©Journal of Sports Science and Medicine (2014) **13,** 881-887
http://www.jssm.org

Research article

Effects of Synchronization between Cardiac and Locomotor Rhythms on Oxygen Pulse during Walking

Shinta Takeuchi [1]✉, Yusuke Nishida [2] and Takashi Mizushima [1]
[1] Hamamatsu University School of Medicine, University Hospital, Department of Rehabilitation, Shizuoka, Japan
[2] Rehabilitation Sciences, Seirei Christopher University, Shizuoka, Japan

Abstract
The objective of the study was to investigate whether the occurrence of cardiac–locomotor synchronization (CLS) affects oxygen pulse (O_2 pulse, mL/beat) during walking. Twelve healthy men were studied under two treadmill protocols. The CLS protocol involved subjects walking at a frequency of their heart rate (HR) to induce CLS. The free protocol (reference) involved subjects walking at a self-selected cadence. The treadmill load was equal between the two protocols and was adjusted so that the subject's HR was maintained at approximately 120 bpm. Electrocardiographic signals, foot switch signals, and oxygen consumption (VO_2) were measured continuously for 10 min after the heart rate reached a steady state. VO_2, O_2 pulse, and mean HR were calculated. VO_2 and O_2 pulse were significantly higher in subjects in the CLS protocol compared to those in the free protocol. However, mean HR was not different between the two groups. The synchronization strength was significantly related to the increase in O_2 pulse in subjects in the CLS protocol compared with those in the free protocol. These results suggest that the occurrence of CLS enhances O_2 pulse by increasing the strength of CLS during walking.

Key words: Heart rate, step rate, coupling, entrainment, oxygen consumption stroke volume.

Introduction

When humans and other mammals rhythmically exercise, heartbeats interact with other biological rhythms or external rhythms, and synchronization between the heartbeat and the other rhythms is observed (Glass, 2001). Synchronization between the heartbeat and locomotor activity rhythms (cardiac–locomotor synchronization; CLS) occurs in humans during walking and running (Kirby et al., 1989; Niizeki et al., 1993, 1996; Nomura et al., 2001, 2003). CLS has been proposed to be an efficient phenomenon for exercising the body (Kirby et al., 1989; 1992) and is thought to optimize muscle blood flow and minimize cardiac afterload based on the hypothesis that peak intra-arterial pressure due to cardiac contraction occurs at the lowest phase of the intramuscular pressure cycle. CLS also increases stroke volume (SV) associated with increase in venous return by the Frank–Starling law based on the hypothesis that increase in venous return due to muscular pump action occurs during cardiac diastole. Increase in SV results from decrease in peripheral vascular resistance and changes in pressure in the ascending aorta caused by vertical body movement during running (O'Rourke and Avolio, 1992). In fact, Phillips et al. (2013) reported that CLS provided a performance improvement when running long distances. If CLS also has physiological significance for blood supply to muscles by cardiac contraction during walking, it could be applied to rehabilitation program for patients with depressed left ventricular ejection function and elderly people. However, few studies have reported the functional significance of CLS during walking (Niizeki and Saitoh, 2014).

The ratio between oxygen consumption (VO_2) and heart rate (HR) defines the oxygen pulse (O_2 pulse), which is numerically equal to the product of SV and the arteriovenous oxygen difference (a-vO_2 difference), according to Fick's equation (Wasserman et al., 1999). O_2 pulse also independently predicts SV during submaximal exercise in healthy subjects (Bhambhani et al., 1994; Whipp et al., 1996). Therefore, we examined whether CLS has physiological significance for blood supply during walking, using O_2 pulse as an alternative SV index.

Methods

Subjects

Twelve healthy men (mean height: 169.4 cm, range: 1.64.0–1.79 m; weight: 57.9 kg, range: 48.4–68.6 kg; age: 21.2 years, range: 19–25 years) with no history of cardiopulmonary diseases participated in this study (Table 1). Each subject provided an informed consent after being provided with a verbal explanation of the intent and the experimental procedures. This study protocol was approved by the Ethics Committee of the University. Physical activity as well as alcohol and caffeinated beverage consumption were prohibited 24 h before testing. Drinking and eating, except water, were also prohibited 3 h before testing.

Table 1. Subject characteristics (n= 12) and applied treadmill load.

