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Aim and Scope

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

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Editorial – Volume 6, Number 2

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***Address correspondence to**: Rex L. Cannon, PhD, BCN, Knoxville Neurofeedback Group, 7147 Kingston Pike, Ste 103, Knoxville, TN 37919, USA. Email: rcannonphd@gmail.com

Welcome to *NeuroRegulation* 6, Issue 2; thanks for joining us for the latest issue. In the current issue authors utilize a variety of research techniques and several case reports demonstrating interesting findings. Ashlie N. Bell, Donald Moss, and Robert J. Kallmeyer present data of a controlled study examining LORETA Z-Score neurofeedback and HRV biofeedback for chronic posttraumatic stress disorder (PTSD). Michela Balconi and Maria Elide Vanutelli present data for optical imaging and neurofeedback intervention for emotional behavior regulation in schizophrenia. Jon A. Frederick, Andrew S. Heim, and Kelli N. Dunn present data concerning self-prompted discrimination and operant control of the alpha frequency domain. Rubén Pérez-Elvira, José A. Carrobles, Diego J. López Bote, and Javier Oltra-Cucarella present case study data for the efficacy of Live Z-score neurofeedback training in chronic insomnia. And finally, George Lindenfeld, George Rozelle, John Hummer, Michael R. Sutherland, and James C. Miller present a case study of remediation of PTSD in a combat veteran.

NeuroRegulation thanks these authors for their valuable contributions to the scientific literature for neurofeedback, neuroscience, and learning. We strive for high quality and interesting empirical topics. We encourage the members of ISNR and other biofeedback and neuroscience disciplines to consider publishing with us. We extend an invitation to all researchers and clinicians interested in human performance, the human brain, and methods to improve its functionality to submit reviews, theoretical articles, and research data. It is important to stress that publication of case reports is also always useful in furthering the advancement of an intervention for both clinical and normative functioning. We encourage researchers, clinicians, and students practicing neurofeedback to submit case studies, or groups of case studies!

NeuroRegulation has made great strides for increasing the scientific integrity of neurofeedback, biofeedback, and applied neuroscience. We would like to thank our editorial board, reviewers, and contributors for this success. When writing this editorial, I decided to conduct a search of PubMed with the term “neurofeedback” dated from 1995 to current and there is a substantial increase in the number of articles over the last few years, and we expect this trend to continue. If we are clear to purpose, consistent with methods and publishing outcomes, then we are capable of much. I look forward to more discoveries and processes uncovered to aid in improving human performance across all functional domains.

We thank you for reading *NeuroRegulation*!

Rex L. Cannon, PhD, BCN
Editor-in-Chief
Email: rcannonphd@gmail.com

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NeuroRegulation

Healing the Neurophysiological Roots of Trauma: A Controlled Study Examining LORETA *Z*-Score Neurofeedback and HRV Biofeedback for Chronic PTSD

Ashlie N. Bell [*], *Donald Moss, and Robert J. Kallmeyer*

Saybrook University, Oakland, California, USA

Abstract

Introduction: Posttraumatic stress disorder (PTSD) has been linked to abnormalities within three neural networks: default mode (DMN), salience (SN), and central executive (CEN). This study examined the effectiveness of LORETA *z*-score neurofeedback (LZNF) training for altering current source within these networks and reducing symptoms associated with PTSD. **Methods:** Twenty-three adults with chronic PTSD were randomly assigned to 15 sessions of either LZNF (n = 12) or heart rate variability biofeedback (HRVB; n = 11). Psychosocial and physiological assessments were completed at baseline and postintervention. **Results:** The LZNF group showed very large, statistically significant decreases in symptoms on the PTSD Checklist for DSM-V (PCL-5; p = .003, d = 2.09) and Beck Anxiety Inventory (BAI; p = .003, d = 2.13). The HRVB group also showed very large decreases on the PCL-5 (p = .006, d = 1.40) and medium effects on the BAI (p = .018, d = 0.76). Between-group comparisons showed medium to large effects of group type in favor of LZNF (PCL-5 d = 0.57; BAI d = 0.94), although not statistically significant. LZNF Responders (n = 9) demonstrated very large, statistically significant decreases in abnormal *z*-scores within all targeted networks (DMN p = .012, d = 0.96; SN p = .008, d = 1.32; CEN p = .008, d = 1.33). **Conclusion:** The positive outcomes of this study provide preliminary evidence to support LZNF training as a specific, effective, and tolerable intervention for adults with chronic PTSD.

Keywords: traumatic stress; PTSD; EEG biofeedback; neurofeedback; LORETA; neurophysiology

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***Address correspondence to**: Ashlie Bell, PhD, 3333 S. Wadsworth Blvd., Ste 160, Lakewood, CO, 80227-5122, USA. Email: abell@saybrook.edu

Edited by:
Rex L. Cannon, PhD, SPESA Research Institute, Bloomfield Hills, Michigan, USA; Knoxville Neurofeedback Group, Knoxville, Tennessee, USA

Reviewed by:
Randall Lyle, PhD, Mount Mercy University, Cedar Rapids, Iowa, USA
Tanju Surmeli, MD, Living Health Center for Research and Education, Sisli, Istanbul, Turkey

Introduction

Everything we think, feel, and do is largely governed by a single organ: the human brain. In fact, numerous neuroimaging studies have revealed that alterations in cognition, behavior, mood, and arousal are closely linked to the functional integrity of various brain regions and networks (Bluhm et al., 2009; Daniels et al., 2010; Lanius, Frewen, Tursich, Jetly, & McKinnon, 2015; Menon, 2011). While decades of research have been dedicated to finding solutions for physical brain injuries and neurodegenerative disorders, less research has examined interventions that target the neurophysiological consequences of something the large majority of humans will face at least once in their lifetime: traumatic stress (Kessler et al., 2017).

Neurophysiological Abnormalities

Posttraumatic stress disorder (PTSD) has been linked to a number of abnormalities in neural activation patterns, particularly within three intrinsic connectivity networks: the default mode network (DMN), salience network (SN), and central executive network (CEN; Dunkley et al., 2015; Engdahl et al., 2010; Imperatori et al., 2014; Jokić-Begić & Begić, 2003; Patel, Spreng, Shin, & Girard, 2012; Todder et al., 2012; van der Kolk, 2006; Wahbeh & Oken, 2013).

The DMN is known for its role in both autobiographical and interpersonal functioning, especially in relation to self-awareness and identity (Menon, 2011). Neuroimaging studies have observed that individuals with PTSD tend to show altered functional connectivity within this network, which might underlie some common experiences reported by trauma survivors, such as relational challenges, depersonalization, and identity alterations (Bluhm et al., 2009; Daniels et al., 2010; Lanius et al., 2015; Patel et al., 2012).

The SN is involved in shifting attention toward or away from internal and external stimuli (Menon, 2011). Individuals with PTSD often show either an overengagement or underengagement of this network, as well as altered connectivity within the network (Lanius et al., 2015). These neurophysiological patterns might contribute to alterations in arousal (e.g., hyperarousal or dissociation), misinterpretation of ambivalent stimuli (e.g., hypervigilance, heightened startle response, etc.), and avoidance (Lanius et al., 2015; Patel et al., 2012; Simmons et al., 2008; Simmons, Strigo, Matthews, Paulus, & Stein, 2009).

The CEN is known for its role in higher-level cognitive functioning, such as attention, decision-making, planning, working memory, verbal learning, and time perception (Menon, 2011). PTSD has been associated with a failure to properly recruit this network, which might underlie impairments in cognition, difficulty concentrating, and altered time perception during flashbacks (Daniels et al., 2010; Lanius et al., 2015; Patel et al., 2012). The extensive evidence behind such neurophysiological abnormalities provides a strong rationale for interventions that directly target these underlying patterns.

Neurofeedback Training for PTSD

Neurofeedback training is a psychophysiological intervention designed to alter brain activation patterns toward healthier levels of functioning. This intervention utilizes neuroimaging and a brain-computer interface to read neural activity in real time and feed that information back to clients in the form of audiovisual cues to assist them in self-regulating their brainwave activation patterns (Engelbregt et al., 2016; Lanius et al., 2015). Numerous studies have found neurofeedback to be effective for alleviating symptoms associated with a wide variety of cognitive, emotional, and neurological disorders (Arns et al., 2017; Arns, de Ridder, Strehl, Breteler, & Coenen, 2009; Panisch & Hai, 2018; Reiter, Andersen, & Carlsson, 2016). Moreover, neuroimaging studies have shown alterations in both the functional activation patterns and structural volume of targeted brain regions following neurofeedback training (Ghaziri et al., 2013; Markiewicz, 2017).

An extensive systematic review of the literature by the first author found 10 studies that provided quantifiable data of preintervention to postintervention changes following neurofeedback (Bell, 2018). All studies observed medium to large improvements in PTSD symptoms and/or related neural activity, in accordance with the particular variables measured (Foster & Thatcher, 2015; Gapen et al., 2016; Huang-Storms, Bodenhamer-Davis, Davis, & Dunn, 2006; Kluetsch et al., 2014; Paret et al., 2014; Peniston & Kulkosky, 1991; Peniston, Marrinan, Deming, & Kulkosky, 1993; Pop-Jordanova & Zorcec, 2004; Ros, Baars, Lanius, & Vuilleumier, 2014; Smith, 2008; van der Kolk et al., 2016; Walker, 2009). Three of these studies also conducted follow-up assessments, which found improvements to be maintained over an extended period (1–26 months) in most participants. However, most studies utilized convenience samples, and only three included a control or comparison group. Of these, the most recent randomized controlled trial found neurofeedback to produce more significant improvements in affect regulation, identity impairments, abandonment concerns, and overall PTSD symptoms than a treatment-as-usual condition (i.e., psychotherapy and medication; van der Kolk et al., 2016).

The large majority of these studies utilized 20 to 40 sessions of traditional surface electroencephalogram (EEG) neurofeedback. Only one small case series by Foster and Thatcher (2015) utilized a newer modality called low resolution electromagnetic tomography analysis (LORETA) *z*-score neurofeedback. The case series examined 11 veterans with comorbid PTSD and traumatic brain injury, and the number of sessions ranged from 11 to 27. The authors reported significant ($p < .01$) changes in LORETA current source density (CSD) within the region of training for all subjects, yielding very large effect sizes (mean $d = 1.78$) for nine of the veterans and moderate effects (mean $d = 0.466$) for the other two. These neurophysiological changes were also accompanied by substantial improvements in symptoms. Promising results such as these justify further exploration into the use of this newer neurofeedback modality as an intervention for PTSD and other mental health disorders.

LORETA *Z*-Score Neurofeedback

LORETA *z*-score neurofeedback (LZNF) is one of the most advanced, comprehensive, and targeted

modalities of neurofeedback training available. LORETA utilizes a 19-channel EEG cap and three-dimensional (3-D) source imaging to determine the specific source of an electric dipole (Pascual-Marqui, Michel, & Lehmann, 1994). As such, while surface EEG is known to have poor spatial resolutions (i.e., 22–37 cm^3), the use of LORETA brings these levels down to 7 mm^3, all while maintaining the optimal temporal resolutions of EEG within the millisecond time domain (Pascual-Marqui, Esslen, Kochi, & Lehmann, 2002). Thus, the use of this imaging technology allows for targeted, real-time training of individual brain regions, even deeper within the cortex (Krigbaum & Wigton, 2014; Thatcher, 2010).

Power and connectivity metrics for each Brodmann area can then be compared against the FDA registered NeuroGuide normative database of age-matched, *neurotypical* individuals (i.e., without neurological or psychological impairments; Thatcher, North, & Biver, 2005; Thatcher, Walker, Biver, North, & Curtin, 2003). From this comparison, a *z*-score is derived for each metric, which assumes a normal Gaussian distribution to define the level of deviation from the average of that normative population (Thatcher & Lubar, 2009). During LZNF training, the *z*-scores for all targeted metrics are computed in real time and trained in the direction of $z = 0$. Although limited, research thus far has demonstrated that LZNF produces clinically-meaningful improvements in both symptoms and brain activity for a variety of disorders, including traumatic brain injury (Koberda, 2015a), depression (Koberda et al., 2014b), anxiety (Koberda et al., 2014b; Lambos & Williams, 2015a), addiction (Cannon, Lubar, Sokhadze, & Baldwin, 2008), seizures (Frey & Koberda, 2015; Koberda, 2015b), attention-deficit/hyperactivity disorder (Decker, Roberts, & Green, 2015; Koberda et al., 2014a), autism (Koberda, 2012), cognitive dysfunction (Koberda, 2014b; Lambos & Williams, 2015b), and cerebrovascular accident (Koberda, 2014a). These outcomes were produced after an average of 10 to 20 sessions, which is less than the 30 to 40 sessions generally required for traditional neurofeedback.

Method

Study Design

The purpose of this study was to assess the effectiveness and specificity of LZNF training, as compared to HRVB training, for reducing mental health symptoms, improving autonomic regulation, and regulating abnormal brainwave activity in adults with chronic PTSD (i.e., symptoms for a minimum of 6 months following a traumatic event).

HRVB as an active control for LZNF. Heart rate variability (HRV) is a measure of beat-to-beat heart rate intervals that is often used as a measure of autonomic regulation (McCraty & Shaffer, 2015; Thayer, Ahs, Fredrikson, Sollers, & Wager, 2012). HRV biofeedback (HRVB) training utilizes electrocardiography and a respiratory belt, paired with a breath pacer and audiovisual feedback, to train the heart toward healthier levels of HRV (Thayer et al., 2012). This modality of biofeedback has previously demonstrated effectiveness for reducing PTSD symptoms, even when compared to various control conditions (Ginsberg, Berry, & Powell, 2010; Reyes, 2014; Tan, Dao, Farmer, Sutherland, & Gevirtz, 2011; Zucker, Samuelson, Muench, Greenberg, & Gevirtz, 2009). This qualified HRVB training as an active control condition for the experimental LZNF intervention in this study. It also offered a more ethical option than sham neurofeedback for this sensitive population. The use of HRVB for comparison also provided the opportunity to closely match most of the LZNF training conditions, such as real-time measurement of psychophysiological data, self-regulation training with audiovisual cues, resting time in front of a computer monitor, and interactions with a therapist. To maintain similar levels of placebo and nocebo between the groups, all participants were provided brief psychoeducation around the intervention they would receive and were told that, “as far as we know, both interventions provide equal opportunity for benefit, although neither is guaranteed to benefit.”

Eligibility and Enrollment

Following approval of all aspects of this study by the Saybrook Institutional Review Board, adults between the ages of 18 and 80 were recruited via advertisements on social media, in health and mental health centers, and in various community locations throughout the greater Denver/Boulder area. Eligibility criteria was defined prior to recruitment and all interested individuals completed prescreening. Individuals were eligible if (a) they self-reported having experienced a traumatic event, (b) 6 months or more had passed since the traumatic event, (c) their total score on the PTSD Checklist for DSM-V (PCL-5) was greater than 20, (d) they were proficient in English, and (e) they were between the ages of 18 and 80. Exclusion criteria included (a) moderate to severe brain injury, (b) current diagnosis of a seizure disorder, (c) current diagnosis of a personality disorder, (e) active psychosis, (f) active suicidal ideation, and (g) pregnancy. Participants were also asked to refrain from making changes in their current treatment regimens or engaging in other brain-oriented interventions for the duration of this study.

Eligible participants were officially enrolled in the study upon signing the IRB-approved informed consent form, which spelled out the procedures, risks, and potential benefits of the study.

Measures and Procedures

This study aimed to examine the effectiveness of LZNF training for reducing PTSD symptoms, improving HRV, and normalizing neural activation patterns associated with PTSD. Seven outcome measures were assessed within approximately one week prior to starting training (Time 1) and one week after the 15th training session (Time 2).

Demographic and presession questionnaires. Prior to initiating training, all participants completed a demographic questionnaire, which assessed for general demographic data (e.g., age, gender, etc.) as well as potential confounding variables (e.g., concurrent practices, medication, etc.). Additionally, participants completed a presession questionnaire at the beginning of each session to track subjective changes in symptoms and assess for factors that could impact physiological measures that day, such as pain, substance use, and sleep quality.

Psychosocial assessment. For each assessment, participants completed two self-report symptom questionnaires: the PTSD Checklist for DSM-V (PCL-5) and the Beck Anxiety Inventory (BAI). The PCL-5 closely correlates with the symptoms outlined in the Diagnostic and Statistical Manual of Mental Disorders (5th ed.; DSM-V; American Psychiatric Association, 2013; Blevins, Weathers, Davis, Witte, & Domino, 2015) and assesses the frequency and severity of PTSD symptoms using a Likert-type scale. For this study, PTSD symptom scores were computed by summing the total score for all symptoms, producing a continuous score ranging from 0 to 80. The BAI assesses symptoms of anxiety up to three levels of severity. This questionnaire was utilized to more thoroughly examine changes in psychophysiological anxiety symptoms associated with PTSD. The severity level for each item was attributed a number (i.e., 0–3) and summed for a total anxiety score ranging from 0 to 63.

Psychophysiological assessment. EEG and HRV data were recorded in the initial and final assessment sessions. A third recording was completed around the midpoint of the intervention to check in on participants' response to training and update training protocols in accordance with changing psychophysiological states. Interim assessments such as this are common, and often necessary, in clinical practice.

***HRV recording and artifacting*.** HRV data was recorded simultaneous with the EEG recording using the NeXus-4 amplifier, an EXG sensor cable, Meditrace disposable electrodes, a respiration sensor, and BioTrace+ software (Mind Media BV, Herten, Netherlands). Electrocardiographic activity was recorded using the forearm placement method, which is a minimally invasive placement that is less susceptible to artifact than placements such as the hand (Shaffer & Combatalade, 2013). Participants placed the respiration belt around their own waists approximately 2 inches above the navel.

Prior to analyzing this data, visible artifacts were manually removed within the Biotrace+ software. The file was then imported into Kubios 2.1 software (Biosignal Analysis and Medical Imaging Group, Kuopio, Finland) for more detailed artifacting and analysis. For this study, the HRV analyses examined the standard deviation of intervals between normal heart beats (SDNN) and the root mean square of successive differences (RMSSD).

***EEG recording and artifacting*.** Scalp voltages were recorded using a 19-channel electrode cap (Electro-cap International, Inc., Eaton, OH) corresponding to the 10-20 international system and referenced to linked ears. Electrode sites were prepared until the impedance level at each site was less than 5 kΩ, and electrical signals were amplified using the Brainmaster Discovery 24E amplifier (BrainMaster Technologies, Inc., Bedford, OH). For each assessment, 10 min of EEG data (i.e., 5 min with eyes open and 5 min with eyes closed) were recorded in an at-rest condition using the NeuroGuide 2.9.1 software (Applied Neuroscience, Inc., Largo, FL).

Each EEG recording was first edited using the automatic artifacting feature in the NeuroGuide 2.9.1 software to remove stereotypical artifacts such as eye blinking and electrode pops. This was followed by a manual scan of the full EEG recording to remove any artifact data that the software had incorrectly selected (e.g., pulse artifact, lateral eye movement, electromyographic activity from temporal or frontal muscles, etc.) and add any true EEG data that it had inaccurately omitted (e.g., abnormal EEG activity). The total selection in each recording included a minimum of 2 minutes of clean EEG data, which is the recommended minimum in accordance with the algorithm of the NeuroGuide database (R. Thatcher, personal communication, August 10, 2017).

Training Protocol Selection and Procedures

All participants attended 15 sessions of the training to which they were assigned (i.e., LZNF or HRVB) at a

rate of two sessions per week. Each session included 20 minutes of direct training, divided into 4 rounds of 5 min. A third-party software, Zukor Media Player (Zukor Interactive, Inc., Las Vegas, NV) was utilized to provide identical audiovisual feedback between the two groups. This feedback was provided in the form of movies, which were chosen by participants from a limited selection. The chosen movie was then connected to the individual's training protocol so that the screen and volume zoomed in and out as participants' physiological measures moved in and out of the set thresholds.

LZNF training protocol. As a way of standardizing an individualized training modality, NeuroGuide's Symptom Checklist-Neural Network Match (SCL-FNM) method was utilized to generate each participant's training protocol (Thatcher, 2013). Three networks (i.e., CEN, SN, and DMN) and 5 metrics (i.e., amplitude, coherence, phase, phase shift, and phase lock) were selected for each LZNF participant. The software then automatically compared the LORETA metrics from the client's baseline EEG recording to those of the NeuroGuide normative database, ultimately selecting all metrics within these networks that showed abnormal levels of activity in the individual's brain. The Z-Tunes method was utilized for reward provision, which required two selection criteria to be met for a reward to be received: (1) 70% of the targeted metrics were within the set *z*-score threshold and (2) the average of the remaining 30% were moving in the direction of $z = 0$ (i.e., a negative slope over time). The *z*-score threshold was manually adjusted throughout each session to maintain a reward rate of 24 to 36 rewards per minute (i.e., 40%–60%). When participants successfully achieved a 50%–60% reward rate, the *z*-score threshold was decreased by 1 or 2 tenths of a *z*-score for the next 5-min round (e.g., $z = 2.9$ to $z = 2.8$). In the operant conditioning paradigm, this process has been termed *shaping* and refers to the reinforcement of successive approximations toward a targeted outcome (Strehl, 2014). Thus, the video feedback in this study guided participants to systematically lower *z*-scores for the trained brain regions, promoting a gradual normalization of the three neural networks.

HRVB training protocol. The HRVB protocol for this study was largely based on the resonant frequency training protocol outlined by Lehrer, Vaschillo, and Vaschillo (2000). This is one of the most common protocols in HRVB training and has previously demonstrated effectiveness for reducing PTSD symptoms (Tan et al., 2011). Each participant's resonant frequency was determined through assessment of five different breathing rates and analyzed for the best convergence of features (e.g., phase relations between heart rate and breathing, peak-trough amplitude, etc.). A breath pacer was then matched to the rate of each participant's resonant frequency and added to the training screen. The combination of breath pacer and video feedback guided participants to breathe at the resonant frequency and increase HRV metrics.

Data Analysis

The data for this study was analyzed using SPSS software, version 25. For each outcome measure, the difference from Time 1 to Time 2 was first measured within each of the groups separately and then assessed for differences between the groups. Due to the small, heterogenous sample of this study, nonparametric, signed rank Wilcoxon and Mann-Whitney U analyses were utilized in place of paired and independent samples *t*-tests. Statistical significance was set at $\alpha = .050$ for all analyses and SPSS output was a p value. Cohen's d effect sizes were also calculated to assess the magnitude and practical importance of observed changes (Weaver & Goldberg, 2012). These effect sizes are commonly categorized as small ($d = 0.20$), medium ($d = 0.50$), and large ($d \geq 0.80$).

LORETA CSD *z*-scores. The final selection of EEG data from each Eyes Open recording was run through NeuroGuide's LORETA 3-D source analysis, which compares the CSD of each Brodmann area against the LORETA normative database to generate *z*-scores. These *z*-scores were then exported from NeuroGuide and imported into an Excel spreadsheet for further analysis. The center voxel was selected for each frequency and Brodmann area within the targeted neural networks and then separated for individual network analyses. Due to the canceling effects of averaging negative and positive *z*-scores, all *z*-scores were converted to absolute values prior to any further analysis. To counter the dampening effects of averaging a large quantity of *z*-scores (i.e., 600–780 *z*-scores per network), the total number of significant (i.e., beyond ±1.96) *z*-scores was summed for each of the targeted neural networks. Higher numbers reflect higher levels of abnormal brain activity.

LZNF responders. Another challenge inherent to LORETA *z*-score analyses is that, due to significant heterogeneity from participant to participant, as well as differences in baseline levels of absolute and relative power (e.g., overall low power), some participants might show an overall increase in significant *z*-scores while others show a decrease.

Similar to averaging positive and negative *z*-scores, this can lead to cancelation effects. For this reason, a subgroup of the LZNF group (*n* = 9), termed *LZNF Responders*, was analyzed further for each of the neural network analyses. This subgroup consisted of participants in the LZNF group who showed any amount of decrease from Time 1 to Time 2 in the total number of significant CSD *z*-scores within the targeted networks. This provided a more accurate measurement of the size and significance of changes in brainwave activity within the majority (75%) of LZNF participants.

Results

Participant Demographics

Twenty-four eligible adults were enrolled on a first-come, first-served basis and alternately assigned between the LZNF group and HRVB group according to the order in which they returned their prescreening materials. Only one participant assigned to the HRVB group withdrew participation prior to completion of the study. Thus, the final sample included 12 participants in the LZNF group and 11 in the HRVB group. Enrolled participants ranged from age 30 to 60 with a mean age of 44. Of the 23 participants that completed the study, 21 (91%) reported at least one comorbid psychiatric disorder, 18 (78%) were taking psychiatric medication, and 19 (83%) were concurrently receiving outside psychotherapeutic support. The LZNF group reported a larger number of comorbid diagnoses at baseline (i.e., LZNF = 21, HRVB = 15). The latter two variables were similar between the two groups at baseline. Participants engaged in psychotherapy had been attending psychotherapy for several months to several years prior to enrollment in this study, and no participants began psychotherapy during their participation in the study.

All participants endorsed having experienced multiple traumatic events, with a mean of 6 direct experiences per participant reported on the PCL-5 Life Events Checklist. The most commonly endorsed traumatic experiences included sexual trauma (65%), physical assault (61%), childhood abuse or neglect (52%), life-threatening illness or injury (48%), natural disaster (35%), work-related trauma (e.g., first responders; 26%), and military combat (13%). Mean baseline measurements were similar between the LZNF and HRVB groups for most variables (see Table 1). The largest baseline differences were in the HRV measures, for which the LZNF group had higher initial levels. There was also substantial variability from participant to participant, particularly in the three network analyses. Such variability is common when examining psychophysiological measurements.

Table 1
Baseline Mean and Median Measurements for LZNF and HRVB Groups

	HRVB Group		LZNF Group	
	Mean (*SD*)	Median	Mean (*SD*)	Median
Age	43.73 *(8.79)*	44.0	44.58 *(13.06)*	41.0
PCL-5 Total Score	49.82 *(10.16)*	47.0	46.17 *(14.23)*	45.0
BAI Total Score	24.91 *(8.77)*	26.0	25.50 *(8.08)*	22.5
CEN Total Sig *Z*-scores	69.09 *(71.94)*	31.0	66.17 *(99.79)*	46.0
SN Total Sig *Z*-scores	89.09 *(82.74)*	61.0	82.00 *(119.83)*	48.0
DMN Total Sig *Z*-scores	74.27 *(73.82)*	51.0	70.50 *(105.04)*	39.5
SDNN	23.59 *(11.62)*	19.5	37.82 *(23.51)*	28.80
RMSSD	22.18 *(12.13)*	18.1	34.42 *(17.82)*	29.00

Note. LZNF group *n* = 12; HRVB group *n* = 11; *SD* = standard deviation; Sig = significant (i.e., absolute *z* > 1.96).

Psychosocial Outcomes

For the psychosocial measures utilized in this study (i.e., PCL-5 and BAI), a decrease in scores represents a decrease in negative symptoms and is thus desirable.

PTSD symptoms. For the HRVB group, total scores on the PCL-5 decreased significantly (p = .006) from Time 1 (M = 49.82, SD = 10.16) to Time 2 (M = 31.18, SD = 13.53) with a very large effect (d = 1.40). For the LZNF group, PCL-5 scores also decreased significantly (p = .003) from Time 1 (M = 46.17, SD = 14.23) to Time 2 (M = 18.08, SD = 12.65) with a very large size of effect (d = 2.09). Considering both groups demonstrated very large, statistically significant improvements, the MWU analysis found the difference between the LZNF and HRVB groups to be statistically nonsignificant (p = .414). The Cohen's d analysis, however, found a medium effect of group type (d = 0.57). Figure 1 represents the amount of pre–post change in PCL-5 scores, which was about 40% greater in the LZNF group compared to the HRVB group.

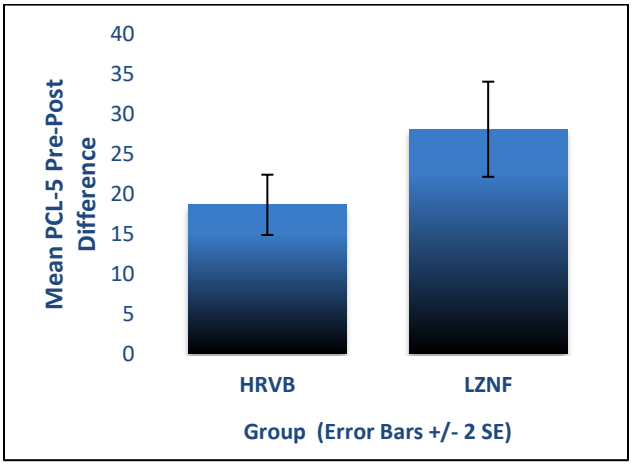

Figure 1. PTSD Checklist for DSM-V pre–post difference in the LZNF and HRVB groups.

Physiological anxiety symptoms. For the HRVB group, total scores on the BAI decreased significantly (p = .018) from Time 1 (M = 24.91, SD = 8.77) to Time 2 (M = 18.18, SD = 8.9) with a medium effect size (d = 0.76). For the LZNF group, BAI scores decreased significantly (p = .003) from Time 1 (M = 25.50, SD = 8.08) to Time 2 (M = 9.83, SD = 6.52), yielding a very large effect size (d = 2.13). Similar to the PCL-5 analyses, MWU results found the BAI difference between the LZNF and HRVB groups to be statistically nonsignificant (p = .214). However, Figure 2 shows that the amount of change from the start to the end of training was about two times larger for the LZNF group than the HRVB group, with a large effect of group type (d = 0.94).

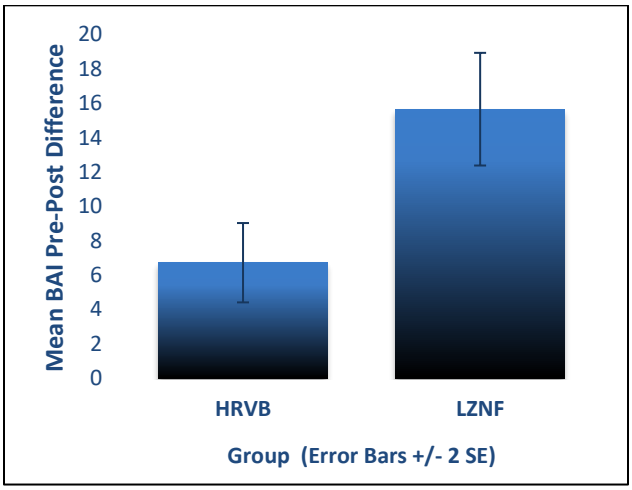

Figure 2. Beck Anxiety Inventory pre–post difference in the LZNF and HRVB groups.

