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Investigation of vagal afferent functioning using the Heartbeat Event Related Potential

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ABSTRACT

Although there has been much support for HRV Biofeedback as an effective intervention for various disorders, there is a lack of comprehension of the underlying mechanisms. The predominant theories of increased vagal efferents and baroreflex gain are insufficient in explaining the frequent observations that HRV Biofeedback impacts changes in constructs beyond ANS mediation, such as emotion regulation, attentional control, and self-regulatory reserve. It has been suspected that vagal afferent functioning may be the underlying mechanism, but little research has explored this. Previously, researchers measured cortical evoked potentials contingent to the heart, or an indication of vagal afferent functioning (Schandry et al., 1986). Twenty-five participants were randomly stratified to HRV Biofeedback or EMG Biofeedback for four sessions. Repeated measures ANOVAs revealed that the HRV group exhibited statistically significantly increased baseline Heartbeat Event-Related Potentials (updated term for 'evoked potential') while the relaxation control group did not. The results of this study provide initial support to the premise that HRV Biofeedback stimulates changes in the vagal afferent pathway that are longer lasting than simply the short term effects of breathing.

1. Introduction

In recent years, there has been much evidence supporting Heart Rate Variability (HRV) Biofeedback as an effective and efficacious treatment for a wide range of disorders, including anxiety, gastrointestinal, cardiac disorders, and trauma (Brown and Gerbarg, 2005; Del Pozo et al., 2004; Gevirtz, 2013; McKee, 2008; Moravec, 2008; Nolan et al., 2008; Sowder et al., 2010; Swanson et al., 2009; Tan et al., 2011; Zucker et al., 2009). However, the mechanism by which HRV Biofeedback works and specifically which pathways are stimulated remains unclear (Lehrer et al., 2003; Weydert et al., 2003; Wheat and Larkin, 2010). Knowledge of the underlying mechanisms, effects of atrophied and stimulated pathways, and relationship to various disorders could assist with more accurate clinical diagnoses, inform tailoring more efficient and cost-effective treatment, and promote better understanding of many diseases.

1.1. Baroreceptor reflex

Frequently, increased vagal efferent functioning, or "vagal tone," is a mediator for HRV Biofeedback treatment related symptom reduction given typically observed improvements in HRV and baroreflex gain (Gevirtz, 2007; Lehrer et al., 2003; Porges, 2009; Sowder et al., 2010; Thayer, 2007; Thayer and Lane, 2000). Baroreflex refers to pressure sensors in the major arteries that communicate with the sinus node of the heart to influence and maintain blood pressure homeostasis through both vagal breaking during rising blood pressure epochs and sympathetic stimulation during blood pressure dips. The baroreflex elicits reciprocal autonomic responses with inverse relationships between afferent and efferent parasympathetic and sympathetic traffic. That is, when there is an increase in afferent baroreflex signals, efferent sympathetic nerve traffic decreases while efferent parasympathetic traffic increases. Furthermore, there is a known relationship between baroreflex activity and the brain, including the brainstem and certain neural structures of the limbic system, including the amygdala and hypothalamus (Henderson et al., 2004). Therefore, baroreceptor reflex activation could potentially serve as a cogent explanation for the frequently observed gains in limbic system mediated constructs such as emotion/affect regulation and self-regulatory reserve (defined as one's inherent and semi-pre-determined capacity to change and inhibit thoughts, emotions, impulses, or behaviors). In fact, the baroreflex response has been the only proposed underlying mechanism of HRV Biofeedback to

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date. However, these clinical changes have often been observed even in the absence of observable baroreflex gains, achieved autonomic balance, and physiological coherence, which is the synchronization of the two branches of the Autonomic Nervous System, with a reduction in the Sympathetic branch and elevation in the Parasympathetic branch (Henriques et al., 2011; Lehrer, 2007; McKinney and Gatchel, 1982). Furthermore, while breathing at resonance frequency boosts the baroreflex response, improved baroreflex sensitivity effects have been shown to be significant and enduring even after controlling for the immediate effects of respiration rate (Lehrer et al., 2003).

Therefore, increased HRV and baroreflex gain are insufficient to explain evidence that HRV Biofeedback training is associated with the aforementioned complex constructs that are not known to be entirely ANS mediated (Appelhans and Luecken, 2006; Ginsberg et al., 2010; Gyurak and Ayduk, 2008; Porges, 1991; Reynard et al., 2011; Segerstrom and Solberg Nes, 2007). It may be that the underlying mechanism for the frequent observation of these improved constructs is less complicated.

In considering vagal pathways alone, there has been much recent supporting evidence in the literature that stimulating the afferent pathways of the vagus nerve (Vagus Nerve Stimuation or VNS) that innervate brain regions important in mood regulation, such as the locus coeruleus, orbitofrontal cortex, insula, hippocampus, amygdala, and subgenual cingulate gyrus, can produce mood-stabilizing effects (Cristancho et al., 2011; Daban et al., 2008; George et al., 2008; Mayberg et al., 2005; Nahas et al., 2005; Sackeim et al., 2001). While this literature is promising, the highly invasive quality of the procedure does not render VNS to be an effective or feasible form of treatment for many.

This study therefore aims to systematically investigate possible underlying mechanisms of HRV Biofeedback by departing from the common practice of simultaneously studying both the efferent and afferent pathways that are inherent in the baroreflex and instead, focusing on solely the vagal afferent pathways, or the sensory communication of parasympathetic viscera to the brain (Appelhans and Luecken, 2006; Grundy, 2002; Karavidas et al., 2007; Patron et al., 2013; Porges, 2009; Porges, 2009; Siepmann et al., 2008; Thayer, 2007; Thayer and Lane, 2000). This is especially due to recent discoveries via functional neuroimaging that a vast majority of vagal fibers are afferent and innervate the insula, somatomotor, and cingulate cortices (Critchley et al., 2004; Grundy, 2002; Pollatos et al., 2005a, 2005b). Furthermore, due to a historical bias to focus on the efferent pathways as well as dearth of available methods that can measure afferent pathways, very little research to date has explored the vagal afferents alone.

1.2. Heartbeat Event Related Potential

Decades ago, German researchers Schandry, Sparrer, and Weitkunat were inspired by their observation that certain individuals were more adept at perceiving their own heartbeats, which led them to postulate that there must be a cortical component behind a seemingly automatic process. They developed the “Heartbeat Evoked Potential” (HEP) to measure cortical influences contingent to the heartbeat (Schandry et al., 1986) to test their hypothesis that certain involuntary bodily functions could be influenced by conscious control. Unlike conventional event related potentials, the HEP is a method that utilizes the heartbeat itself (specifically the R-wave of the EKG), as opposed to an external cue, as the stimulus for EEG measurement (Gray et al., 2007; Leopold and Schandry, 2001; Montoya et al., 1993; Pollatos et al., 2005a, 2005b; Pollatos and Schandry, 2008; Schandry et al., 1986). Each EEG sweep measurement was programmed to commence at 100 msec before the R-wave to 600 msec after the R-wave, totaling 700 msec per EEG sweep (Schandry et al., 1986). After many trials, researchers found that individuals previously determined to have good heartbeat perception had significantly larger HEP amplitudes than individuals with poor heartbeat perception. Largest significant differences in HEP activity were detected at frontocentral electrodes. These sites are correlated with vagal afferent sources previously observed in the insular, anterior cingulate, and somatosensory cortices (Gray et al., 2007; Leopold and Schandry, 2001; Montoya et al., 1993; Pollatos et al., 2005a, 2005b; Pollatos and Schandry, 2008; Schandry et al., 1986).

