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Postural-induced phase shift of respiratory sinus arrhythmia and blood pressure variations: insight from respiratory-phase domain analysis

Kiyoshi Kotani,[1] Kiyoshi Takamasu,[2] Yasuhiko Jimbo,[1] and Yoshiharu Yamamoto[3]

[1]*Graduate School of Frontier Science, The University of Tokyo, Chiba; and Graduate Schools of* [2]*Engineering and* [3]*Education, The University of Tokyo, Tokyo, Japan*

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Kotani K, Takamasu K, Jimbo Y, Yamamoto Y. Postural-induced phase shift of respiratory sinus arrhythmia and blood pressure variations: insight from respiratory-phase domain analysis. *Am J Physiol Heart Circ Physiol* 294: H1481–H1489, 2008. First published January 25, 2008; doi:10.1152/ajpheart.00680.2007.—The purpose of this study is to evaluate the multiple effects of respiration on cardiovascular variability in different postures, by analyzing respiratory sinus arrhythmia (RSA) and respiratory-related blood pressure (BP) variations for systolic BP (SBP), diastolic BP (DBP), and pulse pressure (PP) in the respiratory-phase domain. The measurements were conducted for 420 s on healthy humans in the sitting and standing positions, while the subjects were continuously monitored for heart rate and BP variability and instantaneous lung volume. The waveforms of RSA and respiratory-related BP variations were extracted as a function of the respiratory phase. In the standing position, the waveforms of the BP variations for SBP, DBP, and PP show their maxima at around the end of expiration (π rad) and the minima at around the end of inspiration (2 π rad), while the waveform of RSA is delayed by ~0.35 π rad compared with the BP waveforms. On the other hand, in the sitting position, the phase of the DBP waveform (1.69 π rad) greatly and significantly ($P < 0.01$) differs from that in the standing position (1.20 π rad). Also, the phase of PP is delayed and that of RSA is advanced in the sitting position ($P < 0.01$). In particular, the phase shift of the DBP waveform is sufficiently large to alter whole hemodynamic fluctuations, affecting the amplitudes of SBP and PP variations. We conclude that the postural change associated with an altered autonomic balance affects not only the amplitude of RSA, but also the phases of RSA and BP variations in a complicated manner, and the respiratory-phase domain analysis used in this study is useful for elucidating the dynamic mechanisms of RSA.

heart rate variability; Hilbert transform; respiratory phase; blood pressure variability

RESPIRATION HAS STRONG AND multiple effects on the cardiovascular system. The best known effect of respiration is respiratory sinus arrhythmia (RSA) (12, 13, 26), i.e., fluctuations in heart rate (HR), depending on the phases of inspiration and expiration. RSA mainly reflects the modulation of the central autonomic outflow caused by respiration-related factors, such as spontaneous oscillations of respiratory centers and pulmonary stretch receptor afferents (8), and hemodynamic factors through the baroreflex and the Bainbridge reflex (30), which interact with each other in a complicated manner (4).

Blood pressure (BP) is also affected by multiple interactions of these factors. To describe quantitatively the effects of respiration on HR and BP, Saul et al. (21) constructed a model in which HR is determined by the sum of central vagal and sympathetic activity, low-pass filtered and time delayed due to peripheral neurotransmitter kinetics. Arterial BP, determining the baroreceptor activity, is influenced by HR with some (mechanical) time delays. Then they incorporated the respiratory effects on HR and BP in two ways. First, instantaneous lung volume (ILV) has a (respiration-related) inhibitory effect on the central nervous system, which is known to be the inhibitory effect of inspiratory neurons and pulmonary stretch receptors on the activity of vagal motoneurons in the nucleus ambiguus (4, 10, 25) and further influences HR via vagal and sympathetic efferents. Second, the first derivative of ILV [i.e., $-\mathrm{d(ILV)}/\mathrm{d}t$] also influences the arterial BP, by which the effect of changes in the intrathoracic pressure on hemodynamics is modeled. Saul et al. (21) compared the transfer relations from ILV and arterial BP to HR under the conditions of pharmacological neural blockade and change in position and reported good agreement of this model with experimental results.

The respiratory phase dependence of hemodynamics and the resultant reflex control of the cardiovascular system are, however, much more complicated than those considered in the study by Saul et al. (21). For example, the effect of cardiac filling caused by a decrease in the intrathoracic pressure, through the Frank-Starling mechanism, influences systolic BP (SBP), while the windkessel BP reduction process, altered by the length of interbeat intervals, affects diastolic BP (DBP). Therefore, a more detailed description of the relationships between respiration, HR, and hemodynamic fluctuations, including those of SBP and DBP, is needed to elucidate the dynamic mechanisms of RSA.

To investigate the multiple effects of respiration on cardiovascular control, power spectral analysis (20, 26), cross-spectral analysis (5, 21), and multivariate autoregressive analysis (3) have been used. However, these methods cannot describe a precise phase relation between respiration and multiple cardiovascular variables, because respiration is not a linear or harmonic oscillator. One solution to this problem is to use paced respiration (12, 24, 31), but this investigates the respiratory influence only in a specific condition, and the pacing itself may result in unnatural hyperventilation or an alteration in the autonomic balance (19). Therefore, an analysis that represents respiration as a nonlinear oscillator, thus focusing on the respiratory phase, is required. For this purpose, some recent studies (9, 15, 16) have used so-called respiratory-phase domain analysis to study RSA, where the HR variability signal is resampled equidistantly with respect to an extracted respiratory

Address for reprint requests and other correspondence: K. Kotani, Graduate School of Frontier Science, The Univ. of Tokyo, 5-1-5 Kashiwanoha, Kashiwa, Chiba 277-8653, Japan (e-mail: kotani@k.u-tokyo.ac.jp).