Neural Network Outcomes

When analyzing changes in neural networks, a decrease in the total number of significant LORETA CSD z-scores is desirable and indicates positive change.

Default mode network. The HRVB group showed a slight decrease in the number of significant DMN z-scores from Time 1 (M = 74.27, SD = 73.82) to Time 2 (M = 68.27, SD = 81.18), although this effect was nonsignificant (p = .790) with a negligible size of effect (d = 0.08). The LZNF group also showed a decrease in DMN z-scores from Time 1 (M = 70.50, SD = 105.04) to Time 2 (M = 54.33, SD = 96.13) yielding a small effect (d = 0.27), although this difference was also statistically nonsignificant (p = .213). It is important to note this analysis included nine LZNF participants who showed an overall decrease, as well as three LZNF participants who showed an overall increase, thus producing a cancelation of effects. When these canceling effects were removed by analyzing a subgroup of LZNF Responders (n = 9) separately, the LZNF training was shown to produce large (d = 0.96), statistically significant (Wilcoxon p = .012) decreases in the total number of significant DMN z-scores.

The MWU analysis found the DMN difference between the HRVB and full LZNF groups to be statistically nonsignificant (p = 1.00) with a small effect of group type (d = 0.17). Descriptive analyses,

however, revealed that the amount of change from preintervention to postintervention in the LZNF group was more than 2.5 times that of the HRVB (see Figure 3). For the LZNF Responders, the amount of pre–post change was double that of the full LZNF group and over six times that of the HRVB group.

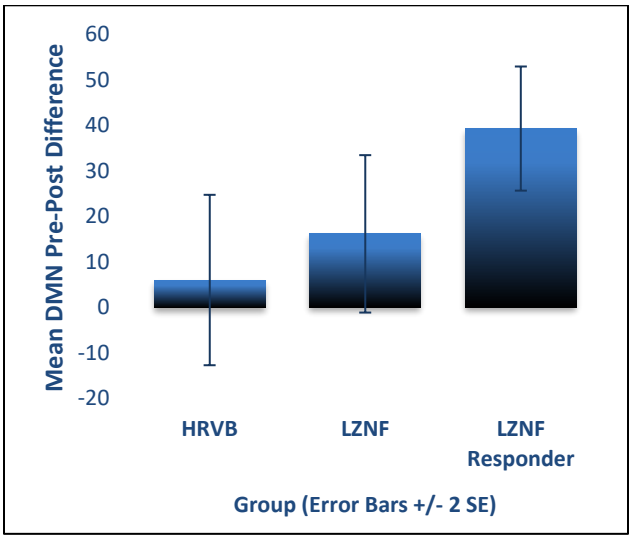

Figure 3. Default mode network pre–post difference in the HRVB, LZNF, and LZNF Responder groups

Salience network. For the HRVB group, there was a modest decrease in the number of significant SN *z*-scores from Time 1 (*M* = 89.09, *SD* = 82.74) to Time 2 (M = 74.91, SD = 115.85), although this difference was statistically nonsignificant (*p* = .625) and yielded a small effect size (*d* = 0.14). The LZNF group also showed a decrease in SN *z*-scores from Time 1 (*M* = 82.00, *SD* = 119.83) to Time 2 (*M* = 54.42, *SD* = 102.05) with a small/medium size of effect (*d* = 0.49), although this difference was also found nonsignificant (Wilcoxon *p* = .213). As with the DMN, this analysis included some participants who showed an increase from pretest to posttest. The LZNF Responders subgroup, however, showed very large (*d* = 1.32), statistically significant (*p* = .008) effects of training from Time 1 (*M* = 101.67, *SD* = 133.38) to Time 2 (*M* = 51.44, *SD* = 117.30).

MWU results found the SN difference between the HRVB group and full LZNF group to be statistically nonsignificant (*p* = 1.00) with a very small effect of group type (*d* = 0.18). Figure 4, however, shows that the amount of pre–post SN change in the LZNF group was about twice that of the HRVB group. The pre–post difference in the LZNF Responders was almost twice that of the full LZNF group and over 3.5 times that of the HRVB group.

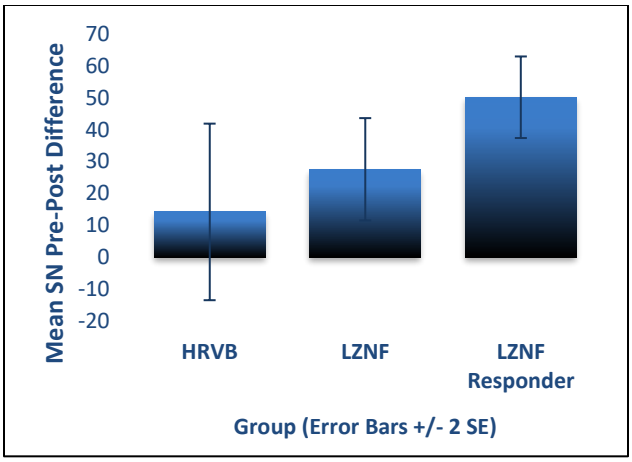

Figure 4. Pre–post SN difference in the HRVB, LZNF, and LZNF Responders groups.

Central executive network. The HRVB group showed a slight pre–post decrease in the number of significant *z*-scores within the CEN from Time 1 (*M* = 66.00, *SD* = 69.42) to Time 2 (*M* = 57.75, *SD* = 94.41). This difference was not statistically significant (*p* = .790) and was very small (*d* = 0.10). The LZNF group showed a larger pre–post change in CEN *z*-scores from Time 1 (*M* = 66.17, *SD* = 99.79) to Time 2 (*M* = 42.50, *SD* = 81.27) with a medium effect size (*d* = 0.59), although this difference did not reach statistical significance (*p* = .084). The LZNF Responders subgroup showed the greatest amount of change from Time 1 (*M* = 83.44, *SD* = 110.48) to Time 2 (*M* = 43.11, *SD* = 95.11), with a very large (*d* = 1.33), statistically significant (*p* = .008) effect of LZNF training.

The MWU analysis found the CEN difference between the HRVB group and LZNF group to be statistically nonsignificant (*p* = .414) with a small effect of group type (*d* = 0.29). Figure 5 reveals that the amount of change from the start to the end of the intervention was two to three times greater in the LZNF group than the HRVB group. The pre–post difference for the LZNF Responders was 1.5 times that of the full LZNF group and almost 4.5 times the magnitude of the HRVB group.

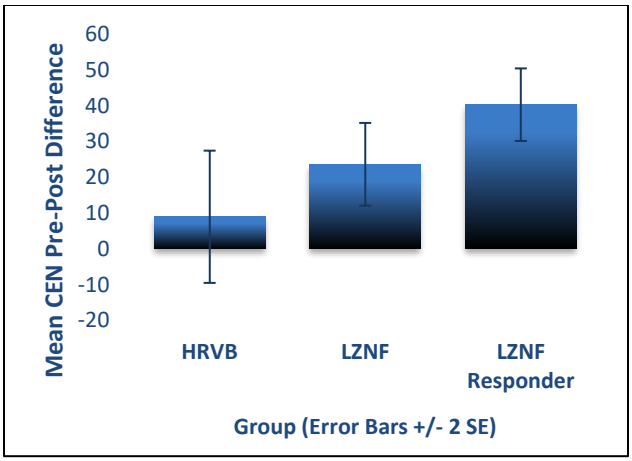

Figure 5. Pre–post CEN difference in the HRVB, LZNF, and LZNF Responders groups.

Heart Rate Variability Outcomes

When analyzing HRV metrics, an increase in SDNN and RMSSD scores is desirable.

Standard deviation of the NN Interval (SDNN). For the HRVB group, mean SDNN scores increased from Time 1 (M = 24.90, SD = 11.97) to Time 2 (M = 29.82, SD = 17.73) with a small effect size (d = 0.36), although this difference was not statistically significant (p = .182). The LZNF group started with a higher mean SDNN and showed a slight decrease (d = 0.11) from Time 1 (M = 37.82, SD = 23.51) to Time 2 (M = 36.53, SD = 18.32), although this change was nonsignificant (p = .814). When comparing the HRVB and LZNF groups, the effect of group type was of medium size (d = 0.58), although not statistically significant (p = .684).

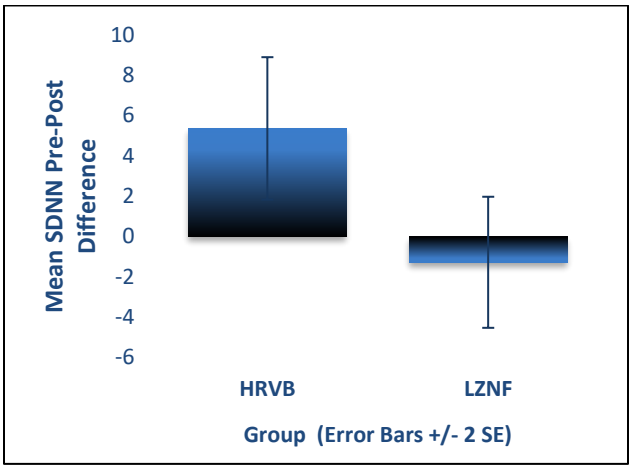

Figure 6. SDNN pre–post difference in the HRVB and LZNF groups.

Root mean square of the successive differences (RMSSD). For the HRVB group, RMSSD means increased from Time 1 (M = 22.18, SD = 12.13) to Time 2 (M = 23.93, SD = 16.77), although by a very small amount (d = 0.12) not reaching statistical significance (p = .722). Similar to the SDNN analyses, the LZNF group showed a slight decrease in RMSSD from Time 1 (M = 34.42, SD = 17.32) to Time 2 (M = 31.51, SD = 12.74), although this effect was small (d = 0.25) and nonsignificant (p = .530). The difference between groups was nonsignificant (p = 1.00) with a medium effect of group type (d = 0.50).

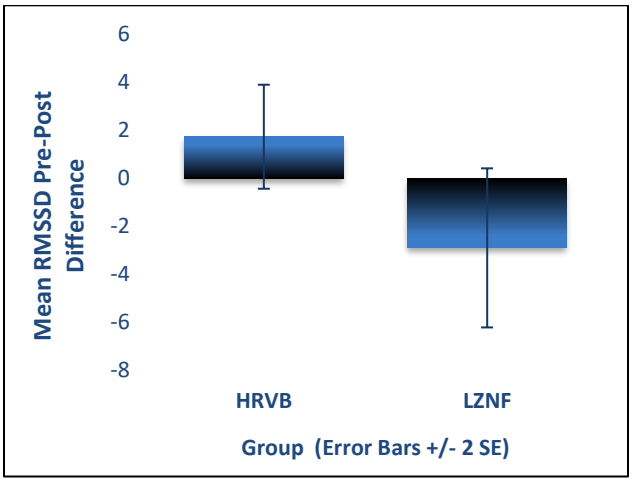

Figure 7. RMSSD pre–post difference in the HRVB and LZNF groups.

Discussion

This was the first active-controlled study to examine the effectiveness of LZNF training for altering neural activation patterns and alleviating mental health symptoms associated with chronic PTSD. In alignment with prior neurofeedback research, these findings support the notion that neurofeedback is likely an effective intervention for this debilitating condition. Only 15 sessions of LZNF training produced very large, statistically significant effects on both measures of PTSD symptomology. These outcomes were comparable or larger than the active control condition, HRVB, which produced medium to very large decreases in these symptoms. Moreover, these positive outcomes were produced in less than half the number of sessions than the average for traditional neurofeedback modalities (i.e., 30–40 sessions).

The effect sizes for the psychosocial measures in this study compare well with those of common conventional interventions for PTSD, such as eye

movement desensitization and reprocessing (EMDR), prolonged exposure, cognitive-behavioral therapy, and pharmacotherapy (van der Kolk et al., 2016). Meta-analyses have found the latter three to produce mild to moderate effects in 60% of participants (Bradley, Greene, Russ, Dutra & Westen, 2005; Erford et al., 2016; Hoskins et al., 2015; Jonas et al., 2013; Swift & Greenberg, 2012). Additionally, the rates of completion for the interventions utilized in this study were very high at 100% for the LZNF group and 92% for the HRVB group. These retention rates supersede those of psychotherapy and pharmacotherapy, which have been found to vary widely from a maximum average of 80% to as low as 2% (Najavits, 2015; Swift & Greenberg, 2012; Watts et al., 2014). Future research should directly compare LZNF training to these conventional interventions as well as assess any added benefits of an integrated approach.

While many conventional modalities require re-exposure to traumatic memories and emotions, LZNF directly targets the underlying neurophysiological patterns without requiring verbal processing. Therefore, LZNF might be especially beneficial for clients who are too hyperaroused, dissociated, or otherwise dysregulated to tolerate processing of traumatic stimuli. Neurofeedback might also be a more appealing, less stigmatizing, and less painful alternative to conventional methods, leading to higher retention rates. Furthermore, many psychotherapists have reported that clients receiving concurrent neurofeedback are better able to self-regulate while processing traumatic content and are thus able to go deeper into the therapeutic process.

Specificity of effects. Although the differences between the LZNF and HRVB groups were not statistically significant, the effects of group type provide preliminary evidence that the effects of each intervention are likely specific to their physiological targets. For example, the LZNF group showed larger effect sizes for both symptom assessments and all three neural networks, with small to large effects of group type; the HRVB group, on the other hand, showed greater improvements in both HRV metrics with medium effects of group type.

Responders vs. Nonresponders

For the purposes of this study, participants whose *z*-scores moved toward neurotypical levels (i.e., toward $z = 0$) were considered LZNF Responders, and those whose *z*-scores did not move in this expected direction were termed *nonresponders*. The rate of responders to nonresponders in this study (i.e., 75% to 25%) was similar to rates observed in other neurofeedback studies (Othmer, 2012). It is worth noting, however, that all three nonresponders in this study did show pre–post changes in their brainwave activity, although this change involved an overall increase in *z*-scores rather than the expected decrease. Of these three participants, two started with low-powered EEGs at baseline and showed an increase in overall power by the end of the study; this might have caused regions and frequencies that were relatively higher to begin with to be boosted over the predefined threshold ($z > 1.96$), resulting in an overall increase in the number of significant *z*-scores. The greatest increases for all participants were within the alpha and beta frequency bands, and two participants showed concurrent decreases in slow wave activity. Slow waves can sometimes indicate neural weakness, so it is possible that a decrease in these slow waves with a concurrent increase in faster frequencies could be representative of decreased neural weakness and increased cortical excitability (R. Thatcher, personal communication, July 29, 2018).

Furthermore, prior research has found alpha brainwaves to be associated with a state of calmness, flow, and mindfulness, and low beta frequencies have been associated with calm, focused attention (Kluetsch et al., 2014; Thompson, Thompson, & Reid-Chung, 2015). In fact, a study by Kluetsch et al. (2014) observed a significant increase in alpha power following alpha desynchronization neurofeedback, which was accompanied by feelings of calmness and enhanced functional connectivity within both the DMN and SN. Therefore, an overall increase in these frequencies might not necessarily be undesirable. In line with this thought, the nonresponders in this study reported increases in feelings of calmness, openness, and present moment awareness by the end of the study.

Avoidance and emotional numbness. Nonresponders showed maximal increases in *z*-scores at the midpoint assessment, accompanied by a brief increase in symptoms at some point during the initial stages of training. By the final assessments, however, these *z*-scores had decreased from the midpoint scores (although still higher than baseline) and participants subjectively reported large improvements in symptoms, specifically in relation to memory cohesion, mental clarity, and ability to cope. Notably, all three nonresponders reported a history of significant childhood trauma associated with primary caregivers, as well as prominent symptoms of avoidance and emotional numbing. Two reported extreme difficulty remembering large parts of their traumatic experiences as well. Thus, the initial

increases in *z*-scores and overall EEG power might be interpreted as a breaking out of avoidance and numbness into more appropriate levels of feeling and processing. Such clients might require additional sessions to first increase overall EEG power and then bring down relatively higher brainwave activity once it becomes more detectable to the training software. Future research should further investigate different subtypes of trauma survivors as they relate to EEG activity and LZNF training.

Limitations, Delimitations, Recommendations for Future Research

There are a number of variables to consider when interpreting the results of this research. The most significant limitation of this study was the small sample size. Due to the lack of adequate prior research examining LZNF, the available data was insufficient to conduct an accurate power analysis (Leon, Davis, & Kraemer, 2011). In such cases, authors have proposed the most appropriate sample for this early stage of research should be 10–30 participants per group (Johanson & Brooks, 2010; Julious, 2005). In line with these recommendations, the final sample in this study was 11–12 participants per group. Nonetheless, a small sample increases the probability of Type II error and might have underpowered this study to achieve statistical significance on outcome measures with lower effect sizes, such as between-group comparisons. A priori sample size calculations using the neural network effect sizes observed in this study determined that, for 80% statistical power and an alpha level of .05, the minimum required sample to achieve statistical significance within the LZNF group would have been 94 participants. For the between-group comparisons, a minimum of 188 participants per group would have been necessary. Even so, some outcome measures (i.e., within-group psychosocial assessments and LZNF Responder network changes) produced large enough effects to achieve the hypothesized significance despite the limitations of a small sample.

In the planning of this study, it was understood that it might be underpowered to accurately measure statistical significance; however, considering this was the first controlled study to examine LZNF training as an intervention for PTSD, the purpose of the study was to provide important preliminary data to support future research. For this reason, descriptive statistics and Cohen's d effect sizes were provided for all measures, and nonparametric analyses were utilized in place of inferential statistics for hypothesis testing. Researchers should utilize the methods, outcomes, and lessons learned in this small study to guide the planning of a larger study.

Sample heterogeneity and comorbid diagnoses. Another challenge that arises in both PTSD and psychophysiological research is the significant heterogeneity from subject to subject. The current diagnostic criteria outlined in the DSM-V allows for over 636,000 possible clinical presentations, and different clinical presentations might have different underlying neurophysiological patterns (Galatzer-Levy & Bryant, 2013). Epidemiological surveys have also estimated that about 80% of adults with PTSD have at least one comorbid mental health disorder and/or substance abuse disorder, which might further diversify neurophysiological patterns in this population (Brady, Killeen, Brewerton, & Lucerini, 2000; Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995). To limit the participants in this study to "pure" PTSD (i.e., devoid of comorbidities) would not be fully representative of the PTSD population. Thus, the inclusion criteria for this study was less limiting than some other, more rigorous PTSD studies. Consequently, the resulting sample included a wide diversity of backgrounds, trauma histories, and comorbidities. While such a sample maintains ecological validity, it also presents complications, both for the intervention as well as interpretation of outcomes. Furthermore, the majority of this study's participants reported a history of childhood trauma, which has been found to alter the structural and functional development of the brain (Cassiers et al., 2018). As such, individuals with multiple comorbidities and/or a history of childhood trauma might require additional sessions, as well as a more integrative approach.

In addition to a diversity of trauma histories and symptomology, the participants in this study also showed extensive variability in baseline levels of psychophysiological dysregulation. For example, one participant in the LZNF group started with 113 significant *z*-scores in the CEN while another started with only 8. Participants with higher levels of dysregulation might require more than 15 sessions for complete resolution, while those with lower numbers have little room for statistical improvement (i.e., ceiling effect). Such heterogeneity of the data also leads to a large number of outliers on both ends of the spectrum. The use of nonparametric, signed rank analyses in this study reduced the impact of outliers on hypothesis testing, although the descriptive statistics still reflected this variability. Extensive variability also reduces the statistical power of a study (Dufek, Bates, & Davis, 1995). Future studies might benefit from predefining eligibility criteria based on a specified range of psychophysiological parameters. A larger sample would also provide the option to cluster participants into different subtypes according

to symptom presentation, comorbidities, and baseline physiological measures.

Active control vs. sham. This study employed an active comparison group that received HRVB training in place of LZNF training. While this was an appropriate and ethical control condition, findings might have been more robust with the use of a sham (i.e., placebo) control. Sham controls are generally considered the gold standard for assessing the efficacy of an intervention while ruling out the most common confounding variables, such as placebo. However, sham neurofeedback might not be an ethical option for sensitive. Trauma survivors often experience feelings of powerlessness and helplessness, which could be exacerbated by sham conditions in which they are powerless to affect change (Brewin, Andrews, & Rose, 2000). Moreover, there is some evidence to suggest that sham feedback might reduce a person's ability to effectively learn from future neurofeedback training (Kluetsch et al., 2014; van Boxtel et al., 2012). The World Medical Association's Declaration of Helsinki, which outlines ethical principles for medical research with human participants, recommends that when another effective intervention exists for a particular ailment, an experimental intervention should be tested against that intervention rather than placebo due to the potential for harm related to nontreatment or delayed intervention (Carlson, Boyd, & Webb, 2004; World Medical Association, 2013).

For these reasons, HRVB was determined to be an ethical control condition while maintaining scientific rigor and controlling for many of the same confounding variables as sham neurofeedback. However, participants were unblinded to the training they were undergoing, which is a complication inherent to the use of active controls. Future research comparing these two conditions might effectively blind participants to the condition by connecting them to both EEG and HRV apparatuses for all training sessions; in this way, all participants would receive true psychophysiological feedback without knowing whether or not that feedback was based on brain activity or heart activity. This would allow for at least a single-blinded condition while still providing the opportunity for all participants to benefit.

Another challenge in comparing an experimental intervention against an active control is that an active control is, by definition, an effective intervention for the target population. This requires experimental conditions to achieve an even larger effect in order to produce statistically significant differences in between-group comparisons. On the other hand, equivalency of outcomes between an experimental condition and another proven intervention actually demonstrates effectiveness in and of itself. In fact, guidelines for evaluating the clinical efficacy of psychophysiological interventions state that, for an experimental intervention to be considered "efficacious," it must be at least "equivalent to a treatment of established efficacy in a study with sufficient power to detect moderate differences" (La Vaque et al., 2002). Although the statistical power of this study was insufficient to declare efficacy, the fact that the LZNF condition was at least equivalent to the HRVB condition makes it a promising alternative for the treatment of chronic PTSD.

Challenges in statistical analysis of LORETA *z*-scores. The neural analyses in this study calculated the total number of significant, absolute *z*-scores, which resolved many challenges inherent to LORETA *z*-score analyses, such as negative–positive *z*-score cancelations, minor shifts within neurotypical ranges, and dampening effects of averaging multiple *z*-scores. Nonetheless, this method still presented some complications of its own. For example, measuring the CSD for all Brodmann areas and frequencies within each network resulted in a very large number of metrics per network, which increased the extent of intersubject variability and reduced statistical power. Additionally, grouping all frequencies together in a single analysis did not allow for separate examination of changes within each frequency band, thus reducing the ability to adequately assess compensatory dynamics.

However, it would be challenging to find a single brain region and frequency band that would be dysregulated within all participants, especially considering the extensive heterogeneity of the PTSD population. The examination of entire networks in this study increased the chances of encompassing various patterns of dysregulation within a diverse sample, as well as assess changes in overall dysregulation throughout large-scale neural networks. However, limiting LORETA data analyses to a single metric might have provided a less confounded analysis of the size and significance of change, with increased statistical power. Future researchers might consider predetermining a region of interest and creating eligibility criteria based on EEG parameters for that region. As an alternative, future studies could design a reproducible method for selecting a different metric of interest for each participant, such as the region and frequency with the most significant *z*-score.

This study's method of data analysis also failed to account for individuals starting with low-power EEGs, which might have been responsible for the observed increases in *z*-scores for some of the nonresponders. Although assessment of the LZNF Responders subgroup resolved this issue for the pre–post analyses of that subgroup, all analyses containing the full LZNF group were impacted by these canceling effects. Furthermore, changes were only counted once they surpassed the set cut-off threshold (i.e., 1.96) in either direction. For example, if a *z*-score for 20 Hz in Brodmann area 13 decreased from 3.4 down to 2.1, it was still above the 1.96 threshold and thus counted as if there was no change (i.e., 1 stays 1). On the other hand, if a *z*-score for 10 Hz in Brodmann area 24 increased by a much smaller amount, such as a shift from 1.94 to 1.97, it was counted as significant (i.e., 0 becomes 1) because it surpassed the predefined threshold. Future research might reduce this complication by measuring changes in the means of all absolute *z*-scores above the 1.96 threshold.

Challenges in statistical analyses of HRV metrics. For the HRV analyses, it is possible that the LZNF group experienced ceiling effects due to high baseline levels of HRV, which were higher than baseline means for the HRVB group. Some participants also showed higher baseline levels of variability due to more chaotic heart rate patterns, such as sudden increases or decreases in heart rate. However, this activity was not in phase with their breathing. Over time, the raw data during training sessions showed improvements in phase relations between heart rate and breathing rate, but this data was not reflected in the predetermined amplitude analyses for this study. Future PTSD research might utilize HRV coherence training in place of amplitude training as well as analyze pre–post changes in coherence.

Additional confounding variables. Within the time frame of this study, many participants were exposed to stressful situations and confounding variables. For example, some participants: (a) experienced significant losses or conflictual periods in their relationships, (b) were re-exposed to trauma-related triggers or people, (c) endured a physical illness or injury, (d) had changes in their job status, (e) were undergoing final examinations in school, (f) were experiencing changes related to seasonal shifts (i.e., fall to winter), and (g) experienced additional stress related to holiday events. Within a naturalistic setting, it is difficult to avoid exposure to such confounding variables. Since one of the key characteristics of PTSD is being triggered by a variety of stimuli, it would not have been appropriate to remove all triggered participants from analysis. However, such events might have had an impact on both training effectiveness and assessments. Future research might explore ways to reduce these variables. Importantly, many participants who were exposed to triggers and stressors reported feeling lower levels of stress reactivity and enhanced levels of self-regulation in response to these stressors than they had prior to the study.

Optimal training targets and thresholds. Future research is needed to further parse out the effectiveness of various neurofeedback training modalities. Research should also assess for optimal reward rates, the optimal number of metrics to be trained simultaneously, and differences in effectiveness and tolerability between the Z-Tunes and All-or-None methods. Differences in audiovisual feedback should also be assessed, taking into account variables such as the effectiveness of direct feedback versus more obscure feedback, as well as levels of motivation and reward to reinforce a desired activation pattern. For example, while bar graphs might provide more direct feedback, movies might be more motivating and thus induce a larger dopamine reward.

A more individualized approach. In order to maintain reproducibility, the training in this study was confined to brain regions within the three predefined networks. However, many participants, including the three nonresponders, showed additional dysregulated brainwave activity outside these networks—sometimes to a greater extent than dysregulation within the networks. It is possible that dysregulated activation patterns of untrained regions might have negatively impacted the training process, especially if overactivation of the trained regions was a compensatory mechanism for dysregulation in outside regions. Consequently, a more individualized, comprehensive training program might have produced even more optimal outcomes for the participants in this study. Future research and clinical practice might utilize this study's protocol design as a starting point and add a manualized method for further individualizing protocols to each client's needs. Alternatively, the SCL-FNM method could be used to select regions associated with an individual's primary symptoms rather limiting the training to predefined networks.

Integration of LZNF and HRVB. Considering both interventions demonstrated positive effects, future research might include a third group to assess for added benefits of integrating LZNF training with HRVB training. Although LORETA neuroimaging can

reach deeper regions of the cortex than surface EEG neurofeedback, it cannot effectively reach deeper subcortical regions such as the hypothalamus. Any LZNF-induced changes in deeper limbic regions are likely related to modulatory feedback loops between cortical and subcortical regions. HRVB might also exhibit effects on these subcortical regions via feedback loops between the peripheral nervous system and subcortical brain regions (Thompson et al., 2015). In fact, this type of "bottom-up" regulation might have contributed to the positive symptom changes reported by participants in the HRVB group. Future research might utilize fMRI neuroimaging to further explore the effects of each intervention on subcortical regions associated with PTSD. Furthermore, the integration of HRVB and LZNF training might prove more effective than either intervention alone by targeting dysregulated activation patterns from both directions.

Conclusion

Chronic PTSD is a debilitating condition that, despite conventional treatment attempts, continues to impact millions of lives around the world. Neuroimaging studies have found strong associations between symptoms of PTSD and abnormal neurophysiology, particularly within three large-scale neural networks: the DMN, SN, and CEN. Such evidence demonstrates a need for interventions that more directly target these underlying neurophysiological roots, such as LZNF training. This was the first controlled study to assess the effectiveness of LZNF training for alleviating symptoms, improving autonomic regulation, and regulating abnormal brainwave activity in adults with chronic PTSD.

Despite the aforementioned limitations, the findings of this study provide strong preliminary evidence that LZNF training of the DMN, SN, and CEN is highly effective for reducing both PTSD symptoms and physiological anxiety symptoms in adults with chronic PTSD. HRVB training was also largely effective for reducing these symptoms, and the integration of these interventions might produce even greater outcomes. LZNF training produced large to very large, significant effects on all three targeted neural networks within the majority of trainees (i.e., LZNF Responders). These outcomes were produced in less than half the average number of sessions for traditional neurofeedback modalities. Positive outcomes were also observed across a wide diversity of individuals and comorbidities, indicating that LZNF training might be beneficial for a variety of trauma populations and conditions.

Furthermore, both interventions demonstrated very high rates of attendance and completion, suggesting high levels of feasibility and tolerability. These interventions might also offer a more appealing alternative to psychotherapy and medications, especially for professional populations such as military personnel, firefighters, and police officers. All in all, the outcomes of this study provide promising preliminary evidence to support future research with larger sample sizes.

