Biofeedback treatment increases heart rate variability in patients with known coronary artery disease

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Objectives To determine if cardiorespiratory biofeedback increases heart rate variability (HRV) in patients with documented coronary artery disease (CAD).

Background Diminished HRV has been associated with increased cardiac morbidity and mortality. Evidence suggests that various lifestyle changes and pharmacologic therapies can improve HRV. The objective of this study was to determine if biofeedback increases HRV in patients with CAD.

Methods Patients with established CAD (n = 63; mean age, 67 years) were randomly assigned to conventional therapy or to 6 biofeedback sessions consisting of abdominal breath training, heart and respiratory physiologic feedback, and daily breathing practice. HRV was measured by the standard deviation of normal-to-normal QRS complexes (SDNN) at week 1 (pretreatment), week 6 (after treatment), and week 18 (follow-up).

Results Baseline characteristics were similar for the treatment and control groups. The SDNN for the biofeedback and control groups did not differ at baseline or at week 6 but were significantly different at week 18. The biofeedback group showed a significant increase in SDNN from baseline to week 6 ($P < .001$) and to week 18 ($P = .003$). The control subjects had no change from baseline to week 6 ($P = .214$) and week 18 ($P = .27$).

Conclusions Biofeedback increases HRV in patients with CAD and therefore may be an integral tool for improving cardiac morbidity and mortality rates. (Am Heart J 2004;147:e11.)

Low heart rate variability (HRV) is an independent risk factor for sudden cardiac death, all-cause death, and cardiac event recurrence.[1,2] HRV is defined as the fluctuations in heart rate (HR) from beat-to-beat as measured in milliseconds. The standard deviation of normal-to-normal beats (SDNN) is significantly related to cardiac function, specifically to left ventricular dysfunction, peak creatine kinase, and Killip class.[3] HRV is most commonly measured at each interval between QRS complexes. This is called a normal-to-normal (NN) interval. SDNN is the primary measure used to quantify HRV change, since "SDNN reflects all the cyclic components responsible for variability in the period of recording."[3] In recent decades, it has become a prominent predictor and diagnostic tool for cardiovascular disease.

Many studies have found low HRV to be of prognostic value in the prediction of all-cause death for those who have had myocardial infarction, congestive heart failure, and coronary artery disease (CAD).[1,4–8] For example, Kleiger et al[1] found a 4-fold increase in relative risk of death in 808 patients after myocardial infarction with low HRV (<50 ms) compared with those with high HRV (>100 ms). HRV remained the strongest single predictor of death after accounting for medications, demographics, and multiple clinical factors.

Lehrer et al[9] demonstrated that training subjects to maximize peak HR differences with visual and auditory feedback can increase homeostatic reflexes, lower blood pressure, and improve lung function. They postulate that this reflects improved homeostatic functions within the sympathetic and parasympathetic nervous systems. Although the underlying physiologic mechanism is not fully understood, the literature supports biofeedback and breathing retraining as a treatment to help reverse the decrease in HRV that occurs with heart disease.[10–12]

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Although limited in number, several studies have attempted to use biofeedback to alter HRV. Reyes del Paso et al[11] examined whether respiratory sinus arrhythmia (RSA) feedback, the variation in heart rate that accompanies breathing, could increase voluntary control of HRV in healthy volunteer subjects. They found that the group with breathing instruction combined with biofeedback, as well as the group with breathing instruction alone, increased RSA faster than did control subjects. The group with combined breathing instruction and biofeedback had the best performance. Cowan et al[12] are the only investigators to date to have used biofeedback training to increase HRV in cardiac patients. After biofeedback treatment, HRV increased significantly through the use of SDNN time-domain measures. Unfortunately, there were only 6 subjects, and there was no control group.

Many studies measuring HRV use 24-hour Holter monitoring. There is evidence, however, that short-term power spectral measures of HRV are also powerful predictors of all-cause death, cardiac-related deaths, and arrhythmic deaths. Two- to 15-minute analyses have been found to correlate highly with 24-hour values.[2,13]

Based on current research, HRV biofeedback appears to be a promising technique for HRV increase. We performed a prospective study to more conclusively determine if biofeedback can improve HRV in patients with known CAD.

