Title: Resonance breathing is associated with improvements in depression and anxiety symptoms during heart rate variability biofeedback sessions

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Abstract

Heart rate variability (HRV) appears to be a transdiagnostic biomarker for health and disease. Although initial studies using HRV biofeedback (HRVB) to regulate HRV as a potential adjunctive treatment to gold-standard interventions seem promising, more research is needed to determine which aspects of HRVB training provide the most clinical benefits to those suffering from mental health symptoms. In the current study, we sought to investigate whether time spent in resonance, between-person differences in resonance frequency, and/or within-person resonance frequency trajectory across repeated HRVB sessions were related to changes in depression and/or anxiety symptoms during a 12-week digital mental health intervention that contains HRVB as part of the treatment protocol. We used a retrospective cohort study to examine these associations among 387 participants in the Meru Health Program. For depression, we found that average resonance time per HRVB session, but not total time in resonance, was significantly associated with decreased depression as measured by the Patient Health Questionnaire 9-item scale (PHQ-9) across treatment ($b=-0.38$, 95% CI $[-0.76,-0.01]$, $t(377)=-1.99$, $p=.047$). For anxiety symptoms as measured by the Generalized Anxiety Disorder 7-item scale (GAD-7), we found neither association significant. Within-person effects were significant for both depression and anxiety, with steeper slopes of time spent in resonance significantly related to reductions in PHQ-9 and GAD-7 symptoms, respectively. Between-person effects were not significant for either depression or anxiety. Our results demonstrate that improvements in resonance efficiency over time in treatment, independent of how each participant starts, are related to reductions in depression and anxiety symptoms.

Keywords: Heart rate variability, biofeedback, mHealth intervention, resonance breathing, depression, anxiety

Introduction

Heart rate variability (HRV), or the changes in the time intervals between consecutive heart beats, has been conceptualized as a transdiagnostic biomarker for health and disease (Kemp and Quintana 2013; Beauchaine and Thayer 2015)). HRV can be modified for better or worse by various biopsychosocial factors including environmental, psychological, and physical stress (Shaffer and Ginsberg 2017) and is thought to be regulated by cognitive and affective regulatory neural regions of the brain (Mather and Thayer 2018; Shaffer, McCraty, and Zerr 2014; Shaffer and Ginsberg 2017; Thayer et al. 2009). In general, higher HRV (i.e., greater variability in heart rate fluctuations) has been associated with positive health outcomes and is thought to indicate a greater ability to flexibly adjust to environmental demands, while lower HRV is associated with deleterious mental health outcomes as well as subsequent morbidity and mortality (Kemp and Quintana 2013). Therefore, HRV may serve as a putative biological mechanism whereby stressors exert effects on individuals as explained by the stress diathesis model of health (Kemp, Koenig, and Thayer 2017). Importantly, HRV is plastic and has bidirectional associations with neural regions (Mather and Thayer 2018), indicating that HRV may be a modifiable transdiagnostic biomarker amenable to clinical interventions. One such intervention, HRV biofeedback (HRVB), involves providing participants beat-to-beat heart rate data during exercises of slow, paced breathing with the goal of maximizing HRV. Through its practice, HRVB may provide one avenue for volitionally upregulating HRV with potentially indirect cognitive and affective benefits.

