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Cardiolocomotor phase synchronization during rhythmic exercise

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Abstract Biological rhythms can be entrained by internal oscillatory processes and often become synchronized with each other. For integrated physiological systems, there is evidence to show that coupling can exist between cardiorespiratory and locomotor systems. Phase synchronization, which has been well documented in articles describing cardiac and locomotor rhythms for individuals engaged in rhythmic activity such as walking, running, or cycling, is called "cardiolocomotor synchronization" or "cardiolocomotor coupling". Although this coupling has been hypothesized to play a functional role during exercise, the nature of this interaction, its physiological relevance, and the underlying mechanism behind this phenomenon are not fully understood. This review summarizes research findings to date on cardiolocomotor synchronization, and aims to provide the method for identification of phase synchronization between cardiac and locomotor rhythms. In addition, the mechanisms responsible for the synchronization and possible physiological function of this interaction are discussed.
Keywords : heartbeats, locomotion, entrainment, phase response, synchrogram

Introduction

Biological rhythms interact with external rhythmic stimuli and other intrinsic rhythms. The phenomenon in which two oscillators with different periodicity are led to oscillate "in step", by interacting with each other, is called "synchronization" or "entrainment"[1]. For integrated physiological systems, such synchronization has been reported among the cardiac, respiratory, and locomotor systems. Recently, a number of studies have focused on the synchronization between cardiac and respiratory systems and have reported episodic phase synchronization between these two oscillatory processes in resting humans[2-4]. Interestingly it has been found that the degree of synchronization dramatically changes with the sleep-stage transition[4]. Phase synchronization between heartbeats and locomotor activity also occurs. Starting from the pioneering work of Coleman[5,6] in 1921, cardio-locomotor synchronization (CLS) has been documented in humans performing various locomotor activities, such as walking, running and cycling[7-13]. Surrogate data analysis has indicated that the emergence of CLS is more than just a coincidence of the rhythmic processes of cardiac and locomotor cycles, but is likely a consequence of heartbeat entrainment by locomotor rhythms due to interaction[12,13]. However, the exact physiological mechanisms responsible for CLS are not well understood. Furthermore, the identification of such CLS raises the question as to whether this interaction is related to any physiological functions during exercise. This review focuses on the literature evidence for CLS and its underlying mechanism, as well as the physiological significance of this interaction.

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Literature evidence for CLS

The earliest study on the synchronization between cardiac and locomotor rhythms dates back to the reports by Coleman[5,6]. He observed the cadence and heart rate (HR) of a variety of species at the London Zoological Gardens, identifying the HR by noting the apical pulsations of the heart against the chest wall or the pulsation of the carotid artery in the neck when the animal stopped moving. Comparing the heart and exercise rates, he often noted 1:1 integer ratio between them. After that, he made a number of similar observations for humans during walking exercise tests[5]. For instance, it was reported that the heartbeat rhythm coincided with a metronome rhythm as the subjects sat and stood up from a chair repeatedly in accordance with a metronome rhythm. However, his method of measuring HR was based on palpation, and therefore synchronization was not objectively established.

Kirby and collaborators note CLS during walking and running on a treadmill, as well as during a cycle ergometer exercise in humans[7]. In their experiment, CLS was considered to be present if the difference between the heart and step rates were less than 1.0%. They reported that the CLS was physiological and a real phenomenon based on the following criteria: 1) CLS was sufficiently stable to last for up to 2 min; 2) CLS resumed after a disruption caused by intentional alteration of the tread-

mill speed; 3) HR and cadence frequency rose together, maintaining CLS as the exercise intensity increased; 4) with increasing exercise intensity, the HR often appeared to approach the cadence more rapidly, suggesting an association between the rates. Assuming that vertical movement of the viscera during rhythmic exercise may enhance expulsion of blood from the heart, Kirby et al.[14] examined how the coupling frequency was modulated when vertical body movements were accentuated. They examined whether CLS frequently occurred during hopping and skipping rope activity but failed to induce a consistent phase relationship between the rates, suggesting that the visceral piston is unimportant in the induction of CLS. In humans, hopping and skipping are not generally used for moving, so Baudinette et al.[15] examined a mammal that chiefly uses hopping to move. They examined the relationship between cardiac and gait rhythms in tammar wallabies hopping on a treadmill and found no correlation between locomotor and cardiac cycles. Udo et al.[16] found that, in running humans, HR decreased when the R wave appeared at a phase less than the initial one-fourth of a step cycle, and that it was increased when the R wave shifted into the later three-fourths of the cycle. They inferred that the HR was modulated depending on the phase difference to the step cycle, via some unknown mechanism. Niizeki et al.[10] reexamined Kirby's experiments and analyzed the interactions among cardiac, respiratory, and locomotor rhythms during treadmill exercise. They found that the strength of coupling between cardiac and respiratory rhythms, as estimated by coherence function, decreased in the presence of CLS, indicating that cardiac rhythm is influenced not only by respiration but also by locomotor rhythm. Later, Blain et al.[17] showed, during cycling exercise, that the cardiac chronotropic activity was modulated by pedaling frequency, and that this modulation significantly increased with an increase in workload. Nomura et al.[18] compared the characteristics of CLS in running and cycling exercise in humans. They observed that CLS occurred for relatively prolonged periods at specific regions of relative phase difference during running, whereas in cycling, CLS occurred intermittently and was not phase specific. Novak et al.[19] examined the effects of aging on CLS using treadmill walking at incremental speeds, and revealed a significant relationship between step intervals and beat-to-beat cardiac cycles for elderly people; but not for young participants. They assumed that the attenuations in RSA and vagally mediated baroreflex with aging may have induced enhanced coupling.