Montoya et al. (1993) furthered the theory by providing evidence that the degree of cortical influence on cardiac processes could be manipulated with training in that individuals trained to have greater interoceptive awareness exhibited larger HEP amplitudes after training.

When taking into account the definition of vagal afferents and the empirical support that the HEP can detect the brain waves linked to the heartbeat (an ANS function), it is suspected that the HEP may actually measure vagal afferents. If the Heartbeat Event Related Potential (referred to as HERP for the remainder of this document; same as HEP but changed to reflect updated terminology) really does assess vagal afferent functioning as it has been empirically supported, then it would follow that the HERP would be a good way to measure if increased vagal afferent functioning is actually occurring with HRV Biofeedback training. Recently, MacKinnon et al. (2013) investigated the connection between HRV and HEPs during different emotional states and found that HRV was consistently associated with increased HEP amplitudes, especially during resonance frequency breathing.

The purpose of this controlled study was to assess vagal afferent activity by comparing changes in the Heartbeat Event-Related Potential (HERP) before and after training in HRV Biofeedback versus a relaxation control group of Progressive Muscle Relaxation that received feedback via facial EMGs. It was hypothesized that individuals in the HRV treatment condition would exhibit increased amplitude in HERPs during both baseline and training segments after four weekly sessions of HRV paced breathing training while the EMG relaxation control group would not, which would indicate that HRV Biofeedback training can uniquely improve vagal afferent functioning. Additional hypotheses were based on aforementioned frequently reported observations of the clinical effects of improved HRV due to training and sought to confirm whether HRV biofeedback would be associated with greater improvements in sleep, anxiety, and mood as compared to the EMG group. The exploratory hypothesis sought to validate the findings of Montoya et al. (1993) that interoception, as measured by the heartbeat perception task, could be increased with training. It was hypothesized that participants in the HRV treatment condition would demonstrate improved interoceptive sensitivity as compared to individuals in the EMG relaxation control condition.

2. Method

2.1. Pilot study

The original HERP research utilized four sites of EEG measurement according to the 10-20 EEG system: Cz, F3, Fz, and Pz, and determined these sites as having had the most significant HERP changes during a heartbeat perception task (Montoya et al., 1993; Schandry et al., 1986). Since EEG analysis techniques have improved significantly since the original HERP experiments, validation pilot data were collected. The pilot study was approved by the Alliant International University Institutional Review Board and utilized Schandry's (1981) heartbeat perception protocol to select six participants: three who met criteria as “good” heartbeat perceivers, and three as “poor” perceivers. Each participant was recruited from first-year graduate Clinical Psychology, Ph.D. students at Alliant International University. All participants selected were between 18 and 45 years old in order to account for the slight attenuation of HRV found with increasing age. Additionally, participants were eligible for inclusion only if they had minimal exposure to HRV Biofeedback or VNS, not be taking prescription medications that are reported to affect HRV, including opiates, stimulants, tricyclic antidepressants, benzodiazepines, and cardiac drugs such as

beta blockers, not wear pacemakers, or meet criteria for any clinical psychiatric diagnoses. Pilot study participants did not participate again in the main study due to exposure to resonant frequency breathing during the pilot.

EKG was simultaneously recorded using J & J Engineering C2 + hardware and Use3 software (J & J Engineering, Poulsbo, Washington). An Independent Component Analysis was conducted to determine the most significant brain regions and scalp locations involved in heartbeat perception, resonance frequency paced breathing tasks, and hence location of vagal afferent pathways via origination sites while accounting for lateral electrical charge movements of scalp potentials. A total of 136 channels of EEG were recorded using Ag/AgCl electrodes that were connected via a head stretch cap with a chin-strap enclosure (ActiveTwo System, Biosemi, The Netherlands). Electrodes were injected with Signa conductive electrode gel and electrode sites were validated using ultrasound technology. Additionally, eight electrodes were placed on the individual's face and forehead with electrode tape. Scalp abrasion and/or skin preparation were not necessary as the equipment is programmed to have active amplification at each electrode to enhance signal over noise even in the presence of high impedance and 60-Hz interference, therefore reducing electrode placement time, participant discomfort, and infection risk.

Pilot data consisted of 24 min of before and after baseline recordings in which participants were engaged in a distraction task to prevent deliberate focus on heartbeat perception or slower conscious breathing. The beginning distraction baseline task consisted of three silent videos that were four minutes in duration each. Participants were then asked to attempt to perceive their heartbeats for 10 min, followed by 10 min of slow, diaphragmatic breathing paced to their approximate resonance frequency with Breath-Sync music (BK Specialities, Inc., Elgin, Illinois), and then an additional 10 min of heartbeat perception. Lastly, three more silent videos that were four minutes each were shown as the ending baseline. Total continuous measurement per participant during the pilot phase totaled 54 min. Total time commitment per pilot participant averaged approximately two hours to account for the additional time of applying and removing the electrodes.

Results from the pilot study revealed that while many different areas of the brain showed activation during breathing tasks, the ICA validated evidence from the comprehensive literature review that fronto-central sites were frequently prominent during resonant frequency paced breathing (see Figs. 1, 2, and 3). Therefore, the sites of Cz, F3, Fz and Pz were chosen and recorded for the main study as these validated previous research (Montoya et al., 1993; Schandry et al., 1986).

2.2. Main study

2.2.1. Participants

Recruitment began via approaching graduate students enrolled at Alliant International University and by referral from individuals already