Methods

This study was conducted at Scripps Clinic, Scripps Green Hospital, and Scripps Center for Integrative Medicine between February 2001 and November 2001. All patients provided written informed consent, and the study was approved by the institutional review board at Scripps Clinic.

The participant population included cardiac patients ages 45 to 84 years with CAD. A total of 63 participants were enrolled for the entire study. Every participant had documented CAD defined by one of the following according to their medical records: ≥50% blockage of the left anterior descending artery, right coronary artery, or circumflex artery on coronary angiography; a reversible perfusion defect on chemical stress testing (cardiolite, PET, or thallium); inducible wall motion abnormality on a stress echocardiogram; a history of percutaneous coronary intervention (angioplasty, stent, atherectomy, or laser); or a history of coronary artery bypass surgery. Participation was delayed if potential participants had a myocardial infarction within 2 weeks of enrollment or a coronary intervention within 6 months of enrollment.

Potential participants were excluded from the study if they met the criteria for class IV congestive heart failure according to the New York Heart Association, had a pacemaker, atrial fibrillation, or other arrhythmia precluding the use of HRV measurements, or if they were currently participating in another investigational clinical trial. The 61 patients who met the criteria for the study were randomly assigned to the treatment or control group and were asked to refrain from caffeine, alcohol, and vigorous exercise for 4 hours before each appointment. Participants were instructed to take all medications as usual.

HRV measurements were taken at week 1, 6, and 18. All groups were measured in a standardized fashion, using a 15-inch laptop computer connected to a Cardiopro monitor (Thought Technology; Montreal, Canada). The Cardiopro sampled heart rate 256 times every second, and SDNN was calculated to quantify HRV. In addition, we analyzed 2 other time-domain indexes, the root mean square of successive differences (RMSSD) and the standard deviation of the average of normal-to-normal beats (SDANN). The Cardiopro recorded data for 15 minutes and divided it into three 5-minute epochs. Electrocardiography was recorded with three electrodes attached to the chest. Respiration was recorded with a 2 PS-1 strain gage/tube filled with conduction fluid with a range of 0 to 100 units of relative strength.

The treatment groups received biofeedback treatment once per week for 45 minutes at weeks 1 through 6. Biofeedback treatment sessions consisted of breath retraining with an emphasis on abdominal breathing, as well as cardiac and respiratory feedback. This was accomplished by using a C2 biofeedback machine (J & J Engineering; Poulsbo, Wash) and a 15-inch laptop computer. Physiological feedback was monitored visually on the computer screen. Participants were trained to practice breathing at their peak RSA, attempting to increase peak/valley amplitude of the HR signal. Various color screens were displayed, reflecting depth and frequency of respiration, HR, and HRV. A 3-D screen showed heart rate frequencies and grouped them into high, low, or very low.[12,14] A session-by-session description has been published elsewhere.[9] Each participant was given a weekly chart on which to log daily breathing practice, exercise, other stress management techniques, and any change in medications. Participants were encouraged to practice abdominal breathing for at least 20 minutes per day, and they received written material to help facilitate home practice.

All participants were measured for HRV and blood pressure at week 1, week 6, and week 18. Each participant was measured for 15 minutes, at the same time each day, seated in a comfortable chair, while listening to a neutral travel tape to provide a standardized stimulus minimizing movement artifact.

All data were carefully edited through the use of visual screening and the manual corrections program on the Cardiopro. Artifact was discovered and edited by following the Installation and User's Manual for the Cardiopro, coinciding with several experts' agreed-upon method for editing. Experimenters were kept blind about what group participants were in. After generating each participant's session, we visually examined each 5-minute tachogram for suspected artifact. We then examined the corresponding heart beat, splitting the beat if it recorded approximately twice the expected value, adding 2 heart beats if it recorded approximately half the expected value, or averaging 2 beats if it recorded one elongated beat followed by an unusually short beat. Since deletion of beats can bias the results, no beats were manually deleted in the editing process. Recommendations were followed concerning signal-to-noise ratio, common mode rejection, and bandwidth according to the Task Force.[3]