CLS has also been reported in some species of birds. Aulie[20] examined the relationship between wing beats and cardiac rhythm in small birds (finches and budgerigars) flying freely in a wind tunnel. He recorded an electrocardiogram via a copper wire positioned on the sternum and an electromyogram from the pectoral muscle, which is the working muscle of birds during flight. In the budgerigar, wing beat remained at a relatively constant frequency during flight, and HR increased at the start, synchronizing with the wing beat about 3 min after the flight began. The synchronization between the wing beat and heartbeats at maximal rate was in the ratio of 1:1 in the budgerigar and 1:2 in the finches, indicating some degree of coordination between them. He noted that the heart was rarely activated simultaneously with the pectoral muscles. Aulie[21] also examined synchronization in pigeons and reported that 72% of the observed heartbeats were activated out of phase with activation of the pectoral muscles, suggesting that the bird coordinates the timing of flight muscles and heartbeats in such a way that simultaneous activations are relatively few.

Simmons et al.[22] examined CLS in quadrupedal animals (dogs). They investigated, in unanesthetized dogs, whether cardiac rhythm was coupled with locomotor rhythm, during a trotting exercise on a treadmill. Although the dogs did not exhibit strong coupling, they observed that heartbeats often occurred immediately before crossing a hind and front leg. Elongation or shortening of the heartbeat interval occurred primarily during the diastolic phase of the cardiac cycle, suggesting that transient CLS may be a function of locomotor and ventilatory influences on venous return and/or ventricular ejection. In a natural field setting, stride rate, speed, and direction of the animal are factors that are forced to change constantly. This causes stride-by-stride variation in the venous return from skeletal muscle, in the respiratory pump, and in the ejection fraction from the ventricles through reflexes such as the baroreflex, Bainbridge reflex, and Frank-Starling mechanism. Thus, the authors suspected that these reflex-induced variations in venous return and ventricular ejection during exercise might render absolute CLS impractical in dogs. Coupling has also been shown to occur by passive mechanical oscillation in dogs. Bhattacharya et al.[23] demonstrated, in dogs, that heartbeats were coupled with the body acceleration applied in the direction of the body axis. Although the criterion for CLS is different among studies, coupling (adjustment of rhythms due to interaction) is evident between the rhythms.

Detecting and quantifying CLS

CLS can be interpreted as a consistent occurrence of heartbeats at the same relative phases as consecutive locomotor cycles. To corroborate a relative phase relationship, we need to know the instantaneous phase of the two oscillators. Two approaches have dominated the calculation of the instantaneous phase: the method based on marker events or the analytic signal approach. In the former method, marker events that characterize the cycle of the oscillator are determined. For both cardiac and locomotor rhythms, the timing of each successive QRS spike of an electrocardiogram (ECG) and that of each successive onset of locomotion (or onset of muscle contraction) is

measured (Fig. 1A). Each successive marked event is equivalent to one oscillatory cycle. Within one oscillatory cycle, the instantaneous phase is $\phi(t)=2\pi(t-t_k)/(t_{k+1}-t_k) + 2\pi k$, where t_k is the time of the k_{th} marked event. A second approach is the reconstruction of the instantaneous phase from the time series of an oscillatory signal in the complex plane[24]. The complex analytic signal for an oscillatory signal *x(t)* is calculated as $\zeta(t) = x(t) + i\tilde{x}(t)$, where the real part *x(t)* is the actual data, and the imaginary part $\tilde{x}(t)$ is given by the Hilbert transform of the signal. The instantaneous phase $\phi(t)$ is then obtained by taking the complex argument as $\phi(t) = \tan^{-1}[\tilde{x}(t)/x(t)]$ (Fig. 1B).

The relative phase for the occurrence of the QRS spike with respect to the locomotor cycle is calculated as $\Psi(t_k) = [\phi_L(t_k) \bmod 2\pi]/2\pi$, where t_k is the time of the k_{th} occurrence of the QRS spike and $\phi_L(t_k)$ is the instantaneous phase of locomotion. The plot of $\Psi(t_k)$ over t_k defines the cardiolocomotor synchrogram. If the two rhythmic processes are independent, then there should be no preferred phase; thus, random distribution of $\Psi(t_k)$ will be expected. Alternatively, if n:m (cardiac:locomotor) phase synchronization occurs, $\Psi(t_k)$ attains exactly the same *n* different values within the *m* locomotor cycle, and in the synchrogram, *n* parallel horizontal lines are observed.

