

Heart Rate Variability Biofeedback as a Method for Assessing Baroreflex Function: A Preliminary Study of Resonance in the Cardiovascular System

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This study describes the use of a biofeedback method for the noninvasive study of baroreflex mechanisms. Five previously untrained healthy male participants learned to control oscillations in heart rate using biofeedback training to modify their heart rate variability at specific frequencies. They were instructed to match computer-generated sinusoidal oscillations with oscillations in heart rate at seven frequencies within the range of 0.01–0.14 Hz. All participants successfully produced high-amplitude target-frequency oscillations in both heart rate and blood pressure. Stable and predictable transfer functions between heart rate and blood pressure were obtained in all participants. The highest oscillation amplitudes were produced in the range of 0.055–0.11 Hz for heart rate and 0.02–0.055 Hz for blood pressure. Transfer functions were calculated among sinusoidal oscillations in the target stimuli, heart rate, blood pressure, and respiration for frequencies at which subjects received training. High and low target-frequency oscillation amplitudes at specific frequencies could be explained by resonance among various oscillatory processes in the cardiovascular system. The exact resonant frequencies differed among individuals. Changes in heart rate oscillations could not be completely explained by changes in breathing. The biofeedback method also allowed us to quantify characteristics of inertia, delay, and speed sensitivity in baroreflex system. We discuss the implications of these findings for using heart rate variability biofeedback as an aid in diagnosing various autonomic and cardiovascular system disorders and as a method for treating these disorders.

KEY WORDS: biofeedback; heart rhythm variability; respiratory sinus arrhythmia; baroreflex; resonance; Fourier filtration procedure; transfer functions.

INTRODUCTION

The baroreflexes (BRs) are important mechanisms for cardiovascular regulation (Eckberg & Sleight, 1992). Changes in blood pressure (BP) are detected by pressure

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receptors (baroreceptors) in the large blood vessels (principally the aorta and carotid artery). Neural input from the baroreceptors triggers reflexes that produce contingent changes in heart rate (HR) and vascular tone (VT). The increases in BP produce decreases in HR and VT, and decreases in BP produce increases in HR and VT. These changes help to modulate changes in blood pressure. By mechanical action, BR-induced increases in HR and in VT produce increases in BP, whereas BR-induced decreases in HR and in VT produce decreases in BP. Oscillations in BP therefore produce oscillations in HR and in VT, which, in turn, maintain the oscillatory activity in BP, and modulate it, thus regulating BP. There are at least two branches of the baroreflex system: a HR baroreflex and a VT baroreflex (DeBoer, Karemaker, & Strackee, 1987; Kirchheim, 1976; Taylor & Eckberg, 1996). Thus far the HR baroreflex has been the main focus of investigation.

In some approaches to studying BR activity, changes in BP are induced by chemical or mechanical stimulation, and contingent changes in HR are examined. In other procedures, naturally-occurring oscillatory changes are assessed. As we will point out below, all of these methods may be either insensitive to naturally-occurring BR function or unrepresentative of it. This study illustrates how biofeedback can be used for more precise noninvasive assessment of BR function, and for modeling the BR system using transfer function analysis of biofeedback-induced oscillations in heart rate and blood pressure.

Heart Rate and Cardiovascular Variability

Normal heart rate variability (HRV) has been described as having a pattern of several overlapping oscillatory frequency components. Three of these have been identified: a “high-frequency” rhythm (0.15–0.4 Hz), which usually corresponds to respiration, and is known as “respiratory sinus arrhythmia” (RSA); a “low-frequency” rhythm (0.05–0.15 Hz), which some studies have associated with BP oscillations (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology [Task Force], 1996; Zingerman, Konstantinov, Menitsky, Logvinov, & Vaschillo, 1988) and BR function (DeBoer et al., 1987; Vaschillo, 1984); and a “very low frequency” rhythm (0.005–0.05 Hz), which seems to be related to control of VT and temperature (Shusterman, Anderson, & Barnea, 1997; Task Force, 1996; Zingerman et al., 1988).

Oscillatory rhythms have been found in many physiological functions, including HR, BP, VT, and respiration. In the cardiovascular system they appear to reflect the health and adaptability of autonomic regulation, and have been used for examining the prognosis of some cardiovascular diseases (Bernardi et al., 1997; Task Force, 1996). There is evidence that the relative proportions of various frequency spectrum components change correspondingly with changes in autonomic balance (Berntson et al., 1997; Task Force, 1996; Vaschillo, 1984; Zingerman et al., 1988), and that the relationship between HR and BP oscillations reflects BR action (Akselrod, 1988; Bernardi et al., 1994; DeBoer et al., 1987; Eckberg & Sleight, 1992; Saul et al., 1991; Sleight et al., 1995; Taylor & Eckberg, 1996). Different mechanisms appear to underlie oscillations at each frequency range (Berntson et al., 1997; Task Force, 1996). We have proposed that the amplitude and complexity of the oscillatory pattern represents homeostatic capacity because the oscillation at each frequency represents a specific control mechanism in the body. A complex oscillatory pattern would therefore reflect the operation of multiple control mechanisms, which, in

turn, would reflect a strong capacity for regulatory control (Giardino, Lehrer, & Feldman, 2000).

Problems in the Investigation of HR Baroreflex Activity

One commonly used method for estimating BR activity is to calculate the slope between changes in BP and HR (Steptoe & Sawada, 1989). Although it is commonly used, this method is often unrepresentative of naturally-occurring BRs, because a large majority of such naturally-occurring changes fail to meet amplitude criteria for clear calculation of BR activity (e.g., changes of at least 2 ms in cardiac interbeat interval and corresponding changes of at least 1 mmHg in BP for each of three consecutive beats). Cross-spectral analysis of HR and BP also has been used for assessing BR activity. Here also, however, low oscillation amplitudes do not produce valid estimates of BR activity because cross-spectral estimations cannot be reliably calculated if the signal-to-noise ratio is low (i.e., HR and BP signals have low coherence, Berger, Saul, & Cohen, 1989; Eykhoff, 1974).

Methods used for increasing the amplitude of HR and BP changes have been used, but these may obscure the naturally-occurring processes by which BR activity ordinarily operates. Such methods have included the Valsalva maneuver (Eckberg & Sleight, 1992), head-up tilt (Taylor & Eckberg, 1996), and neck suction to the carotid sinus region (Bernardi et al., 1994; Eckberg & Sleight, 1992). The Valsalva maneuver is difficult to standardize as a physiologically meaningful stimulus, because effort and pressure may vary from person to person and from time to time. The neck suction method is problematic because it affects only the carotid BRs, and not the BRs in the aorta. Biochemical stimulation also has been used (e.g., with phenylephrine, which rapidly constricts the blood vessels, producing an immediate increase in BP and decreases in HR and VT). This method may effectively isolate the effect of specific reflexes but it is invasive and therefore may not accurately demonstrate the natural interplay among the various respiratory–cardiovascular rhythms and reflexes.

Voluntary alterations in respiratory patterns also have been used (Saul et al., 1991). This method is closest to the method we propose below, but it is inherently limited, because it cannot be used to study BR effects at very low oscillation frequencies, beyond the range of possible respiratory control. As will be illustrated below, examining very low frequency bands can detect the influence of various operating characteristics of the cardiovascular system, and their influence both on BR activity and in explaining biofeedback effects on cardiovascular oscillations and the BRs.

In previous studies cross-spectral analysis has been used for examining the amplitude and phase relationships between HR and BP. In doing so, investigators computed transfer functions between HR and BP across relatively broad frequency bands (0–0.4 Hz, Akselrod, 1988; Bernardi et al., 1994; DeBoer et al., 1987; Saul et al., 1991; Sleight et al., 1995; Taylor & Eckberg, 1996). However, this analysis only gives reliable estimations when the coherence between BP and HR oscillations is 0.5 or more (DeBoer et al., 1987; Saul et al., 1991). Methods used for increasing the amplitude of HR and BP changes do not provide sufficiently high coherence between BP and HR oscillations at all frequencies within this range; so conclusions about the relationships between variables at specific frequencies cannot be made. Also this approach may obscure some of the finer frequency-tuning that characterizes BR function.

Biofeedback Training to Increase the Amplitude of Heart Rate Variability

It has long been known that the amplitude of RSA increases when people breathe slowly (Brown, Beinghtol, Koh, & Eckberg, 1993; Cooke et al., 1998). Mechanisms that have been proposed for this include reflexes induced by increased intrathoracic pressure due to deeper breathing, chemical changes caused by slow breathing, and various chronotropic reflexes originating in the brain stem (Clynes, 1960; Malkin & Gora, 1996). Eckberg and Eckberg (1982) have proposed that the increase in RSA amplitude reflects the time required for hydrolyzation of acetylcholine, such that acetylcholine expressed by vagus nerve activity is more fully hydrolyzed only at slower respiration rates. If this is the case, the higher RSA amplitudes at slower respiration rates do not necessarily reflect increased vagus nerve traffic when people breathe more slowly.

Biofeedback researchers have recently become interested in training people to increase the amplitude of HRV rhythms as a method for improving autonomic homeostasis, for example, for treating irritable bowel syndrome (Gevirtz, 1999) and essential hypertension (Herbs, Gevirtz, & Jacobs, 1993). However, there has been little research on either human ability to perform this task or on the mechanisms by which increase heart rate variability (HRV) amplitude occurs. Similarly there has been little research on the effects of HRV amplitude training on homeostatic capacity. This paper describes a preliminary study of biofeedback-induced changes in heart rate oscillations, explores the various patterns of heart rate oscillations that can be produced at specific frequencies, and calculates the parameters for the various mechanisms of HRV biofeedback effects.

Below, we show exploratory data showing that people are capable of producing very high amplitudes of HRV, but only at specific frequencies, where processes underlying two or of the oscillatory functions in HR and BP can potentiate *each other*. We will show how this pattern reflects resonance characteristics in the cardiovascular system (DeBoer et al., 1987; Vaschillo, 1984) and will use these resonance characteristics to model baroreflex function.

Advantages of Biofeedback as a Method for Studying BR Activity

Previous studies (Vaschillo, 1984; Vaschillo, Zingerman, Konstantinov, & Menitsky, 1983) have demonstrated that biofeedback can be used to produce stationary high-amplitude sinusoidal HR and BP oscillations at specific target frequencies within the low (0.05–0.15 Hz) and very low (0.01–0.05 Hz) frequency ranges. Sinusoidal oscillations at each target frequency can be induced for sufficiently long periods to allow accurate calculation of transfer functions at each frequency using a Fourier filtration procedure (Eykhoff, 1974). This method allows calculation of the amplitude and phase values of transfer functions at specified frequencies. This contrasts with more widely used Fourier transformation, which only examines frequency *bands*. By varying the target frequency of the biofeedback procedure, the dynamic interplay between HR and BP can be measured very precisely. An additional advantage of this procedure is that it allows observation of naturally-occurring baroreflex action, not distorted by chemical or mechanical stimulation.

