structural pathologies. Increases in low-frequency (2–4 Hz) and high-frequency (14–44 Hz) power in pain patients compared to healthy controls has been previously observed (Vanneste et al., 2018). Our participants displayed similar spectral data at baseline. After the float intervention, excess spectral power in all frequency bands was reduced, suggesting a healthier pattern (Supplements 2 and 3). These broad spectra significant improvements are shown in Figure 5. Significant changes were observed across all frequency bands, with the greatest spectral changes being decreases in delta (1–4 Hz), theta (4–8 Hz), and beta (17–30 Hz; Figure 1).

### EEG Pain Network

The pain network is comprised of several ROIs in addition to the primary motor cortex, such as the insula, thalamus, amygdala, and habenula. While the motor cortex is responsible for the localization of pain, the interpretation and internalization of this signal take place in other regions of the brain. The thalamus is classically described as the gatekeep for inbound stimuli, while other areas like the insula, amygdala, and cingulate cortex play a central role in the "chronification" of pain (Lindsay et al., 2021).

Delta (1–4 Hz) activity is seen in deep, dreamless sleep. It has implications in pain, as Li, Ge, and colleagues (2020) found that elevated delta power is seen in increased neuropathic pain, while decreases in delta power are correlated with pain attenuation (Li, Ge, et al., 2020). Changes in delta activity at 4 Hz are represented in Figure 2 (Experimental) and Figure 3 (Control). Improvement in delta band frequencies in pain patients may help to regulate sleep and nociceptive signaling.

Theta (4–8 Hz) occurs in both sleep and wakeful states. Increased spectral theta power is seen in chronic pain (Fallon et al., 2018). Pinheiro and colleagues (2016) conducted a review and surmised that chronic pain patients display higher power in lower frequencies at rest compared to healthy individuals (Pinheiro et al., 2016).

Healthy qEEG spectra resemble a bell curve with a peak in the alpha band (Furman et al., 2020). Alpha can be viewed as a conveyer system that carries one from internal (slower frequencies) to external (faster frequencies) states of arousal. Healthy, synchronous alpha activity helps one to effectively maneuver between concentration and relaxation cycles (Sterman et al., 1994). Dysregulated alpha power can lead to interruptions in this cycle, impacting cognitive performance. Pain patient spectra tend to show dampened and slowed alpha activity, with increased power in the theta and beta bands. Other known disease states with cognitive impairment as their hallmark tend to present with a similar alpha/theta pattern (Özbek et al., 2021). Some researchers suggest that slower alpha may indicate increased sensitivity to pain (Furman et al., 2020). In this study, we observed a rightward shift in alpha band activity toward a healthier spectral presentation. Theta/alpha dysregulation is a hallmark of thalamocortical dysregulation and is

especially noted in pain patients (Prichep et al., 2018). Regulation toward healthy, normal spectra may indicate movement toward symptom reduction and overall improvement in cortical activity.

The increase in the delta band is associated with internal stressors including poor pain processing, kinesiophobia, and rumination (Li, Ge, et al., 2020). An increase in the beta band amplitude is associated with external pain-stressors such as societal stressors, loss of work, and back pain associated stigmas (Teixeira et al., 2022). These processing centers are overworked and cannot effectively communicate with one other, which is necessary to resolve the issues outlined above. Essentially, these processing centers are overworking with little to show for it. Therefore, our qEEG spectral shifts translate into a more efficient conveyer and decreased workload on the processing centers, translating to a significantly more efficient system (Zolezzi et al., 2023). Ergo, the experimental group is showing fewer disease-related qEEG signatures, such as thalamocortical dysrhythmias, which may translate to an improved quality of life.

Increased high beta activity has been observed in the chronic pain population. Excess high-beta power can lead to psychological discomfort and feelings of stress or anxiety (Díaz et al., 2019). Reducing the increase in beta power is often a target for neurofeedback interventions aiming to improve both chronic pain symptoms and pain-related comorbidities (Hassan et al., 2015; Vučković et al., 2019; Wang et al., 2019). Regulation of the beta band serves to improve symptoms of pain and anxiety alike.

### EEG in Default Mode Network

Numerous recent works have shown alterations in the DMN in chronic pain states (Alshelh et al., 2018; Loggia et al., 2013). The DMN is classically discussed as the network invoked when there is a light cognitive load. However, the DMN plays a key function in many self-awareness and introspective tasks. The DMN is a relatively young evolutionary by-product because of the required advancements in cortex development and focus on internal stimuli instead of extrinsic rewards (Smallwood et al., 2021). The DMN also has close ties to the somatosensory and motor cortices. Therefore, it is not a far stretch of the imagination that the literature has shown a connection between the decrease in DMN activity and increased pain rumination (Kucyi et al., 2014). In addition, alterations to the DMN contribute to neural deficits associated with cognitive impairment in many disease states like AD, depression, ADHD, and Parkinson's disease (Mohan et al., 2016).