HRV and Mental Health

HRV represents the temporal variation in beat-to-beat intervals between consecutive heart beats and is thought to be controlled by vagally mediated higher-order inhibitory cortico-subcortical neural circuitry spanning the medial and orbitofrontal aspects of the prefrontal cortex, anterior insula, cingulate cortex, central nucleus of the amygdala, and the brainstem (Kemp and Quintana 2013; Thayer et al. 2009). Many of these same brain regions have been implicated in emotion regulation and cognitive control, which may explain why higher resting HRV is associated with greater emotion regulation and psychological flexibility (Kemp and Quintana 2013; Mather and Thayer 2018). In contrast, lower HRV has been found in a host of psychiatric disorders, including depression (Kemp et al. 2010), anxiety (Chalmers, Quintana, and Abbott 2014), Bipolar Disorder (Henry et al. 2010; Lee et al. 2012), Attention Deficit Hyperactivity Disorder (Buchhorn et al. 2012), Schizophrenia (Berger et al. 2010), Alcohol Use Disorders (Quintana et al. 2013), and Conduct Disorder (Beauchaine, Gatzke-Kopp, and Mead 2007). Furthermore, severity of psychiatric disorder appears to be associated with greater decreases in HRV such that there is, for example, a negative correlation between depression severity and HRV (Kemp et al. 2010). Owing to the links between HRV and mental health disorders, researchers have started to examine whether improvements in HRV could have ameliorative effects on mental health symptoms.

HRVB As an Adjunctive Treatment for Depression.

One way to directly increase heart rate variability is through HRVB. During HRVB, participants are shown real-time heart rate data and prompted to breathe at a prescribed rate which corresponds to "resonance" frequency, which maximizes HRV or heart rate oscillations (P. Lehrer 2013). This resonance frequency is thought to improve physical and emotional resilience by strengthening homeostatic functions through increasing cardiac vagal activity and exercising the baroreflexes. For example, these processes may help provide homeostatic control of blood pressure through changes in heart rate (P. M. Lehrer et al. 2003). For an in-depth HRVB protocol and further explanation, see Lehrer et al. (2013).

Recent meta-analyses have found that the practice of HRVB is associated with significant reductions in depression (P. Lehrer et al. 2020), anxiety, and stress (Goessl, Curtiss, and Hofmann 2017) with low to moderate effect sizes. As mentioned above, HRV has bidirectional vagal circuitry to inhibitory cortico-subcortical neural circuitry. This theoretical ascending biological pathway may explain how many behavioral interventions, including meditation, yoga, paced breathing, exercise, and HRVB have their salutary effects (Kemp, Koenig, and Thayer 2017; P. M. Lehrer and Gevirtz 2014).

Current Study

While initial HRVB studies are promising as a potential adjunctive treatment to gold-standard interventions, more research is required to examine these effects in sufficiently powered and controlled studies. In particular, we still do not know which aspects of HRVB training provide the most clinical benefits to those suffering from mental health symptoms. In the current study, we sought to study more nuanced explanations for the significant improvements seen in mental health outcomes after practicing HRVB. Specifically, we were interested in investigating whether 1) indicators of time spent in resonance (total and average time), 2) between-person differences in resonance frequency, and/or 3) within-person resonance frequency trajectory across repeated HRVB sessions (i.e., slope) were related to changes in depression and anxiety symptoms during a digital mental health intervention that contains HRVB as part of the treatment protocol. We hypothesized that indicators of greater resonance breathing resulting from HRVB practices during the Meru Health Program (MHP), an evidence-based digital mental health intervention, would be related to decreases in depressive and anxiety symptoms. We did not, however, have a priori hypotheses for which aspects of HRVB training (e.g., total time in resonance, average time in resonance, slope over time) would be related to changes in these mental health symptoms, so these analyses should be considered exploratory.

Materials and Methods

Participants and Recruitment.

Patients presented to the MHP via several different avenues. The MHP has been described in detail in prior publications (Economides et al. 2019, 2020; Goldin et al. 2019). Briefly, the MHP is a 12-week digital mental health intervention (originally developed as an 8-week program) with evidence-based components delivered asynchronously via a smartphone app. The program incorporates a continuous care model that includes frequent interaction with a dedicated, licensed clinical therapist and as-needed consultations with medical doctors, including psychiatrists. Some were recruited to the MHP via online Facebook advertisements, while others were referred by healthcare providers or via employee assistance programs. Inclusion/exclusion criteria of the MHP require patients to have at least mild levels of depression, anxiety, or burnout, own a smartphone, and not have an active substance use disorder, a previous suicide attempt, severe active suicidal ideation with a specific plan, severe self-harm, or a history of Bipolar Disorder or psychosis. In addition, patients agree to spend up to 20 minutes per day on the program, 6 days per week. All patients enrolled signed informed consent to participate and have their collected, deidentified data used for research purposes. Data collected as part of care, including engagement data, HRVB data, and depression and anxiety outcomes data, is stored in Health Insurance Portability and Accountability Act-compliant electronic medical records that includes protected health information. All measures examined in this study were collected in the MHP app before, during, and at end-of-treatment. Institutional review board exemption for this analysis was granted by the Pearl Institutional Review Board for analyses of previously collected and de-identified data.