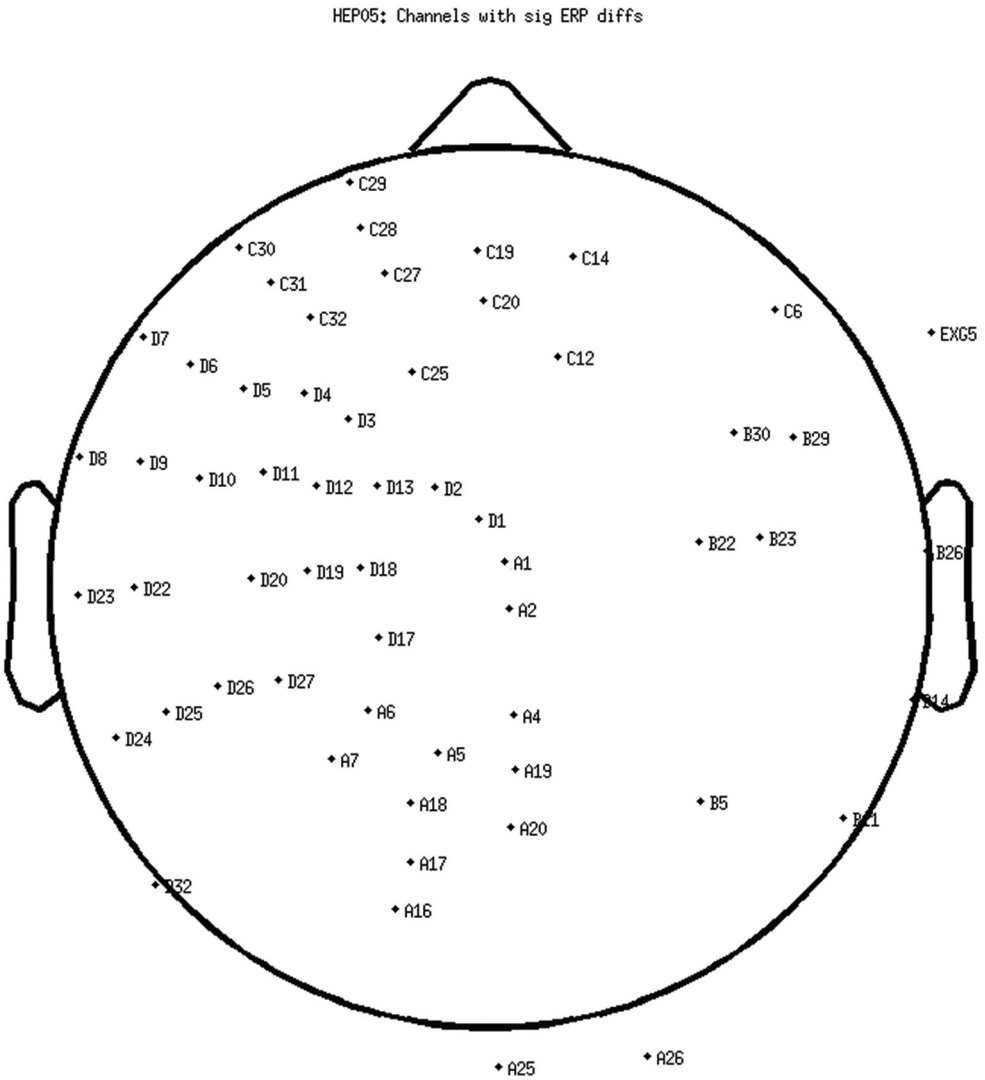


Fig. 1. Plot of all channel ERPs after removal of artifacts to composite a heart-locked ERP. Channel locations shown are sites that had significant ($p < 0.001$) differences between conditions.

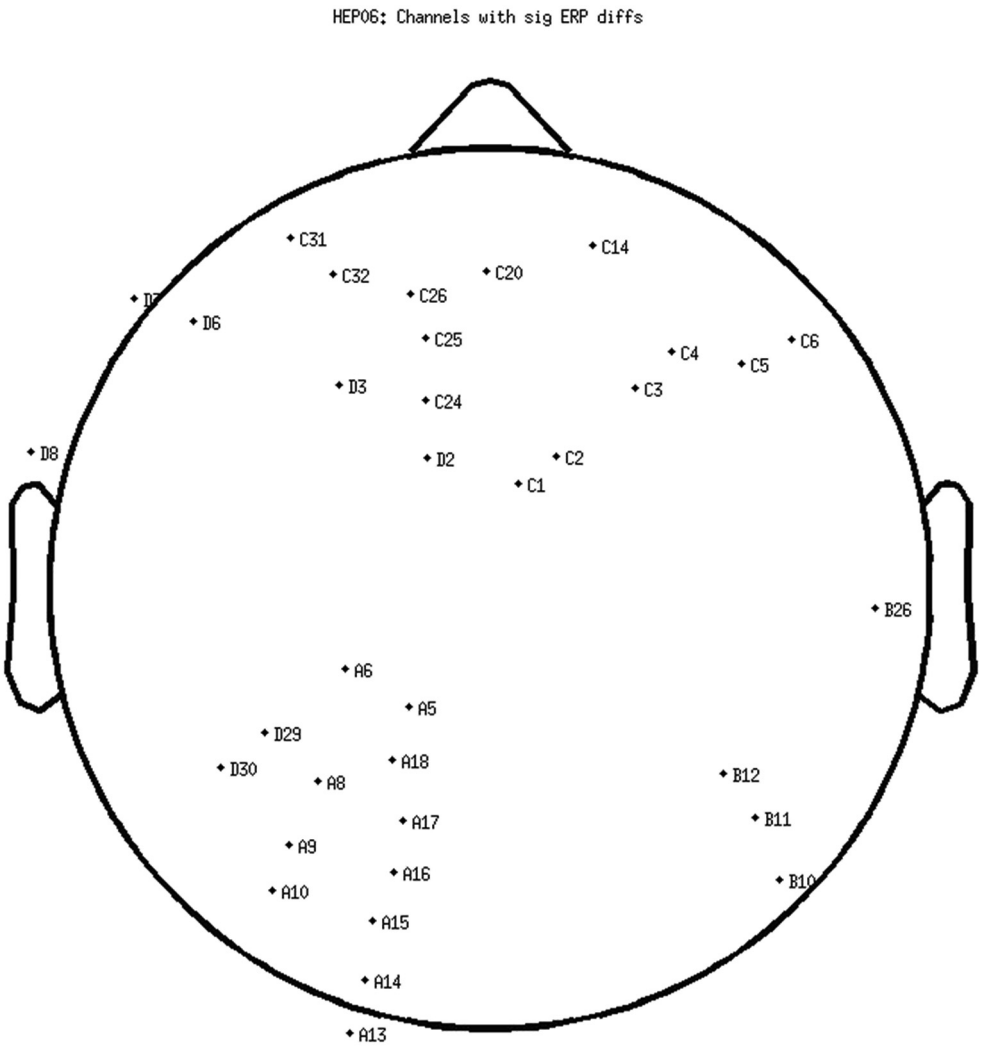


Fig. 2. Plot of all channel ERPs after removal of artifacts to composite heart-locked ERP. Channel locations shown are sites that had significant ($p < 0.001$) differences between conditions.

recruited through utilization of a snowball sampling approach. Inclusion and exclusion criteria were the same as used for the pilot study. Participants were not informed of the true purpose of the study until after completion of all four training sessions and were recruited with the premise that they would learn a form of relaxation training. Participants were informed that the purpose of the study was to examine the effect of various forms of relaxation on the brain to explain the need for electrode placements on the scalp. Participants received free treatment but no financial compensation. The Structured Clinical Interview for DSM Disorders (SCID) was utilized to screen each prospective candidate for clinical psychopathology and appropriateness of inclusion in this study. Individuals who met criteria for DSM-IV TR Axis I and II diagnoses were referred to professional psychologists within the community instead of invited to participate in the study. The study included 28 participants with 14 individuals in each treatment condition. Due to evidence that HRV attenuates with increasing age, preliminary statistical analyses were conducted to ensure that the groups did not differ significantly in terms of age, gender, or preliminary ability to perceive their own heartbeats.