The DMN is comprised of the precuneus, posterior cingulate, medial prefrontal cortex, and bilateral temporoparietal junction (BA 2, 7, 10, 11, 19, 29, 30, 31, 35, 39, 40). The DMN is one of the most widely studied resting-state neural networks. This network is considered to oppose the central executive network as it is dominant in resting states when the brain is not actively involved in a task and, conversely, becomes deactivated during externally oriented cognitive processing.

Delta frequencies are imperative for memory formation, especially in the DMN (Neuner et al., 2014). Delta also plays a role in cognitive processing, with increases in power being observed during cognitive tasks (Harmony, 2013). In clinical populations, dysregulation in delta power and connectivity is observed in the DMN and is believed to be the underpinnings of psychopathology (Baenninger et al., 2017). Regulation in delta frequency power could be helpful in cognitive flexibility, sleep, and memory. Delta frequencies are highly correlated with DMN activity and the Para-hippocampal gyrus, and it is believed that this link in the delta frequencies is imperative for memory (Neuner et al., 2014).

Like delta, theta power increases during cognitive load (Diaz-Piedra et al., 2020). Frontal theta power is observed during mental processing and is negatively correlated with DMN activity. The inability to regulate frontal midline theta power can inhibit DMN activation (Scheeringa et al., 2008). Increased widespread slow-wave activity (delta and theta) in the DMN is a biomarker for AD (White et al., 2013).

Alpha, the brain's idling rhythm, is the predominant rhythm of the DMN. Alpha activity in the DMN is dominant when internal processing occurs, such as self-referential thinking and has implications in memory (Klimesch et al., 2008; Knyazev et al., 2011). The alpha oscillations help to keep the brain disengaged from external stimuli whilst engaging in introspection during resting state (Foxe & Snyder, 2011). Alpha band dysregulation in the DMN is observed in neuropsychiatric disorders such as AD, schizophrenia, and posttraumatic stress disorder (PTSD; Jafari et al., 2020; Tu et al., 2020). Decreased alpha power is thought to be the underpinning of hypervigilance in PTSD populations. Alpha band activity is believed to be imperative for information sharing in the DMN and, therefore,

regulation of this band is vital for the overall health of the network.

Beta activity in the posterior cingulate is observed in cross-network interaction and functional integration of information (de Pasquale et al., 2012). This frequency band in resting states is believed to be one of the mechanisms used in the predictive coding of stimuli (Betti et al., 2021). Engel and Fries argue that beta rhythms maintain brain states, and alterations in beta activity are representative of detriments in cognition (Engel & Fries, 2010).

### Clinical Impact

Each frequency band impacts the function and connection between hubs within networks. Alterations in oscillations can impact cognition, sensation, movement, perception, and behavior. The health of the DMN affects the health and behavior of the entire brain. In this study, REST flotation shifts qEEG to reflect healthier spectral power in two key pain networks, the DMN and pain network. Initially, our population varied from healthy, pain-free spectra. Typically, normal pain-free spectra clearly display a peak in the alpha frequency band; however, thalamocortical dysrhythmias tend to show increases in theta and beta frequencies that reflect symptomatic pain experiences (Prichep et al., 2018). Restoration of the natural, alpha-dominant frequency may lend to the improvement of a wide array of symptoms (Kisler et al., 2020; Schuurman et al., 2023). In our experimental intervention, we see a significant decrease in beta/theta bands with a slight increase in the alpha band. While these findings are preliminary, these significant neural network changes are often seen before behavioral outcomes. Therefore, with a further longitudinal investigation, REST flotation may prove beneficial as a supplemental nonpharmacological treatment for CLBP because it improves regulation across neural networks.

## Conclusion

Thalamocortical dysrhythmias are observed in many neuropsychiatric and neurodivergent populations. Dysregulated neural oscillations can manifest in various behavioral and symptomatic experiences. A CLBP population was the center of this investigation because of the abhorrent alterations caused by chronic pain and the pervasiveness of CLBP. Our overall goal was to determine what, if any, effect REST flotation may have on neural networks. If REST flotation is able to improve neural networks, then it may prove useful as a supplemental nonpharmacological treatment for CLBP. In both networks of interest, we observed significant changes towards healthy pain-free spectra in the float group, while no significant changes were seen in the controls. These improvements demonstrate the effectiveness of REST flotation in altering neural networks. Therefore, REST flotation shows promise as a supplemental intervention for CLBP.

### Limitations and Future Work

There are several key limitations to note in this investigation. First, this is a pilot investigation with a relatively small number of participants. Further investigation is needed to verify these data and trends, and a greater sample size is also needed to cross-examine the effects of biological sex on pain processing. These findings could be further corroborated by incorporating more expository investigational modalities, such as functional magnetic resonance imaging, to investigate changes in deeper neural networks. Also, additional behavioral outcomes should be assessed to substantiate these findings. Results from this study could be partially due to a mild reduction in inflammation, which could be further elucidated via serum biomarkers. Lastly, more diverse pain syndromes should be investigated to determine whether these findings translate to other populations.