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phase, and a stable waveform of RSA is obtained by ensemble averaging over the whole respiratory phase, so that the precise phase relation between RSA and respiration can be identified. Here, we extend this method to BP variability to investigate the respiratory phase dependence of hemodynamic fluctuations in the sitting and standing positions with different HR and BP variability levels.

METHODS

Experimental procedures. Healthy men, with ages ranging from 23 to 27 yr, were tested in experimental sessions in sitting and standing positions while in a state of rest. Each subject gave informed consent to participate in this institutionally approved study after the test protocol had been fully described. Data were recorded for 420 s in each session. More than 480 s were allowed between the sessions to stabilize the cardiovascular variables affected by the change in position. Eight subjects performed the experiments in the standing position first and then in the sitting position. Ten subjects performed the experiments in the opposite order to evaluate the effects of the order. The 18 sets of data obtained included data from seven subjects who performed two sets of experiments, each containing two sessions, which were conducted in both orders. Another four subjects performed only one set of experiments.

During the experiments, continuous recordings were made of electrocardiographic R-R intervals (RRI) (AC-601, Nihon-Koden), radial artery BP, by means of a tonometric device (JENTOW, Nihon Colin), ILV, by means of an elastic chest band (TR-753T, Nihon-Koden), and the motion of the laryngeal prominence, by means of an accelerometer (8304B2, Kistler). The electrocardiogram, BP, and the motion of the laryngeal prominence were digitized at a sampling frequency of 1,000 Hz, while ILV was digitized at a sampling frequency of 100 Hz. In 11 of the 18 data sets, calibration was performed before each session. The calibration was performed through the inspiration of 0.5 liter of air, and linear fitting was conducted for the states before and after inspiration, on the assumption that the lung is a rectangular parallelepiped, one axis of which is changed by inflation. It is of note that the phase obtained was not altered by the presence or absence of this calibration procedure.

Signal processing. The averaged waveforms of RSA, SBP, DBP, and pulse pressure (PP) were extracted in the respiratory-phase domain as follows. First, interval tachograms of RRI and time series of SBP, DBP, and PP were obtained. SBP is the maximum value and DBP is the minimum value of the BP in a cycle of interbeat intervals. PP was obtained as the subtraction of DBP from SBP. SBP, DBP, and PP were aligned for the occurrence of the same heartbeat (i.e., R-wave on the ECG), as shown in Fig. 1*A*.

The subsequent signal processing procedures are shown in Fig. 1*B*. The data of RRI and the three indexes of BP were interpolated, whereas that of respiration was transformed to obtain its instantaneous phase. RRI was interpolated by the inverse of the derivative of the cubic spline interpolation with the equation

$$M(t_k) = \int_{t_0}^{t_k} m(t)\mathrm{d}t = k \qquad (1)$$

where t_k ($k = 0, 1, 2, \ldots, n$) is the times at which heartbeats are observed; $m(t)$ is the instantaneous HR; and $M(t)$ is the continuous integral of $m(t)$ (11). The inverse of this function $m(t)$ was used as instantaneous RRI. As for the BP indexes, SBP, DBP, and PP were interpolated by the cubic spline function.

The instantaneous phase of respiration was calculated after filtering ILV. The raw ILV data contain low-frequency trends and electrical noise, and both of these affect the calculation of the respiratory phase. Therefore, raw ILV data were passed through a linear phase finite impulse response filter, of which the pass-band was 0.1–10.0 Hz and the order was 4,001. The upper frequency limit is sufficiently high compared with the respiratory frequency to preserve the harmonics of the respiratory oscillation. The instantaneous respiratory phase was estimated by using an analytic signal approach, which was first introduced for respiration signals by Schäfer et al. (22, 23). The analytic signal $\psi(t)$ is a complex function of time defined by

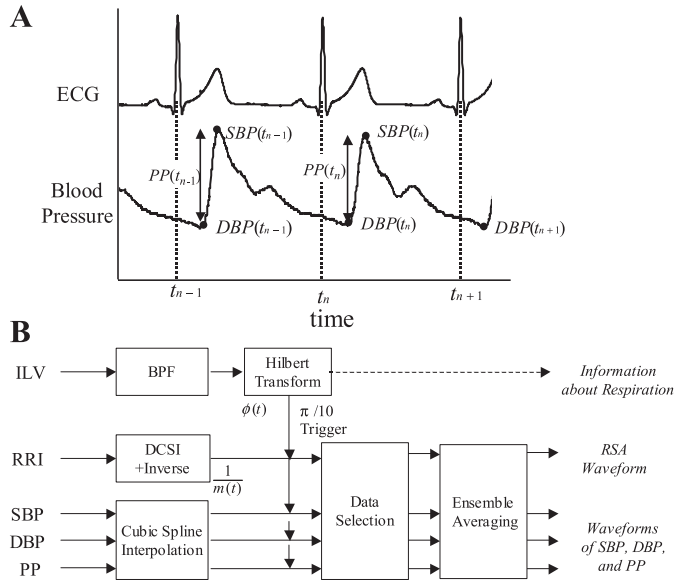

Fig. 1. *A*: waveforms of the electrocardiogram and blood pressure. Systolic blood pressure (SBP), diastolic blood pressure (DBP), and pulse pressure (PP) against time are defined. *B*: schematic diagram of the signal-processing method for extracting the respiratory sinus arrhythmia (RSA), SBP, DBP, and PP waveforms using respiratory-phase domain analysis. BPF, band-pass filtering: ILV, instantaneous lung volume; RRI, R-R interval; DCSI, derivative of cubic spline interpolation; t_n, *time n*.

$$\psi(t) = s(t) + j\tilde{s}(t) = A(t)e^{j\phi(t)} \qquad (2)$$

where j is the imaginary unit; A is amplitude; $s(t)$ is the ILV data in this case; and the function $\tilde{s}(t)$ is the Hilbert transform of $s(t)$,

$$\tilde{s}(t) = \pi^{-1}\mathrm{PV}\int_{-\infty}^{\infty} \frac{s(\tau)}{t-\tau}\mathrm{d}\tau \qquad (3)$$

where τ is the variable for integration, and PV means that the integral is taken in the sense of Cauchy's principal value. The instantaneous phase $\phi(t)$ of the signal $s(t)$ was thus uniquely defined from *Eq. 2*.