Variable	Mean (±SD)
Age (year)	21.2 (2.1)
Height (m)	1.69 (.05)
Weight (kg)	57.9 (6.5)
Body mass index (kg/m2)	20.2 (2.1)
Treadmill speed (km/h)	5.7 (.2)
Treadmill grade (%)	3.3 (1.0)
First protocol (CLS/Free)	5/7

Protocols

We determined each subject's treadmill load (treadmill speed and grade) at which their HR was maintained at

Received: 08 May 2014 / Accepted: 26 August 2014 / Published (online): 01 December 2014

approximately 120 beats per min (Table 1). Target heart rate was derived from the 50-70 percent of estimated maximal heart rate, which is formula of optimal heart rate during exercise for heart failure patients in Japan. Subjects walked on a treadmill (Autorunner AR-200, Minato Medical Science Co. Ltd, Osaka, Japan), and the treadmill speed was increased gradually in the range which subjects can walk (limited at 6.0 km/h). When the load was insufficient, the treadmill grade was increased until the target HR was achieved. The subjects walked at the determined treadmill speed and grade for at least 5 min to confirm the appropriate load.

The subjects then rested at least 15 min during which they were instrumented for data collection. Electrodes for electrocardiogram (ECG), a foot switch sensor, and a mask connected to an expired gas analyzer were placed on the chest, right heel, and face of the subjects, respectively. Thereafter, the subjects were instructed to conduct the two treadmill protocols in a random order. In the first protocol, subjects walked at the frequency of their HR to induce synchronization between heartbeat and locomotor activity (CLS protocol). In the other protocol, subjects walked at their preferred pace (free protocol as reference data). Both protocols were performed at the determined treadmill load for each subject for 20 min. First 10 min was warm-up period. Next 10 min was measurement period. The treadmill load (treadmill speed and grade) was fixed while each protocol. Therefore treadmill load and walking time were equal between the two protocols. Subjects rested in a sitting position for at least 15 min between the two protocols.

In the CLS protocol, firstly they walked at each treadmill load for 5 min. Next, they walked for 5 min with a buzzer signal, which was generated by an ECG monitor (Bedside monitor BSM-2400 series Life Scope 1, Nihon Kohden Corp., Tokyo, Japan). The buzzer sounded with the occurrence of each R waves, so subject's heart rate and the frequency of the buzzer were same. After their HR reached a steady state, they walked with a buzzer signal for 10 min. We collected data during the last 10 min of the synchronized walking period.

In the free protocol, firstly they walked at each treadmill load for 10min. Next, they walked at their preferred pace for 10 min. We collected data during the last 10 min of the preferred walking period. Because SV and the a-vO_2 difference vary between individuals, depending on the degree of obesity at rest and submaximal exercise (Vella et al., 2011), the value at rest was not appropriate to use as reference data. Thus, we set equal treadmill load and exercise time for both protocols.

Data collection

The R-R interval (RRI) was measured continuously from a surface ECG using standard bipolar leads (CM5). The ECG signal was amplified and filtered to distinguish the R waves of the QRS complex. We set the filtering frequency band to 10–300 Hz to avoid movement artifacts. The ECG signal was digitized with a sampling frequency of 1 kHz using a personal computer-based system (Chart 5 for Windows, AD Instruments, Shanghai, China) equipped with an analogue-to-digital converter (ML880 PowerLab 16/30, AD Instruments). The heel contact interval (HCI) was also measured by a foot switch sensor (Inline Foot Contact Sensor, Noraxon) from the right heel. The foot switch signal was collected with a sampling frequency of 1.5 kHz using a personal computer-based system (MyoResearch XP, Noraxon). The ECG and foot switch signals were reported by separate computers; therefore, we started maintaining records at the same time. In addition, subject's VO_2 was measured breath by breath throughout the exercise period from expired gases with an AE-300S aero monitor (Minato Ikagaku Co., Tokyo, Japan) and calculated on a personal computer.

Data analyses

We translated the RRI and HCI data into text files and opened them as worksheets in Microsoft Office Excel 2007 (Redmond, WA, USA). Each successive HCI signal was halved to estimate the foot switch data for both legs. The time at which each R-wave occurred and the onset of each step cycle were calculated by adding the first onset time and the interval times. To obtain the relative phase relationship between cardiac and locomotor rhythms ($\varphi_{r,h}$), the time (t_r) at which the rth R-wave occurred in a one-step cycle was calculated from the onset of the step cycle, where t_r is the time of the rth marked event. We then set the onset of the step cycle as T_h. The relative phase ($\varphi_{r,h}$) of the rth heartbeat in the one-step cycle was calculated as follows:

$$\varphi_{r,h} = \frac{t_r - T_h}{T_{h+1} - T_h}$$

where r and h are integers (Figure 1).