### Acknowledgement

A special thanks to J. H. Stovall and B. Rawls for their review of this manuscript. In addition, we would like to thank J. Ramadan and J. Suffridge for their technical expertise.

### Author Disclosure

The authors have no disclosures.

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**Received:** April 06, 2023
**Accepted:** April 23, 2023
**Published:** June 29, 2023

# Appendix

## Supplemental Materials

**Supplement 1**
*Participant Medications Verified via Chart Review*

| Participant | Medication | Purpose/Class |
|---|---|---|
| Float 1 | Dexedrine 10mg PO Daily | Stimulant |
| | Adderall XR 30mg PO Daily | Stimulant |
| Float 2 | Allegra 30 mg PO Daily | Allergy |
| | Flonase PRN | Allergy |
| | Naproxen 1000 mg PRN | NSAID |
| Float 3 | Methotrexate 2.5mg PO Daily | Antimetabolites |
| | Enbrel 50 mg SubQ weekly | TNF Blocker |
| Float 4 | Adderall XR 20mg BID | Stimulant |
| | Methocarbamol 500mg PRN | Muscle Relaxer |
| Float 5 | No prescribed medications | |
| Float 6 | No prescribed medications | |
| Nap 1 | Duloxetine 20mg PO Daily | Antidepressant |
| Nap 2 | No prescribed medications | |
| Nap 3 | Buspar 10mg BID | Anxiolytic |
| | Trazadone | Antidepressant |
| | Colchicine 0.6mg PRN | Gout |

## Supplement 2:

| Pain Network t-Test | | Delta | | | Theta | | | Alpha | | | Beta | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ROI NAME | ROI LOCATION | 1 Hz | 2 Hz | 3 Hz | 4 Hz | 5 Hz | 6 Hz | 7 Hz | 8 Hz | 9 Hz | 10 Hz | 11 Hz | 12 Hz | 13 Hz | 14 Hz | 15 Hz | 16 Hz | 17 Hz | 18 Hz | 19 Hz | 20 Hz | 21 Hz | 22 Hz | 23 Hz | 24 Hz | 25 Hz | 26 Hz | 27 Hz | 28 Hz | 29 Hz | 30 Hz |
| 1 - L | Post Central Gyrus | 0.020 | NS | 0.034 | 0.021 | 0.044 | 0.016 | 0.041 | 0.034 | 0.033 | NS | 0.016 | 0.034 | 0.024 | NS | NS | NS | 0.040 | 0.023 | 0.039 | 0.041 | 0.045 | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| 1 - R | Post Central Gyrus | NS | NS | 0.018 | 0.028 | 0.043 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | 0.029 | 0.041 | 0.032 | NS | NS | 0.036 | 0.047 | NS | NS | NS | NS | NS |
| 2 - L | Post Central Gyrus | 0.010 | 0.029 | 0.022 | 0.014 | 0.027 | 0.012 | 0.028 | NS | NS | NS | 0.029 | NS | 0.047 | NS | NS | 0.045 | NS | 0.035 | NS | 0.022 | 0.029 | 0.044 | NS | NS | NS | 0.037 | NS | 0.044 | | |
| 2 - R | Post Central Gyrus | 0.045 | 0.036 | 0.015 | 0.025 | 0.034 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | 0.014 | 0.022 | 0.024 | NS | 0.023 | 0.025 | NS | NS | 0.049 | NS | | |
| 3 - L | Post Central Gyrus | 0.020 | NS | 0.030 | 0.019 | 0.036 | 0.014 | 0.045 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | 0.035 | NS | NS | 0.034 | NS | NS | NS | NS | 0.050 | 0.049 | NS | 0.050 | |
| 3 - R | Post Central Gyrus | 0.040 | 0.047 | 0.015 | 0.029 | 0.044 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | 0.018 | 0.030 | 0.029 | NS | NS | 0.042 | 0.039 | NS | NS | NS | NS | |
| 4 - L | Pre-Central Gyrus | 0.021 | NS | 0.044 | 0.032 | NS | 0.026 | NS | NS | NS | NS | 0.029 | NS | NS | NS | NS | NS | NS | 0.036 | NS | NS | 0.044 | NS | NS | NS | NS | NS | NS | NS | | |
| 4 - R | Pre-Central Gyrus | NS | NS | 0.016 | 0.038 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | 0.016 | 0.033 | 0.030 | NS | NS | NS | NS | NS | NS | NS | | |
| 5 - L | Parietal Lobe | NS | NS | 0.032 | 0.026 | 0.037 | 0.039 | NS | 0.011 | 0.019 | NS | NS | NS | 0.040 | NS | NS | NS | 0.025 | 0.020 | 0.022 | 0.030 | NS | NS | NS | 0.046 | NS | NS | NS | NS | | |
| 5 - R | Parietal Lobe | NS | NS | 0.041 | 0.035 | NS | NS | NS | 0.021 | 0.031 | NS | NS | NS | NS | NS | NS | NS | 0.026 | 0.039 | 0.007 | 0.026 | 0.041 | NS | NS | 0.050 | NS | NS | NS | NS | | |
| 13a - L | Anterior Insula | 0.007 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | | |
| 13a - R | Anterior Insula | 0.015 | NS | 0.007 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | | |
| 24 - L | Anterior Cingulate Gyrus | 0.013 | NS | NS | 0.044 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | | |
| 24 - R | Anterior Cingulate Gyrus | 0.015 | NS | 0.035 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | | |
| 32 - L | Anterior Cingulate Gyrus | 0.015 | NS | 0.035 | 0.006 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | | |
| 32 - R | Anterior Cingulate Gyrus | 0.016 | NS | 0.005 | 0.010 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | | |
| 33 - L | Anterior Cingulate | 0.011 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | | |
| 33 - R | Anterior Cingulate | 0.014 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | | |
| Thal - L | Parasubiculum hippocampal region | 0.049 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | | |
| Thal - R | Parasubiculum hippocampal region | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | | |
| Hab - L | Habenula | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | | |
| Hab - R | Habenula | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | 0.032 | NS | NS | NS | NS | NS | 0.010 | NS | NS | NS | | |
| Amy - L | Amygdala | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | | |
| Amy - R | Amygdala | 0.040 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | 0.028 | NS | NS | 0.028 | NS | NS | NS | 0.049 | 0.044 | NS | NS | NS | NS | NS |