Participants were included in analyses if they had participated in the MHP after December 02, 2018 and before November 11, 2020. Our initial sample consisted of 588 participants; however, 201 did not have 6 or more HRVB sessions, which was necessary for estimating a slope for an individual (see Statistical Analysis for more information). There were significant differences between those who were included and those who were excluded based on this criterion, with included participants having more total active days in the MHP ($W = 12{,}094.5$, $p < 0.001$), being younger ($W = 34{,}676$, $p = 0.024$), and being more likely to complete the MHP ($\chi^2(1) = 183.28$, p < .001) than excluded participants. No other significant differences were observed.

After excluding the 201 participants with less than 6 HRVB sessions, the analytic sample was left with 387 participants (Mean age = 39.7, SD = 9.6, range: [20, 67]; 79.3% females), who collectively had 16,109 HRVB sessions (mean sessions per individual = 20.18, SD = 17.46). There were significant differences between individuals in the two different versions of the MHP (8-week versus 12-week; see below section for more information regarding program weeks) for total HRVB minutes, baseline PHQ-9 scores, last GAD-7 scores, PHQ-9 change scores, time spent in resonance intercept, and gender, which are reported in Table 1.

Assessment & Treatment Procedures.

We examined existing baseline and end-of-treatment clinical outcomes data collected from patients treated with the MHP as well as daily HRVB data. The HRVB component of the program, referred to as "resonance breathing exercises," start at a duration of 5 minutes and gradually increase up to a maximum of 20 minutes per daily, with participants directed to adjust the duration in 5-minute increments accordingly. At the onset of the MHP, each participant is sent a heart rate sensor (see below for more details). In addition, they receive a brief written introduction to HRV and resonance breathing, including how to use the sensor. During each HRV-B session, participants are guided by a visual pacer that expands during inhalation for 4 seconds and contracts during exhalation for 6 seconds, achieving resonance breathing at a rate of approximately 6 breaths per minute. The visual pacer is supplemented with recorded breaths that matched the rate of the visual pacer. Below the pacer, participants are shown a real-time visual trace of their heart rate which is green during periods of high resonance and amber during low resonance. At the end of the practice participants are shown summary feedback detailing the session duration and time spent in high and low resonance.

Measures.

Depressive and Anxiety Symptoms. Depressive symptoms were measured at baseline and every 2 weeks through the program's end by the Patient Health Questionnaire-9 (PHQ-9), a widely used instrument used to screen for depression (Kroenke, Spitzer, and Williams 2001). The PHQ-9 is comprised of a list of nine depressive symptoms with response options ranging from 0 (not at all) to 3 (nearly every day). The PHQ-9 has excellent internal consistency (Cronbach's α of 0.89 in primary care settings), and test-retest reliability (Arroll et al. 2010). Anxiety symptoms were measured at baseline and every two weeks through the program's end by the Generalized Anxiety Questionnaire-7 (GAD-7), a widely used instrument in outpatient and primary care settings to screen for the presence and severity of an anxiety disorder. The GAD-7 has excellent internal consistency and test-retest reliability (Löwe et al. 2008; Spitzer et al. 2006).

HRVB. Participants self-administer HRVB via the Meru Health app using a HeartMath Bluetooth photoplethysmography (PPG) sensor, which collects interbeat intervals (IBIs) from an earlobe. IBI data are then collected and sent to a secure database, which can then be subsequently preprocessed and used for analyses.