Statistical analysis

A mixed analysis of variance and 2 one-way analyses of variance were carried out to examine SDNN. Mixed analyses were also used to examine SDANN and RMSSD. The within-group subject factor was time; the between-group subject factor was treatment. Specific differences among the three measurement sessions were examined by using independent and paired Student t tests. A P value $< .05$ was regarded as significant. A manipulation check was done to examine low frequency (LF) during and between treatment sessions by using a mixed analysis of variance. All the data were analyzed with the use of SPSS, version 9.0 (SPSS Incorporated, Chicago, Ill). Nondefault functions were not used. The assumption of sphericity occurs in repeated-measures analyses of variances with more than 2 levels. The Huynh-Feldt correction was used for the analyses to correct for type I error created by the violation of the sphericity assumption. All P levels reported are therefore Huynh-Feldt corrected.

Results

One hundred twenty-two patients were screened over the telephone for the study and 69 participants met the criteria and were randomly assigned. Six participants (8.7%) did not complete the study: 2 participants listed time conflict as a reason for dropping out of the study and 4 participants did not list a reason. No significant differences were found on demographic variables between those who discontinued the study and those who completed the study. There were no significant differences between treatment and control groups on demographic or clinical features, including ejection fraction, as shown in Table I. Similarly, no significant pretreatment differences existed for SDNN measures between the groups, ($P = .072$ and $P = .162$, respectively) (Table II). Baseline respiratory rate and heart rate did not significantly change across the three measurement sessions ($P = .073$ and $P = .217$, respectively).

Expected diaphragmatic breathing practice at home was 20 minutes per day. Compliance of 100% was considered 2520 minutes over the course of the 18-week treatment. There was a broad range of reported compliance with the recommended treatment program: 38% fulfilled 90% or more of the required practice, 32% fulfilled between 50% to 89% of the required practice, and 30% of participants fulfilled between 16% and 49% of the required practice. The mean practice time was 1908 minutes (SD = 979.58), or 75%, over the 18 weeks. This averages to approximately 15 minutes per day. There was not a significant correlation between self-reported practice and SDNN [$r = 0.104$, $P = .593$].

SDNN over the three 5-minute epochs was averaged for each measurement session. The means and standard deviations are shown in Table II. There was a significant interaction (Table II) and a significant effect over time for the treatment group (simple effects analysis). The control subjects, however, did not show a significant time effect. This group actually showed a trend for reduced HRV as measured by SDNN.

As shown in Table II, the groups did not significantly differ at time 1. However, at time 3, the groups did differ significantly. The treatment group increased HRV significantly between week 1 and week 6 and week 1 and 18 but not between week 6 and 18. The control group did not change significantly between week 1 and 6 or between week 6 and 18; however, it significantly decreased SDNN between week 1 and week 18. Overall, the treatment group increased SDNN 39.2%, whereas the control group decreased SDNN by 9.9% (Figure 1).

Besides SDNN, 2 other primary measures of HRV are the SDANN (standard deviation of the average of NN intervals) and the RMSSD (square root of the mean squared differences of successive NN intervals). There was a significant time by treatment interaction, such that the treatment group improved over time whereas the control group remained the same for the SDANN

