Physiological interdependence of the cardiovascular and postural control systems under orthostatic stress

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Garg A, Xu D, Laurin A, Blaber AP. Physiological interdependence of the cardiovascular and postural control systems under orthostatic stress. Am J Physiol Heart Circ Physiol 307: H259–H264, 2014. First published May 23, 2014; doi:10.1152/ajpheart.00171.2014.—The cardiovascular and postural control systems, including the skeletal muscle pump, work together to maintain homeostasis under orthostatic challenge. The behavior of the two systems under orthostatic challenge was studied through novel adaptations of signal processing techniques. To this effect, the interactions between the two systems were assessed with two metrics, coherence and phase lock value, based on the wavelet transform. Measurements from the cardiovascular system (blood pressure), lower limb muscles (surface electromyography), and postural sway (center of pressure) were acquired from young healthy adults (n = 28, men = 12, age = 20–28 yr) during quiet stance. The continuous wavelet transform was applied to decompose the representative signals on a time-scale basis in a frequency region of 0.01 to 0.1 Hz. Their linear coupling was quantified through a coherence metric, and the synchrony was characterized via the phase information. The outcomes of this study present evidence that the cardiovascular and postural control systems work together to maintain homeostasis under orthostatic challenge. The inferences open a new direction of study for effects under abnormalities and extreme environmental conditions.

cardiovascular system; orthostatic challenge; postural control; EMG; blood pressure

THE ORTHOSTATIC CHALLENGE experienced in daily life can lead to serious adverse outcomes in some populations. Orthostatic hypotension and postural instability frequently occur in the elderly (26, 27), patients with neurodegenerative diseases (5), and astronauts (9, 32) and in many cases occur concurrently. Orthostatic and postural reflexes in day-to-day life involve complex interaction between multiple physiological systems to maintain homeostasis and stability. Standing reduces blood pressure (BP) above heart level (e.g., the brain), which is mitigated by baroreflex regulation manifested by increased heart rate, cardiac contractility, and peripheral vascular resistance (30). Additionally, during prolonged standing, contractions of the skeletal musculature play a critical role to maintain BP. These contractions compress the underlying veins, which lead to the pumping of venous blood pooled in the lower limbs back to the heart (i.e., skeletal muscle pump). Absence of this compressive action may lead to fainting under prolonged standing and requires further study. While studies have observed that maintenance of postural orientation integrates sensory information from a wide variety of sources including somatosensory, visual, and vestibular pathways to make appropriate balance corrections through musculoskeletal activation (12), the skeletal muscle pump activation has been shown to be essential to maintain venous return and BP during standing (18) and after exercise (10). These observations suggest that postural orientation control may very well integrate information from BP in addition to known balance variables.

It has been known from past observations that leg movement while standing upright helps maintain BP (30). Only recently has research been conducted to investigate the control relationship between the skeletal-muscular and cardiovascular systems. A conceptual model of cardiac-locomotor coupling was recently proposed where, as a result of the force generated by muscle contraction during walking, the skeletal muscle group acts as a pump, rhythmically propelling venous blood to the right atrium (28). Claydon and Hainsworth (11) revealed that certain individuals with poor orthostatic tolerance with a tilt test but no history of syncope or presyncope had increased postural sway in upright stance, which most likely enhanced venous return and prevented fainting. The potential interaction between BP and postural sway has also been investigated in terms of their relationships to lower limb and trunk discomfort (1). These studies suggest the presence of compensatory mechanism via the activation of skeletal muscle pump in cardiovascular regulation. This speaks to the importance of an integrated BP and postural control system, particularly with poor or impaired vascular control.

Based on our observations of the correlation between postural sway and BP (3), we have developed a new physiological model that integrates the cardiovascular and postural control systems through the skeletal muscle pump (Fig. 1). In this model we hypothesize a baroreflex-induced interaction between BP regulation and lower limb muscle activation. Subsequent studies based on this model have confirmed the existence of cardiopostural interactions during quiet stance and validated the use of wavelet transform in characterizing the interactions (13, 14). Wavelet transform coherence analysis applied in this study has been in part applied in other physiological investigations (20–23, 33).

