

SPECIAL ISSUE



Heart Rate Variability Anatomy and Physiology

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Keywords: heart rate variability, respiration, autonomic nervous system, biofeedback

Heart rate variability (HRV) is generated by the interaction of multiple regulatory mechanisms that operate on different time scales. This article examines the regulation of the heart, the meaning of HRV, Thayer and Lane's neurovisceral integration model, the sources of HRV, HRV frequency and time domain measurements, Porges's polyvagal theory, and resonance frequency breathing. The medical implications of HRV biofeedback for cardiovascular rehabilitation and inflammatory disorders are considered.

Regulation of the Heart

The Heart

The heart is a hollow, muscular organ, about the size of a closed fist. The heart beats about 100,000 times a day and 2.5 billion times during a typical lifetime. The heart contains four chambers, two atria and two ventricles. The atria are upper chambers that receive returning venous blood. The ventricles are located below the atria and pump blood from the heart into the arteries.

Deoxygenated blood enters the right atrium through the superior and inferior vena cava. After passing through the right atrioventricular orifice (tricuspid valve), blood flows into the right ventricle and is pumped via the pulmonary arteries to the lungs. There, wastes are removed and oxygen is replaced. Oxygenated blood returns through the pulmonary veins to the left atrium and passes through the left atrioventricular orifice (mitral valve) and into the left ventricle. During contraction, blood is ejected through the aorta to the arterial system.

The Cardiac Cycle

The cardiac cycle consists of systole (ventricular contraction) and diastole (ventricular relaxation). During systole

(about 0.3 seconds), blood pressure (BP) peaks as contraction by the left ventricle ejects blood from the heart. Systolic BP is measured here. During diastole (about 0.4 seconds), BP is lowest as the left ventricle relaxes. Diastolic BP is measured at this time (see Figure 1).

Pacemakers

The heart contains autorhythmic fibers that spontaneously generate the pacemaker potentials that initiate cardiac contractions. These fibers continue to initiate heartbeats after surgeons sever all cardiac nerves and remove a heart from the chest cavity for transplantation. Autorhythmic fibers function as pacemakers and provide a conduction pathway for pacemaker potentials.

The sinoatrial (SA) node and atrioventricular (AV) node are the two internal pacemakers that are primarily responsible for the heart rhythm. The electrocardiogram (ECG) records the action of this electrical conduction system (see Figure 2).

Cardiac Conduction

In a healthy heart, the SA node initiates each cardiac cycle through spontaneous depolarization of its autorhythmic fibers. The SA node's firing of about 100 action potentials per minute usually prevents slower parts of the conduction system and myocardium (heart muscle) from generating competing potentials. The AV node can replace an injured or diseased SA node as pacemaker and spontaneously depolarizes 40 to 60 times per minute. The SA node fires an impulse that travels through the atria to the AV node in about 0.03 seconds and causes the AV node to fire. The P wave of the ECG is produced as contractile fibers in the atria depolarize and culminates in contraction of the atria (atrial systole).

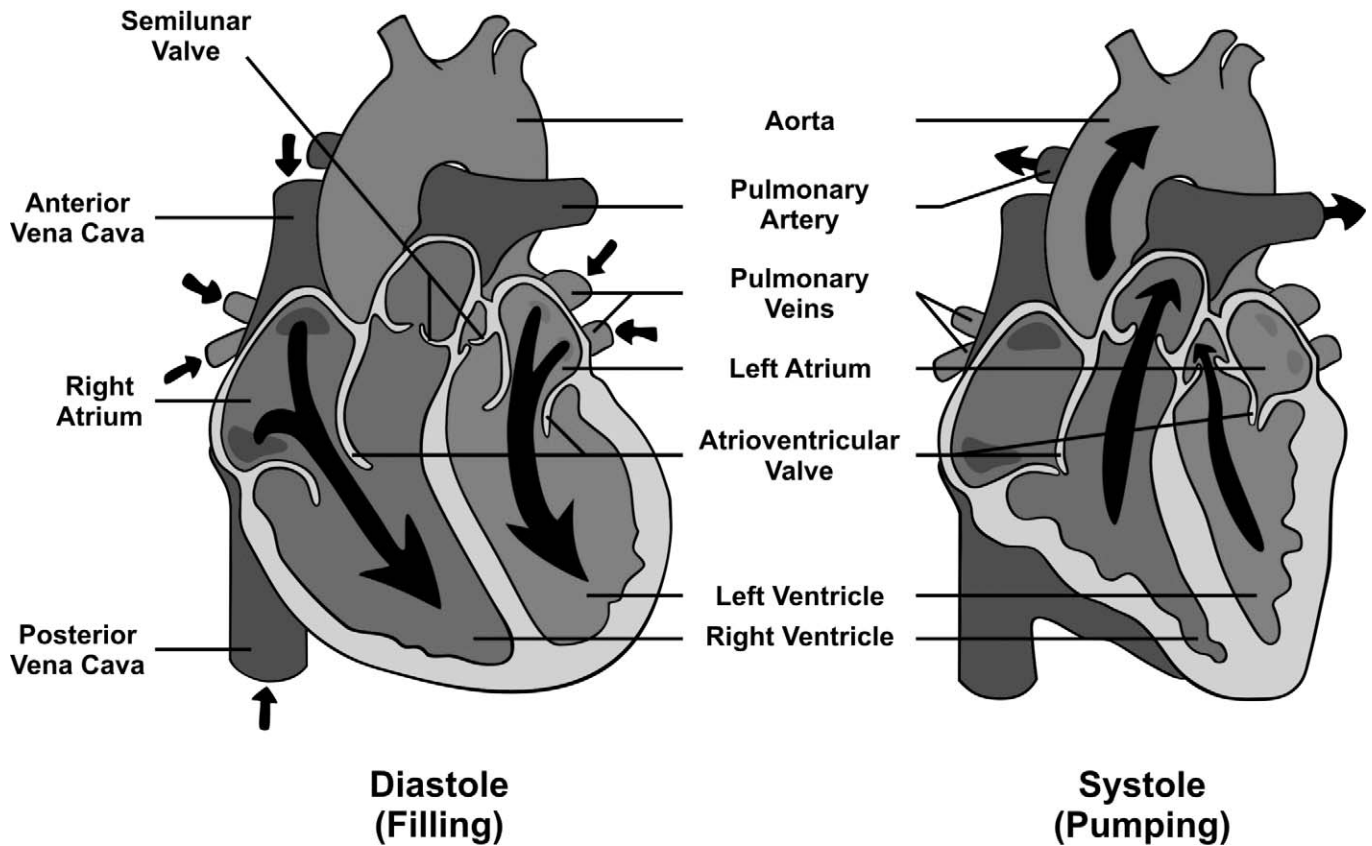


Figure 1. Systole and diastole. Credit: udaix/Shutterstock.com.

The signal rapidly spreads through the AV bundle reaching the top of the septum. These fibers descend down both sides of the septum as the right and left bundle branches and conduct the action potential over the ventricles about 0.2 seconds after the appearance of the P wave. Conduction myofibers, which extend from the bundle branches into the myocardium, depolarize contractile fibers in the ventricles (lower chambers), resulting in the QRS complex. The ventricles contract (ventricular systole) soon after the emergence of the QRS complex, and this continues through the S-T segment. The repolarization of ventricular contractile fibers generates the T wave about 0.4 seconds following the P wave. The ventricles relax (ventricular diastole) 0.6 seconds after the P wave begins.