Then the interpolated RRI, SBP, DBP, and PP variations were resampled at every $\pi/10$ rad of the respiratory phase, yielding an equidistantly sampled RRI and BP variability. After that, the physiologically abnormal data were removed as a function of the data selection box. The data containing respiration frequency lower than 0.15 Hz or overly rapid respiration (abrupt respiration and phase slipped data due to noise), in which the difference of continuous respiratory points exceeds $\pi/10$ rad in the phase, were removed. In addition, the time of swallowing was detected by an accelerometer, and the data containing the respiration during swallowing were also removed. Following the results of our laboratory's previous study (16), if swallowing was observed between inspiration and expiration (i.e., around 2 π rad), the data for one respiration after swallowing were also removed. To remove such data, the phase between a $\pi/2$ rad and the next $\pi/2$ rad was determined to be one respiration so that the inspiratory period (i.e., from π rad to 2 π rad) and tachycardia associated with the inspiration were contained in one

respiration. Then inappropriate data for corresponding respiratory cycles were removed.

Finally, in the ensemble-averaging box, mean waveforms of RSA, SBP, DBP, and PP were obtained. These waveforms were ensemble averaged over the entire respiratory cycle (the phase between a $\pi/2$ rad and the next $\pi/2$ rad) to extract the stable mean waveforms. In this analysis, both the first and last 20 s were eliminated by filtering, and the remaining 380 s were used.

Statistical analyses. For the statistical analyses, three parameters characterizing respiratory phase-dependent waveforms were obtained. The time-varying waveform $y(\theta)$ as a function of the respiratory phase θ,

$$y(\theta) = A\cos(\theta + \alpha) + B \quad (4)$$

where A is the amplitude, B is the mean value, and α is the phase lag, was estimated by the nonlinear least squares method (the range of α is between 0.5 π rad and 2.5 π rad). In this study, there were 12 parameters, as each of the four waveforms (RSA, SBP, DBP, and PP) had 3 parameters (A, B, and α). For all of these 12 parameters, statistical differences caused by the body position and the order of the experiments were tested by the linear mixed model (29) by using an SAS package. In this analysis, the data are fit to a model of

$$Y_{i,j,k} = \mu + \alpha_i + \beta_j + (\alpha\beta)_{ij} + p_k + \varepsilon_{ijk} \quad (i = 1,2;\ j = 1,2;\ k = 1, \ldots, 11) \quad (5)$$

where $Y_{i,j,k}$ is the experimental value, μ is the mean value, α_i is the fixed effect coefficient of positions, β_j is the fixed effect coefficient of orders, and $(\alpha\beta)_{ij}$ is their interactions. In addition, p_k is the random effect coefficient that results from intersubject variability, and ε_{ijk} is the independent random value for error. In addition, we calculated the mean interval and amplitude of respiration from the selected respirations in each data set. The fitting of the mixed linear model was conducted in the same way, although the data for the amplitude of respiration were not tested statistically, because not all of the sets of respiration data were calibrated.