The present study is among the first to systematically conduct a quantitative investigation of interactions between the cardiovascular and postural systems during quiet standing. The interdependence was assessed using both signal coherence and synchrony based on wavelet transform. To further distinguish muscle contractions induced by postural adjustments from those initiated by baroreflex, representative signals from the...
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CARDIOPOSTURAL INTERACTIONS UNDER ORTHOSTATIC STRESS

Cardiovascular control
SBP

Postural control
COPr

Fig. 1. The hypothesized cardiopostural integration loop with the 3 controls centers, their representative signals, and the inter system interaction. EMG, electromyography; SBP, systolic blood pressure; COPr, resultant center of pressure.

cardiovascular system [systolic BP (SBP)], lower limb muscle activation [electromyography (EMG)], and postural sway [center of pressure (COP)] were measured and analyzed. We hypothesized that 1) The three (cardiovascular, posture, muscular) systems interact in a sporadic manner either pairwise or all together, representing different physiological mechanisms; 2) the majority of lower limb EMG activity is associated with postural sway since these two are known to be closely related; 3) baroreflex mediated EMG activation exists and can be observed through interactions between EMG and SBP where other interactions are absent; and 4) the interactions between the systems are frequency dependent within the physiologically relevant range. The hypothesized interactions between the two systems provide a potential for understanding the unexplained system level physiological integration.

METHODS

Protocol and Data Collection

Data were collected from 28 young individuals (12 men, age = 25 ± 2.2 yr, height = 172 ± 9.3 cm, weight = 65 ± 12.4 kg) during a sit-to-stand test. All participants were screened for any cardiovascular disease or postural complications through questionnaire and verbal confirmation. All participants were required to refrain from exercise and caffeine for 24 h before the experiment.

The experiments were conducted in a sensory input-reduced environment within an enclosed space. The participants changed into loose, comfortable clothing before height and weight measurement. After all the physiological monitoring sensors were fixed to the participant, they were seated and checked for foot placement, signal acuity, and general comfort. The sit-to-stand test required the participant to remain seated for 5 min and maintain quiet stance for 5 min after passive-assisted transition from sitting phase. The purpose of this procedure was to challenge the cardiovascular system and monitor responses. This 10-min procedure was conducted blindfolded, and eyes closed with an imaginary eye-level gaze. The eyes-closed condition was selected as postural sway increases with the removal of visual input, which leads to elevated levels of muscle activation and an increased ability to isolate posture and BP related contractions. It is known that visual cues affect sway responses in the studied frequency range (29). Quiet standing on level ground was chosen to minimize modifications of sway effects that are caused by fear of falling (8). The experiment protocol was approved to be of minimal risk by Simon Fraser University’s research ethics board. Written informed consent was obtained from each participant before the experiment.

Throughout the 10-min period, bilateral lower leg EMG was collected from four leg muscles: tibialis anterior, medial gastrocnemius, lateral gastrocnemius, and medial soleus, chosen in accordance with the observations by Joseph et al. (19). Transdermal differential recording of signals was performed using an eight-channel EMG system (Myosystem 1200, Noraxon, AZ). For signal transduction, Ag/AgCl dual electrodes (2-cm interelectrode distance) were used at the muscle sites, and a single Ag/AgCl electrode was placed at the right lateral malleolus as a reference electrode. The sites of electrode placement were chosen in accordance with the recommendations for placement of electrodes from the SENIAM project (17). Electrocardiography signals were acquired (LifePak 8, Medtronic) using the lead II configuration. Continuous BP measurements were acquired by photoplethysmography using a finger cuff (Finapres, Ohmeda 2300, Ohmeda, OH) and adjusted to heart level via a hydrostatic correction. Postural sway data, in terms of coordinates of the body COP (COPx and COPy), were computed from the force and moment data collected with a force platform (Accusway Plus, Advanced Medical Technologies). Feet were placed in a parallel foot configuration with a distance of 5 cm (measured at the first toe and heel) between them. The data were stored as 16-bit digital, acquired at a sampling rate of 1,000 Hz with a 32-along input channel DAQ card and Labview 8.2 software (National Instruments).

Data Analysis

The last 4 min of the quiet stance phase were used for analysis. Beat-by-beat time series of SBP were obtained from the maximum pressure values of the BP waveform for each beat identified through the R-wave detection in the electrocardiography signal. Response and control of the overall postural system were the main focus of this study. To this end, aggregate EMG was obtained by addition of rectified, zero-mean, EMG recordings from all individual leg muscles as in previous studies (4, 14). Similarly, the overall resultant COP (COPr) was obtained from COPx (medial-lateral sway) and COPy (anteroposterior sway). All data were resampled to 10 Hz before the application of wavelet transform.

Data analyses were implemented in MatLab (MathWorks, Natick, MA), and the results are presented as means ± SE unless noted otherwise.