Author Disclosure

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NeuroRegulation

Neurofeedback Intervention for Emotional Behavior Regulation in Schizophrenia: New Experimental Evidences from Optical Imaging

Michela Balconi[1,2*] *and Maria Elide Vanutelli*[2,3]

[1]Department of Psychology, Catholic University of Milan, Milan, Italy
[2]Research Unit in Affective and Social Neuroscience, Catholic University of Milan, Milan, Italy
[3]Department of Philosophy, Università degli Studi di Milano, Milan, Italy

Abstract

Recent neuroscience research tried to identify biological markers underlying schizophrenia's (SZ) symptoms. Results showed a functional hypofrontality in SZ patients during both cognitive and emotional tasks. Here, we submitted an experimental (E) group of patients to a neurofeedback (NF) training during emotion induction (T1) and assessed its efficacy by comparing the frontal neural activity before (T0) and after it (T2), with regard to a control (C) group. Functional near-infrared spectroscopy (fNIRS) was used during an emotional task with valence and arousal rating. Behavioral results showed that patients of both groups could identify pictures' valence, both in T0 and T2. However, a significant interaction effect revealed that negative and positive stimuli received more positive values in T2 compared to T0 only in E group, as a consequence of an alleged more functional management of negative feelings. Such results were paralleled by imaging data that showed increased O2Hb levels over frontal areas for positive and negative pictures compared to neutral ones, which were even more evident in the E group in T2. The preliminary results of the present study highlight the possible application of NF training to sustain patients' achieving more awareness and regulation during emotion processing.

Keywords: emotional behavior; fNIRS; neurofeedback; prefrontal cortex; schizophrenia

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***Address correspondence to**: Michela Balconi, Department of Psychology, Catholic University of the Sacred Heart, Milan, Largo Gemelli, 1, 20123 Milan, Italy. Email: michela.balconi@unicatt.it

Edited by:
Rex L. Cannon, PhD, SPESA Research Institute, Bloomfield Hills, Michigan, USA; Knoxville Neurofeedback Group, Knoxville, Tennessee, USA

Reviewed by:
Rex L. Cannon, PhD, SPESA Research Institute, Bloomfield Hills, Michigan, USA; Knoxville Neurofeedback Group, Knoxville, Tennessee, USA
Tanju Surmeli, MD, Living Health Center for Research and Education, Sisli, Istanbul, Turkey

Introduction

Schizophrenia (SZ) is a chronic and severe neuropsychiatric syndrome that affects reasoning, feelings, and behaviors, with a substantial social and relational dysfunction. In recent years, researchers from the neuroscientific field tried to identify some biological markers and neural correlates which could represent the symptoms underlying SZ deficits and support the diagnosis (Linden & Fallgatter, 2009) that is usually made by observable symptoms. Such research engaged patients in different experimental protocols and recorded their neural activity by using different neuroimaging techniques like functional magnetic resonance imaging (fMRI), positron emission tomography (PET), and, more recently, functional near-infrared spectroscopy (fNIRS). A relatively new technique, fNIRS allows a photometrical measurement of changes in the concentration of oxy (O2Hb) and deoxyhemoglobin (HHb) in brain tissue (Jobsis, 1977). Compared to other functional neuroimaging techniques, fNIRS has some disadvantages, such as a lower spatial resolution and the inability to reach deep brain regions. However, it was successfully applied in studies involving neuropsychiatric patients, since it is portable and can be easily and noninvasively positioned in naturalistic environments (even at the

bedside). More importantly, it doesn't impose movement limitation and it is completely silent. That's why it became especially popular in research with patients suffering from SZ spectrum disorders.

Previous fNIRS research with SZ patients mainly focused on cognitive impairment, by assessing verbal fluency (Ehlis, Herrmann, Plichta, & Fallgatter, 2007; Kubota et al., 2005; Takizawa et al., 2008), divergent thinking (Takeshi, Nemoto, Fumoto, Arita, & Mizuno, 2010) and insight (Pu et al., 2013), as well as attentive (Shoji et al., 2013) and executive functions (Zhu et al., 2010). The results of these studies consistently showed reduced prefrontal activation during the cognitive tasks in SZ patients (functional hypofrontality) compared to healthy controls (see also Shinba et al., 2004; Watanabe & Kato, 1999). Moreover, instead of overall activation effects in SZ patients, Falgatter and Strik (2000) found a specific hemispheric effect with a lack of lateralized activity, interpreted as a sign of reduced specific lateralized frontal reactivity.

However, prefrontal and frontal regions are also core regions during emotional/social regulation. As pointed out by Doi and colleagues (Doi, Nishitani, & Shinohara, 2013), fNIRS is really suitable at quantifying emotional functioning in the prefrontal cortex, which is also significantly impaired in SZ patients. In fact, although positive symptoms usually tend to respond to pharmacological treatment, negative symptoms tend to persist in the form of affective flattening, alogia, anhedonia, asociality and emotion dysregulation. As pointed out by Balconi and colleagues (Balconi, Tirelli, & Frezza, 2015), emotional deficits in SZ affect different processes, such as emotional experience (Taylor et al., 2012), expression (Blanchard & Cohen, 2006), and recognition (Horan et al., 2012). Of course, this is particularly important, since these symptoms affect patients' personal and interpersonal dimensions, as well as their social functioning. Despite the significant interest of this topic, few previous research applied neuroimaging techniques to explore emotional dysfunction in SZ patients (for a review see Balconi, Tirelli, et al., 2015). For example, Egashira and colleagues (Egashira et al., 2015) found that SZ patients showed less activation in the superior frontal, orbital frontal, and middle temporal regions during an emotional go/no-go task compared to healthy subjects. In addition, Pu and colleagues (Pu et al., 2016) explored the relation between frontal activity during a working memory task and social cognition in SZ patients. The authors found the presence of a significant relation between the activity within the lateral PFC and theory of mind scorings.

Interestingly, some other studies demonstrated how the brain activity is associated with SZ severity and with some symptoms that affect patients' everyday life. For example, Nishimura and colleagues (Nishimura et al., 2011) found that the abnormal activity over prefrontal and frontopolar regions during response inhibition is associated with excitement symptoms. Also, Watanabe and colleagues (Watanabe, Urakami, Hongo, & Ohtsubo, 2015) found that O2Hb values within the frontal areas reflect disease severity and the degree of social adjustment. In fact, patients with increased frontal activation were better socially adjusted than those with lower responses.

However, another important issue about SZ research that should be addressed by the neuroscientific approach is related to the assessment of treatment effects. In fact, although imaging techniques are contributing to the knowledge of the impaired frontal networks in SZ in both cognitive and emotional domains, the clinical applications in treatment monitoring are still inconsistent. Nonetheless, considering the resistance of emotional and social symptoms to the pharmacological treatment, there is the urgency to validate and develop new interventions based on objective data in support of more conventional and subjective outcome measured according to patients' reports. In recent years, neurofeedback (NF) was introduced as an innovative method to improve patients' awareness about some cognitive or emotional symptoms. In fact, as a behavioral approach by operant conditioning paradigm and shaping procedure (Sherlin et al., 2011), it can reinforce voluntary control on some forms of neural activity, such as the electrophysiological modulation, by eliciting desirable brain waves and inhibiting abnormal responses (Kouijzer, van Shie, de Moor, Gerrits, & Buitelaar, 2010). The efficacy of NF on SZ has been demonstrated starting from the pioneering studies (Balconi, Frezza, & Vanutelli, 2018; Schneider et al., 1992), in which attention breakdown of schizophrenic patients was improved by regulating the slow cortical potentials. Also, in an in-depth case study, Schummer (2008) uncovered favorable effects of NF in executive functioning. Similar results have been also found by Naimijoo and colleagues (Naimijoo, Rezaei, & Feizzadeh, 2015) on a larger sample. Another examples of NF application to the cognitive domain in SZ is the work of Surmeli and colleagues (Surmeli, Ertem, Eralp, & Kos, 2012), which showed increased attentive scorings after the NF intervention, as well as improved symptoms severity. In addition, a single-case intensive training conducted by Nan and colleagues (Nan et al., 2017) showed an

improvement in short-term memory, mood, and speech after NF.

For what concerns the emotional domain, instead, Ruiz and colleagues (Ruiz et al., 2013) trained nine schizophrenic patients to up- and downregulate anterior insular cortex activity by fMRI neurofeedback to improve face emotion recognition. Moreover, by following a specific theoretical model on emotion processing lateralization, Gruzelier and colleagues (Gruzelier, Hardman, Wild, & Zaman, 1999) trained patients to shift EEG negativity away from their functionally dominant hemisphere. Specifically, they induced a rightward direction in the Active syndrome with left-sided functional biases, and a leftward direction in the Withdrawn syndrome with right-sided functional biases.

However, the existing studies are only preliminary and generally not exhaustive in term of experimental paradigm (no imaging evidences after NF treatment; Naimijoo et al., 2015), sample size (only single or few cases; Schummer, 2008) or specific type of treatment. Thus, the aim of the present study was to evaluate the efficacy of a NF intervention to improve emotional regulation in a pilot sample of SZ patients. The procedure included an initial assessment during a passive emotional task (T0) to explore the brain mechanisms related to emotional processing before and after the training (pre/post) by means of fNIRS covering the frontopolar area. Together with stimuli presentation, the explicit subjective evaluation of emotional stimuli was assessed. Then, a NF intervention was planned and performed for the following 5 weeks (T1). It consisted in an emotional training by the modulation of delta–theta EEG range. Following the same idea of Gruzelier and colleagues (Gruzelier et al., 1999) about lateralization enhancement, we trained patients to intensify such range in the less responsive hemisphere, based on a previous assessment. It was proposed only to a group of patients assigned to the experimental (E) group, while the other half was assigned to the control (C) group.

Subsequently, the emotional assessment was repeated (T2) exactly as in T0. According to previous research (Kring & Moran, 2008) we expected preserved capacity to discriminate stimulus valence yet increased in T2 for the E group. For what concerns the neural level, instead, we expected a significant effect of the training over prefrontal brain activity for the E group in T2, which could also be more lateralized according to stimuli valence (Fallgatter & Strik, 2000; Balconi, Grippa, & Vanutelli, 2015a; Balconi, Vanutelli, & Grippa, 2017).

Materials and Methods

Participants

The study recruited a pilot sample of 25 institutionalized patients, 12 females (M_{age} = 32.10; *SD* = 4.76; range = 28–40). The sample is an extension of a preliminary data acquisition on 19 patients (see Balconi, Frezza, et al., 2018). Establishment of diagnoses was based on semi-structured interviews which were conducted by an expert psychiatrist according to the criteria of the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (SCID-I: Structured Clinical Interview for DSM IV Axis I Disorders; American Psychiatric Association, 2000). Informed consent was obtained after full explanation of purpose and procedure of the study. Inclusion criteria were: (1) age between 18 and 45 years old; (2) fair psychopathological compensation; (3) stable pharmacological program followed for at least 4 weeks before the beginning of the study. Exclusion criteria were as follows: (1) visual or auditory impairment; (2) concurrent substance abuse (abstinence for at least 3 months); (3) Diagnosis of moderate or severe mental retardation (IQ < 55); (4) neurological damage; (5) anamnesis of brain injury.

Then, patients have been randomly assigned to either the C group, composed of 11 patients, 6 females (M_{age} = 34.78; *SD* = 5.04; range = 27–40), or the neurofeedback (NF) group, composed of 14 patients, 6 females (M_{age} = 35.23; *SD* = 4.09; range = 28–38). The two groups were comparable in term of emotional intelligence (as assessed by the Mayer-Salovey-Caruso Emotional Intelligence Test, MSCEIT), cognitive competencies (as assessed by the Wechsler Adult Intelligence Scale Fourth Edition, WAIS-IV) and neuropsychological profile (as assessed by the Brief Assessment of Cognition in Schizophrenia, BACS). Patients in the C group followed the Treatment-As-Usual (TAU), while patients in the NF group followed both TAU and NF training.

The study included a first phase of assessment (T0), the NF intervention (T1), and a second assessment (T2) to evaluate the treatment efficacy. Procedures in T0 and T2 were identical to allow direct comparison of their measures (for the original protocol, see Balconi, Cotelli, et al., 2018). The assessment consisted of the recording of hemodynamic parameters by means of fNIRS during a passive emotional task, and of subjective ratings in terms of valence and arousal of stimuli, by means of the Self-Assessment Manikin (SAM; Russell, 2003).

The study and its procedures followed the principles of the Declaration of Helsinki and were approved by the Ethics Committee of the Department of Psychology of the Catholic University of the Sacred Heart. Written informed consent for the enrollment of patients included in the experimental cohort was obtained from their legal representatives.

Stimuli

Patients were required to observe and then evaluate affective patterns at the end of the stimuli processing. One hundred pictures were taken from the International Affective Picture System (IAPS) (Bradley & Lang, 2007), depicting 40 positive and 40 negative pictures (20 low and 20 high arousing, each), and 20 neutral stimuli, based on valence and arousal ratings obtained from a prior validation study (Balconi, Brambilla, & Falbo, 2009). IAPS subjective ratings were obtained with the SAM scale, using an easier adapted 5-point version (Bradley & Lang, 2007). For IAPS codes, see (Balconi, Grippa, & Vanutelli, 2015b).

Procedure

Patients were seated in a dimly lit room, facing a computer monitor that was placed 70 cm from the subject. The stimuli were presented using STIM2 software (Compumedics Neuroscan, Charlotte, NC) running on a personal computer with a 15-in. screen. Participants were required to observe each stimulus during fNIRS recording, and they should attend to the images the entire time of exposition. Pictures were presented in a random order in the center of a computer monitor for 6 s, with an inter-stimulus interval of 12 s. 120-s eyes-closed and 120-s eyes-open resting baselines were registered at the beginning of the experiment before the picture series. After the experimental phase, patients had time to rate their emotional experience on the SAM scale evaluating valence and arousal on a bipolar scale applied to each picture.

fNIRS Recording and Analysis

fNIRS measurements were conducted with a NIRScout system (NIRx Medical Technologies, LLC, Los Angeles, CA) using a 6-channel array of optodes (4 light sources/emitters and 4 detectors) covering the prefrontal area. Emitters were placed on positions AF3-AF4 and F5-F6, while detectors were placed on AFF1-AFF2 and F3-F4 (see Figure 1). Emitter–detector distance was 30 mm for contiguous optodes and a near-infrared light of two wavelengths (760 and 850 nm) was used. With NIRStar (NIRScout acquisition software), changes in the concentration of oxygenated (O2Hb) and deoxygenated hemoglobin (HHb) were recorded continuously throughout the paradigm. Signals obtained from the 6 NIRS channels were measured with a sampling rate of 6.25 Hz, analyzed and transformed with nirsLAB software (v2014.05; NIRx Medical Technologies, LLC, Glen Head, NY), according to their wavelength and location, resulting in values for the changes in the concentration of O2Hb and HHb for each channel. The raw data of O2Hb and HHb from each channel were digitally band-pass filtered at 0.01–0.3 Hz. Then, the mean concentration of individual channel was calculated by averaging data across trials from the trial onset for 6 s. The mean concentration value of 6 s immediately before each trial was used as event-related baseline. Based on the mean concentrations in the time series, we calculated the effect size in every condition for each channel within a subject, calculated as the difference of the means of the baseline (m1) and trial (m2) divided by the standard deviation (s) of the baseline: $d = (m1 - m2)/s$. Then, the effect sizes obtained from the 6 channels were averaged in order to increase the signal-to-noise ratio. These normalized effect sizes could be averaged regardless of the unit (for this procedure, see Balconi, Grippa, et al., 2015a, 2015b; Balconi, Vanutelli, Bartolo, & Cortesi, 2015). To interpret the event-related responses to stimuli with respect to each baseline, signs have been inverted.

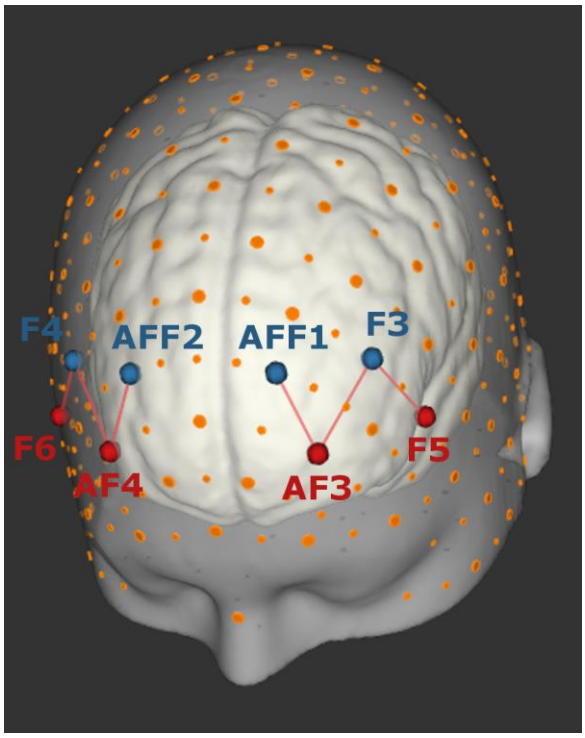

Figure 1. Location of NIRS sources (red) and detectors (blue) over the frontopolar areas.

Neurofeedback Training

The training consisted in a 5-week successive training period. The experimental group completed 10 sessions, each lasting approximately 25 minutes with 2 intervals of 2 min in between. The sessions were performed in the same room as the assessment phases. NF was administered using a ProComp2 device (Thought Technology Ltd, Montreal, Canada) and the task was created and presented by BioGraph Infiniti software package (Thought Technology Ltd, Montreal, Canada). Before each training session, a 2-min resting baseline was recorded with eyes open. Patients were instructed to reduce muscle activity and control eye blinks. EEG was recorded by placing an electrode in correspondence to the left (F3) or the right hemisphere (F4), according to each patient's electrophysiological pattern as assessed in a preliminary session. Thus, training was lateralized as a function of preliminary patient's baseline left or right higher activity. The reference was placed on the contralateral earlobe, and ground electrode on the ipsilateral earlobe. The main visual feedback and reward tool was a video made up of IAPS pictures different from those used during the initial assessment phase: when the EEG band of interest reached values over the established reward-threshold, the video proceeded and showed different affective stimuli. Thus, patients had to learn to enhance the low-frequency range within the less active hemisphere. The reward threshold is automatically managed by the software such that a fixed 80% reward level is provided. The band values were as follows: reward = 0.5–5.5 Hz; inhibit-low = 0.1–0.5 Hz; inhibit-high = 50–64 Hz.

Results

SAM Ratings

Arousal and valence subjective scorings (dependent measures) were analyzed with two separated three repeated factor (2 arousal; 3 valence; 2 time) and one between factor (2 group, C group vs. NF group) mixed-model ANOVAs. For all ANOVA tests, degrees of freedom were corrected by Greenhouse–Geisser epsilon where appropriate. Moreover, due to multiple independent analyses and comparisons, we applied Bonferroni test for inequality. Contrast analyses (paired comparisons) were applied to significant main or interactions effects.

For valence ratings, Valence main effect was significant ($F(2, 49) = 8.13$, $p < .01$). Indeed, negative valence stimuli received significantly ($p < .01$) lower values ($M = 1.86$; $SD = 0.03$) than positive stimuli ($M = 3.84$; $SD = 0.41$), with intermediate level for neutral ones ($M = 2.27$; $SD = 0.34$), which were significantly higher ($p < .01$) than negative, and lower ($p < .01$) than positive pictures. Also, Time main effect was significant ($F(1, 24) = 7.45$, $p < .01$), with increased/decreased values based on valence for all conditions in T2 (for positive $M = 3.77$; $SD = 0.18$; for negative $M = 2.40$; $SD = 0.16$) than T0 (for positive $M = 3.02$; $SD = 0.09$; for negative $M = 1.74$; $SD = 0.10$). Finally, the Valence × Time × Group interaction effect was significant, with negative pictures evaluated as more positive ($p < .05$) by NF group in T2 ($M = 2.88$; $SD = 0.13$) than T0 ($M = 1.65$; $SD = 0.12$) and positive pictures evaluated as more positive ($p < .01$) by NF group in T2 ($M = 3.80$; $SD = 0.18$) than T0 ($M = 1.84$; $SD = 0.10$). In contrast, C group did not show this significant effect. For arousal ratings, instead, no significant effect emerged (see Figure 2).

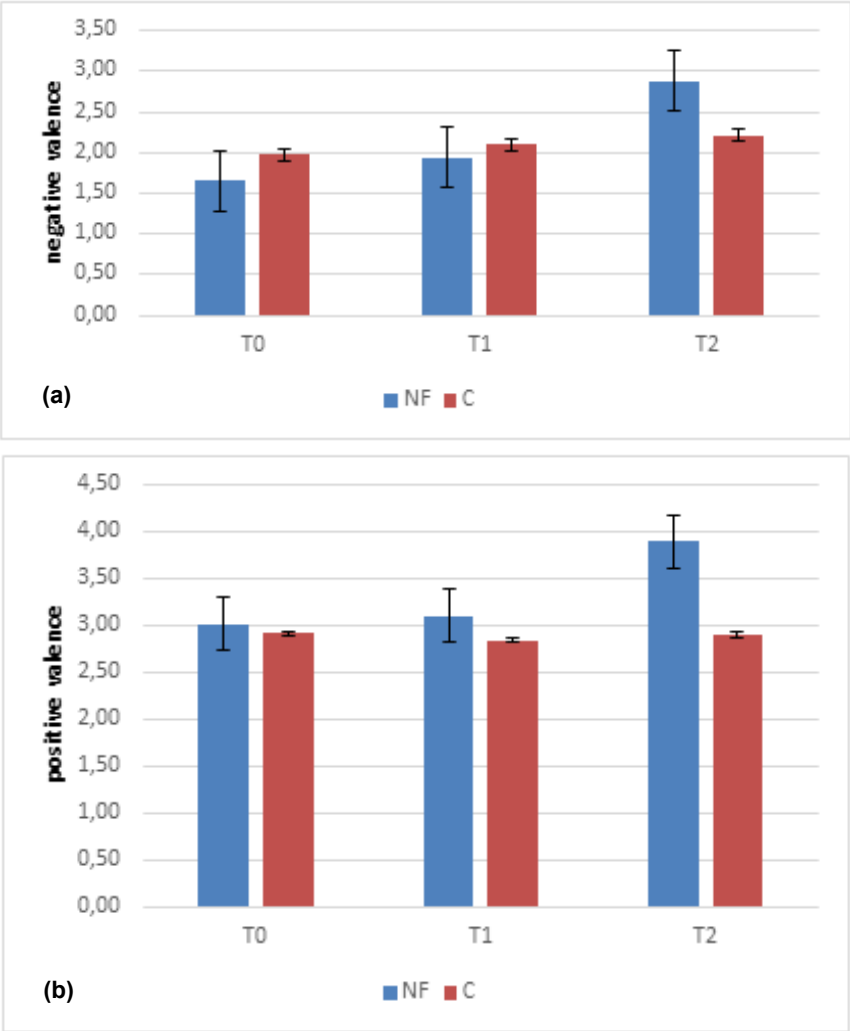

Figure 2. SAM ratings as a function of group, valence and time for (a) negative and (b) positive pictures.

fNIRS Results

About fNIRS recordings, repeated measure ANOVAs were applied with respect to D dependent measure of O2Hb concentration in all the channels (Ch1-Ch6). Successively, for a second set of analysis data were averaged considering left (Ch1: AF3-F3; Ch2: AF3-AFF1; Ch3: F5-F3) and right (Ch4: AF4-F4; Ch5: AF4-AFF2; Ch6: F6-F4) regions to obtain an inclusive index based on the specific lateralized NF application.

The first set of analysis was aimed at assessing the effect of figure valence on brain activation before and after NF (Group × Valence × Channel × Time) and showed a significant effect for figure valence ($F(2,48) = 8.78$, $p < .01$), with increased activity for positive and negative that neutral stimuli (Figure 3). In addition, Group × Valence × Time × was significant ($F(2, 48) = 8.13$, $p < .01$), with increased activity for NF compared to C for positive ($F(1, 28) = 6.90$, $p < .01$) and negative ($F(1, 48) = 7.34$, $p < .01$) stimuli in T2. No significant effect was found for arousal.

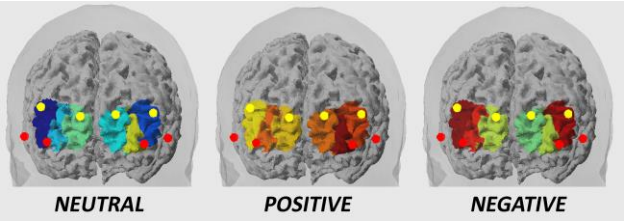

Figure 3. Projection of raw O2Hb activation in response to neutral (left), positive (middle), and negative (right) pictures from one exemplificative subject.

The second set of analysis was aimed at assessing the lateralized hemodynamic effect (Group × Valence × Lateralization × Time) before and after NF. Results showed a significant Group × Valence × Lateralization effect ($F(2, 48) = 8.55$, $p < .01$). Indeed, the NF group presented increased O2Hb levels in T2 within the right side in response to negative stimuli ($F(1, 48) = 7.13$, $p < .01$) compared to the C group. In addition, NF group showed increased O2Hb levels in T2 within the left side in response to positive stimuli ($F(1, 48) = 7.98$, $p < .01$) compared to the C group (see Figure 4). No significant effect was found for arousal.

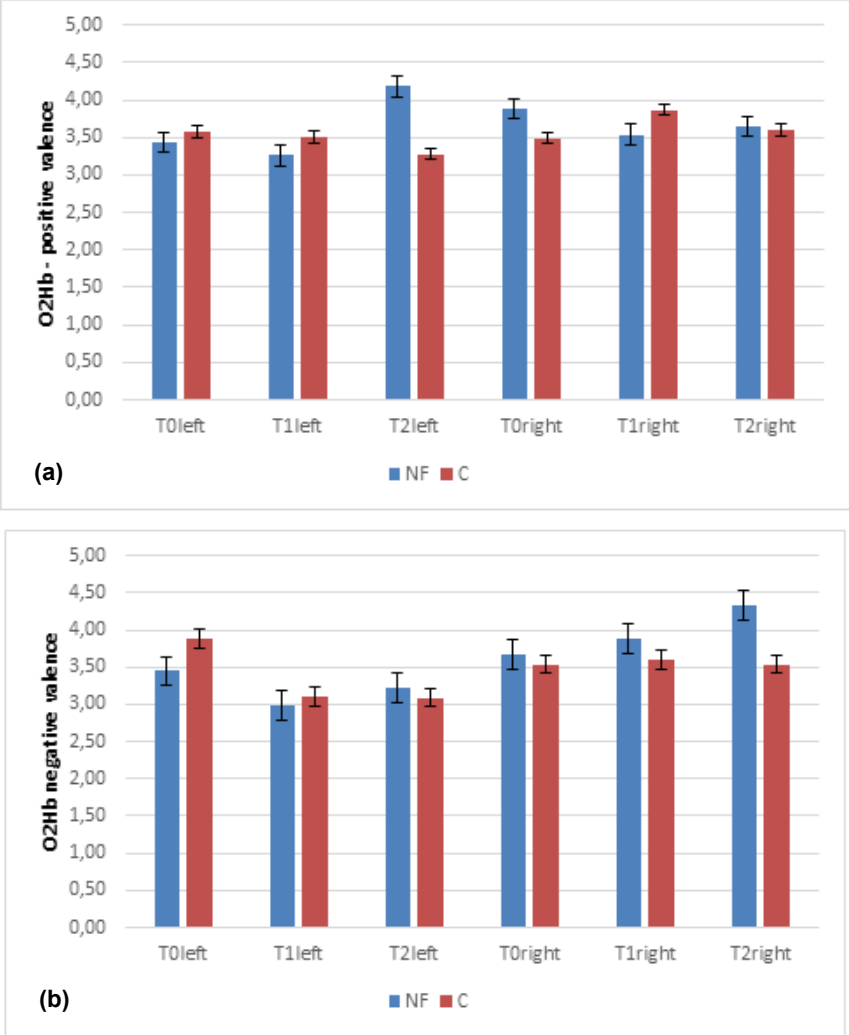

Figure 4. O2Hb activation as a function of group, valence and time for positive (a) and negative (b) pictures.

Discussion

The present research aimed at investigating the effects related to a NF training over the prefrontal neural activity in a small sample of SZ patients. The experiment was subdivided into three different sections, with the neurophysiological assessment being proposed at T0 and T2, and the NF training administered in between (T1) and only to the experimental (E) group. The training was meant to provide the patients the capacity to self-regulate their own cortical activity while processing different affective pictures. The study highlighted different significant results both at a behavioral and a neurophysiological level.

For what concerns valence and arousal ratings, the analysis showed that patients of both groups were

able to correctly identify the hedonic valence of IAPS stimuli, both in T0 and T2. In fact, they identified negative stimuli as more negative than positive ones, and vice versa. This result is in line with previous research (Balconi, Frezza, et al., 2018**,** Kring & Moran, 2008) that identified preserved attributional processes in SZ patients. Indeed, it is possible to argue that this capacity does not depend on the NF training. However, a significant interaction effect showed that both negative and positive stimuli received more positive values in T2 compared to T0 only in the E group. This specific enhancement effect towards positive feelings could, instead, be attributed to the NF training as a consequence of an alleged more functional management of negative effects (Balconi, Tirelli, et al., 2015). On the other hand, patients faced more difficulties in discriminating the arousing power of pictures, which could derive from an impairment in detecting the motivational significance of external stimuli (Williams et al., 2004). At this regard, future research could better investigate this issue by using a combined bio + neurofeedback to provide a clearer signal to be modulated by the arousal dimension.

For what concerns the neural level, instead, a first result revealed that, irrespective of group and time, the O2Hb levels increased over the frontopolar regions for positive and negative stimuli if compared to neutral ones. This result is in line with previous work (e.g., see Balconi & Vanutelli, 2016, 2017; Herrmann et al., 2008) assessing emotional pictures as being more activating than neutral ones. Such a mechanism could be interpreted as finalized to alert the emotional behavior in response to the highly significant emotional stimuli patients are interacting with (Balconi & Vanutelli, 2016). Moreover, this is also in line with the behavioral result confirming patients' preserved ability to detect hedonic valence.

