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Utilizing Heartbeat Evoked Potentials to Identify Cardiac Regulation of Vagal Afferents During Emotion and Resonant Breathing

Starr MacKinnon · Richard Gevirtz · Rollin McCraty · Milton Brown

Abstract The importance of the bi-directional communication between the heart and brain has been known for over 100 years (Lane et al. in NeuroImage 44:213–222, 2009a, Psychosom Med 2:117–134, 2009b) and plays an important role in many of the prominent theories of psychophysiology today. Utilizing heartbeat evoked potentials (HEPs), we sought to determine whether heart rate variability (HRV) was related to the strength of the connection between the heart and brain. We also hypothesized that differing emotion states would result in differing amplitudes of HEPs. Participants were induced into emotional states with an autobiographical script of their happiest and saddest memory. HEPs were also recorded during diaphragmatic breathing at six breaths per minute. The evoked potentials during the emotional conditions, especially negative emotion were most attenuated. We believe that the signal from the heart to the brain may be filtered by central limbic structures affecting the level of the signal at the cortex. It also appears that HRV affects the strength of HEPs, especially during resonant breathing. Significant neurocardiac gender differences were also present across all conditions. The results of this study support the theory and speculation of many authors who believe vagal afferents play a role in brain function.

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S. MacKinnon (✉) · R. Gevirtz · M. Brown
CSPP, Alliant International University, Daley Hall, 10455 Pomerado Road, San Diego, CA 92131-1799, USA
e-mail: smackinnon@alliant.edu

R. McCraty
HeartMath Research Center, 14700 West Park Avenue, Boulder Creek, CA 95006, USA

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Introduction

The importance of the bi-directional communication between the heart and brain has been known for over 100 years (Lane et al. 2009a, b). It plays an important role in many of the prominent theories of psychophysiology today such as the Neurovisceral Integration Model (Thayer and Lane 2000), and the PolyVagal Theory (Porges 1995). Research has shown that cognitive, affective, and physiological regulation are all associated with vagally mediated cardiac function (Lane et al. 2007, 2008, 2009a, b; Nugent et al. 2007; Pu et al. 2010).

Afferent and efferent vagal neurons facilitate neurocardiac communication and are critical to visceral and autonomic homeostasis. The afferent pathway consists of the nerve structures that carry information from the body to the brain stem and cerebral cortex (Tortora and Grabowski 1996). Conversely, the efferent pathway contains the nerve structures through which an impulse passes away from the brain, targeting the effector organs, glands, and muscles (Tortora and Grabowski 1996). The majority (80–90 %) of vagal nerve fibers are afferent, communicating the state of the body to the brain (Berthoud and Neuhuber 2000). Since the vagal efferents dominate cardiac control (Levy 1990), and the vagus contains a high percentage of afferent fibers (Porges 1995), it is theorized that both the input and output of the Central Autonomic Network (CAN) in the brain are directly linked to HRV (Thayer and Lane 2009).

Currently, there are a few studies aimed directly at investigating the afferent vagal pathways. Many researchers

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would argue that considering the pivotal role it plays in visceral physiology it is relatively understudied (Undem and Weinreich 2005). Afferent input from the heart not only affects the homeostatic regulatory centers in the brain, but also influences the activity of higher brain centers involved in perceptual, cognitive, and emotional processing, thus in turn affecting many and diverse aspects of our experience and behavior (McCraty et al. 2009). McCraty et al. (2009) demonstrated that by modifying subjects' emotional states, the brain's activity, which is naturally synchronized to that of the heart, is altered which in turn modifies the afferent neurological input from the heart to the brain. Subjects experiencing negative emotions exhibited more chaotic or disordered HRV, and subjects experiencing positive mood states exhibited increased order or resonance in the HRV. Additional research completed on emotional affect and HRV has shown a decrease in HRV with negative mood states (Carney 2009; Kemp et al. 2010; Lyonfields et al. 1995; Movius and Allen 2004; Rechlin et al. 1994), and an increase in HRV with positive mood states (Beauchaine 2001; DiPietro et al. 1992; Gruber et al. 2008). Emotion related modulation of cardiac activity by the cortex appears to be primarily vagally mediated (McCraty et al. 2009; Thayer and Lane 2009; Lane et al. 2009a, b).

Vagal Nerve Stimulation and HRV biofeedback are interventions that target the function of the afferent pathways of the ANS. Afferent vagal nerve stimulation (VNS) has become a treatment option especially for those suffering from treatment resistant depression. Manta et al. (2009) have demonstrated the direct clinical mechanism of VNS through the increased firing rate of serotonin and norepinephrine. HRV Biofeedback is designed to increase HRV and stimulate baroreceptors through slow diaphragmatic breathing. During the slow breathing, resonant frequency is reached between respiratory induced oscillations and naturally occurring oscillations in the body (Lehrer et al. 2000). As breathing patterns approach six breaths per minute, there is an increase in HRV, RSA amplitude, and baroreceptor sensitivity during which several biological rhythms become synchronized. Regular practice of the HRV biofeedback techniques increases vagal tone and decreases blood pressure (Lehrer et al. 2000).

HRV biofeedback appears to result in the same benefits as VNS with increases in HRV and improvement of depressive symptoms. Several studies have shown significant clinical improvement in depressive symptoms following biofeedback treatment (Karavidas et al. 2007; Siepmann et al. 2008). HRV biofeedback would clearly be a preferred method of treatment over VNS which is an invasive and expensive procedure with consequent risks of infection, voice alteration, dysphasia, or pain, and a cost of $12,000–$25,000 per patient (Rush et al. 2000). Many studies investigating VNS and HRV biofeedback note that further research is required to elucidate the specific mechanism of vagal control of mood and the heart (Andrade et al. 2010; Siepmann et al. 2008).

Heartbeat Evoked Potentials (HEPs) can be used to identify the specific mechanism of afferent input from the heart to the brain during different emotions and HRV Biofeedback. Heart beat evoked potentials (HEPs) are segments (averaged microvolts) of electroencephalogram (EEG) that are synchronized to the heartbeat. The ECG R-wave is used as a timing source for the signal averaging resulting in waveforms known as HEPs. Each segment of EEG between 100 and 700 ms following each R-wave are averaged into an evoked potential (in microvolts). Changes in HEP amplitude (higher or lower microvolts) serve as an indication of an increase or reduction in afferent signals from the heart to the brain (McCraty 2003). By observing changes in HEPs during the different conditions, one can evaluate the differences in cardioafferent activity.