Supplement 3:

| Default Mode Network t-Test | | Delta | | | Theta | | | Alpha | | | Beta | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ROI-Name | ROI - LOCATION | 1 Hz | 2 Hz | 3 Hz | 4 Hz | 5 Hz | 6 Hz | 7 Hz | 8 Hz | 9 Hz | 10 Hz | 11 Hz | 12 Hz | 13 Hz | 14 Hz | 15 Hz | 16 Hz | 17 Hz | 18 Hz | 19 Hz | 20 Hz | 21 Hz | 22 Hz | 23 Hz | 24 Hz | 25 Hz | 26 Hz | 27 Hz | 28 Hz | 29 Hz | 30 Hz |
| 2 - L | Post Central Gyrus | 0.010 | 0.029 | 0.022 | 0.041 | 0.022 | 0.012 | 0.023 | NS | NS | NS | 0.029 | NS | 0.047 | NS | NS | 0.045 | NS | 0.035 | NS | NS | 0.029 | 0.044 | NS | NS | NS | 0.037 | 0.037 | NS | 0.044 |
| 2 - R | Post Central Gyrus | 0.045 | 0.036 | 0.015 | 0.025 | 0.034 | 0.021 | 0.028 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | 0.014 | 0.022 | 0.024 | NS | 0.023 | 0.026 | NS | NS | 0.049 | NS | NS |
| 7 - L | Supramarginal Gyrus | 0.022 | 0.040 | 0.011 | 0.020 | 0.010 | 0.012 | 0.033 | 0.021 | NS | NS | 0.050 | NS | 0.029 | NS | NS | NS | 0.024 | 0.033 | 0.033 | NS | 0.038 | NS | NS | 0.039 | NS | NS | NS | NS | NS | NS |
| 7 - R | Supramarginal Gyrus | NS | NS | 0.026 | 0.022 | 0.044 | NS | NS | NS | NS | NS | NS | 0.045 | NS | NS | NS | NS | NS | 0.050 | 0.022 | NS | 0.043 | NS | NS | 0.031 | NS | NS | NS | NS | NS | NS |
| 10 - L | Pre-Frontal Cortex | 0.100 | 0.045 | 0.034 | 0.022 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| 10 - R | Pre-Frontal Cortex | 0.016 | 0.043 | 0.011 | 0.042 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| 11 - L | Orbital Frontal | 0.011 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| 11 - R | Orbital Frontal | 0.012 | NS | 0.007 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| 19 - L | Occipital Cortex | NS | NS | 0.037 | 0.030 | NS | 0.037 | 0.038 | NS | NS | NS | NS | NS | NS | NS | NS | NS | 0.011 | 0.038 | 0.032 | NS | 0.037 | NS | NS | NS | NS | NS | NS | 0.049 | NS | NS |
| 19 - R | Occipital Cortex | NS | NS | 0.040 | 0.047 | 0.044 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | 0.035 | 0.043 | 0.015 | 0.035 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| 29 - L | Posterior Cingulate & Superior Transverse Temporal Gyrus | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| 29 - R | Posterior Cingulate & Superior Transverse Temporal Gyrus | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | 0.019 | NS | 0.024 | NS | 0.018 | 0.014 | 0.046 | 0.035 | 0.003 | 0.023 | 0.033 | NS | 0.045 | NS |
| 30 - L | Posterior Cingulate & Cuneus | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | 0.039 | 0.044 | NS | 0.048 | NS | NS | 0.042 | 0.022 | 0.046 | 0.014 | NS | NS | 0.033 | NS | NS |
| 30 - R | Posterior Cingulate & Cuneus | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | 0.017 | 0.016 | NS | 0.042 | 0.022 | 0.046 | 0.014 | NS | NS | NS | NS | NS | NS |
| 31 - L | Dorsal Posterior Cingulate | NS | NS | 0.040 | 0.022 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | 0.031 | NS | 0.022 | NS | 0.046 | NS | NS | NS | 0.020 | NS | NS | NS | NS | NS |
| 31 - R | Dorsal Posterior Cingulate | NS | NS | 0.044 | 0.030 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | 0.031 | NS | 0.022 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| 35 - L | Medial Temporal Lobe & Parahippocampal Gyrus | 0.022 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| 35 - R | Medial Temporal Lobe & Parahippocampal Gyrus | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | 0.041 | NS | 0.047 | 0.016 | NS | NS | NS | 0.040 | 0.029 | NS | NS | NS | NS | NS |