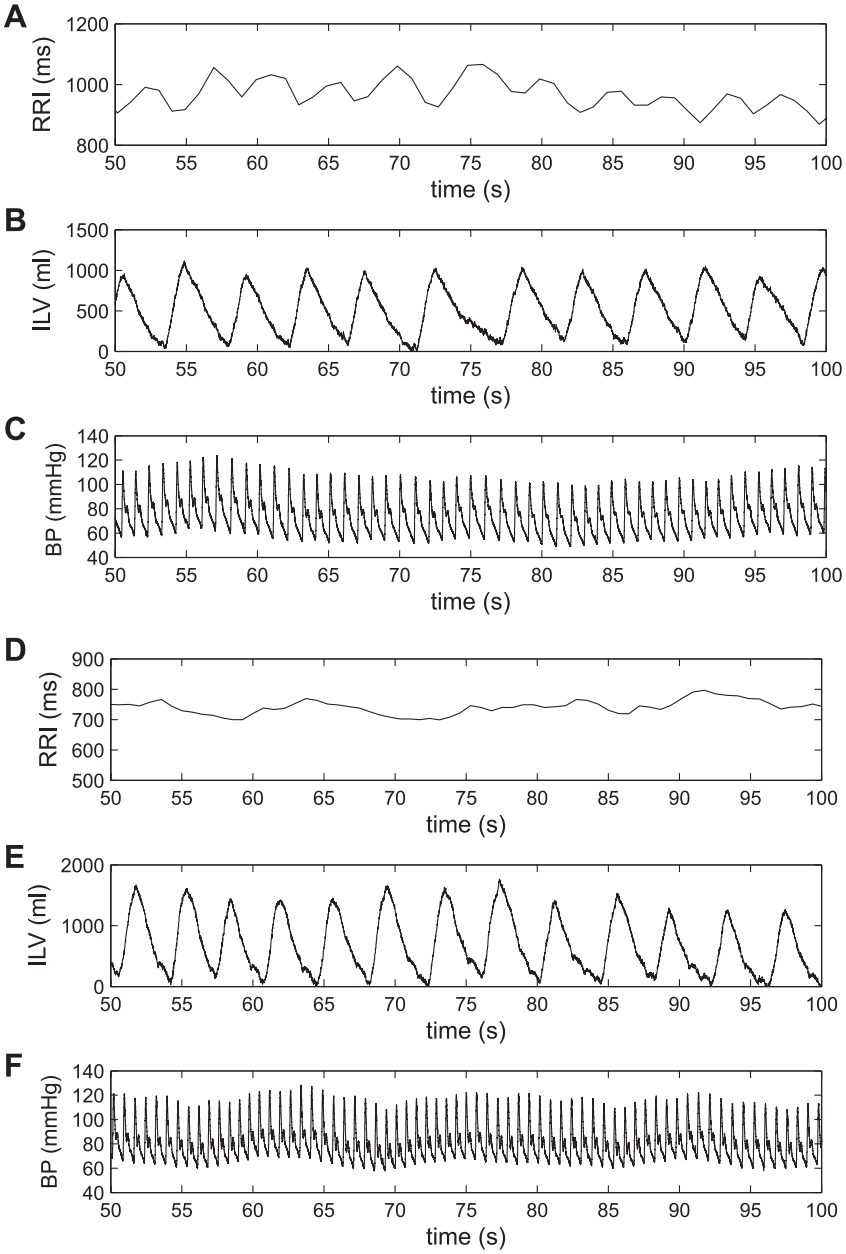

Fig. 2. Data of three variables in the sitting (*A–C*) and standing (*D–F*) positions. *A* and *D*: heartbeat. *B* and *E*: respiration. *C* and *F*: blood pressure.

RESULTS

Figure 2 shows the raw data for each variable (*A–C* in the sitting position and *D–F* in the standing position). The respiratory fluctuation of RRI is largely suppressed in the standing position, with smaller average RRI than that in the sitting position, although the shapes of respiration are not much different between the sitting (Fig. 2*B*) and standing (Fig. 2*E*) positions.

Figure 3 indicates how the signal processing method works; ILV and its instantaneous phase are shown in Fig. 3, *A* and *B*, respectively. The respiratory phase increases slowly for the period of slow respiration (arrows) and quickly for the period of fast respiration. The data after resampling at each π/10 rad of the respiratory phase are shown in Fig. 3*C*, where fluctuations synchronous to the respiration (i.e., their wavelength is 2 π rad in the respiratory phase) are observed in both RRI and SBP data. However, the signal-to-noise ratios appear not to be so high, and ensemble averaging is needed to increase the signal-to-noise ratio.

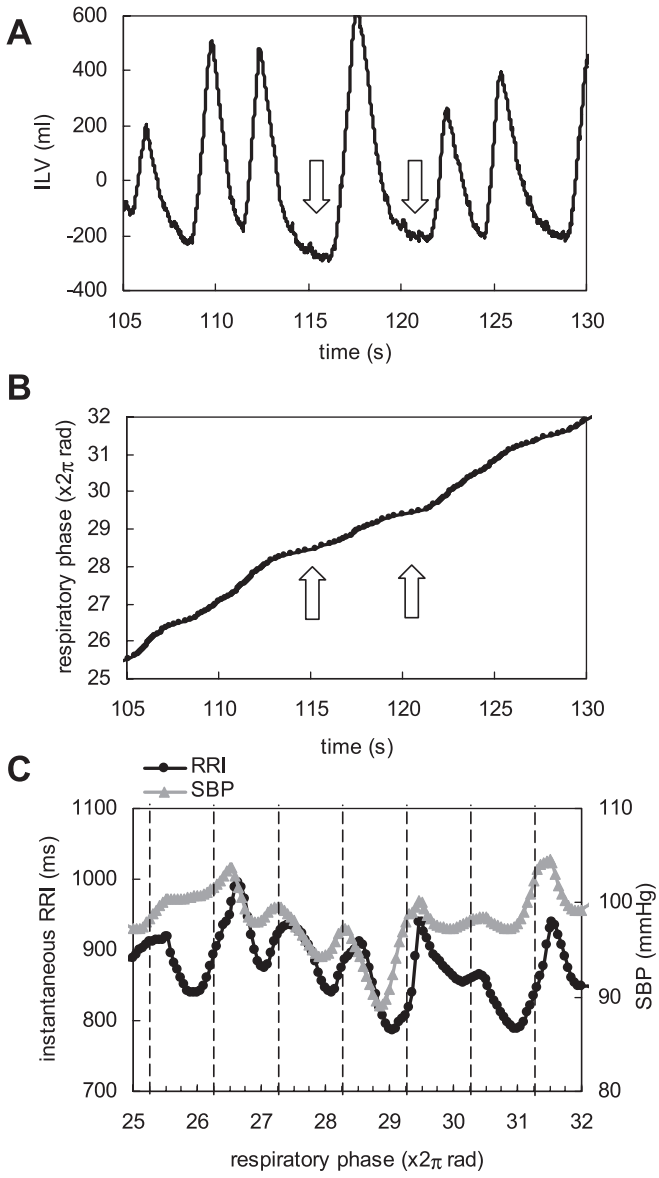

Fig. 3. *A*: ILV waveform. *B*: respiratory phase of *A*. It can be seen that the respiratory phase increases slowly when the respiration is slow (open arrows in *A* and *B*). *C*: resampled data of RRI and SBP variability in the respiratory-phase domain. The data were resampled at each π/10 rad in the respiratory phase. The dotted line is the separation of the data at one respiration.