HRVB Preprocessing. Preprocessing of the HRVB sessions was conducted using the RHRV package (Rodriguez-Linares et al. 2019). First, we extracted the non-interpolated instantaneous heart rate signal. We then used a filtering algorithm which removed beats based on whether they were 13 bpm away from the RR interval, the subsequent RR interval, or the average of 50 previous RR intervals, which was standard protocol within the preprocessing step in the RHRV package. Additionally, beats were removed if they were above or below 25 or 200 bpm, respectively. We then interpolated the heart rate signal with a linear method using a frequency of 4 Hz. In order to ascertain the power spectral density for each session, we used the Lomb-Scargle periodogram. This allowed us to determine the spectral density between specific frequency bands (e.g., within the resonance frequency of 0.08 Hz – 0.12 Hz vs outside the resonance frequency > 0.12 Hz) in order to ascertain the density within the range versus outside the range of resonance frequency. We excluded any frequencies below 0.08 Hz because not all HRVB sessions were long enough in duration to accurately capture low frequency patterns.

Time Spent in Resonance Calculation. Once we extracted the spectral density of the different frequency bands, we could then estimate total time spent in resonance. In order to do this, we found the specific frequency that had the maximum spectral density value for each session within the 0.08 Hz – 0.12 Hz band. The equation for Spectral Density (SD) is the following $SD=\frac{S^2}{Hz}$, with seconds denoted as "*S*" and frequency denoted as "*Hz*." We were able to estimate the amount of time (in seconds) spent at the highest given spectral density within the previously noted frequency band by rearranging the equation as follows: $S=\sqrt{SD\,x\,Hz}$.

Covariates. Various patient demographics and clinical characteristics collected at baseline as well as engagement metrics collected during the MHP were examined as correlates of changes in both depression and anxiety symptom response. These variables included age, gender, location of program (Finland or United States), length of program (8 weeks versus 12 weeks), baseline level of depression and anxiety symptoms, and average number of days active (e.g., engaging in any program practices, watching content, or messaging) with the MHP. These covariates were selected based on prior studies showing significant associations with changes in mental health symptoms after treatment (Trivedi et al. 2006) as well as with changes in HRV (Wong et al. 2001). Program completion was defined as watching at least half of the weekly psychoeducation video lessons during the program (e.g., at least 4 in the 8-week program and at least 6 in the 12-week program). Because using approaches such as stepwise regression to select covariates have led to overfitting, model instability, and issues replicating key findings (Steyerberg et al. 2000; Babyak 2004), we adjusted our analyses for the aforementioned covariates pre-selected based on literature showing significant relationships with HRV as well as with depression and/or anxiety.

Statistical Analysis

All statistical analyses were conducted in R (version 4.0.2). Statistical significance was defined using *p*-values < .05. Descriptive statistics (i.e., n and percentages or mean and standard deviations) were calculated for each patient demographic and clinical variable, engagement characteristic, and each outcome variable (see Table 1). Outcome measures were analyzed using an intention-to-treat (ITT) analysis, in which all participants with outcome measures at baseline were included, regardless of intervention engagement or attrition, and last observation carried forward was used for the final PHQ-9 and GAD-7 scores.

In our first analysis, we ran a linear regression where we used total time spent and average time spent in resonance per session throughout the MHP as predictors of changes in PHQ-9 and GAD-7 scores, after adjusting for relevant covariates including baseline PHQ-9 and GAD-7, days spent in program, age, and gender.

For our second set of analyses, we first ran a multilevel model using the lme4 package (Bates et al. 2014) in R to disaggregate within-person and between-person differences in resonance by grouping HRVB sessions within individuals. We adjusted for the duration of the HRVB session and created individual slopes by including a "days" variable, with 0 being the first day an individual used the HRVB device. We then scaled this variable and added it in as both a random and fixed effect. This model allowed us to extract individual intercepts (i.e., mean resonance per session across treatment) and slopes (i.e., trajectory of time in resonance across treatment).