| 39 - L | Angular Gyrus & Inferior Parietal Lobe | 0.001 | 0.018 | 0.009 | 0.012 | 0.015 | 0.022 | 0.025 | 0.039 | 0.048 | NS | NS | NS | 0.038 | NS | 0.041 | NS | 0.020 | 0.032 | 0.023 | 0.036 | 0.018 | NS | NS | 0.033 | NS | 0.044 | 0.038 | NS | NS |
| 39 - R | Angular Gyrus & Inferior Parietal Lobe | NS | NS | 0.031 | 0.031 | 0.040 | 0.024 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | 0.050 | 0.019 | 0.038 | 0.019 | NS | NS | 0.029 | 0.017 | NS | NS | NS | NS | NS | NS |
| 40 - L | Inferior Parietal Lobe Angular Gyrus | 0.005 | 0.022 | 0.016 | 0.011 | 0.025 | 0.012 | 0.019 | 0.041 | NS | NS | 0.042 | NS | NS | NS | 0.039 | NS | NS | 0.028 | 0.044 | 0.040 | 0.025 | 0.028 | NS | 0.047 | NS | 0.036 | 0.035 | NS | 0.044 |
| 40 - R | Inferior Parietal Lobe Angular Gyrus | NS | 0.044 | 0.018 | 0.022 | 0.030 | 0.024 | NS | 0.041 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | 0.012 | 0.023 | 0.018 | NS | 0.014 | 0.018 | 0.050 | NS | 0.045 | NS | NS |
| Crus1 - L | Cerebellum | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | 0.011 | 0.031 | NS | 0.034 | NS | 0.045 | NS | 0.035 | NS | NS | NS | 0.030 | 0.031 | NS |
| Crus1 - R | Cerebellum | NS | NS | 0.034 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | 0.025 | 0.044 | 0.023 | 0.034 | NS | NS | NS | NS | NS | NS | NS | 0.041 | NS | NS |
| Crus2 - L | Cerebellum | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | 0.017 | 0.035 | NS | NS | NS | NS | NS | 0.043 | NS | NS | NS | 0.030 | 0.029 | NS |
| Crus2 - R | Cerebellum | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | 0.019 | 0.040 | 0.023 | 0.042 | NS | NS | NS | NS | NS | NS | NS | 0.049 | NS | NS |
| Cblm_9 - L | Cerebellum | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | 0.015 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | 0.046 | NS |
| Cblm 9 - R | Cerebellum | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | 0.021 | NS | 0.049 | 0.049 | NS | NS | NS | 0.043 | NS | NS | NS | NS | 0.042 | NS |

**Supplement 4**

| Pain Network | | Talairach Coordinates | | |
|---|---|---|---|---|
| Brodmann Area | ROI LOCATION | X | Y | Z |
| 1 - L | Post Central Gyrus | −41 | −40 | 67 |
| 1 - R | Post Central Gyrus | 45 | −37 | 63 |
| 2 - L | Post Central Gyrus | −44 | −36 | 48 |
| 2 - R | Post Central Gyrus | 46 | −35 | 47 |
| 3 - L | Post Central Gyrus | −40 | −28 | 51 |
| 3 - R | Post Central Gyrus | 40 | −28 | 51 |
| 4 - L | Pre-Central Gyrus | −31 | −24 | 57 |
| 4 - R | Pre-Central Gyrus | 31 | −24 | 57 |
| 5 - L | Parietal Lobe | −11 | −51 | 65 |
| 5 - R | Parietal Lobe | 11 | −51 | 66 |
| 13a - L | Anterior Insula | −34 | 18 | −1 |
| 13a - R | Anterior Insula | 36 | 18 | −4 |
| 24 - L | Anterior Cingulate Gyrus | −4 | 17 | 29 |
| 24 - R | Anterior Cingulate Gyrus | 5 | 16 | 30 |
| 32 - L | Anterior Cingulate Gyrus | −9 | 33 | 29 |
| 32 - R | Anterior Cingulate Gyrus | 11 | 33 | 29 |
| 33 - L | Anterior Cingulate | −3 | 10 | 26 |
| 33 - R | Anterior Cingulate | 4 | 11 | 26 |
| Thal - L | Parasubiculum hippocampal region | −10 | −20 | 8 |
| Thal - R | Parasubiculum hippocampal region | 10 | −20 | 8 |
| Hab - L | Habenula | −4 | −28 | −4 |
| Hab - R | Habenula | 4 | −28 | −4 |
| Amy - L | Amygdala | −16 | −4 | −20 |
| Amy - R | Amygdala | 16 | −4 | −20 |