Table I. Clinical characteristics of study population

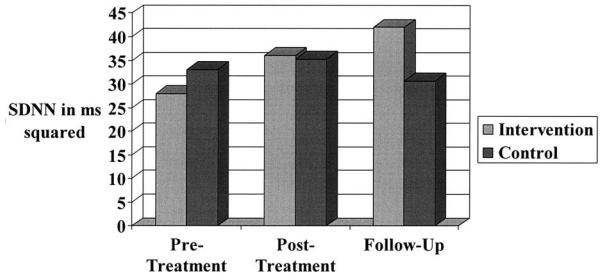
	Treatment	Control	P
Age (y, mean)	66.81 ± 8.4	67.97 ± 8.98	NS
Sex (%)			NS
Female	11 (35.5)	10 (31.3)	
Male	20 (64.5)	22 (68.8)	
Height (in, mean)	67.1 ± 4.28	67.28 ± 3.97	NS
Weight (lbs, mean)	171.47 ± 36.11	167.28 ± 35.22	NS
Height/weight	.397 ± 7.52E-02	.41 ± 7.3E-02	NS
Marital status (married) (%)	21 (67.7)	26 (81.3)	NS
Education (%)			
High-school graduate	30 (100)	31 (96.9)	NS
Graduate level	13 (41.9)	11 (34.4)	
White (%)	31 (100)	31 (96.9)	NS
Medical history (%)			
Myocardial infarction	13 (42)	14 (43.8)	NS
CABG	10 (32.3)	13 (40.6)	NS
Stent	18 (58.2)	13 (40.6)	NS
Diabetes mellitus	3 (9.7)	5 (15.6)	NS
Stoke	2 (6.5)	1 (3.1)	NS
Cancer	6 (19.3)	8 (25)	NS
Smoking			
Duration (y)	16.6 ± 17.12	15.7 ± 17.19	NS
Amount (mean, ppd)	1.1 ± 1.16	.89 ± 1.1	NS
Alcohol (mean per week)	1.7 ± 1.5	2.23 ± 1.25	NS
Medications (%)			
β-Blockers	12 (38.7)	14 (43.8)	NS
ACE inhibitors	5 (16.1)	6 (18.8)	NS
Aspirin	21 (67.7)	19 (59.4)	NS
Ejection fractions	62.78 ± 11	65.01 ± 11.5	NS

Table II. SDNN measured across the 3 measurement sessions

	Week 1	Week 6	Week 18	ANOVA (*P*)
SDNN				<.001
Treatment (mean ± SD)	28.0 ± 15.2	36.1 ± 18.3	42.0 ± 25.8	
Control (mean ± SD)	33.0 ± 12.6	35.2 ± 13.5	30.7 ± 15.4	
Treatment only across time				.004†
Control only across time				NS
Dependent *t* test	NS	NS	.04	
Independent *t* test	Week 1 vs 6	Week 6 vs 18	Week 1 vs 18	
Treatment	<.001	NS	.003	
Control	NS	.01	NS	

ANOVA, Analysis of variance.
*Interaction.
†Simple effects.

Figure 1



SDNN at week 1, week 6, and week 18 for treatment and control groups.

and RMSSD ($P = .001$ and $P = .021$, respectively). For the SDANN, there were no significant differences between the groups at week 1, week 6, or week 18. However, the treatment group significantly increased between week 1 and week 6, between week 1 and week 18 but not between week 6 and week 18. The control group did not significantly change between week 1 and week 6 but did decrease significantly between week 1 and week 18 and also between week 6 and week 18. For the RMSSD measure, there was a significant difference between the treatment and control group at week 1 but no difference at week 6 or week 18. The treatment group significantly increased between week 1 and week 6 and between week 1 and week 18. However, no significant change was found between week 6 and week 18. The control group did not change between any measurement times.

The biofeedback technique emphasized producing heart rate frequencies within a specific LF bandpass (0.05 to 0.14 Hz). Twenty participants in the treatment group were randomly chosen to assess treatment effectiveness within and between sessions. LF was measured by the spectral analyses during treatment sessions 2, 3, 4, and 5. An increase in LF spectrum occurred within each session, whereas the total spectrum (total power) remained the same from the beginning of the session to the end. LF also increased between each session, whereas the total spectrum remained the same from the beginning to end of each session. The total spectrum was controlled to observe a change in LF within and between treatment sessions. This was calculated by averaging the first 2 minutes and last 2 minutes of each treatment session. LF increased within and between sessions ($P < .01$), thus showing an increase in LF throughout treatment.

Summary and discussion of findings

This study showed that HRV increased in patients with CAD with biofeedback treatment as compared with the control subjects. In 6 weeks, the treatment group had increased HRV, as measured by SDNN, SDANN, and RMSSD, whereas the control subjects showed a decreasing trend. These results were maintained at the week 18 follow-up assessment and were of a sufficient magnitude to justify the expectation of clinical improvement.