After ensemble averaging at 2 π rad of the respiratory phase, in Fig. 4, representative individual results of the RSA, SBP, DBP, and PP waveforms in the respiratory-phase domain in the sitting and standing position are shown. In each panel, the *top* trace shows the results for the sitting position, whereas the *bottom* trace shows the results for the standing position. In these figures, the phase between π rad and 2 π rad is an inspiratory period, and the other phase is an expiratory period. In addition, Fig. 5 shows the mean waveforms of all of the data sets, where the mean value (i.e., DC component) of each waveform is eliminated and averaged. In the case of the sitting position, the RSA, SBP, and PP waveforms have their maxima at around π rad and minima at around 2 π rad (the *top* trace of Fig. 4, *A*, *B*, and *D*, and Fig. 5, *A*, *B*, and *D*), indicating that the maximum is roughly observed at the end of expiration and the minimum at the end of inspiration. On the other hand, the waveform of DBP for the sitting position is largely shifted (the *top* trace of Figs. 4*C* and 5*C*). Although the averaged waveform of DBP is not a simple cosine curve because of interindividual differences, its maximum is shifted to around 2 π rad (Fig. 5*C*). In the case of the standing position, DBP has the maximum at around π rad and the minimum at around 2 π rad (the *bottom* trace of Figs. 4*C* and 5*C*), which is closer to the waveforms of RSA, SBP, and PP (the *bottom* trace of Fig. 4, *A*, *B*, and *D*, and Fig. 5, *A*, *B*, and *D*).

Table 1 shows the mean values and standard errors of all of the estimated parameters of the HR and BP variability and the results of statistical tests by a linear mixed model. The interaction between body position and experimental order is not significant in any of the parameters. The statistical results of the order are significant only for the mean values of SBP and DBP (both having $P < 0.05$). On the other hand, there are several parameters that demonstrate statistically significant differences between the sitting and standing positions. First, the amplitude (parameter *A* in *Eq. 4*) in the sitting position is larger in RSA ($P < 0.01$), smaller in SBP ($P < 0.05$), smaller in DBP ($P < 0.05$), and larger in PP ($P < 0.05$) than in the standing position. Second, the mean value (parameter *B* in *Eq. 4*) in the sitting position is larger in RRI ($P < 0.01$) than in the standing position. Third, the phase (parameter α in *Eq. 4*) in the sitting position is larger in RSA, smaller in SBP, larger in DBP, and smaller in PP (all having $P < 0.01$). The larger positive value of the phase indicates that the waveform shifts left in Figs. 4 and 5 and fluctuates earlier on the respiratory phase axis.

Table 2 shows the mean values of the interval and amplitude of respiration. There is no consistent difference in the effects of orders and positions on the interval of respiration.

DISCUSSION

The respiratory influence on RSA and BP differs in phase with a change in body position, which is not described adequately by Saul's model, and this is the most outstanding finding of the present study. Especially, this is clearly observed in the DBP waveform (from 1.20 π rad to 1.69 π rad in α) in