In addition, a significant interaction revealed a higher activity for E compared to C group for positive and negative stimuli in T2. Fallgatter and colleagues (Fallgatter & Strik, 2000) found that, when performing a cognitive task, SZ patients did not display the significant increase in hemispheric asymmetry that was instead evident in controls. Since patients' and controls' behavioral performance did not differ, the author concluded that the absence of this lateralized activation couldn't be attributed to a dysfunctional strategy and interpreted such effect as a different functional response from patients who lacked lateralized activation. Similarly, in our case, although patients showed a congruent hemodynamic response to emotional stimulation (both positive and negative valenced stimuli), the effect of the NF training could have been in the direction of an improved awareness during emotion processing, which resulted in a more positive emotional attribution, as also revealed by SAM data. However, future studies could better explore this issue by administering further questionnaires to assess patients' emotional experience, to be acquired also at long-term distances.

To conclude, as pointed out by the present results, the use of imaging methods such as fNIRS could provide significant evidence about the efficacy of an innovative and noninvasive training such as NF, which could anyhow provide patients with the capacity to self-regulate their own cortical activity during emotion processing. At present, however, since we did specifically acquire data about the microvolt levels for the frequency over time, we did not consider the learning trend during the task. It was due to the main focus of the present research on the hemodynamic analysis and trend evaluation of these parameters to support the training effect.

Starting from this first evidence, firstly future studies should better monitor the modifications of the electrophysiological parameters (in terms of microvolts levels) during the task, discussing their trend for learning. Secondly, the connectivity patterns related to the NF training should be better explored in a way to disclose the underlying mechanisms related to brain plasticity. Also, different kinds of NF training could be compared in a way to find the most efficient way to induce emotional regulation. Finally, a clinical assessment about the generalization of the NF effects should be included, in a way to validate the positive impact found for at both behavioral and neural level.

Author Disclosure

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

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NeuroRegulation

Self-Prompted Discrimination and Operant Control of EEG Alpha

Jon A. Frederick[*]*, Andrew S. Heim, and Kelli N. Dunn*

Middle Tennessee State University, Murfreesboro, Tennessee, USA

Abstract

EEG state discrimination studies may contribute to understanding the role of awareness in physiological self-regulation, but many individuals learn the existing paradigm very slowly. In this study, a self-prompted discrimination paradigm, in which subjects decide when to respond based upon their subjective state, was examined for the rate of learning and its effects on the ability to control EEG alpha. Twenty-nine participants received up to three 40-min sessions in which discrimination training was alternated with training to control alpha in four 10-min sets, compared to 22 participants who received control training only. Discrimination training appeared to facilitate the ability to control alpha amplitude, but only in the first session. The rate of learning of the discrimination paradigm was markedly greater than seen in previous studies. Comparing the time series of postresponse alpha amplitudes suggested that the lowest scoring sessions involved a behavioral inertia, or difficulty switching states, particularly when a higher alpha state was required. However, extreme amplitudes were discriminated better than moderate ones and discrimination task performances significantly exceeded the percent time that alpha amplitude was in the correct state. These two observations suggest that EEG discrimination involves awareness of, and not just manipulation of, one's EEG state.

Keywords: discrimination learning; perceptual motor processes; consciousness states; electroencephalography; biofeedback; neurotherapy

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***Address correspondence to**: Dr. Jon A. Frederick, Department of Counseling, Lamar University, P.O. Box 10034, Beaumont, TX, USA. Email: jfrederick8@lamar.edu

Edited by:
Rex L. Cannon, PhD, SPESA Research Institute, Bloomfield Hills, Michigan, USA; Knoxville Neurofeedback Group, Knoxville, Tennessee, USA

Reviewed by:
Rex L. Cannon, PhD, SPESA Research Institute, Bloomfield Hills, Michigan, USA; Knoxville Neurofeedback Group, Knoxville, Tennessee, USA
Randall Lyle, PhD, Mount Mercy University, Cedar Rapids, Iowa, USA

Introduction

In biofeedback, self-regulation of physiological function is learned by displaying or "feeding back" a physiological signal in real time to the individual producing it. Rewards are provided when the signal exceeds a threshold indicating a desired response, and over time individuals learn to produce the response without feedback (Sherlin et al., 2011). It is sometimes argued that attention to the feedback display increases awareness of otherwise unconscious internal sensations, and this awareness enables or facilitates voluntary control of the process (Brener, 1974; Congedo & Joffe, 2007; Frederick, 2016; Frederick, Heim, Dunn, Powers, & Klein, 2016; Olson, 1987; Plotkin, 1981). While voluntary action is possible without awareness of one's current state (Black, Cott, & Pavloski, 1977; Taub & Berman, 1963), performance can be substantially impaired (e.g., Taub, Bacon, & Berman, 1965). Operant conditioning is also possible without awareness (Becker, Kleinböhl, & Hölzl, 2012), but conscious perception is argued to involve access to more global processing in the brain (Dehaene, Charles, King, & Marti, 2014), allowing for explicit rehearsal processes and the kind of internal reinforcement seen in observational learning (Bandura, 1977).

Awareness of a physiological process has been operationally defined as the ability to discriminate

differences in a physiological signal, where individuals report their perception of whether a variable is high or low. For instance, human subjects have been trained to discriminate EEG alpha (Frederick, 2012; Kamiya, 1968, 2011), the sensorimotor rhythm (Cinciripini, 1984), P300 amplitude (Sommer & Matt, 1990), and slow cortical potentials (Kotchoubey, Kübler, Strehl, Flor, & Birbaumer, 2002).

Despite considerable controversy about the relationship between physiological awareness and control (Frederick et al., 2016), relatively few studies have examined this relationship. Training to control physiological responses has been shown to increase performance for discrimination of heart rate (Brener, 1977; Marshall & Epstein, 1978), galvanic skin response (Baron, 1966; Lacroix, 1977; Stern, 1972), the sensorimotor rhythm (Cinciripini, 1984), and slow cortical potentials (Kotchoubey et al., 2002). The reverse effect, an enhancement of control performance after prior discrimination training, has been reported for heart rate (Brener, 1974, 1977; Brener, Ross, Baker, & Clemens, 1979), a cephalic vasomotor response (Fudge & Adams, 1985), and for EEG alpha (Kamiya, 1968).

Generalization of Skills Between Discrimination and Control of EEG Alpha

Our laboratory (Frederick et al., 2016) found that seven sessions of control training (standard neurofeedback) of EEG alpha dramatically increased discrimination performance in three subsequent sessions. Among the participants who successfully learned to control EEG alpha, the average discrimination task performance was 81% correct (50% is a random performance). However, the reverse was not true. Seven sessions of EEG alpha discrimination training had no effect on three subsequent sessions of the standard neurofeedback task. While these results were consistent with arguments that awareness is not necessary or sufficient to learn physiological control (Black et al., 1977; Lacroix, 1981), our results suggested another possible interpretation. Learning of the discrimination task was relatively weak, the group average never exceeding 55% correct across seven sessions. This rate of learning was consistent with that seen in Frederick (2012), where the successful participants averaged 56% in the 10th session.

Self-prompted Versus EEG-prompted Discrimination

One possible explanation for the lack of robust learning of the discrimination task was that only a small proportion of excursions in alpha amplitude are related to discriminable changes in subjective states. Since the paradigm provided only about three prompts per minute, informative learning trials (that included discernible subjective correlates of the EEG state) might have occurred less than once per minute. Possibly, a higher proportion of informative learning trials might be provided (and more robust learning achieved) if subjects could decide when to respond based on their subjective states rather than the computer prompting based on alpha amplitude differences. For instance, Frederick (2005) reported a case study using this self-prompted discrimination paradigm, where one subject scored 68% in the first session and reached 81% in the 11th session. Figure 1 illustrates the theoretical suggestion, where only a small proportion of alpha amplitude differences involve subjective state differences, but a larger proportion of subjective state differences are associated with alpha amplitude differences.

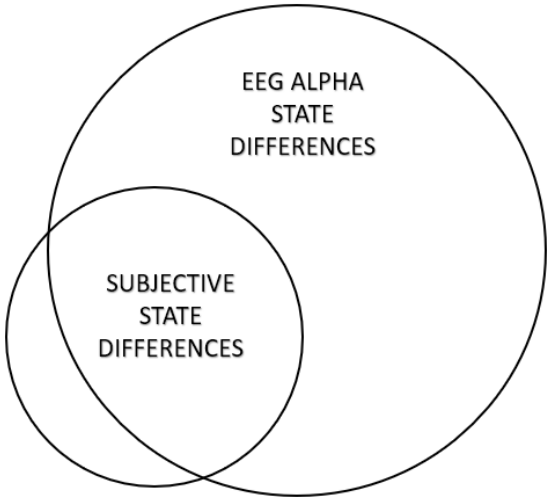

Figure 1. Hypothesized relationship between subjective state differences and EEG alpha state differences, where a discrimination paradigm prompted by subjective state differences might result in faster learning than a paradigm prompted by EEG alpha state differences.

If more rapid learning and a higher level of discrimination task performance could be achieved, then it would be possible to more specifically test whether discrimination training can facilitate learning to control the EEG through standard neurofeedback.

Therefore, this study evaluated the effect of self-prompted discrimination training on standard neurofeedback training. It was hypothesized that dividing session time equally between standard neurofeedback control training and subject-prompted discrimination training would result in greater control of EEG alpha than control training alone.

Discrimination Versus Manipulation of the EEG

The self-prompted responding paradigm involves substantial efforts by the subject to manipulate their EEG. Participants are instructed in the subjective phenomenology of high and low alpha states and asked to press a button when they believe they have reached a high or low alpha state, in alternating order. Black et al. (1977) and Lacroix (1981) theorized that successful discrimination performance probably only involved successful reporting of a subject's voluntary effort to manipulate their state. However, the self-prompted discrimination paradigm allows for a direct test of this theory. During each (high or low) type of trial, it is possible to measure the percentage of time the subject spends in the "correct" EEG amplitude state before responding. A successfully manipulated EEG amplitude would then be correct more than 50% of the time in the self-prompted discrimination paradigm. However, discrimination performances significantly greater than the percent time correct would suggest that subjects are aware of more than just their effort to manipulate the EEG signal.

Psychophysics of Self-Prompted Discrimination

It was previously found that performance in EEG-prompted alpha discrimination was strongest for very high (91–100th percentile) and very low (1–10th percentile) amplitudes compared to moderately high (71–80th percentile) and moderately low (21–30th percentile) amplitudes, consistent with an interpretation of alpha discrimination as a kind of a sensory or perceptual process (Frederick, 2012). It was of interest to see whether a similar pattern would be seen for self-prompted discrimination. Would participants' correct responses tend to cluster closer to the first percentile for low trials and the 100th percentile for high trials? Or, would they cluster just on the correct side of the 50th percentile, when perhaps they perceived some contrast with the previous correct trial, or perceived movement in the right direction?

Response Timing

Previous studies found that it was possible to use intertrial time intervals to "cheat" in the standard Kamiya paradigm, although subjects did not make significant use of this information (Frederick, Dunn, & Collura, 2015; Frederick et al., 2016). It is possible that some of the significantly correct performance in the self-prompted discrimination paradigm could be explained by attention to time cues rather than genuine discrimination. For instance, it might be more time-consuming to "clear the mind" and switch to high alpha than to "activate the mind" and switch to low alpha. Or, if there is significant postreinforcement synchronization after correct trials (Hallschmid, Mölle, Fischer, & Born, 2002; Sherlin et al., 2011), one might expect transitions from low to high trials to go more quickly.

Method

Participants

With the approval of the institutional review boards at Middle Tennessee State University and Saint Cloud State University, 51 participants were recruited from students, faculty, staff, and the local community. To improve motivation, compensation was based partly on performance (Sherlin et al., 2011), where participants received $12 if their scores reached a criterion (67% in the discrimination task or 14% difference between increasing and decreasing alpha in the control task), or $9 otherwise. These criteria were determined by pilot data to make the average payment $10 per session.

Measurements and Apparatus

EEG was recorded at the parietal midline (Pz) using tin electrodes. Reference and ground were randomly assigned to left or right earlobes each session. Impedances were lowered to below 10 kΩ, with no site greater than twice the others. Considering modern amplifier input impedances (Ferree, Luu, Russell, & Tucker, 2001), impedances of up to 15 kΩ were occasionally accepted if repeated preparations would not bring them lower.

EEG was recorded with a BrainMaster Atlantis amplifier and BrainMaster 3.7i software using the default settings as described (Frederick et al., 2016). The alpha band was defined as a 5-Hz band centered at each subject's peak alpha frequency (PAF). For example, if the PAF were 11 Hz, the alpha band was then defined as 9–13 Hz.

For the alpha amplitude control (standard neurofeedback) task, the experimenter maintained a percent reward between 15% and 30% while viewing a 60-s filtered alpha amplitude window and a 60-s running average of the percent time in reward. Adjustments to the reward threshold were made about every 20 seconds. To avoid triggering reward onset/offset, adjustments were only made when the alpha amplitude was not close to the threshold.

Spectral amplitudes were saved in 1-s epochs for delta (1–3 Hz) and for each participant's custom alpha band. Epochs were assumed to include artifact and excluded when the delta amplitude exceeded 30 μV.

During the discrimination task, EEG amplitudes for each 1-Hz band from 1 to 32 Hz were sampled 10 times per second by custom software (*Introspect*, written in C++), which recorded both EEG and task responses. The task and recording were suspended (and an artifact warning tone was played) whenever lodelta (0.5–2.0 Hz) or hibeta (23–32 Hz) amplitude exceeded a threshold. Alpha amplitude was defined as the sum of amplitudes in the five 1-Hz bands centered at the PAF, smoothed over the most recent 2 s, delayed 500 ms. Following Libet's (1985) observation that the readiness potential—the brain's process underlying a decision to act—begins about 500 milliseconds before the action, the delay was introduced both to remove any effect of the readiness potential and to reflect the likelihood that responses indicate conscious contents with at least a 500-ms delay. A sliding baseline consisting of the most recent 600 alpha amplitude samples (60 s) was rank ordered for comparison to the alpha amplitude at the time of each participant response. The baseline was updated every 15 s, with each response, or whenever the experimenter pressed the pause button.

Procedure

After obtaining informed consent, participants were given a set of instructions describing strategies to relax and reduce muscle artifact, and the phenomenology of alpha and nonalpha states (Frederick, 2012; Frederick et al., 2015). Participants sat in a cushioned chair with eyes closed in a dimly lit, sound-attenuated room. The PAF was determined from a 60-s eyes-closed baseline recording.

Participants were randomly assigned to two groups who each received up to three 40-min sessions. In the first group ("control task group"), sessions consisted of alternately rewarding increasing and decreasing alpha amplitude in 5-min runs. In the second group ("discrimination task group"), minutes 1–10 and 21–30 consisted of the same 5-min runs of increasing and decreasing alpha amplitude. However, during minutes 11–20 and 31–40 they received a discrimination task, in which they which they were given a trial type (high or low alpha) and asked to press a button when they believed they were in that state. The trial type would alternate after each correct response but would stay the same after each incorrect response. A response below the 50th percentile was correct for low trial, and a response above the 50th percentile was correct for a high trial. Correct responses triggered a reward (Microsoft "tada") sound, followed by a voice announcing the next trial ("high trial" or "low trial"). Incorrect trials resulted only in the repetition of the trial type. Responses within 2 seconds of the previous response or an artifact were not allowed and would trigger a verbal reminder of this rule.

The control task group included 22 participants (age 18–54, median 24, 10 female) while the discrimination task group included 29 participants (age 18–63, median 25, 15 female). Although the original intent was for the two participant groups to be equal in size, the need for the "percent time correct" measure (which applies only to the discrimination task), was discovered late in the progress of the study (see Frederick & Guetter, 2017). The discrimination group included extra subjects in order to get a larger number (n = 13) with the percent time correct measure.

Results

Improvement Across Sessions

A total of 74 discrimination task sessions were completed among 29 participants. Among these, 23 completed two sessions and 22 completed three sessions. The mean performance significantly improved from 50.8% to 56.4% between the first and third sessions, one-tailed $t(21) = 3.05$, $p = .003$, Cohen's $d = 0.65$ (Figure 2).

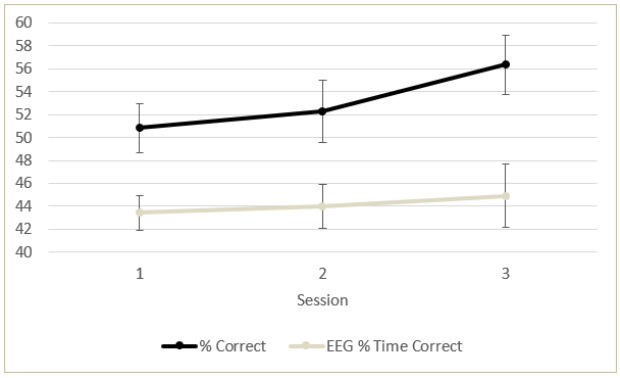

Figure 2. Discrimination performance (% Correct, n = 29, 23, and 22 for sessions 1, 2, and 3, respectively) compared to the percent of time EEG alpha amplitude was in the correct state (EEG % Time Correct, n = 13, 9, and 9). Error bars indicate standard errors.

Performances Significantly Above and Below 50%

Thirty-three of 74 sessions among 16 subjects showed performance significantly *above* 50% with binomial $p < .05$ (by chance alone, five percent or about four out of 74 sessions would be expected to have $p < .05$). However, 22 sessions among 12 subjects showed performance significantly *below* 50% at $p < .05$, about 5.9 times the amount expected by chance (Table 1). For instance, one participant's three session scores were 13/42 (31.0%), 7/38 (18.4%), and 15/43 (34.9%). Earlier sessions scores tended to predict later session scores. Only three of the 12 participants who scored significantly below 50% later scored significantly above 50%.

Table 1
Discrimination Task Performances Significantly Above and Below Null Hypothesis

Discrimination score null hypothesis	50%	50%	44.0%*
Number of subjects	29	13	13
Number of sessions	74	31	31
Sessions $p < .05$ above null hypothesis	33	9	19
Sessions $p < .05$ below null hypothesis	22	11	1
Number expected by chance at $p < .05$	3.7	1.6	1.6
Ratio of observed to expected above	8.9	5.8	12.3
Ratio of observed to expected below	5.9	7.1	0.6

Note. *In the third column, individual session percent times correct were used as the binomial null hypothesis for each discrimination task score, where the mean percent time correct was 44.0%.

Percent Time Correct Adjustment

The high level of "below-chance" performances was unexpected and prompted a revision of the task software to record EEG values between trials every 0.5 s for the final 13 participants. The task software informs the participant that either a "high" or "low" response is required for each trial and then waits for their response. Then, the alpha amplitude for each sample is assigned a percentile ranking from the sliding 60-s baseline, where the participant would be correct on a high trial if the percentile amplitude exceeds 50, incorrect otherwise. On a low trial, the participant would be correct for each sample if the percentile amplitude is 50 or below, incorrect otherwise. Thus, across all samples, it is possible to compute a "percent time correct," or the expected score if the participant responded continuously or randomly across the session. The mean percent time correct, not including the 2 s after each correct response when new responses were not allowed, was 44.0% (*SD* = 5.3) and appeared to change very little between sessions (Figure 2). The percent time correct during high trials (44.5%, *SD* = 4.9) was about the same as during low trials (43.4%, *SD* = 6.3).

A total of 31 sessions were completed by the 13 participants for whom EEG percent time correct was recorded, where nine subjects completed all three sessions. Nine of these 31 sessions were significantly *above* 50% at binomial $p < .05$, and 11 sessions were significantly *below* 50% at $p < .05$ (Table 1).

Among the nine sessions significantly above 50% at $p < .05$, the average score was 60.9% (*SD* = 6.3, range 52.7–75.8), while the mean percent time correct was 48.8% (*SD* = 5.1, range 40.9–54.9).

Among the 11 sessions significantly below 50% at $p < .05$, the average score was 39.5% (*SD* = 3.6, range 35.4–46.5), the mean percent time correct was 38.0% (*SD* = 4.7, range 27.8–46.5). Only four percent time correct values among the 31 recorded were above 50 (range 51.1–54.9), and all four of these were among the nine sessions significantly above 50%.

Performances Significantly Above Percent Time Correct

The observation of the average percent time correct being 44.0% suggested that unlike in the EEG-prompted discrimination paradigm (Kamiya, 1968) where high or low alpha amplitude events trigger a prompt to respond, 50% is not the appropriate null hypothesis, or expected value for a random performance.

When each individual session percent times correct were used as the null hypothesis for the 31 sessions where it was measured, the number of sessions significantly above chance levels increased from 9 to 19 (Table 1). Only one of 13 participants failed to achieve one significant above chance session performance. The number of sessions significantly below chance levels decreased from 11 to 1, a number more consistent with chance levels at $p < .05$.

Psychophysics

For each criterion session ($p < .05$ above chance) for each subject, the percentage of the total trials was counted, separately for low trials and high trials, in each of the following percentile amplitude bins: 0–10, 11–20, 21–30, 31–40, 41–50, 51–60, 61–70, 71–80, 81–90, and 91–100. The mean across all subjects was computed in each percentile bin. These results are summarized in Figure 3.

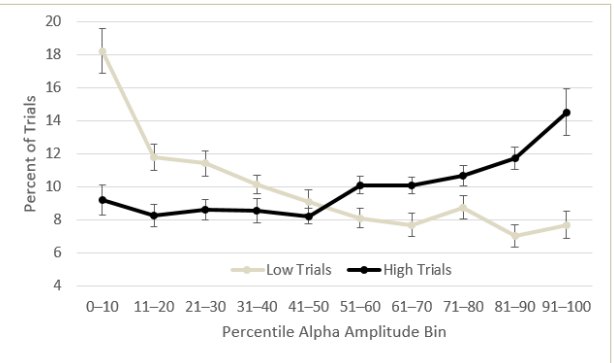

Figure 3. Percent of total trials in each of 10 percentile alpha amplitude bins for high and low trials, where 0–50th percentile is correct for low trials and 51–100th percentile is correct for high trials. Error bars indicate standard errors.

During correct low trials, participants were more likely to select very low (0–10) than moderately low (41–50) alpha amplitude events, one tailed $t(23) = 5.72$, $p < .001$, $d = 1.17$. Similarly, during correct high trials, participants were more likely to select very high (91–100) than moderately high (51–60) percentile amplitude events, one-tailed $t(23) = 2.61$, $p = .008$, $d = 0.53$. However, the reverse was not true. Participants were not more likely to incorrectly respond "low" to a moderately high (51–60) event than a very high (91–100) amplitude event, one-tailed $t(23) = 0.46$, $p = .324$, $d = 0.10$, and they were also not more likely to respond "high" to a moderately low (41–50) than a very low (0–10) percentile amplitude event, one-tailed $t(23) = -1.01$, $p = .839$, $d = -0.21$.

Response Timing

The average session had 115.3 trials ($SD = 42.2$) during the two 10-min sets of trials, or an average of 5.8 trials per minute (or one trial every 10.3 s). The correlation between discrimination performance and the number or frequency of trials was nonsignificant in the first ($r = .134$, $df = 27$), second ($r = .288$, $df = 21$), or third ($r = .223$, df = 20) sessions.

All criterion sessions (significantly above chance at $p < .05$) among 24 subjects were examined for the effect of response timing on performance. These included a total of 5991 trials (not including the first trial in each session for which the intertrial interval was undefined). Among these, 3580 (59.8%) followed a correct trial and were therefore different from the previous trial (because the trial type, high or low, switches after each correct response, or else it stays the same). The number of different trials for each criterion session was counted and summed for each of the following intertrial intervals: 2.1–5.0 s, 5.1–10.0 s, 10.1–15.0 s, and 15.1 s or greater. There were only 12 out of 5991 trials with intertrial intervals of 30.1 s or greater.

Rapid response times were most common, where average percent of total responses was 35.2% for 2.1–5.0 s, 44.0% for 5.1–10.0 s, 14% for 10.1–15.0 s, and 6.9% for 15.1 s or greater.

Repeated measures analysis of variance found that there was no effect of intertrial interval on performance among all the trials, among the high trials or low trials alone, or among the differences between high and low trials.

Postresponse "Behavioral Inertia" in Alpha Amplitude

Since each correct response occurs when alpha amplitude is relatively high or low, it was of interest to see how long it took for alpha amplitude to recover from this deviation. The mean percentile alpha amplitude was computed every 0.5 s after each correct response ($n = 13$) and is shown in Figure 4. On average, it took about 3.5 seconds to reach the 50th percentile for both high and low alpha trials. Note that individual trials (e.g., Figure 5) are more variable than the grand averages shown in Figure 4.

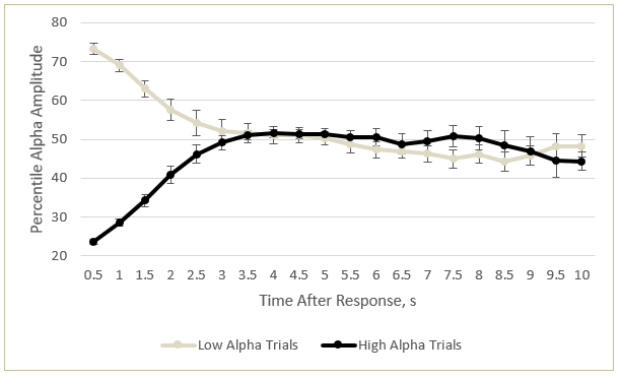

Figure 4. Behavior inertia or recovery time after a correct response (all sessions, *n* = 13 subjects), where each low alpha trial follows a correct high alpha trial and vice versa, *n* = 13. Error bars indicate standard error.

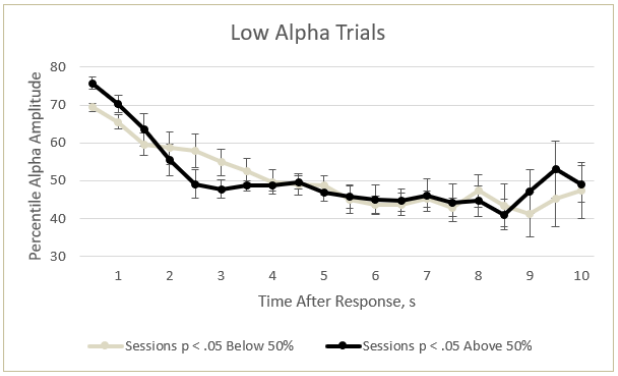

Figure 6. Differences in behavior inertia or recovery times during low alpha trials after a correct high trial for sessions scoring significantly below 50% (*n* = 6 subjects) and above 50% (*n* = 6) subjects. Error bars indicate standard errors.

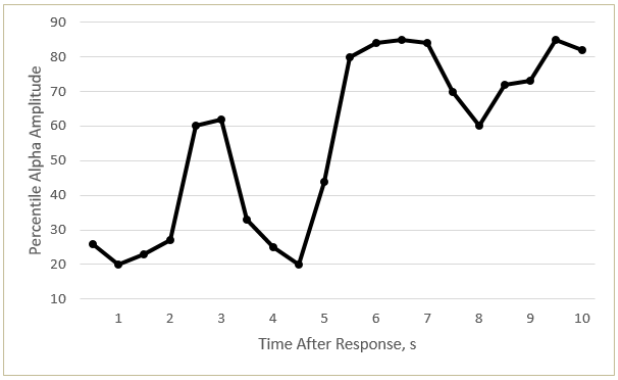

Figure 5. Example time series of alpha amplitude during a single high trial after a correct low trial.

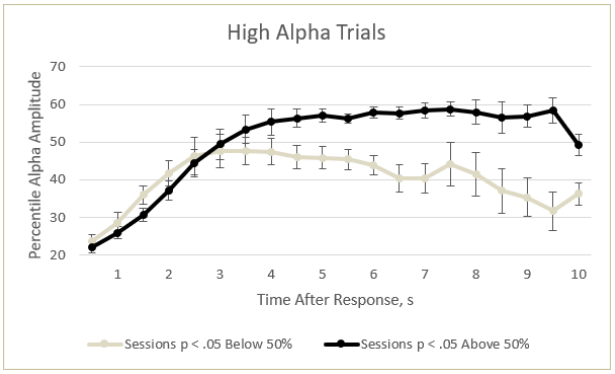

Figure 7. Differences in behavior inertia or recovery times during high alpha trials after a correct low trial for sessions scoring significantly below 50% (*n* = 6 subjects) and above 50% (*n* = 6) subjects. Error bars indicate standard errors.

To determine whether differences in recovery time could explain differences in discrimination task performance, the mean postresponse amplitudes were compared from sessions scoring significantly above 50% (*n* = 6 participants) to those from sessions scoring significantly below 50% (*n* = 6 participants). Among these two groups of six, there were a total of 11 participants, where one participant had both types of sessions. These results are summarized in Figure 6 and Figure 7. Figure 6 shows that for low alpha trials, subjects took about 2.5 seconds to reach the 50th percentile during high-performing sessions, but about 4 seconds during low-performing sessions. Figure 7 shows that during high alpha trials, subjects took about 3 seconds to reach the 50th percentile during high-performing sessions, whereas during low-performing sessions, the average amplitude did not cross the 50th percentile during the first 10 seconds. Note: there are fewer data and measurements become less reliable after 10.3 seconds, the average response time (data not shown).

For purposes of comparison, Figures 8 and 9 show the postresponse alpha amplitudes for the same sessions after incorrect responses. In these situations, participants are recovering from unintentionally low or high alpha. Figure 8 shows after an incorrect "low alpha" response, high-performing subjects appear to reach the 50th percentile in 1.5 seconds, or about 1 second sooner than after a correct trial (Figure 6). However, in low-performing subjects Figure 8 shows how (despite recovering from correct high trials in about 4 seconds on average, Figure 6) the first error in identifying low alpha seems to indicate an ongoing difficulty reaching the low alpha state, where the 50th percentile is not reached until about 8.5 seconds. Figure 8 shows a brief opportunity for a correct high alpha response starting around 3.5 seconds in both groups followed by varying difficulty reaching high alpha.

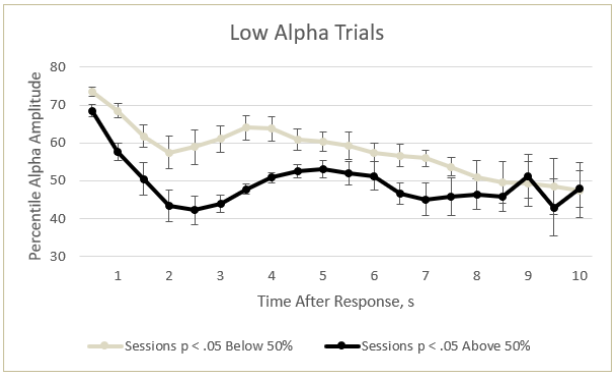

Figure 8. Time series of mean alpha amplitudes in low alpha trials after an incorrect low alpha trial ("same" trial type) for sessions scoring significantly below 50% (n = 6 subjects) and above 50% (n = 6) subjects. Error bars indicate standard errors.