Biofeedback also has the advantage of increasing the proportion of HR and BP oscillations that can be used for calculating BR activity using the slope method (Steptoe & Sawada,

1989). The high amplitudes in BP and HR oscillations at specific frequencies produced by individuals using biofeedback allow inclusion of virtually all oscillations in calculation of BR activity.

The Baroreflex System as a System for Controlling BP

We view the baroreflex system as component in a general system for control of blood pressure. We, therefore, believe it is useful to assess characteristics of this *system*, rather than, as in previous research, just the effects of BP on HR. In a system, the various components control each other; thus, we view the baroreflex system as one in which HR and BP influence each other. We observe their mutual influence in time-linked oscillations that occur in the two variables. Various analytical techniques from systems engineering have been applied to studying system characteristics through analysis of such time-linked oscillations. We apply some of these methods in the current study, and studied some of the system components by experimentally manipulating one of them (HR), and observing the effects on the whole system. Because we conceptualize the goal of the baroreflex system as a component in the control of BP, we have chosen to manipulate HR (as the independent variable), and to examine the effects of this manipulation on BP (as the dependent variable), while assessing the ways in which the two variables interact (i.e., the system characteristics).

We note that the process by which HR affects BP differs from that by which BP affects HR. The direct effects of the baroreflex are on HR, that is, baroreceptors detect changes in BP and provide outputs that trigger reflexive changes in HR. The effects of HR on BP are mechanical, through the effects of blood flow changes on pressure in the vessels.

Transfer Functions of a Control System

We believe that the baroreflex system can be described using linear transfer function analysis. This common method in engineering utilizes a form of cross-spectral analysis, and experimental manipulation of input signals at various frequencies. It is used to examine the dynamic properties of various control systems, such as inertia (time constants), gain, delay, resonance, sensitivity, working frequency range, reaction speed, stability, etc. (Murphy, 1957). To calculate the transfer functions of the baroreflex system we must produce the sinusoidal HR, BP, and VT oscillations and evaluate amplitude and phase relationships among them.

Transfer function analysis allows us to calculate both amplitude and phase characteristics of an interaction between two time-linked oscillating processes (signals). The “amplitude transfer function” is the ratio between amplitudes of the output and input signals of system (i.e., gain of the system) at each frequency, across all frequencies examined, such that frequency dependence of these amplitude transfers can be observed. The “phase transfer function” shows the phase shifts between oscillations in the output and input signals at each frequency.

Linear transfer function analysis can reveal some important properties of a control system (Grodins, 1963). If the amplitude transfer function decreases as frequency increases, the system has inertia. If the system has a delay, the phase transfer function gradually decreases as the frequency increases. If the phase transfer function has positive values (i.e.,

the output signal follows the input signal in time), the system contains a speed sensitivity link. (In a speed sensitivity link, the amplitude of output oscillation is proportional to the rate of change in the input oscillation, and the output follows the input in time with a 90° phase relationship between the two variables.) If the phase transfer function has negative values at all frequencies, the system does not contain a speed sensitivity link. Finally, if the amplitude transfer function has a peak at a single frequency, the system has resonance. This often occurs in a control system with feedback loops, where the input and output signals entrain each other, and stimulate greater amplitudes in each other at a particular frequency.

A Two Closed Loop Model of the Baroreflex System

We know that the baroreflex system is more complex than a control system involving only HR and BP. For example, we know that VT also is affected by BR activity, such that increases in BP trigger decreases in VT and vice versa (Kirchheim, 1976). We propose that the BR system for controlling BP is more accurately modeled as a two closed loop system, as shown in Fig. 1. Here one loop involves HR and BP control systems, and the other VT and BP control systems. The BP control system is a common link to both loops.

The baroreflexes help to modulate BP through their influence on two physiological variables, HR and VT. The two loops are interconnected because they have common elements, namely the baroreceptors and the BP control system. HR, BP, and VT all participate

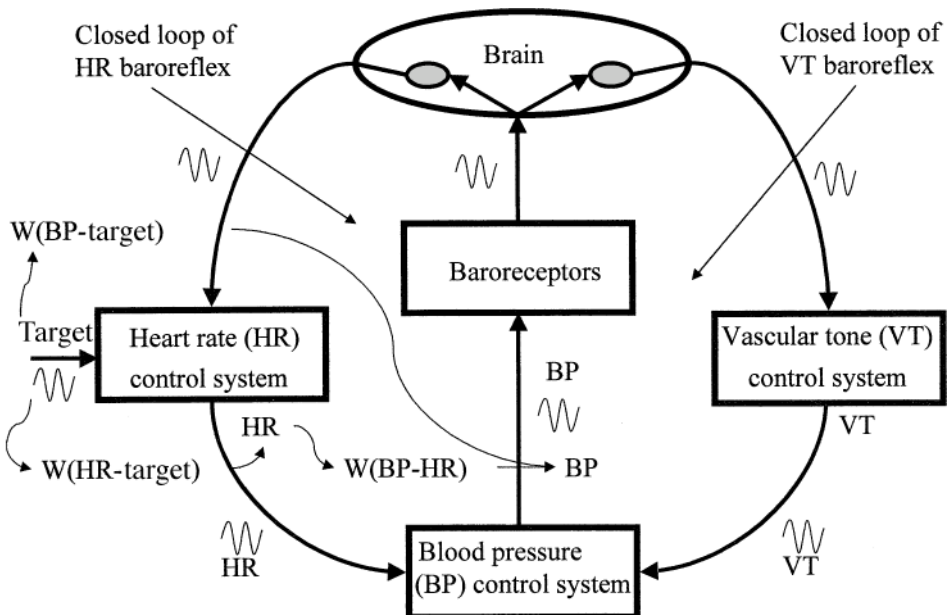


Fig. 1. A two closed loops model of the baroreflex system. $W(\text{HR-target})$, $W(\text{BP-target})$ indicate the transfer functions between the target stimulus as the input and, respectively, HR and BP as the output. $W(\text{BP-HR})$ indicates the transfer functions between HR as the input and BP as the output.

in the operation of these loops. Oscillations in any of these functions cause oscillations in the other two. The two closed loop model implies the following set of interrelated hypotheses.

1. The participant produces HR sinus oscillations using biofeedback.
2. HR sinus oscillations mechanically cause BP sinus oscillations, because of changes in blood flow.
3. The baroreceptors sense BP oscillations and modulate the brain structures that control HR and VT.
4. HR and VT sinus oscillations are produced by efferent neural impulses. These oscillations help to modulate changes in BP.
5. The interrelationships among oscillations in HR, VT, and BP produce sinusoidal oscillations that circulate in both loops of the baroreflex system.

Although we manipulated HR oscillations and studied their effects on BP in this study, we neither manipulated nor measured oscillations in VT. We nevertheless will note below the effects of the VT baroreflex loop that we observed indirectly.

METHODS

Participants and Structure of the Experiments

Five healthy male volunteers, ages 24–27 were repeatedly tested over 20 one-hr sessions, each on a separate day. The participants were Russian cosmonauts, with no previous experience or special prior interest in HRV or psychophysiological self-control. Each session began with a 5-min recording of baseline physiological data. Then the participants were asked to produce HR oscillations at seven specific frequencies within the range of 0.01–0.14 Hz in 5-min tasks. In each task, participants were presented with a sine wave stimulus, and were asked to duplicate this pattern with their own physiological function. They were not informed that the recording of their activity specifically represented HR.

Recording of Physiological Parameters

Prior to each session, electrodes and sensors were placed on the participant to record an electrocardiogram (ECG), a respiration curve (RC), and mean dynamic arterial blood pressure (BP). (The equipment we used provided on output of mean BP, but did not separately assess systolic or diastolic BP.) The ECG was recorded from the thoracic area using electrodes fastened by an elastic strap. The respiration curve was recorded from a carbon sensor stain gauge transducer located around the participant's chest. A DC amplifier without a time constant was used for the respiration signal. Continuous mean dynamic arterial pressure for each heart beat was recorded from sensors located on the fingers of the left hand. Our device (model 028, Krasnogvardeyets plant, Russia) used the same method as used in the well-known Finapres device. Both devices use the Penaz principle (Penaz, 1992). According to this principle, an external pressure is applied to an artery (usually through pressure around a finger). Mean dynamic arterial blood pressure is the "unloaded" artery size. An artery becomes "unloaded" when the external pressure equals the internal pressure. A servo control loop detects the unloaded artery size and traces (follows) its changes.

Apparatus

A polygraph (EEG 4756, Orion, Hungary) was used to record physiological data. All of these measures were transmitted to a computer via an analog-digital converter. ECG was sampled at 500 Hz. A computerized algorithm selected ECG R-spikes and measured cardiac interbeat interval (IBI) with an accuracy of 1 ms. Blood pressure and the respiration curve were sampled at 10 Hz. In order to smooth the curve of R–R intervals, the nonequidistant R–R interval time series was spline interpolated (cubic), and resampled at 10 Hz. Computer software automatically controlled the procedure for each session, with simultaneous processing of the physiological data.

Production of Feedback and Target Stimulus Signals

The participant sat in a comfortable armchair in a half-shaded room in front of a computer screen. Two signals were presented simultaneously on the screen: a feedback signal and a target stimulus signal (sine curve). The target stimulus signal was presented in the upper half of the screen. It consisted of a sine wave showing the frequency and amplitude at which participants were asked to reproduce the lower signal. Both signals were moving points, which left a track similar to an oscillograph ray and moved from left to right at a constant rate of 60 s/sweep. The HR biofeedback signal was presented in the lower half of the screen. The movement of the lower ray vertically reflected the continuous value of the participant's HR, which was calculated from cardiac interbeat interval.

Procedure

Each participant was informed that the position of the lower ray on the screen was associated with his "internal condition," and that the state could be controlled voluntarily. The participant was instructed to change his internal condition in such a way that the lower ray matched the oscillatory movement of the upper ray. The upper ray drew a sinusoidal signal on the screen with a period alternating among 100, 47, 34, 18, 13, 9, or 7 s, (i.e., frequencies $f_i = 0.010, 0.021, 0.029, 0.055, 0.077, 0.111, \text{ or } 0.143$ Hz). These intervals were chosen to provide an equal interval logarithmic scale on the frequency axis, where the difference between the logarithmic values of adjacent frequencies was 0.15 (i.e., $-2.00, -1.70, -1.55, -1.25, -1.10, -0.95, -0.80$). We excluded two values in this sequence (-1.85 and -1.40) to decrease the number of tasks in the experiment.