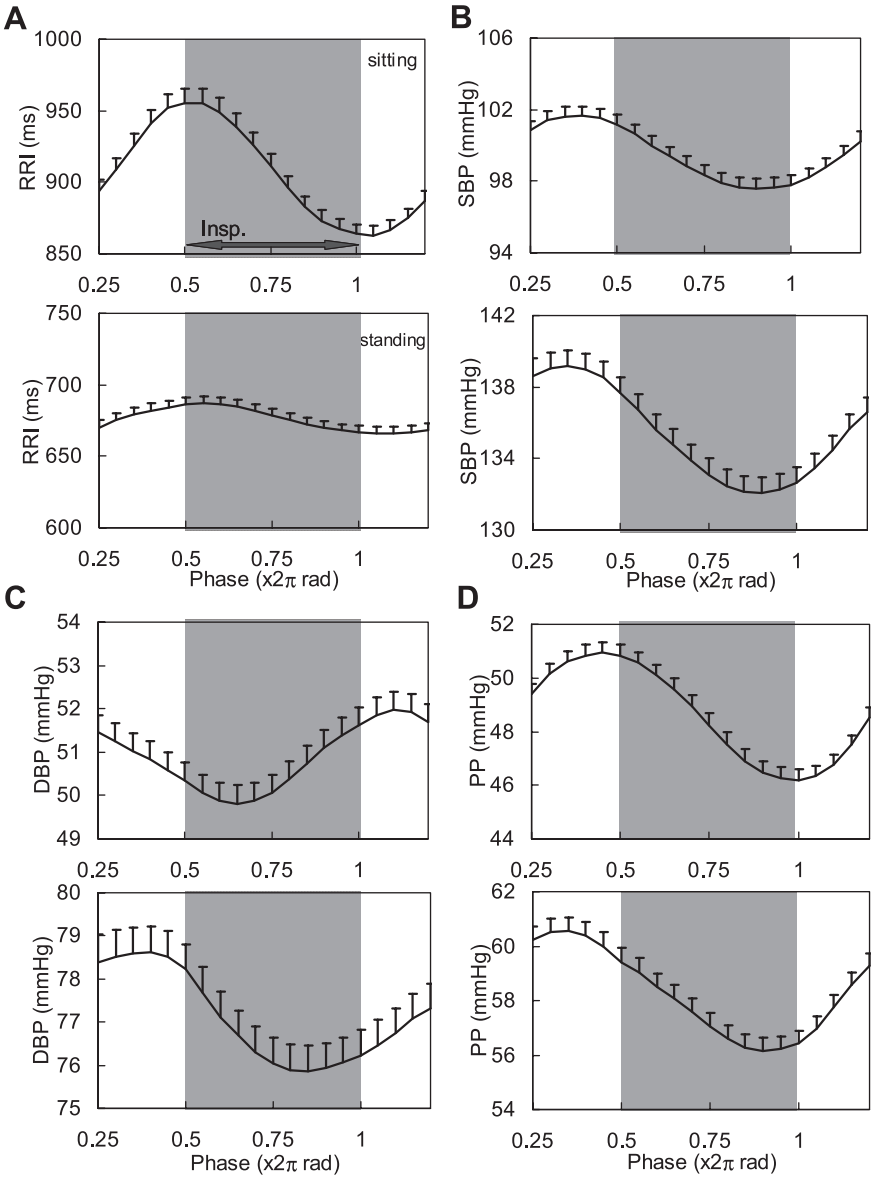

Fig. 4. Waveforms of RRI (*A*), SBP (*B*), DBP (*C*), and PP (*D*) of a representative subject in the sitting (*top* trace) and standing (*bottom* trace) positions. Vertical bars represent SE. The phase between π rad and 2 π rad is inspiratory duration, and the other phase is expiratory duration.

the sitting position (see also Figs. 4*C* and 5*C*, *top* trace). This difference corresponds to ~1 s, because the averaged interval of respiration from all of the data sets is ~4.2 s [(1.69 π − 1.20 π)·4.2/(2 π) ≅ 1.0] and is considered to be sufficiently large to alter the cardiovascular regulation significantly. The mechanism is presumably related to a postural effect on the amplitude of RSA. That is, in the sitting position, the amplitude of RSA is large because vagal activity is higher. Larger RSA makes diastolic duration shorter during inspiration than expiration, and this increases DBP during inspiration. The phase of DBP variation shifts because this effect is opposed to that of the intrathoracic pressure, i.e., the $-d(ILV)/dt$. A previous paper by De Boer et al. (6) has also reported that the phase between DBP and RRI at the respiratory frequency is −90° in the resting condition, although they discuss neither the mechanism of it nor the postural effects on it.

Also, the amplitude of DBP variation is decreased in the sitting position ($P < 0.05$), possibly for a similar reason to the above. There is a competing relation in DBP variation during inspiration between the factor of a decrease due to the effect of the intrathoracic pressure and the factor of an increase due to shortened diastolic duration by the function of RSA. In the standing position, the factor of the increase is minimized because the amplitude of RSA is decreased, while the two factors are competing in the sitting position, leading to the decreased amplitude of DBP variation. An alternative possibility is that these changes in DBP variation are derived from the change in the sympathetic nervous activity to vascular smooth muscles followed by changes in the venous return. However, this effect is considered to be small because the changes in the waveform of PP variation, in which the changes in the venous return appear first, are not so large compared with that of DBP variation.

Furthermore, as for detailed changes in the phase relationships, the phases of the PP and SBP waveforms in the sitting position are smaller than those in the standing position, indicating that these phases in the sitting position are delayed compared with those in the standing position. On the contrary,