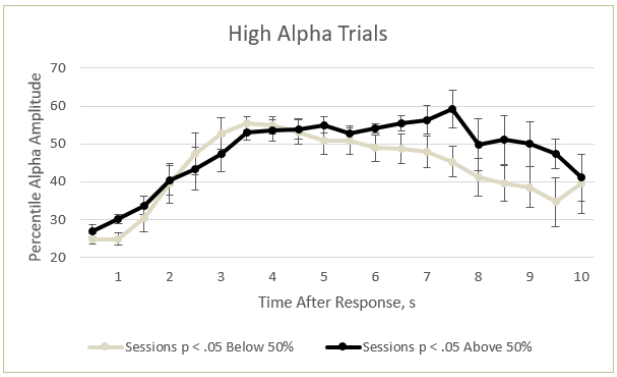

Figure 9. Time series of mean alpha amplitudes after an incorrect high alpha trial ("same" trial type) for sessions scoring significantly below 50% (n = 6 subjects) and above 50% (n = 6) subjects. Error bars indicate standard errors.

Interactions Between Discrimination and Operant Control

Percentage differences between alpha amplitude during the increase and decrease conditions (100 percent times the difference between increase and decrease / average of increase and decrease) were computed for each 10-min segment, which consisted of 5 min of increasing and 5 min of decreasing alpha. The discrimination task group only received the operant control task during minutes 1–10 and 21–30 of the session, so only these segments were used for comparison between groups. Figure 10 shows averages for each 10-min session time interval across three sessions. The first 10 min of the first session was effectively a baseline for the operant control task because the two groups received identical treatments until the 11th minute.

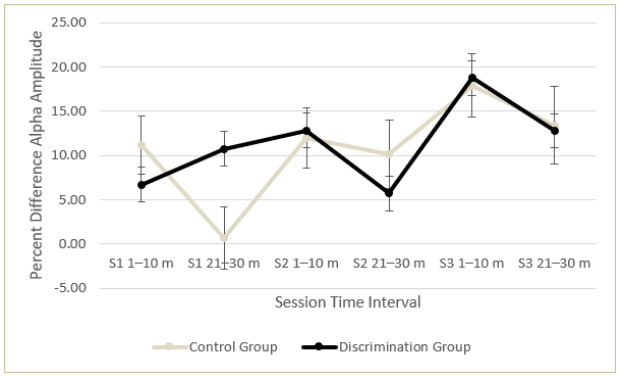

Figure 10. Percent difference in alpha amplitude between increase and decrease conditions during operant control (standard neurofeedback) of alpha.

Performances in the control and discrimination tasks correlated significantly in the first session, Pearson r = .338, n = 28, one-tailed p < .05, and third session, Spearman r = .510, n = 20, one-tailed p = .010, but not the second session, Pearson r = .258, n = 20, one-tailed p = .116 (nonparametric statistics were used whenever variable distributions failed to meet parametric assumptions).

During the first 10 min of the first session (before the treatments were different), the control task-only group achieved an average of 11.1% greater in the increase condition than the decrease condition (SD = 15.5), compared to 6.7% (SD = 15.3) in the discrimination task group, a nonsignificant difference. However, during minutes 21–30, the discrimination task group increased to 10.8% (SD = 14.0) while the control-task only group decreased to 0.7% (SD = 16.4; Figure 10). This group difference was significant, Mann-Whitney W = 185, one-tailed p = .008, n_1 = 22, n_2 = 28, rank-biserial correlation 0.399. However, performances were not significantly different during any of the remaining session time intervals. An alternative analysis was performed in which the session 1 baselines were subtracted from each segment, using a pretest posttest design. While the differences from baseline were greater in the discrimination task group during the second and third sessions, the effect was not significant.

Discussion

Learning of the self-prompted discrimination task was more robust than the learning of EEG-prompted discrimination seen in previous studies. Participants averaged 56.4% by the third session, 12.6% higher than a chance-level (44.0%) performance. By contrast, the mean score for the top 40 of 106 participants in Frederick (2012) was below 52% in the

third session—where a chance-level performance was 50%—and just under 57% by the 10th session. Similarly, in Frederick et al. (2016), 17 participants averaged about 53% in the third session and did not exceed an average of 55% by the seventh session. The greater discrimination performance in this study could be explained by several factors, including the larger number of trials per minute (5.8 compared to 3.0 in Frederick et al., 2016), or generalization of skills from the standard neurofeedback training. It may also indicate that using subjective states to prompt responses more reliably indicates EEG state differences than the other way around, providing more informative opportunities for learning (Frederick, 2006).

The finding that most subjects scored significantly higher than the percent time that the EEG was in the correct state in most sessions supports the interpretation that physiological state discrimination involves some genuine awareness of internal feedback about the physiological state (as suggested by Brenner, 1974). Participants in this study were reporting more than just their awareness of their effort to manipulate their state (as suggested by Black, Cott, & Pavloski, 1977; Lacroix, 1981).

Psychophysics of Self-Prompted Discrimination

The percentage of trials was significantly higher in the lowest (0–10th) percentile amplitude bin for correct low trials and significantly higher in the highest (91–100th) percentile amplitude bin for correct high trials (Figure 3). This observation is consistent with the view of EEG alpha discrimination being a sensory or perceptual process involving some transduction of energy from the objective signal. Although subjects do not report perceiving EEG amplitude directly, it may be indirect, like the amount of visual phosphenes being related to the amount of pressure applied over the eyelid.

There appeared to be little or no significant differences with respect to alpha amplitude among the incorrect low trials, or among the incorrect high trials. For instance, below the 51st percentile on a high trial or above the 50th percentile on a low trial, subjects were equally likely to make moderately wrong and very wrong responses. This finding is mysterious because in the same percentile bins they did demonstrate an awareness of the differences between moderately correct and very correct responses. For instance, on an incorrect high trial, they may have no longer recognized a very low state that they had just correctly identified on a low trial. Possibly, this difference indicates top–down processing where subjects are deploying a kind of search-image for pattern-matching in each type of trial. This finding suggests that high and low alpha states are phenomenologically not just opposites, or one the absence of the other.

Percent Time Correct and Behavioral Inertia in Alpha Amplitude

This study began with the incorrect assumption that a random performance in the discrimination task would be 50% correct. The initial result was that the number of "significantly below chance" scores was 5.9 to 7.1 times the number expected at $p < .05$ (Table 1). However, the "percent time correct"—the percent that would be scored if subjects responded continuously or randomly (on average, 44.0%)—was lower than 50%. This finding could have been predicted from the fact that alpha amplitude is a physiological process that is not distributed randomly but varies with a finite rate of change. Figures 4–9 show how there is a behavioral inertia in alpha amplitude where, after every trial, it takes time for the subject to recover from the voluntary or spontaneous processes that resulted in the previous (currently incorrect) state. When the percent time correct was used as the null hypothesis, number of sessions significantly below the percent time correct was much closer to the 5% expected at $p < .05$ (Table 1).

Figures 6 and 7 suggest that performances significantly below 50% were explained more by a difficulty in achieving high alpha than in achieving low alpha. This difference could correspond to a general difference in achieving high and low states of arousal. For instance, it generally takes at least 5 minutes to fall asleep (Carskadon et al., 1980), but only a few seconds to wake someone up. It would be of interest to see how this greater relative difficulty in returning to high alpha in some subjects relates to measures of mood or arousal regulation.

Future studies should redefine a correct response to take account of the behavioral inertia when switching between trial types. Scores below 50%, resulting from the use of the 50th percentile as the threshold for a correct response, can be demoralizing for participants. A lower threshold for a correct response would allow for shaping, or the reinforcement of successive approximations to the correct response (Sherlin et al., 2011). One method would be to define a correct trial as above the percent time correct (updated each trial based on the 50th percentile) on high trials and below 100 minus the percent time correct on low trials. Another possibility that might produce equivalent results would be to only use the most recent 60 s of the same trial type (instead of just the most recent 60 s).

Response Timing

The lack of relationship between response timing and response performance suggests that self-prompted discrimination may not require complex controlling for the possible use of response timing to "cheat" in the discrimination task (compared to EEG prompted discrimination, Frederick et al., 2015; Frederick et al. 2016).

No evidence of a post-reinforcement synchronization (Hallschmid et al., 2002; Sherlin et al., 2011) was seen in this paradigm. That is, there was no advantage to having a high alpha trial rather than a low alpha trial after a correct response (Figure 4). Alpha amplitude also did not increase more in the few seconds after a correct response (Figures 6 and 7) than after an incorrect response (Figures 8 and 9). Thus, it did not seem generally possible to use a postreinforcement synchronization to cheat on high trials following correct low trials.

Figures 4–9 represent the 500-ms delayed amplitudes used in the task. While it is assumed based on Libet (1985; 1993) that the phenomenal correlates of alpha amplitude represent their corresponding brain states with a 0.5-s delay, this assumption has not been tested. If true, a study comparing discrimination performance with varying 0 to 2-s delays might contrast with Sherlin et al.'s (2011) suggestion that latency between a correct EEG response and the reinforcement should not exceed 250 to 350 milliseconds.

Interactions Between Discrimination and Operant Control

A significant effect of discrimination training on the standard neurofeedback performance was observed in the first session but not in the second and third sessions (Figure 10). This observation is consistent with awareness playing a greater role in the early stages of learning (Frederick, 2016; Fitts & Posner, 1967). However, the lack of effect beyond the first session suggests that further refinement of the paradigm is needed. It is possible that the limited facilitation of operant control performance by discrimination training seen in this study could be an effect of the limited opportunities for generalization of skills between the two tasks. That is, each 40-min session consisted of two 10-min runs of each task, alternating between tasks only three times. Future studies should alternate more frequently between the tasks. For instance, the training paradigm could require a subject to alternate immediately and repeatedly: first achieve a high alpha state, then achieve a low alpha state, then discriminate a high alpha state, then discriminate low alpha state, and repeat. Such an arrangement would maximize the number of opportunities for generalization between the two types of skills. However, it is also possible that the effect of discrimination on control task performance was some idiosyncratic effect of the first session. For instance, subjects may habituate to the novelty of the task(s) and the lab environment after the first session, which may interact with how boredom or fatigue with the control task is interrupted by the discrimination task during minutes 11–20.

It is worth noting that while the discrimination-trained group did not do better during sessions 2 and 3, they did not do worse. This finding suggests that dividing session time equally between standard neurofeedback and discrimination training is at least an equally useful way to do the training. Discrimination training may have benefits other than facilitation of voluntary control, such as increasing client motivation and engagement in the session. While it is possible to sit passively through a standard neurofeedback session without much attention or effort, attention and participation are intrinsic to every trial in the discrimination task. When integrated into a standard neurofeedback session, self-prompted discrimination training may function as "transfer trials" and facilitate generalization of self-regulation skills beyond the clinical setting (Sherlin et al., 2011). Discrimination training measures and trains awareness about the subjective correlates of physiological states. Regardless of how it interacts with voluntary control, the ability to discriminate physiological states may play a role in the clinical efficacy of biofeedback, just as the ability to discriminate emotional states is important in the efficacy of psychotherapy (Lau & McMain, 2005). The explicit training of contrasts between opposing states in discrimination training may improve flexibility or the ability to make transitions between states, as opposed to merely maintaining a desired state. By analogy, the standard neurofeedback approach is like lifting a weight once and holding it up the entire session (with some exceptions, e.g. Strehl, 2009). Finally, the discrimination task score may provide an alternative and more reliable measure of the success of neurofeedback training.

Conclusion

The self-prompted discrimination paradigm in this study was much more readily learned than the EEG-prompted discrimination described in previous studies. The postresponse time series of alpha amplitudes suggested that recovering from correct low alpha trials was a particular challenge for some participants, contributing to session scores

significantly below 50%. However, discrimination task scores frequently and significantly exceeded the percent time the EEG was in the correct state, providing evidence that the discrimination paradigm measures more than just the ability to manipulate EEG amplitude. Observations that extreme amplitude events were discriminated better than moderate ones supported the interpretation that EEG alpha discrimination is more like a sensory than a motor performance. Discrimination training appeared to facilitate performance of the control task in the first session, consistent with awareness being important for early stages of learning. The lack of effect on control task performance in subsequent sessions suggests the need for further development of the paradigm. However, discrimination training may have other benefits, including client motivation and engagement, generalization beyond the clinical setting, and flexibility in making state transitions.

Author Disclosure

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NeuroRegulation

Efficacy of Live *Z*-Score Neurofeedback Training for Chronic Insomnia: A Single-Case Study

Rubén Pérez-Elvira[1], José A. Carrobles[2], Diego J. López Bote[1], and Javier Oltra-Cucarella[3]*

[1]NEPSA Rehabilitación Neurológica, Salamanca, Spain
[2]Departamento de Personalidad, Evaluación y Tratamientos Psicológicos, Universidad Autónoma de Madrid, Madrid, Spain
[3]Departamento de Psychología de la Salud, Universidad de Alicante, Alicante, Spain

Abstract

Objective/Background: Insomnia is the most common sleep disorder in the general population. Pharmacological treatments have shown efficacy in the short term, yet the symptoms return once the treatment has been withdrawn. In the search for treatment options with long-lasting effects, neurofeedback (NF) has arisen as a therapeutic option. Neurofeedback is the application of operant conditioning to brain activity. The aim of this work is to show the effectiveness of Live *Z*-Score NF training (LZT), a paradigm within the field of NF, in a case of insomnia. **Participants:** A 32-year-old male with chronic insomnia since his adolescence. **Methods:** Thirty 35-min sessions of qEEG-guided LZT using patient's highly preferred feedback. The main outcomes of this study were the patient's qEEG metrics and a visual analog scale of sleep quality throughout the intervention. **Results:** qEEG-guided LZT showed an improvement of 90.63% of the patient's qEEG metrics and an 82.55% relief of the clinical symptoms after 30 NF sessions. **Conclusions:** Although more research is needed to establish that NF based on Live *Z*-Score is effective for insomnia, our results suggest that NF might be a therapeutic alternative for the treatment of insomnia.

Keywords: insomnia; neurofeedback; *z*-score; qEEG; *z*-score neurofeedback

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***Address correspondence to**: Javier Oltra-Cucarella, Departamento de Psicología de la Salud, Universidad de Alicante, Campus de San Vicente del Raspeig – 03690 San Vicente del Raspeig, Alicante, Spain. Email: javier.oltra@ua.es

Edited by:
Rex L. Cannon, PhD, SPESA Research Institute, Bloomfield Hills, Michigan, USA; Knoxville Neurofeedback Group, Knoxville, Tennessee, USA

Reviewed by:
Randall Lyle, PhD, Mount Mercy University, Cedar Rapids, Iowa, USA
Nancy L. Wigton, PhD, Grand Canyon University, Phoenix, Arizona, USA

Introduction

About 20% to 30% of adults have some type of sleep disorders (Daley, Morin, LeBlanc, Grégoire, & Savard, 2009; Hammer, Colbert, Brown, & Ilioi, 2011). Insomnia is the most prevalent sleep disorder (Martínez Hernández, Lozano Olivares, & Álamo González, 2016), with around 21% of the population having at least one symptom of insomnia (Ohayon & Sagales, 2010) and between 6% and 10% of the general population presenting the full clinical syndrome of insomnia (Martínez Hernández et al., 2016). Pharmacological treatment for insomnia usually involves the use of benzodiazepines and antidepressants (NIH, 2005). Pharmacological treatments for insomnia have shown efficacy during the first 6 months after the treatment is implemented, with a worsening of sleep quality after treatment withdrawal (Hammer et al., 2011). This lack of long-term effectiveness of pharmacological therapies has highlighted the need to search for pharmacological and nonpharmacological therapy combinations able to maintain clinical improvements. Indeed, the combination of therapies seems to be more beneficial than monotherapy (Hammer et al., 2011).

Regarding nonpharmacological therapies for insomnia, previous studies have analyzed neurofeedback (NF) interventions either as monotherapy or in combination with other therapies.

The findings reported in these studies suggest that NF could be beneficial to improve sleep quality (Hammer et al., 2011), to maintain long-term improvements, to reduce falling asleep latency (Hoedlmoser et al., 2008) and to reduce awakenings during sleep (Cortoos, De Valck, Arns, Breteler, & Cluydts, 2010).

NF is a specialized field of biofeedback focused on the electroencephalographic (EEG) activity control (Carrobles, 2016), based on operant conditioning applications to EEG activity. Operant conditioning is a learning procedure that relies on the use of reinforcement to increase the likelihood of a target response (Skinner, 1938). Rewards are stimuli that are a thing of value to the organism and vary in degree across population. In NF training, the targeted response consists of prespecified patterns of brain waves, and the patient is given the reinforcement every time his or her brain waves match the prespecified pattern (Chapin & Russell-Chapin, 2014).

The EEG activity is recorded by an amplifier and processed with specialized software that allows the breakdown of the EEG into frequency bands, and also to quantify the mean voltage or amplitude of each band in a specific moment (Carrobles, 2016; Demos, 2005). Through the application of NF, it is possible to reinforce, inhibit, or ignore the different bands. For bands that are being reinforced, an amplitude threshold is established that must be exceeded to obtain feedback; for bands that are being inhibited, a threshold is established under which their amplitudes must remain in order to obtain reinforcement. When more than one frequency band is being reinforced and/or inhibited, all set thresholds must be within the range set to receive feedback (Demos, 2005). This feedback, which can be visual (e.g., films, animations), auditory (e.g., music) or mixed, is contingent on the fulfilment of the thresholds for each band in the EEG. The clinician usually selects the amplitude thresholds for each frequency band in order to ensure that the patient receives feedback at least 50% of the time, although learning can take place even with feedback percentages between 20% and 70% (Soutar & Longo, 2011).

Previous studies have shown that the application of NF has beneficial effects in patients with sleep problems (Arns, Feddema, & Kenemans, 2014; Arns & Kenemans, 2014; Halson, 2017; Hammer et al., 2011; Schabus et al., 2014), while others have not shown superior effects compared to placebo (Schabus et al., 2017). However, an important limitation related to the NF protocol is found across these studies. The works by Arns et al. (2014), Arns and Kenemans (2014), Halson et al. (2017), and Schabus et al. (2017, 2014) assessed the effects of NF on the sensorimotor rhythm (SMR), a brain wave with a frequency in the range of 13 to 15 Hz that is recorded over the sensorimotor cortex (Arroyo et al., 1993). The SMR protocol was developed in the first place for the treatment of epilepsy and was later applied as a one-size-fits-all procedure for other conditions including attention-deficit/hyperactivity disorder (ADHD) or insomnia. In the SMR protocol, brain waves are recorded in C3 or Cz sites, and reinforcement are provided when SMR amplitude is increased irrespective of other brain waves in other sites. This means that the SMR protocol is not administered based on the individual's qEEG profile (Cortoos et al., 2010; Hoedlmoser et al., 2008; Schabus et al., 2017, 2014), as waves at different brain sites are not trained.

Hammer et al. (2011) compared a group receiving *Z*-score training guided by qEEG with a group receiving *Z*-score SMR training. As participants receiving *Z*-score SMR training showed large movements toward *Z*-score normalization, these authors concluded that the *Z*-score training was probably more related to improvements in sleep quality than was the SMR element and the rewarding of SMR itself.

The technological advances in recent years have allowed an increase in the possibilities of the NF (Hammer et al., 2011) through different paradigms: *Z*-score-based neurofeedback, infralow frequency neurofeedback, infraslow fluctuation neurofeedback, or low-resolution electromagnetic tomography analysis (LORETA)-based neurofeedback. Some authors (Krigbaum & Wigton, 2015; Lubar, 2015; Wigton & Krigbaum, 2015) indicate that NF based on Live *Z*-Score (LZT) produces faster learning than conventional NF and has shown efficacy in different pathologies such as ADHD, epilepsy, migraine, depression, anxiety, and learning disorders (Guan, 2016; Walker, 2016). Hammer et al. (2011) used a 4-channel LZT neurofeedback protocol based on the qEEG results and showed that it might be effective in improving both overall sleep quality and quantity in individuals with insomnia. However, studies on the application of LZT in insomnia are scarce, both in group designs and in single-case designs. The main objective of LZT is to train patient EEG *Z*-scores, deviated from the norm, to behave normally; it does so with a low probability that waves with a normal amplitude move out of the normal range (Pérez-Elvira et al., 2018). To do this, all the patient's EEG *Z*-scores are computed and collected at all times, the

percentage of *Z*-scores within a specific range (±1 standard deviation *SD*) is calculated, and the patient receives feedback every time the percentage of *Z*-scores within the normal range is equal to or higher than the requested percentage.

The use of LZT is aimed at normalizing extreme *Z*-scores, while outliers are avoided so as to not overtrain them. Thus, the brain has sufficient freedom to choose a path of self-regulation that is not limited to training towards the norm (Collura, Guan, Tarrant, Bailey, & Starr, 2010). In other words, the brain accommodates itself to normalize with a certain degree of flexibility, since the main objective is to place a percentage of waves within the normal range.

Amplitude NF allows for the training of a small number of targets at the same time and does not permit the safe increase of slow waves, such as delta (Soutar & Longo, 2011). With LZT up to 248 simultaneous *Z*-scores (if four EEG channels are used) can be trained at the same time, and delta waves can be raised with a good safety margin since the limit is a normed *Z*-score, which is not the case with NF amplitude (Collura et al., 2010; Gracefire, 2016). With LZT the clinician can read the patient's qEEG deviations in real time and adjust the reinforcement thresholds to optimize the intervention.

There is a scarcity of LZT literature published in peer-reviewed scientific journals (with institutional review board coverage) reporting targeted qEEG change (Krigbaum & Wigton, 2015; Wigton & Krigbaum, 2015). To our knowledge, only one previous study used LZT for insomnia (Hammer et al., 2011). Therefore, the aim of this study is to analyze the efficacy of LZT guided by qEEG in the treatment of chronic insomnia.

Methods

Patient

The patient was a 32-year-old male, adopted when he was eight. He suffered from chronic insomnia since his adolescence. He had been receiving psychological treatment from an early age for night terrors and sensory deprivation suffered before his adoption. He started his schooling at eight years of age, because up to that moment he had environmental and psychosocial problems.

When this study began, he was working as a carpenter and was still receiving psychological treatment aimed at improving social skills for problems related to self-esteem. His educational level was primary school.

Main Complaints

The patient consulted our clinic, looking for a nonpharmacological treatment, because of complaints related to quantity and quality of sleep.

He had problems falling and staying asleep during the night and had frequent and vivid nightmares. The patient was unable to fall asleep, once lying down, until after more than an hour, and woke up frequently during the night without managing to maintain sleep more than 4 hours. Before starting treatment with NF, he received pharmacological treatment for insomnia (quetiapine 100 mg). Yet he often woke up during the night and felt anxious. This fact conditioned the rest of his day, both at work and in his social life. In addition, the patient expressed a desire to withdraw the medication.

The main objectives of the patient were to (1) fall asleep, to reduce the time between lying down and starting to sleep to less than 20 minutes; (2) stay asleep during most of the night, the total sleep time to be at least 6 hours; (3) feel refreshed after sleeping; and (4) withdraw sleep medication without worsening the quantity and quality of sleep.

The patient provided written informed consent for the intervention and the publication of this study, which was undertaken at NEPSA Rehabilitación Neurológica, a neurologic rehabilitation clinic authorized by the Regional Department of Health (Castilla y León, Spain). The Regional Department of Health provided approval for this kind of intervention.

Instruments and Procedure

qEEG Recording and Analysis. A qEEG was obtained before starting the NF intervention, and after every 10 NF sessions. To obtain the EEG, the patient was fitted with a 19-channel (Electro-cap International, Eaton, OH) according to the International 10–20 System with linked-ear montage (Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, and O2). For 3 min, the EEG signals were obtained and collected simultaneously over these 19 channels with a Discovery 20 amplifier (BrainMaster Technologies, Inc., Bedford, OH). The EEG recordings were recorded in eyes-closed condition, using BrainAvatar 4.6.4 software (BrainMaster Technologies, Inc., Bedford, OH).

The EEG signals were then imported into the NeuroGuide v2.9.1 software (Applied Neuroscience, Inc., Largo, FL) for computation and analysis, where artifacts (i.e., activity collected from the EEG that is not produced by the brain) were visually inspected and removed, retaining 1 min and 33 s with a test–

retest value of 0.93. The EEG was processed with linked-ear montage and compared with the NeuroGuide normative database, and *Z*-score values were obtained in order to identify the patient's brain waves that were out of range.

Visual Analog Scale. Prior to starting the NF intervention, the patient rated his sleep quality using a subjective visual scale. The visual scale included a 10 cm line with numbers from 0 to 100, with 0 being no sleep problems and 100 being the worst sleep quality. This scale was administered before the NF intervention and after every 10 sessions during the intervention. The upscale was also administered after 1-, 3-, and 6-month follow-ups.

Intervention

Live *Z*-Score Training (LZT) Neurofeedback. We used qEEG-guided LZT. Since C3, C4, P3, and P4 were the most deviated waves from normal range at pretreatment, they were selected for NF intervention. We used a 4-channel linked ears montage and the BrainAvatar 4.6.4 *Z*-Score PZOKUL protocol (BrainMaster Technologies, Inc., Bedford, OH).

This protocol has a training threshold that auto-adjusts based on the percentage of *Z*-scores within the upper and lower selected limits. In this study, 1 *SD* was used as the upper and lower thresholds (Thatcher & Lubar, 2014). The patient received one 35-min session twice a week for 15 weeks without interruption, with a total of 30 LZT sessions. The patient was offered to choose both the form of feedback (e.g., auditory or visual) and the type of feedback (e.g., sounds, music, videogames, movies, etc.) within each session. According to the patient's preferences, different movies selected by the patient were used to produce the feedback. This procedure is a modification of the procedure used in previous studies where the same form and type of feedback was selected by the researcher and used for all participants. For instance, Schabus et al. (2017, 2014) and Hoedlmoser et al. (2008) used the drawing of a sun along with a sound, whereas other studies did not specify what feedback was used (Cortoos et al., 2010; Hammer et al., 2011). We allowed the patient to choose both the form and the type of feedback in each session because, as previous studies have shown (Fisher et al., 1992; Mangum, Fredrick, Pabico, & Roane, 2012; Piazza, Fisher, Hagopian, Bowman, & Toole, 1996), rewards that are more relevant for the subject have a superior learning effect.

A dimmer was placed in front of the video screen that offered sharpness when the patient met the criteria set by the LZT protocol or became opaque, preventing the video from being viewed, when the criteria were not met.

Statistical Analysis

To analyze the change in EEG values, *Z*-scores were obtained for each location and frequency band, with a total of eight bands (Table 1). These *Z*-scores were dichotomized as within (i.e., ±1 *SD*) or outside the norm. The number of *Z*-scores within the limits of normality every 10 sessions was calculated. The McNemar test was used for related data to analyze whether significant changes occurred after each block of 10 sessions.

To analyze the clinical change, we used the percentage change of the values of the visual sleep quality scale.

Results

The pretreatment qEEG showed that all brain waves were under the lower limit for all four locations in all frequency bands (Table 1), mainly in the delta and beta bands, and in central, parietal, and occipital regions (Figure 1). The patient scored 86 on the visual analog sleep quality scale (Figure 2). The percentage of *Z*-scores within the normal limits was 0% (Tables 2 and 3).

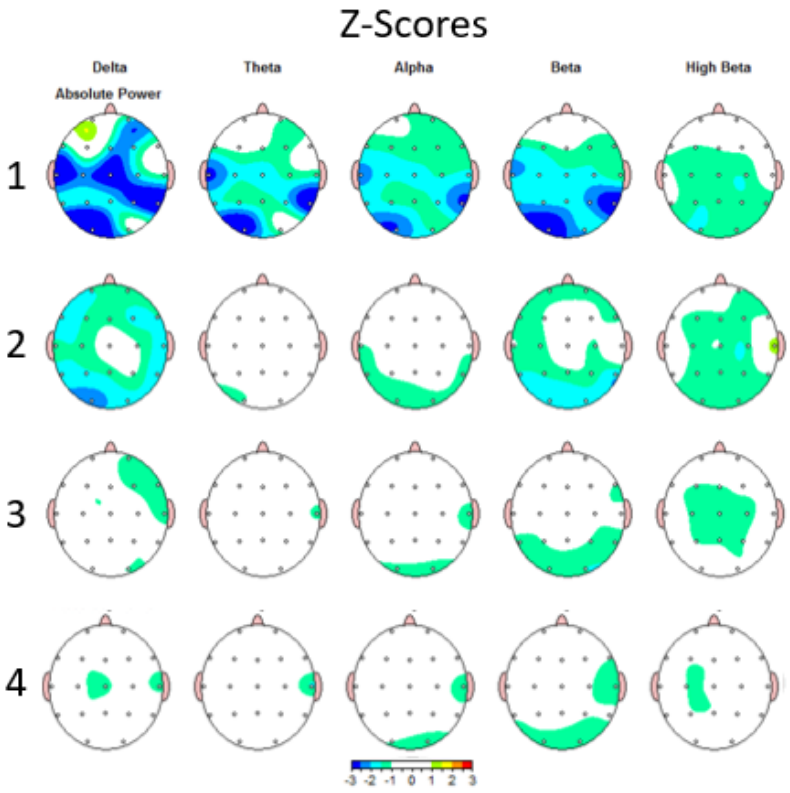

Figure 1. Surface maps of *Z*-scores distribution (full EEG). 1 = Baseline qEEG, 2 = after 10 LZT sessions qEEG, 3 = after 20 LZT sessions qEEG, 4 = after 30 LZT sessions qEEG.

Table 1
Z-scores per channel and frequency, and evaluation.