Linear coupling. The wavelet transform coherence estimates, ranging from 0 to 1, were obtained through implementation of the method proposed and explained in detail by Torrence and Compo (35). The same value of the wavelet coefficient (ω0 = 6) for the Morlet wavelet was used throughout the analysis. A cone of (edge) influence (COI) on the time-frequency map, in which the edge effect is considered nontrivial, was defined as described in Grinsted et al. (16) (Fig. 2B). For each signal pair analyzed, 1,000 pairs of surrogate data were generated with a first-order autoregressive process model whose coefficients were estimated from the actual signals. The wavelet coherence was then calculated for all pairs of surrogate data with the coherence threshold set at the 90th percentile of the coherence sampling distribution at each scale/frequency, as established through the Monte Carlo method (16).

Phase synchrony. Phase dynamics derived from wavelet decomposition of the signals indicate system-level interactions, where a close coupling between two signals is characterized by constant or zero difference in phase (i.e., phase lock) (23).

Traditionally, coherence has been used to represent a measure of linear covariance between two signals, combining the effects of signal amplitude and phase in the interrelationship, whereas the phase synchrony has indicated a direct phase relationship. The degree of synchrony between two signals can be quantified through the metric of smoothed phase lock value (S-PLV) (23, 24). Analogous to coher-
Fig. 2. The results from the wavelet coherence and phase analysis between the cardiovascular and postural control system: A: raw data from one participant of EMG and continuous waveform blood pressure (BP). The upper envelope of this tracing is SBP, AU, arbitrary units. B: time-frequency plot (bottom) of wavelet coherence between EMG and SBP signals from A and summary Venn diagrams (top) from 28 subjects’ significant coherence (%SC) in low-frequency (LF) and very LF (VLF) bands. C: same presentation of results as in B but with wavelet phase lock analysis (smooth phase lock value (S-PLV)). The regions with significant coherence and in phase lock between EMG and SBP in the time-frequency plots (B and C) are red and highlighted with bold black contours. The cone of influence (COI) is shown as a lighter shade. Each Venn diagram (B, top, and C, bottom) is composed of 3 ellipses, each of which represents the number of interactions between a pair of signals [i.e., EMG↔COPr, EMG↔SBP, and COPr↔SBP]. The overlapped regions signify that 2 or more pairs of signals are simultaneously coupled.
The time-frequency plots and Venn diagrams for one representative subject were computed (Fig. 2). The coherence (Fig. 2B, bottom) and S-PLV (Fig. 2C, top) between EMG and SBP signals (Fig. 2A), hypothesized to represent baroreflex-mediated muscle contraction, were computed from one representative participant. The Venn diagrams in both LF and VLF bands (Fig. 2, B, top and C, bottom) pools outcomes for all 28 participants. Total interactions among the three systems (i.e., the area of the Venn diagram) represent ~40% of the total area [%SC: 44.3 ± 4.0% (LF), 47.9 ± 5.2% (VLF); %PL: 36.2 ± 3.0% (LF), 38.7 ± 3.8% (VLF)].

The regions thought to represent baroreflex-mediated muscle contraction (EMG and SBP) were found to make <10% of all observed interactions [%SC: 4.1 ± 0.8% (LF), 3.9 ± 1.9% (VLF); %PL: 5.5 ± 0.8% (LF), 6.2 ± 1.8% (VLF)]. The majority of the EMG interactions were with COPr only [%SC: 25.1% out of 37.0% (LF), 32.0% out of 42.5% (VLF); %PL: 18.1% out of 29.0% (LF), 20.4% out of 32.4% (VLF)]. When combined, the regions where SBP coupled with either COPr or EMG represent almost half of the total interactions [%SC: 19.3 ± 2.8% of 44.3% total (LF), 15.8 ± 3.4% of 47.9% total (VLF); %PL: 18.1 ± 1.8% of 36.3 total (LF), 18.3 ± 2.7% of 38.7 total (VLF)].

Areas where pairs of signals were simultaneously coherent and in phase lock were computed to EMG ↔ SBP (LF: 2.7 ± 0.7%, VLF: 1.9 ± 0.7%), COPr ↔ SBP (LF: 4.5 ± 1.2%, VLF: 3.8 ± 1.6%), and EMG ↔ COPr (LF: 42.0 ± 3.3%, VLF: 35.1 ± 3.6%). From Table 1, we can observe that relative percent contributions of the three interactions display similar behavior regardless of whether coherence or phase lock is used. The unimodal pairwise interactions share the largest time percentage, the bimodal (2 pairs together) are substantially lower, and the trimodal interactions (3 pairs together) are higher than the bimodal interactions but substantially lower than the unimodal interactions (Table 1).

Mean significant coherence and S-PLV values ranged from 0.42 to 0.88 (Table 2). For all paired signals, these values were higher in the LF band. The highest mean values for both coherence and S-PLV in both frequency bands occurred with EMG ↔ COPr.