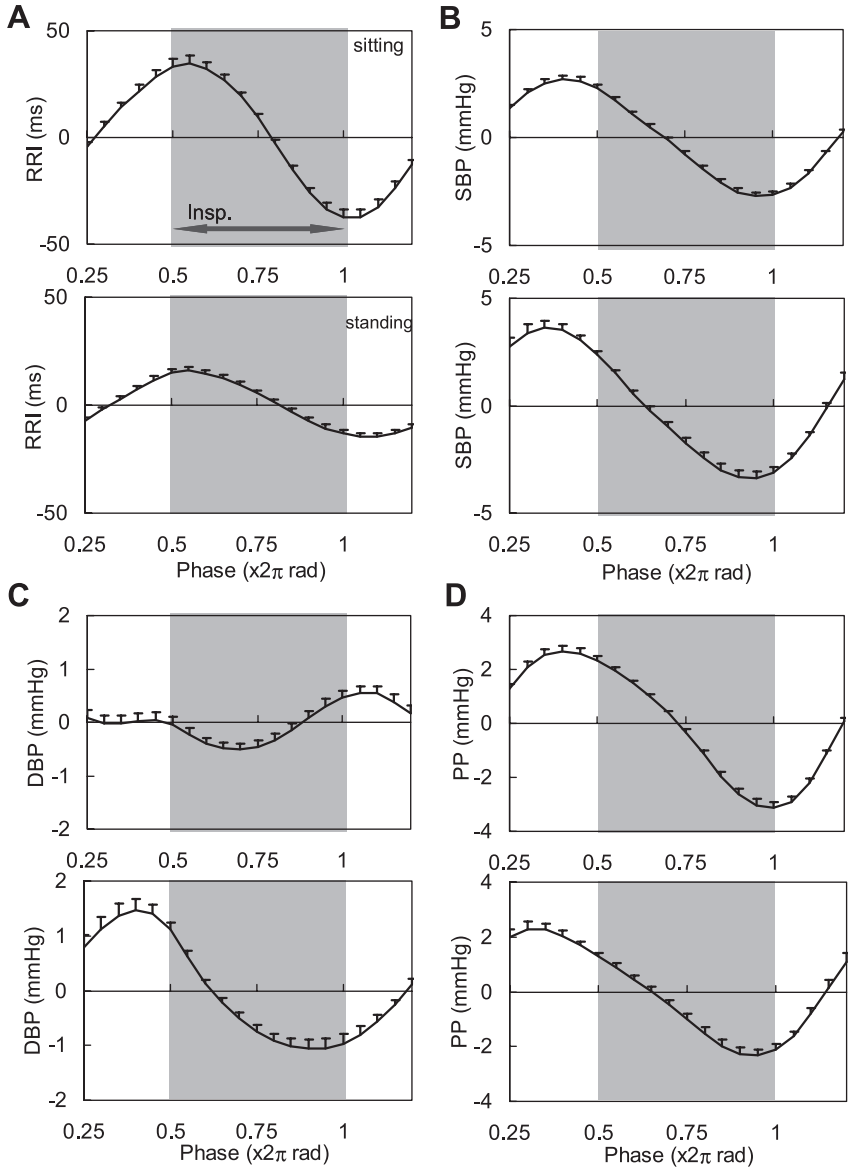

Fig. 5. Averaged waveforms of RRI (*A*), SBP (*B*), DBP (*C*), and PP (*D*) in the sitting and standing positions. In each panel, the *top* trace shows the results for the sitting position, whereas the *bottom* trace shows the results for the standing position. The vertical bars represent interindividual SE. The phase between π rad and 2 π rad is inspiratory duration, and the other phase is expiratory duration.

Table 1. *Parameters of the heart rate and blood pressure indexes and the results of statistical tests*

	Position			Order			
	Sitting	Standing	*P*	First	Second	*P*	Interaction *P*
RSA amplitude, ms	35.95±3.18	15.80±3.18	<0.01	25.57±3.18	26.18±3.18	NS	NS
SBP amplitude, mmHg	2.65±0.28	3.46±0.28	<0.05	3.12±0.28	2.99±0.28	NS	NS
DBP amplitude, mmHg	0.76±0.16	1.28±0.16	<0.05	1.06±0.16	0.97±0.16	NS	NS
PP amplitude, mmHg	2.86±0.23	2.34±0.23	<0.05	2.64±0.23	2.57±0.23	NS	NS
Mean RRI, ms	909.9±21.2	724.5±21.2	<0.01	815.0±21.2	819.4±21.2	NS	NS
Mean SBP, mmHg	109.62±2.62	111.59±2.62	NS	114.04±2.62	107.16±2.62	<0.05	NS
Mean DBP, mmHg	59.67±2.39	61.37±2.39	NS	63.85±2.39	57.19±2.39	<0.05	NS
Mean PP, mmHg	49.96±2.16	50.23±2.16	NS	50.20±2.16	49.98±2.16	NS	NS
RSA phase, ×π rad	0.947±0.024	0.856±0.024	<0.01	0.923±0.024	0.881±0.024	NS	NS
SBP phase, ×π rad	1.121±0.019	1.186±0.019	<0.01	1.162±0.019	1.146±0.019	NS	NS
DBP phase, ×π rad	1.687±0.074	1.199±0.074	<0.01	1.520±0.074	1.366±0.074	NS	NS
PP phase, ×π rad	1.077±0.026	1.195±0.026	<0.01	1.142±0.026	1.130±0.026	NS	NS

Values are estimated mean values ± SE. RSA, respiratory sinus arrhythmia; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; RRI, R-R interval; NS, no statistically significant difference. The larger positive value in the phase indicates that the waveform shifts left and fluctuates earlier in the respiratory phase axis.

Table 2. *Parameters of the indexes of respiration and the results of statistical tests*

	Position			Order			
	Sitting	Standing	*P*	First	Second	*P*	Interaction *P*
Interval of respiration, s	4.10±0.16	4.18±0.16	NS	4.17±0.16	4.10±0.16	NS	<0.01
Amplitude of respiration, liter	0.485±0.099	0.733±0.099		0.620±0.099	0.598±0.099		

Values are estimated mean values ± SE. Statistical tests regarding the amplitude of respiration were not performed.

the phase of RSA in the sitting position is larger; hence it is earlier than in the standing position. These differences are ~0.1 π rad and not large in value compared with that of the DBP waveform, but a strong statistical significance is observed ($P < 0.01$). The possible reasons for these results are as follows. First, the delay in the phases of the PP and SBP waveforms in the sitting position is explained by the balance of the changing intrathoracic pressure and the decreasing diastolic duration due to RSA. The changing intrathoracic pressure occurs earlier in the phase than ILV. However, the changing cardiac filling due to RSA occurs almost in the same phase as that of ILV, assuming that there is a positive correlation between the length of diastolic duration and cardiac filling. Only the earlier effect of the intrathoracic pressure is dominant in the case of the standing position, whereas the two effects are mixed in the case of the sitting position. Therefore, the phase of the PP waveform is delayed in the sitting position, and the phase of the SBP waveform is also delayed because the fluctuation of PP is larger than DBP, and SBP is largely influenced by PP. Second, the earlier phase of RSA in the sitting position than in the standing position is thought to be caused by baroreflex or respiratory effects. One possibility is that the BP variations caused by the intrathoracic pressure, which occur earlier than RSA, affect HR through the baroreflex. However, similar changes can also be caused by respiratory changes via RSA, and indeed several lines of discussion have been conducted regarding whether the correlation between BP and HR at the respiratory frequency is brought about by the baroreflex or not (2, 5, 8). Therefore, further investigation is required into this complicated problem.

Finally, the phase shift of the DBP waveform decreases the amplitude of SBP variation in the sitting position, despite the increased amplitude of PP variation. This is possibly due to the shortened diastolic duration during inspiration absorbing the fluctuation of PP. This result provides evidence that the changes of DBP waveform affect other cardiovascular variables and indicates the importance of our findings.