The predominant use for HEPs in the literature has been to evaluate interoceptive awareness through heartbeat perception tasks (Pollatos and Schandry 2004; Schandry and Montoya 1996; Schandry et al. 1986). A recent article by Terhaar et al. (2012), utlitzed HEPs to evaluate the interoceptive differences between depressed individuals and normal controls. They discovered that less accurate heartbeat perception was significantly associated with reduced HEPs in depressed patients. There have been several studies investigating correlations between the activity of specific brain structures and autonomic parasympathetic activity for cognitive and emotional tasks, but the variations of vagal tone and the relationship with brain activity concerning emotional information has yet to be established (Dufey et al. 2010). There are no current studies investigating the effects of resonant breathing upon the afferent pathway.

There are currently no studies or documented differences in regards to heartbeat evoked potentials between men and women. According to the literature on evoked potentials or event related potentials (ERPs), in general, there are documented differences between men and women during emotion (Lithari et al. 2010: Kemp et al. 2004; Garcia–Garcia et al. 2008). It has been suggested that women are more responsive to emotional stimuli (Kemp et al. 2004; Orozco and Ehlers 1998; Hofer et al. 2007; Lithari et al. 2010; Wrase et al. 2003). Specifically, women display enhanced negative components (N200) in comparison to males when viewing emotional stimuli (Lithari et al. 2010). Women also appear to have greater evoked potential amplitudes as a result of unpleasant or highly arousing stimuli (Garcia–Garcia et al. 2008; Lithari et al. 2010). Gender differences also appear to be most pronounced in the central and left hemisphere areas (Lithari

et al. 2010). These electrophysiological gender differences appear to be present despite their being no difference in subjective emotional ratings (Kemp et al. 2004).

For many years, research has demonstrated a clear connection between changes in HRV and resonant breathing. Current research also shows a definite relationship between HRV and differing emotional states. Extreme prolonged mood states have also been shown to be associated with both physiological and psychosocial changes that are deleterious to the cardiovascular system (Carney et al. 2005a, b). Although, the involvement of the afferent pathway during an emotional task or diaphragmatic resonant breathing have been minimally studied. As a result, the mechanisms underlying the connection between mood states, biofeedback treatment, and HRV remain unclear. Additionally, current literature indicates an attenuation of evoked potentials (N200) during both positive and negative emotion (Schupp et al. 2003), yet the connection between evoked potentials and HRV has not been explored.

Thus, the objective of the current study was to use heartbeat evoked potentials to investigate the cardiac regulation of vagal afferents during emotion induction and resonant breathing. We hoped to gain insight into the mechanism behind HRV biofeedback and add to our understanding of emotions and their connection to our physiology. We hypothesized that higher levels of HRV would be associated with stronger amplitude of the HEPs. We also predicted that differing emotion states would result in a greater amplitude in HEPs than baseline. We believed that positive emotion would result in a stronger HEP than baseline (because positive emotion increases HRV) and negative emotion would result in a smaller amplitude HEP than baseline (because negative emotion decreases HRV). We also predicted that the HEPs during resonant breathing would be significantly stronger than baseline because slow paced breathing increases HRV. Lastly, we believed that the heart rate rhythm or order rate may influence the amplitude of the evoked potential. We used the formula LF/(HF + VLF) as suggested by McCraty et al. (2009) to determine the degree of coherence or order in the HRV pattern. According to McCraty et al. positive emotion results in a more coherent, orderly, and elevated HRV pattern and negative emotion results in a disordered and decreased HRV pattern.

Methods

Participants

This study was approved by the Instructional Review Board (IRB) of the California School of Professional Psychology at Alliant International University, San Diego. The nature and purpose of the investigation was explained to the participants, including the procedures involved and their potential benefits and risk. They were given an opportunity to ask questions and were informed that their participation in the study was voluntary and could be terminated at any time. Participants were given and signed an informed consent and given the California subject's bill of rights. This study followed the guidelines of the Policy and Procedures for the Protection of Human Participants according to Alliant International University.

A total of 30 subjects were recruited as potential candidates for participation in the study (21 females and 9 males; average age = 27; range 23–35). The mean age for women was 27 and mean age for men was 29 with no significant difference ($t = -1.599$, $p = .144$). Inclusion criteria required participants to be physically and psychologically healthy and between the ages of 18–35. Participants who met criteria for a psychiatric disorder according to the Structured Clinical Interview for DSM-IV—Non-patient version (SCID-NP) were excluded from participation. Participants who had pacemakers, irregular heartbeat, or were on medication affecting autonomic function (opiates, stimulants, tricyclic antidepressants, benzodiazepines, and cardiac drugs such as beta-blockers) were also excluded. In terms of the prior experience with diaphragmatic breathing, 25 % ($n = 7$) had no experience, 43 % ($n = 12$) had some experience (6 months or less or did not practice regularly), and 32 % ($n = 9$) were experienced diaphragmatic breathers.

Procedure

All participants were initially screened with the SCID-NP and completed a demographic questionnaire to gather descriptive information including age, gender, and experience with diaphragmatic breathing. This form also included questions about medical conditions, psychiatric illnesses and current medications. Participants also completed an initial Positive and Negative Affect Scale (PANAS) to assess for baseline emotional affect. Chest leads were applied to collect ECG and EEG was measured by placing electrodes at the Cz, C3, and C4 sites according to the 10–20 international standards. Baseline ECG and EEG data was then recorded for 10 min. The subjects' eyes were closed during all conditions to control for unwanted eyeblink interference in the data. Subjects were instructed to keep their eyes closed and fixed forward.

Emotional states were induced using a validated autobiographical script technique (Dougherty et al. 1999; Lane et al. 2009a, b; Mayberg et al. 1999; Pitman et al. 1990). Prior to their arrival at the clinic where data collection took place, each participant was asked to prepare two written autobiographical scripts describing their most recent saddest and happiest moment. The autobiographical scripts

were then verbally reviewed (for 3–5 min) with the investigator prior to each emotional condition in preparation for data collection. During the emotional conditions, subjects were asked to visualize a previously identified moment of their autobiographical script during which the target emotion was experienced most intensely (Lane et al. 2009a, b). The emotional conditions were 5 min in length and the participants were asked to silently visualize their memory with their eyes closed. Immediately following each of the emotion inductions, subjects were again asked to rate their affect on the PANAS. The emotional inductions were counterbalanced and a 2-min neutral condition separated the two conditions.