The participant was not specifically told how to control his internal state. We thus did not limit the methods (e.g., respiratory, muscular, and/or mental activity) by which participants could control their HR oscillations. Participants were instructed not to move, in order to reduce the probability of artifact in the ECG recording. The amplitude of the target stimulus was the same at all frequencies corresponding to a peak-to-peak HR variation of 60 beats/min. This value of amplitude was selected as a target based on preliminary data from a pilot study in which people were encouraged to produce maximum amplitude oscillations.

Mathematical Processing of the Experimental Data

We used the Fourier filtration procedure in order to obtain the values of the transfer functions between input (the target stimulus signal) and output (HR, BP, or RC) at each of the target frequencies. The Fourier filtration method examines the relationship between sine-wave oscillations in two variables at a single frequency. As such, it examines only the linear component of the relationship between the two variables. For each task, we computed the amplitude and phase among these signals for each target frequency. For the baseline tasks the same Fourier filtration procedure was used. The sinusoid amplitudes at baseline HR were computed for each from seven frequencies used in the biofeedback procedure.

The Fourier filtration procedure enabled us to quantify the oscillation amplitude at each specific target frequency. We used the following algorithm (Eykhoff, 1974):

$$C(\omega_i) = \frac{2}{U_0 T} \int_0^T Y(t) \sin(\omega_i t) dt$$

$$D(\omega_i) = \frac{2}{U_0 T} \int_0^T Y(t) \cos(\omega_i t) dt \quad T = K T_i, \quad T_i = 2\pi / \omega_i, \quad \omega_i = 2\pi f_i$$

where t is current time (s), f_i frequency of i th target stimulus sinusoidal signal (Hz), T the time of the task (5 min), K an integer, $Y(t)$ the physiological measure (HR, BP, and RC), and U_0 is the amplitude of the stimulus sinusoidal signal. U_0 was equivalent to 60 beats/min for HR and 30 mmHg for BP. For RC it was equivalent to average respiratory magnitude in the baseline period.

We computed the values of the real $C(\omega_i)$ and imaginary $D(\omega_i)$ parts of the transfer function of the observed process sequentially for each sinusoidal signal ($\omega_i/2\pi = 0.010, 0.021, 0.029, 0.055, 0.077, 0.111, \text{ and } 0.143$ Hz). Using $C(\omega_i)$ and $D(\omega_i)$, we then calculated the amplitude $A(\omega_i)$ and phase $\Phi(\omega_i)$ transfer functions of the observed process as follows:

$$A(\omega_i) = \sqrt{C(\omega_i)^2 + D(\omega_i)^2}$$

$$\Phi(\omega_i) = \arctg \frac{D(\omega_i)}{C(\omega_i)}$$

The value of $A(\omega_i)$ equal to 1 thus corresponds to a HR oscillation amplitude of 60 beats/min, and a BP oscillation amplitude of 30 mmHg. The $\Phi(\omega_i)$ reflects the phase shift in degrees, where positive values indicate that Output variables (as defined below) follow Input variables in time.

We calculated the transfer function (W) of the system by which particular physiological functions are controlled voluntarily, yielding the expression $W(\text{Output-Input})$. In order to assess biofeedback effects, the following transfer functions were calculated with regard to the target stimulus sine curve: $W(\text{HR-target})$ for the HR control system (i.e., the process whereby HR oscillations are influenced by the target stimulus, through the effects of biofeedback), $W(\text{BP-target})$ for the blood pressure control system (i.e., the process whereby BP is indirectly affected by the target stimulus, through biofeedback-induced oscillations in HR), and $W(\text{RC-target})$ for the respiratory control system (i.e., the process whereby

the biofeedback task produced changes in respiration rate). We also calculated the HR–BP transfer function $W(\text{BP}–\text{HR})$, where the input is HR and the output is BP. This was computed by dividing the $W(\text{BP}–\text{target})$ by $W(\text{HR}–\text{target})$. This function assesses HR effects on BP at each target frequency and is the transfer function of the BP control system as it is affected by the baroreflex. This calculation differs from the usual method of assessing baroreflex activity, with BP changes as the input and HR changes as the output. Our approach was dictated by two considerations: (1) our procedure directly manipulated HR, not BP; and (2) this method is consistent with viewing the baroreflex system as part of the body’s apparatus for modulating BP.

In order to evaluate the level of stability and stationarity of sinusoidal oscillations induced on HR during the various tasks we additionally calculated a full frequency spectrum of HR oscillations (0–0.4 Hz) using the Fast Fourier transformation. We estimated the power spectrum component at the target frequency as percent of total power of HR spectrum. Stationarity is assumed to be present where a high proportion of total power occurs at the target frequency. This type of evaluation of stationarity is original, and may not be appropriate when using the traditional Fourier analysis methods, but it is *more* appropriate when using the Fourier filtration, because a high proportion indicates that only a single sinusoidal process has occurred during the testing period, and significant trends and noise both are absent, that is, the power of the all other frequency components, including ultra low and noise components of the total spectrum are small. This is the type of “stationarity” that is assumed by the Fourier filtration method.

Statistical Analysis

The transfer functions and spectral values of HR variability at baseline were averaged across all 20 sessions for each participant separately and for all participants together. The average values of the amplitudes $A(\omega_i)$ and phases $\Phi(\omega_i)$ for each of the seven frequencies and their standard errors also were calculated.

RESULTS

Inducing Stationary Sinusoidal Oscillations in HR, BP, and Respiration (the RC)

The participants were able to produce sinusoidal oscillations in HR at each of the prescribed frequencies. Elevations in each target frequency oscillation also were found in BP. A typical example of physiological function recorded during the HR pattern-tracing task is shown in Fig. 2.

The sinusoidal oscillations induced in HR and BP are clearly visible during each of the tasks. The oscillation amplitudes differ among the various frequencies, as does the relationship between HR and BP oscillation amplitudes [Fig. 2(B) and (D)]. A high amplitude of HR oscillations occurred at a period⁵ of 100 s, and decreased as the frequency

⁵The *period* of oscillation refers to the length of time in each cycle. It is reciprocally related to the *frequency* of oscillations (number of cycles/s, or Hz).

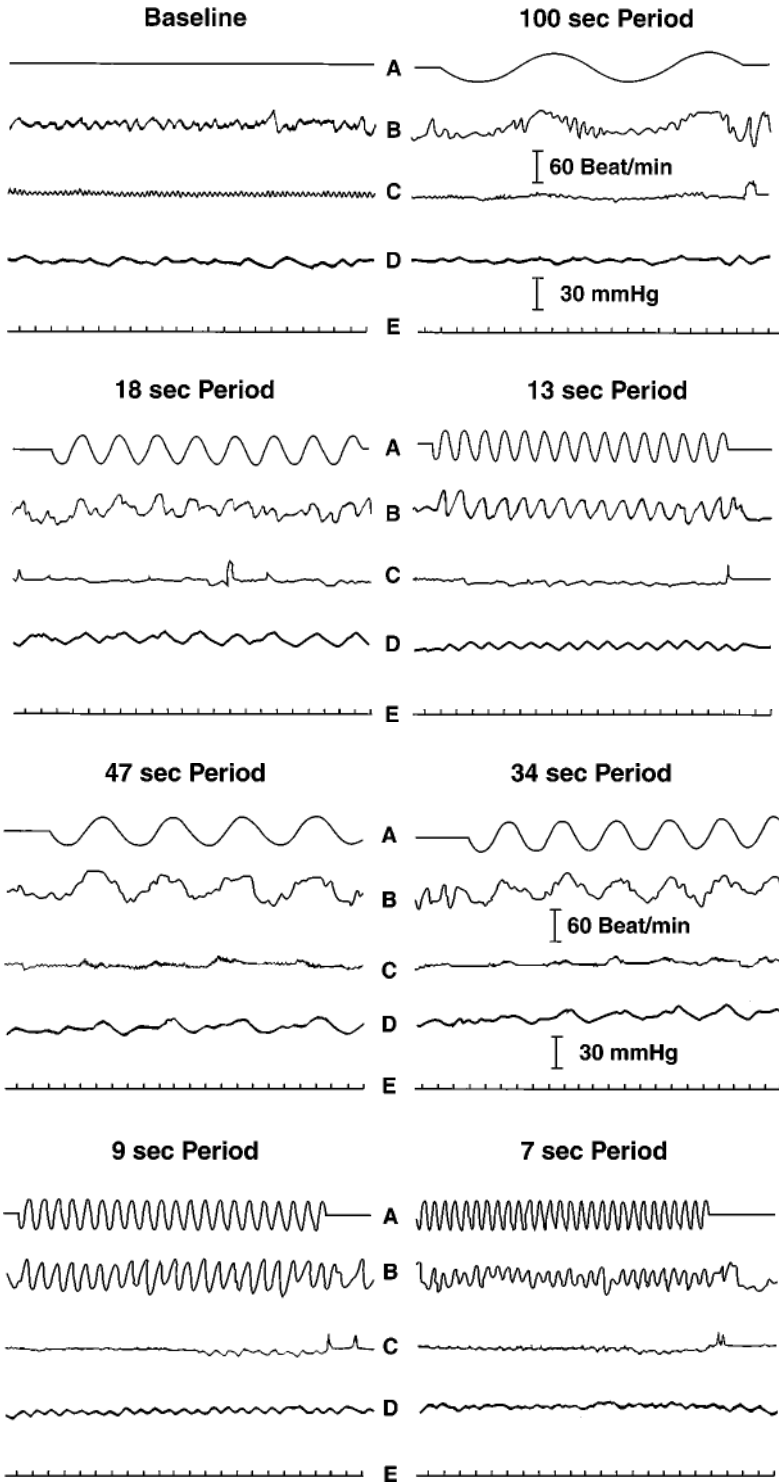


Fig. 2. Experimental records from one participant (S). A – sinusoidal target stimulus signals with a period of 100, 47, 34, 18, 13, 9, and 7 s; B – heart rate (beat/min); C – respiratory curve; D – mean dynamic arterial blood pressure (mmHg); and E – time marker of 10 s.

Table I. Percent of Heart Rate Variability Explained by Target Frequency

Target frequency (Hz) ^a	Mean \pm SD (% of total spectrum power) ^b
0.010	81.1 \pm 4.3
0.021	85.4 \pm 3.8
0.029	73.8 \pm 5.7
0.055	71.6 \pm 6.1
0.077	88.6 \pm 3.8
0.111	91.5 \pm 2.9
0.143	64.2 \pm 3.1

Note. A high percentage of heart rate variability at target frequency indicates stability and stationarity of imposed sinusoidal oscillations into heart rate.