There are several approaches for quantifying the strength of synchronization; these are chi square value[11,12,22], phase coherence[13], Shannon entropy[25], and mutual information indices[26,27]. Here, we consider the phase coherence and Shannon entropy indices. The phase coherence index is based on the coherence spectral estimator for bivariate time series. The time series of $\Psi(t_k)$ in the time window of t_w is quantified using phase coherence λ, which is defined by $\lambda(t_k)=\left\| \frac{1}{N} \sum_{j=k-N}^{k} e^{i\Psi(t_k)} \right\|^2$, where N is the number of heartbeats in the time window of $t_k - t_w/2 \le t_j < t_k + t_w/2$. The value of λ ranges from 0 to 1, with $\lambda = 1$ denoting complete synchronization. The Shannon entropy index is computed from the distribution of $\Psi(t_k)$ in the observation time window. The entropy of the $\Psi(t_k)$ series in the time window is defined as $h(t_k) = -\sum_{j=0}^{N} p_j \ln (p_j)$, where N is the total number of bins, and p_j is the probability of $\Psi(t_k)$ corresponding to the j_{th} bin. This index can be normalized to the maximum entropy, that is achieved for uniform distribution: p_j=1/N for all j, and h reaches its maximum value given by $h_{max} = \ln (N)$. The normalized entropy is then, $h_n(t_k) = [h_{max} - h(t_k)]/h_{max}$ and this quantity has values between 0 and 1. The $h_n(t_k)$ is

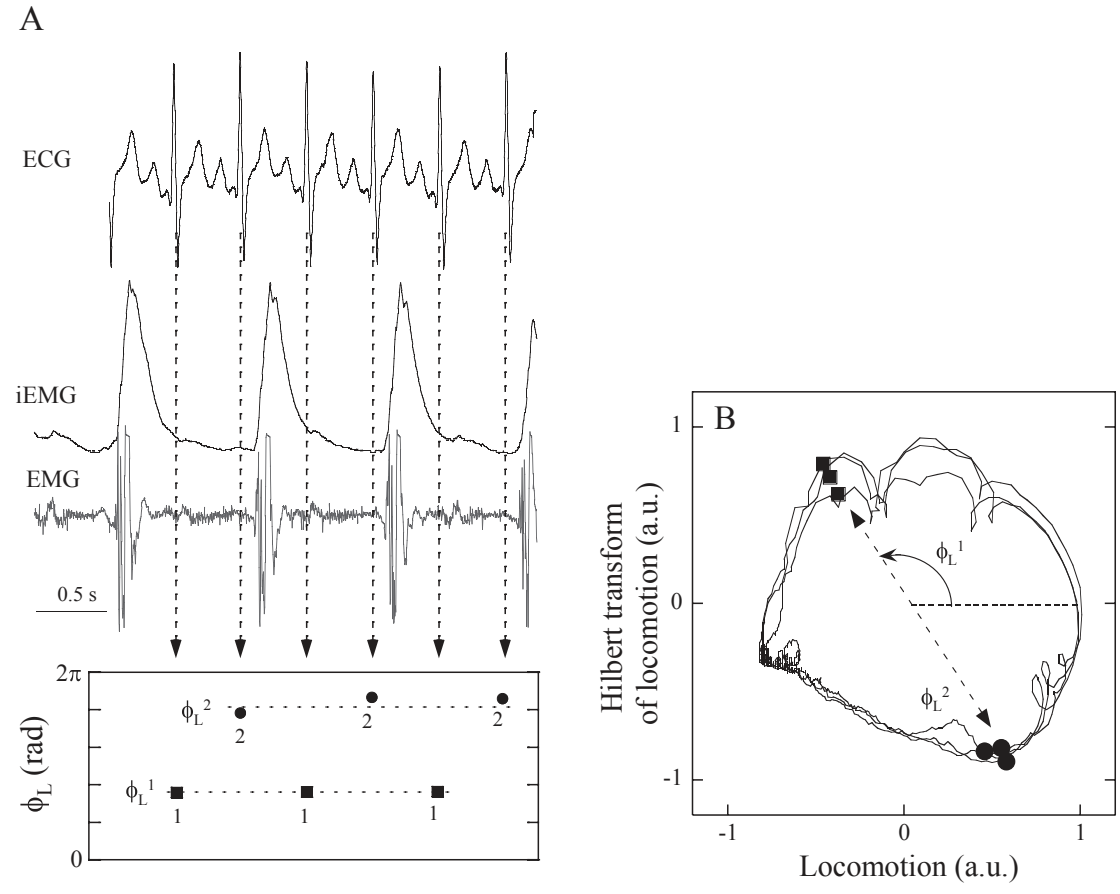


Fig. 1 Derivation of a cardiolocomotor synchrogram from the timing of the QRS spike of the ECG with respect to the gait rhythm estimated from the EMG for a gastrocnemius muscle. The instantaneous locomotor phase ϕ_L is defined as the angle of the gait signal relative to the start of EMG activity (A); alternatively it can be calculated by the analytic signal approach (B).
ECG: electrocardiogram, EMG: electromyogram, iEMG: integrated EMG.

minimal for a uniform probability distribution and maximal in the case of a δ-function probability distribution. Phase coherence is a good measure of how clustered the relative phase is around a single value, while the entropy measure can detect any deviation from a uniform distribution of the relative phase.