Channels	Delta Initial	Delta 10NF	Delta 20NF	Delta 30NF
C3	**−2.38**	**−1.37**	−0.64	−0.69
P3	**−1.83**	**−1.60**	−0.56	−0.83
C4	**−1.82**	−0.92	−0.67	−0.57
P4	**−2.63**	−0.96	−0.83	−0.47

Channels	Theta Initial	Theta 10NF	Theta 20NF	Theta 30NF
C3	**−1.66**	−0.22	0.35	0.33
P3	**−1.46**	−0.52	0.13	0.09
C4	**−1.30**	0.21	0.10	−0.09
P4	**−1.77**	0.12	0.57	0.71

Channels	Alpha Initial	Alpha 10NF	Alpha 20NF	Alpha 30NF
C3	**−1.64**	−0.73	−0.24	−0.36
P3	**−1.46**	−0.90	−0.59	−0.56
C4	**−1.47**	−0.69	−0.41	−0.33
P4	**−1.65**	−0.71	−0.58	−0.44

Channels	Beta Initial	Beta 10NF	Beta 20NF	Beta 30NF
C3	**−1.80**	**−1.19**	−0.57	−0.47
P3	**−1.91**	**−1.43**	−0.98	−0.72
C4	**−1.65**	**−1.08**	−0.78	−0.91
P4	**−2.19**	**−1.22**	**−1.08**	−0.94

Note. Initial = 1st qEEG, 10NF = after 10 NF sessions, 20NF = after 20 NF sessions, 30NF = after 30 NF sessions. Z-scores out of range are marked in blue ink.

Table 1 *(continued).*

Channels	Hi Beta Initial	Hi Beta 10NF	Hi Beta 20NF	Hi Beta 30NF
C3	**−1.32**	**−1.11**	**−1.15**	**−1.01**
P3	**−1.45**	**−1.33**	**−1.01**	−0.89
C4	**−1.42**	**−1.32**	**−1.16**	−0.97
P4	**−1.38**	**−1.25**	**−1.01**	−0.66

Channels	Beta1 Initial	Beta1 10NF	Beta1 20NF	Beta1 30NF
C3	**−1.31**	−0.72	−0.19	−0.34
P3	**−1.58**	**−1.15**	−0.84	−0.72
C4	**−1.21**	−0.45	−0.34	−0.84
P4	**−1.78**	−0.99	−0.98	−0.88

Channels	Beta2 Initial	Beta2 10NF	Beta2 20NF	Beta2 30NF
C3	**−1.39**	−0.97	0.13	0.29
P3	**−1.61**	**−1.19**	−0.47	−0.23
C4	**−1.19**	−0.79	−0.19	−0.13
P4	**−1.69**	−0.69	−0.54	−0.59

Channels	Beta3 Initial	Beta3 10NF	Beta3 20NF	Beta3 30NF
C3	**−1.91**	**−1.53**	**−1.36**	−0.96
P3	**−1.87**	**−1.58**	**−1.28**	−0.87
C4	**−1.87**	**−1.76**	**−1.50**	**−1.30**
P4	**−2.18**	**−1.62**	**−1.34**	**−1.05**

Note. Initial = 1st qEEG, 10NF = after 10 NF sessions, 20NF = after 20 NF sessions, 30NF = after 30 NF sessions. Z-scores out of range are marked in blue ink.

After the first 10 sessions of LZT, 16 of the 32 *Z*-scores (50%) were within the normal range (Tables 2 and 3), which is a statistically significant change relative to baseline assessment ($\chi^2 = 14.06$, $p < .001$). Also, the qEEG maps showed an overall improvement (Figure 1), despite maintaining low voltage in all frequency bands. After these 10 LZT sessions, the patient identified a 22.09% improvement in sleep quality (Figure 2).

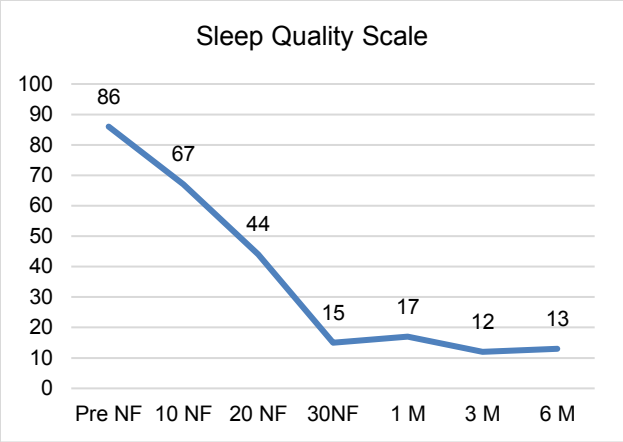

Figure 2. Sleep Quality Visual Analog Scale. Pretreatment, after 10NF, 20NF, and 30NF sessions, and 1-month (M), 3 M, and 6 M follow-up. 100 = worst sleep quality, 0 = best sleep quality.

After 20 LZT sessions, the maps again showed an overall improvement (Figure 1), with higher voltage in all bands and 71.88% of *Z*-scores within the norm (Tables 2 and 3), a significant change compared to the previous measurement ($\chi^2 = 5.14$, $p = .011$). The patient identified an improvement of 48.83% compared to the previous assessment on the analogue visual scale (Figure 2) measuring sleep quality.

Table 2
Percentage of Z-scores within the normal limits for every measurement distributed by frequency.

	Number of *Z*-scores within the limits	% within the limits
Initial	0	0.00%
10NF	16	50.00%
20NF	23	71.88%
30NF	29	90.63%

Note. Initial = First qEEG, 10NF = after 10 sessions qEEG, 20NF = after 20 sessions qEEG, 30NF = after 30 sessions qEEG.

Table 3
Percentage of Z-scores within the normal limits for every measurement distributed by channel.

Number of Z-scores within the limits	C3	P3	C4	P4
Initial	0	0	0	0
10NF	4	2	5	5
20NF	6	6	6	5
30NF	7	8	7	7
% within the limits	**C3**	**P3**	**C4**	**P4**
Initial	0%	0%	0%	0%
10NF	50.0%	25.0%	62.5%	62.5%
20NF	75.0%	75.0%	75.0%	62.5%
30NF	87.5%	100.0%	87.5%	87.5%

Note. Initial = First qEEG, 10NF = after 10 sessions qEEG, 20NF = after 20 sessions qEEG, 30NF = after 30 sessions qEEG.

After 30 LZT sessions, additional improvements were found in the qEEG maps (Figure 1), with higher voltage in all bands and an improvement of 82.5% in sleep quality compared to the initial measurement (Figure 2). It can be observed that 90.63% of *Z*-scores were in the normal range after the last LZT session (Tables 2 and 3), which is a statistically significant improvement compared to baseline assessment ($\chi^2 = 4.17$, $p = .02$).

Regarding the channel scores, P3 showed 100% of the *Z*-scores within the normal range after 30 sessions of NF, whereas C3, C4, and P4 showed 87% of *Z*-scores within the normal range. As can be seen in Table 1, none of the waves within the normal range deviated from normality (i.e., ±1 *SD*).

Data on subjective perception of sleep quality after 1-, 3-, and 6-month follow-ups showed no difference compared to the last measurement of the intervention phase, indicating a maintenance of the improvements achieved after 30 sessions of LZT.

Discussion

This study aimed to analyze the efficacy of LZT neurofeedback intervention for the treatment of chronic insomnia. A qEEG-guided LZT protocol was designed for this purpose. The results showed that LZT was effective in modifying EEG patterns and bringing EEG metrics within the normal range after thirty 35-min sessions of NF. In addition, the patient was able to discontinue the use of sleep medication after 20 sessions.

These results are consistent with previous works. Hammer et al. (2011) found improvements in sleep after 10 LZT sessions in people with insomnia. Krigbaum and Wigton (2015) analyzed 10 individuals with different conditions (attention-deficit/hyperactivity disorder, anxiety disorder, and Asperger's disorder) using 19-Channel *Z*-score NF during 6 to 15 NF sessions. They identified the sites of interest as any electrode sites which had *Z*-scores of either $Z \geq 1$ or $Z \leq -1$, and then analyzed those that moved towards values of $Z = 0$. Their findings showed that 45 sites of interest out of 50 (90%) moved in the targeted direction, a finding similar to the results reported in the present study using a similar methodology, even though we used the criterion of *Z*-scores falling within the normal range (*Z*-scores between ±1) rather than moving toward $z = 0$.

Our data indicate that after 10 sessions of LZT there was a trend towards normalization of *Z*-scores, and after 30 sessions the total computation of *Z*-scores was very close to normal. Likewise, the patient interrupted the pharmacological treatment and identified an improvement of 83% in the subjective perception of the quality of sleep. Sleep quality was measured with a visual analog scale during the intervention and in the follow-up, with maintenance of sleep quality at the end of the intervention and withdrawal of the medication. Our results showed a difference of 71 points between baseline and the last NF session. This difference, which is higher than the difference considered clinically relevant by Zisapel and Nir (2003) using a 100 points visual analog scale for measuring quality of sleep, highlights the clinical importance of the LZT and supports the clinical relevance reported in previous works (Hammer et al., 2011; Krigbaum & Wigton, 2015; Wigton & Krigbaum, 2015).

One of the strengths of this work is that the effects of NF were assessed both immediately after treatment and after 1-, 3-, and 6-months follow-ups. This is an improvement over other studies which, as far as we know, either did not follow up (Hoedlmoser et al., 2008; Schabus et al., 2017, 2014) or only did it at one time. For instance, Hammer et al. (2011) had a 6- to 9-month follow-up, and Cortoos et al. (2010) had a

2-week follow-up after the treatment was completed. Interestingly, our results after 6 months of follow-up are similar to those reported by Hammer et al. (2011), who found a good sleep quality in their participants after 6 months of follow-up. Additionally, it must be noted that the improvement in sleep quality in the patient described here continued even after the patient withdrew the medication.

In the present study, qEEG was used to guide treatment with LZT, which allowed specification of the brain waves that would be the sites of interest for the intervention. This could explain the differences with the study by Schabus et al. (2017), who concluded that treatment with NF was not superior to placebo for insomnia. It should be noted that in their study they used the SMR protocol, which was not qEEG-guided and was applied similarly to every participant. Regarding feedback, stimulus used to work as reinforcer for some subjects might not work for others (Mangum et al., 2012). The NF is based on the application of the operant conditioning for the modulation of the EEG activity, so it is important that the feedback is a real reinforcer relevant for the individual patient (Fisher et al., 1992). The feedback used by Schabus et al. (2017) appears to have little probability of being a true reinforcer for the subjects in their study because they were not selected by the subjects and might not work as a reinforcer. It should be added that the results of Schabus et al. (2017) contradict other studies that showed that the use of different NF protocols improved sleep latencies in children and adults with ADHD (Arns et al., 2014; Arns & Kenemans, 2014). Both the protocol and the feedback used by Schabus et al. (2017) could partially explain their negative results. In contrast, our study used patient's highly preferred feedback, so it is are assumed to have a higher reinforcing value (Fisher et al., 1992; Piazza et al., 1996).

The results of this case suggest the need to investigate the efficacy of LZT not only as a treatment for insomnia but also as a tool to normalize brain activity, including low-voltage cases. Despite our results, this study had numerous limitations, including sample size, which was reduced to a single case without a control group. In the protocol used in the present study, following the fundamental principles of operant conditioning, and in order to ensure that feedback had real reinforcing value, the patient was allowed to choose the feedback to be used. Although this could guarantee the reinforcing value of the material, this procedure makes our results not comparable with previous works that did not allow the patient to select a relevant reinforcer. Also, sleep quality was measured with a visual analog scale, as used in previous research on insomnia (Zisapel & Nir, 2003), but it probably only reflects very generally the quality of sleep. It is therefore necessary to include objective measures of sleep quality to correlate subjective improvements with objective physiological measures. Similarly, the effect of reinforcer selection on the neurometric results of the intervention with LZT and other types of NF should be analyzed. As for the measures of sleep quality, insomnia is a multicausal pathology and with several dimensions to take into account (e.g., hours of sleep, latency time until conciliation of the same, awakenings during the night). Thus, scales and other instruments are needed that could sufficiently cover the different dimensions of sleep.

In conclusion, LZT seems to be a good approach to NF not only because of its rapid resolution of symptoms and normalization of brain activity but also because of its safety margin for increasing slow waves. In the case of insomnia, LZT may be a better option than pharmacological treatment. As shown by this 30-session intervention, NF may achieve long-lasting effects, may normalize the EEG, and may also improve subjective quality of sleep in chronic insomnia, without producing adverse reactions or side effects.

Author Disclosure

The authors declare that they have no grants, financial interests, or conflicts of interest to disclose.

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NeuroRegulation

Remediation of PTSD in a Combat Veteran: A Case Study

George Lindenfeld[1], George Rozelle[2], John Hummer[3], Michael R. Sutherland[4], and James C. Miller[5]*

[1]Reset Therapy Professional Institute, LLC, Sarasota, Florida & Hendersonville, North Carolina, USA
[2]MindSpa Integrative Wellness Center, Sarasota, Florida, USA
[3]James H. Quillen VA Medical Center, Johnson City, Tennessee, USA
[4]University of Massachusetts, Amherst, Massachusetts, USA
[5]U.S. Air Force Research Laboratory, Corpus Christi, Texas, USA

Abstract

The posttraumatic stress disorder (PTSD) condition is a systemic neuroinflammatory state that emanates from a failure to recover from traumatic occurrence(s). Major complications associated with PTSD include problems with impulse control and issues related to verbal and physical outbursts of anger and rage. The Veteran's Administration (VA) projects a post–9/11 veteran population of around 3.5 million by 2019. Emotional problems are prevalent among combat service members and veterans with about half of the group suffering from various symptoms of PTSD. Three in four among them report they are reliving traumas in the form of flashbacks and nightmares. Current mental health treatments have not fully remediated the negative impact that results from PTSD. We present a case study of a novel and transformative treatment approach called Reconsolidation Enhancement by Stimulation of Emotional Triggers (RESET) Therapy. The intervention uses binaural sound to unlock the memory reconsolidation process, thereby releasing the emotional component of experienced trauma. RESET Therapy offers a compelling therapeutic adjunct to the practicing biofeedback/neurofeedback clinician, who is under constant pressure to deliver interventions that are rapid, tolerable, and cost-effective. Additionally, the treatment spares the therapist from repeated exposures to the raw limbic activity of traumatized patients, thereby minimizing the potential for vicarious traumatization.

Keywords: posttraumatic stress disorder; trauma; memory reconsolidation; binaural sound; the neuronal network of PTSD

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***Address correspondence to**: Dr. George Lindenfeld, Glenhouse Drive GL-327, Sarasota, FL 34231, USA. Email: glindy123@gmail.com

Edited by:
Rex L. Cannon, PhD, SPESA Research Institute, Bloomfield Hills, Michigan, USA; Knoxville Neurofeedback Group, Knoxville, Tennessee, USA

Reviewed by:
Randall Lyle, PhD, Mount Mercy University, Cedar Rapids, Iowa, USA
Nancy L. Wigton, PhD, Grand Canyon University, Phoenix, Arizona, USA

The included case study aims to introduce the neurofeedback practitioner to a promising new neurofeedback-based intervention called Reconsolidation Enhancement by Stimulation of Emotional Triggers (RESET) Therapy, a type of brief nonverbal exposure therapy utilizing auditory stimulation via an individually-intonated binaural beat. We demonstrate the RESET procedure using a case study involving a veteran volunteer who took part in a larger pilot study (Lindenfeld, Rozelle, Soutar, Hummer, & Sutherland, 2019).

Background

Psychological trauma inflicts a shock to the central nervous system that results in a reduction in connectivity between limbic and cortical processes. The varied consequences reverberate throughout the brain over time depending upon the patient's previous history, physiological status, and the ongoing social distress encountered. Severe anxiety and depression are likely to be concomitant states which vary over time and circumstance, reflected in hemispheric asymmetries. The

posttraumatic stress disorder (PTSD) condition is a systemic neuroinflammatory disorder that emanates from a failure among many human beings to recover from traumatic occurrence(s). Inability to recover from trauma can occur following the experience of stress-induced "fight, flight, or freeze" event(s). Unlike other mammalian species who can "shake it off," humans may lock recall of their adverse experience into the long-term memory system of the brain and body (Levine & Frederick, 1997).

Psychological symptoms of PTSD are accompanied by a neuroinflammatory process in the brain and body, where oxidative stress and excitotoxicity takes an adverse toll over time (Soutar, Hopson, & Longo, 2016; Bam et al., 2016). Soutar et al. (2016) outlined successive stages of the oxidative stress process and its adverse effects upon brain activation patterns as depicted via a series of quantitative electroencephalograms (qEEGs). Patients with PTSD vary in their stage of the stress response, as reflected in their brain physiology (Soares, Marques, Magalhães, Santos, & Sousa, 2014). Any effort to oversimply PTSD by looking for a singular qEEG brainwave "signature" misses the condition's variability point, as it reflects a failure to grasp the dynamic and degrading nature of the stress response syndrome over time.

Presently, there is no single unified or encompassing model of PTSD. It is generally accepted, however, that individuals with chronic PTSD encounter difficulties in the regulation of attention and arousal, self or other emotional awareness, and social–emotional processing. These processes depend upon the functional integrity of large-scale brain networks encompassing cortical, subcortical, and brainstem structures.

We begin the article by summarizing some of the current neuroscience understanding of PTSD, followed by a limited review of psychological, biofeedback, and neurofeedback research addressing the treatment of PTSD. We present a heuristic neuronal model of PTSD to provide testable hypotheses for the clinician using the RESET method, and then present our case study of a veteran successfully treated with RESET to demonstrate the method and how it can be replicated via future research.

Remediation of PTSD

Remediation of PTSD is an ongoing topic of discussion among many mental health practitioners because we have been unable to restore the impacted individual to a full state of prior functioning. While advised by leading governmental agencies such as the National Institute of Mental Health (NIMH) in the use of frontline therapies, we are still seemingly not able to meet the demand of those most impacted by the condition. As noted in the NIMH (2019) description of treatments for PTSD, the primary interventions discussed are talk based psychotherapy, medications, or both. With the Veteran's Administration (VA) projecting numbers in the millions of those affected by PTSD, (Tanielian & Jaycox, 2008) finding better answers to enable mental health professionals to restore those altered by PTSD are critical.

A recent letter to the editor Krystal et al. (2017) reported a 2017 consensus statement of the PTSD Psychopharmacology Working Group. They advise that "there seems to be no visible horizon for advancements in medications that treat symptoms or enhance outcomes in persons with a diagnosis of PTSD" (p. e51). A follow-up letter by another group of researchers, Lipov, Tukan, and Candido (2018), comments that "with only 50% of veterans seeking care and a 40% recovery rate, current strategies will effectively reach no more than 20% of all veterans who need PTSD treatment" (p. e17).

Neuroscience Underpinnings

Rauch, Shin, and Phelps (2006) outlined a neurocircuitry model of PTSD that emphasizes the role of the amygdala, as well as its interactions with the ventral/medial prefrontal cortex including but not limited to the anterior cingulate, prefrontal cortex, orbitofrontal cortex, and hippocampus. Rauch et al. (2006) proposes a diathesis–stress model involving a fear-conditioning process that could include any possible combination of amygdala hyperresponsivity, ventromedial prefrontal cortex deficiency, hippocampal deficiency, or exaggerated sensitivity or susceptibility to the effects of stress. They cite earlier fMRI studies that showed the right amygdala hyperactivity and decreased left prefrontal, Broca's area activity. Brain imaging research has tended to provide evidence that an overactive right hemisphere is involved in persistent posttraumatic stress (Engdahl et al., 2010; Engels et al., 2007; Lanius, Frewen, Tursich, Jetly, & McKinnon, 2015; Rauch et al., 2006). Underarousal of the left prefrontal/frontal cortex has been demonstrated in depression (Davidson & Hugdahl, 1996; Herrington et al., 2010). Broca's area becomes underactive in psychological trauma, speechless horror, followed by fragmentation of, or lack of, verbal story or narrative as noted by van der Kolk, McFarlane, and Weisaeth (1996).

At least three large-scale brain networks—also referred to as intrinsic connectivity networks—have been implicated in psychiatric disorders, including PTSD. These include the default mode network (DMN), salience network, and central executive control network (Lanius et al., 2015). Networks, both large-scale and mesoscale, tend to be bihemispheric (Laird et al., 2011). Network activity has been established via functional neuroimaging (e.g., fMRI) studies.

Resting-state conditions are observed through changes in blood flow in the brain, assessed via the blood-oxygen-level-dependent (BOLD) signal in fMRI. Because the brain is always active even in the absence of task involvement, any brain region will have spontaneous fluctuations in the BOLD signal. The resting state is used to assess the brain's functional organization connectivity or communication level and to evaluate whether it is altered in neurological and psychiatric conditions (Sporns, 2010). Functional connectivity lasting seconds is reflected by varied brain region intercommunication that share functional properties and is an expression of network behavior underlying high-level cognitive functions. These networks increase and decrease in activation in proportional and antagonistic manners during the performances of emotional and cognitive tasks.

Default Mode Network (DMN). The DMN involves the anterior and posterior medial cortices and the lateral parietal lobes, and it is most active when an individual is in a waking, resting state. It activates an internal focus, such as daydreaming, retrieving autobiographical information, self-monitoring, inner reflection upon one's emotional state, imagining the future, focus upon personal values and morals, and theory of mind thinking about others, wondering socially about the perceptions, feelings, and motivations of others. The default state encompasses emotional reasoning, social judgment, episodic memory recalling specific events in time, and story comprehension understanding and remembering a narrative. The DMN also focuses on future goals and internally valued rewards.

The DMN has been hypothesized to be relevant to disorders including Alzheimer's disease, autism, schizophrenia, depression, chronic pain, PTSD, among other disorders (Menon, 2015; Sporns, 2010). Lower connectivity between brain regions has been found across the DMN in persons with long-term trauma such as childhood abuse or neglect and disrupted attachment. In PTSD, lower activation has been found in the posterior cingulate gyrus, and in severe posttraumatic stress (PTS), lower overall connectivity within the DMN. If the DMN is altered, it changes the way one perceives events, one's social and moral reasoning, and makes a person more susceptible to major depression-like symptoms.

Salience Network. The salience (vigilance) network (SN), which involves the dorsal anterior cingulate and frontoinsular cortex, is involved in maintaining a sustained state of alertness, involving the right frontal and right parietal lobes. As opposed to the narrow, task-focused attention of the left hemisphere, the right hemisphere employs a broader and more vigilant orientation to the environmental, allowing rapid detection of the location of a stimulus—especially an infrequent or unexpected stimulus (Posner & Raichle, 1994; McGilchrist, 2009), it plays a crucial role in salience detection—directing behavior to the most pertinent actions. The anterior insula of the SN is thought to meditate the engagement of the central executive network (CEN) and disengagement of the DMN, and hence the dynamic interplay between the externally and internally focused attention and cognitive–affective processing.

Central Executive Network (CEN). The CEN involves the dorsolateral prefrontal cortex and the posterior parietal cortex. It is responsible for high-level cognitive functions, notably the control of attention and working memory. It acts as a controller that directs the engagement of other areas that contribute sensory or conceptual content to network operations. For example, coordination of the prefrontal and posterior parietal areas channels the flow of sensory and motor activity to prepare for perceptual-motor processing which involves the dorsolateral prefrontal cortex and the posterior parietal cortex; it is critical to verbal learning and executive functioning (Bressler & Menon, 2010).

Lanius et al. (2015) reviewed experimental neuroimaging research demonstrating disrupted internetwork activity in PTSD, as opposed to healthy controls. When given a working memory task, healthy controls readily shifted to engage the CEN, whereas the PTSD group showed difficulty shifting out of DMN activity. By contrast, when the task involved autobiographical memory retrieval, the PTSD group showed decreased recruitment of DMN networks, relative to healthy controls. Memories recalled in first-person perspective elicited greater medial temporal amygdala activity than third-person perspective. Interestingly, the emotional intensity of the memory was associated with increased frontal-

parietal CEN activity in healthy controls but decreased frontal-parietal activity within the CEN among PTSD participants. There was a positive correlation between dissociative experiences and communication between the DMN and CEN in PTSD patients.

While healthy controls engage the CEN on working-memory tasks, PTSD subjects engage brain regions irrelevant to the task, such as the DMN, engaging in self-referential processes rather than outwardly directed task behavior, signaling cognitive dysfunction. Findings demonstrate that the ability to engage and shift between task-relevant CEN and task-irrelevant DMN brain networks during processing tasks which are partly mediated by the anterior insula is impaired in PTSD (Lanius et al., 2015). A brain that is dysregulated from trauma cannot recall, evaluate, explain, plan, or coordinate complex cognitive and emotional processes (Soutar, in press).

Synthesis of Findings

From the research above, we can synthesize the following findings: the amygdala shows increased activation, which translates to overactivation of the fear circuit with exaggerated fight or flight responses, in PTSD. The prefrontal cortex shows decreased activation, which translates to weakening the influence of the thinking or executive brain over other areas or networks. The cingulate cortex shows decreased activation, translating to decreasing emotional regulation. The insula may show increased or decreased activation, reflecting active versus numbing states experienced in the body. The amygdala's connections to the prefrontal cortex are strong, whereas the prefrontal cortex's ability to inhibit the amygdala weakens in PTS.

In PTS, the amygdala's influence upon connections to the anterior cingulate cortex emotional regulation system is strong, whereas the anterior cingulate reciprocal connections to the amygdala are weakened. The right prefrontal and frontal cortex must increase in activation elevating amplitudes in the beta, and high beta frequency ranges to exert inhibitory control over the right amygdala. The inhibitory aspect is a form of a compensatory process (Merabet & Pascual-Leone, 2010) characteristic of deregulated self-organizing neurobiological systems where timing has become disrupted (Othmer, Othmer, & Kaiser, 1999) where some brain areas are running too slowly, other brain areas are running too rapidly—hence, brain too slow; brain too fast. Similarly, the right parietal cortex must increase its activation elevating amplitudes in the beta, and high beta frequency ranges to control the hyperaroused reticular activating system (RAS) in the brainstem. The delicate normal asymmetry pattern between the left and right hemispheres is now reversed, whereas the left hemisphere becomes underactive.

Swingle (2008) has noted a phenomenon called alpha blocking in PTSD. Alpha amplitudes normally increase by 30% to 60% when eyes are closed, particularly in the occipital regions. Many PTSD subjects do not show the expected normal pattern of alpha amplitude increases in the eyes-closed condition. They also tend to have lower than average theta amplitudes in the occipital areas. The phenomenon of alpha blocking has been largely based on clinical observation and practice and may require further empirical investigation.

Veterans with PTSD and TBI

About veterans with PTSD and traumatic brain injury (TBI), Brenner (2011) reviewed neuroimaging and neuropsychological data on veterans returning from Iraq and Afghanistan. Focusing specifically on PTSD research, Brenner concluded that neurobiological activation influences functioning. He noted that chronic activation of, or alteration to, structures in the limbic system and prefrontal cortex is detrimental to long-term physical and mental well-being. Reduced hippocampal volume and other premorbid neurobiological risk factors from exposure to developmental and premilitary stressors contribute to the development of combat-related PTSD.

Hypothesis

We hypothesize that the PTSD condition is a systemic neuroinflammatory disorder that emanates from a failure among many human beings to recover from traumatic occurrence(s). Inability to recover from trauma can happen following the experience of stress-induced fight, flight, or freeze event(s). As an example of how other mammal species who can shake it off, whereas humans may lock recall of their adverse experience into the long-term memory system of the brain and body, Levine and Frederick (1997) inform us that "tigers don't get ulcers"; thus insinuating that the predator is not vulnerable to stress as are humans.

We will proceed with clarification of different elements of our hypothesis, beginning with the systemic aspect of PTSD. By systemic, we mean the impact of an adverse effect on multiple body

organs and tissue, systemwide. Next, we specifically discuss the neuroinflammatory component that may be initiated in response to the impact of stress. And finally, we will explain the memory component within the context of the reconsolidation process.

PTSD as a Systemic Disorder

Among Australians who served in Iraq or Afghanistan, the estimate of those incurring PTSD is 16.5%. Those who served in Vietnam suffered a lifetime incidence rate of 20.9% (McLeay et al., 2017). Among these Australian veterans, many experienced accompanying physical comorbidities, including chronic disease (McLeay et al., 2017), suggesting that PTSD should not be seen as a mental condition but rather as a systemic disorder. Other investigators (Mellon, Gautam, Hammamieh, Jett, & Wolkowitz, 2018) found increased rates of somatic comorbidities in those with PTSD in comparison to those without it, including immune dysfunction and cardiovascular disease. Their findings support the perspective that PTSD may be a systemic condition. They conclude with the position that PTSD with its accompanying comorbid conditions places affected individuals at increased mental and physical health risk.

PTSD as a Neuroinflammatory Contributor

Microglia, comprising 10% of the central nervous system (CNS) population, are the immune cells of the CNS, which play essential roles in mediating neuroinflammatory responses. Their primary function appears to be that of coordinating the interaction between the immune system and the brain. Unfortunately, their low turnover rate makes them susceptible to the proinflammatory effects of stress, injury, or age. The extent of neuroinflammation is dependent on the situation, length of time, and the intensity of the trauma effects. Chronic low-level effects trail the acute phase of trauma, leading to diminished neuronal plasticity and accompanying impairment in cognitive functioning. Increased degrees of the chronic effect are associated with actual damage to the nervous system that is target specific for neurodegenerative diseases.

Chronic or traumatic stressors promote an increased neuroinflammatory profile involving both microglia and bone marrow-derived macrophages. With the activation of the above process, the immune system is thought to relay information to the brain, which consequently promotes prolonged anxiety-like behavior. Chronic stress appears to be associated with impairment to intellectual abilities, accelerating a decline in the effectiveness of cognitive abilities (DiSabato, Quan, & Godbout, 2016).

A 2018 systematic review of literature explored the possible association between PTSD and low-grade inflammation. Speer, Upton, Semple, and McKune (2018) found evidence for the presence of inflammatory biomarkers that were elevated across included studies in the varied PTSD groups but not in the control groups.

A recent study found that enhanced inflammatory processes across a wide range of psychiatric diagnoses are thought to disrupt neurobiological mechanisms that regulate cortical plasticity and cognition suggesting that a cross-conditional approach be considered for managing disrupted cognition in psychiatric patients (Fourrier, Singhal, & Baune, 2019).