^aThe frequencies in this table correspond to the seven oscillation periods shown in Fig. 2.

^bAveraged power of target frequency component in HR spectrum across 5 subjects and 20 sessions.

increased (i.e., as the period decreased). At a period of 18 s, the amplitude of HR oscillations was at a minimum. The low amplitude of BP oscillations at a period of 100 s increased as the frequency increased and reached a maximum peak at a period of 18 s. As the frequency further increased, BP oscillation amplitude decreased whereas HR oscillation amplitude increased, to a maximum peak at a period of 9 s.

The biofeedback-induced HR oscillations were stable and stationary at each target frequency, as shown by the high proportion of total spectral power explained by oscillations at the target frequency. The target frequency component always dominated the HR oscillation spectrum (see Table I).

For respiration [Fig. 2(C)] the stimulus sinusoidal oscillations were not visible clearly at all times, suggesting that the voluntarily-induced HR and BP oscillations were *not* induced entirely by alterations in respiration. Also the changes in the pattern of the RC while executing the tasks were not always correlated with changes in HR or BP oscillations. (See Fig. 2, the first and second halves of the 13- and 9-s period sinusoid tracing tasks.)

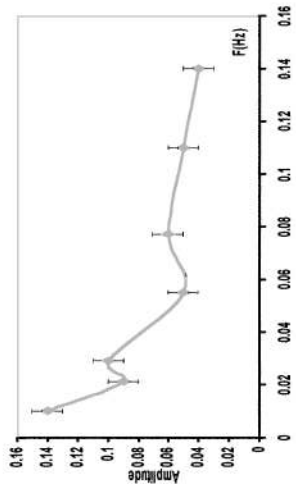
Baseline Recording

The amplitudes of sinusoidal HR oscillations at the target frequencies during the baseline task are presented in Fig. 3. At baseline, HR oscillations were present at low amplitudes at all seven target frequencies (Fig. 3). Very low frequency sinusoid amplitudes (with a frequency less than 0.03 Hz) were greater than low frequency (>0.05 Hz) sinusoid amplitudes for all participants, as found in other studies (Sleight et al., 1995).

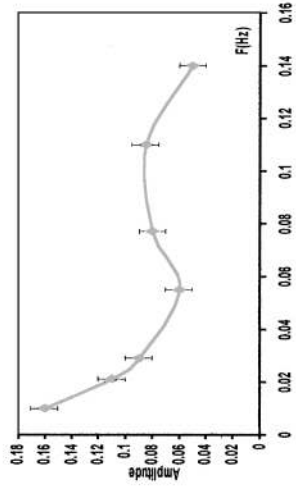
Transfer Functions of the HR Control System: $W(\text{HR-Target})$

Figure 4 shows that, in general, HR oscillation amplitudes at target frequencies were 4–10 times greater than HR oscillation amplitudes at baseline. (Compare Figs. 3 and 4. Note differences in scale of the *Y*-axis.) The maximum amplitude tended to be achieved

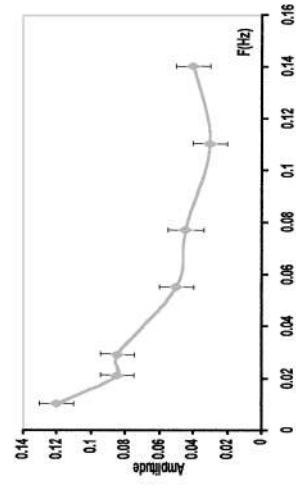
Average P, K, S, T, Ch



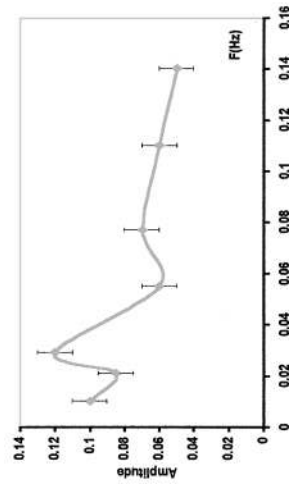
P



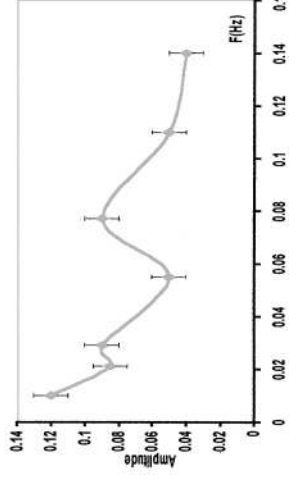
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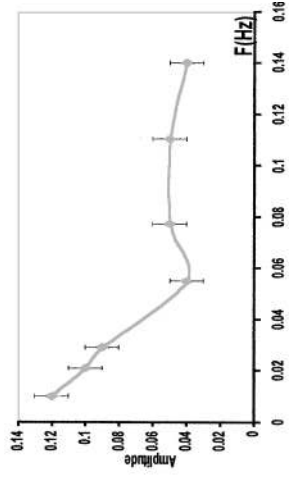


Fig. 3. Average spectral values of heart rate variability at baseline. Data are for participants P, K, S, T, and Ch, together and separately, across 20 sessions. Vertical lines (bars) represent ± 2 standard errors. An amplitude value of 1.0 represents 60 beats/min.

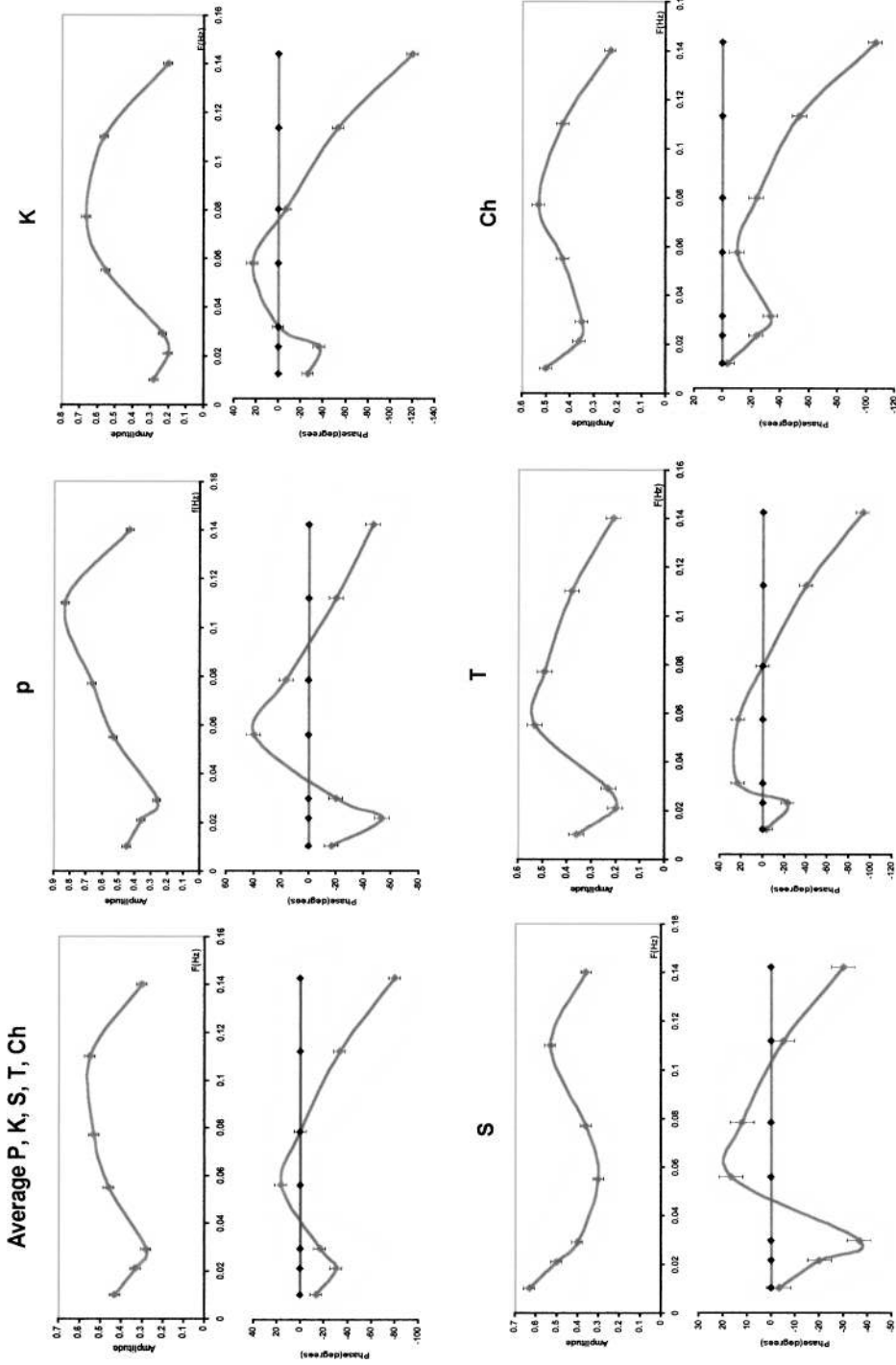


Fig. 4. Averaged amplitude and phase transfer functions of heart rate with regard to the target stimulus. This graph shows the transfer function $W(\text{HR-target})$ for all five participants P, K, S, T, and Ch, together and separately, across 20 sessions. Vertical lines (bars) represent ± 2 standard errors. An amplitude value of 1.0 represents 60 beats/min. Each value represents the HR oscillation amplitude divided by the amplitude of the stimulus sinus wave (coefficient of amplification). The amplitude of the stimulus sinus wave corresponds to 60 beats/min (NB! The scale of the Y-axis in Fig. 3 differs from the scale of Fig. 4).

in the lower half of the low frequency range (0.055–0.11 Hz) and was lowest within the very low frequency range (0.02–0.055 Hz). Although the exact amplitudes and frequencies of the maximum and minimum peak amplitudes and the phase transfer functions differed among participants, the shape of the curve is the same for all participants.

Transfer Functions of the BP Control System: $W(\text{BP-Target})$

Just as with $W(\text{HR-target})$, the patterns of the $W(\text{BP-target})$ transfer functions (Fig. 5) also have very similar shapes across all participants. However, the shape of this function is markedly different from that for HR. The amplitude at 0.01 Hz is low, but grows across frequencies within the very low frequency range (i.e., until 0.055 Hz). The amplitude then decreases at the low and high frequency ranges. The phase of the transfer functions decreases from an initially positive value at 0.01 Hz. The speed of this decrease differs among participants.

