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Increased cardio-respiratory coupling evoked by slow deep breathing can persist in normal humans☆

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ABSTRACT

Slow deep breathing (SDB) has a therapeutic effect on autonomic tone. Our previous studies suggested that coupling of the cardiovascular to the respiratory system mediates plasticity expressed in sympathetic nerve activity. We hypothesized that SDB evokes short-term plasticity of cardiorespiratory coupling (CRC). We analyzed respiratory frequency (fR), heart rate and its variability (HR&HRV), the power spectral density (PSD) of blood pressure (BP) and the ventilatory pattern before, during, and after a 20-min epoch of SDB. During SDB, CRC and the relative PSD of BP at fR increased; mean arterial pressure decreased; but HR varied; increasing ($n=3$), or decreasing ($n=2$) or remaining the same ($n=5$). After SDB, short-term plasticity was not apparent for the group but for individuals differences existed between baseline and recovery periods. We conclude that a repeated practice, like pranayama, may strengthen CRC and evoke short-term plasticity effectively in a subset of individuals.

1. Introduction

Cardiovascular and respiratory control systems are coupled reciprocally. While each system affects the other, respiration, the slower oscillation, has a stronger influence on the cardiovascular system than arterial blood pressure has on the breathing pattern. Due to the strength of the effect of respiration, the influence of breathing on heart rate (HR) and blood pressure (BP) was recognized early in the development of Western medicine. In his overview of milestones for understanding heart rate variability (HRV), Billman (2011) credited Reverend Stephen Hale for reporting respiration's influence on HR and BP in 1733 and Walter Cannon for measuring increases in HR and BP during inspiration (respiratory sinus arrhythmia (RSA) and Traube–Hering waves, respectively) approximately 100 years later. Then just 50 years ago, Hon and Lee (1963a,b) made the translational step from bench to bedside by identifying the clinical relevance of HRV as a biomarker for fetal health. An absence of HRV preceded death.

Although various analytical tools can measure HRV, the standards of measurement, physiological interpretation, and theoretical clinical use of HRV became defined in the 1996 white paper, a joint publication in journals of Cardiology Societies in both North American and Europe. But despite wide spread involvement of leading scientists, the interpretation and usefulness of HRV is not accepted universally. Indeed, these issues have been debated in the literature. For example, "Cardiovascular variability is/is not an index of autonomic control of circulation" was one of the earliest topics considered in Point:Counterpoint published

Abbreviations: ABP, arterial blood pressure; BP, blood pressure (in this manuscript, the reader can assume we are referring to ABP); BPM, beats per minute; BrthPM, breaths per minute; CRC, cardiorespiratory coupling; ECG, electrocardiography; f_R, respiratory frequency (brthpm); HR, heart rate; HRV, heart rate variability; PSD, power spectral density; Rel PSD_{BP}, relative PSD of blood pressure; Rel PSD_{VP}, relative PSD of the ventilatory pattern; RSA, respiratory sinus arrhythmia, a property of CRC referring to the influence of respiration on heart rate; RRI, RR intervals where the time difference in the peaks of two consecutive R waves in the QRS complex is used to measure cardiac cycle duration.; SDB, slow, deep breathing; SDRR, standard deviation of RR intervals, measured as the distance of the point from the origin in a Poincaré plot; SDSD, standard deviation of successive differences between RRIs; SNA, sympathetic nerve activity; τ, time delay, no. of RRI from the current RRI; TPV_{TD}, temporal Poincaré variability over multiple time delays; TPV_A, temporal Poincaré variability over averages.

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by Journal of Applied Physiology (Parati et al., 2006 and Taylor and Studinger, 2006, respectively). This was followed by another Point:Counterpoint entitled "Respiratory sinus arrhythmia is due to a central mechanism versus respiratory sinus arrhythmia is due to the baroreflex mechanism" (Eckberg, 2009 and Karemaker, 2009, respectively).

Even the underlying physiologic purpose for cardio-respiratory coupling (CRC) is not clear. Teleologically, CRC should enhance the efficacy of gas exchange by matching ventilation with perfusion, filling the lungs with well-oxygenated air during inspiration is coupled to increase blood flow to the lungs. Indeed, this concept was verified in a well-designed study performed in canines, where the RSA is dramatic compared to humans (Hayano et al., 1996). However, in a theoretical study using optimal control theory as well as a computational model of gas exchange, RSA minimized the cardiac work while maintaining physiological gas levels (Ben-Tal et al., 2012). While modelling did not support improve gas exchange efficiency, it supported CRC as physiologically significant and not simply an epiphenomenon, the appendix of homeostatic control.