Considerations for HRV Biofeedback Training

Clinicians should examine the morphology of the ECG for evidence of arrhythmias, ischemia, and prolonged Q-T intervals that could endanger patient safety (Drew et al., 2004) as part of the assessment for heart rate variability (HRV) biofeedback training.

Regulation by the Cardiovascular Center

Although the SA node generates the normal heartbeat cardiac rhythm, autonomic motor neurons and circulating hormones and ions influence the interbeat interval (time between adjacent heartbeats) and the force of the myocardial contraction. The cardiovascular center, located in the medulla of the brain stem, integrates sensory information from proprioceptors (limb position), chemoreceptors (blood chemistry), and baroreceptors (BP) and information from the cerebral cortex and limbic system. The cardiovascular center responds to sensory and higher brain center input by adjusting autonomic balance via sympathetic and parasympathetic motor neurons.

Sympathetic Control

Sympathetic cardiac accelerator nerves target the SA node, AV node, and the bulk of the myocardium (heart muscle). Action potentials conducted by these motor neurons trigger norepinephrine (NE) and epinephrine (E) release and binding to beta-adrenergic (β_1) receptors located on cardiac muscle fibers. This speeds up spontaneous depolarization in the SA and AV nodes (increasing heart rate [HR]) and

Normal

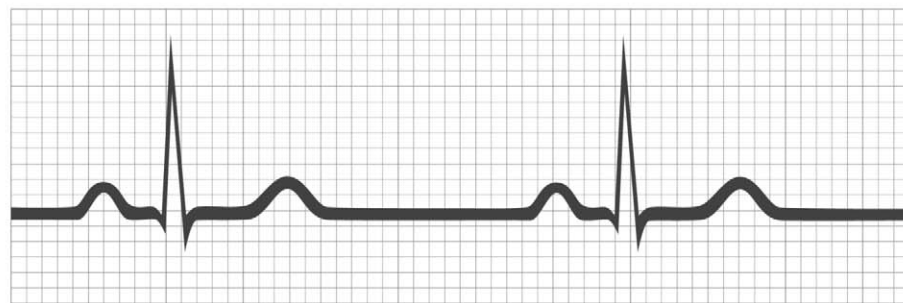
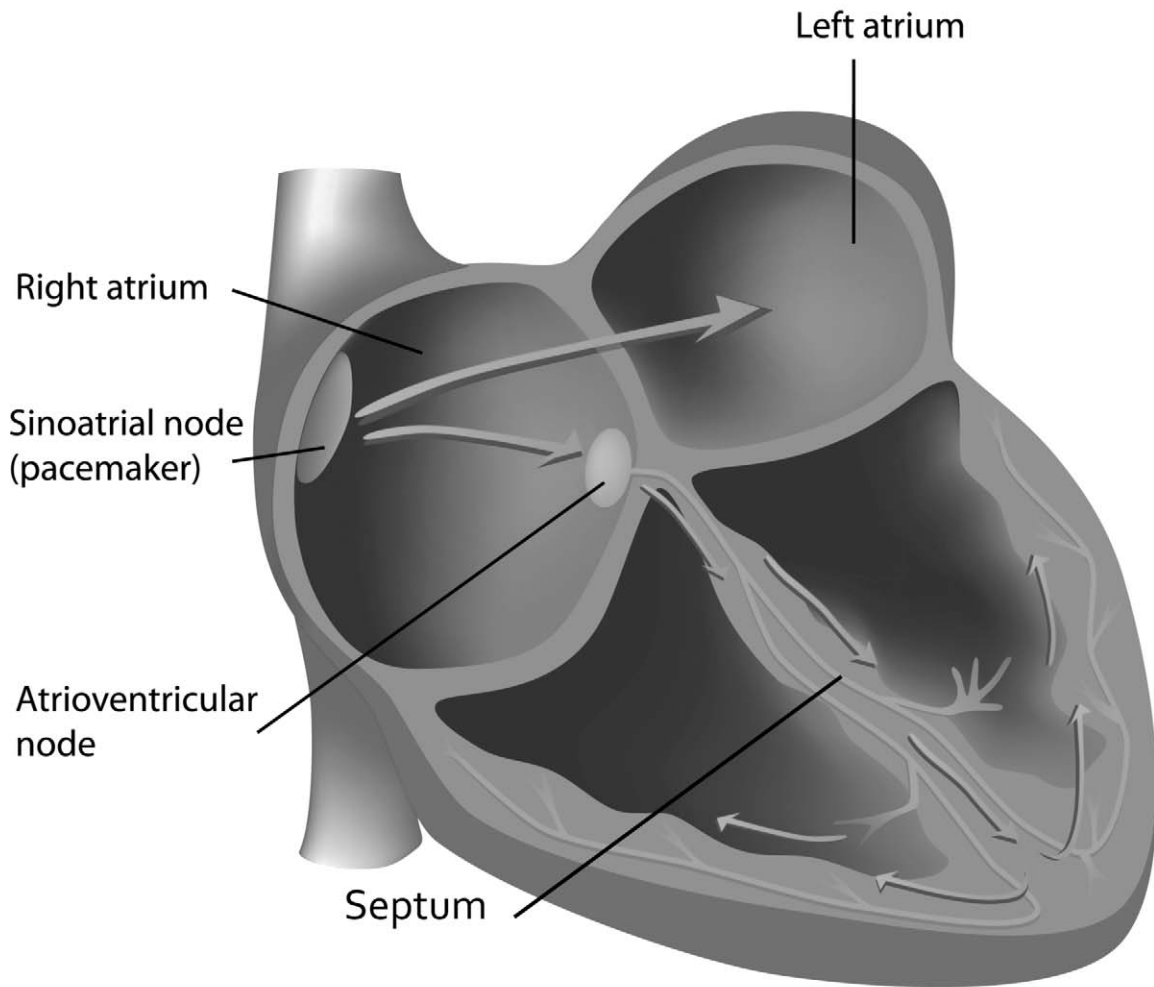


Figure 2. The generation of the electrocardiogram. Credit: Alila Sao Mai/Shutterstock.com.

strengthens the contractility of the atria and ventricles. The number of beta-adrenergic receptors is reduced, and their cardiac muscle contraction in response to NE and E binding is weakened in failing hearts (Ogletree-Hughes et al., 2001).

Parasympathetic Control

The parasympathetic vagus (X) nerves similarly innervate the SA node, AV node, and atrial cardiac muscle. Firing by these motor neurons triggers acetylcholine release and binding to muscarinic (mainly M2) receptors. This decreases the rate of spontaneous depolarization in the SA and AV nodes (slowing HR). Because there is sparse vagal innervation of the ventricles, vagal tone minimally affects the ventricular contractility.

Autonomic Balance

In a healthy heart, there is a dynamic balance between sympathetic nervous system (SNS) and parasympathetic nervous system (PNS) influences. PNS control predominates at rest, resulting in an average HR of 75 beats per minute (bpm). This is significantly slower than the SA node's intrinsic rate, which decreases with age, from an average 107 bpm at 20 years to 90 bpm at 50 years (Ophthof, 2000). The parasympathetic branch can slow the heart to 20 or 30 bpm or briefly stop it (Tortora & Derrickson, 2012). This illustrates the response called accentuated antagonism (Olshansky et al., 2008). Parasympathetic nerves exert their effects more rapidly (<1 second) than sympathetic nerves (>5 seconds; Nunan, Sandercock, & Brodie, 2010).