We then used a linear regression model utilizing extracted individual resonance intercepts and slopes to predict changes in depressive and anxiety symptoms across treatment after controlling for relevant covariates including baseline PHQ-9 and GAD-7, days spent in program, age, and gender.

Finally, in order to extrapolate our findings for relevance to clinical settings, we took the unstandardized betas of the slopes from the linear regression models to determine how much a unit increase in slope was related to reductions in depressive and anxiety scores.

Results

Analyses.

Total and Average HRVB Resonance and PHQ-9. Total time in resonance across the MHP was not significantly related to PHQ-9 change ($b=0.01$, 95% CI $[0.00, 0.01]$, $t(377)=1.27$, $p=.210$), but average resonance time per HRVB session was significantly associated with decreased PHQ-9 score across treatment ($b=-0.38$, 95% CI $[-0.76, -0.01]$, $t(377)=-1.99$, $p=.047$).

Total and Average HRVB Resonance and GAD-7. Neither total time in resonance across MHP ($b=0.01$, 95% CI $[0.00, 0.01]$, $t(377)=1.91$, $p=.057$), nor average time in resonance per HRVB session ($b=-0.28$, 95% CI $[-0.61, 0.04]$, $t(377)=-1.72$, $p=.086$) were related to change in GAD-7.

MLM Descriptives. The fixed-effects slope for scaled days of all individuals was $\hat{\beta}=-0.07$, 95% CI $[-0.10, -0.04]$, while the random-effects for the slope had a standard deviation of 1.40. The fixed-effects intercept was $\hat{\beta}=2.10$, 95% CI $[1.99, 2.21]$, while the random-effects for the slope had a standard deviation of 0.29.

Within Person Effects of Time in Resonance on PHQ-9 and GAD-7. First, we used the individual slopes (within-person effects) of time spent in resonance as predictors of changes in depression (PHQ-9) and anxiety (GAD-7) symptom scores in separate models. Steeper positive slopes of time spent in resonance were significantly related to reductions in PHQ-9 scores across treatment ($b=-2.33$, 95% CI $[-4.44, -0.22]$, $t(376)=-2.17$, $p=.031$). In order to determine whether the slope variable was predicting a significant portion of the variance, we removed it from the model to see if there was a significant change in R^2. When comparing a model with the slope included and with the slope excluded, there was a significant change ($\Delta R^2 = 0.01$, $p=$ ¿ .025). Next, we wanted to determine whether changes in GAD-7 scores were predicted by changes in slope. Steeper slopes of time spent in resonance were significantly related to reductions in GAD-7 scores across treatment ($b=-1.84$, 95% CI $[-3.66, -0.01]$, $t(377)=-1.98$, $p=.049$). Again, we removed the slope value from the model to determine its explanatory value, and it did significantly add explanatory value to the model ($\Delta R^2 = 0.01$, $p=$ ¿ .049).

Between Person Effects of Time in Resonance on PHQ-9 and GAD-7. Individual intercepts were not significantly associated with changes in PHQ-9 scores ($b=-0.19$, 95% CI $[-0.53, 0.15]$, $t(376)=-1.08$, $p=.282$). The average intercept was also not associated with changes in GAD-7 scores ($b=-0.01$, 95% CI $[-0.31, 0.28]$, $t(377)=-0.08$, $p=.937$).

Clinical Relevance. Extrapolating our findings for relevance to clinical settings, we find that a 0.1 unit increase in slope of each adjusted peak in the depression and anxiety model is associated with a 1.23-point reduction in PHQ-9 and a 0.96-point reduction in GAD-7, respectively.

