The emphasis on the sympathetic nervous system (SNS) in cardiology has recently shifted to a view recognizing the extraordinarily protective role that the (parasympathetic) vagus nerve plays in prevention and rehabilitation of heart muscle and pacemaker function. This article summarizes some of the epidemiological evidence supporting this premise and describes biofeedback-based interventions that may play a role in the future of cardiac disease prevention and rehabilitation.

The Vagus Nerve, Parasympathetic Activity, and Cardiovascular Disease

In recent years in cardiac rehabilitation, there has been a shift in emphasis from interventions that reduce chronic sympathetic activation to a more balanced view that includes activation of the parasympathetic system, especially the vagus nerve (Curtis & O’Keefe, 2002). The vagus, the 10th cranial nerve, is responsible for inhibitory pathways to the heart and lungs. According to Olshansky et al. (2011), “Vagal ‘tone’ predominates over sympathetic tone at rest. Under normal physiological conditions, abrupt parasympathetic stimulation will inhibit tonic sympathetic activation and its effects at rest and during exercise. This response is known as ‘accentuated antagonism’” (p. 863).

Traditionally, the sympathetic branch of the autonomic nervous system (ANS) was considered the major player in the onset and maintenance of cardiovascular disease. The thinking was that the adaptive SNS arose as needed for fight or flight as appropriate for survival thousands of years ago, but when activated in modern life on a chronic basis, it may produce the deleterious effects associated with cardiovascular disease. On the other hand, it is also well known that diminished SNS function can have deleterious effects on health and level of functioning such as producing lethargy or dysphoria. The longstanding view that SNS overactivation was the main risk for cardiovascular disease has led to the liberal use of beta blockers. This has had mixed results (Curtis & O’Keefe, 2002).

More recent analyses emphasize a balance between the two ANS branches: “Any therapy that chronically activates the sympathetic nervous system and/or diminishes the parasympathetic (vagal) tone will increase the risk of cardiovascular events. In contrast, any therapies that tip the autonomic balance toward parasympathetic dominance and decrease sympathetic tone will improve prognosis” (Curtis & O’Keefe, 2002, p. 47).

Epidemiological evidence from large longitudinal studies reinforces this point with regard to cardiac disease onset and rehabilitation (Nishime, Cole, Blackstone, Pashkow, & Lauer, 2000). For example, Nishime et al. (2000) found that 5-year mortality rates in patients referred for exercise ECGs went from 2% in participants with a robust heart rate recovery in the minute after exercise (a decrease of 25–30 breaths/minute) up to 13% for those patients with a decrease of 10 breaths/minute or less. Recovery after exercise is known to be dependent on vagal tone.

Heart rate variability (HRV), the variation in cardiac beat-to-beat intervals averaged over time, is largely determined by the vagus exerting inhibitory effects on the sinus node (pacemaker) of the heart. It then follows that poor HRV would produce poor outcomes after a cardiac event such as a myocardial infarction. Figure 1 shows the survival curves for two groups of patients, those with poor (lower) HRV vs. those with normal HRV. As can be seen, the two groups differed dramatically on survival (Måkikallio et al., 1999; Måkikallio, Huikuri, Hintze et al., 2001; Måkikallio, Huikuri, Måkikallio et al., 2001).

One manifestation of the shift in emphasis from reduction of SNS activity to boosting parasympathetic or vagal tone can be seen in the recent work with vagal nerve stimulation (VNS). Earlier work had shown that stimulation of the vagal afferent pathway may have had profound effects on depression of seizure activity (Chae et al., 2003; D. T. George et al., 1989; M. S. George et al., 2000; Rush et
al., 2000). More recently, stimulation of the vagal efferent pathway has been shown to be helpful in the treatment of heart failure (Sabbah et al., 2011). Benefits after 3 months of VNS were seen in improved left ventricular ejection fraction (LVEF) and distance walked in 6 minutes (Sabbah et al., 2011). “Vagus nerve stimulation derives these potential clinical benefits from multiple mechanisms of action. These include reduced heart rate, restoration of heart rate variability and baroreflex sensitivity, suppression of proinflammatory cytokines, and antiarrhythmic effects” (Kuschyk & Borggrefe, 2011, p. 21).

Another pathway that has been recently discovered involving the parasympathetic system has been called the cholinergic anti-inflammatory system (Czura, Friedman, & Tracey, 2003; Pavlov & Tracey, 2005; Pavlov, Wang, Czura, Friedman, & Tracey, 2003; K. J. Tracey, 2002; K. J. Tracey, 2007; W. R. Tracey, Alexander, Eyre, & Singh, 1985). “The regulation of the innate immune response is critical for controlling inflammation and for the prevention and treatment of diseases. We recently demonstrated that the efferent vagus nerve inhibits proinflammatory cytokine release and protects against systemic inflammation, and termed this vagal function ‘the cholinergic anti-inflammatory pathway’” (Pavlov & Tracey, 2005, p. 493). Thus, aspects of cardiovascular or other disease that involve an unchecked inflammatory response might be targeted with vagal stimulation, either electrically or behaviorally.

“Behavioral modification, meditation, hypnosis, biofeedback, and cognitive and relaxation therapies, which have been advocated for treatment of inflammation, can stimulate vagus nerve activity. It should now be possible to determine clinically whether these or other approaches activate the cholinergic anti-inflammatory pathway” (K. J. Tracey, 2007, p. 291). This work has led to investigations using an implantable device that stimulates the vagal pathway to the heart (Zitnik, 2011a, 2011b).