Cardiac Regulation by Hormones and Ions

Circulating hormones and ions also influence the heart. E, NE, and thyroid hormones increase HR and contractility. The cations (positive ions) K⁺, Ca²⁺, and Na⁺ significantly affect cardiac function. Although elevated plasma levels of K⁺ and Na⁺ decrease HR and contraction force, elevated intracellular Ca²⁺ levels have the opposite effect (Tortora & Derrickson, 2012).

What Is HRV?

HRV consists of changes in the time intervals between consecutive heartbeats (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology [Task Force], 1996). HRV is produced by the interaction of multiple regulatory mechanisms that operate on different time scales (Moss, 2004). Circadian rhythms, core body temperature, and metabolism contribute to 24-hour HRV recordings, which represent the

gold standard for clinical HRV assessment. The autonomic, cardiovascular, and respiratory systems produce short-term (e.g., 5-minute) HRV measurements (see Figure 3).

Why Is HRV Important?

A Healthy Heart Is Not a Metronome

When the time intervals between heartbeats significantly change across successive breathing cycles, this shows that the cardiovascular center can effectively modulate vagal tone. During inhalation, the cardiovascular center withdraws vagal inhibition of the S-A node (speeding the heart). Conversely, during exhalation, it restores vagal inhibition (slowing the heart) via the release of acetylcholine (Eckberg & Eckberg, 1982). This phenomenon, called respiratory sinus arrhythmia (RSA), is mediated by the vagus nerve and is largely responsible for generating HRV (Lehrer, 2013). The modulation of vagal tone helps maintain the dynamic autonomic balance critical to cardiovascular health. Autonomic imbalance due to deficient vagal inhibition is implicated in increased morbidity and all-cause mortality (Thayer, Yamamoto, & Brosschot, 2010).

HRV Is a Marker for Disease and Adaptability

Reduced HRV Is Associated with Disease and Loss of Adaptability

Reduced HRV is associated with vulnerability to physical and psychological stressors and disease (Lehrer, 2007). Low HRV is a marker for cardiovascular disorders, including hypertension, especially with left ventricular hypertrophy; ventricular arrhythmia; chronic heart failure; and ischemic heart disease (Bigger et al., 1995; Casolo, Balli, Taddei, Amuhasi, & Gori, 1989; Maver, Struel, & Accetto, 2004; Nolan et al., 1992; Roach, Wilson, Ritchie, & Sheldon, 2004). Low HRV predicts sudden cardiac death, especially due to arrhythmia following myocardial infarction, and post-heart attack survival (Bigger et al., 1992; Bigger, Fleiss, Rolnitzky, & Steinman, 1993; Kleiger, Miller, Bigger, & Moss, 1987).

Reduced HRV is also seen in disorders with autonomic dysregulation, including anxiety and depressive disorders and asthma, and vulnerability to sudden infant death (Agelink, Boz, Ullrich, & Andrich, 2002; Carney et al., 2001; Cohen & Benjamin, 2006; Giardino, Chan, & Borson, 2004; Kazuma, Otsuka, Matsuoka, & Murata, 1997).

Lehrer (2007) believes that HRV indexes adaptability and marshals evidence that increased RSA represents more

ECG and electrical activity of the myocardium

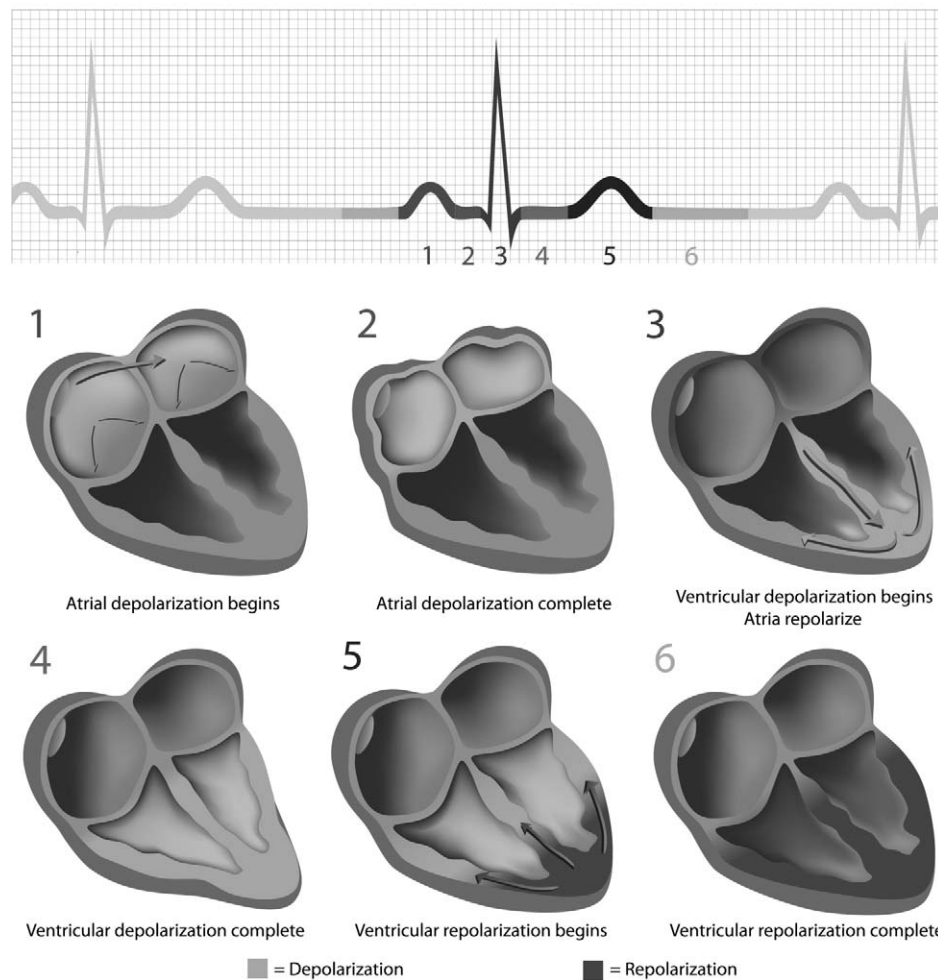


Figure 3. The generation of the electrocardiogram. Credit: Alila Sao Mai/Shutterstock.com.

efficient regulation of BP, HR, and gas exchange by synergistic control systems. He speculates in this special issue of *Biofeedback* that HRV biofeedback might reduce anxiety and depression because the nucleus of the solitary tract (NST), which controls the baroreflexes, is centrally located within the limbic pathways.

Thayer and Lane (2000) outline a neurovisceral integration model that describes how a central autonomic network links the brain stem NST with forebrain structures (including the anterior cingulate, insula, and ventromedial prefrontal cortex, and the amygdala and hypothalamus) through feedback and feed-forward loops. They speculate that a breakdown in negative feedback may produce the increased SNS arousal that characterizes anxiety disorders. Thayer et al. (2012, p. 754) contend that regions that include the amygdala and medial prefrontal cortex, which

evaluate threat and safety, help regulate HRV through their connections with the NST.

How Is HRV Detected?

Clinicians use ECG or photoplethysmograph (PPG) sensors to detect the interbeat interval. The ECG method is more

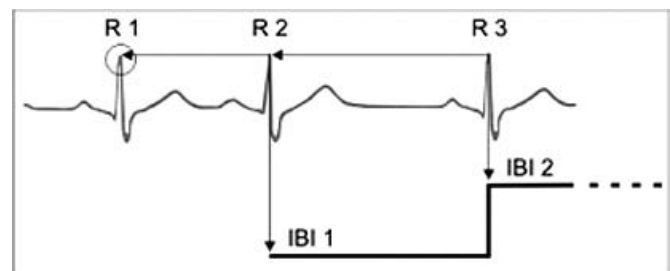


Figure 4. Interbeat interval.