Initially, 41 individuals expressed interest in participating in the study through email and phone calls. Of these 41 individuals, 13 did not participate in the study due to scheduling conflicts, increased demands at work and therefore lack of time to participate in the study, or were ruled out according to the aforementioned exclusion criteria. None of the 28 participants involved in the study dropped out. Of the 28 participants who received treatment, data from 25 participants were analyzed after removal of outliers. The HRV Biofeedback group included 12 individuals: six female and six male participants, ranging in ages from 26 to 37 with a relatively even spread. The only ages that had more than one participant of that age were 30 years (two participants) 32 years (two participants), and 37 years (three participants). The EMG Biofeedback group included a total of 13 participants: eight female and five male individuals ranging in ages from 24 to 37. The spread included one participant of each age, the exception being two participants aged 26 and 28 each.

2.2.2. Measures

Prospective participants were screened for exclusion and inclusion criteria using the Structured Clinical Interview for DSM Disorders (SCID) and demographic questionnaire that queried participants on age, gender, medications, sleep, and previous exposure to biofeedback. Participants that met all criteria were then invited to continue with the study and completed the psychometrically valid and reliable measures of BAI, STAI-Y, PSQI, and HBP at both pre and post time points. The Beck Anxiety Inventory (BAI; Beck, 1990) and State-Trait Anxiety Inventory, Form Y (STAI Form Y; Spielberger et al., 1970) were used to assess anxiety on various dimensions, including subjective, neurophysiological, autonomic, and panic related aspects (BAI) as well as differentiating between temporary and emotional anxiety versus long-term, personality-based anxiety (STAI Form Y). The Pittsburgh Sleep Quality Index (PSIQ; Buysse et al., 1989) assessed for sleep quality and disturbances, and lastly, the heartbeat perception (HBP) task as outlined by Schandry (1981) was utilized for the random stratification procedure to ensure equivalent distribution of “good” and “poor”

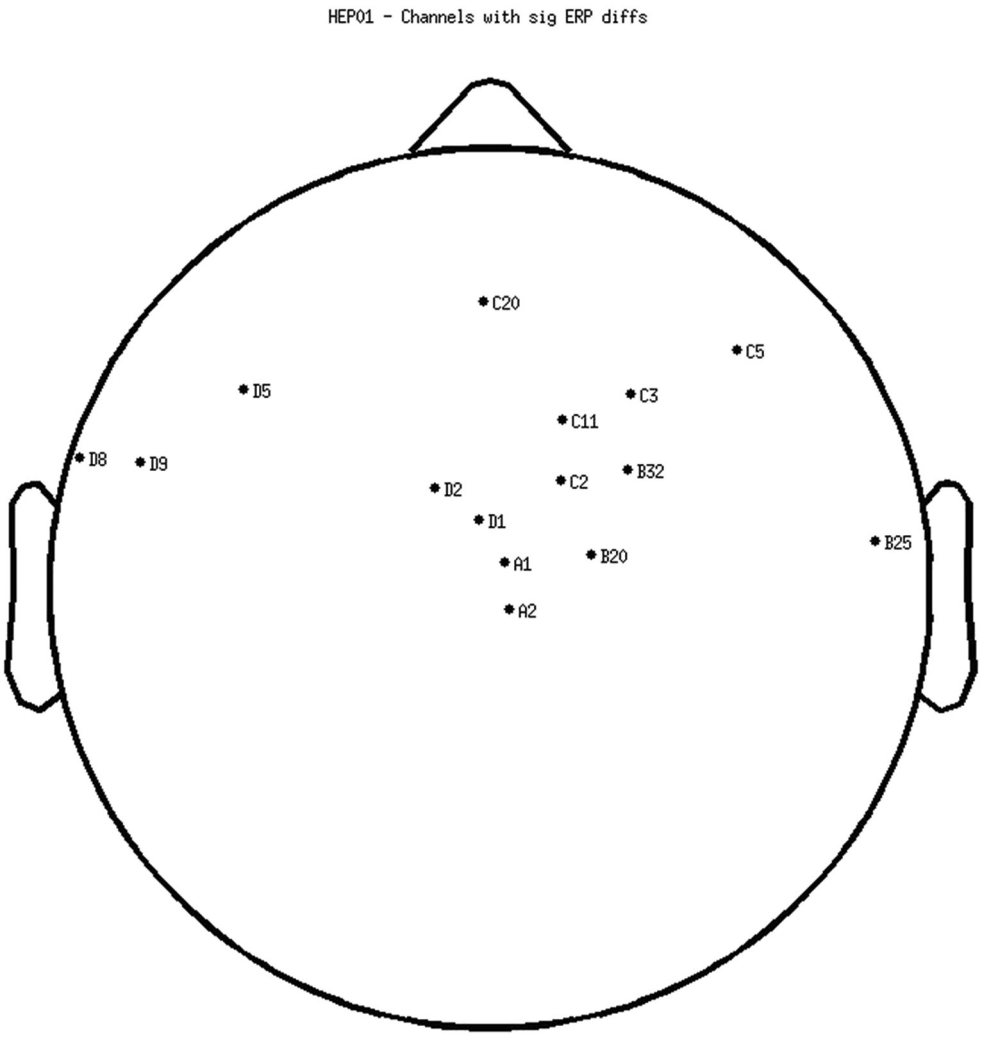


Fig. 3. Plot of all channel ERPs after removal of artifacts to composite heart-locked ERP. Channel locations shown are sites that had significant ($p < 0.001$) differences between conditions.

heartbeat perceivers into each treatment condition. To safeguard against the possibility of shared method variance, non self-report physiological assessment of HRV was included. The standard deviation of normal to normal peaks (SDNN), root mean square of successive differences (RMSSD), and natural log of high frequency (lnHF) were reported and analyzed. Physiological baseline measurements of resting heart rate, skin conductance, finger temperature, and average breathing rate were recorded for 10 min for baseline measurements.

2.2.3. Psychophysiological assessment

J & J Engineering I-330 C2 hardware and accompanying Use3 Physiolab software (J & J Engineering, Poulsbo, Washington) loaded onto an Acer laptop was used for HRV Biofeedback training. Assessment of ANS functioning was collected via gel free wrist EKG electrodes that were held in place with athletic cotton wristbands. A magnetic, stretchable respiration sensor belt was placed around the participant's midsection and approximately on top of the maximum distension of the diaphragm to measure respiration. Finger surface temperature and skin conductance were assessed with reusable Velcro finger electrodes and accompanying thermistor on the index and middle fingers of the non-dominant hand to minimize muscle and hand movement contamination. A non-abrasive, opaque conductance gel helped ensure a better signal through each non-EEG electrode.

For the relaxation condition consisting of Progressive Muscle Relaxation (PMR) with facial EMG feedback, individuals had an additional two EMG electrodes on the forehead to enhance facial muscle relaxation training. Although this is not a conventional part of PMR, this was included in the control condition to mimic the same amount of visual feedback present as in the treatment condition.