### Applying Heart Rate Variability Training to Cardiac Rehabilitation Populations

Our group as well as others (see especially Morovec et al., 2013, this issue) have been investigating the use of HRV biofeedback in the cardiac rehabilitation setting. HRV biofeedback is a technique that uses electrocardiogram (or photoplethysmograph) displays of beat-to-beat changes in heart rate (HR) to encourage the client to maximize the increase in heart rate during inhalation and decrease during exhalation regulated by the vagus (respiratory sinus arrhythmia [RSA]). With daily practice, this technique has been shown to be effective in increasing homeostasis of the autonomic nervous system and strengthening the baroreflex (Gevirtz, 2000, 2007, 2011; Gevirtz & Lehrer, 2003; Gevirtz & Schwartz, 2003; Giardino, Lehrer, & Feldman, 2000; Lehrer, 2007; Lehrer, Smetakin, & Potapova, 2000; Lehrer et al., 2006).

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![Figure 1. Survival (in days) following an ECG referral for patients with high (good) versus low (poor) heart rate variability.](Image)
Figure 2. SDNN (a measure of cardiovascular adaptive ability) over three time periods. The treatment group received HRV biofeedback while the controls received treatment as usual (Del Pozo et al., 2004).

Figure 3. Distance walked in 6 minutes by two groups of heart failure patients; those receiving HRV biofeedback vs. those getting an EEG feedback signal. Note this graph only represents the participants with left ventricular ejection fractions (LVEF) over 30 (Swanson et al., 2006).
Our original premise was that, by stimulating parasympathetic activity, we might tip the balance away from sympathetic dominance and improve cardiac function. In this light, students in our group completed two studies involving cardiac patients. Jan van Dixhoorn in the Netherlands had already shown that carefully taught, slow, functional breathing techniques could have an effect on cardiac morbidity and mortality (van Dixhoorn, 1997, 1998, 2007; van Dixhoorn & Duivenvoorden, 1985, 1999; van Dixhoorn, Duivenvoorden, & Pool, 1990; van Dixhoorn, Duivenvoorden, Pool, & Verhage, 1990; van Dixhoorn, Duivenvoorden, Staal, & Pool, 1989; van Dixhoorn, Duivenvoorden, Staal, Pool, & Verhage, 1987; van Dixhoorn & White, 2005). We (Jessica Del Pozo was the principal investigator) tested the efficacy of HRV biofeedback in postmyocardial infarction patients. After seven sessions of training with encouraged home practice, we followed up at the 18-week mark. Compared to a wait list control, the biofeedback-trained patients showed significant improvement in SDNN, a general measure of cardiac health and variability (Del Pozo, Gevirtz, Scher, & Guarneri, 2004). The SDNN is the standard deviation of the beat-to-beat interval, the time between R waves, and is a widely utilized index of variability. Most patients approached a healthy level of variability (see Figure 2).

Next, we tried HRV biofeedback compared to a pseudo-EEG feedback (alternating enhance/inhibit alpha/theta) with heart failure patients (Swanson, Gevirtz, Spira, & Guarneri, 2006). For those patients with a very low LVEF (a very sick heart), we did not see much change. But for those with a LVEF over 31 (still not good, but not as severe), the biofeedback led to significantly greater distance walked in 6 minutes (see Figure 3).

In fact, this outcome is almost identical to the data reported by Sabbah using an electrical stimulus to the vagus (Sabbah, 2011).

**New Horizons: Heartbeat Evoked Potential**

This led us to wonder if HRV biofeedback (and probably thousands of years of various meditative breathing techniques) might be stimulating the vagus such that both efferent and afferent pathways would be effective. To investigate this possibility, we (Starr MacKinnon was the Principle Investigator and Rollin McCraty of the Heart-Math institute worked with us) are now studying a phenomenon called heartbeat evoked potential (HEP). Each time the heart beats, the R wave, reflecting the left ventricle’s contraction, is sent coursing through the body. It is easily seen in EEG waves unless filtered out. By concentrating the EEG on a 1-second window a short time...
(250 millisecond) after the R wave, an event related or evoked potential is measurable from central brain locations. It has been shown that good heart rate perceivers have a higher amplitude in the wave, presumably reflecting a stronger afferent pathway (Pollatos, Kirsch, & Schandry, 2005a, 2005b; Pollatos, Matthias, & Schandry, 2007; Pollatos & Schandry, 2004; Pollatos, Schandry, Auer, & Kaufmann, 2007; Schandry, 1981, 2003; Schandry, Bestler, & Montoya, 1993; Schandry, Sparrer, & Weitkunat, 1986; Schandry & Weitkunat, 1990). We tested this idea by looking at the HEP during a recalled positive or negative emotion and during slow (6/minute) breathing compared to a baseline. The preliminary results (partially shown in Figure 4) were that negative emotion reduced the HEP amplitude, positive emotion had no significant effect, and slow breathing enhanced it.

This technique may help us discover what mechanisms are involved in HRV biofeedback, in interoception, in body awareness, and so forth.

Conclusions: Biofeedback and Breath Training Offer Tools for Cardiac Rehabilitation

In summary, biofeedback and/or other breathing techniques seem to offer useful tools in the field of cardiac rehabilitation. We may be able to understand mechanisms that would lead to a meaningful integration of pharmacology, electrical devices, and biofeedback techniques to further our efforts to prolong and improve the life of cardiac patients.

References


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