A synchronization index, λ, was calculated to quantify the strength of phase locking between the heartbeats and the step cycle as follows:

$$\lambda - \left(\frac{1}{N}\sum_{j=r-N}^{r}\sin(\varphi_{r,h}\times 2\pi)\right)^2 + \left(\frac{1}{N}\sum_{j=r-N}^{r}\cos(\varphi_{r,h}\times 2\pi)\right)^2$$

where N indicates the number of consecutive data samples. The λ value was calculated from 60-point (approximately 30 s) windows with a sliding window of 10 points. The mean λ value was calculated by averaging the entire measurement period in each protocol. The fractional points were rounded down when the point of the relative phases was insufficient at the end of the calculations. The λ value is restricted to the unit interval $0 \le \lambda \le 1$ and is maximal for strong phase locking between the two rhythms and is minimal for weak or no phase locking.

Furthermore, a surrogate data technique was applied to determine the probability of entrainment between the cardiac and locomotor rhythms (Seidel and Herzel, 1998; Nomura et al., 2001). Surrogate data were generated by randomly shuffling the original order of the HCI, which was not halved. The successive RRI remained the same as for the actual data. A new relative phase between the two rhythms was created as compared with the original data after random shuffling of the HCI order. The phase relationships between the heartbeat and locomotor activity rhythm were destroyed because of the random

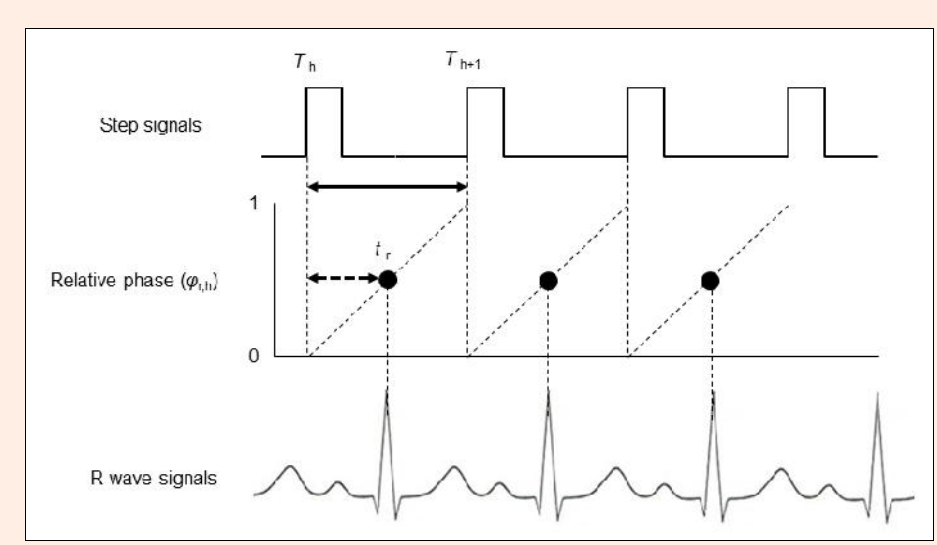


Figure 1. The computational theory used to calculate the relative phase relationship between the heartbeat and locomotor activity rhythms ($\varphi_{r,h}$). The square waves are step signals. Elevation of the wave indicates heel contact. The waves at the bottom of the panel are electrocardiogram signals. The sharply elevated wave is the R wave.

order of the HCI. If the two rhythms had an exact phase relationship, a similar relative phase to the original relative phase occurred in the surrogate data. By computing multiple trial-shuffled estimates (100 shuffles), a distribution of values under the null hypothesis was obtained (Niizeki, 2005). The average λ value from the original data was compared with that of the surrogate data calculated from an identical choice in the observation window.

We calculated the mean HR, standard deviation of HR (SDHR), mean step rate (SR), standard deviation of SR (SDSR), VO_2, and O_2 pulse as mean values for 10 min in each protocol to investigate the CLS physiological response. HR, SDHR, SR, and SDSR were calculated with the RRI data and HCI data, respectively. The O_2 pulse value was obtained by dividing mean VO_2 by mean HR.

Statistical anlyses

Values are shown as means ± standard deviations. The λ values were compared between the two protocols using the paired t-test to determine whether phase synchronization significantly occurred during the CLS protocol. In addition, the λ values from the original and surrogate data in both protocols were compared using paired t-tests to determine whether phase synchronization occurred by entrainment. Mean HR, SDHR, mean SR, SDSR, VO_2, and O_2 pulse were compared between the two protocols using paired t-tests to examine the effect of inducing CLS on the physiological data during walking. Furthermore, we investigated the relationship between the changes in λ value and O_2 pulse in the CLS protocol compared with that in the free protocol using Pearson's product–moment correlation coefficients. All statistical analyses were performed using the SPSS version 19 for Windows software (SPSS Japan, Inc., Tokyo, Japan). $P < 0.05$ was considered to be statistically significant.