Discussion

The current study investigated the association between time spent in HRVB resonance (total and average time per session) and changes in depressive and anxiety symptoms. Additionally, we also examined whether individual HRVB resonance trajectory (within-person effects) of time spent in resonance and individual HRVB resonance intercepts (between-person effects) were associated with depressive and anxiety symptom changes. The findings provided partial support for our hypothesis. Average resonance time per HRVB session was associated with decreasing PHQ-9 scores across treatment, but not GAD-7 scores. This indicates that individuals who spent more time, on average, in resonance within a session were likely to have greater reductions in PHQ-9 scores. In contrast, total time spent in resonance across the MHP was not associated with reductions in PHQ-9 or GAD-7 scores. These findings were in line with our hypothesis of significant associations between HRV indicators and depression but not anxiety. Because our analyses were exploratory and the sample size needed to detect significant differences was not calculated *a priori*, the lack of significant finding for anxiety associations could be due to inadequate power. Additional powered analyses are needed to explore and confirm these associations.

In addition, when examining within-subject effects across treatment, we found that the steeper an individual's slope of time spent in resonance (i.e., improvements in resonance efficiency) across the MHP, the greater the reductions in both PHQ-9 and GAD-7 scores. In contrast, the intercepts at the mid-point of the program for each individual were not associated with PHQ-9 or GAD-7 scores. This indicates that the within-person effects (i.e., changes in an individual's resonance efficiency over time) are related to changes in mental health scores, while between-person effects (i.e., individual ability of resonance breathing) was not related to changes in mental health scores.

These findings confirm results from prior studies that have found significant associations between HRVB practice and improvements in mental health outcomes (Caldwell and Steffen 2018), and provide important clinical implications for incorporating HRVB into mental health treatments. Specifically, one's general ability to achieve resonance (i.e., intercept) was not associated with anxiety and depressive outcomes, while improvements (regardless of starting point) in the ability to achieve resonance over time (i.e., slope or resonance efficiency) were associated with significant reductions in depression and anxiety symptoms across treatment. These findings suggest that HRVB is a malleable and trainable skill in mental health settings, such that patients can learn how to achieve resonance breathing with practice, regardless of their initial ability, which in turn is associated with improvements in mental health outcomes. Furthermore, because resonance breathing was significantly associated with outcomes above and beyond all covariates, including engagement, it suggests that including HRVB as a component of a mental health intervention likely has a generalizable impact on clinical outcomes regardless of patient demographic backgrounds or total time spent engaging in other program activities.

Limitations and Future Directions.

The robustness of the sample, made up of nearly 387 individuals with 16108 HRVB sessions between them, was a strength of the study. Additionally, the use of standardized outcome variables (PHQ-9 and GAD-7) collected at multiple times during the intervention was another strength. Despite these strengths, however, our results should be interpreted within the context of several limitations. First, no clinical oversight was provided to help each study participant achieve resonance breathing, as the intervention was delivered remotely. Each individual was taught to breathe at a rate of approximately six breaths per minute, which is not always the precise rate by which people achieve resonance breathing. Future studies should allow more flexibility in breathing rate to account for individual differences in optimal resonance breathing. Second, these are only findings from one sample of participants of a single mental health intervention; thus, replication of these findings and application to other types of samples is needed. In addition, our results only generalize to users of the MHP who practiced HRVB at least 6 times and should be interpreted as such. Third, it could be possible that individuals who improve at adhering to protocols, overall, are more likely to have improvements in mental health (which would, as a byproduct, lead to improved resonance breathing), although we did adjust our analyses for total time of engagement with the MHP and still found significant associations between mean number of minutes of resonance per HRVB session and depression improvements. Additionally, traditional HRVB is measured with both a PPG and a respiration monitor. Unfortunately, for this study, participants only had a PPG device to collect pulse information, and we were unable to use data from a respiration monitor to assess resonance breathing. Lastly, this study did not include other treatment arms with interventions expected to have similar effects to HRVB on mental health outcomes, such as paced breathing, which precludes the ability of this study to conclude that beneficial effects came from resonance breathing specifically, rather than the alternate forms of adjunctive components within the MHP. For example, one study found that HRVB had no significant improvement when compared to a slowed breathing protocol in controlling physiological arousal and reducing anxiety (Wells et al., 2012), indicating that a simple breathing exercise may have comparable effectiveness without the need for HRVB devices, which would reduce the overall cost of treatment.