Martone (2019) found a correlation between an overactivated immune response and the advancement of psychiatric symptoms. He notes the presence of harmful effects on cognition and behavior, whereas subduing inflammation can considerably improve mood and sensorium. Particular brain regions that trigger alarm and arousal appear to be predominantly vulnerable to the effects of inflammation.

Sumner et al. (2017) found PTSD to be associated with heightened cardiovascular disease risk by fostering a neuroinflammatory state. They suggest that impaired endothelial function and increased inflammation may serve as a pathway through which chronic PTSD may increase a cardiovascular disease risk factor.

As substantiated above, varied investigators are increasingly exploring the long-term effects that emerge due to trauma exposure (Miller, Lin, Wolf, & Miller, 2018). Many early-onset conditions are noted, including dementia and other neurocognitive disorders. Miller et al. (2018) report a strong association of trauma activation with related neurobiological pathways within the context of a state of heightened physiological arousal. These researchers propose that the molecular consequences of the syndrome activate elevated systemic levels of oxidative stress. The long-term results of the induced chronic state include accelerated cellular aging.

Ryder, Azcarate, and Choen (2018) conducted a meta-analysis focused on the long-term consequences of chronic PTSD. They found strong

evidence for elevated risk of musculoskeletal, metabolic, and cardiovascular conditions among those with the PTSD condition. Earlier, Sumner et al. (2017) explored the association between trauma exposure, chronic PTSD, and biomarkers of inflammation in middle-aged women in the Nurses' Health Study II. Their results revealed an increase in inflammation as well as impaired endothelial function leading to the speculation that the inflammation might be the vehicle through which chronic PTSD may increase cardiovascular disease risk.

There is little remaining doubt that PTSD impacts selective organs in the body. A large-scale consortium study was conducted by the Psychiatric Genomics Consortium (PGC)–Enhancing Neuroimaging Genetics through Meta-Analysis (ENIGMA) PTSD Working Group; the group achieved the most extensive neuroimaging study of PTSD to date analyzing data from 1,868 subjects consisting of both PTSD and control group participants. Eight subcortical structures were subjected to a standardized image analysis and quality-control neuroimaging analysis. The results of the meta-analysis revealed a smaller hippocampus size in those participants with PTSD (Logue et al., 2018).

Finally, a significant step is in place through the development of a comprehensive PTSD Biomarker Database (PTSDD) focused on fluid-based biomarkers. Information was collected from over 100 PTSD-related articles ranging from 1997 to 2017. For inclusion in the database, it was necessary for the article authors to evaluate fluid-based biomarkers in humans comparing PTSD patients to control populations. The goal of the project is to investigate whether single biomarkers such as cortisol may emerge as a systemic indicator from at least 900 physiological markers to assist in the early identification of those who will develop PTSD (Domingo-Fernández et al., 2019).

There appears to be cumulative research producing substantial evidence supporting our perspective that PTSD creates a neuroinflammatory state within the afflicted individual. It is likely that the long-term effects contribute to delayed onset PTSD (Frueh, Grubaugh, Yeager, & Magruder, 2009) as well as to the differential found between combat veterans and noncombat veterans in regards to the later emergence of dementia in their functioning as they attain an older age (Health, 2010).

Memory Reconsolidation Process

Before the turn of the century (2000), it was thought that memory was permanently stored in the mind in an unalterable fashion. In truth, the hypothesis of memory consolidation was proposed by Müller and Pilzecker about 100 years ago, as cited in McGaugh (2000). The first time a memory is permanently stored in the brain, it is referred to as consolidation. The stronger the memory, such as that which occurs in a traumatic event, the more robust the storage aspect will be.

After a trauma encounter, each time the memory is brought into awareness, it then goes through a reconsolidation process. We have found that such a natural occurrence provides us with an opportunity to alter what is to be restored and what emotional aspect may be dropped out. Thus, parts of the memory become briefly vulnerable to change during the period before it reconsolidates or hardens into long-term memory again. The primary brain region associated with the reconsolidation process is the hippocampus (Dudai, Karni, & Born, 2015). Our specific goal in RESET Therapy is to sustain the memory detail but erase the negative and traumatic part of it so that it no longer adversely triggers the patient. The individual still has the memory, but it becomes something diminished in the distance and will no longer be experienced as intrusive or disrupting.

We consider RESET Therapy to be a transformative approach wherein specified emotional aspects of the traumatic memory are diminished or erased from long-term memory. The extrinsic memory of the event remains, but the intrinsic emotional aspect has dropped out once the memory has reconsolidated (Ecker, Ticic, & Hulley, 2012). We find that trauma remediation is possible through brief disruption of the memory reconsolidation process by a neuro-modulated sound tuned in to resonate and target with a particular trauma frequency (Lindenfeld & Bruursema, 2015).

As elucidated by Ecker et al. (2012), we have based our understanding of their working model of memory reconsolidation related to their transformative memory reconsolidation principles. We have found that when selectively tuned in and a binaural sound is correctly applied to maladaptive cortical circuitry, disruption of memory reconsolidation occurs that permits the brain to return to homeostatic norms. We believe that our contribution to a working model of brain plasticity allows the fine-tuning of new protocols for the treatment of PTSD and other treatment-resistant conditions (Lindenfeld & Rozelle,

2015). Added to the use of a binaural sound protocol is the conceptual model of neuronal networks and how emotionally related circuits alter the effects of trauma on the memory reconsolidation process (Falconer et al., 2008).

Other therapies are being applied based on the same model, such as the use of Propranolol for disrupting memory reconsolidation of PTSD symptoms (Giustino, Fitzgerald, & Maren, 2016). An example of a verbally based therapy using transformative principles is Rapid Resolution Therapy (RRT; Harnes, 2010). Within the RRT approach, the therapist seeks to emotionally elicit a traumatic experience while concurrently creating a positive experience, thereby resulting in a mismatch phenomenon.

Changes produced through memory reconsolidation interventions are long-lasting as noted by Monfils, Cowansage, Klann, and LeDoux (2009). Additionally, Beckers and Kindt (2017) noted that "... a recurring theme will be how further basic research and theoretical progress regarding the nature of emotional memory and its modification will inform the future of memory reconsolidation interference as an effective intervention for emotional disorders" (p. 2).

We find that RESET Therapy accomplishes the above-stated objectives without the necessity of drug usage with its accompanying adverse side effects (American Addiction Centers, 2019). Also, because the intervention is nonverbal, it protects the practitioner from exposure to raw limbic system emotional material, thereby protecting the therapist from the secondary effects of PTSD (Penix, Kim, Wilk, & Adler, 2019).

Our review of the use of binaural sound or the use of any sound for the remediation of PTSD symptomology has found a sparsity of positive results. Alternatively, the literature is replete with instances of sound used primarily as a noxious stimulus (Golkar, Tjaden, & Kindt, 2017; Schroyens, Beckers, & Kindt, 2017). We have found that there exists a functional neuroanatomical basis for the proposed therapeutic process (Miller & Lindenfeld, 2017).

In contrast, rather extensive recent research efforts are related to varied applications of binaural sound such as allocating attention (Colzato, Barone, Sellaro, & Hommel, 2017); enhancing long-term memory (Garcia-Argibay, Santed, & Reales, 2017); synchronization of working memory (Beauchene, Abaid, Moran, Diana, & Leonessa, 2017); assisting older patients with depression (Sung et al., 2017); patients undergoing general anesthesia (Flanagan & Kerin, 2017); Parkinson's Disease (Gálvez, Recuero, Canuet, & Del-Pozo, 2017); relapse prevention (Sewak & Spielholz, 2018); and reducing preoperative anxiety in dentistry (Isik, Esen, Büyükerkmen, Kilinç, & Menziletoglu, 2017).

Therapeutic Strategies

The current use of counteractive procedures in the treatment of PTSD includes extinction (Helpman et al., 2016) and cognitive-behavioral strategies (Monson & Shnaider, 2014). These procedures are designed to prevent symptom arousal by arranging for a more desired state of mind to emerge as an outcome; similar interventions would include the teaching of relaxation skills to counteract anxiety (Dahlgaard et al., 2019). Another therapeutic strategy would include the cultivation of positive rational thoughts to counter automatic depressive or anxious ones (Agbu, 2015).

Extinction Methods

Extinction methods are suppressive (Dunsmoor, Niv, Daw, & Phelps, 2015). They compete against unwanted learning by building up preferred learning and reactions intended to override and suppress the adverse response (Gieselmann et al., 2019). Furthermore, extinction is imperfect, and while some emotional responses may weaken and discontinue, other less desirable emotions are evoked or triggered due to unforeseen circumstances (Pfitzer, 2008). The suggestion here is that deletion or elimination of the original implicit memory did not occur as intended. Maren and Holmes (2016) and Widholm (2010) found that extinction methods have a very high relapse rate in the treatment of addiction indicating that, while the neuronal circuits may become dormant for new learning, they retain their sensitized or potentiated state; once reactivated, old urges (memories) emerge with their former strength.

Biofeedback and Neurofeedback-based Interventions for PTSD

Biofeedback and neurofeedback are client-centered and empirical data-driven approaches. Feedback informs and empowers the client. Transparency of the procedures allows skeptical patients to observe for themselves what is happening in their brain and body during a session, and to evaluate the trustworthiness of the process and the practitioner quickly.

Biofeedback researchers established an association between chronic sympathetic hyperarousal from posttraumatic stress and cardiovascular disease risk (Buckley & Kaloupek, 2001; Kibler, 2009), especially among veterans diagnosed with PTSD (Orr et al., 2000; Orr, Meyerhoff, Edwards, & Pitman, 1998). Persistently elevated heart rate and attenuated heart rate variability in response to chronic and situational stress was predictive of postdeployment PTSD (Nagpal, Gleichauf, & Ginsberg, 2013; Chalmers, Quintana, Abbott, & Kemp, 2014; Dennis et al., 2016; Pyne et al., 2016).

Such alarming findings prompted biofeedback scientists and practitioners to begin using heart rate variability coherence training among traumatized veterans to help them learn balancing of sympathetic and parasympathetic activity (Lake, 2015; Lande, Williams, Francis, Gragnani, & Morin, 2010; Tan, Dao, Farmer, Sutherland, & Gervitz, 2011; Tan, Wang, & Ginsberg, 2013; Wahbeh & Oken, 2013; White et al., 2017). Breathing retraining techniques were incorporated as a treatment adjunct to aid in the reduction of PTSD symptoms (Polak, Witteveen, Denys, & Olff, 2015).

Despite the very promising findings of various individual studies, biofeedback was not recommended for management of posttraumatic stress in the VA or Department of Defense (DOD; Psychological Health Center of Excellence, 2018), having failed to meet the "burden of evidence" required by most VA/DOD publications. A seminal study published by Peniston and Kulkosky (1989) demonstrated that a combination of biofeedback and neurofeedback gives veterans a substantially better outcome than treatment-as-usual in a residential addiction treatment setting. Working with veterans at a VA facility in Colorado, Peniston and Kulkosky used techniques developed by Elmer Greene (Greene & Greene, 1977) to access luminal states of awareness. In addition to treatment-as-usual such as 12-step programs, individual psychotherapy, medication management, and milieu therapy, an experimental group received biofeedback training which included hand-warming, autogenic exercises, and progressive muscle relaxation to lower autonomic arousal. They then underwent 30 consecutive daily individual sessions of alpha-theta neurofeedback where reinforcing amplitude increases in alpha and theta and inhibiting subconscious states where memories and associated emotions are stored, bringing them to conscious awareness. The results were remarkable. Compared with treatment-as-usual controls, veterans in the experimental condition had abstinence rates as high as 70%, and these results were maintained at a follow-up.

Peniston and Kulkosky (1991) turned their attention to Vietnam veterans with combat PTSD. They recruited 29 Vietnam veterans suffering from chronic war-related PTSD, including frequent anxiety-evoking nightmares and flashbacks. In comparison to 14 control group participants who received psychotropic medications including tricyclic antidepressants, antipsychotics, and anxiolytics, the 15 experimental group participants received biofeedback training to reduce sympathetic arousal, followed by 30 sessions of alpha-theta neurofeedback, each session lasting 30 min. Some veterans experienced strong emotional reactions during the alpha-theta sessions, supported and encouraged through the session by Dr. Kulkosky. By the end of treatment, outcome measures showed significant symptom reduction, consistent with patient reports. At a 30-month follow-up, all the control participants who received medication treatment alone had experienced a recurrence of PTSD symptoms, whereas only 20% (3 of 15) of the experimental participants reported a recurrence of PTSD symptoms.

The alpha-theta protocol was tested in dually diagnosed veterans having PTS with addiction by Peniston, Marrinan, Deming, and Kulkosky (1993). Peniston et al. (1993) reported that alpha-theta brainwave training significantly reduced anxiety-provoking nightmares, flashbacks, cravings, and urges. Only 20% of veterans (4 of 20) who underwent the alpha-theta protocol reported relapse of alcohol or substance use. Many participants reported that traumatic recollections no longer elicited anxiety. The alpha-theta protocol has since been well replicated in several residential addictions' programs throughout North America (Moore et al., 2000).

In the millennium, researchers continue to replicate Peniston and Kulkosky's basic findings with slight modifications in methodology in veteran and military samples. As part of a military-related stress reduction program, Putnam (2000) showed a relaxation induction video followed by one-channel alpha and low beta amplitude enhancement training at site Pz using visual feedback in a sample of 77 Army reservists. He found that increases in alpha amplitude eyes-open training was associated with reports of increases in energy level, positive mood, reduced arousal, and, in some cases, reduced vigilance.

In a doctoral dissertation, Smith (2008) studied 10 military veterans with PTSD-induced depression and decreased levels of attention. After 30 sessions of neurofeedback alpha-theta training, all participants showed a significant reduction in PTSD and depression symptoms and an increase in attention levels. In the aftermath of Operations Iraqi Freedom and Enduring Freedom, mental health researchers in the middle east have replicated the Alpha-Theta protocol with traumatized soldiers (Noohi, Miraghaie, Arabi, & Nooripour, 2017; Rastegar, Dolatshahi, & Dogahe, 2016).

Using low-resolution electromagnetic tomography (LORETA) *z*-score training, Foster and Thatcher (2015) reported on the results of the first 16 veterans from an ongoing study of combat veterans with comorbid PTSD and mTBI. Training multiple neural networks implicated in PTS, they reported normalization of the affected networks together with rapid resolution of PTSD symptoms, using protocols customized to the individual aspects and needs of the veteran.

These studies suggest that, regardless of the specific method used, positive outcomes in PTSD are likely using a combination of biofeedback and neurofeedback—each approach complementing the other. The primary limitations of biofeedback and neurofeedback are cost and time. The cost of training, equipment, staff, and malpractice insurance can be daunting. Most insurance plans do not yet recognize neurofeedback as a cost-effective intervention; most patients must pay out of pocket for services. Despite the invaluable information that they provide, qEEG brain maps are relatively expensive, and it may not be practical to use qEEG or neurofeedback as a first-tier treatment approach.

Even when delivered by an experienced and highly skilled practitioner, a minimum of 10 to 20 neurofeedback sessions are necessary before the client consistently experiences positive changes. All neurofeedback practitioners have to deal with the frustrating reality of no-shows and dropouts. The practitioner is under a great deal of pressure to deliver results rapidly, lest impatient clients give up prematurely because progress is taking too long and perceived as too costly. The problem is further magnified in the case of the veteran with PTSD or combined PTSD/TBI with low frustration tolerance, impulsivity, avoidance tendencies, and a high threshold for developing trust.

Rapid remediation of combat-incurred PTSD re-engages the prefrontal cortex the center for reasoning, planning, and understanding and establishes the essential trust that motivates the veteran to continue in their biofeedback and neurofeedback treatments. Suffice it to say that following remediation of PTSD symptoms, the veteran's brain still needs a rebalancing of normal asymmetry and stabilization/regulation of thalamocortical, limbic, and brainstem circuits. The veteran's autonomic nervous system must be rebalanced in terms of healthy levels of sympathetic versus parasympathetic arousal. He or she needs to learn readily-usable strategies for managing bodily reactions to stress and sustaining therapeutic gains. Integration of the remediated traumatic memory into one's personal identity to derive new meaning allows a new sense of purpose and future, as opposed to being stuck in the moment. Biofeedback and neurofeedback have essential roles to play in the long-term therapeutic process.

BAUD Biofeedback Device

In line with the above objective, we have adopted the Bio-Acoustical Utilization Device (BAUD) as the vehicle through which to provide the binaural sound effect (Lawlis, 2006). The BAUD is a handheld, battery-powered device and was FDA approved as a class 2 accessory medical device (Biofeedback device 21 CFR 882.5050) in 2006. The FDA approval is for use in relaxation and stress reduction. The BAUD provides sound through a set of headphones. It has independent volume controls for the left and right ears. It also has a tone (frequency) knob to adjust the sound frequency as well as a "disrupter" adjustment (offset) knob which produces a sound in the left ear that is slightly different than that provided in the right ear. The frequency knob ranges from 30 to 360 Hz (square wave), heard initially in both ears but later in the right ear. The disruptor knob adds an offset ranging from 0 to 20 Hz, heard in the left ear (see Figure 1).

Figure 1. BAUD and varied setting dials.

BAUD therapy based upon Lawlis's basic principles has been available worldwide, and the BAUD protocol was founded on his perception that:

> The underlying acoustical physics entrain the general EEG ranges by creating a third tone from the interference ratios between the two frequencies. It is thus purported to influence brain functioning at the unconscious level and perceived emotional functioning at the conscious level (Lawlis, 2010, p. 3).

"We now know that PTSD is often the result of a physical injury to the brain" (Lawlis, 2011, p. 13–14).

Advances in neuroscience have provided greater clarity related to entrainment and brain damage involvement within the PTSD context. RESET Therapy has integrated these updated findings, consequently leading to our understanding that RESET Therapy is a transformative rather than an entrainment process. Furthermore, while injury to the brain may be concurrent to PTSD among our returning veterans, it is no longer seen as being among the causative factors. Instead, TBI and PTSD are recognized as "signature wounds of war" among those deployed to Afghanistan and Iraq (Tanielian & Jaycox, 2008). Thus, we have come to perceive of RESET Therapy as a further modification and scientifically-based advancement of Lawlis's foundational work with the BAUD.

RESET Versus BAUD

RESET Therapy is the treatment process utilizing the BAUD which interferes with targeted trauma memories. Through the specialized use of binaural sound, the intervention blocks the restoration of trauma material after it is selectively lit up in the emotional part of the brain through the patient's intentional focus. We use the term "target" in RESET Therapy and suggest that we are going to turn off the "switch" in the brain that produces the PTSD symptoms (Lindenfeld & Rozelle, 2015).

Specifics that differentiate RESET from BAUD Therapy include

> (a) Patient preparation based on information related to memory consolidation/reconsolidation factors. The patient is taught that the memory aspect of trauma is the primary problem that perpetuates PTSD, not the traumatic incident itself. Significant recent changes in our understanding of how long-term memory is established and maintained are shared with the treatment participant;
>
> (b) Patient's sole focus directed towards activating sensory aspects of traumatic experiences. Coaching is next provided in the identification and targeting of physiological sensations as a primer to the activation of critical emotional circuits;
>
> (c) Targeting varied sensitized brain circuitry beyond trauma circuitry for remediation purposes such as that of unresolved grief;
>
> (d) Informing the participant of a 5-hour vulnerability period following the resetting of cortical circuitry. Therapeutically, the veteran is advised to maintain a stress-reduced environment for the stated period. Through following the prescribed procedure, we accomplish Joseph LeDoux's objective of reshaping memory but without the use of drugs or invasive procedures (Bergstein, 2014).

Brain Map EEG Alterations. We find that when neuronal RESET occurs, survival reactions to trauma based on instinct reassume a secondary position within the context of earlier experienced traumatic events. Support for the "shifting" perspective is present in a recent study of acute stress-related disorders wherein the authors found selective enhancement of threatening variables as well as an apparent decoupling between the dorsolateral prefrontal cortex and the amygdala (Luo et al., 2018). Further support for the position is present in a unique 2017 study that investigated EEG brain map alterations in arousal and reactivity in combat-veterans with PTSD. Bangel, Buschbach, Smit, Mazaheri, and Olff (2017) hypothesized that PTSD-afflicted individuals appear to be highly sensitive to subconscious auditory changes in sound patterns. The authors suggest that PTSD-involved individuals are susceptible due to primary survival mechanisms that place executive functioning in an inferior secondary position.

The above finding supports our perspective of sensitivity to sound and frequency variables that appear to be related to trauma effects that produce a "bottom-up" shift in attention. Some perceive the reaction as being a maladaptive alteration in the neuronal network, which in theory we support. We also view such a shift as being related to survival purposes rather than higher thinking processes (Schmidt, Belopolsky, & Theeuwes, 2015).

Reptilian Brain. Rosenthal (2015) refers to the Triune Brain model, introduced by neuroscientist Paul D. MacLean, explaining the primitive aspect of the reptilian brain stem which assumes control in traumatic experience(s).

> The reptilian brain takes control, shifting the body into reactive mode. Shutting down all non-essential body and mind processes, the brain stem orchestrates survival mode. During this time the sympathetic nervous system increases stress hormones and prepares the body to fight, flee or freeze…for those 20 percent of trauma survivors who go on to develop symptoms of post-traumatic stress disorder (PTSD)—an unmitigated experience of anxiety related to past trauma—the shift from reactive to responsive mode never occurs. Instead, the reptilian brain, primed to threat and supported by dysregulated activity in significant brain structures, holds the survivor in a constant reactive state (p. 2).

Methods

Our 54-year-old, three-times-married male, Special Forces veteran (MED) attained 32 years of active service as well as 84 months of combat-involved engagements. He agreed to participate in the case study regarding family violence issues to potentially assist other service members with similar difficulties. MED's primary objective was to alter the deteriorating family situation in which he was currently involved. He had previously been diagnosed with PTSD, social anxiety disorder, and depressive mood disorder. He was facing felony charges in a state judicial court due to intimate partner violence. Consequent to his legal matters, he was court-ordered to leave home with limited visits established between himself and his two young children. He was to avoid all contact with his wife. The events leading up to his consideration for participation in RESET Therapy included a suicidal near-miss as well as a family violence incident that in his mind was directly linked to his PTSD condition. To protect both his family as well as his identity, details related to these matters will remain protected.

Our investigation protocol was approved by the research ethics committee of The QuietMind Foundation of Pennsylvania which is registered with the U.S. Department of Health and Human Services (DHHS), Office for Human Research Protections (OHRP), IORG 0004684 and IRB 0005585. Following a diagnostic intake with the primary investigator (Lindenfeld), MED underwent the following sequence within the context of his evaluative and treatment process. He provided documentation indicating an honorable discharge from military service. Additionally, he was provided with a consent form for participation and acknowledged that while his identity would be protected, results emanating from his treatment would possibly be used in research articles.

The sequence of his participation for which results are provided included (a) psychometric assessments: Clinician-Administered PTSD Scale for DSM-5 (CAPS-5) and Personal Assessment of Intimacy in Relationship Scale (PAIR); (b) brain mapping in the form of surface qEEG and LORETA anaylsis; (c) four RESET Therapy treatment sessions; (d) post-treatment reassessment (repeat CAPS-5 and PAIR; repeat qEEG) and debriefing. The present study hypothesis is straightforward. Within four treatment sessions of RESET Therapy, MED will demonstrate (1) significant reduction of PTSD symptoms as indicated in his CAPS-5 scores, and (2) qEEG changes that reflect improvement toward normalization.

Psychometric Assessments

Clinician-administered PTSD Scale for DSM-5 (CAPS-5). The CAPS-5 is the gold standard in PTSD assessment used by clinicians and clinical researchers at both the VA and DOD who have a working knowledge of PTSD. The full interview takes 45 to 60 minutes to assess 20 DSM-5 PTSD symptoms. The CAPS-5 requires the identification of a single index trauma to serve as the basis for symptom inquiry. The selected trauma is also utilized within the treatment context to serve as the initial target for frequency and binaural sound offset setting. The questions in the scale target the onset and duration of symptoms, subjective distress, impact of symptoms on occupational and social and functioning, improvement in symptoms since a previous administration, overall response validity, and overall PTSD severity. For each symptom, standardized questions and probes are provided. Scores on the instrument are based on a possible total of 80 points (Weathers et al., 2013). Cutoff scores between 31 and 33 are considered to be optimal for the effective diagnosis of PTSD (Bovin et al., 2016). Scores are derived by combining the frequency and intensity of a particular item into a single severity rating. Each item in the scale is combined to represent intensity scores ranging from 0 (*Absent*) to 4 (*Extreme*). A severity score at 2 or above on a particular item suggests clinical significance.

Personal Assessment of Intimacy in Relationship Scale (PAIR). Schaefer and Olsen (1981) created the Personal Assessment of Intimacy Scale (PAIR). The primary focus of the scale is to describe the partner relationship regarding how each currently perceives it. Permission was sought from the

authors and approved for the use of the scale to determine pretreatment versus posttreatment changes in a specified individual related to intimacy issues.

The five types of intimacy utilized in the above scales are (a) Emotional Intimacy, experiencing a closeness of feeling with others; (b) Social Intimacy, having common trends and similarities in social networks; (c) Intellectual Intimacy, the experience of sharing ideas; (d) Sexual Intimacy, the experience of sharing general affection and/or sexual activity; and (e) Recreational Intimacy, the sharing experience of interest in hobbies such as mutual participation in sporting events. The PAIR instrument does not have cutoff scores, although average scores are expected to be around the mean. The higher the score on each variable, the more likely that a positive outcome on that variable will be more forthcoming (Schaefer & Olson, 1981).

Brain Mapping

Surface qEEG. A qEEG is a painless and relatively noninvasive experience. A cap with 19 electrodes is placed on the scalp with two additional linked references placed on the earlobes. A conductive paste is inserted into 19 openings in the cap to ensure a proper connection with the scalp. Each electrode records brain electrical activity in a different region of the scalp, which is a good approximation of activity in the underlying neocortex. The patient is asked to follow standard procedures such as to sit quietly and still, with eyes closed or open, and to reduce eye movement. For RESET cases, the patient may be asked to imagine an emotionally disturbing triggering event during the recording.

The results of the spectral analysis are displayed in color-coded topographic maps. The reported qEEG was based upon at least 60 seconds of edited raw EEG data for each testing condition. Analysis of edited raw EEG data is matched for age, gender, and handedness (Kaiser, 2006). qEEG brain electrical activity was recorded with a 19-channel Electro-Cap (Electro-Cap International, Inc., Eaton, OH), using the 10-20 International Electrode Placement System referenced to linked ears, on a Brainmaster Discovery 24E amplifier (BrainMaster Technologies, Inc., Bedford, OH) with the DC Offset reduced to less than 30 millivolts. The sampling rate was 256 samples per second. No activation procedures were used. The raw recording was digitized for data storage and analysis and later manually edited to reduce artifact (eye movement, EMG, body movement, etc.) and subjected to quantitative spectral analysis.

For purposes of analysis, the raw data were imported into NeuroGuide Deluxe software (Applied Neuroscience, Inc., Largo, FL). Signal amplification and processing were accomplished with an eyes-closed resting EEG (default state) recorded for 5 min as a pretreatment baseline. Next, with eyes closed, the veteran was asked to focus attention upon the selected combat-related trauma utilized as a target for the CAPS-5 interview. The recommended state replicates the “activate the target” component of the RESET procedure. Hence, an eyes-closed baseline (default state) and an eyes-closed trigger condition (trauma network activation) were obtained for utilization as a pretreatment baseline.

Low-Resolution Brain Electromagnetic Tomography (LORETA). Pascual-Marqui et al. (2011) published reliable research support about a new mathematically based method of analyzing electric neuronal activity (EEG) distributions. Low-resolution brain electromagnetic tomography (LORETA) uses a mathematical inverse solution to determine the relative activity of various regions in the brain using surface electrodes (Thatcher, North, & Biver, 2005). In contrast to surface qEEG, the LORETA method estimates current source densities at deeper cortical levels using 19 channels of EEG data. Advanced source-correlation software is utilized permitting deep brain structures to become visible in the form of a 3D display (Thatcher, 2011). The validation of the procedure permits functional localization, but, more importantly, it provides the methodology to assess dynamic functional connectivity.

Todder et al. (2012) sought to identify and differentiate changes in brain structure between those with PTSD from those without the condition. Statistically significant findings in the theta band range (4–7 Hz) thought to represent the activity of the limbic system was noted. Specific regions of the brain identified among the PTSD group as compared to the non-PTSD group included the right and left frontal lobes regions as well as the right temporal lobe.

Cannon et al. (2012) ascertained the validity and reliability of the qEEG over 30 days. Results were good to very good with comparative LORETA calculations at 1 Hz. Across time reveal robust similarity. Data analysis found good to excellent reproducibility of qEEG measures and LORETA. Cannon, Lubar, Thornton, Wilson, and Congeto

(2004) utilized LORETA to explore the effects of anger in the limbic region of the brain as well as to identify the primary EEG frequencies produced by emotional activation. The participants were asked to elicit memories of anger and to maintain it during the measurement period. Significant differences between the baseline and anger conditions in both frontal and limbic regions supported the perspective that effective memory recollection could be captured for comparative purposes between varied PTSD and non-PTSD groups. An interesting difference observed was that in some cases, the amygdala and uncinate gyrus was activated by beta frequencies (12–32 Hz). The identified hemispheric asymmetries produced by the above research lend support related to the apparent lateralization of hemispheric activity during to affective reactivity.

RESET Therapy Protocol

The RESET Therapy protocol is copyright-protected and, as stated, utilizes the commercially available BAUD instrument for producing binaural beats. Those practitioners who perform RESET must be appropriately trained. Although the protocol is described in sufficient detail to allow independent replication, there are nuances as well as caveats that can be learned only by hands-on instruction, observation, and practicum. That training is currently available through the RESET Therapy Professional Institute, LLC.

Guidelines. Before starting each session of RESET:

(1) Dispense with the words *Think* and *Feel*. Remove them from your vocabulary. These words are evaluative and will engage the left hemisphere. Our goal is, as much as possible, to minimize the involvement of the left hemisphere, and shift into right-brain experiential processing (sensory focus on pictures, sounds, odors, tastes, and bodily sensations). The right brain can respond with single words (e.g., Yes, No) without much conscious evaluation.