**Supplement 5**

| Default Mode Network | | Talairach Coordinates | | |
|---|---|---|---|---|
| Brodmann Area | ROI LOCATION | X | Y | Z |
| 2 - L | Post Central Gyrus | −44 | −36 | 48 |
| 2 - R | Post Central Gyrus | 46 | −35 | 47 |
| 7 - L | Supramarginal Gyrus | −20 | −66 | 51 |
| 7 - R | Supramarginal Gyrus | 21 | −66 | 52 |
| 10 - L | Pre-Frontal Cortex | −14 | 58 | 9 |
| 10 - R | Pre-Frontal Cortex | 15 | 58 | 9 |
| 11 - L | Orbital Frontal | −15 | 41 | −13 |
| 11 - R | Orbital Frontal | 15 | 41 | −13 |
| 19 - L | Occipital Cortex | −29 | −75 | 6 |
| 19 - R | Occipital Cortex | 30 | −74 | 5 |
| 29 - L | Posterior Cingulate & Superior Transverse Temporal Gyrus | −9 | −45 | 11 |
| 29 - R | Posterior Cingulate & Superior Transverse Temporal Gyrus | 8 | −44 | 11 |
| 30 - L | Posterior Cingulate & Cuneus | −15 | −37 | −13 |
| 30 - R | Posterior Cingulate & Cuneus | 16 | −37 | −14 |
| 31 - L | Dorsal Posterior Cingulate | −5 | −55 | 38 |
| 31 - R | Dorsal Posterior Cingulate | 5 | −55 | 38 |
| 35 - L | Medial Temporal Lobe & Parahippocampal Gyrus | −16 | −13 | −25 |
| 35 - R | Medial Temporal Lobe & Parahippocampal Gyrus | 14 | −13 | −24 |
| 39 - L | Angular Gyrus & Inferior Parietal Lobe | −44 | −64 | 28 |
| 39 - R | Angular Gyrus & Inferior Parietal Lobe | 45 | −64 | 29 |
| 40 - L | Inferior Parietal Lobe Angular Gyrus | −45 | −46 | 43 |
| 40 - R | Inferior Parietal Lobe Angular Gyrus | 46 | −46 | 44 |
| Crus1 - L | Cerebellum | −37 | −66 | −33 |
| Crus1 - R | Cerebellum | 38 | −68 | −33 |
| Crus2 - L | Cerebellum | −29 | −74 | −39 |
| Crus2 - R | Cerebellum | 32 | −70 | −41 |
| Cblm_9 - L | Cerebellum | −11 | −50 | −47 |
| Clbm 9 - R | Cerebellum | 9 | −50 | −47 |

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# Reflections on the Increase in Autism, ADHD, Anxiety, and Depression: Part 1 – Bonding, Screen Time, and Circadian Rhythms

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**Abstract**

Over the past 2 decades, there has been a significant increase in the prevalence of autism, attention-deficit/hyperactivity disorder (ADHD), anxiety, depression, and pediatric suicidal behavior. Based upon the evolutionary perspectives of Nassim Taleb and educator Joseph C. Pearce, discussed are three identified behavioral risk factors that may contribute to activate, maintain, and increase the prevalence and severity of these disorders. These include the reduction of infant and caretaker bonding, increase in screen time, and disruption of circadian rhythms. Prevention strategies are suggested to reduce the risk factors.

***Keywords***: autism; ADHD; anxiety; screen time; circadian rhythm; prevention

**Citation**: Peper, E. (2023). Reflections on the increase in autism, ADHD, anxiety, and depression: Part 1 – bonding, screen time, and circadian rhythms. *NeuroRegulation, 10*(2), 134–138. https://doi.org/10.15540/nr.10.2.134

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## Introduction

Over the past 2 decades, there has been a significant increase in the prevalence of autism, attention-deficit/hyperactivity disorder (ADHD), anxiety, depression, and pediatric suicidal behavior. Autism rates have risen from 1 in 150 children in 2000 to 1 in 36 children in 2020 (CDC, 2023), while ADHD rates have increased from 6% in 1997 to approximately 10% in 2018 (CDC, 2022). The rates of anxiety among 18- to 25-year-olds have also increased from 7.97% in 2008 to 14.66% in 2018 (Goodwin et al., 2020), and depression rates for U.S. teens ages 12–17 have increased from 8% in 2007 to 13% in 2017 (Geiger & Davis, 2019; Walrave et al., 2022). Pediatric suicide attempts have also increased by 163% from 2009 to 2019 (Arakelyan et al., 2023), and during the COVID-19 pandemic, these rates have increased by more than 25% (WHO, 2022; Santomauro et al., 2021). In addition, the prevalence of these disorders has tripled for U.S. adults during the pandemic compared to before (Ettman et al., 2020).