To measure the HERP, Thought Technology (Thought Technology, Ltd., Montreal, Canada) Procomp Infiniti hardware and Biograph and Developer Tool software were loaded onto a Windows partition on a MacBook Pro laptop. The Procomp Infiniti physical channels that were used provided even signal fidelity at 256 samples per second across EEG and EKG measurements. Checks of the equipment and inter-electrode impedances were conducted before each session with a goal of below 5 K. Heart rate was measured with electrocardiograph (EKG-Flex/Pro) sensors that were attached to non-latex, removable, and pre-gelled disposable UniGel electrodes. The R-wave time-linked scalp potentials were assessed with electroencephalograph (EEG) sensors. All electrodes used were bipolar gold-plated cup cables. Positive leads were applied onto the scalp, with all negative leads combined into a detachable extender DIN cable that attached as a common linked right gold ear lobe electrode clip. Another linked gold ear clip attached to the left ear lobe and into extenders off each of the four EEG sites to serve as a singular common reference ground electrode. Gold plated EEG cup electrodes were placed at the 10-20 EEG sites of Cz, F3, Fz and Pz using Ten20 EEG conductive paste to reduce skin impedance. As an extra measure of signal clarity, scalp sites were measured using measuring tape and cleaned with isopropanol and tissue paper before electrodes were applied. The R-wave of the EKG served as the stimulus for each EEG sweep measurement, which was programmed to commence at 100 msec before the R-wave to 600 msec after the R-wave, totaling 700 msec per EEG sweep (Schandry et al., 1986). HERP measurement was assessed

for the duration of each session so that approximately 1200–2000 heartbeats were calculated (variation in total heartbeats analyzed depended on individual's average heart rate and degree of heart rate variations), and each EEG sweep was averaged to a composited running average HERP. Sensors were removed at the end of each session with a Q-tip and tissue paper, and light water was applied to the individual's scalp to further remove the conductive paste.

Participants in the HRV treatment group received 50 min of HRV Biofeedback instruction once weekly for four weeks. During the first session, participants were taught diaphragmatic breathing and resonance frequencies were determined, thus extending the length of the first session by an average of 10 min. Participants were instructed to complete a daily practice log to chronicle their daily relaxation practice, sleep quality, and exercise for each day in between sessions, with the daily diaphragmatic breathing practice targeted at 10–20 min. Each subsequent session recording commenced with 10 min measurement of body physiology with an audio distraction task that served as the "in-session baseline distraction segment," followed by 5 min of self-directed, natural breathing without visual feedback from the computer ("self-pace"), 5 min of paced breathing with the computer, 2 min of stressor task, and 5 min of paced breathing ("recovery"). The stressor task consisted of simple mental arithmetic in the form of serial 7 s, or subtracting by sevens. HERPs were assessed continuously during each session and across all four sessions to compare changes across time. At the fourth and final session, participants completed the measures of BAI, STAI-Y, PSQI, and HBP for post measures. At this point, participants were debriefed on more details of the study and the purpose of measuring the HERP.

For the EMG Biofeedback control group, J & J Engineering I-330 C2 + hardware and Use 3 Physiolab software was also used to assess EMG facial electrodes. Facial EMG feedback helped to facilitate a relaxed face throughout the exercise as well as awareness of this conscious effort to disengage from the facial muscles. All participants were asked to either turn off their cell phones and any other electronic devices (pagers, Ipads, Ipods) or to place devices across the room to minimize electrical impedance. The relaxation control group was modeled after the HRV Biofeedback treatment group in terms of amount of time spent with a therapist, length and number of treatment sessions, and degree of physiology that is visualized with a computer and provided as feedback to the participant. Participants in this treatment condition were required to attend weekly treatment sessions lasting 50 min each. During the first session, the nature and explanation of Progressive Muscle Relaxation (PMR) was given as well as ensuing discussion on any limitations the participant had in terms of tensing muscles. No participants expressed concern with tensing muscles, although a few requested a different seating position or extra cushion for subsequent sessions. More detailed discussion on the facial EMG feedback was provided, and participants were taught how to read the feedback screen to measure their degree of facial muscle relaxation throughout the exercise. The nature of the weekly diary card was also introduced and similar to the Biofeedback condition, participants in the control condition were encouraged to practice PMR for 10 to 20 min daily. The first session on average lasted 10 min longer than subsequent sessions due to baseline measurements. The first 10 min of each session also began with the same in-session baseline distraction segment measurement using the same audio distraction task. A conventional Progressive Muscle Relaxation protocol and script was then employed (Bourne, 2011) but all breathing components, including directives to focus on the breath during the script were removed. HERPs were also recorded during all sessions to allow for analysis of changes over time. During the last session, the same procedures were followed. Participants completed the same measures of BAI, STAI-Y, PSQI, and HBP for post measures. Participants were debriefed on more details of the study and the purpose of measuring the HERP.

2.2.4. Data analysis

To analyze changes in HRV, an internal interbeat-interval (IBI) algorithm was computed into the Procomp Infiniti channel set in order to calculate and automatically remove artifacts in EKG due to muscle movements, eyeblinks, and other data points that exceeded the conventional ranges observed for EKG. Data were then exported in IBI format to Kubios 2.0 for calculation of HRV statistics (SDNN, RMSSD, lnHF).

For analysis of HERPs, one site per participant was selected for analysis, and this was determined by choosing the site that provided readings with minimal interference, hereby referred to as the "optimal site." Of the four sites measured: Cz, Fz, Pz, and F3, Cz was chosen 5% of the time as the optimal site, Fz: 13%, Pz: 24%, and F3: 58%. HERPs were interpreted as amplitudes occurring between 200 and 300 ms after the occurrence of the R-wave, in accordance with Schandry et al. (1986). Data were uploaded into IBM SPSS 21 for statistical analysis. All data were inspected three times to account for data entry errors.

To account for the possibility of type I error, the total number of planned comparisons was carefully limited to the number recommended by Keppel and Wickens (2004). Additionally, the Huynh-Feldt correction was reported for all repeated measures analyses of variance F statistics.

3. Results

Independent samples *t*-tests and chi square tests were conducted to ensure that the groups were reasonably equivalent only on the factors of age and pre-experimental heartbeat perception as these factors had the potential of confounding the experimental results. A chi-square test indicated that the biofeedback and relaxation control groups did not significantly differ in terms of age of participants: $X^2(1, N = 25) = 10.644$, $p = 0.50$ and that the distribution of ages amongst participants adhered to a normal bell curve. An independent samples *t*-test provided evidence that the two groups did not differ in terms of the stratification variable of baseline heartbeat perception: $t(25) = 0.202$, $p = 0.841$. Independent samples *t*-tests were also validated that the groups were equivalent in all baseline mood measures of BAI, STAI-Y, and PSQI as well as the seven subscales of the PSQI (Tables 1 and 2).

Three outliers were identified in terms of change of HERP amplitude over time and change of HRV (as measured by SDNN) over time. Two individuals reported multiple simultaneous adverse life events that likely confounded the experimental manipulation as well as their ability to adhere to the daily practice required for each condition. The third outlier was identified as having remarkably large baseline HERP amplitude at session one and HRV despite his lack of prior experience with biofeedback. This case was removed due to the observation of the ceiling effect and the low likelihood of the experimental manipulation being able to further improve this participant's HERP amplitude and HRV values. After removal of these outliers, violations of sphericity and equivalent dependent variable covariance matrices were no longer evident, and change of HERP amplitude over time and change of HRV over time adhered to a normal distribution. There were no other violations of sphericity and equivalent dependent variable covariance matrices after removal of outliers.