Results

Figure 2 shows representative RRI (Figure 2A, A') and HCI (Figure 2B, B') time series, and the trace of λ value (Figure 2C, C') recorded from one subject while he performed CLS protocol (Figure 2A, B, C) and free protocol (Figure 2 A', B', C') for last 10min.

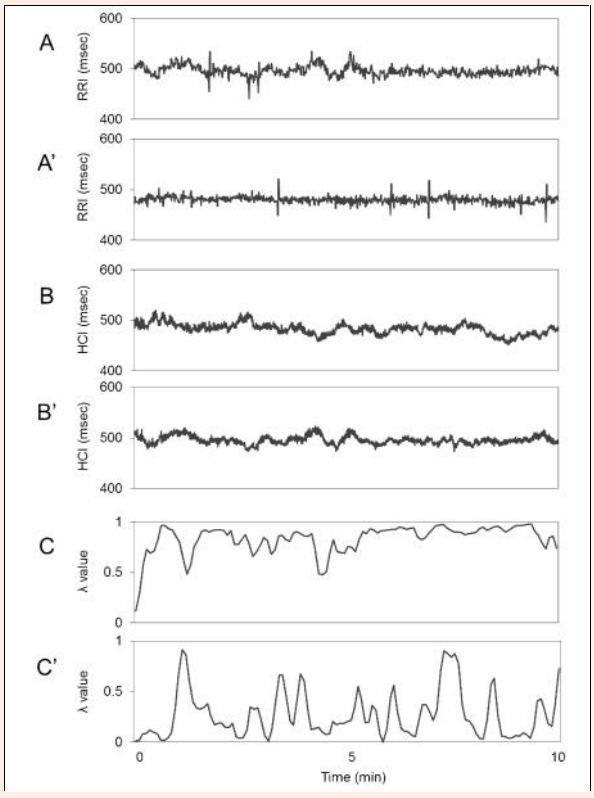


Figure 2. Representative time series variation of cardiac rhythm, locomotor rhythm, and λ value in one subject. Shown are the time series of R-R interval (RRI) (A, A'), heel contact interval (HCI) (B, B') and the trace of the λ value (C, C') during CLS protocol (A, B, C) and free protocol (A', B', C').

Table 2. Comparison of physiological data during walking between the CLS and the free protocols. Data are expressed as mean (± standard deviation).

Variables	CLS protocol	Free protocol
Oxygen consumption (ml·kg^{-1}·min^{-1})	29.2 (5.3) *	28.3 (4.9)
Oxygen pulse (average difference) (ml/beat)	14.2 (2.7) (3.04) *	14.0 (2.7) (3.06)
Mean heart rate (beat/min)	118.4 (5.5)	117.2 (7.6)
Standard deviation of heart rate	2.85 (.70) *	3.34 (.71)
Mean step rate (step/min)	118.7 (4.5)	122.9 (6.4)
Standard deviation of step rate	3.04 (.49)	2.71 (1.87)

In the CLS protocol, subjects walked at the pace of their heart rate rhythm to induce phase synchronization between the heartbeat and locomotor activity. In the free protocol, subjects walked at their preferred pace. * $p < 0.05$ compared with the free protocol

The mean λ value in the CLS protocol increased significantly compared with that in the free protocol (0.56 ± 0.18 vs 0.08 ± 0.08, $p < 0.05$) and from the surrogate data (0.56 ± 0.18 vs 0.25 ± 0.09, $p < 0.05$), indicating that phase synchronization was the result of heartbeat entrainment by locomotor activity. The mean λ value in the free protocol was not different from the surrogate data (0.08 ± 0.08 vs 0.07 ± 0.07, not significant), indicating that phase synchronization did not occurred in the free protocol.

Table 2 shows the comparison of the physiological responses during walking between the CLS and free protocols. Despite an identical treadmill load during the two protocols, VO_2, and O_2 pulse during the CLS protocol were significantly higher than those during the free protocol, respectively. SDHR was significantly lower in the CLS protocol. Mean HR, mean SR, and SDSR were not significantly different between the two protocols.

Figure 3 shows the relationship between the difference in λ value (Δ λ value, range 0.16–0.66) and the difference in O_2 pulse in the CLS and free protocols (Δ O_2 pulse, range, −0.08–0.51). A correlation analysis revealed a significant relationship between the Δ λ value and Δ O_2 pulse ($r = 0.70$, $p < 0.05$), indicating that as the subjects walked with increasing synchronization strength between heartbeat and locomotor activity during the CLS protocol, they showed increased O_2 pulse values in the CLS protocol compared with normal walking at the same treadmill load.