Transfer Functions of the HR Baroreflex System: $W(\text{BP-HR})$

The transfer function of the HR baroreflex system similarly has the same distinctive form for all participants (see Fig. 6, solid lines). The amplitude transfer functions have a clearly defined maximum in the very low frequency range (0.02–0.055 Hz). The phase transfer functions are positive for the frequencies close to 0.01 Hz. As frequency increases, phase values become negative, and the negativity gradually increases.

For each participant, we found a frequency at which $W(\text{BP-HR})$ had a phase angle of 180° , that is, HR and BP were oscillating in perfectly opposite directions. This frequency was always within the low-frequency range [near 0.1 Hz]. At this frequency, the $W(\text{HR-target})$ amplitude was invariably at its maximum level (see Fig. 4 and Fig. 6, dashed lines), that is, participants produced very high amplitude HR oscillations at this frequency. We also found a frequency at which $W(\text{BP-HR})$ had a phase angle of 0° , that is, where HR and BP were oscillating in phase with each other. At this frequency (which invariably was within the very low frequency range) the $W(\text{HR-target})$ was always at its minimum level (see Figs. 4 and 6).

Transfer Functions of the Respiratory Control System: $W(\text{RC-Target})$

The transfer functions between RC and the target stimulus signal (see Fig. 7) show that the participants' respiration did not have higher amplitude sinusoidal oscillations during biofeedback than at baseline for any target stimulus frequency. The amplitude of these oscillations was always lower than resting respiration amplitude (see Fig. 7, where an amplitude transfer function value of 1.0 corresponds to each participant's respiration amplitude at baseline).

Participants' breathing strategies were inconsistent even within specific tasks (e.g., Fig. 2). Also Fig. 7 shows a very high standard error for each frequency, further suggesting a great inconsistency in respiratory strategies. Thus no reliable differential RC response could be determined in response to the various frequencies of the HR pattern-tracing task.

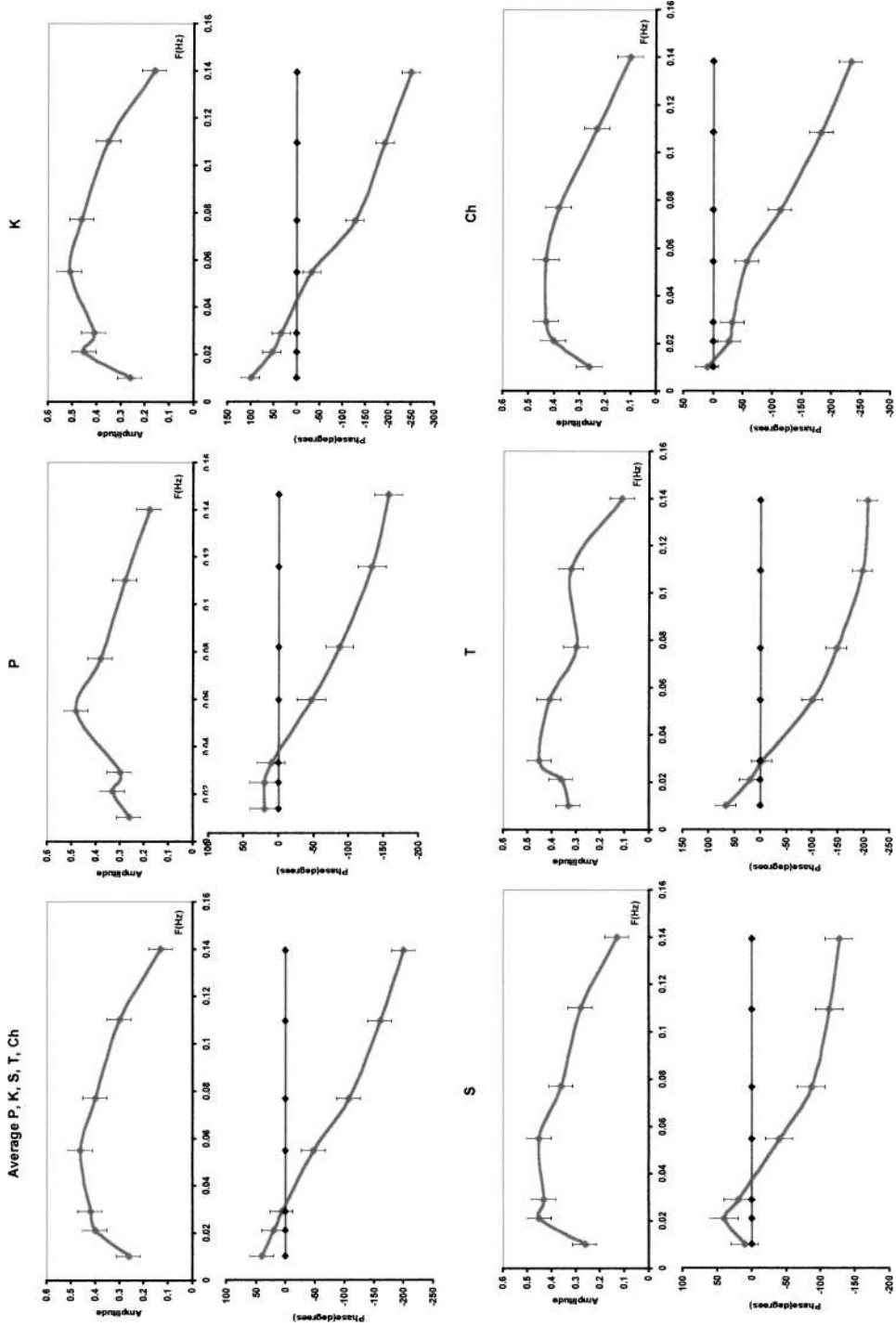


Fig. 5. Amplitude and phase transfer functions of arterial blood pressure with regard to the target stimulus. This graph shows the transfer function $W(BP-target)$ for all five participants P, K, S, T, and Ch, together and separately, averaged across 20 sessions. Vertical lines (bars) represent ± 2 standard errors. An amplitude value of 1.0 represents 30 mmHg. Each value represents the BP oscillation amplitude divided by the amplitude of the stimulus sinus wave (coefficient of amplification). The amplitude of the stimulus sinus wave corresponds to 30 mmHg.

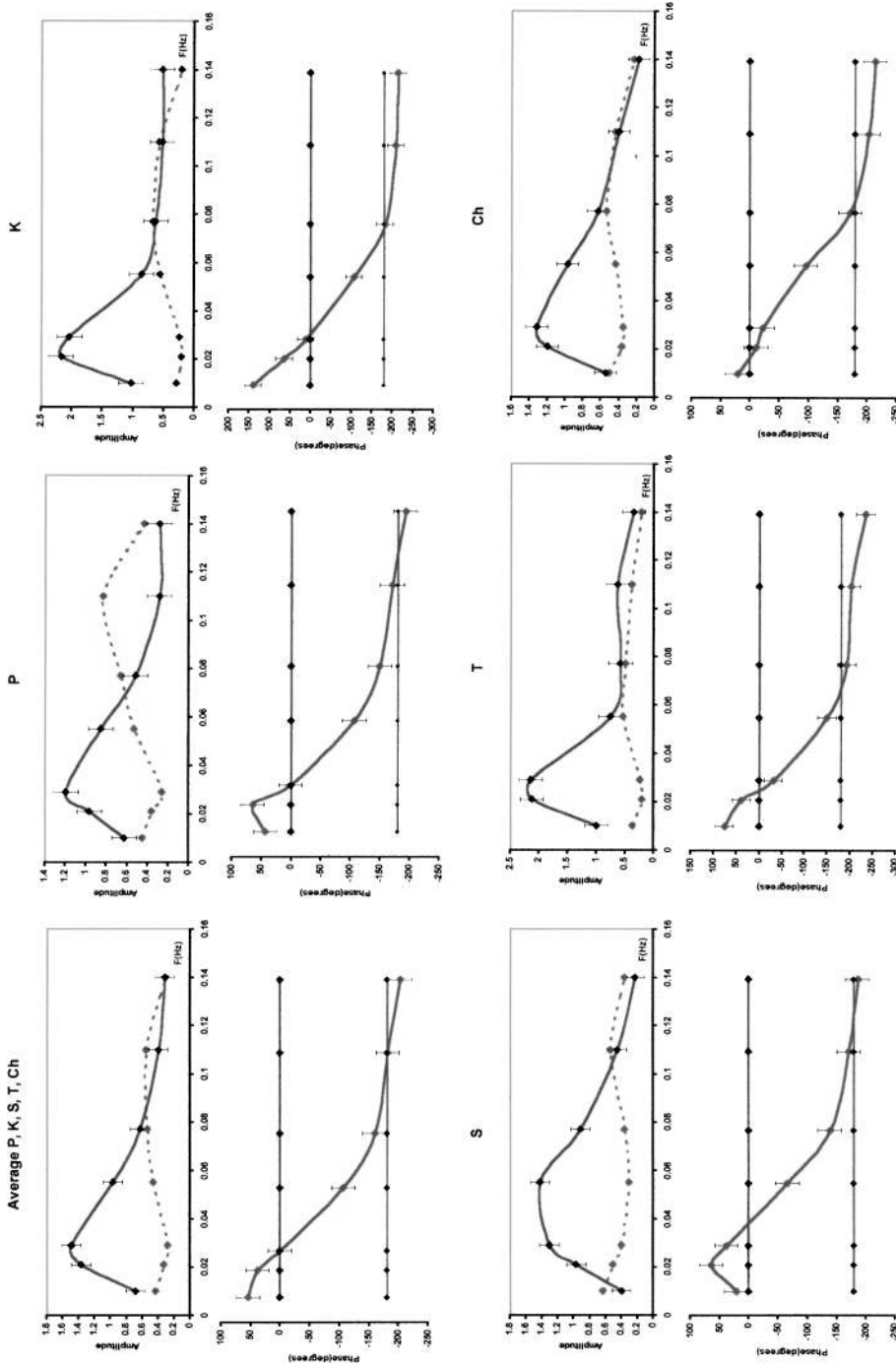


Fig. 6. Amplitude and phase transfer functions of the blood pressure relating to heart rate. This graph shows the transfer function $W(\text{BP}-\text{HR})$ (solid lines) and the amplitude transfer functions of the heart rate with regard to the target stimulus sine curve, $W(\text{HR}-\text{target})$ (dashed lines) for all five participants P, K, S, T, and Ch, together and separately, averaged across 20 sessions. Vertical lines (bars) represent ± 2 standard errors. Y-axis values are the ratios of BP/HR in units of amplification coefficients (see footnotes to Figs. 4 and 5). An amplitude value of 1.0 represents 30/60 = 0.5 mmHg/beat per min.