Table 1
Group equivalence for demographics.

Demographics	HRV Biofeedback			EMG Biofeedback			*t* or X^2	Sig.
	N	M	SD	*N*	M	SD		
Age	12	32.25	3.75	13	29.38	4.09	10.64	0.56
Baseline HBP	12	0.70	0.19	13	0.68	0.28	0.202	0.84

Table 2
Group equivalence at baseline for mood measures.

Measure scale	HRV Biofeedback			EMG Biofeedback			*t*	Sig.
	N	M	SD	*N*	M	SD		
Beck Anxiety Inventory	12	9.42	7.10	13	8.77	8.75	0.20	0.84
State-Trait Anxiety Inventory		32.92	7.40		30.08	7.25	0.97	0.34
Pittsburgh Sleep Quality Index Global Scale		6	2.56		5	2.31	1.03	0.32
Subjective sleep quality		1	0.60		0.54	0.52	2.06	0.051
Sleep latency		0.83	0.84		1	1.16	− 0.41	0.69
Sleep duration		0.67	0.65		0.77	0.83	− 0.34	0.74
Habitual sleep efficiency		0.67	0.99		0.62	0.96	0.13	0.90
Sleep disturbances		1.33	0.65		1.23	0.60	0.41	0.69
Use of sleep medications		0.42	1.00		0.15	0.56	0.82	0.42
Daytime dysfunction		1.08	0.67		0.77	0.60	1.24	0.23

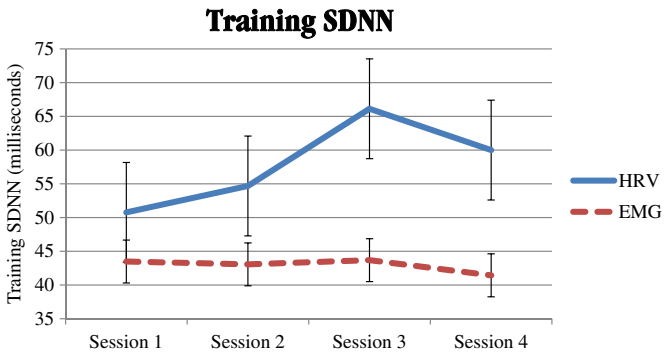


Fig. 4. Significant interaction of time and group on HRV measured by SDNN for 10 min training segments for HRV Biofeedback (HRV) and EMG Biofeedback (EMG) groups. Error bars represent ± 1 standard deviation.

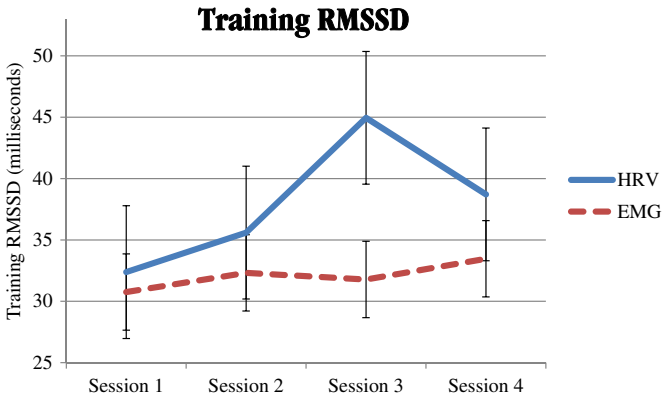


Fig. 5. Significant interaction of time and group on HRV measured by RMSSD for 10 min training segments for HRV Biofeedback (HRV) and EMG Biofeedback (EMG) groups. Error bars represent ± 1 standard deviation.

3.1. HRV assessment

Significant interactions in HRV could be observed once the groups engaged in training sessions: training SDNN, $F(3, 69) = 3.896$, $p = 0.013$; and training RMSSD, $F(3, 69) = 3.558$, $p = 0.025$ (see Fig. 4 for training SDNN and Fig. 5 for training RMSSD). Analysis of simple effects revealed that the two groups began to differ significantly in SDNN and RMSSD at session three, $t(23) = 2.606$, $p = 0.016$; and session four, $t(23) = 2.343$, $p = 0.028$.

3.2. HERP amplitudes

A 2(group) × 2(time) repeated measures analysis of variance (RM ANOVAs) of in-session baseline distraction segment HERP amplitudes yielded a significant 2-way interaction between group and time: $F(1, 23) = 6.072$, $p = 0.022$, partial eta squared = 0.209, thus providing supportive evidence that the HRV Biofeedback group demonstrated greater in-session baseline distraction segment HERP amplitudes as compared to the EMG Biofeedback condition. Analysis of the simple effects via independent samples *t*-test revealed that the significant difference was due to the groups' in-session baseline distraction HERP amplitude differences in session four, $t(23) = 3.561$, $p = 0.002$, while they began reasonably equivalent at session one, $t(23) = 0.450$, $p = 0.659$ (see Fig. 6). Analysis of training segment HERP amplitudes over time yielded a non-significant 2-way interaction: $F(1,23) = 3.545$, $p = 0.072$, partial eta squared = 0.134 (see Fig. 7).

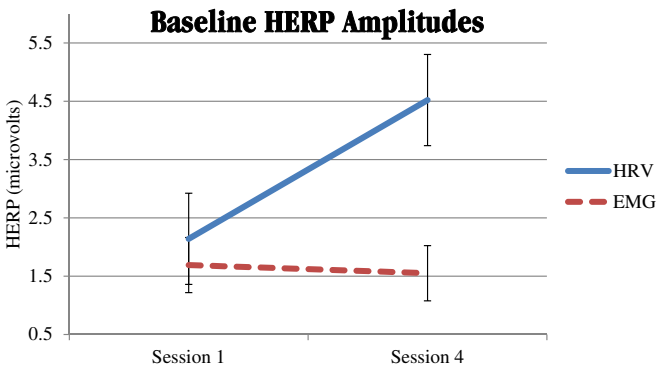


Fig. 6. Significant 2-way interaction of average HERP amplitudes measured in μV for 10 min in-session baseline distraction segments for HRV Biofeedback and EMG Biofeedback (Relaxation Control) condition groups from pre to post measurement. Error bars represent ± 1 standard deviation.

3.3. Behavioral measures

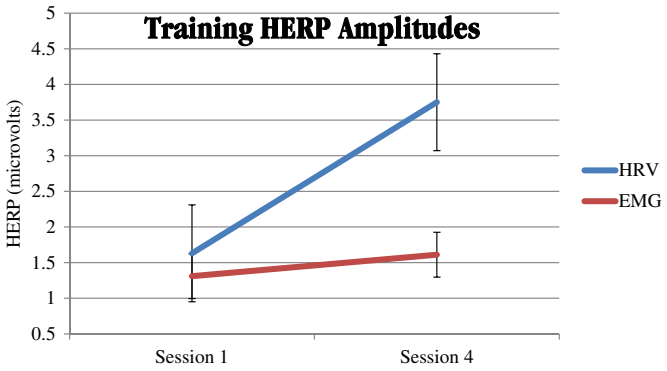
Non-significant 2-way interactions were yielded for all behavioral measures between the two treatment conditions: BAI, $F(1, 23) = 0.008$, $p = 0.931$; STAI-Y, $F(1, 23) = 0.139$, $p = 0.713$; and PSQI global, $F(1, 23) = 0.081$, $p = 0.779$ (Figs. 8–15).