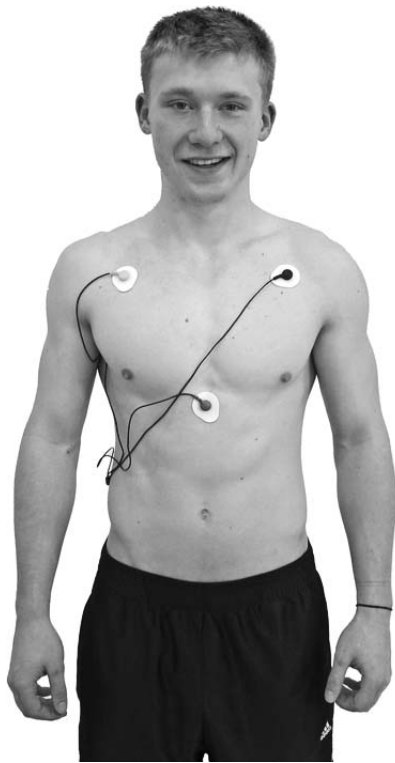


Figure 5. Electrocardiogram chest placement.

accurate than the PPG method because software algorithms can more easily detect the sharp upward spike of the R-wave than the curved peak of the blood volume pulse signal (see Figure 4, courtesy of Thought Technology Ltd.).

An ECG chest placement locates active and reference electrodes over the right and left coracoid processes, respectively, and a second active electrode over the xiphoid process (see Figure 5).

Sources of HRV

Analogous to the electroencephalogram, we can use power spectral analysis to separate HRV into its component rhythms that operate within different frequency ranges. The Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (1996) divided HR oscillations into four frequency bands. The autonomic contribution to the ultra-low-frequency (ULF), very-low-frequency (VLF), and low-frequency (LF) bands remains controversial because measurements profoundly vary with testing conditions (P. M. Lehrer, personal communication, 2012).

ULF Band

The ULF band (≤ 0.003 Hz) indexes fluctuations in interbeat intervals with a period from 5 minutes to 24 hours and is measured using 24-hour recordings (Kleiger et al., 2005). ULF power is highly correlated with the SDANN time domain index (Bigger et al., 1992). Although there is no consensus regarding the mechanisms that generate ULF power, very slow-acting biological processes are implicated. Circadian rhythms, core body temperature, metabolism, and the renin-angiotensin system operate over a long time

Table 1. HRV frequency domain measurements (Task Force, 1996)			
HRV Band	24-Hour Recording	5-Minute Recording	Processes
Ultra low frequency	≤ 0.003 Hz		Very slow biological processes that include circadian rhythms, core body temperature, metabolism, and the renin-angiotensin system and possible PNS and SNS contributions
Very low frequency	0.003–0.04 Hz	$\approx \leq 0.04$ Hz	Temperature regulation, plasma renin fluctuations, endothelial and physical activity influences, and possible PNS and SNS contributions
Low frequency	0.04–0.15 Hz	0.04–0.15 Hz	PNS, SNS, and baroreflex activity (when breathing at resonance frequency)
High frequency	0.15–0.40 Hz	0.15–0.40 Hz	Inhibition and activation of the vagus nerve by breathing (respiratory sinus arrhythmia)
<i>Note.</i> HRV = heart rate variability, PNS = parasympathetic nervous system, SNS = sympathetic nervous system.			

period and may contribute to these frequencies (Bonaduce et al., 1994; Task Force, 1996). There is disagreement about the contribution by the PNS and SNS to this band (see Table 1). Because of its long cycle length (>5 hours), ULF activity is too gradual to train using conventional biofeedback (Stauss, 2003).

VLF Band

The VLF band (0.003–0.04 Hz) requires a recording period of at least 5 minutes. VLF power is strongly correlated with the ASDNN (SDNN index) time domain index, which averages 5-minute standard deviations for all NN intervals over a 24-hour period. There is uncertainty regarding the physiological mechanisms responsible for activity within this band (Kleiger et al., 2005). VLF power may be generated by physical activity (Bernardi, Valle, Coco, Calciati, & Sleight, 1996), thermoregulatory, renin-angiotensin, and endothelial influences on the heart (Akselrod et al., 1981; Claydon & Krassioukov, 2008). PNS activity may contribute to VLF power because parasympathetic blockade almost completely abolishes it (J. A. Taylor, Carr, Myers, & Eckberg, 1998). In contrast, sympathetic blockade does not affect VLF power, and VLF activity is seen in tetraplegics, whose SNS innervation of the heart and lungs is disrupted (Berntson et al., 1997; Task Force, 1996).

The Baroreceptor Reflex Mechanism

The cardiovascular system, central nervous system, endocrine system, peripheral nervous system, respiratory system, and baroreceptors and chemoreceptors influence HRV over a brief time period and contribute to the very low to high frequencies of the HRV spectrum. Baroreceptors, which are BP sensors located in the aortic arch and internal carotid arteries, contribute to HRV. When you inhale, HR increases. BP rises about 5 seconds later. Baroreceptors detect this rise and fire more rapidly. When you exhale, HR decreases. BP falls 5 seconds later (Gevirtz & Lehrer, 2003; Lehrer & Vaschillo, 2008). The baroreflex (see Figure 6) makes possible the respiration-driven speeding and slowing of the heart via the vagus nerves, called respiratory sinus arrhythmia (Karemaker, 2009).

LF Band

The LF band (0.04–0.15 Hz) requires a recording period of at least 2 minutes. There is disagreement regarding the sources of activity within this band. LF power may be produced by both the PNS and SNS and BP regulation via baroreceptors (Akselrod et al., 1981; Berntson, Quigley, & Lozano, 2007; Lehrer, 2007; Task Force, 1996) or by

baroreflex activity alone (Goldstein, Benthoo, Park, & Sharabi, 2011).

HF Band

The high-frequency (HF) or respiratory band (0.15–0.40 Hz) requires a recording period of at least 1 minute. HF power is highly correlated with the pNN50 and RMSSD time domain measures (Kleiger et al., 2005). HF power is generated by the inhibition and activation of the vagus nerves by breathing at normal rates and is primarily parasympathetic. HF power is an index of the sensitivity of the baroreflex, which regulates BP and HR (Task Force, 1996).

LF/HF Ratio

Power is the signal energy contained within a frequency band. The ratio of LF to HF power is called the LF/HF ratio. The interpretation of the LF/HF ratio is controversial because of disagreement about the sources of the LF band. The SNS component of LF activity profoundly varies with testing conditions (P. M. Lehrer, personal communication, 2012). Recall that LF power may be generated by PNS, SNS, and baroreflex mechanisms, whereas HF power is produced by the PNS. A low LF/HF ratio appears to reflect parasympathetic dominance and can be observed when we conserve energy and engage in “tend-and-befriend” behaviors described by S. E. Taylor (2006; see Figure 7).

In contrast, a high LF/HF ratio may indicate sympathetic dominance and may be observed when we engage in fight-or-flight behaviors (see Figure 8).

Time Domain Measurements of HRV

HRV time domain indices quantify the amount of variability in the interbeat intervals between successive heartbeats. Frequently used measurements include the SDNN, SDRR, SDANN, pNN50, HR Max – HR Min, and RMSSD (see Table 2). All measures of HRV are affected by physical conditioning (P. M. Lehrer, personal communication, 2012). Nunan et al. (2010) reported that although the published short-term values for healthy adult subjects were lower than Task Force (1996) 24-hour norms, there was homogeneity among several time domain indices across 44 studies meeting inclusion criteria that enrolled 21,438 participants.