Future studies are needed to confirm the findings of the present investigation. All individuals in this study were instructed to breathe at a rate of 6 breaths per minute, which might not be the optimal rate for some to achieve resonance frequency breathing. Two prior studies have indicated that breathing at resonance frequency may produce better outcomes than breathing at resonance frequency plus one breath per minute or having all subjects breathe at 6 breaths per minute (Steffen et al. 2017; Lin, Tai, and Fan 2014), which suggests that future studies should incorporate a step to find each individual's resonance frequency breathing rate as part of the treatment program. These studies can also test whether other ranges of LF breathing, such as 0.75 to 0.11, might lead to more precise findings and/or determine the robustness of the conclusions.

Conclusion

To our knowledge, this is the first study that has examined the association between different resonance metrics indicated during HRVB sessions and mental health outcomes such as depressive and anxiety symptoms. Our results demonstrate that changes in mental health symptoms are related to resonance breathing and HRVB practice. More specifically, we have found that improvements in resonance efficiency over time, independent of how one starts, are related to reductions in depression and anxiety symptoms. It is an important first step of determining how patients should be advised to practice HRVB in order to maximize its benefits.

Declarations

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Drs. Pettitt and Nelson are employed by Meru Health Inc. and receive salary from the company. Mr. Ranta serves as the Chief Executive Officer (CEO) at Meru Health, Inc., owns a large share of stocks, and raises salary from the company. Mr. Nazander serves as the Chief Technology Office (CTO) at Meru Health Inc., owns a large share of stocks, and raises salary from the company. Drs. Gevirtz and Lehrer are advisors of Meru Healtlh, Inc. and own options of the company. Dr. Forman-Hoffman is employed by Meru Health, Inc., receives salary from the company and owns options of the company.

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Table 1

Characteristic	Overall, N = 387	12 Weeks, N = 320[1]	8 Weeks, N = 67[1]	p-value[2]
Total HRVB Minutes	156.86 (135.89)	140.76 (122.98)	233.71 (166.25)	**<0.001**
Total Active Days	38.03 (19.07)	37.75 (20.11)	39.36 (13.04)	0.2
Baseline PHQ9	11.73 (6.14)	11.03 (6.22)	15.10 (4.45)	**<0.001**
Last PHQ9	6.71 (5.30)	6.28 (5.23)	8.81 (5.15)	<0.001
Baseline GAD7	11.73 (4.64)	11.68 (4.79)	12.00 (3.84)	0.5
Last GAD7	6.78 (4.37)	6.56 (4.38)	7.85 (4.19)	**0.017**
Completion Status				0.063
completer	361 / 387 (93%)	295 / 320 (92%)	66 / 67 (99%)	
dropout	26 / 387 (6.7%)	25 / 320 (7.8%)	1 / 67 (1.5%)	
PHQ9 Change Score	-5.02 (5.41)	-4.75 (5.32)	-6.30 (5.72)	**0.010**
GAD7 Change Score	-4.95 (4.76)	-5.12 (4.88)	-4.15 (4.11)	0.14
Time in Resonance Intercept	2.15 (1.42)	2.07 (1.41)	2.51 (1.41)	**0.011**
Time in Resonance Slope	-0.07 (0.21)	-0.07 (0.20)	-0.09 (0.26)	0.2
Total HRVB Sessions	22.21 (15.93)	21.71 (15.97)	24.64 (15.63)	0.052
Age	39.66 (9.58)	40.06 (10.08)	37.73 (6.46)	0.2
Gender				**0.035**
Female	307 / 387 (79%)	247 / 320 (77%)	60 / 67 (90%)	
Male	80 / 387 (21%)	73 / 320 (23%)	7 / 67 (10%)	

[1]Statistics presented: mean (SD); n / N (%)

[2]Statistical tests performed: Wilcoxon rank-sum test; Fisher's exact test; chi-square test of independence

PHQ9 = Patient Health Questionnaire – 9, GAD7 = General Anxiety Disorder – 7, HRVB = Heart Rate Variability BioFeedback