3.4. Exploratory analyses

As a correlate to the idea that participants in the HRV Biofeedback condition would exhibit significantly larger HERP amplitudes than the EMG Biofeedback condition, an exploratory analysis was conducted on possible changes seen in participants' ability to perceive their own heartbeats before and after training. The 2(group) × 2(prepost) RM ANOVA yielded a non-significant 2-way interaction, $F(1, 23) = 0.05$, $p = 0.823$. There were no significant main effects for time, $F(1, 23) = 1.45$, $p = 0.241$; or group, $F(1, 23) = 0.126$, $p = 0.726$, as well.

To further explore the relationship between groups, heart rate variability (HRV) as measured by the standard deviation of normal to normal peaks (SDNN), and heartbeat event-related potential (HERP)

Fig. 7. Non-significant 2-way interaction of average HERP amplitudes measured in μV for 10 min training segments for HRV Biofeedback and EMG Biofeedback (Relaxation Control) condition groups from pre to post measurement. Error bars represent ± 1 standard deviation.



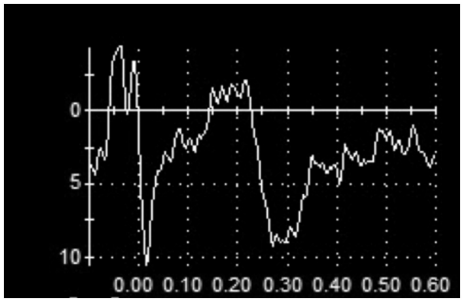


Fig. 8. Example of in-session baseline distraction segment running average HERP for HRV Biofeedback participant at session one.

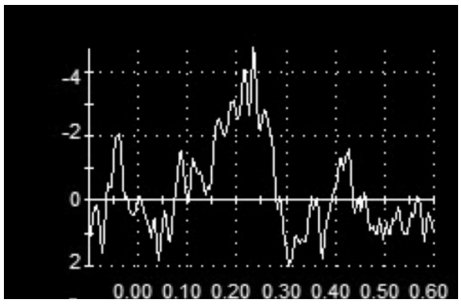


Fig. 9. Example of in-session baseline distraction segment running average HERP for HRV Biofeedback participant at session four.

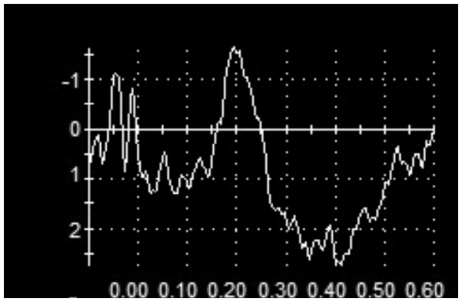


Fig. 10. Example of training segment running average HERP for HRV Biofeedback participant at session one.

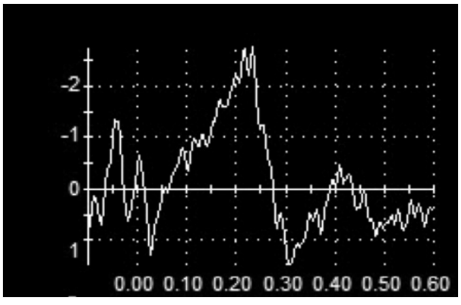


Fig. 11. Example of training segment running average HERP for HRV Biofeedback participant at session four.

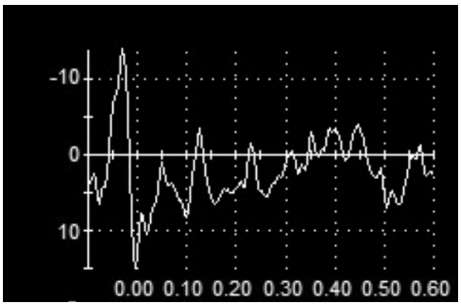


Fig. 12. Example of in-session baseline distraction segment running average HERP for EMG Biofeedback participant at session one.

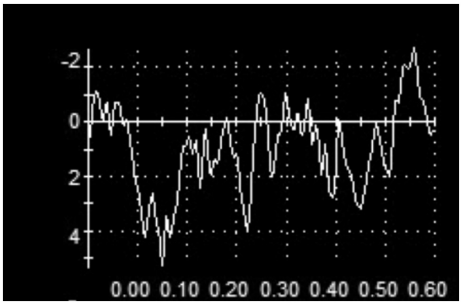


Fig. 13. Example of in-session baseline distraction segment running average HERP for EMG Biofeedback participant at session four.

amplitudes, correlational analyses were conducted. Results confirmed a significant relationship between group and change in in-session baseline segment HERPs over time, $r(23) = -0.457$, $p = 0.022$ as well as significant correlation between in-session baseline HERPs and training HERPs over time, $r(23) = 0.560$, $p = 0.004$.

Change in training HERPs did not significantly correlate with group,

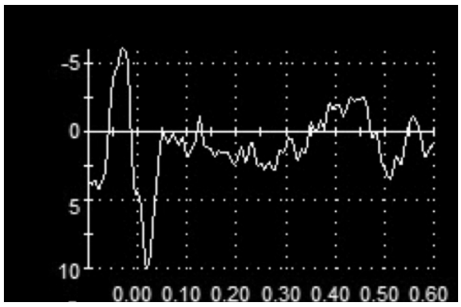


Fig. 14. Example of training segment running average HERP for EMG Biofeedback participant at session one.

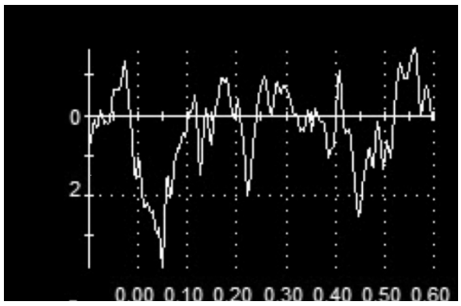


Fig. 15. Example of training segment running average HERP for EMG Biofeedback participant at session four.

$r(23) = -0.365$, $p = 0.072$. Change in training HERPs significantly and positively correlated with change in SDNN for the HRV Biofeedback group, $r(23) = 0.434$, $p = 0.030$. However, this correlation was not significant for the EMG Biofeedback group, $r(23) = -0.345$, $p = 0.248$.