Following the baseline and two emotion conditions, participants completed a resonant breathing condition. Prior to the resonant condition, the subjects were taught a diaphragmatic breathing technique until they were able to breathe comfortably at resonant frequency. Resonance was reached when subjects slowed their breathing to six breaths per minute amplifying 0.1 Hz oscillations, which is known to produce large fluctuations in heart rate and blood pressure (Lehrer et al. 2000). During the 5-min resonant breathing condition, the subjects were asked to close their eyes and were cued by an auditory stimulus to breathe in and breathe out at a pace of six breaths per minute. The equipment was then removed and participants were given an opportunity to debrief. Table 1 illustrates the data collection procedure for each participant.

Digitized data files were transferred to a PC workstation and analyzed using DADiSP 2002 (DSP Development Corp., Newton, MA) signal processing software. The individual continuous recordings of the ECG and 3 EEG channels were reshaped into 800 ms. long segments time locked to the ECG R-wave. Segments began 200 ms. before and ended 600 ms. after the R-wave of each ECG cycle. Individual averages using 260 segments were computed for each electrode site resulting in 1 ECG and 3 EEG waveforms for each condition. All segments were manually reviewed for artifacts; segments with extreme baseline drift and noisy uncharacteristic signal were not used in the HEP waveform. A baseline correction was also performed by subtracting the mean of the first 75 ms., before the ECG R-wave onset, from the entire segment prior to computing the HEP waveform average (Montoya et al. 1993).

HRV data cleaning and analysis was completed using Kubios HRV analysis software developed by the Biosignal Analysis and Medical Imaging Group (BSAMIG, Version 2.0) at the Department of Physics of the University of Kuopio in Finland. This software allows for frequency domain analysis and the ability to correct for complex or slow linear trends that are characteristic of HRV data, as well as removal of ectopic or irregular data points (Tarvainen and Niskanen 2008). Each participant's IBI data was manually reviewed and ectopic beats were replaced with the mean average of the previous and following beat. The "smooth priors" Kubios artifact rejection was also utilized.

Table 1 Data collection procedure

1. Informed consent presented, reviewed, and signed by the subject
2. Demographics Questionnaire
3. SCID-NP Completed
4. Baseline PANAS
5. Baseline ECG and EEG data recorded for 10 min
6. Verbal review of first autobiographical script (positive or negative emotion script based on counterbalanced order). The content deemed to evoke the highest amount of emotion was designated by the subject and primary investigator
7. The subject was instructed to close their eyes and was then cued verbally by the primary investigator to recall the pre-designated content of the autobiographical script. Data was recorded during this time for 5 min
8. PANAS completed
9. 2 min neutral condition
10. The opposite emotion condition (positive or negative based on the initial emotional condition) was completed following the same procedures as the initial emotional condition. Data was recorded for 5 min during the recall of the pre-designated script segments
11. PANAS completed
12. Subjects unfamiliar with resonant breathing were taught diaphragmatic breathing. Subjects were given the opportunity to practice paced breathing with the 6 breaths per minute audio pacer for up to 1 min
13. Data was recorded for 5 min while subjects breathed diaphragmatically at 6 breaths per minute following the audio pacer
14. Equipment was removed and subjects were given the opportunity to debrief

Physiological Monitoring

BioPac MP35 4-Channel Data Acquisition System with Student Lab Pro software version 3.7 was used to collect the EEG and ECG signals. Three EEG sensors and one ECG sensor were utilized. The EEG was measured by placing electrodes at the Cz, C3, and C4 sites. All data was collected with a sampling rate of 1,000 samples/second. Grass 10 mm gold cup electrodes with Weaver Ten20 electrode paste were used for recording the EEG. The EEG electrodes were referenced to linked ears. Disposable pre-gelled silver/silver chloride snap electrodes were used to record the ECG. The ECG was recorded using a chest modified V5 (CMV5) arrangement. The active electrode was placed over the 6th rib along the left anterior line with the reference electrode located on the right Manubrium border of the Sternum. The ground electrode was on the lower right rib margin over bone.

Psychological Measures

The SCID-NP (First et al. 2002) is a semi-structured interview used to identify DSM-IV Axis I disorders. It is considered to be the "gold standard" of diagnostic assessment (Shear et al. 2000; Steiner et al. 1995). There are at least 700 studies in which the SCID was the diagnostic screening instrument used (Lobbestael et al. 2010). The non-patient version is for use in studies where subjects are not psychiatric patients. Research has demonstrated superior reliability and validity for the SCID over standard intake screening interviews (Basco et al. 2000; Fennig et al. 1994, 1996; Kranzler et al. 1995, 1996; Lobbestael et al. 2010). The SCID-NP contains sections pertaining to substance use, anxiety, eating disorders, somatoform disorders, psychotic disorders, adjustment disorders, and mood disorders. The SCID-NP takes approximately 15–30 min to administer.

HRV Measures

Heart rate (HR) and HRV were measured continuously during the baseline, emotion, neutral, and resonance conditions. HRV was measured as the standard deviation of the normal-to-normal inter-beat intervals (SDNN). SDNN is considered to be the most complete measure of HRV encompassing all possible sources of variability (Task Force Special Report by the European Society for Cardiology and the North American Society of Pacing and Electrophysiology 1996). HRV was also evaluated using the low frequency (LF) domain of the heart rate between 0.04 and 0.15 Hz, which can be influenced by both SNS and PNS activity (Task Force, 1996). The LF/HF ratio was also included in analysis, which is considered to reflect the balance between parasympathetic and sympathetic autonomic activity in long-term ambulatory recordings (Task Force, 1996). Higher scores on SDNN, LF, and LF/HF ratio indicate higher levels of HRV.

The high frequency (HF) domain of HRV was examined to contrast the changes in LF especially during resonant breathing (Task Force 1996). HF is thought to be predominantly influenced by efferent vagal activity. The square root of the mean squared differences of successive NN intervals, or RMSSD, as well as pNN50, or the divided proportion of the number of NN interval differences of successive NN intervals larger than 50 ms, were also both evaluated. Both are thought to be short-term variation estimates of high frequency HRV (Task Force 1996).