The manipulation check examined the treatment session changes as measured by the spectral analysis. The increase in LF power with the percentage of overall power in the spectral analysis remaining the same suggests that the resulting increase in HRV was related to the increase in RSA amplitude during treatment. This may reflect an increase in overall parasympathetic function, an increase in the sympathetic/parasympathetic balance, or an improvement in baroreflex sensitivity. It has been hypothesized that the body's systems (such as the circulatory system) function best when the sympathetic and parasympathetic nervous systems are in balance. Lack of homeostasis may increase cardiovascular disease risk.[5,6]

Despite the lack of systematic normative data, associations found between HRV measures and health have led to the commonly used cutoffs of 50 ms and 100 ms for SDNN. Kleiger et al[1] reported the relative risk of death to be 5.3 times higher for people with SDNN of <50 ms compared with those over 100 ms and 1.6 times higher for people with SDNNs of 50 ms to 100 ms compared with those >100 ms. Therefore, >100 ms is considered "healthy," between 50 ms and 100 ms is considered "compromised health," whereas <50 ms is considered "unhealthy."[1] This suggests that some participants in the treatment group improved their SDNN enough to benefit their risk status, improving

from the "unhealthy" range to the "compromised health" range. This, together with the fact that most subjects in the treatment group but not the control group showed substantial gains in HRV, indicates that HRV biofeedback may be able to produce meaningful physiologic changes and improved clinical outcomes.

These findings are consistent with prior literature that showed that participants were able to control cardiac responses with behavioral treatments.[10–12,15,16] The mechanism of change in HRV is not fully understood; however, Lehrer et al[17] found RSA heart rate biofeedback training increased the variability in interbeat-interval measurements and also "exercised" the baroreflexes resulting in more efficient operation of the baroreceptors (which control blood pressure). They postulated that RSA training reregulates the autonomic nervous system and balances the sympathetic and parasympathetic branches.

Interestingly, the main effect of our study was seen in the first 6 weeks, and although it persisted at 3 months, there was no further significant improvement after the initial change. In addition, HRV improvement was not correlated with the amount of home practice. This suggests that the most powerful intervention is the initial teaching and counseling about biofeedback, and sustained benefits probably persist over the long term.

Study Limitations

This study has several limitations. First of all, we did not have a placebo control. However, we did include a control group, which is an improvement over prior published studies. It is difficult to hypothesize how a placebo could affect HRV, but we cannot rule it out in the absence of a placebo. Our study was ethnically and socioeconomically homogenous; therefore the results may not be directly applicable to all patient populations. However, we did have a relatively large patient group, which were representative of the patient population at Scripps Clinic. Although we provided a 3-month follow-up, we did not measure actual clinical outcomes. Instead, we used the well-established surrogate marker of HRV. Several reviews claim HRV to be the single greatest predictor for mortality and morbidity, especially for people with cardiovascular disease[1,5–8,18]; therefore, it is possible that any increase in HRV is beneficial to the health of a patient with compromised HRV. Up to this time, it has not been clear whether or not disease populations would be able to increase HRV through behavioral interventions such as biofeedback. The current findings can be strengthened by measuring other meaningful clinical outcomes such as cardiac event recurrence, mortality rates, and cardiac test results, but in absence of such results, increases in HRV are still promising. Future research needs to measure long-term morbidity and mortality rates to explore whether the increase in SDNN is meaningful in the reduction of cardiac-related risk. In addition, future studies would improve our current study by enrolling a more heterogeneous socioeconomic group of patients, with the use of a sham biofeedback as a placebo, and looking at patient populations more diverse than those with CAD.

Conclusions

The current study indicates that patients with decreased HRV from CAD can be trained to increase HRV as measured by SDNN. Over a 6-week period, participants were able to learn to increase SDNN through diaphragmatic breathing and cognitive efforts during HRV biofeedback training. These changes were maintained at follow-up measurement 3 months later. If clinical outcomes verify the HRV findings, cardiorespiratory biofeedback may become a useful tool in cardiac rehabilitation.

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