Surrogate data analysis

To test the significance of the phase synchronization indices, we need to know their distribution under a null hypothesis of independent pairs of cardiac and locomotor rhythms. The distribution of the index computed from surrogate ensembles, in which pairs of oscillatory activity variables are drawn randomly, can be considered as an approximation of the null distribution[28]. This can be achieved by randomly shuffling the original instantaneous phase of the locomotor rhythm $\phi_L(t)$ to secure the statistical properties of the original data. The sequence of the instantaneous phase of heartbeats remains the same as for the actual data. Then, a new relative phase between the two rhythms is created. By computing multiple trial shuffled estimates, a distribution of the synchronization index computed from surrogate ensembles can be considered as an approximation of the null hypothesis. Nomura et al.[12] and Takeuchi et al.[13] provided the evidence, using surrogate data analysis, which allowed rejection of the hypothesis that CLS occurs by chance during running and walking exercises. Fig. 2 shows an example of a cardiolocomotor synchrogram for a subject who walked at a speed of 6.2 km/h. The CLS is appreciable during the period from 800 to 1200 sec after exercise began, as indicated by the increases in λ and h_n values. The histogram of the original $\Psi(t)$ distribution shows two distinct peaks, whereas $\Psi(t)$ distribution for the surrogate data looks more uniform (Fig. 2C).

Mechanism(s) for producing CLS

The specific mechanism leading to CLS remains elusive. It is generally accepted that the synchronization phenomenon between two rhythms is a manifestation of

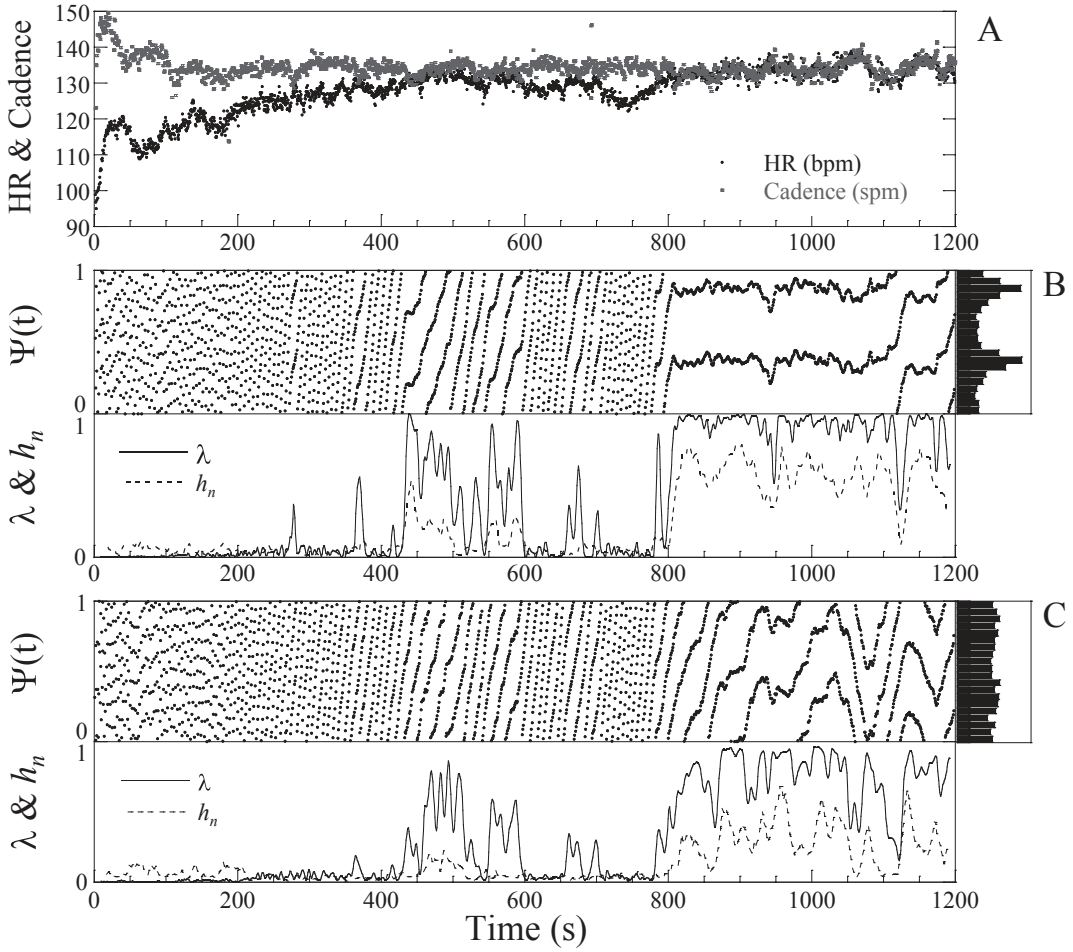


Fig. 2 Time series of the heart rate and cadence (A), and the corresponding cardiolocomotor synchrogram with a histogram of the distribution of $\Psi(t)$ (B), and the synchronization indices λ (B, *solid line*) and h_n (B, *dotted line*) for a subject who walked at 6.2 km/h on a treadmill for 20 min. A 2:1 (heartbeats:gait) phase synchronization was noted at around 450 s and from 800 s to 1200 s after exercise began. An example of the surrogate data analysis is shown in C, where the original instantaneous phase of the locomotor rhythm was randomly shuffled.