Emotional Measures

Subjects were asked to rate their experience of the emotions on the PANAS at baseline and following each emotional condition to validate the success of the affect induction. The PANAS is a 20 item self-report measure used to provide independent measures of positive and negative affect (Watson et al. 1988). Subjects are instructed to rank each feeling according to a five point scale of 1 = Not at all or very slightly, 2 = A little, 3 = Moderately, 4 = Quite a bit, and 5 = Extremely. Possible total scores on each subscale range from a minimum of 10 to a maximum of 50. High negative affect (NA) on the PANAS represents the level of unpleasurable engagement with the environment and subjective distress (Crawford and Henry 2004). High positive affect (PA) represents the absence of NA and the extent of pleasurable engagement with the environment (Crawford and Henry, 2004). Overall, the PANAS has high levels of reliability (PA .86–.90, NA .84–.87) and is known to be a valid measure of the construct it is intended to assess (Crawford and Henry 2004). There is also a large amount of normative data available for this measure.

Statistical Analysis and Design

Analysis

Using SPSS 20.0 statistical software, pairwise comparisons were completed to evaluate the success of the emotion induction. All mean assumptions of ANOVA were evaluated and met including homogeneity of variance, normality, and independence of observation. A repeated measures ANOVA was conducted to evaluate the difference in heartbeat evoked potentials (HEPs) between conditions. The HEP waveform following the R wave was split into two separate time points of analysis: the first being 20–180 ms, and the second being 180–240 ms (N200). Pairwise comparisons were evaluated to examine the difference in N200s between specific conditions. An independent samples *t* test was completed to compare male to female N200s across the conditions. Heart rate data was analyzed using SDNN, pNN50, and RMSSD from the IBI data. HRV was also evaluated using the frequency domains of the heart rate. Specifically, the low frequency (LF) and high frequency (HF) bands of the HRV and the ratio between low frequency and high frequency or LF/HF Ratio were evaluated. Pearson bivariate correlations were completed to evaluate the relationship between HRV variables and N200s in each condition. The heart rate rhythm was also evaluated across conditions to evaluate differences in the order of the heart rate using the formula LF/(HF + VLF), which is used to determine the degree of coherence or order in the HRV pattern (McCraty et al. 2009). A stringent bonferonni correction (.01) was used to correct for familywise error due to the multiple comparisons.

Sample Characteristics

Thirty individuals were screened using the SCID-NP. Participants were eliminated from the study if there was any indication of alcohol or substance abuse. A physical exam and routine ECG's were not completed because the subjects were young healthy adults recruited from a college population. Of the 30 interested participants, one individual was excluded as a result of substance abuse, and another was excluded for meeting DSM criteria for a mood disorder. All other participants were not reportedly taking medication, had no current medical issues, and did not meet criteria for a DSM disorder according to the SCID-NP. A total of 28 subjects met criteria for inclusion and participated in the study. One of the subject's data was unusable due to repetitive ectopic heartbeats and was excluded from the analysis. EEG and ECG data for 27 participants were included in the final analysis. One of the remaining subject's data contained HEPs outside of the standard range and was Winsorized to reduce the effect of spurious outliers.

Results

Emotion Induction

Success of each emotion induction was assessed with the Positive and Negative Affect Scale (PANAS). The manipulation check was given at baseline and following each emotion condition. Overall, positive and negative affect were successfully induced during each emotion condition and were significantly different from baseline (see table xxx) The subjects reported significantly higher positive emotion than negative emotion during the positive emotion condition and significantly higher negative emotion than positive emotion during the negative emotion condition The baseline PANAS scores for the subjects in the present study resulted in scores consistent with the normative data in a neutral condition from a large non-clinical sample (Crawford and Henry 2004). The baseline mean score for positive affect in the present study was 28.75 (SD = 4.8) and the norm is 30.62 (SD = 7.9), and the baseline mean score for negative affect was 15.00 (SD = 4.4) and the norm is 14.00 (SD = 5.9) (Crawford and Henry 2004). Scores are also consistent with PANAS scores following a mood induction by Pretz et al. (2010). This study showed mean scores close to 28 for PA and 25 for NA, which is similar to means obtained in the current study of 32 for PA and 22 for NA. This suggests that the mood inductions did in fact elicit changes in targeted affect. Figure 1 shows the PANAS scores following the mood inductions.

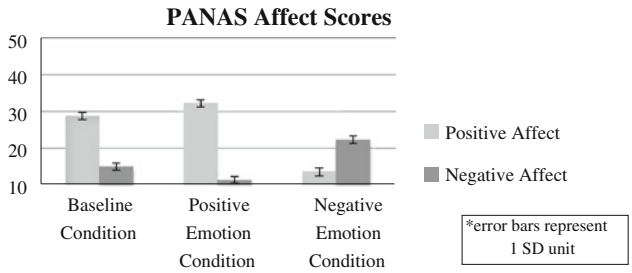

Fig. 1 Mean PANAS ratings at baseline and following each emotion condition

Heart Beat Evoked Potentials (HEPs in Microvolts)

The repeated measures ANOVA indicated significantly different N200s across conditions on all EEG placements (see Table 2) There was no significant difference between subjects based on the order of the emotion condition experienced (Cz $F(1, 25) = .544$ $p = .467$, C4 $F(1, 25) = .346$, $p = .562$, C3 $F(1, 25) = 1.53$, $p = .227$). There was also no significant difference between subjects based on the level of experience with diaphragmatic breathing (Ch 1 $F(1, 25) = 1.09$, $p = .353$, Ch 2 $F(1, 25) = 1.37$, $p = .274$, Ch 3 $F(1, 25) = 1.04$, $p = .368$). There was no significant difference between the emotion induction conditions in the HEP waveform between 20 and 180 ms (Cz $F(3,78) = .286$, $p = .835$, C4 $F(3,78) = .682$, $p = .566$, C3 $F(3,78) = .057$, $p = .982$). The period following 240 ms was not examined to avoid interference of the blood pressure wave. Figure 2 displays the grand average of all 3 EEG channels for all participants across the conditions.