The rapid increase of these disorders is not solely due to improved diagnostic methods, genetic factors, or the COVID-19 pandemic. The pandemic amplified preexisting increasing trends. More likely individuals who were at risk had their disorders triggered or amplified by harmful environmental and behavioral factors. Conceptually, genetics loads the gun; epigenetics, behavior, and environment pull the trigger.

While behavioral strategies such as neurofeedback, cognitive behavior therapy, biofeedback, meditation techniques, and pharmaceuticals can treat or ameliorate these disorders, the focus concurrently needs to be on prevention and risk reduction. In some ways, treatment can be likened to closing the barn doors after the horses have bolted.

### Evolutionary Perspective to Reduce Risk Factors

Nassim Taleb (2012) in his book*, Antifragile: Things That Gain from Disorder (Incerto)*, provides an evolutionary perspective and offers simple rules of health by reducing risk factors:

- Assume that anything that was not part of our evolutionary past is probably harmful.
- Remove the unnatural or unfamiliar (e.g., smoking or e-cigarettes, sugar, digital media).
- We do not need evidence of harm to claim that a drug or an unnatural (via positive) procedure is dangerous. If evidence of harm does not exist, it does not mean harm does not exist.
- Only resort to medical techniques when the health payoff is very large (to save a life) or exceeds its potential harm, such as incontrovertibly needed surgery or lifesaving medicine (penicillin).
- Avoid the iatrogenics and negative side effects of prescribed medication.

Taleb's suggestions are reminiscent of the perspective described by the educator Joseph C. Pearce (1993) in his book, *Evolution's End*. Pearce argued that modern lifestyles have negatively affected the secure attachment and bonding between caregivers and infants. The lack of nurturing and responsive caregiving in early childhood may lead to long-term emotional and psychological problems. He points out that we have radically adapted behaviors that differ from those that evolved over thousands of generations and that allowed us to thrive and survive. In the last 100 years, babies have often been separated from their mothers at birth or early infancy by being put in a nursery or separate room, limited or received no breastfeeding with the use of formula, exposed to television for entertainment, lacked exploratory play outdoors, and absent of constant caretakers in high-stress and unsafe environments.

As Pearce pointed out:

> If you want true learning, learning that involves the higher frontal lobes—the intellectual, creative brain—then again, the emotional environment must be positive and supportive. This is because at the first sign of anxiety the brain shifts its functions from the high, prefrontal lobes to the old defenses of the reptilian brain. These young people need audio-vocal communication, nurturing, play, body movement, eye contact, sweet sounds and close heart contact on a physical level. (Mercogliano & Debus, 1999)

To optimize health, eliminate or reduce those factors that have significantly changed or were not part of our evolutionary past. The proposed recommendations are based upon Talib's perspective that anything that was not part of our evolutionary past is probably harmful; thus, remove the unnatural or unfamiliar and adapt the precautionary principle which states that if evidence of harm does not exist, it does not mean harm does not exist (Kriebel et al., 2001). This article is the first of a two-part series. Part 1 focuses on increasing reciprocal communication between infant and caretaker, reducing screen time, and reestablishing circadian rhythms. Part 2 focuses on reducing exposure to neurotoxins, processed foods, and supporting the human biome.

## Part 1 – Increase Bonding, Reduce Screen Time, and Reestablish Circadian Rhythms

### Increase Bonding Between Infant and Caretaker

Infants develop emotional communication through reciprocal interactions with their caregiver, during which the caregiver responds to the infant's expressions. When this does not occur, it can be highly stressful and detrimental to the infant's development. Unfortunately, more and more babies are emotionally and socially isolated while their caregivers are focused on and captured by the content on their digital screens. Moreover, infants and toddlers are entertained (babysat) by cellphones and tablets instead of dynamically interacting with their caretakers. Screens do not respond to the child's expressions; the screen content is programmed to capture the infant's attention through rapid scene changes. Without reciprocal interaction, babies often become stressed, as shown by research conducted by developmental psychologist Professor Edward Tronick, who conducted the "Still Face" experiment (Tronick & Beeghly, 2011; Weinberg et al, 2008).

The Still Face experiment illustrated what happened when caregivers did not respond to infants' communication. The caregivers were asked to remain still and unresponsive to their babies, resulting in the infants becoming increasingly distressed and disengaged from their surroundings. Not only does this apply to infants but also to children, teenagers, and older individuals. Watch the

short Still Face experiment which illustrates what happens when caretakers do not respond to the infants' communication.

https://www.youtube.com/watch?v=vmE3NfB_HhE

***Recommendation***. Do not use cellphone and digital media in the first 2 years of life while being with an infant. It is important for caregivers to limit their cellphone use and prioritize reciprocal interactions with their infants for healthy emotional and psychological development.