Discussion

The main finding of the present study was that O_2 pulse increased with the synchronization strength between the heartbeat and locomotor activity during walking. Furthermore, the synchronization strength of the CLS protocol was significantly greater than that of the surrogate data and the free protocol, indicating that the difference in physiological data between the two protocols could show a physiological response when CLS occurs. These results suggest that CLS could increase O_2 pulse during walking. VO_2 and O_2 pulse increased significantly during the CLS protocol compared with those during the free protocol, despite an identical treadmill load (Table 2). In addition, a strong positive correlation was observed between Δ O_2 pulse and Δ λ value (Figure 3), indicating that the increase in O_2 pulse is related to the occurrence of CLS. Although Δ O_2 pulse was small as a mean value, it was different for each subject and related to Δ λ value (Figure 3). Ciske et al. (1986) showed that 4 weeks of aerobic training significantly increased 0.9-ml/beat O_2 pulse at a fixed treadmill load (speed, 1.7 mile/h; grade, 10%) in patients with

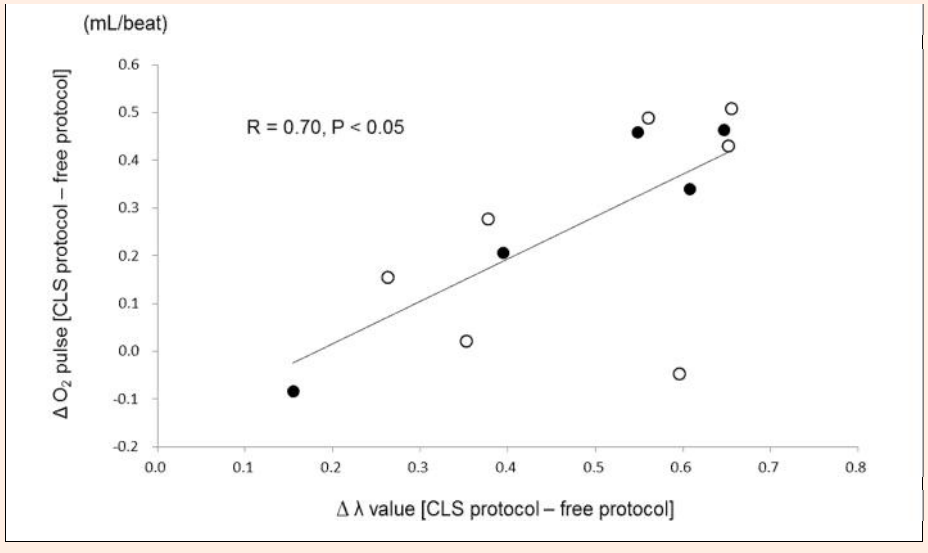


Figure 3. The relationship between the Δ λ value and Δ O_2 pulse. An increase in Δ O_2 pulse with the Δ λ value was determined by Pearson's product–moment correlation coefficient. λ, synchronization index. Black circle, subject who performed the CLS protocol as the first protocol. White circle, subject who performed the free protocol as the first protocol

coronary heart disease. Sullivan et al. (1989) showed that digoxin administration increased 1.6-ml/beat O_2 pulse at submaximal exercise in patients with heart failure. In the present study, Δ O_2 pulse was 0.51 ml/beat in the subject whose Δ λ value was the highest. Therefore, CLS could have an effect of the half of aerobic training or third effect of digoxin administration on O_2 pulse. However in the present study, it was unclear what affected increase in O_2 pulse, such as an increase in SV, an increase in a-vO_2 difference, or both. Research in similar subjects who were induced with CLS during running (Dhindsa et al., 2012) has demonstrated an increase in SV with subsequent increase in the cardiac output. In the present study the main factor for the increase in O_2 pulse also may be increase in SV.