There was no significant difference between the positive and baseline condition on any of the EEG channels. On channel 1 (CZ) the N200 s were significantly stronger during the resonant breathing condition than in the baseline condition. On channel 2 (C4) and 3 (C3) the resonant breathing condition produced elevated N200 s but did not result in a statistically significant higher amplitude than baseline The resonant breathing condition produced significantly stronger

Table 2 Heart beat evoked potentials across conditions and placements (in microvolts), means (SDs)

Condition	Cz***#	C4***	C3***
Baseline	−.689 (1.04)	−.814 (1.02)	−.934 (1.07)
Positive	−.617 (.790)	−.614(.924)	−.704 (.789)
Negative	−.352 (.750)	−.364 (.984)	−.391 (.719)
Resonance breathing	−.961 (.735)	−.894 (.955)	−.934 (1.07)

***$p < .001$ for ANOVAs across conditions Baseline, Positive, Negative

# $p < .05$ for baseline versus positive emotion condition and resonance breathing condition

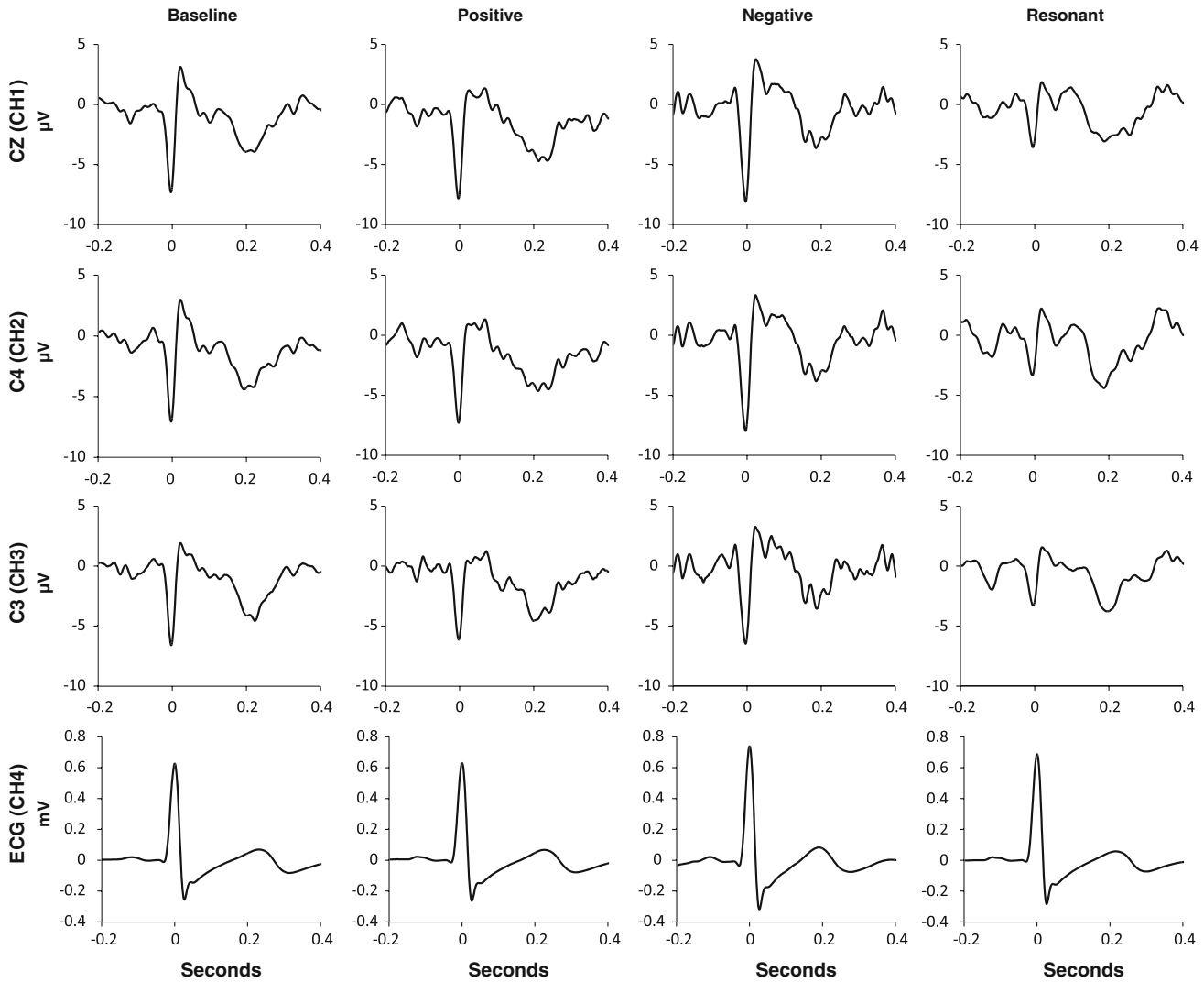

Fig. 2 Heartbeat evoked potentials by channel and condition. *Note*: μV = Microvolts, mV = Millivolts

HEPs than the positive condition on Channels 1 and 2. There was not a significant difference between the resonant breathing condition and the positive condition on channel 3 (C3). Figure 3 shows the differences in condition by channel.

Correlations Between HRV Variables and N200s

Bivariate correlations were completed to evaluate the relationship between the N200s and HRV variables. A modified Bonferoni correction was used to correct for multiple comparisons and the alpha level was reduced to .01. The results of the correlations can be seen in Table 3.

SDNN

It appears that there is some relationship between SDNN and the amplitude of the N200s. The correlations in this study were seen as exploratory in nature and should be interpreted with caution. Although, many of the correlations between HRV and N200s were not significant so no mediation analyses were completed.

LF/HF Ratio

For both positive and negative emotions, the higher the LF/HF ratio, the lower the N200 amplitude

Low Frequency (LF)

There does appear to be a relationship between the LF variable and N200s during resonant breathing especially on the central channel. The higher the LF value, the higher the resulting evoked potential.

Table 3 Correlations between N200 heart beat evoked potentials and heart rate variability parameters

Condition	HRV measure	N200 site		
		Cz	C4	C3
	SDNN			
Baseline		−.155	−.104	−.147
Positive		−.326	−.338	−.498**
Negative		−.413	−.302	−.391
Slow breath		.456*	.323	.382
	LF/HF			
Baseline		−.213	−.218	−.264
Positive		−.382	−.325	−.265
Negative		−.322	−.322	−.245
Slow breath		.049	−.007	.226
	HF			
Baseline		.251	.181	.139
Positive		.559*	.580*	.755*
Negative		.912**	.506**	.588**
Slow breath		−.267	−.414*	.243
	LF			
Baseline		−.258	−.266	−.336
Positive		.557**	−.498**	−.570**
Negative		−.453*	−.385	−.437*
Slow breath		.452*	.352	.412
	RMSSD			
Baseline		.119	.194	.223
Positive		.189	.181	.095
Negative		.224	.329	.265
Slow breath		−.274	−.362	−.204
	PNN50			
Baseline		.189	.198	.316
Positive		.294	.306	.289
Negative		.255	.080	.303
Slow breath		−.341	−.396*	−.287

SDNN standard deviation of normal to normal interbeat intervals, *LF/HF* ratio of high frequency to low frequency variability data, *HF* high frequency variability data, *LF* low frequency variability data, *RMSSD* root mean square of successive differences, *PNN50* percent of sequential intervals greater than 50 ms, *N200* amplitude of the Evoked potential at 200 ms, CZ, C4, and C3 = scalp sites

High Frequency

There also appears to be a relationship between the HF variable and N200s. The lower the HF value, the higher the N200 potential.