All of the above findings on the detailed postural effects on phasic hemodynamics can only be obtained by the respiratory-phase domain analysis employed in this study. Although the model by Saul et al. (21) well describes the property of RSA and BP variations, it does not describe adequately the differences in phase induced by the activity of the autonomic nervous system that are shown in our results. Regarding this, there are a few studies that have dealt with the phase of RSA and BP variations in changing autonomic nervous activity, although these papers neither investigate precise phase relationships between respiratory and other hemodynamic variables, nor observe the phase shift of the DBP waveform.

Gilad et al. (9) found that the phase of RSA advances in the supine position compared with the upright position, which is consistent with our results. However, their analysis has limitations in assuming that the respiratory phase increases at a constant speed during one respiration (therefore, the waveforms are largely changed if the rates of inspiration and expiration are changed) and in not controlling the effect of changing gravity on the lungs between the supine and the upright positions (18). On the contrary, our results suggest that this difference of the phase of RSA does not result from the changes in the gravity to the lungs or in respiratory patterns, but from the changes in autonomic nervous activity.

As for the phase relation between RSA and BP variations, Cooke et al. (5) analyzed the phase angle between RSA and SBP variation at a respiratory frequency and found that the latency of RSA with respect to SBP variation decreases as the tilt angle decreases. In our experiment, it is also observed that this latency decreases in the sitting position. This is derived from the two statistically significant effects of advanced RSA and delayed SBP variation against the respiratory phase with the mechanisms that are discussed above.

Furthermore, as for the changing amplitude of these waveforms, Toska et al. (28) found that the variance of the mean arterial pressure at the respiratory frequency increased after cholinergic blockade by atropine, and Taylor and Eckberg (27) also found that the changes in the variances of SBP and DBP at the respiratory frequency increased with a change in body position from supine to a 40° tilt. Our results also show larger amplitudes of SBP and DBP variations in the standing position than in the sitting position. The possible reason why the amplitude of DBP variation increases in the standing position has already been discussed above, and this change in the amplitude of DBP variation also possibly increases the amplitude of SBP variation in the standing position.

The possibility exists that changes in respiratory patterns due to the change in posture affect the BP and RSA indexes. In fact, the amplitude of respiration is decreased without a consistent

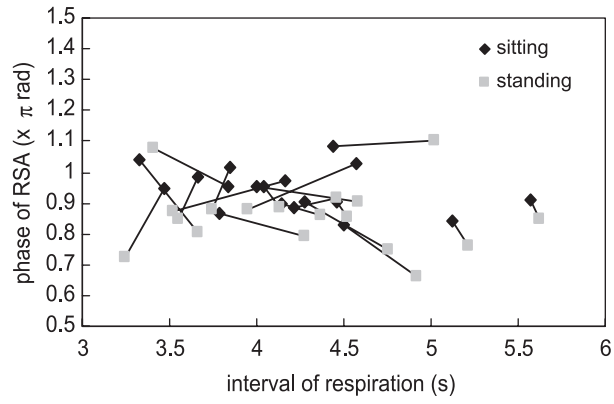

Fig. 6. Relationship between the phase of RSA and the interval of respiration. There is no consistent relation between them.

decrease in the interval of respiration in the sitting position. It may also affect the decrease in the changes in the intrathoracic pressure and respiration-induced BP variations. This may partially explain why the amplitude of SBP and DBP variations decreases in the sitting position. However, the effect of respiratory change by body position alone cannot account for the large phase difference in the DBP waveform and increase the amplitude of PP variation in the sitting position. Also, it is known that the interval of respiration affects the phase between RSA and respiration (1, 7). However, the difference in the phase of RSA in our results seems not to be produced by this factor, because there is no consistent difference in the respiratory interval between positions. For confirmation of this, Fig. 6 shows the relationship between the respiratory interval and the phase of RSA. The lines showing the difference due to body positions have both the left side up and the right side up, and there is no consistent relation between them. Therefore, it is considered that the difference in the phase of RSA possibly results from the changes in autonomic nervous activity. While previously the relationship between the phase of RSA and respiration has mainly been studied with intervals of respiration (1, 7), further analyses are required for the relationships between the phases of hemodynamic fluctuations and detailed respiratory information other than intervals of respiration (e.g., amplitude, maximum rate of inspiration).

In physiological experiments examining the effects of posture, comparative tests have frequently been conducted between the supine and upright positions (9, 21). In this study, however, a comparison is made between the sitting and standing positions, because the sitting position has the same vector of gravity to the lungs as the standing position, and this avoids the risk of changing the vector of gravity to the abdominal wall and the intrathoracic pressure (9, 18). Furthermore, the elastic chest band, used for the measurement of respiration, would have to be set up again if the shape of the trunk altered, as it would in changing position from supine to upright. Although it is known that the difference in the autonomic nervous activity is relatively small in the comparison of the sitting and standing positions, we observe significant effects of posture on mean RRI, as well as the amplitude of RSA.

In summary, we conclude that the postural change associated with an altered autonomic balance affects not only the amplitude of RSA, but also the phases of RSA and BP variations in a complicated manner. It is of note that the phase of the DBP waveform in the sitting position largely differs from that in the standing position, which is caused by the factor that RSA changes the diastolic duration. This phase shift is sufficiently large to alter the cardiovascular regulation ($\sim$1 s); due to this effect, the amplitude of SBP variation decreases in the sitting position, despite the increased amplitude of PP variation. Also, this change in PP variation is possibly caused by changing diastolic duration via the venous return. Furthermore, it is also found in this experiment that the phase of PP variation is delayed and that of RSA is advanced in the sitting position by changing the balance of autonomic nervous activity. Thus the respiratory-phase domain analysis used in this study is useful for elucidating the dynamic mechanisms of RSA and the sources of "complexity" in cardiovascular variability (14, 17).

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GRANTS

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