nonlinear biological oscillators in which mutual interaction is involved[1]. To determine whether the CLS is mutual or not, a more sophisticated analysis is necessary. Our view on this issue is that the CLS occurs by the influence of locomotion on heartbeats. The beat-by-beat changes in cardiac rhythm due to muscular contraction suggest that CLS is mediated through a neuronal origin. Previous studies addressing the link between respiratory and exercise rhythms have suggested the possible involvement of the reflex arc between peripheral receptors in the muscles and the pontomedullary junction[29-31]. It has also been demonstrated that the respiratory rhythm is entrained to the stimulus frequency by repetitive electrical stimulation of the somatic afferent nerves[32,33]. These studies have suggested the existence of a neural circuit originating in the periphery that leads to respiratory-locomotor entrainment. Therefore, it is possible to infer that cardiac rhythm is also influenced by some neural circuit arising from peripheral inputs. One possible candidate of the afferent fibers that are activated concomitantly with muscle contraction could be the sensory fibers in muscles. It has generally been accepted that the thin sensory fibers classified into group III and IV types can be stimulated by pressure and pain and by certain metabolic substances produced by muscular contractions, and that this stimulation causes increased cardiorespiratory responses[34]. Kaufman and coworkers[35,36] have been studying the response of afferent fibers (group III and IV) to exercise. Although the conduction velocity of thin group III fibers has been considered to be slow[35], several observations have demonstrated that these fibers are stimulated by dynamic exercise[36,37], and that their reflex affects the autonomic nervous system[38]. Thus, synchronization may involve the interaction of a cardiac pacemaker with an afferent signal arising from the stimulation of mechano- and chemosensitive receptors in the contracting muscles, perhaps through the parasympathetic nervous system, because the sympathetic nervous system cannot respond as quickly to the frequency of locomotor activity[39], and because cardiac responses to sympathetic stimulation are phase independent[40].

For the cardiac-respiratory systems, it is well documented that the efferent vagal discharges to the heart are influenced by the respiration phase[41], and that the timing at the start of vagal discharge during the pacemaker cycle alters the next occurrence time of a heartbeat[42,43]. This suggests the existence of phase dependency of the cardiac pacemaker in response to vagal activity. In fact, phase dependency of pacemaker activity in cardiac tissue has been demonstrated[44]. Thus, it is possible to infer that afferent signals from contracting muscles may result in phase-dependent changes in the pacemaker cycle length through the parasympathetic nervous system. The timing of the muscle contraction within the cardiac cycle has been shown to influence the muscular-cardiac interaction (Fig. 3A): a positive chronotropic response (normalized ϕ_d is greater than 0.5, Fig. 3B) is provoked when muscle contractions occur during systole; whereas muscle contractions occurring during diastole result in a negative chronotropic response (normalized ϕ_d is less than 0.5, Fig. 3B)[45] This investigation leads us to speculate that cardiac rhythm is so coordinated that the period of muscle contraction does not override the systolic phase of the cardiac cycle. Nomura et al.[46] also observed that, during running exercise, positive chronotropic changes in the heart

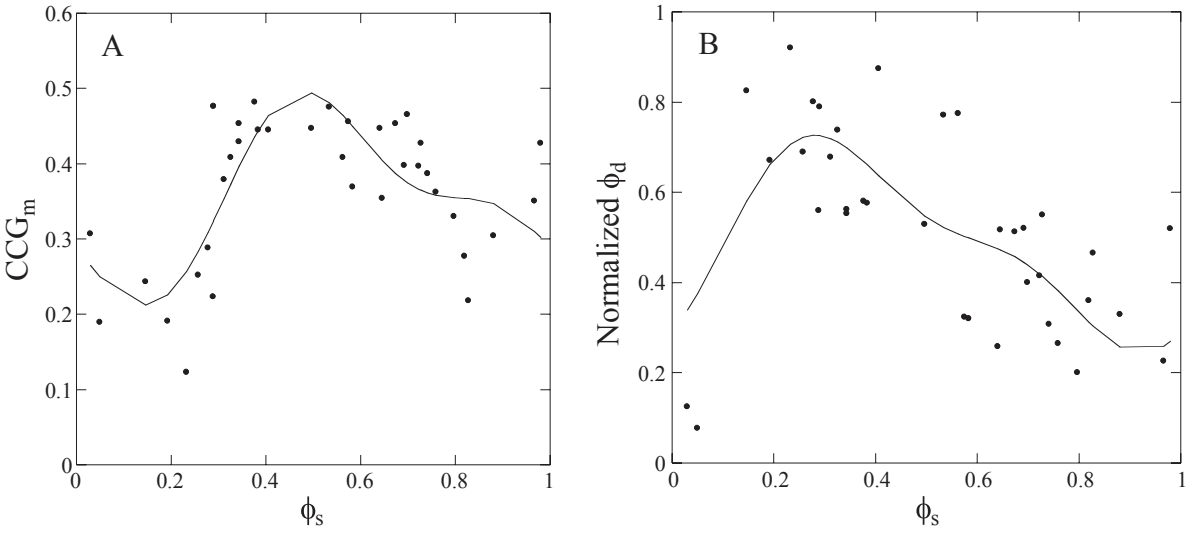


Fig. 3 The influences of muscle contraction timing (ϕ_s) within the R-R interval on cardiac-muscle contraction coupling (A), and phase shift (B) during a hand grip exercise. Solid lines indicate the second-order Fourier regression lines fitted to data by the least square method. CCG_m: maximum cross-correlation value between cardiac and muscle contraction rhythms, ϕ_d: phase shift defined as the difference between the time showing the peak of the cross-correlation and the zero lag time. Note that CCG_m is lower and normalized ϕ_d is greater, if muscle contraction occurs during systole. Data modified from the study by Niizeki and Miyamoto[45].

were elicited when lower extremity muscular contraction (footfalls) occurred early in the cardiac cycle, i.e., during systole.