RMSSD

There were no significant correlations between the RMSSD HRV measure and the N200s.

pNN50

There was a significant correlation between pNN50 and the N200s at the C4 site during resonant breathing. The higher the pNN50 value the higher the evoked potential.

Heart Rate Variability

SDNN

Heart rate variability variables including SDNN, LF/HF Ratio and LF were analyzed to evaluate the differences in HRV across conditions. A repeated measures ANOVA was completed evaluating the differences in SDNN across the four conditions. The observed F value was statistically significant at $F(3,78) = 28.55$, $p < .001$. Pairwise comparisons revealed significant differences between all conditions except the comparison between the positive and negative conditions. Both emotional conditions produced significantly lower SDNN and the resonant frequency produced significantly higher SDNN relative to the baseline condition. Table 4 displays the results.

LF/HF Ratio

A repeated measures ANOVA was completed to evaluate the differences in LF/HF Ratio across the four conditions. The observed F value was statistically significant, $F(3,78) = 48.78$, $p < .001$. Results for the pairwise comparisons for LF/HF Ratio between the conditions are displayed in Table 5. The LF/HF ratio was significantly greater than baseline during the positive emotion condition. Additionally, the LF/HF ratio during the resonant breathing condition was significantly greater than all of the other conditions.

Low Frequency (LF)

A repeated measures ANOVA was completed to evaluate the differences in LF across the conditions. The observed F value was statistically significant at $F(3,78) = 35.78$, $p < .001$. During the resonant breathing condition, LF was significantly higher than LF in all of the other conditions. Pairwise comparisons between the conditions are displayed in Table 6.

High Frequency (HF)

A repeated measures ANOVA was completed to evaluate the differences in HF across the conditions. The observed F value was statistically significant at $F(3,78) = 46.43$, $p < .001$. HF was significantly higher during the baseline condition in comparison to all of the other conditions.

Table 4 Paired differences for standard deviation of normal to normal R-waves (SDNN)

Pair	Pair desc.	M	SD	SEM	95 % CI		t	*df*	Sig. (2 tailed)
					Lower	Upper			
1	Baseline—positive	48.62	19.80	2.15	.413	9.25	2.248	26	.033
		43.79	15.12						
2	Baseline—negative	48.62	19.80	2.67	.505	11.48	2.245	26	.034
		42.63	12.92						
3	Baseline—resonant	48.62	19.80	5.19	−36.93	−15.60	−5.06	26	.000
		74.89	25.34						
4	Positive–negative	43.79	15.12	1.56	−2.06	4.38	.741	26	.465
		42.63	12.92						
5	Positive—resonant	43.79	15.12	5.42	−42.25	−19.95	−5.73	26	.000
		74.89	25.34						
6	Negative—resonant	42.63	12.92	5.10	−42.75	−21.77	−6.32	26	.000
		74.89	25.34						

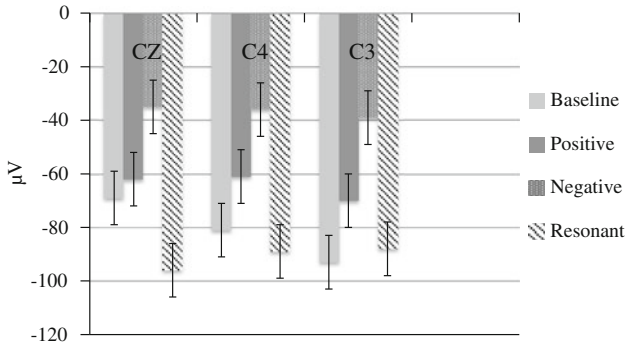

Fig. 3 N200 heartbeat evoked potentials on each EEG channel during each condition. *Note*: μV = Microvolts

Gender and Heart Beat Evoked Potentials

Although there was an imbalance between males and females within the study, the assumptions of ANOVA were carefully evaluated and were not violated. There was a significant difference between men and women across the conditions on all channels (Ch1 $F(1,25) = 5.60$, $p = .026$, $\eta^2 = .18$, Ch2 $F(1,25) = .010$, $p = .920$, $\eta^2 = .22$, Ch3 $F(1,25) = 5.01$, $p = .034$, $\eta^2 = .17$). Gender differences in HRV are displayed in Table 7.

Heart Rate Coherence

Heart rate rhythms were also evaluated to assess the order versus disorder in the heart rate between conditions. Order

Table 5 Paired differences for LF/HF ratio

Pair	Pair desc.	Paired differences					t	*df*	Sig. (2 tailed)
		M	SD	SEM	95 % CI				
					Lower	Upper			
1	LF/HF baseline	1.62	1.57	.277	−1.151	−.0124	−2.10	26	.046
	LF/HF positive	2.21	2.25						
2	LF/HF baseline	1.62	1.57	.325	−1.288	.0506	−1.90	26	.069
	LF/HF negative	2.24	1.99						
3	LF/HF baseline	1.62	1.57	1.76	−16.560	−9.321	−7.34	26	.000
	LF/HF resonant	14.57	9.27						
4	LF/HF positive	2.21	2.25	.315	−.6844	.6111	−.116	26	.908
	LF/HF negative	2.24	1.99						
5	LF/HF positive	2.21	2.25	1.82	−16.099	−8.617	−6.79	26	.000
	LF/HF resonant	14.57	9.27						
6	LF/HF negative	2.24	1.99	1.73	−15.879	−8.764	−7.11	26	.000
	LF/HF resonant	14.57	9.27						