SDNN is the standard deviation of the interbeat interval of normal sinus beats measured in milliseconds. “Normal” means that abnormal beats, like ectopic beats, have been removed. Both SNS and PNS activity contribute to SDNN, and it is highly correlated with VLF and LF band power (Umetani, Singer, McCraty, & Atkinson, 1998). This

Baroreceptor Reflex

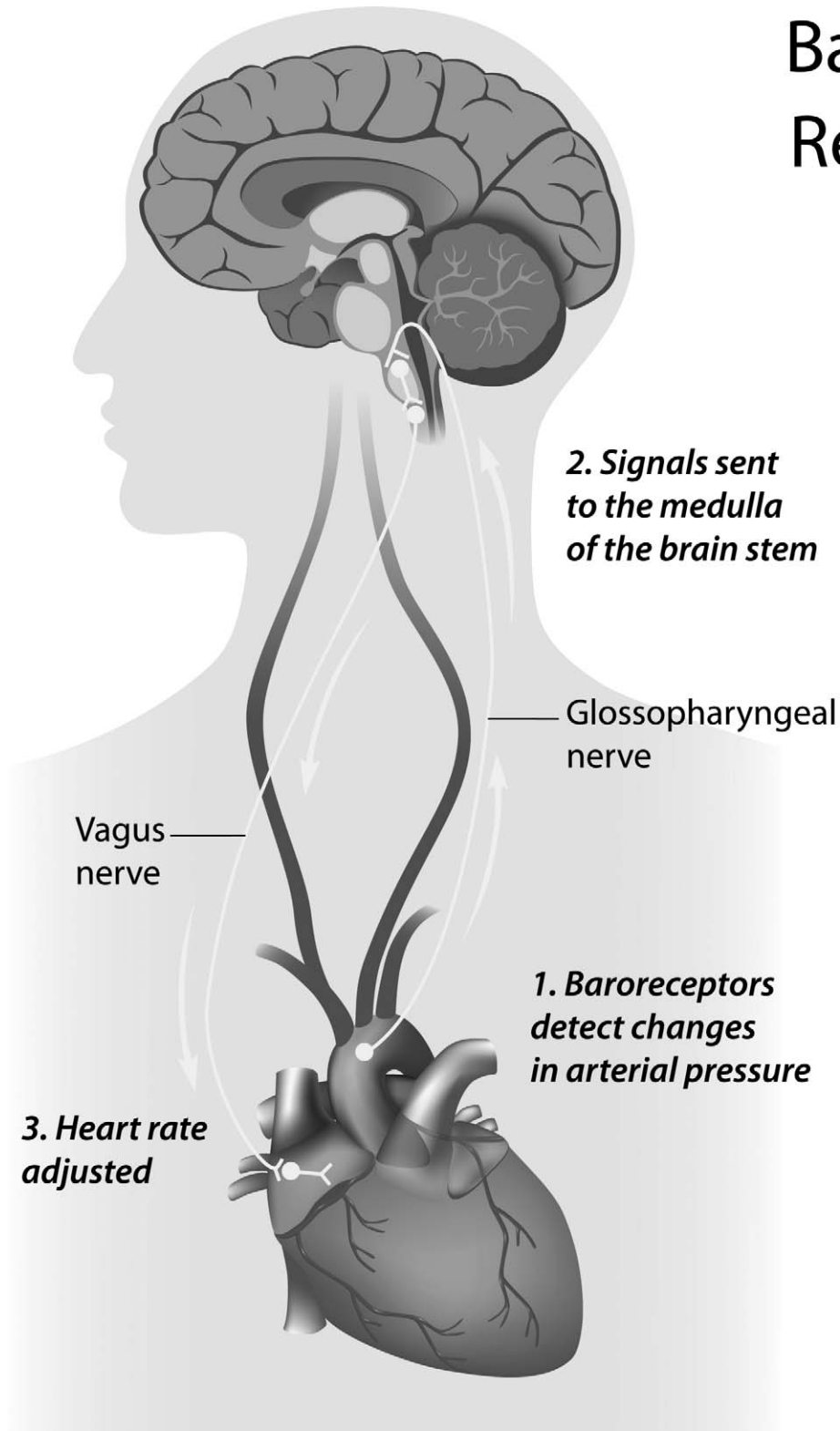
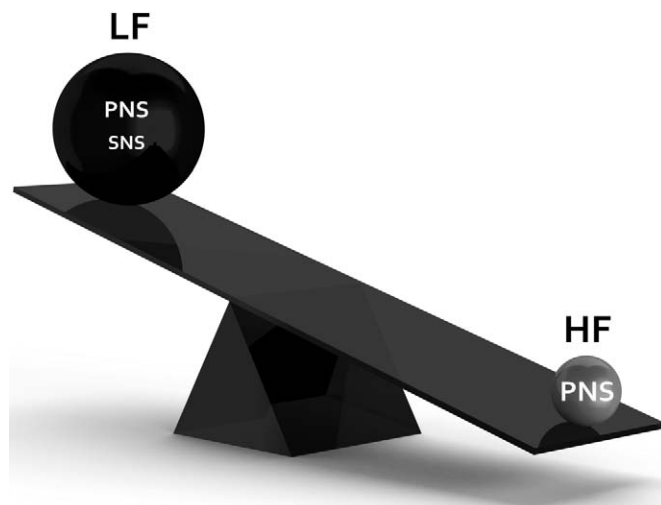


Figure 6. Baroreflex. Credit: Alila Sao Mai/Shutterstock.com.

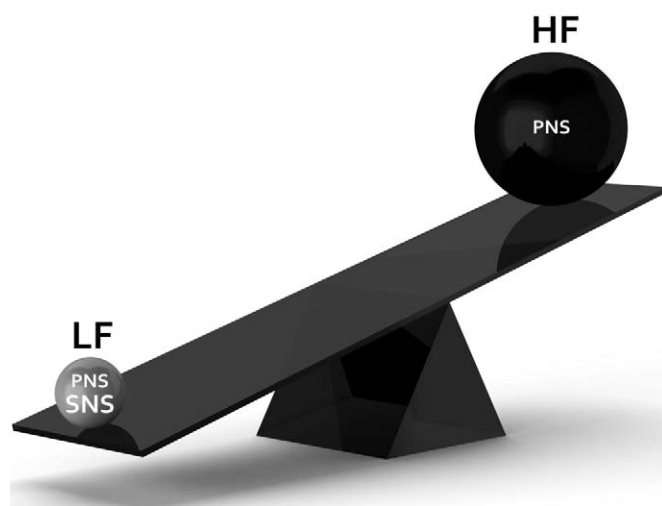


A low LF/HF ratio reflects parasympathetic dominance

Figure 7. Low low-frequency/high-frequency ratio. Credit: luchschen/Shutterstock.com.

relationship depends on the measurement conditions. When these bands have greater power than the HF band, they contribute more to SDNN.

SDNN is more accurate when calculated over 24 hours than during the shorter periods monitored during biofeedback sessions. However, half-hour recording periods may approximate 24-hour values. Longer recording periods



A high LF/HF ratio reflects sympathetic dominance

Figure 8. High low-frequency/high-frequency ratio. Credit: luchschen/Shutterstock.com.