The mean synchronization index during the CLS protocol was 0.56 ± 0.18. This value was different for each subject (range, 0.16–0.83) but was significantly greater compared with that in the surrogate data. The lack of strong synchronization between the heartbeat and locomotor activity may have occurred because of multiple factors associated with the cardiac activity. Two factors appear to affect the cardiac activity (Nomura et al., 2006). The first is that a peripheral neural circuit with ascending signals from mechanoreceptors within active skeletal muscle may modulate the heartbeat interval (Legramante et al., 2000; McWilliam and Yang, 1991; Niizeki, 2005). The second is a non-neural mechanism such as the intrinsic property of the heart without modification of the autonomic nervous activity (Bernardi et al., 1990; Casadei et al., 1996; Kohl et al., 1999; Simmons et al., 1997). Novak et al. (2007) reported that cardiac–locomotor entrainment is enhanced in elderly people. They hypothesized that the muscle forces generated during the gait cycle may exert a greater effect on the cardiac cycle with the attenuation of autonomic feedback mechanisms due to aging. Blain et al. (2009) showed that cycling continuously modulates the cardiac chronotropic response to exercise and that a workload increase during intense exercise further accentuates synchronization between the cardiac and locomotor rhythms. It appears that the strength of CLS is associated with the balance of neural and non-neural mechanisms and depends on the exercise intensity. In the present study, SDHR was significantly lower in the CLS protocol, which was similar result of previous study (Niizeki et al. 1993). However we set the treadmill load at a level to maintain the subject's HR at approximately 120 beats per min. This treadmill load may have been insufficient for inducing CLS in several subjects. Difference of relative exercise intensity for each subject would cause the variability in λ value between subjects.

Numerous studies (Kirby et al., 1989; Niizeki, 2005; 1993; Nomura et al., 2006) have proposed that CLS optimizes blood flow to contracting muscles and minimizes the energy cost of cardiac muscle contraction. For example, Niizeki (2005) reported that simulated CLS by rhythmic cuff occlusion of the thigh improves muscle perfusion. In addition, Kimura et al. (2010) found that CLS attenuates systolic blood pressure and cardiac afterload and increases SV, as shown by an electrical muscle stimulation experiment. However, direct reliable evidence for CLS during exercise is rare. Donville et al. (1993) showed evidence for CLS during cycling and concluded that any functional significance of CLS is unrelated to metabolic efficiency. However, their method of analyzing synchronization was not based on phase synchronization but on frequency synchronization, which is inappropriate for analyzing biological rhythms (Rosenblum et al., 1998; Schäfer et al., 1999). In addition, Nomura et al. (2003) found that during running, CLS likely results from entrainment, whereas during cycling, it results from chance, occurring when the cardiac rhythm approached the locomotor rhythm. Therefore, the results of Donville et al. (1993) may have lower reliability. In recent years, Dhindsa et al. (2012) showed evidence for CLS during running and demonstrated that SV and cardiac output were elevated when heart rates and step rates were synchronized. The SV and cardiac output were calculated with beat-by-beat analysis, but the method of analyzing synchronization was not based on phase synchronization. In the present study, we showed the physiological responses of CLS were based on phase synchronization during walking. These results support the physiological significance of CLS as proposed by previous studies.

Four limitations of the present study should be mentioned. First, we did not measure the SV and a-vO_2 difference. Therefore it was unclear what affected increase in O_2 pulse in the present study. Second, we were unable to validate the effect of respiratory rhythm on the relationship between cardiac and locomotor rhythms. Respiration could indirectly influence the occurrence of CLS in two ways. Respiratory sinus arrhythmia modulates the heartbeat through neural effects (Schafer et al., 1998), and ventilation modulates venous return through movement of the diaphragm (Miller et al., 2005). Further study is required to test these respiratory effects. Third, we were unable to validate instant CLS responses. One sample value was actually quite far from the correlation line (Figure 3) suggesting that O_2 pulse did not increase despite the occurrence of CLS in that case. Thus, we need to analyze beat-by-beat CLS physiological responses. However, O_2 pulse values were calculated from two parameters, which were sampled at different frequencies. In addition, computation of the synchronization strength required a number of relative phase relationships between cardiac and locomotor rhythms. Therefore, we used the mean for the last 10 min in each protocol. As a result, the beat-by-beat CLS physiological response during exercise was unclear. Forth, our results should be carefully applied to other subjects because they were obtained in healthy young males.

Conclusion

Our findings provide the first evidence that CLS increases O_2 pulse during walking. We believe that our results could have important implications for investigating other CLS physiological responses during exercise.

Acknowledgements
This work was supported by JSPS KAKENHI Grant Numbers 24650311.

References

Bernardi, L., Salvucci, F., Suardi, R., Soldá, PL., Calciati, A., Perlini, S., Falcone, C. and Ricciardi, L. (1990) Evidence for an intrinsic mechanism regulating heart rate variability in the transplanted and the intact heart during submaximal dynamic exercise? *Cardiovascular Research* **24**, 969-981.

Bhambhani, Y., Norris, S. and Bell, G. (1994) Prediction of stroke volume from oxygen pulse measurements in untrained and trained men. *Canadian Journal of Applied Physiology* **19**, 49-59.