Table 6 Low frequency pairwise comparisons

Pair	Pair desc.	Paired differences					t	*df*	Sig. (2 tailed)
		M	SD	SEM	95 % CI				
					Lower	Upper			
1	Baseline LF	6.68	1.19	.1466	−.2774	.3255	.164	26	.871
	Positive LF	6.66	.964						
2	Baseline LF	6.68	1.19	.1620	−.2734	.3927	.368	26	.716
	Negative LF	6.62	1.02						
3	Baseline LF	6.68	1.19	.2550	−2.228	−1.180	−6.68	26	.000
	Resonant LF	8.39	.692						
4	Positive LF	6.66	.964	.1135	−.1978	.2690	.313	26	.756
	Negative LF	6.62	1.02						
5	Positive LF	6.66	.964	.2529	−2.248	−1.208	−6.83	26	.0001
	Resonant LF	8.39	.692						
6	Negative LF	6.62	1.02	.2491	−2.276	−1.251	−7.08	26	.000
	Resonant LF	8.39	.692						

Table 7 Differences in N200 evoked potentials males versus females

Condition	Gender	Cz		C4		C3	
Baseline			*t* test,		*t* test		*t* test
	Male	.006 (.724)	2.46**#	−.056 (.724)	2.82***#	.322 (1.08)	2.03
	Female	−.982 (1.03)		−1.13 (.924)		−1.19 (.987)	
Positive							
	Male	−.125 (.641)	2.258*	−.052 (.673)	2.19*	−.210 (.568)	2.28*
	Female	−.823 (.766)		−.851 (.926)		−.912 (.786)	
Negative							
	Male	−.034 (.680)	1.458	.089 (.688)	1.59	−2.19 (.824)	.798
	Female	−.486 (.757)		−.554 (1.04)		−.463 (.680)	
Resonance							
	Male	−.183 (.640)	2.83**#	−.353 (.606)	2.20*	−.549 (.395)	1.99
	Female	−1.19 (.915)		−1.09 (.861)		−1.13 (.783)	

Uncorrected p values:* $p < .05$, ** $p < .01$, *** $p < .001$.
Significant with Bonferroni correction

in the rhythm was evaluated by averaging the Low Frequency over the sum of High Frequency and Very Low Frequency (LF/(HF + VLF)) within the heart rate domains (McCraty et al. 2009). A within subjects ANOVA resulted in a significant F value, $F(3,78) = 54.86$, $p < .001$. Pairwise comparisons revealed significantly more ordered heart rhythm during the positive emotion condition in comparison to baseline (Baseline $M = 1.36$, SD = 1.32, Positive $M = 1.81$, SD = 1.91, $t = -2.28$, $p = .031$), as well as significantly more ordered heart rhythm during the resonant condition in comparison to all of the other conditions (Baseline $M = 1.36$, SD = 1.32, Positive $M = 1.81$, SD = 1.91, Negative $M = 1.83$, SD = 1.59, Resonant $M = 12.06$, SD = 7.11, $p < .001$).

Discussion

The results of this study support the theory and speculations of many authors who believe vagal afferents play a role in brain function. Beginning with Claude Bernard in the late 1800 s, many researchers have attempted to conceptualize and demystify the nervous system pathways between the heart and the brain. The present study offers evidence to further these theories and findings. It appears that heart rate variability (HRV) influences the afferent input to the brain during the experience of emotion as well as during resonant breathing. The level of engagement of neuroanatomical structures also appears to affect the amplitude of potential at the scalp. This study additionally

provides interesting findings on gender differences in heart-brain dynamics.

The attenuation of HEP N200s during both positive and negative emotion supports current literature on evoked potentials during emotion (Schupp et al. 2003). A review was completed on ERPs during emotional processing by Olofsson et al. (2008) spanning 40 years of literature. The Olofsson et al. review confirmed attenuated ERPs during emotion with stronger effects following negative emotional stimuli (Crawford and Cacioppo 2002; Schupp et al. 2003; Olofsson et al. 2008). It is hypothesized that this may be the result of rapid processing of aversive information by the amygdala (Olofsson et al. 2008; Morris et al. 1998). Negative emotion is also known to engage the amygdala (Morris et al. 1996; Breiter et al. 1996), insula (Reiman et al. 1997), and other limbic structures (Lane et al. 2007) more than positive emotion, which in the present study resulted in the lowest N200.

Emotion engages many neural structures such as the amygdala, anterior insula, anterior cingulate cortex, medial prefrontal cortex, superior frontal gyrus, thalamus, hypothalamus, and the superior temporal gryus (Carla and Hamann 2006; Fernandez-Carriba et al. 2002; Lane et al. 2007; Vytal and Hamann 2010). The induced emotions also involved other neural processes such as visualization and memory, which engage additional neuroanatomical structures. During processing of emotion, we assume that due to the extensive neural processing in addition to influences of heart rate variability, there is an interference of the flow of information from the heart to the cortex resulting in a reduced evoked potential.

Overall, it does appear that there is some relationship between the level of variability produced by the heart and the N200 amplitude. The negative emotion condition resulted in reduced HRV and also the weakest evoked potentials. We believed that the positive emotion condition would result in higher HRV and in turn elevated N200 s, when in reality the positive emotion condition resulted in reduced HRV, which also resulted in reduced N200 s. Due to the exploratory nature of this study and multiple variables, many comparisons were made. As a result, the alpha level was reduced to account for multiple correlations and many of the HRV variables during the emotional conditions as well as the resonant breathing condition did not result in significant correlations. Mediation analyses were not performed as a result of the sporadic significant correlations between the HRV variables and N200s.

The low frequency domain of the heart rate appears to be particularly connected to the amplitude of the evoked potentials. Low frequency is believed to represent baroreflex activity as well as in some conditions reflecting the effects of both sympathetic and parasympathetic efferent activity (Task Force 1996). During the emotional conditions, the higher low frequency values were associated with weaker evoked potentials at the scalp. Increased neural processing may be occurring based on the amplitude of the heart signal to the brain. For the resonant breathing condition, there was a converse result: the higher the low frequency the higher the evoked potential. This makes sense according to the neural processing theory since the heart brain connection during resonant breathing is much more mechanical and requires engagement of less neural processes. The high frequency domain resulted in an opposite result demonstrating lower high frequency values during the emotional and resonant breathing conditions.

For the SDNN variable, both positive and negative emotion resulted in significantly lower SDNN than baseline. Additionally, the resonant breathing condition produced significantly higher SDNN than baseline. The differences in SDNN match the N200 trends across the conditions: both the positive and negative emotional conditions produced lower N200s and the resonant breathing condition produced higher N200s. The results of the bivariate correlations resulted in similar findings showing higher levels of heart rate variability were correlated with stronger N200 amplitudes. Although, especially with the alpha correction, not all bivariate correlations resulted in significant Pearson values. The RMSSD variable did not result in significant correlations and the pNN50 variable resulted in only one significant correlation during resonant breathing. Overall, it does appear that there is a connection between the level of HRV and the resulting amplitude of the N200. With a larger sample size, we may have been able to reach levels of significance between HRV and the N200s.