Ironically, a plausible role for CRC acting as pathophysiologic mechanism in hypertension is being established (Braga et al., 2006; Zoccal et al., 2007, 2008, 2009a,b, 2011; Simms et al., 2009a,b; Zoccal and Machado, 2010, 2011). In particular, upregulation of chemoreceptor sensitivity and the recruitment of expiratory motor activity have been associated with an additional burst of SNA in expiration, which may lead to neurogenic hypertension (Abdala et al., 2009; Molkov et al., 2010, 2011). While this work was initiated in an animal model of hypertension, in which hypertension was evoked by chronic intermittent hypoxia, enhanced coupling between respiration and sympathetic activity has been extended to other hypertensive rat models (Simms et al., 2009b; Abdala et al., 2012; Paton et al., 2013). Thus, increased activity of the chemoreceptors could trigger sympathetic activity directly and through the network underlying CRC. We have focused on CRC and its role in evoking plasticity.

Western medicine is just one, scientifically as well as empirically based approach to health. Medical practices in the Eastern hemisphere include breathing exercises to enhance health and reduce anxiety. Recently, the National Center for Complementary and Alternative Medicine has suggested slow deep breathing (SDB) exercises as a relaxation technique that could help an individual achieve better health (NIH WEBpage, http://nccam.nih.gov/health/stress/relaxation.htm). In SDB as therapy, relaxation would complement SDB in decreasing heart rate, blood pressure, oxygen consumption and levels of stress hormones. While mechanisms evoked during SDB and other relaxation techniques counteract the stress response, these techniques require that positive effect outlasts the stimulus. Specifically, we speculate that the neural network underlying CRC mediates the neural plasticity evoked by SDB and that the reduction in stress is permissive allowing the plasticity to occur.

In summary, CRC is a biomarker of health and may underlie processes of health and disease. CRC deteriorates in sepsis and increases in highly-trained athletes. Similarly, CRC deteriorates in stress and is enhanced in relaxation and slow-wave sleep. SDB enhances CRC. But in order to act therapeutically, there has to be a lasting effect.

In this paper, we present the effect of a single episode of SDB on HRV assessing HRV in the frequency domain from spectral analysis of arterial blood pressure and in the time domain from Poincaré plots. These data were obtained in healthy human subjects that did not practice yoga. Short-term plasticity is evident after SDB in individuals but not for the group. We discuss these results in the context of our previous reports indicating that plasticity in the cardio-sympathetic control is mediated through mechanisms similar to those that mediate plasticity in the respiratory system.

2. Materials and methods

2.1. Subjects

Healthy young adult male subjects ($N = 10$, mean age 26.7 ± 1.4) were recruited from Rochester, MN and its surrounding area. All experiments and procedures were approved by the Institutional Review Board at the Mayo Clinic and conformed to the Declaration of Helsinki. All subjects signed an approved informed consent form. The data were de-identified to comply with HIPAA rules and regulations for data analysis.

We sought to include subjects that encompassed a wide range of resting breathing frequencies (fR). Although textbooks define a resting fR between 12 and 15 breaths/min (BrthPM) as normal, fR can range from 6 to 31 BrthPM (Benchetrit, 2000). A standard pulmonary function test consisting of simple spirometry was administered at the screening day to rule out any pulmonary pathology. Subjects were normotensive (systolic BP < 130 mmHg, diastolic BP < 90 mmHg). The subjects were non-obese (body mass index <30), non-smokers, non-diabetic, and normally active (neither sedentary nor actively training). Subjects were screened rigorously for disease and were ineligible if they had acute or chronic disorders associated with cardiovascular structure or function and if they were being treated with anti-hypertensive or other medications. All subjects reported that they did not practice yoga, meditation and breathing exercises.

2.2. Recording

Arterial pressure was monitored continuously using a 20 ga, 5 cm catheter, which was inserted aseptically in the brachial artery of the non-dominant arm with ultrasound guidance and local anesthesia (2% lidocaine). The catheter was connected to a pressure transducer and flushed continuously at 3 ml/h with heparinized saline. Heart rate was measured with a standard 3-lead ECG. Respiratory rate and pattern were monitored using a double pneumobelt system (ribcage and abdominal belts) calibrated using a 1 L balloon.

2.3. No respiratory pacing

Subjects were positioned in a comfortable resting supine position with all instrumentation for the duration of the study. A resting period of measurements of respiration and BP was obtained for 20 min, then subjects were instructed to perform slow breathing for 20 min followed by a 20 min recovery period of endogenous rate. The recording was continuous from baseline to slow deep breathing and recovery. In this study, subjects were given minimal instructions on how to breathe slowly and had no visual, auditory or verbal feedback. Subjects were told to breathe at a slower frequency than their normal breathing and at a rate and depth of their choosing based on their comfort level. They were not cued to breathe at a particular pace with any devices or metronome pacing.

2.4. Data analysis

Data files were converted to a file format compatible with Spike 2 (Fig. 1). Complete 20-min epochs were analyzed; transitions between changes in fR were abrupt. Data were not interpolated; voids in the ABP due to sampling blood at the end of an epoch were not included in the analysis. Breaths were not excluded; sighs were few, and paradoxical rib change contraction with abdominal expansion did not occur. False negatives from not scoring small breaths could have occurred; breaths with a tidal volume less than two standard deviations from the mean were difficult to identify and could have been excluded unintentionally.