**Figure 1.** *Reduce Screen Time (Television, Social Media, Streaming Videos, Gaming)*


**Note.** The critique of social media does not imply that there are no benefits. If used judiciously, it is a powerful tool to connect with family and friends or access information needed.

From an evolutionary perspective, screen time is an entirely novel experience. Television, computers, and cellphones are modern technologies that have significantly impacted infants and young people's development. To grow, infants, toddlers, and children require opportunities to explore the environment through movement, touch, and play with others, which is not possible with screen time. Research has shown that excessive screen time can negatively affect children's motor development, attention span, and socialization skills, as well as contribute to obesity and other health problems (Carson et al., 2016; Hinkley et al., 2014; Mark, 2023).

When 4-year-olds watch fast-paced videos, they exhibit reduced executive functions and impulse control, which may be a precursor for ADHD, compared to children who engage in activities such as drawing (Lillard & Peterson, 2011; Mark, 2023). Furthermore, excessive screen time and time spent on social media are causal in increasing depression as was discovered when Facebook became available at selected universities.

Researchers compared the mental health of students at similar universities where Facebook was or was not available and observe how the students' mental health changed when Facebook became available (Braghieri et al., 2022). Their research showed that

> college-wide access to Facebook led to an increase in severe depression by 7% and anxiety disorders by 20%. In total, the negative effect of Facebook on mental health appeared to be roughly 20% the magnitude of what is experienced by those who lose their job. (Walsh, 2022)

Exposure to digital media has also significantly reduced our attention span from 150 s in 2004 to an average of 44 s in 2021. The shortening of attention span may contribute to the rise of ADHD and anxiety (Mark, 2023, p. 96).

***Recommendations***. Reduce time spent on social media, gaming, mindlessly following one link after the other, or watching episode after episode of streaming videos. Instead, set time limits for screen use, turn off notifications, and prioritize in-person interactions with friends, family, and colleagues while engaging in collaborative activities. Encourage children to participate in physical and social activities and explore nature.

To achieve this, follow the guidelines from the American Academy of Pediatrics' recommendation on screen time (Council on Communications and Media, 2016), which suggests limiting screen time for children of different age groups:

- Children under 18 months of age should avoid all screen time, except for video chatting with family and friends.
- Children aged 18–24 months should have limited screen time and only watch together with a caretaker.
- Children aged 2–5 years should have no more than 1 hr of screen time per day with parental supervision.
- For adolescents, screen and social media time should be limited to no more than an hour a day.

In our experience, when college students reduce their time spent on social media, streaming videos, and texting, they report that it is challenging; however, they then report an increase in well-being and performance over time (Peper et al., 2021). While it may require more effort to provide children with actual experiential learning and entertainment than allowing them to use screens, having children perform activities and play outdoors (a green environment) appears to reduce ADHD symptoms (Louv, 2008; Kuo & Taylor, 2004).

### Reestablish Circadian (Daily) Rhythms

Our natural biological and activity rhythms were once regulated by natural light until the 19th century. It is hard to imagine not having light at night to read, work on the computer, or answer email. However, light not only illuminates but also affects our physiology by regulating our biological rhythms. Exposure to light at night can interfere with the production of melatonin, which is essential for sleep. Insufficient sleep affects 30% of toddlers, preschoolers, school-age children, and the majority of adolescents. The more media is consumed at bedtime, the more delayed bedtime and reduced total sleep occur (Hale et al., 2018). Reduced sleep is a contributing factor to increased ADHD symptoms of inattention, hyperactivity, and impulsivity (Cassoff et al., 2012).

***Recommendations***. Support the circadian rhythms. Avoid screen time an hour before bedtime. This will reduce exposure to blue light and also reduce the sympathetic arousal triggered by the content on the screen or reacting to social media and emails. Sleep in total darkness and establish a regular bedtime and waking time to avoid social jetlag, which can negatively affect health and performance (Caliandro et al., 2021). Implement sleep hygiene strategies such as developing a bedtime ritual can also improve sleep quality (Stager et al., 2023; Suni, 2023). Thus, go to bed and wake up at the same time each day, including weekends as well as avoiding large meals, caffeine, and alcohol before bedtime. Consistency is key to success.

## Conclusion

To optimize health, eliminate or reduce those factors that have significantly changed or were not part of our evolutionary past and explore strategies that supports our behaviors that have allowed the human being to thrive and survive. Improve clinical outcome and optimize health by enhancing reciprocal communication interactions, reducing screen time, and reestablishing the circadian rhythm.

### Author Disclosure

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

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**Received:** April 05, 2023
**Accepted:** April 12, 2023
**Published:** June 29, 2023