(2) Use the words *You* and *I*. Dispense with the words *We* or *Us*.

(3) Use the patient's own words (descriptions of sensations) rather than your words. The meaning of words can be easily misconstrued, so it is best to reiterate their words (e.g. the flicker/tightness in your chest, the lump in your throat, etc.)

(4) Closely observe the patient's behavior for signs of shifts in arousal, both during the tuning-in phases and during the actual exposure trials.

(5) Keep talking to a minimum.

(6) When first working with a new patient, choose a memory with a Subjective Unit of Distress Scale (SUDS; Kaplan, Smith, & Coons, 1995) rating of about a 6 or 7, based on a 10-point range (10 most intense) rather than a higher SUDS memory.

(7) Before doing your first RESET session, get familiar with the technique of ideomotor signaling. Ideomotor signaling was effectively used in medical hypnosis by LeCron (1964). It is a form of nonverbal communication, akin to nodding the head *Yes*, turning the head from side to side *No*, or shrugging the shoulders with *I don't know*. Patients are taught how to allow the subconscious mind to signal a response, while the patient is simultaneously and intensely focusing attention upon his or her subjective sensory/bodily experiencing and the sound of the tone.

(8) Phase 1 of the RESET assessment phase involves having the patient activate or "light up the target" from the present adult perspective (looking back at the disturbing memory). We can anticipate that the patient will start in a relaxed state with eyes closed (alpha) but will rapidly shift to a state of negative arousal once the bodily sensations resonate with the BAUD frequency tone being adjusted by the therapist.

(9) Phase 2 of the RESET assessment phase invites the patient's subconscious mind to become involved by engaging a child-like perspective. The dominant EEG rhythm in children is theta, which is associated with daydreaming, fantasy, and creativity. Theta is also the frequency in the adult where subconscious memory and emotion can be most readily accessed. We seek to engage subcortical areas as well as the right cerebral hemisphere, to process sensory and perceptual experience associated with the memory of the traumatic event(s). The subconscious mind is very literal and concrete, child-like in many aspects. When we fine-tune the BAUD settings while the client is accessing an unembellished state of awareness, we obtain the best results.

(10) If the patient is having difficulty zeroing in a key memory, ask him or her to remember back to a time when things were "normal" or trouble free. Then ask at what point things began to change (a specific stressor or series of stressors). Hence, ask the patient to go back chronologically through the emergence of the trauma. If the patient is dissociated (has difficulty identifying bodily sensations), use a lower intensity target. If dissociative, the therapist may have to do a couple of Eye Movement Desensitization and Reprocessing (EMDR) sessions first.

RESET Therapy with MED

Clarification was provided in detail to MED that it was necessary to light up the target in the emotional region (limbic system) of the brain. He was informed that the sensory aspects of a selected trauma experience need to be activated rather than merely thinking about it. The veteran was told that the best way to create the experience was to imagine being in the experience fully and entirely by bringing in all the involved senses and thoughts that were present at the time of the experience, including sight, sound, smell, and skin sensation.

An explanation was provided about the SUDS, utilized in the study ranged from a level of 0 to 10, to determine the subjective level of intensity of the targeted trauma. MED identified an intensity score at the most exhaustive point during the period of imagery and then again following the treatment intervention. The therapist observed and monitored physiological reactivity, including facial expression, respiration rate, and muscle tension.

Treatment Summary. MED completed his treatment involvement following three RESET Therapy sessions perceiving that all his trauma-related symptoms remediated. He was consequently able to provide clarity related to many associated triggers that had considerably weakened his ability to contain his rage and anger. He described these triggers as follows:

> [The first event was when] I conducted a battlefield assessment for what was known as the "Highway of Death"—Highway 80 between Kuwait and Iraq. During that event, I witnessed burnt and charred bodies in different states of decay that left a lasting negative impression on me. I lost my faith in religion, and, quite frankly, I lost a lot of faith in mankind.
>
> The second event occurred on the job in Iraq in 2007 where we did a "sensitive site exploitation" related to an attack by around 500 insurgents on a special forces team where an estimated 350 to 400 attackers were killed. The amount of destruction put on those individuals was rather grotesque. Large caliber Gatlin Gun bullets and explosive bombs/missiles were used that pretty much ripped those guys apart. The two events were similar. The only difference was that the bodies were much fresher than the ones I'd seen earlier.
>
> The third event was the loss of a good friend during the invasion of Afghanistan. I went through the Special Forces selection with him, including the Forces qualification course. We went to the same Special Forces group and maintained a close relationship. His loss hit me pretty hard, and it was one of those things that stuck with me. Not being able to see him again, hear him and wishing I could be with him. The level of friendship between us was very close. It was a significant loss.

In his first 5-min trial RESET Therapy treatment, MED recalled that when the sound frequency reached a certain level:

> My body tensed up to a point where it felt like a muscle spasm. One-third of the way through it, I had an internal dialogue—stop trying to control everything. I experienced a pulsing from inside to the back of my head and then tingling through the rest of my body. My right leg jumped a couple of times. At first, I rated the level at a 6/7 on a 10-point scale. After the 5-min trial, it was at a 0. I can't bring it up right now (MED, personal communication, March 15, 2018).

Before his second treatment, MED shared that he usually tries to avoid trigger situations:

> I was curious about how the treatment took, so I tested it at home with stuff from Desert Storm and Iraq. I imagined seeing dead guys. Also, the smell of barbeque would trigger me. I couldn't put myself into it. My sleep was different because I got a good and deep rest. A court veteran employee who also went through the program testified, and the judge reduced my charges to a misdemeanor. I was also able to move back into the home because my wife testified that I was no longer a danger to her. I'm now back in the house with my wife and kids

(MED, personal communication, March 27, 2018).

At his third and final treatment visit, MED reported that his wife was no longer drinking, and he was feeling great. He was told to focus on the loss of his close friend in a treatment tweak that I have called, "talking to your dead buddies(s)." He reported the following:

> When Doc asked me to be with my dead buddies, in my mind, I thought, "oh great, I'm going to be a seance kind of thing." I thought, "you know what—I'll try anything at this point." It turned into a unique experience. I started in the aftermath of the event of his loss. I went into sadness at what it meant, but then transitioned into a conversation with my buddy. He's funny, and he laughed about his death. If he could laugh about his death, then I shouldn't be so sad. He told me he's in a good place. I hugged him. Seeing his face again, I could feel happy tears on my face. I let go of a lot of suppressed emotion. I don't feel I have to lock everything in anymore because I've released the poison. I'm now at a 0 on the skepticism scale.
>
> By the time we finished the third treatment, I had decided that Doc George was on to something. There's no question that my life has finally changed, all for the better. P.S. I completed my homework assignment with flying colors by watching "Twelve Strong," a film about Special Forces from my time. I actually enjoyed it! (MED, personal communication, April 16, 2018).

Results

CAPS-5 Results

MED's pretreatment CAPS-5 score of 58, as seen in Figure 2, was well within the range expected for those who are diagnosed with PTSD. In contrast, his posttreatment CAPS-5 scores dropped significantly to 5 following three 20-min RESET Therapy treatments. Following his brief treatment, he no longer met the criteria for the PTSD diagnosis. We may thus assume that his trauma-initiated behavior has reverted (remediated) to a homeostatic level permitting a full range of effective expression as compared to a prior restricted range based primarily on survival needs.

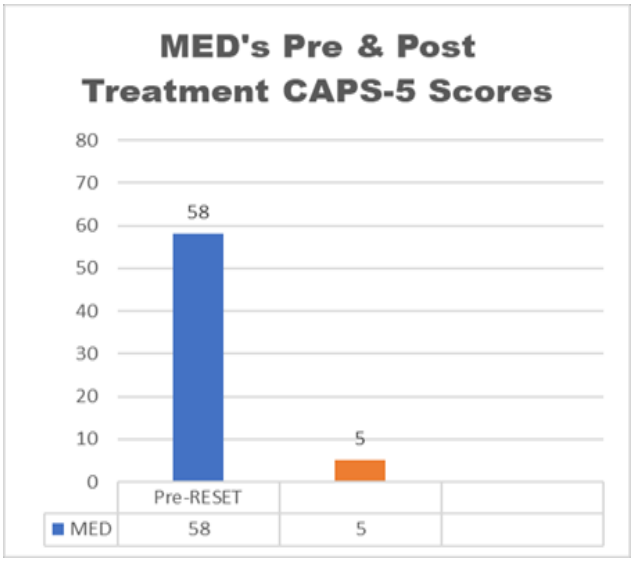

Figure 2. MED's Pre- and posttreatment CAPS-5 scores. The blue bar represents MED's pretreatment score, while the orange bar is the posttreatment status perspective.

PAIR Results

MED's PAIR results, as noted in Figure 3, reveal a significant shift in relationship interest and participation, with higher posttreatment scores relative to pretreatment scores, on all measured variables. By far, the most dramatic change is evident on the Sexual variable with a pretreatment score of 20 changing to a posttreatment score of 92. His transformative changes across many measured variables are supportive of his verbal report of his change in the ability to express positive emotions

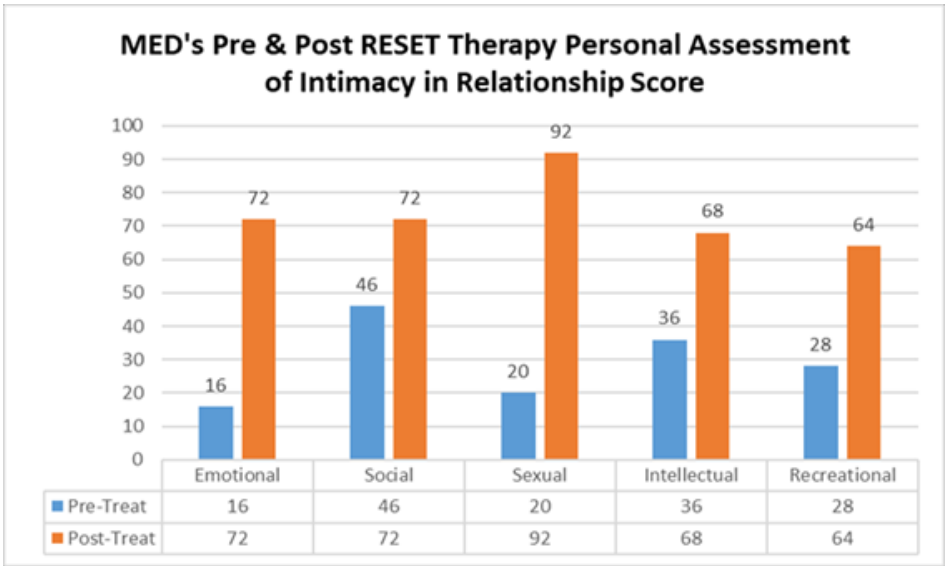

Figure 3. MED's Pre-& Post Personal Assessment of Intimacy in Relationship Score. The blue bars represent pre-treatment, while the orange bars are post-treatment scores.

Surface qEEG Results

Resting Baseline. As displayed in Figures 4 through 7, the *z*-score values for the absolute and relative power are represented by a color palette. The green colors represents ±1.0 *z*-scores and corresponds to the middle 68% of the observed population and considered within the average, *z*-score values greater than 1.0 (yellow/orange) or less than −1.0 (light blue) represent dysregulated brain frequencies, and *z*-score values greater than 3.0 (red) or less than −3.0 (dark blue) represent very dysregulated brain frequencies. For asymmetry, coherence, and phase measures, the *z*-score values are represented by red or blue lines, with red indicating above average (i.e., hyper) and blue below average (i.e., hypo) values.

MED's pretreatment eyes-closed resting baseline findings revealed absolute power measures with elevations in delta (1–4 Hz) and theta (4–8 Hz) as well as in the bilateral frontal, temporal, and parietal regions. Alpha, beta, and high beta showed left frontal focal dysregulation. Increased delta and theta levels suggested a state of under arousal while at rest.

There was global hypocoherence in all frequency bands, especially in delta, with a corresponding phase lag. These indicators represent a neuronal disconnect suggesting white matter damage. On pretesting, the left side showed the most substantial deviation from normal. The right side showed slowing, but the left overshadowed it. The left side of BA 9 is involved in attention to negative emotion and recall of negative experiences. Posttesting results revealed the left side to have normalized quite well, with the right-side slowing more visible. The finding of improved qEEG following three RESET Therapy sessions suggests that much of his pretreatment condition was likely due to residual trauma effects.

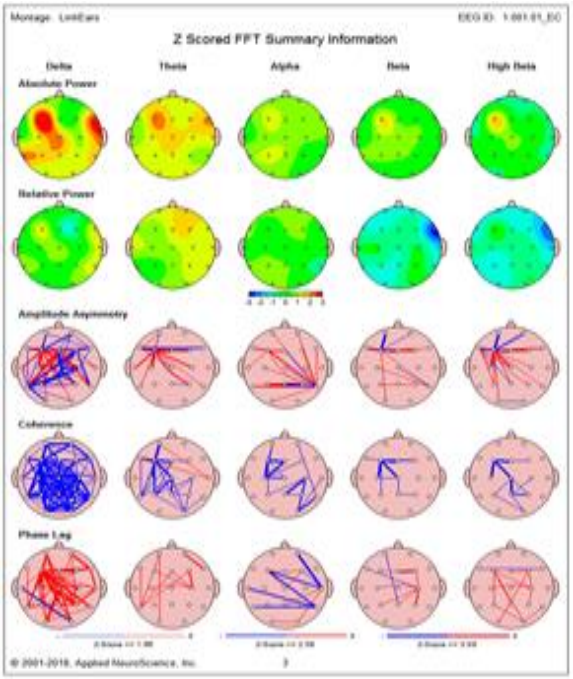

Figure 4. MED eyes-closed resting baseline pretreatment.

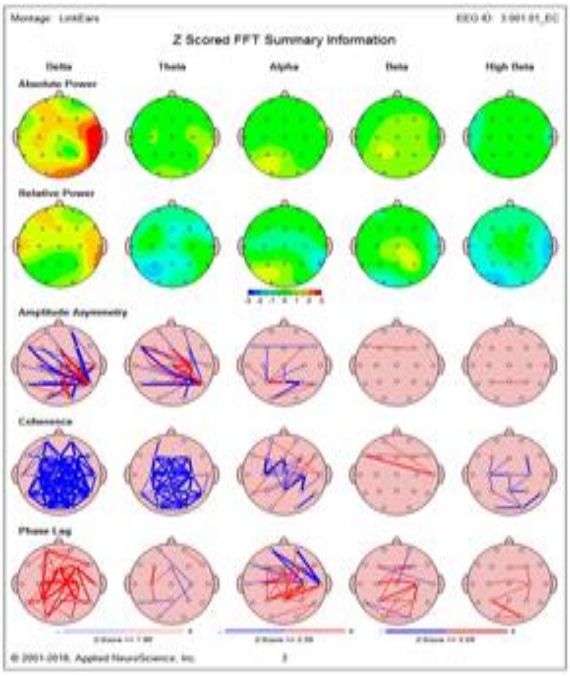

Figure 5. Eyes-closed resting baseline posttreatment.

Trauma Recall: A second 5-min pretreatment recording (Figure 6) was then repeated with MED focused on activating combat-related trauma experiences which presented primarily in the theta range (Dunkley et al., 2015). Elevations that are similar have been found to serve as a protective disengagement mechanism for the veteran. Simultaneously, bilateral frontal lobe dysregulation also was present in the theta pattern suggesting disinhibition of impulse control. Within the assigned task, he visually appeared to be more agitated with increased and shallow thoracic breathing, facial grimacing, and notable muscle tension.

Trauma activation posttreatment qEEG (Figure 7) revealed a significant reduction in the excess delta, and normalization of theta, alpha, beta, and high beta. Coherence and phase were slightly improved. He visually appeared to be more relaxed with normative breathing evidence. A previously unseen elevation (red area) is evidenced in the delta, right prefrontal region suggesting activation of a region of the brain that engages in impulse control as well as social involvement.

The initial enhancement of activation will likely subside over time as MED adjusts to his new persona. The effect will be further explored within the context of a one-year follow-up re-evaluation. It thus appears that his recorded qEEG changes reveal an atypical yet significant treatment effect. The posttreatment qEEG results provides tentative support to our position that the afflicted PTSD neuronal network has reverted to a pretrauma homeostatic setting.

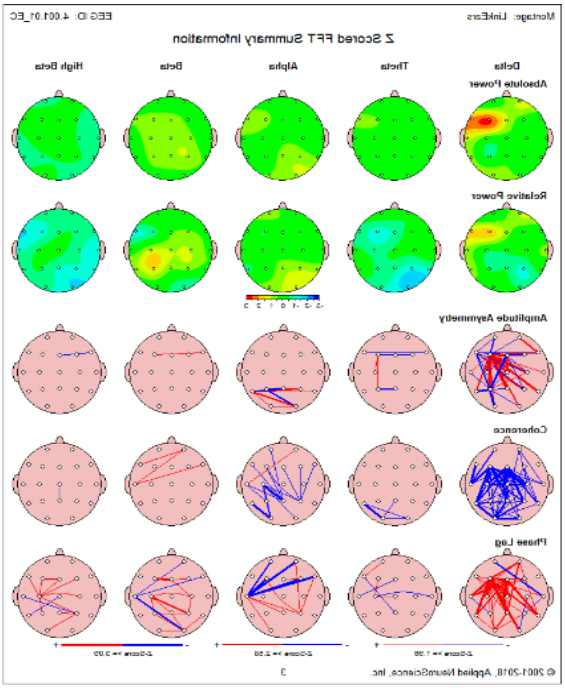

Figure 6. MED trauma recall pretreatment.

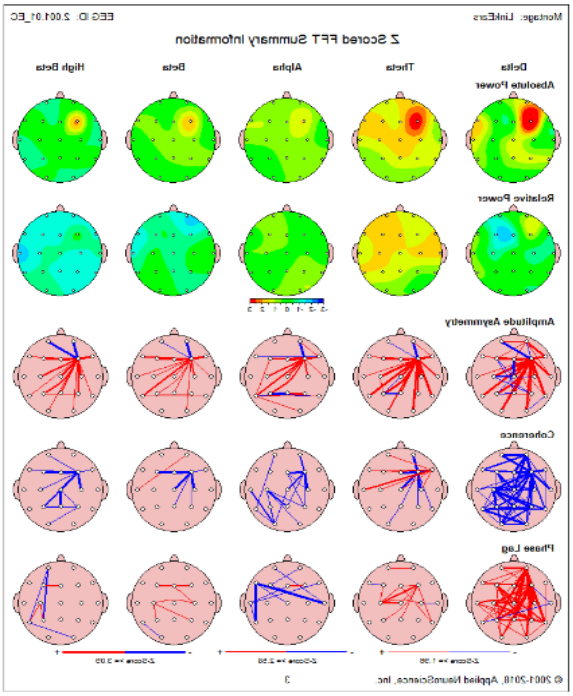

Figure 7. MED trauma recall posttreatment.

LORETA Results

As displayed in Figures 8 through 11, LORETA results depict the CSD localization findings and calculated cortical generators as found for the MRI co-registered Talairach coordinates. The red in the image indicates greater CSD amplitude at single hertz frequencies as contrasted to the normative sample.

MED's areas of greatest dysregulation appear to be Brodmann areas (BA); BA 9, 45, resting baseline and in the trigger condition, making it difficult to measure precise changes in these areas when triggered by emotional memories. Frontal lobe dysregulation would result in reduced executive functioning, poor impulse inhibition, depression, and poor sustainment of attention. BA 9 showed the greatest dysregulation in the trigger condition with excess 7 Hz and 28 Hz, showing the most significant deviations (Figures 8 and 9).

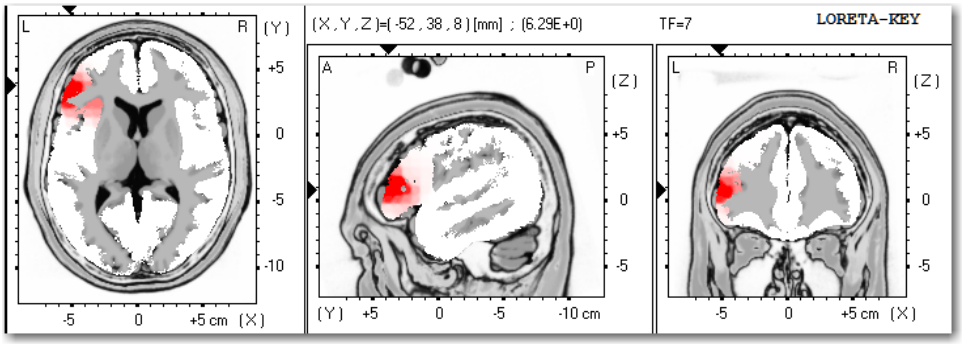

Figure 8. MED trauma recall pretreatment LORETA slice 7 Hz.

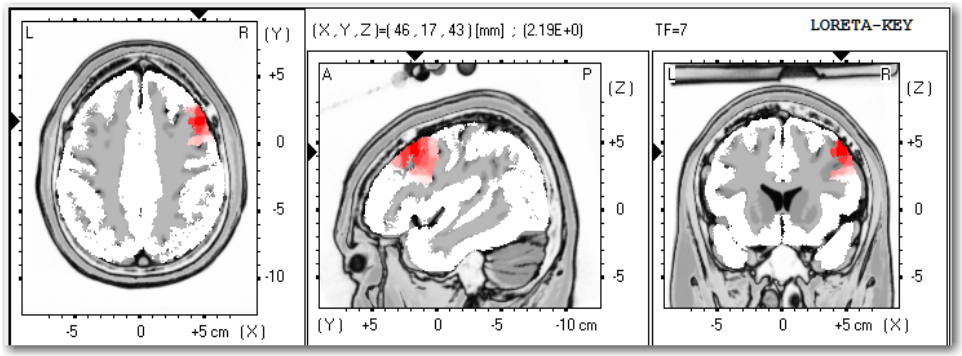

Figure 9. MED trauma recall pretreatment LORETA slice at 28 Hz.

In the posttreatment LORETA data, shown in Figure 10, continual 7-Hz effects appear present in similar areas including Brodmann area 9, the frontal lobe, and superior frontal gyrus.

In contrast, as evidenced in Figure 11, in the 28-Hz frequency, all indicators are normative. As noted earlier, the LORETA alteration occurred within the context of three RESET Therapy sessions.

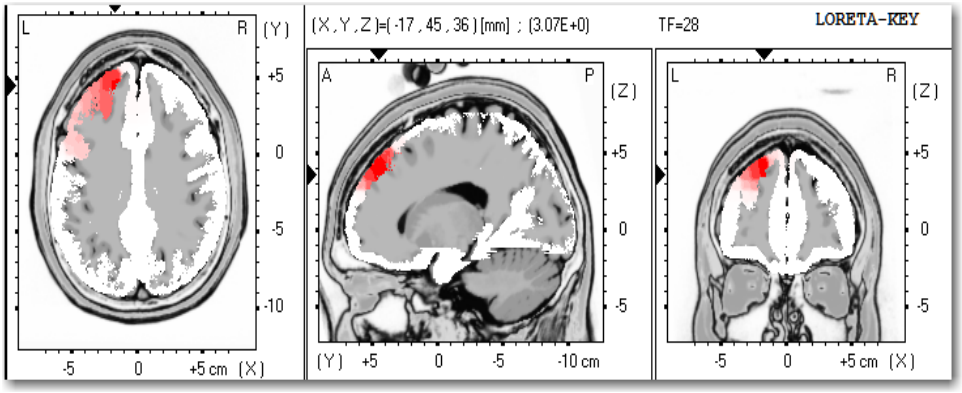

Figure 10. MED trauma recall posttreatment LORETA slice at 7 Hz.

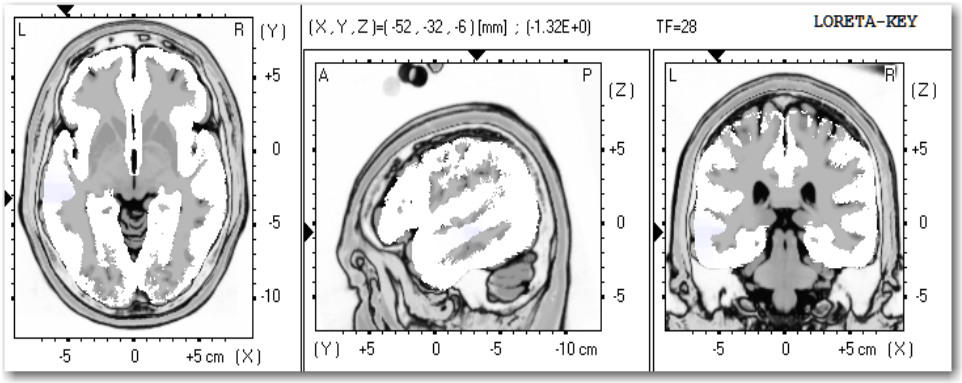

Figure 11. MED trauma recall posttreatment LORETA slice at 28 Hz.

Discussion

The experiential material later verbalized by the veteran and former Special Forces member certainly makes it understandable how he came to be previously diagnosed with PTSD. MED's pretreatment qEEG also helps us to recognize how he sought to control the rage that was locked within him by cortically disengaging from the unpleasantries that troubled him. Unfortunately, his survival process also served to disinhibit his impulse control abilities. Aside from how MED previously functioned, the changes forthcoming from his involvement with a brief intervention called RESET Therapy appears to have altered his life back to one of relative normality and sanity. We are striving to bring RESET Therapy to the next level—a thorough scientific research study, including a control group to obtain scientific support for this noninvasive, nonverbal transformative therapy.

We believe that the quest to finally end the ongoing nightmare of PTSD for active service members, veterans, first responders, and civilians who are chronically afflicted with the PTS condition is a worthy challenge to pursue. For our case study purpose, we did not solicit a detailed history before treatment other than to establish that there was significant combat-related PTSD that occurred through his military service. The specific content of the PTSD was irrelevant to the RESET Therapy approach as we have come to consider that for many, the nature of PTSD is that the person cannot fully recall details, tries to avoid remembering emotionally charged events, and has trouble fully articulating events.

Based upon previous fMRI and qEEG studies of PTSD, we hypothesized that brain mapping (surface qEEG & LORETA) would capture the anticipated changes forthcoming from the RESET Therapy intervention. For example, we postulated that the PTSD condition would include overactivation of the limbic system and underactivation of the medial frontal lobe and Broca's speech area.

We also hypothesized that there would be left and right temporal focal dysregulation present. Baseline measures matched our expectations regarding the neuronal pattern of PTSD hypotheses. We believe

that silently activating and consequently recalling trauma events assisted in triggering and, therefore, fully capturing the pretreatment brain map findings. It is important to note that pre- and posttreatment qEEGs were recorded with the same imaginal exposure to a specifically referenced combat-incurred trauma. Additionally, the data was recorded at the same time of day. As found in Figure 7 (trauma recall posttreatment), MED's brain map revealed significant normalization of the qEEG in the regions of interest related to PTSD.

Conclusion

Based on our preliminary findings, we find initial support for our hypothesis related to the systemic aspect of PTSD, apparent neuroinflammatory element, and memory component within the context of the reconsolidation process. For example, the rather dramatic changes seen on the qEEG results, including LORETA, as well as CAPS-5 and PAIR scores seem to substantiate that binaural sound serves as a key to unlock and alter the emotional aspects of long-term memory. Our results appear to be consistent with other transformation-based interventions. While our sample size is limited, the preliminary findings from our unique case study provides objective as well as subjective evidence of change in brain circuitry.

Indeed, sound has been a universal means to energize warriors to enter the fray of battle. Paradoxically, it may also prove to be the means to transform the warrior back to the socialized being that existed before his or her engagement in military life. Sound used for the healing of the soul and body has long existed in numerous cultures throughout time. Perhaps we will soon harness sound for resetting the aberrant circuitry in the brain created by the trauma exposure effect.

While our article is a single qEEG case study, we would hope to explore the RESET phenomenon further and to refine our procedures within the context of a formal research study. The RESET protocol shows initial promise for adding an alternative noninvasive intervention for the treatment of PTSD. Due to the rapidity of response to treatment, we perceive that increased numbers of afflicted individuals could be assisted in shorter periods than our current traditional therapies. Furthermore, due to its nonverbal aspect, it may extend the viability of the trauma therapist's efficiency by shielding the practitioner from the effects of secondary exposure.

From a broader perspective, the neuronal pattern of PTSD appears to be a valid prognostic indicator that captures the varied effects of the PTSD and trauma condition using surface qEEG, LORETA, and psychometric measurements such as the CAPS-5. Further inquiry into the impact that binaural sound may have on the DMN is also a ripe area for further investigation. Finally, utilization of the qEEG serves as validation of change within brain circuitry as well as providing further clarification of the possible presence of underlying traumatic brain injury.

While not intending to overstate our findings, we need to restate the critical need to find interventions that offer the potential to fully remediate those who continue to experience the residual and chronic effects of combat and trauma incurred through their service to our country. We as a country currently lose 20 veterans a day to suicide; it is critical that we do something better to serve those who served us. It is plausible that RESET therapy could be utilized to allow soldiers to recover from trauma-related PTSD and return to work and remain productive soldiers. Those who serve now, and who have served previously, deserve no less.

Limitations

The results of the provided three RESET Therapy sessions require a final reassessment after a year from the veteran's last treatment date. Tracking MED's ongoing judicial status will provide another way to determine if his interpersonal changes remain intact. Additionally, alcohol abuse within the family context appeared to be an aggravating factor further weakening the husband–wife bond. The above elements require ongoing monitoring over the designated one-year re-evaluation period.

Author Disclosure

Lindenfeld is the owner of the RESET Therapy Professional Institute, LLC, which is dedicated to the permanent healing of emotional trauma. No financial interest is involved in the sale of equipment (BAUD) utilized as the primary treatment vehicle. The RESET Therapy Professional Institute, LLC has affiliated with the Sarasota Community Foundation (501c3) to seek funding for research purposes. To date, all research efforts have been the results of pro bono contributions of professionals involved. Training leading to certification is in the planning stage for future offerings. None of the other coauthors have financial interests of any kind related to these research efforts.

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