We also believed that the resonant breathing condition would result in increased HRV and larger N200s than the other conditions. During the resonant condition in the present study, the N200s at the central EEG site were significantly greater than baseline. There were also significantly greater N200s at two of the electrode sites when comparing the resonant condition to the positive condition and significantly greater N200s at all three of the sites in comparison to the negative condition. It is clear that there was an elevated N200 response at the scalp during the diaphragmatic breathing condition, even for subjects who had never practiced the technique previously. We speculate that the pathway from the heart to the cortex is less interrupted during diaphragmatic breathing resulting in a stronger signal at the scalp. The increases in the N200 following resonant breathing supports evidence from Lehrer et al. (2003), McCraty et al. (2009), and Gevirtz (2000) that HRV biofeedback may operate on the brain by way of the afferent pathway. Perhaps vagal afferent mediation of depression symptoms using HRV biofeedback can be explained or partially explained through this mechanism (Karavidas et al. 2007).

The findings surrounding gender differences are similar to current research on evoked potentials (Lithari et al. 2010: Kemp et al. 2004; Garcia–Garcia et al. 2008). Generally, females produce higher evoked potentials for emotional stimuli in comparison to men (Kemp et al. 2004; Orozco and Ehlers 1998; Wrase et al. 2003; Hofer et al. 2007; Lithari et al. 2010). In terms of heartbeat evoked potentials, females also appear to have higher evoked potentials and potentially a greater heart-brain connection. These findings may indicate that the female brain is more receptive to afferent information than the male brain. Prior research has also shown the most pronounced differences between men and women in the central and left hemisphere areas (Lithari et al. 2010). However for this study, the largest differences across the conditions appeared to be at C4 on the right side of the brain. Also consistent with prior research on gender differences, there was no difference in the subjective emotional ratings between men and women despite the electrophysiological differences (Kemp et al. 2004).

This is the first study to examine the pathway from the heart to the brain during emotion and resonant breathing. The pathway from the heart to the brain is an important area of research that has been minimally investigated. Due to differences in HRV during emotion, we speculated that there may be afferent differences mediating the presentation and experience of happy versus sad mood states. In the present study, levels of HRV were reduced during positive emotion in contrast to some of the prior literature, which led us to conclude that despite the misdirection of our predicted findings, there still appears to be a connection between the evoked potentials and levels of HRV. Additionally, the findings were difficult to interpret due to the engagement and potential interference of the many neuroanatomical structures involved in the processing of emotion.

One could speculate that negative emotion is filtered by the underlying neuroanatomy more than positive emotion as a result of its functional relevance. Negative emotion is evolutionarily more functional for means of survival and protection, thus a higher activation in the limbic and environmental response areas of the brain is observed. Conversely, positive emotion is functionally more appropriate in the brain areas facilitating higher order consciousness such as planning, abstract thinking, and meaning making. During the resonant breathing condition, it appears that the signal from the heart is less interrupted in its path to the cortex. This breathing is similar to what is practiced in yoga and meditation, which are thought to increase cortical thickness and may broaden higher levels of consciousness and awareness (Lazar et al. 2005). We know that regular resonant breathing leads to beneficial physiological changes (Gevirtz 2000; Hassett et al. 2007; Lehrer et al. 2000; Nolan et al. 2005) but aside from a reduction in symptoms further research is needed to examine the overarching psychological benefits resulting from this technique.

We also intended to examine the underlying mechanisms of biofeedback and speculated that an increase in the afferent pathway may be mediating the effects of improvement. It appears that two simultaneous or congruent processes may be occurring leading to our findings. We believe that the level of variability (size of peak valley differences) may be sending increased afferent signals to the brain, which in turn mediates the amplitude of N200s. We also believe that the N200s may be filtered by central limbic structures, especially during the emotional conditions, which may be affecting the signal of the N200s at the cortex.

This specific area of interest has minimal prior research, and as a result the present study was exploratory in nature. Weaknesses of this study include a small sample size, limited equipment and minimal number of electrodes. It does appear though that there is some relationship between the HRV variables and the N200s that may have been discoverable with a larger sample size or more EEG sites. Our analyses may also have led to additional findings by examining the entire HEP waveform and not limiting our scope to the N200 time point. It may have also been beneficial to include a measure of respiration. Although in the current study there were no significant differences between the conditions based on respiration rates (Baseline $M = 13.11$, Positive Emotion $M = 13.00$, Negative Emotion $M = 13.22$, $F(2,52) = .072$, $p. = .930$). Furthermore, the use of the Bonferoni correction may have increased type II error in an attempt to correct for type I error.

The emotion induction procedures can also be viewed as a potential limitation due to the transient and subjective nature of emotion itself. For future studies it may be beneficial to add a measure for skin conductance to improve the evaluation and analysis of the emotion inductions. Longer periods of emotional induction may have also increased the level of emotional expression and allowed for further clarification of the differences between conditions. While it may have also been beneficial to evaluate blood flow and specific areas engaged during the present study, scalp recorded potentials are considered to be a powerful and informative way to evaluate affective processing in the brain (Britton et al. 2006; Olofsson et al. 2008; Smith et al. 2005). Additionally, the use of evoked potentials in this study was of particular interest to evaluate the temporal nature of the heart to brain connection.

Future directions based on the results of this study include the exploration of heart beat evoked potentials in a clinical sample such as a depressed population or individuals struggling with emotion regulation. It is known that

the risk for emotion related disorders such as depression are higher for women (American Psychiatric Association 1994). Differences in physiology may lead to a greater understanding of these gender differences in depression and other mood related disorders (Kessler 2004). It would also be beneficial to compare the differences in evoked potentials prior to and following diaphragmatic breathing training. The majority of the participants in the present study did not practice breathing at resonant frequency on a regular basis. Future directions for biofeedback equipment may even include the development of software displaying the changes in amplitude of heart beat evoked potentials. Continued exploration of this area of research will bring clarity to the underlying mechanisms affecting autonomic and emotional function and will also guide the development of new interventions for psychological and physiologically based disorders.

Conflict of interest None.

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