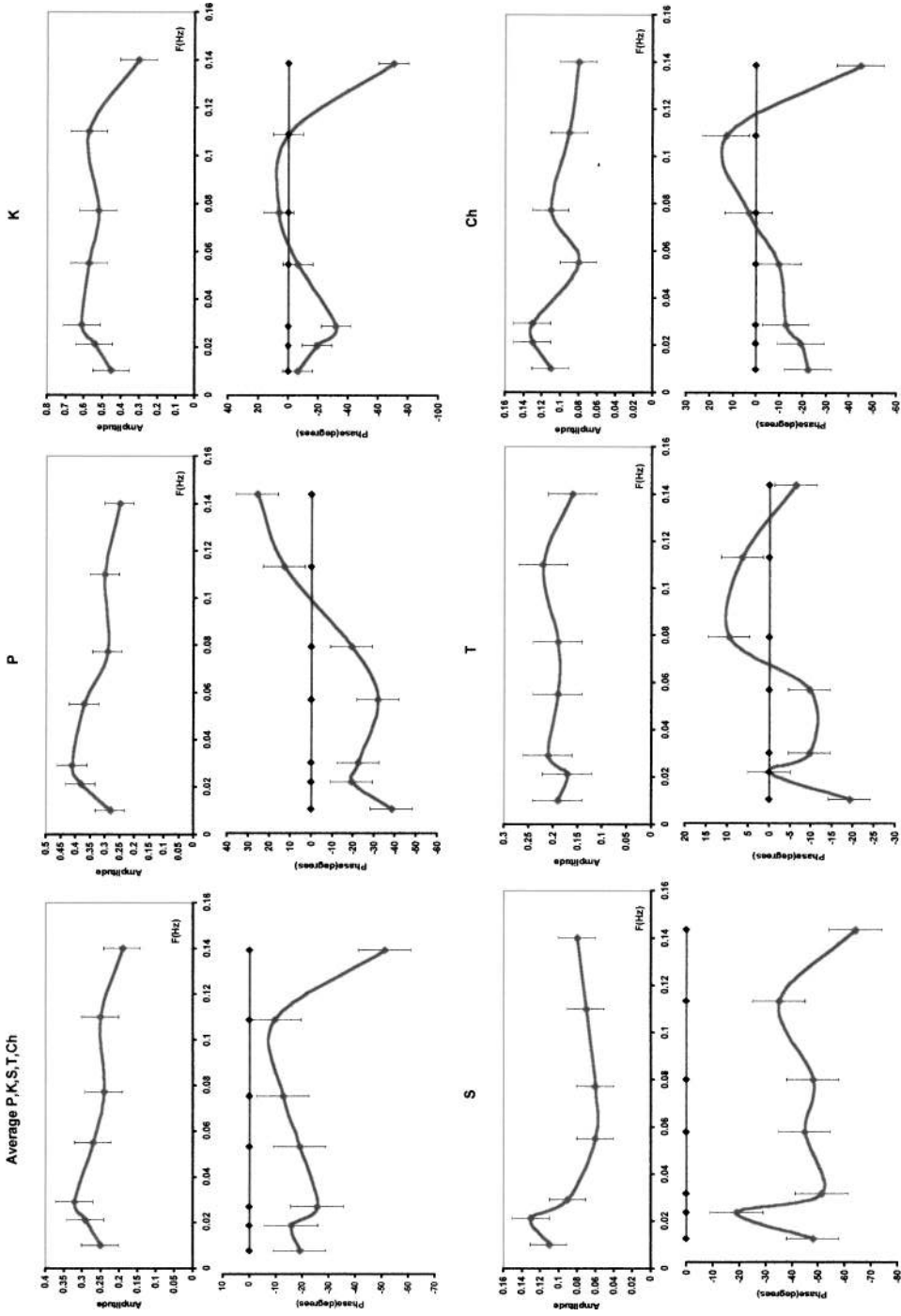


Fig. 7. Amplitude and phase transfer functions of the respiration curve with regard to the target stimulus. This graph shows the transfer function $W(RC-target)$ for all five participants P, K, S, T, and Ch, together and separately, averaged across 20 sessions. Vertical lines (bars) represent ± 2 standard errors. An amplitude value of 1.0 represents baseline respiration amplitude. Each value represents the respiration amplitude divided by the amplitude of the stimulus sinus wave (coefficient of amplification). The amplitude of the stimulus sinus wave corresponds to the baseline respiration amplitude.

DISCUSSION

Adequacy of Biofeedback Procedure for Meeting Assumptions Underlying Transfer Function Analysis

The validity of transfer function analysis depends upon certain characteristics of the data, all of which were met in this study: (1) high amplitude of oscillations at each frequency; (2) linearity of the relationship between input and output oscillations; (3) stationarity of the spectral components during the measurement period; (4) high coherence between input and output signals; and (5) reliability of the spectral relationships from one person to another.

High Amplitude of Oscillations at Each Frequency

The biofeedback task consistently produced oscillations in HR and BP of sufficiently high amplitude for calculation of transfer functions at all frequencies we measured. The amplitudes of the oscillations in HR and BP were both several times higher than the respective frequency components of naturally-occurring oscillations at all frequencies, for example, during the baseline period. (Compare the oscillations at each frequency in Figs. 4 and 5 with baseline oscillations at each frequency in Fig. 3.) Indeed the biofeedback-induced HR fluctuations were up to 50 beats/min at some frequencies in this study (Fig. 4). Although these amplitudes appear to be startlingly high, they are characteristic of the amplitudes achieved in our laboratory using this and similar procedures among young, healthy, previously untrained participants, after approximately four sessions of training.⁶

Stability of Transfer Functions Across Sessions

Sufficiently stable HR and BP oscillations were achieved by all participants even in the first few sessions. In our preliminary data analysis, we compared averages of the transfer functions across the last 15 sessions and across all 20 sessions for each of the seven target frequencies. The *t* test found no significant differences ($\alpha = .05$).

Biofeedback allowed us to obtain consistently more reliable transfer functions than other investigators found when examining spontaneous HR and BP fluctuations (DeBoer et al., 1987), or when using paced breathing at various frequencies (Cooke et al., 2000; Saul et al., 1991).

Linearity of the Relationship Among Oscillatory Variables

Transfer function analysis assumes linearity between input and output signals (Grodins, 1963; Murphy, 1957). The relationship between output and input signals was close to linear in all cases, because, in all cases, sinusoidal input signals produced sinusoidal output signals at the same frequencies.

⁶Session-by-session training data are not described in the current report, and will be the topic of a separate report.

High Coherence Between Input and Output Signals

High coherence between input and output signals is one of the requirements for calculating transfer functions for using Fourier procedures (Cooke et al., 2000; Eykhoff, 1974; Saul et al., 1991). The linearity between input and output signals, the high oscillation amplitudes at target frequencies and the high signal-to-noise ratio (i.e., ratio between oscillations at target frequencies vs. at all other frequencies) indicate that coherence was very high for calculation all transfer functions. Oscillations at the target frequency in this experiment completely dominated the full frequency band from 0 to 0.4 Hz. All other frequency components accounted for less than 30% of the full spectral power. The coherence between any pairs of sinusoidal input and output signals was never less than 0.73.

Stationarity of the Spectral Components During the Measurement Period

We interpreted the single spectral peak for each task as evidence of stationarity. Shifts in spectral patterns during the tasks would have produced multiple frequency peaks. This did not occur. Similarly the low levels of spectral activity in the ultra low frequency range (i.e., below 0.005 Hz) indicates that our data were not contaminated by the occurrence of very slow oscillatory patterns or linear trend.

Reliability of the Spectral Relationships From One Person to Another

The transfer function curves had very similar shapes across all participants (see Figs. 4–6). This strongly suggests that our estimate of transfer function parameters is highly reliable.

System Characteristics of the HR Baroreflex

In this study we applied statistics to HR and BP variability that are conventionally used in analysis of systems. In doing so, we believe we have quantified the operating characteristics of the systems that control HR and BP, and by which HR and BP control each other. As described below, these system characteristics include resonance, inertia, delay, and speed sensitivity. We will describe below how each of these characteristics is relevant to biofeedback therapy, as well as to understanding the nature of the body's system for controlling these physiological variables.

Although the oscillations occurred at sufficiently high amplitudes at all frequencies for calculating transfer functions, sine wave oscillation amplitudes were particularly high at specific frequencies for HR and BP. The highest amplitudes of HR oscillations occurred in the frequency band of 0.055–0.11 Hz. The lowest amplitudes of HR oscillations occurred in the frequency band of 0.02–0.055 Hz (Figs. 2 and 4). However, for BP the highest amplitudes of oscillations occurred in the frequency band of 0.02–0.055 Hz (Figs. 2 and 5). We note that, where HR oscillation amplitudes were high, BP oscillation amplitudes were low, and vice versa.

These characteristics of biofeedback-induced oscillations in HR and BP allowed us to perform a detailed analysis of the operating characteristics of the systems describing

voluntary control of HR and BP oscillations [$W(\text{HR-target})$ and $W(\text{BP-target})$, respectively], as well as the characteristics of the system by which HR and BP control each other [the baroreflex system, denoted as $W(\text{BP-HR})$].

Resonance: HR

When the peak of the amplitude transfer function occurs at a single frequency, a system contains resonance (Grodins, 1963; Murphy, 1957). Such amplitude peaks occurred for $W(\text{HR-target})$ in the low-frequency range (Fig. 4) and for $W(\text{BP-target})$ in the very low frequency range (Fig. 5). Thus resonance occurred at these respective frequencies in the two physiological variables. The specific frequency at which these peaks occurred for each participant is the resonant frequency for the particular physiological function in each individual. Although resonant frequencies are not identical between individuals, they all occur within the respective frequency ranges described above for each physiological variable. Conversely, we propose that the occurrence of resonance between the effects of biofeedback and the baroreflexes cause the oscillations to have the highest amplitudes at these particular frequencies. At these frequencies, the effects of biofeedback resonate with other sources of oscillation in these two physiological variables. We propose that the latter sources of oscillation are the effects of the HR and VT baroreflex loops, respectively.