On the other hand, a command of central neurogenic origin has been shown to drive circulation and locomotion, in parallel, during exercise in animals[47]. Using a "fictive" locomotion animal model, it has been suggested that the existence of neuronal circuits leads to coupling between the central locomotor rhythm and the respiratory rhythm[48], and to coupling between the central locomotor rhythm and the cardiac rhythm[49]. This, possibly, causes a tight coupling of cardiac rhythm to locomotor rhythm in animals, probably by interacting with the efferent feedforward signals from the locomotor centers. Hence, the possibility remains that such central control mechanisms may contribute to the coupling between rhythms.

Furthermore, an alternative explanation for the mechanism of CLS could be locomotor-induced changes in thoracic and abdominal pressures, which vary the rate of venous return, thus changing the ventricular ejection, and thereby influencing the cardiac rhythm[22]. The venous return from skeletal muscles can be expected to vary in sync with the locomotor rhythm. It has been shown in animal experiments that myocardial stretch produced by volume or pressure overload or direct distension of a muscle strip leads to significant electrophysiological changes[50]. Stride-by-stride changes in venous return lead to an alteration in heart muscle activity, and thereby may contribute to the occurrence of CLS.

Using computer-assisted bilateral thigh cuff occlusion to simulate rhythmic intramuscular pressure (IMP) changes during bipedal locomotion in the human, Niizeki[25] found that synchronization between cardiac rhythms and IMP changes can be achieved with no muscle contraction while sitting. In this situation, afferent signals from active muscles and central command can be eliminated as a possible mechanism responsible for phase synchronization. In addition, this would indicate that vertical motion per se may not be necessary to induce CLS. It has been shown in humans that HR increased in response to the pulsed compression of the thigh muscle, even under resting conditions[51]. Thus, the mechanical stimulus of synchronous IMP may contribute, to some degree, to producing phase synchronization, irrespective of whether the subject is under resting conditions or performing exercise.

It seems quite difficult to draw any conclusive explanation as to the primary mechanism responsible for CLS. The possible mechanisms mentioned above are not mutually exclusive, and all could play a role in producing CLS. Further studies are required to gain a broader insight into the mechanism of CLS.

Physiological significance of CLS

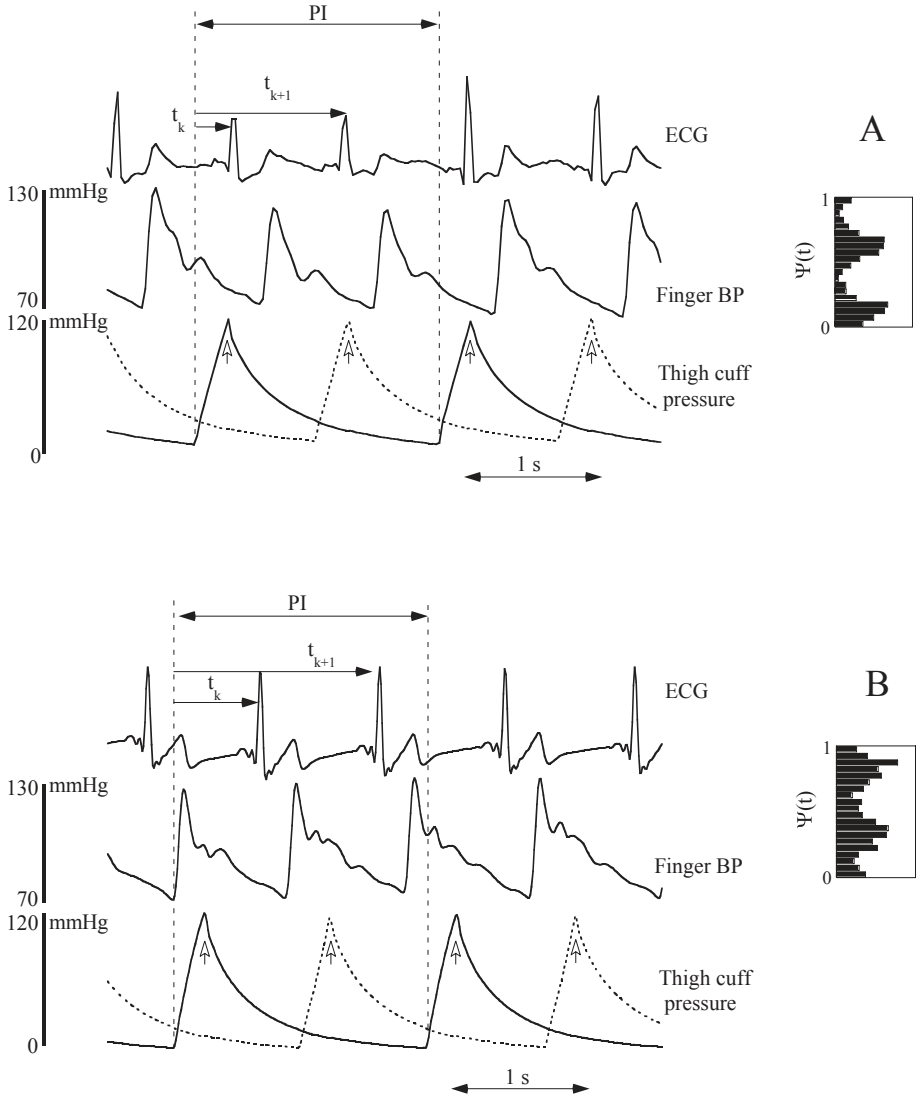
The identification of CLS raises the question as to whether or not the phenomenon is related to physiological functions. Reports of CLS on birds have suggested a mechanical linkage between heartbeats and wing muscle. Aulie[20,21] suggested that the pectoral muscles in small birds may work like a "venous pump" during flight by contracting every time the heart is in the diastolic phase. The pectoral muscle is the largest muscle driving the power stroke (down stroke) of the wing cycle, and when it contracts intrathoracic pressure is increased. This increase results in blood being pumped back to the heart like a "venous pump". Therefore, venous return will be maximized when the pectoral muscle activates during the diastolic phase of the cardiac cycle. Inversely, if the pectoral muscles are not activated during the systolic phase of the cardiac cycle, the blood flow to the pectoral muscles will be maximized. However, no experimental evidence of such a function has been provided thus far, possibly because of the difficulty of blood flow measurement during wing stroke.