Table 2. HRV time domain indices	
Time Domain Index	Mechanisms
SDNN/SDRR/SDANN	Sympathetic and parasympathetic
pNN50	Parasympathetic
HR Max – HR Min	Parasympathetic
RMSSD	Parasympathetic

provide data about cardiac reactions to a greater range of environmental stimulation. In addition to cardiorespiratory regulation, extended measurement periods can index the heart's response to changing workloads, anticipatory central nervous activity involving classical conditioning, and circadian processes, including sleep-wake cycles (P. M. Lehrer, personal communication, 2012). SDNN is the gold standard for medical stratification of cardiac risk when recorded using a Holter monitor over a 24-hour period (Task Force, 1996).

SDNN values predict both morbidity and mortality. Based on Holter monitoring, patients with SDNN values less than 50 milliseconds are classified as unhealthy, those with values 50–100 milliseconds have compromised health, and those with values greater than 100 milliseconds are healthy. Movement to a higher category increases a patient's probability of survival. For example, a shift from low to moderate SDNN can decrease mortality 400% (Kleiger et al., 1987).

SDRR is the standard deviation of the interbeat interval for all sinus beats (including abnormal or false beats) measured in milliseconds. Abnormal beats may reflect cardiac dysfunction or noise that masquerades as HRV.

SDANN is the standard deviation of the average N-to-N intervals. This index is usually calculated over 5 minutes.

The pNN50 is the percentage of adjacent N-to-N intervals that differ from each other by more than 50 milliseconds. pNN50 is closely correlated with PNS activity (Umetani et al., 1998). This may be a more reliable index than short-term SDNN measurements for the brief samples used in biofeedback.

HR Max – HR Min is the average difference between the highest and lowest HRs during each respiratory cycle. This index is especially sensitive to the effects of respiration rate, independent of vagus nerve traffic. Instead of directly indexing vagal tone, it reflects RSA. This measure is particularly influenced by respiration rate, in ways that may not reflect autonomic function. Because longer exhalations allow greater acetylcholine metabolism, slower

Autonomic Nervous System/Endocrine Component	Autonomic Branch	Activated/Inhibited by	Responses
Unmyelinated vagus (dorsal vagal complex)	Parasympathetic	Survival threats activate	Feigning death, immobilization, passive avoidance, shutdown (post-traumatic stress disorder)
Sympathetic-adrenal-medullary system	Sympathetic	Survival threats activate	Mobilization, fight-or-flight, active avoidance
Myelinated vagus (ventral vagal complex)	Parasympathetic	Social engagement and facial muscle relaxation activate; daily stressors inhibit	Bonding, calming, inhibition of sympathetic-adrenal activation, respiratory sinus arrhythmia

respiration rates can produce higher RSA amplitudes that are not mediated by changes in vagal firing (P. M. Lehrer, personal communication, 2012).

The range for 20-year-olds is 5–10 bpm, whereas it can reach 50 bpm for elite athletes. HR Max – HR Min is typically 3–5 bpm for those older than 50 years. Physically active individuals show wider ranges than those who are sedentary (Moss, 2004).

RMSSD, the square root of the mean squared difference of adjacent N-to-N intervals, is mediated by the parasympathetic branch and is correlated with HF power (Otzenberger et al., 1998). RMSSD is more influenced by the PNS than SDNN (R. Gevirtz, personal communication, 2012). Lower RMSSD values are correlated with higher scores on a risk inventory of sudden unexplained death in epilepsy (DeGiorgio et al., 2010).

Porges's Polyvagal Theory

The vagus, the 10th cranial nerve, inhibits the heart and increases bronchial tone in the lungs. The vagus contains specialized subsystems that control competing adaptive responses. Porges's (2011) controversial polyvagal theory proposes competing roles for the unmyelinated vagus (dorsal vagal complex) and newer myelinated vagus (ventral vagal complex). He hypothesizes that the parasympathetic unmyelinated vagus responds to threats through immobilization, feigning death, passive avoidance, and shutdown. From his perspective, the unmyelinated vagus is activated in post-traumatic stress disorder as patients believe that they will die (see Table 3).

The SNS, in concert with the endocrine system, responds to threats to our safety through mobilization,

fight-or-flight, and active avoidance. The SNS responds more slowly and for a longer period of time (i.e., more than a few seconds) than the parasympathetic vagus system.

In Porges's view, the SNS inhibits the unmyelinated vagus to mobilize us for action. In contrast, the parasympathetic myelinated vagus rapidly adjusts cardiac output and promotes social engagement (the tend-and-befriend response). Daily stressors inhibit the myelinated vagus.

Resonance Frequency Breathing

Lehrer, Vaschillo, and Vaschillo (2004) propose that each individual's cardiovascular system has a unique resonance frequency, which is caused by the delay in the baroreflex. Inertia in the blood supply accounts for most of this delay. Taller people and men have lower resonance frequencies than women and shorter people do, because the former have larger blood volumes. Breathing, rhythmic muscle tension, and emotional stimulation at this frequency can activate or stimulate the cardiovascular system's resonance properties (P. M. Lehrer, personal communication, 2012).

When clients breathe at this rate, which varies in adults from 4.5–6.5 breaths per minute, they “exercise” the baroreflex. HR and BP oscillations are 180° out of phase, the baroreflex is strongest, and RSA is greatest (DeBoer, Karemaker, & Strackee, 1987; Vaschillo, Lehrer, Rische, & Konstantinov, 2002). The perfect phase relationship between HR and respiration results in the most efficient gas exchange and the greatest oxygen saturation (Bernardi, Gabutti, Porta, & Spicuzza, 2001; Vaschillo, Vaschillo, & Lehrer, 2004; Yasuma & Hayano, 2004).

With practice, clients can learn to breathe at their cardiovascular system's resonance frequency. This aligns

the three oscillators (baroreflex, HR, and BP) at that frequency and moves the peak frequency from the HF range (≈ 0.2 Hz) to the LF range (≈ 0.1 Hz). Breathing at the resonance frequency more than doubles the energy in the LF band of the ECG (0.04–0.15 Hz) and centers the peak frequency at the cardiovascular system's resonance frequency. This corresponds to Institute of HeartMath's concept of coherence, in which a client produces a "narrow, high-amplitude, easily visualized peak" from 0.09–0.14 Hz (Ginsberg, Berry, & Powell, 2010, p. 54; McCraty, Atkinson, Tomasino, & Bradley, 2009).

Although HRV biofeedback training immediately produces large-scale increases in baroreflex gain, months of steady practice can increase gain when clients are not receiving feedback (Lehrer, 2013; Lehrer et al., 2003). Increased baroreflex gain is analogous to a more sensitive thermostat. The body regulates BP and gas exchange more effectively. Increased baroreflex gain means that the cardiovascular system produces large-scale HR increases and decreases when a client inhales and exhales. This, in turn, translates into greater HRV.

Remodeling Failing Hearts

Moravec and McKee (2013) report preliminary evidence in this issue that HRV biofeedback may act like a left ventricular assist device to help remodel failing hearts. Patients trained to slow their breathing down to 8–9 breaths per minute increased the numbers of β_1 receptors on cardiac muscle fibers and cardiac muscle contraction in response to NE and E. HRV biofeedback for heart failure patients represents a paradigm shift. Instead of only targeting sympathetic activation, HRV biofeedback teaches patients to restore autonomic balance by decreasing SNS arousal while simultaneously increasing PNS activity.