The mechanism for the resonance effects in the HR baroreflex loop is explicitly described by the phase relationships between HR and BP (Fig. 6). For each participant, at a single frequency within the low-frequency range, the effects of the HR baroreflex appear to augment the effects of biofeedback. The amplitude of biofeedback-induced HR oscillations is highest (Fig. 4) at the frequency where HR and BP oscillations are completely out of phase, 180° (Fig. 6). Invariably, this frequency occurs within the low frequency range. Note that the HR baroreflex causes HR to rise as BP falls, and to fall as BP rises. Thus, as the effects of biofeedback cause HR to rise at this resonant frequency, the effects of the HR baroreflex simultaneously cause it to rise. When the effects of biofeedback cause HR to fall the effects of the HR baroreflex simultaneously cause it to fall. This explains the source of the resonance effects we found at this particular frequency. As shown by the amplitude transfer function, the HR baroreflex is the most sensitive at this resonant frequency.

The particularly low HR oscillation amplitudes we found for each participant at a specific frequency in the very low frequency range (Figs. 2(B) and 4) describe the effects of *negative* resonance at this frequency. At this frequency oscillations between HR and BP are completely in phase, 0° (Fig. 6). Thus, at this frequency, as the biofeedback effects cause HR to rise, baroreflex effects cause HR to fall, and as the biofeedback effects cause HR to fall, baroreflex effects cause HR to rise. Thus, at this frequency, *negative* resonance between biofeedback and the HR baroreflex partially cancel each other's effects. As shown by the amplitude transfer function, the HR baroreflex is least sensitive at this frequency of negative resonance.

Resonance: BP

Although this study did not specifically manipulate BP or VT, resonance effects on these functions also are illustrated by our results. At frequencies within the very low

frequency range (0.02–0.055 Hz), the $W(\text{BP}–\text{HR})$ amplitude characteristic was at a clearly defined maximum (see Fig. 6). The maximum amplitude of BP oscillations also was obtained at this frequency [see Fig. 2(D)]. This suggests that BP resonance in the cardiovascular system occurred at this frequency for all participants. As with HR, each participant had his own BP resonant frequency, but in this case resonance always occurred within the very low frequency range.

Our data cannot explain these frequency characteristics for BP data. We hypothesize that the mechanics of BP resonance can be modeled by analogy to those of HR resonance. We hypothesize that BP resonance results from the VT baroreflex (Fig. 1), which was not studied in this experiment. The occurrence of resonance at the frequency in 0.02–0.055 Hz could be explained by a hypothesized phase relationship of 180° between VT and BP oscillations at this frequency. Supporting this hypothesis is evidence from other studies that BP oscillations in the frequency range of 0.02–0.055 Hz are due to variability in vasomotor activity (Akselrod et al., 1985; Shusterman et al., 1997). Oscillations in the VT loop of the two closed loop baroreflex system may arise at lower frequency than these in the HR baroreflex loop, because of the dampening effects of blood vessel plasticity.

The possibility of BP resonance in the very low frequency range supports our interpretation of negative HR resonance in this range. The resonant frequency of the VT baroreflex appears to be the frequency at which HR and BP oscillations are in phase (see Fig. 6). At this frequency resonant BP oscillations suppress the same-frequency HR oscillations.

Delay

The gradual decrease in the phase transfer function $W(\text{BP}–\text{HR})$ as frequency increases shows that a delay between HR and BP changes occurs in the closed loop of the baroreflex system. The greater the negative frequency-dependent slope of the phase transfer function between HR and BP, the greater is the time lag between HR and BP variations. The length of the delay can be calculated from the frequency at which the input and output variables are completely out of phase (180°), that is, in our study, at the HR resonant frequency. The length of the delay is equal to one half of the oscillation period of this frequency. The specific length of the delay varied between 4.5 and 9 s in all participants. Other researchers also have found a delay between HR and BP variations in same range (Wichterle et al., 2000). The length of the delay probably, as suggested above, reflects the effects of sympathetic influence on vascular tone and vascular tissue plasticity.

Inertia

The decrease in the amplitude transfer function $W(\text{BP}–\text{HR})$ as frequency increases shows inertia. Thus there appears to be an upper limit for the working frequency range of the baroreflex system. This study did not examine the physiological factors that contribute to inertia. Contributions to it could include the inertia of blood mass, the effects of blood vessel plasticity, and the relatively slow process of acetylcholine hydrolyzation in the parasympathetic nervous system. Inertia limits the working frequency range of the baroreflex system at the upper end. Level of inertia can be expressed as a time constant for each individual.

Speed Sensitivity

The decrease in amplitude of the $W(\text{BP}-\text{HR})$ transfer function as frequency decreases in the very low frequency range and the positive value of the phase transfer function shows that the baroreflex system contains a speed sensitivity link. It is known that the baroreceptors respond only to relatively fast BP changes and do not sense a constant BP values or very slow BP changes (Eckberg & Sleight, 1992). Thus the baroreceptors can be considered as the speed sensitivity link in the system that controls BP. The speed sensitivity limits the working frequency range of the baroreflex system at the lower end.

Working Range of the Baroreflex System

This study found that, within the frequency range of 0.01–0.14 Hz, baroreflex action depends on the oscillation frequency of BP and HR. This range includes both low-frequency (0.055–0.14 Hz) and very low frequency (0.01–0.055) oscillations. This study revealed resonance in the cardiovascular system within both of these ranges. Baroreflex effects tended to enhance HR oscillations at a specific frequency within the low frequency range, and to enhance BP oscillations at a specific frequency within the very low frequency range. They also tended to depress HR and BP oscillations at specific frequencies within the very low and low frequency ranges, respectively. However, at all frequencies, participants were able to override the negative resonance effects, and to use biofeedback to produce higher-amplitude oscillations in both HR and BP than under baseline conditions.

Usefulness of Biofeedback as a Method for Assessing Cardiovascular System Dysfunction

We have shown that our biofeedback procedure allowed us to determine various specific parameters of the baroreflex system in our small group of young healthy adults. This method may be applied assessing other populations; and it is possible that divergencies in various system values may reflect specific physiological problems among individuals with various abnormalities in the cardiovascular system, including stiffening of the arterial walls, neural abnormalities, and other abnormalities that might be expected to affect heart rate variability and/or cause baroreflex dysfunction. Although in the past biofeedback has generally been used as a *treatment* modality, the results of this study suggest that it also might have advantages as a *diagnostic* modality for cardiovascular system dysfunction and consequent disorders.

Lack of Respiratory Mediation

Others have found a link between naturally-occurring oscillations in respiration and those in both BP (Akselrod et al., 1985; DeBoer et al., 1987; Saul et al., 1991) and HR (Berntson et al., 1997; Saul et al., 1991; Task Force, 1996). However, if respiratory processes have an important link in oscillatory control of the baroreflexes, they were not demonstrated in the current study. This result surprised us because subjects did report having actively

manipulated their respiratory patterns in order to achieve the desired frequency oscillations in HR. However, low amplitudes of RC sinusoidal oscillations during the HR pattern tracing tasks indicate that the subjects did not always breathe in rhythm with the stimulus sinusoids. Large oscillations in the RC did not occur at the same frequencies as HR and BP oscillations (see Fig. 7). These results correspond to conclusions of a paper by Badra et al. (2001), which documents the independence of low-frequency rhythms in HR and BP from respiratory activity and notes that the mode of breathing did not influence low-frequency oscillations in their study.

Although the respiratory patterns in HR-tracing biofeedback tasks differ from the pattern at baseline (see Fig. 2), they do not usually include frequencies of the target stimulus sinusoid, particularly at very low frequencies. In their responses to a questionnaire, study participants reported that they had used a combination of respiration, changes in muscle tension and emotional imagery. Our study did not reveal the precise mechanism by which subjects produced the voluntary HR and BP oscillations. However, we hypothesize that the HR effects found in this study reflect voluntary activity in several psychophysiological functions, including respiration, muscle tension, and mental imagery of emotionally meaningful situations. Participants tended to select and alternate among these methods.

Hypotheses Based on the Resonance Properties of the Cardiovascular System

1. We hypothesize that other variables in addition to respiration may be involved in producing high-amplitude HR oscillations during RSA biofeedback, because participants did not always breathe at the target frequencies when they produced this effect.
2. We hypothesize that the sinusoidal HR and BP oscillations within the frequency range of 0.01–0.14 Hz are caused by resonance properties of the cardiovascular system. Movement, respiration, emotions, and other internal processes produce cardiovascular system changes with a white noise spectrum. The sinusoidal HR and BP oscillations appear because the resonance systems act as narrow-band filters and amplify oscillations only at resonant frequencies.

Implications for Biofeedback Therapy

The results of this study explain why voluntary increases in HRV always occur in the low-frequency range (Chernigovskaya, Vaschillo, Petrash, & Rusanovsky, 1990; Lehrer et al., 1997) where HR resonance can occur. Our results show that people can produce large-amplitude fluctuations in HR, and that these appear to stimulate BR activity. We have hypothesized that frequent high-amplitude stimulation can increase the efficiency of certain reflexes (Chernigovskaya et al., 1990; Vaschillo, 1984). It is possible that this could be the case for biofeedback procedures that teach people to increase the amplitude of HRV.

Stimulation of BR activity by voluntarily-induced HR fluctuations also is consistent with clinical applications of HRV biofeedback, where biofeedback is used to treat conditions characterized by autonomic hyper-reactivity, which presumably can be modulated

more effectively by more efficient BR activity. Repeated high-amplitude stimulation of the baroreflexes may sensitize these reflexes, and increase their efficiency. We have had positive results using RSA biofeedback for treatment of patients with various functional disorders of the vegetative and central neural system (Chernigovskaya et al., 1990) and asthma (Lehrer, Smetankin, & Potapova, 2000).

However, it is still not known, whether the mechanism of effects in clinical studies do indeed reflect the effects of biofeedback on baroreflex activity. Future research is necessary to explore this link. In previous biofeedback studies to increase HRV amplitude people often used respiratory strategies to induce high-amplitude HR fluctuations (i.e., by breathing at the individual's resonant frequency, usually within the low-frequency range) (Chernigovskaya et al., 1990; Lehrer et al., 1997). An extreme example of voluntarily-produced high-amplitude HR oscillations comes from a recent study of Zen monks, who breathed within the low and very low frequency ranges, and produced very large oscillatory increases in HRV (Lehrer, Sasaki, & Saito, 1999). The mechanisms by which biofeedback influenced HR fluctuations in this study were not specifically investigated. Data from the present study suggest that producing changes in respiratory activity is not the exclusive mechanism by which voluntary changes in HRV can be induced.

The resonance characteristics of the baroreflex system also suggest possible technical components of a biofeedback protocol. We have suggested (Lehrer, Vaschillo, & Vaschillo, 2000) that each individual's resonant frequency be determined prior to training the individual to increase the amplitude of RSA. This can be done by instructing the person to breathe at various frequencies in the neighborhood of 0.1 Hz, and determining the frequency at which RSA amplitude is highest. Although the results of the current study suggest that paced breathing is not the only mechanism by which people can induce high-amplitude HR oscillations, it can be effectively used in this way. This use of paced breathing may considerably facilitate training, and may even obviate the need for a home-trainer device.