Early in 1921, Coleman[5] studied a subject who reproducibly felt breathless when climbing a hill; he observed that once the subject started breathing and stepping in unison with his pulse, he was able to walk without breathlessness. Donville et al.[9] tried to find the efficiency of metabolic cost during a cycle ergometer exercise when CLS occurred. In their experiment, subjects tried to synchronize their pedaling rate with their heartbeat at a ratio of 1:1 by listening to an auditory cue, while breath-by-breath oxygen uptake was measured. They showed neither a consistent phase relationship nor increased metabolic efficiency during episodes when the pedaling rate and HR were matched. On the other hand, Udo et al.[16] observed in a human while running, that oxygen uptake is significantly less when CLS occurs than when it does not. It should be noted, however, that their analysis was based on data from single subject designs. Kirby and collaborators[7,8,14] previously proposed in their series of experiments that CLS might improve blood supply to the contracting muscles to minimize skeletal muscle ischemia and/or minimize the energy cost of cardiac muscle contraction. They noted that muscle blood flow through active muscles is periodically occluded during each contraction phase of rhythmic exercise, possibly because IMP often rises beyond the level of systolic blood pressure during contraction[52,53]. Therefore, synchronizing the heartbeat and muscle contraction rhythm would be functionally favorable when it occurs in the latter half of the cardiac phase in rhythmic exercise. However, experimental evidence supporting this hypothesis is lacking. Using thigh-cuff occlusion rhythm, it has been shown that there is a significant tendency for the heartbeat to occur at particular phases in the IMP cycle, where the peak blood pressure measured in the finger is not overlapped by the peak cuff pressure[25]. Since the timing of the systolic phase of blood pressure measured in the finger has been shown to be almost identical with that of peak arterial flow for the thigh[25], it is speculated that the heart expels

blood when the IMP is lower (Figs. 4A and 4B). In the thigh, the timing of the coupling phase during walking are similar to those of the IMP cycle, as shown in Figs. 4C and 4D (Niizeki, unpublished observation). In that study, the IMP profile during walking was assumed to be proportional to the change in intra-cuff pressure of the thigh cuff placed over the thigh muscle belly of the subject. These observations suggest that CLS is involved in the enhancement of blood delivery to the locomotor muscles. Resolving how vascular perfusion adjusts to the pattern of motor activity will provide more solid evidence for the functional meaning of CLS. Recently, Phillips and Jin[54] demonstrated that, when CLS was ensured by pacing the stride rate according to the measured heartbeat during running, the time taken to run 3 miles was less than that taken for runs where the stride rate was not paced. This indicates that CLS may have a beneficial effect on running performance.

O'Rourke and Avolio[55] speculated that the vertical movements during running generate positive and negative pressures in the aorta due to gravity. If the body movement is synchronized with the HR in such a way that negative pressure is generated during cardiac systole and positive pressure is generated during diastole, it may beneficially augment ventricular ejection during systole and enhance myocardial blood supply during diastole. In the modeling studies, the authors showed that when two pumps—representing left ventricular ejection and leg muscle contraction—were perfectly entrained in antiphase, the cardiac performance, as estimated by the left ventricular tension-time index (TTI), improved. Although the relevance of this hypothesis to humans has not yet been explored, such an acceleration effect exists in dogs. Bhattacharya et al.[23] tried to assess the effect of body acceleration on cardiovascular function in supine dogs and found that cardiovascular function improved when the acceleration waveform was imposed along the spinal axis and at a frequency equal to the heart frequency. They demonstrated that stroke volume and cardiac work were maximal when the peak force was positive in early diastole, and negative in late diastole and early systole.