Modulation of Immunity

Resonance frequency breathing, like vagal nerve stimulation (VNS), may influence the parasympathetic cholinergic cytokine control system that modulates immunity through interleukins and interferons (Gevirtz, 2013; Tracey, 2007). Interleukin-6 (IL-6) may increase the risk of myocardial infarction by promoting inflammation in coronary arteries (Ridker, Rifai, Stampfer, & Hennekens, 2000).

Lehrer et al. (2010) demonstrated that subjects trained to breathe at their resonance frequency minimized the reduction of HRV, headache, and eye photosensitivity following an injection of lipopolysaccharide, which is an inflammatory cytokine. Purcell, Urlakis, and Shaffer (2010) reported preliminary evidence that resonance frequency breathing can reduce levels of IL-6.

Summary

The SA node generates the fundamental cardiac rhythm, which is modulated by autonomic motor neurons and circulating hormones and ions. There is a dynamic balance between sympathetic and parasympathetic branches in a healthy heart. HRV is generated by multiple regulatory mechanisms that operate on different time scales. HRV biofeedback exercises the baroreflex and can produce large-scale HR changes and greater respiratory efficiency. Resonance frequency breathing may increase resilience against stressors, reduce hypertension, and improve the prognosis of patients diagnosed with cardiovascular and respiratory disorders. This behavioral intervention may have the potential to help remodel failing hearts and modulate immunity via the parasympathetic cholinergic cytokine control system.

Acknowledgments

The authors want to express their profound thanks to Richards S. Gevirtz and Paul Lehrer for their generous contributions to this article, and to Winston Vanderhoof for his graphics.

References

- Agelink, M. W., Boz, C., Ullrich, H., & Andrich, J. (2002). Relationship between major depression and heart rate variability: Clinical consequences and implications for antidepressive treatment. *Psychiatry Research, 113*, 139–149.
- Akselrod, S., Gordon, D., Ubel, F. A., Shannon, D. C., Barger, A. C., & Cohen, R. J. (1981). Power spectrum analysis of heart rate fluctuation: A quantitative probe of beat-to-beat cardiovascular control. *Science, 213*, 220–222.
- Bernardi, L., Gabutti, A., Porta, C., & Spicuzza, L. (2001). Slow breathing reduces chemoreflex response to hypoxia and hypercapnia, and increases baroreflex sensitivity. *Journal of Hypertension, 19*, 2221–2229.
- Bernardi, L., Valle, F., Coco, M., Calciati, A., & Sleight, P. (1996). Physical activity influences heart rate variability and very-low-frequency components in Holter electrocardiograms. *Cardiovascular Research, 32*, 234–237.
- Berntson, G. G., Bigger, J. T., 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.
- Berntson, G. G., Quigley, K. S., & Lozano, D. (2007). Cardiovascular psychophysiology. In J. T. Cacioppo, L. G. Tassinary, & G. G. Berntson, (Eds.), *Handbook of psychophysiology* (3rd ed., pp. 182–210). New York: Cambridge University Press.
- Bigger, J. T., Fleiss, J. L., Rolnitzky, L. M., & Steinman, R. C. (1993). The ability of several short-term measures of RR variability to predict mortality after myocardial infarction. *Circulation, 88*, 927–934.

- Bigger, J. T., Fleiss, J. L., Steinman, R. C., Rolnitzky, L. M., Kleiger, R. E., Rottman, J. N., et al. (1992). Frequency domain measures of heart period variability and mortality after myocardial infarction. *Circulation*, *85*, 164–171.
- Bigger, J. T., Fleiss, J. L., Steinman, R. C., Rolnitzky, L. M., Schneider, W. J., Stein, P. K., et al. (1995). RR variability in healthy, middle-aged persons compared with patients with chronic coronary heart disease or recent acute myocardial infarction. *Circulation*, *91*, 1936–1943.
- Bonaduce, D., Marciano, F., Petretta, M., Migaux, M. L., Morgano, G., Bianchi, V., et al. (1994). Effects of converting enzyme inhibition on heart period variability in patients with acute myocardial infarction. *Circulation*, *90*, 108–113.
- Carney, R. M., Blumenthal, J. A., Stein, P. K., Watkins, L., Catellier, D., Berkman, L. F., et al. (2001). Depression, heart rate variability, and acute myocardial infarction. *Circulation*, *104*, 2024–2028.
- Casolo, G., Balli, E., Taddei, T., Amuhasi, J., & Gori, C. (1989). Decreased spontaneous heart rate variability in congestive heart failure. *American Journal of Cardiology*, *64*, 1162–1167.
- Claydon, V. E., & Krassioukov, A. V. (2008). Clinical correlates of frequency analyses of cardiovascular control after spinal cord injury. *American Journal of Physiology—Heart and Circulatory Physiology*, *294*, H668–H678.
- Cohen, H., & Benjamin, J. (2006). Power spectrum analysis and cardiovascular morbidity in anxiety disorders. *Autonomic Neuroscience: Basic and Clinical*, *128*, 1–8.
- 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—Heart and Circulatory Physiology*, *253*, H680–H689.
- DeGiorgio, C. M., Miller, P., Meymandi, S., Chin, A., Epps, J., Gordon, S., et al. (2010). RMSSD, a measure of vagus-mediated heart rate variability, is associated with risk factors for SUDEP: The SUDEP-7 Inventory. *Epilepsy and Behavior*, *19*, 78–81.
- Drew, B. J., Califf, R. M., Funk, M., Kaufman, E. S., Krucoff, M. W., Laks, M. M., et al. (2004). Practice standards for electrocardiographic monitoring in hospital settings: An American Heart Association scientific statement from the Councils on Cardiovascular Nursing, Clinical Cardiology, and Cardiovascular Disease in the young. *Circulation*, *110*, 2721–2746.
- Eckberg, D. L., & Eckberg, M. J. (1982). Human sinus node responses to repetitive, ramped carotid baroreceptor stimuli. *American Journal of Physiology—Heart and Circulatory Physiology*, *242*, H638–H644.
- Gevirtz, R. (2013). The nerve of that disease: The vagus nerve and cardiac rehabilitation. *Biofeedback*, *41*, 32–38.
- Gevirtz, R. N., & Lehrer, P. (2003). Resonant frequency heart rate biofeedback. In M. S. Schwartz & F. Andrasik (Eds.), *Biofeedback: A practitioner's guide* (3rd ed., pp 245–250). New York: The Guilford Press.
- Giardino, N. D., Chan, L., & Borson, S. (2004). Combined heart rate variability and pulse oximetry biofeedback for chronic obstructive pulmonary disease. *Applied Psychophysiology and Biofeedback*, *29*, 121–133.
- Ginsberg, J. P., Berry, M. E., & Powell, D. A. (2010). Cardiac coherence and posttraumatic stress disorder in combat veterans. *Alternative Therapies*, *16*, 52–60.
- Goldstein, D. S., Benth, O., Park, M. Y., & Sharabi, Y. (2011). Low frequency power of heart rate variability is not a measure of cardiac sympathetic tone but may be a measure of modulation of cardiac autonomic outflows by baroreflexes. *Experimental Physiology*, *96*, 1255–1261.
- Karemaker, J. M. (2009). Counterpoint: Respiratory sinus arrhythmia is due to the baroreflex mechanism. *Journal of Applied Psychology*, *106*(5), 1742–1743.
- Kazuma, N., Otsuka, K., Matsuoka, I., & Murata, M. (1997). Heart rate variability during 24 hours in asthmatic children. *Chronobiology International*, *14*, 597–606.
- Kleiger, R. E., Miller, J. P., Bigger, J. T., Moss, A. J., & the Multicenter Post-Infarction Research Group. (1987). Decreased heart rate variability and its association with increased mortality after acute myocardial infarction. *American Journal of Cardiology*, *59*, 256–262.
- Kleiger, R. E., Stein, P. K., Bigger, J. T. (2005). Heart rate variability: Measurement and clinical utility. *Annals of Noninvasive Electrocardiology*, *10*(1), 88–101.
- Lehrer, P. M. (2007). Biofeedback training to increase heart rate variability. In P. M. Lehrer, R. M. Woolfolk, & W. E. Sime (Eds.), *Principles and practice of stress management* (3rd ed.). New York: Guilford Press.
- Lehrer, P. M. (2013). How does heart rate variability biofeedback work? Resonance, the baroreflex, and other mechanisms. *Biofeedback*, *41*, 26–31.
- Lehrer, P., Karavidas, M. K., Lu, S. E., Coyle, S. M., Oikawa, L. O., Macor, M., et al. (2010). Voluntarily produced increases in heart rate variability modulate autonomic effects of endotoxin induced systemic inflammation: An exploratory study. *Applied Psychophysiology and Biofeedback*, *35*, 303–315.
- Lehrer, P. M., & Vaschillo, E. (2008). The future of heart rate variability biofeedback. *Biofeedback*, *36*(1), 11–14.
- Lehrer, P. M., Vaschillo, E. V., & Vaschillo, B. (2004). Heartbeat synchronizes with respiratory rhythm only under specific circumstances. *Chest*, *126*, 1385–1386.
- Lehrer, P. M., Vaschillo, E., Vaschillo, B., Lu, S. E., Eckberg, D. L., Edelberg, R., et al. (2003). Heart rate variability biofeedback increases baroreflex gain and peak expiratory flow. *Psychosomatic Medicine*, *65*, 796–805.
- Maver, J., Strucl, M., & Accetto, R. (2004). Autonomic nervous system and microvascular alterations in normotensives with a family history of hypertension. *Blood Press*, *13*, 95–100.
- McCarty, R., Atkinson, M., Tomasino, D., & Bradley, R. T. (2009). The coherent heart: Heart-brain interactions, psychophysiological coherence, and the emergence of system-wide order. *Integral Review*, *5*(2), 10–115.
- Moravec, C. S., & McKee, M. G. (2013). Psychophysiological remodeling of the failing human heart. *Biofeedback*, *41*, 7–12.
- Moss, D. (2004). Heart rate variability (HRV) biofeedback. *Psychophysiology Today*, *1*, 4–11.
- Nolan, J., Flapan, A. D., Capewell, S., MacDonald, T. M., Neilson, J. M., Ewing, D. J. et al. (1992). Decreased cardiac parasym-