Implications for Further Research

In addition to confirming our findings on a larger sample, further research is needed where VT is directly manipulated, to directly examine the characteristics of the VT loop of our model. Additionally, the effects of clinical HRV biofeedback on BR gain requires investigation, as does the expected effect of increased BR gain on improved homeostatic modulation of the cardiovascular system. BR gain can be assessed by the various methods described above. The effects on autonomic homeostasis should be measurable as smaller and less persistent cardiovascular reactions in response to various psychological and physical stressors, as well as improvement in stress-related disease.

In addition, the clinical effects of training subjects to increase amplitude of BP and/or VT oscillations remains to be studied. Promising applications may be to treating such diseases as orthostatic hypotension, labile hypertension, anxiety disorders, and asthma, all of which involve dysfunctional reactions to *changes* in environmental or psychological demand, that is, the hypothesized domain of baroreflex modulation.

Similarly, this biofeedback method may be useful for comparing cardiovascular system function in various populations (e.g., various ages, degrees of fitness, disease, etc.) in order to quantify the effects of these dimensions on dynamic characteristics of the cardiovascular system.

ACKNOWLEDGMENTS

Work on this paper was supported in part by Grant #1 R01 HL/A158805-01A1 to Paul Lehrer from the Heart Lung and Blood Institute of the National Institutes of Health. It also was partially supported by NASA (under grants NAGW-4080, NAG5-5095, and NRA-97-MTPE-05), NSF (CDA-9711582, IRI-9409661, and HRD-9707076), ARO (DAAH04-96-1-0049 and DAAH04-96-1-0278), DoI (CA-5280-4-9044), NATO (HTECH.LG 931449), AFRL (F30602-98-C-0037), and the State of Florida.

REFERENCES

- Akselrod, S. (1988). Spectral analysis of fluctuations in cardio-vascular parameters: Quantitative tool for the investigation of autonomic control. *Trends in Pharmacological Science*, 9, 6–9.
- Akselrod, S., Gordon, D., Madwed, J. B., Snidman, N. C., Shannon, D. C., & Cohen, R. J. (1985). Hemodynamic regulation: Investigation by spectral analysis. *American Journal of Physiology*, 249 (*Heart and Circulatory Physiology*, 18), H867–H875.
- Badra, L. J., Cooke, W. H., Hoag, J. B., Crossman, A. A., Kuusela, T. A., Tahvanainen, K. U. O., & Eckberg, D. L. (2001). Respiratory modulation of human autonomic rhythms. *American Journal of Physiology (Heart and Circulatory Physiology)*, 280, H2674–H2688.
- Berger, R. D., Saul, J. P., & Cohen, R. J. (1989). Transfer function analysis of autonomic regulation. 1. Canine atrial rate response. *American Journal of Physiology*, 256 (*Heart and Circulatory Physiology*, 25), H142–H152.
- Bernardi, L., Leuzzi, S., Radaelli, A., Passino, C., Johnston, J. A., & Sleight, P. (1994). Low frequency spontaneous fluctuations of R–R interval and blood pressure in conscious humans: A baroreceptor or central phenomenon? *Clinical Science*, 87, 649–654.
- Bernardi, L., Rossi, M., Leuzzi, S., Mevio, E., Fornasari, G., Calciati, A., et al. (1997). Reduction of 0.1 Hz micro-circulatory fluctuations as evidence of sympathetic dysfunction in insulin-dependent diabetes. *Cardiovascular Research*, 34, 185–191.
- Berntson, G. G., Bigger, J. T., Jr., Eckberg, D. L., Grossman, P., Kaufmann, P. G., Malik, M., et al. (1997). Heart rate variability: Origins, methods, and interpretive caveats. *Psychophysiology*, 34, 623–648.
- Brown, T. E., Beightol, L. A., Koh, J., & Eckberg, D. L. (1993). Important influence of respiration on human R–R interval power spectra is largely ignored. *Journal of Applied Physiology*, 75, 2310–2317.
- Chernigovskaya, N. V., Vaschillo, E. G., Petrash, V. V., & Rusanovsky, V. V. (1990). Voluntary regulation of the heart rate as a method of functional condition correction in neurotics. *Human Physiology*, 16, 58–64.
- Clynes, M. (1960). Respiratory sinus arrhythmia: Laws derived from computer simulation. *Journal of Applied Physiology*, 15, 863–874.
- Cooke, W. H., Ames IY, J. E., Crossman, A. A., Cox, J. P., Kuusela, T. A., Tahvanainen, K. U. O., et al. (2000). Nine months in space: Effects on human autonomic cardiovascular regulation. *Journal of Applied Physiology*, 89(3), 1039–1050.
- Cooke, W. H., Cox, J. P., Diedrich, A. M., Taylor, J. A., Beightol, L. A., Ames IY, J. E., et al. (1998). Controlled breathing protocols probe human autonomic cardiovascular rhythms. *American Journal of Physiology*, 274, H709–H718.
- DeBoer, R. W., Karemaker, J. M., & Strackee, J. (1987). Hemodynamic fluctuations and baroreflex sensitivity in Humans: A beat-to-beat model. *American Journal of Physiology*, 253 (*Heart and Circulatory Physiology*, 22), H680–H689.
- Eckberg, D. L., & Eckberg, M. J. (1982). Human sinus node responses to repetitive, ramped carotid baroreceptor stimuli. *American Journal of Physiology*, 242 (*Heart and Circulatory Physiology*, 11), H638–H644.
- Eckberg, D. L., & Sleight, P. (1992). *Human baroreflexes in health and disease*. Oxford: Clarendon Press.
- Eykhoﬀ, P. (1974). *System identification: Parameter and state estimation* (p. 684). New York: Wiley-Interscience.
- Gevirtz, R. (1999). Resonance frequency training to restore autonomic homeostasis for treatment of psychophysiological disorders. *Biofeedback*, 4, 7–9.
- Giardino, N., Lehrer, P. M., & Feldman, J. (2000). The role of oscillations in self-regulation: Their contribution to homeostasis. In D. Kenney & F. J. McGuigan (Eds.), *Stress and health: Research and clinical applications* (pp. 27–52). Amsterdam: Harwood.
- Grodins, F. S. (1963). *Control theory and biological systems* (255 pp.) New York and London: Columbia University Press.
- Herbs, D., Gevirtz, R. N., & Jacobs, D. (1993). *The effect of heart rate pattern biofeedback for the treatment of essential hypertension*. First prize research paper at the 19th Biofeedback Society of California (November)

- meeting and Citation Poster at the 25th annual meeting of the Association for Applied Psychophysiology and Biofeedback, Atlanta, GA.
- Kirchheim, H. R. (1976). Systemic arterial baroreceptor reflexes. *Physiology Reviews*, *56*, 100–176.
- Lehrer, P. M., Carr, R. E., Smetankine, A., Vaschillo, E. G., Peper, E., Porges, S., et al. (1997). Comparison of respiratory sinus arrhythmia and neck/trapezius EMG biofeedback for asthma: A pilot study. *Applied Psychophysiology and Biofeedback*, *22*, 95–109.
- Lehrer, P. M., Sasaki, Y., & Saito, Y. (1999). Zazen and cardiac variability. *Psychosomatic Medicine*, *61*, 812–821.
- Lehrer, P., Smetankin, A., & Potapova, T. (2000). Respiratory sinus arrhythmia biofeedback therapy for asthma: A report of 20 unmedicated pediatric cases using the Smetankin method. *Applied Psychophysiology and Biofeedback*, *25*, 193–200.
- Lehrer, P. M., Vaschillo, E., & Vaschillo, B. (2000). Resonant frequency biofeedback training to increase cardiac variability: Rationale and manual for training. *Applied Psychophysiology and Biofeedback*, *25*, 181–192.
- Malkin, V. B., & Gora, E. P. (1996). The participation of the respiration in the rhythmic interactions in the body. *Success in Physiological Science*, *27*, 61–77.
- Murphy, G. J. (1957). *Basic automatic control theory*. Princeton, NJ: Van Nostrand.
- Penaz, J. (1992). Criteria for set point estimation in the volume clamp method of blood pressure measurement. *Physiology Research*, *41*, 5–10.
- Saul, J. P., Berger, R. D., Albrecht, P., Stein, S. H., Chen, M. H., & Cohen, R. J. (1991). Transfer function analysis of the circulation: Unique insights into cardiovascular regulation. *American Journal of Physiology*, *261* (Heart and Circulatory Physiology, *30*), H1231–H1245.
- Shusterman, V., Anderson, K. P., & Barnea, O. (1997). Spontaneous skin temperature oscillations in normal human subjects. *American Journal of Physiology*, *273*, R1173–R1181.
- Sleight, P., La Rovere, M. T., Mortara, A., Pinna, G., Maestri, R., Leuzzi, S., et al. (1995). Physiology and pathophysiology of heart rate and blood pressure variability in humans: Is power spectral analysis largely an index of baroreflex gain? *Clinical Science*, *88*, 103–109.
- Stephoe, A., & Sawada, Y. (1989). Assessment of baroreceptor reflex function during mental stress and relaxation. *Psychophysiology*, *26*, 140–147.
- Task Force of the European Society of Cardiology and the North American Society of Racing and Electrophysiology. (1996). Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. *Circulation*, *93*, 1043–1065.
- Taylor, J. A., & Eckberg, D. L. (1996). Fundamental relations between short-term RR interval and arterial pressure oscillations in humans. *Circulation*, *93*, 1527–1532.
- Vaschillo, E. G. (1984). *Dynamics of slow-wave cardiac rhythm structure as an index of functional state of an operant* (p. 230). Doctoral dissertation. Saint Petersburg, Russia: Institute of Experimental Medicine.
- Vaschillo, E. G., Zingerman, A. M., Konstantinov, M. A., & Menitsky, D. N. (1983). Research of the resonance characteristics for cardiovascular system. *Human Physiology*, *9*, 257–265.
- Wichterle, D., Melenovsky, V., Simek, J., Nekasova, L., Kautzner, J., & Malik, M. (2000). Cross-spectral analysis of heart rate and blood pressure modulations. *Pace-Pacing and Clinical Electrophysiology*, *23*(9), 1425–1430.
- Zingerman, A. M., Konstantinov, M. A., Menitsky, D. N., Logvinov, V. S., & Vaschillo, E. G. (1988). Entropy-statistical, spectral, conditionally-stochastic and determined characteristics of heart rate under different functional conditions of a person. *Success in Physiological Science*, *19*, 40–55.