4. Discussion

The main aim of this study was to investigate firstly if the HERP could be replicated and if this could be shown to increase in amplitude with HRV Biofeedback training to serve as an indication of increased vagal afferent functioning. While a handful of previous studies have focused on utilizing the HERP mainly for other purposes, this study is the first to our knowledge to be paired with HRV Biofeedback for the purpose of specifically investigating the vagal afferent pathway and how it may be affected by Biofeedback training. This study validated that the HERP amplitude could only be observed in individuals in the HRV Biofeedback condition as well as that HERP amplitudes during in-session baseline distraction segments increase only with more HRV biofeedback sessions and not EMG Biofeedback with PMR. Interestingly, while nearly the same effect was also observed for HERPs during resonance frequency breathing, this was not nearly as strong a result, perhaps suffering from the small sample size and insufficient power to detect a difference even if there was one. There are a number of factors that could explain why HERP amplitudes were slightly diminished during training segments however. Given that participants were deliberately selected based on their lack of prior exposure to Biofeedback and other forms of meditation or relaxation that focused on slow breathing, smaller HERPs during breathing segments could be reflective of participants' lack of familiarity with slow breathing and therefore focused attention to adhere to the breathing pattern, or slight discomfort due to underdeveloped diaphragmatic strength.

The results that showed a non-significant difference between the two groups in terms of sleep, overall and state/trait anxiety may be due to a number of factors. The fact that this study focused on exploring the possible mechanism of HRV Biofeedback using the HERP and therefore selected for a non-clinical sample could have inadvertently created a floor effect on the behavioral measures. Since both groups experienced decreases on the BAI after four sessions, this could be interpreted as an additional manipulation check for the EMG Biofeedback with PMR condition and support its use as a relaxation tool.

The preliminary result that HERP is not necessarily related to HRV from the correlation analysis is interesting and requires further investigation. For now, it seems relevant to postulate that while HRV is reputably a valid indicator of vagal efferent functioning, the HERP has gained support as an indicator of vagal afferent functioning. Perhaps these two pathways are not necessarily correlated. However, much more research is required on this area alone before assumptions or theories about the vagal pathways can be formulated.

Similarly, the results suggesting that HBP and the HERP were not significantly correlated in this study need to be replicated in order for more conclusive statements to be made. The observation that there was great variability and lack of a general trend in terms of participants' improvements in the HBP task at pre and post measurements likely confounded the results. Firstly, it seemed that the HBP task was rather sensitive to external factors. For example, a few participants reported feeling too distracted to focus on the HBP task, particularly in later trials that required counting of heartbeats for longer stretches of time. Other participants reported that they struggled with the HBP task due to still feeling flustered from having dealt with traffic and other issues associated with their jobs just before session commencement. However, an important factor to consider may be the brevity of the interventions in this research design. While this study accounted for a four-session treatment, this is much shorter than the average clinical treatment typically lasting eight weeks. It is a possibility that while four weeks is just enough time to cultivate adequate diaphragmatic strength to sustain breathing at a six to eight breath per minute pace (as opposed to the regular 12–20 resting breath per minute pace typical of adults), this may not be enough time to develop associated interoceptive sensitivity and mindfulness of the body.

While the results of this study are promising, there were a few limitations to the study worthy of discussion. While the sample size of 28 was initially computed to purposely ensure that the study would be adequately powered, removal of outliers rendered many of the statistical analyses insufficiently powered. It would be interesting to revisit many of the analyses that did not quite garner statistical significance after obtaining a larger sample size and power. Much of the design of this study was to specifically account for confounds and subtle variations that could interfere with the discreet manipulations intended. For example, the relaxation control condition was designed to match the HRV group in terms of number of sessions, length of sessions, time spent with the therapist, degree of technological hookups, and degree of visual feedback provided during the sessions. However, perhaps the sheer nature of PMR and its inherent differences from HRV Biofeedback could have served as a confound. The nature of the PMR script guided participants through systematic tensing and relaxing of muscles every 10 s. It is possible that the frequent task shifting inherent in PMR, as opposed to the longer five-minute task segments in the HRV condition, created sufficient attentional distraction to interfere with cultivation of the HERP. This could also explain the observation of a slightly diminished HERP during breathing segments for the HRV group given that all participants were deliberately selected for their lack of familiarity with breathing. Future studies could focus on comparing an HRV group to a resting control or to an active control that utilizes frontal surface electromyography (sEMG) biofeedback. However, the observation that the EMG Biofeedback with PMR condition did not exhibit larger HERP amplitudes even during in-session baseline distraction segments may make this idea of the importance of prolonged attention to a familiar task as inherent in HERP amplitudes unlikely.

In this study, the fact that HERP amplitudes could only be observed in individuals undergoing training in HRV Biofeedback as well as the finding that in-session baseline HERP amplitudes steadily increased throughout time only in the HRV condition have a few implications.

These results are promising towards the idea that HRV Biofeedback stimulates changes in the vagal afferent pathway that are more enduring than the short- term effects of a single session of resonance frequency breathing. However, the results of this study need to be replicated and validated. Applying the same manipulations of this study and including a larger sample size to achieve adequate power is warranted. One of the goals of this research is to apply this research design to a clinical population, particularly individuals struggling with depression and/or anxiety, in order to assess if depression and anxiety symptoms could be mitigated with HRV Biofeedback and in concordance with changing HERP amplitudes.

Although this study utilized a design of four sessions due to limitations of time and money, this research warrants further analysis of the longitudinal effects of the manipulations. For example, greater HERP amplitudes were observed to endure on at least a weekly basis (given the frequency of the sessions) and beyond the time frame of in-session differences. This longer-term effect begins to parallel other reported longer-term changes associated with HRV Biofeedback, including enhanced emotion and affect regulation, attention, and self-regulation of behaviors. An understanding of the various changes that occur as a result of HRV Biofeedback and how long these changes last seems necessary in elucidating additional clues to the various pathways stimulated with HRV training.

Returning to this study's findings supporting the idea that HRV Biofeedback stimulates enduring changes in vagal afferent pathways, the result that significant differences were more pronounced between the two treatment conditions during in-session baseline segments is particularly intriguing since this segment marked when participants were not actively engaged in either of the treatment tasks. This finding raises interesting questions regarding the role of conscious awareness on the HERP. Given that the design of this study precluded the role of conscious awareness on the HERP by keeping participants blind to the true purpose of the study, it can be concluded that the increased HERP amplitudes were unintended on the part of the participants. However, a valuable future study could focus on whether conscious awareness could incrementally increase the HERP amplitude and whether resonance frequency breathing that is idiosyncratic to HRV Biofeedback is necessary, essential, or simply a pleasant additive in increasing HERP amplitudes. Studies comparing HRV Biofeedback to other forms of relaxation that involve different styles of breathing and meditation would also illuminate important clues to the vagal pathways. That is, focused attention into possible mediators and moderators may help guide theories to more precisely pinpoint these obviously complex and stunning vagal pathways.

Referring back to the studies on VNS and superficial stimulation of the auricular branch via the outer ear, the finding that anti-depressive, anti-anxiety, anti-epileptic, and anti-nociceptive effects were observed suggests that the vagal afferents are tied to a variety of mood disorders and conditions with neurobiological etiologies. With further understanding of the vagal pathways, it is possible that a form of HERP Biofeedback could be developed as an intervention for specifically treating ailments and disorders associated with deficient vagal afferent functioning while reducing intervention costs and personal risks associated with surgical procedures and undergoing repeated electric shock as in VNS and auricular branch vagal stimulation. It is the sincere hope and ultimate goal of this research to develop interventions that could provide a significant number of individuals with relief that is currently beyond the reach of contemporary treatments.

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