Blain, G., Meste, O., Blain, A. and Bermon, S. (2009) Time-frequency analysis of heart rate variability reveals cardiolocomotor coupling during dynamic cycling exercise in humans. *American Journal of Physiology. Heart and Circulatory Physiology* **296**, H1651-H1659.

Casadei, B., Moon, J., Johnston, J., Caiazza, A. and Sleight, P. (1996) Is respiratory sinus arrhythmia a good index of cardiac vagal tone in exercise? *Journal of Applied Physiology* **81**, 556-564.

Ciske, P.E., Dressendorfer, R.H., Gordon, S. and Timmis, G.C. (1986) Attenuation of exercise training effects in patients taking beta blockers during early cardiac rehabilitation. *American Heart Journal* **112**, 1016-1025.

Dhindsa, M.S., Sugawara, J. and Tanaka, H. (2012) Hemodynamic impacts of entrainment of heart rate and stride rate. *Artery Research* **6**, 136-140.

Donville, J.E., Kirby, R.L., Doherty, T.J., Gupta, S.K., Eastwood, B.J. and MacLeod, D.A. (1993) Effect of cardiac-locomotor coupling on the metabolic efficiency of pedaling. *Canadian Journal of Applied Physiology* **18**, 379-391.

Glass, L. (2001) Synchronization and rhythmic processes in physiology. *Nature* **410**, 277-284.

Kimura, T., Kameda, N. and Moritani, T. (2010) Impact of phase difference between cardiac systole and skeletal muscle contraction on hemodynamic response during electrically-induced muscle contractions. *Journal of Electromyography and Kinesiology* **20**, 572-579.

Kirby, R.L., Atkinson, S.M., Donville, J.E., Urdang, M.F., Stanley, D.A., Gupta, S.K. and MacLeod, D.A. (1992) Failure of accentuated vertical body movements to induce cardiac-locomotor coupling. *Journal of Applied Physiology* **72**, 1368-1374.

Kirby, R.L., Nugent, S.T., Marlow, R.W., MacLeod, D.A. and Marble, A.E. (1989) Coupling of cardiac and locomotor rhythms. *Journal of Applied Physiology* **66**, 323-329.

Kohl, P., Hunter, P. and Noble, D. (1999) Stretch-induced changes in heart rate and rhythm: clinical observations, experiments and mathematical models. *Progress in Biophysics and Molecular Biology* **71**, 91-138.

Legramante, J.M., Raimondi, G., Adreani, C.M., Sacco, S., Iellamo, F., Peruzzi, G. and Kaufman, M.P. (2000) Group III muscle afferents evoke reflex depressor responses to repetitive muscle contractions in rabbits. *American Journal of Physiology. Heart and Circulatory Physiology* **278**, H871-H877.

McWilliam, P.N. and Yang, T. (1991) Inhibition of cardiac vagal component of baroreflex by group III and IV afferents. *The American Journal of Physiology* **260**, H730-H734.

Miller, J.D., Pegelow, D.F., Jacques, A.J. and Dempsey, J.A. (2005) Skeletal muscle pump versus respiratory muscle pump: modulation of venous return from the locomotor limb in humans. *The Journal of Physiology* **563**, 925-943.

Niizeki, K. (2005) Intramuscular pressure-induced inhibition of cardiac contraction: implications for cardiac-locomotor synchronization. *American Journal of Physiology. Regulatory, Integrative and Comparative Physiology* **288**, R645-R650.

Niizeki, K. and Saitoh, T. (2014) Cardiolocomotor phase synchronization during rhythmic exercise. *The Journal of Physical Fitness and Sports Medicine* **3(1)**, 11-20

Niizeki, K., Kawahara, K. and Miyamoto, Y. (1993) Interaction among cardiac, respiratory, and locomotor rhythms during cardiolocomotor synchronization. *Journal of Applied Physiology* **75**, 1815-1821.

Niizeki, K., Kawahara, K. and Miyamoto, Y. (1996) Cardiac, respiratory, and locomotor coordination during walking in humans. *Folia Primatologica; International Journal of Primatology* **66**, 226-239.

Nomura, K., Takei, Y. and Yanagida, Y. (2001) Analysing entrainment of cardiac and locomotor rhythms in humans using the surrogate data technique. *European Journal of Applied Physiology* **84**, 373-378.

Nomura, K., Takei, Y. and Yanagida, Y. (2003) Comparison of cardiolocomotor synchronization during running and cycling. *European Journal of Applied Physiology* **89**, 221-229.

Nomura, K., Takei, Y., Yoshida, M. and Yanagida, Y. (2006) Phase-dependent chronotropic response of the heart during running in humans. *European Journal of Applied Physiology* **97**, 240-247.