- pathetic activity in chronic heart failure and its relation to left ventricular function. *British Heart Journal*, 67, 482–485.
- Nunan, D., Sandercock, G. R. H., & Brodie, D. A. (2010). A quantitative systematic review of normal values for short-term heart rate variability in healthy adults. *Pacing and Clinical Electrophysiology*, 33, 1407–1417.
- Ogletree-Hughes, M. L., Stull, L. B., Sweet, W. E., Smedira, N. G., McCarthy, P. M., Moravec, C. S., et al. (2001). Mechanical unloading restores beta-adrenergic responsiveness and reverses receptor down-regulation in the failing human heart. *Circulation*, 104, 881–886.
- Olshansky, B., Sabbah, H. N., Hauptman, P. J., & Colucci, W. S. (2008). Parasympathetic nervous system and heart failure: Pathophysiology and potential implications for therapy. *Circulation*, 118, 863–871.
- Opthof, T. (2000). The normal range and determinants of the intrinsic heart rate in man. *Cardiovascular Research*, 45, 177–184.
- Otzenberger, H., Gronfier, C., Simon, C., Charloux, A., Ehrhart, J., Piquard, F., et al. (1998). Dynamic heart rate variability: A tool for exploring sympathovagal balance continuously during sleep in men. *American Journal of Physiology*, 275, H946–H950.
- Porges, S. W. (2011). *The polyvagal theory: Neurophysiological foundations of emotions, attachment, communication, and self-regulation*. New York: W. W. Norton & Company.
- Purcell, E., Urlakis, M., & Shaffer, F. (2010). Physical and emotional effects of resonant diaphragmatic breathing. *Applied Psychophysiology and Biofeedback*, 35, 327.
- Ridker, P. M., Rifai, N., Stampfer, M. J., & Hennekens, C. H. (2000). Plasma concentration interleukin-6 and the risk of future myocardial infarction among apparently healthy men. *Circulation*, 101, 1767–1772.
- Roach, D., Wilson, W., Ritchie, D., & Sheldon, R. (2004). Dissection of long-range heart rate variability: Controlled induction of prognostic measures by activity in the laboratory. *Journal of the American College of Cardiology*, 43, 2271–2277.
- Stauss, H. M. (2003). Heart rate variability. *American Journal of Physiology: Regulatory, Integrative and Comparative Physiology*, 285, R927–R931.
- Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. (1996). Heart rate variability: Standards of measurement, physiological interpretation, and clinical use. *Circulation*, 93, 1043–1065.
- Taylor, J. A., Carr, D. L., Myers, C. W., & Eckberg, D. L. (1998). Mechanisms underlying very-low-frequency RR-interval oscillations in humans. *Circulation*, 98, 547–555.
- Taylor, S. E. (2006). Tend and befriend: Biological bases of affiliation under stress. *Current Directions in Psychological Science*, 15, 273–277.
- Thayer, J. F., Ahs, F., Fredrikson, M., Sollers, J. J., & Wager, T. D. (2012). A meta-analysis of heart rate variability and neuroimaging studies: Implications for heart rate variability as a marker of stress and health. *Neuroscience and Biobehavioral Reviews*, 36, 747–756.
- Thayer, J. F., & Lane, R. D. (2000). A model of neurovisceral integration in emotion regulation and dysregulation. *Journal of Affective Disorders*, 61, 201–216.
- Thayer, J. F., Yamamoto, S. S., & Brosschot, J. F. (2010). The relationship of autonomic imbalance, heart rate variability and cardiovascular disease risk factors. *International Journal of Cardiology*, 141, 122–131.
- Tortora, G. J., & Derrickson, B. H. (2012). *Principles of anatomy and physiology* (13th ed.). New York: John Wiley & Sons, Inc.
- Tracey, K. J. (2007). Physiology and immunology of the cholinergic anti-inflammatory pathway. *Journal of Clinical Investigation*, 117, 289–296.
- Umetami, K., Singer, D. H., McCraty, R., & Atkinson, M. (1998). Twenty-four hour time domain heart rate variability and heart rate: Relations to age and gender over nine decades. *Journal of the American College of Cardiology*, 31, 593–601.
- Vaschillo, E., Lehrer, P., Risse, N., & Konstantinov, M. (2002). Heart rate variability biofeedback as a method for assessing baroreflex function: A preliminary study of resonance in the cardiovascular system. *Applied Psychophysiology and Biofeedback*, 27, 1–27.
- Vaschillo, E., Vaschillo, B., & Lehrer, P. (2004). Heartbeat synchronizes with respiratory rhythm only under specific circumstances. *Chest*, 126, 1385–1386.
- Yasuma, F., & Hayano, J. (2004). Respiratory sinus arrhythmia: Why does the heartbeat synchronize with respiratory rhythm? *Chest*, 125, 683–690.



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