Another interesting aspect of the research concerns the use of electrical stimulation to achieve muscle contraction for therapeutic purposes. Kimura et al.[56] examined how



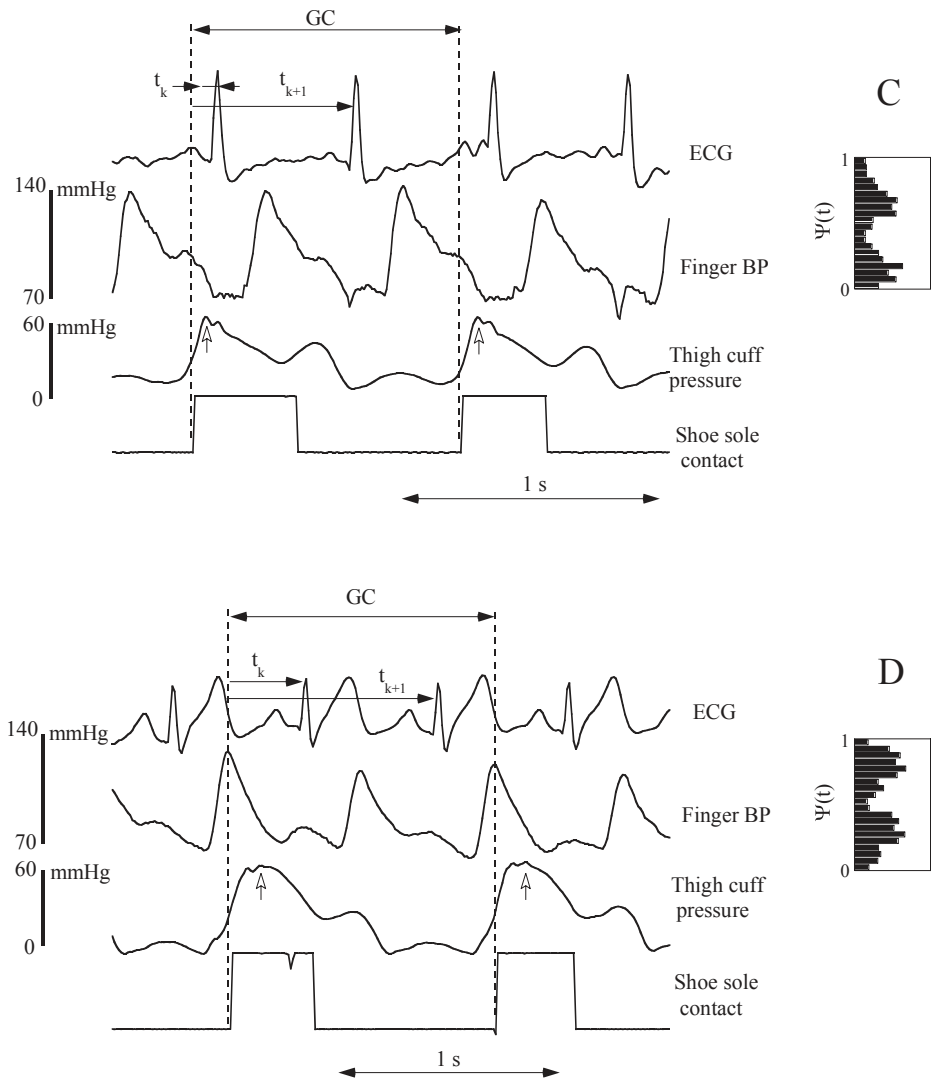


Fig. 4 The relationship between the period of cardiac cycle and the phase of thigh cuff pressure that most frequently occurred in the presence of synchronization during alternative bilateral thigh-cuff occlusion while sitting (A and B, see Niizeki[25] for details) and walking (C and D, Niizeki, unpublished observation). A histogram of the relative phase difference Ψ(t) probability distribution is also shown. During walking, a subject walked on a treadmill with a thigh cuff placed over the thigh muscle belly. When the thigh muscles contract, the circumference of the thigh muscle increases, resulting in an increase in intra-cuff pressure. It was assumed that the intra-cuff pressure profile can be used as a signal that is proportional to the changes in intramuscular pressure. There were two patterns of coupling; the peak cuff pressure occurred in the proximity of the QRS wave (A and C) or immediately after the T wave of the ECG (B and D). Note that each of the peak intra-cuff pressures (open arrows) do not coincide with the systolic blood pressure in both cases. GC: gait cycle, PI: cuff pressure interval.

muscle contraction timing related to the cardiac cycle affects hemodynamic responses during intermittent muscle contractions evoked by electrical stimulation. They demonstrated that systolic blood pressure and peripheral vascular resistance were lowered when muscle contraction started after the R wave of the ECG. This would indicate that if muscle contraction can be induced to be synchronous with heartbeats with an appropriate phase difference, elevations in blood pressure and peripheral resistance would be preventable. It remains to be clarified whether the induction of CLS could be used, for example, for physical rehabilitation in patients with cardiopulmonary diseases, whose exercise capacity is typically lower than that of healthy individuals.

Summary

Cardiolocomotor synchronization has been demonstrated in various types of locomotion. The physiological significance of such coordination has been suggested as a system of economical coaction and one that is energetically advantageous to the organism. However, direct evidence, showing the functional significance of CLS in humans under conditions that may mimic real-life physiological scenarios, is scarce. We expect that future studies will enhance our understanding of the functional role of CLS during exercise. Fundamental questions concerning the synchronization of these rhythmic processes include how these rhythms interact with each other under differ-

ent physiological conditions and whether this interaction is essential to life. The nature and mechanism of this coupling still need to be clarified.

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