**DISCUSSION**

Our analysis has revealed evidence of an interdependent behavior between the cardiovascular and postural systems. The present work is the first attempt to systematically investigate and characterize the interdependent behavior of the posture and cardiovascular control systems under postural and orthostatic challenge. This link was hypothesized to exist via the activation of the skeletal muscle pump as a physiological response to cardiovascular perturbations and vice versa. To obtain evidence in support of the hypothesis, we conducted a passive sit-to-stand test with data collected from the cardiovascular (SBP), posture (COPr), and muscular (EMG) systems. A wavelet transform method, suitable for analysis of nonstationary
signals, was adopted to obtain coherence and phase lock estimates with time-frequency resolution.

The hypothesized model (Fig. 1) of cardiopostural interactions has three primary paths of pairwise interaction and activation: the posture control-mediated (EMG ↔ COPr), baroreflex control-mediated (EMG ↔ SBP), and the cardioposturally mediated (COPr ↔ SBP) interactions. The central goal of this study was to distinguish between the baroreflex-mediated activation of the skeletal muscle pump and postural activation of skeletal muscle.

Significant coherence and S-PLV over the last 4 min of the 5-min stand (Tables 1 and 2) confirm the existence of the hypothesized pairwise interactions. More specifically, the existence of EMG ↔ SBP interaction when EMG ↔ COPr interaction was absent (Fig. 2, B, top and C, bottom) suggests activation of posture-related muscle groups for BP, rather than direct posture-related reasons. This observation supports our third hypothesis of the existence of baroreflex-mediated EMG activation of posture-related muscle groups. While bimodal or trimodal interactions could indeed be mediated by BP requirements, only in the unimodal case can we rule out blood movement caused by unconstrained sway.

Analogously, we observed regions where COPr ↔ SBP interaction existed, while EMG ↔ COPr interaction was absent. This suggests that some postural sway interacts with BP without being mediated by the chosen calf muscles. This could theoretically represent the effects of body movement initiated by muscle activity not measured in our study (e.g., upper limb and abdominal muscles, breathing), which have a significant impact on BP. This presents an area of interest for further investigation into cardiopostural interactions.

Together, the regions where SBP coupled with either EMG or COPr were found to represent almost half of the total interactions (Table 1). This leads the authors to conclude that during quiet standing, BP and postural variables cannot be considered as independent in the chosen frequency bands. The highest time percentage of significant coherence and phase lock was with the EMG ↔ COPr pair (Table 1), which also had the highest corresponding average values (Table 2). This is not surprising given the strong coupling between postural sway and lower limb muscle contraction (6, 18).

The modal frequencies for postural sway during quiet stance range 0.30–0.45 Hz, both in the lateral and anteroposterior directions (31). Since these modal frequencies are well above the range at which the vascular system can respond to stimuli and since significant interaction between COPr and SBP occur only about 20% of the studied time, it is clear that BP regulation is neither the main driver for postural sway in the first 5 min of standing, nor vice versa. Rather, it is possible that cardiopostural interactions constitute a secondary response. These would become apparent only when predominant cardiovascular responses fail to successfully regulate pressure. Determination of such a causal relationship would necessitate analysis methods capable of distinguishing direction. The results from this study suggest that cardiopostural integration can possibly occur in two subpathways: 1) mediated by postural stimuli (COPr → EMG → SBP) and 2) mediated by cardiovascular stimuli (SBP → EMG → COPr), i.e., BP could demand muscle activation which affects COPr, or postural sway could affect BP through muscle activation. This in turn suggests that at a given time, the individual systems contribute to driving a pathway, while being driven in another. Again, the determination of causality in this context presents a clear direction for further investigation.

The data in this study were limited to young healthy male participants under no active perturbation and provide baseline characteristics on a systems level. Since it is well known that aging affects cardiovascular regulation, postural control, and underlying neurological systems, it is the authors' opinion that this type of study could shed light on the importance of cardiopostural interactions in healthy aging. Similarly, it would be of interest to clarify the role of these interactions in other conditions such as concussions, anxiety disorders, diabetic neuropathies, and orthostatic intolerance.

In conclusion, the current article presents evidence to confirm that the cardiovascular and posture control systems work together during the maintenance of upright posture. This novel finding counters the common belief that the systems work independently under conditions of orthostatic challenge. From the current study, it is evident that the cardiovascular and postural systems should not be viewed in isolation when investigating effects on either cardiovascular or postural controls. This would enable us to further understand and predict the adverse effects of one system on another in a timely fashion and prevent health-related issues such as orthostatic hypotension and postural instability.

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