Novak, V., Hu, K., Vyas, M. and Lipsitz, L.A. (2007) Cardiolocomotor coupling in young and elderly people. *The Journal of Gerontology. Series A, Biological Sciences and Medical Sciences* **62**, 86-92.

O'Rourke, M. and Avolio, A. (1992) Improved cardiovascular performance with optimal entrainment between heart rate and step rate during running in humans. *Coronary Artery Disease* **3**, 863-869.

Phillips, B. and Jin, Y. (2013) Effect of adaptive paced cardiolocomotor synchronization during running: a preliminary study. *Journal of Sports Science & Medicine* **12**, 381-387.

Rosenblum, M.G., Kurths, J., Pikovsky, A., Schäfer, C., Tass, P. and Abel, H.H. (1998) Synchronization in noisy systems and cardiorespiratory interaction. *IEEE Engineering in Medicine and Biology Magazine* **17**, 46-53.

Schäfer, C., Rosenblum, M.G., Abel, H.H. and Kurths, J. (1999) Synchronization in the human cardiorespiratory system. *Physical Review. E, Statistical Physics, Plasmas, Fluids, and Related Interdisciplinary Topics* **60**, 857-870.

Schäfer, C., Rosenblum, M.G., Kurths, J. and Abel, H.H. (1998) Heartbeat synchronized with ventilation. *Nature* **392**, 239-240.

Seidel, H. and, Herzel, H. (1998) Analyzing entrainment of heartbeat and respiration with surrogates. *IEEE Engineering in Medicine and Biology Magazine* **17**, 54-57.

Simmons, A.D., Carrier, D.R., Farmer, C.G. and Gregersen, C.S. (1997) Lack of locomotor-cardiac coupling in trotting dogs. *The American Journal of Physiology* **273**, R1352-R1360.

Sullivan, M., Atwood, J.E., Myers, J., Feuer, J., Hall, P., Kellerman, B., Forbes, S. and Froelicher, V. (1989) Increased exercise capacity after digoxin administration in patients with heart failure. *Journal of the American College of Cardiology* **13**, 1138-1143.

Vella, C.A., Ontiveros, D. and Zubia, R.Y. (2011) Cardiac function and arteriovenous oxygen difference during exercise in obese adults. *European Journal of Applied Physiology* **111**, 915-923.

Wasserman, K., Hansen, J., Sue, D., Casaburi, R. and Whipp, B. (1999) *Principles of Exercise Testing and Interpretation*. 4th edition. Baltimore: Lippincott Williams & Wilkins. 2-129.

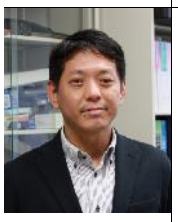
Whipp, B.J., Higgenbotham, M.B. and Cobb, F.C. (1996) Estimating exercise stroke volume from asymptotic oxygen pulse in humans. *Journal of Applied Physiology* **81**, 2674-2679.

Key points

- Twelve healthy men walked at a frequency of their heart rate (CLS protocol) and at a self-selected cadence (free protocol).
- Walking at the frequency of heart rate would induce the CLS by entrainment.
- Oxygen pulse was significantly higher in subjects in the CLS protocol compared to those in the free protocol.
- The occurrence of CLS enhances oxygen pulse by increasing the strength of CLS during walking.

AUTHORS BIOGRAPHY

Shinta TAKEUCHI
Employment
Hamamatsu University School of Medicine, University Hospital, Department of Rehabilitation, 1-20-1 Handayama, Higashi-ku, Hamamatsu, Shizuoka 431-3192, Japan
Degree
PhD
Research interests
Dynamics of biological rhythms during exercise
E-mail: take.shin1110@gmail.com



Yusuke NISHIDA
Employment
Rehabilitation Sciences, Seirei Christopher University, 3453 Mikatahara-cho, Kita-ku, Hamamatsu, Shizuoka 433-8558, Japan
Degree
PhD
Research interests
Autonomic nervous system
E-mail: yuusuke-n@seirei.ac.jp

Takashi MIZUSHIMA
Employment
Hamamatsu University School of Medicine, University Hospital, Department of Rehabilitation, 1-20-1 Handayama, Higashi-ku, Hamamatsu, Shizuoka 431-3192, Japan
Degree
MD
Research interests
Autonomic nervous system/Muscle sympathetic nerve activity
E-mail: mizusima@hama-med.ac.jp

✉ **Shinta Takeuchi**
Hamamatsu University School of Medicine, University Hospital, Department of Rehabilitation, 1-20-1 Handayama, Higashi-ku, Hamamatsu, Shizuoka 431-3192, Japan