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Evidence of an association between cardiac-locomotor synchronization and lower leg muscle blood perfusion during walking

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Abstract. [Purpose] The purpose of this study was to investigate whether the occurrence of cardiac-locomotor synchronization (CLS) improves lower leg muscle blood perfusion during walking. [Subjects and Methods] Eleven healthy men were studied while performing two treadmill protocols. The CLS protocol involved subjects walking at the 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 identical in the two protocols. Electrocardiographic signals for HR, foot switch signals for step rate and near-infrared spectroscopy (NIRS) signals for total haemoglobin (total Hb) in the lower leg muscles were measured continuously for 10 min after HR reached a steady state. [Results] The mean HR and mean step rate did not differ between the CLS and free protocols. However, total Hb was significantly higher in the CLS protocol than in the free protocol. The rate of increase in total Hb positively correlated with the strength of CLS. [Conclusion] These results suggest that the occurrence of CLS enhances lower leg muscle blood perfusion by increasing the strength of CLS during walking.
Key words: Walking, Heart rate, Phase synchronization

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INTRODUCTION

Continuous blood supply to active muscles is necessary to maintain exercise. In patients with cardiovascular diseases, exercise capacity is often limited due to depression of cardiac and arterial function. It has been suggested that synchronization between the heart beat and locomotor rhythm [cardiac-locomotor synchronization (CLS)] can optimise blood flow to muscles and minimise cardiac load[1, 2)]. The mechanism of this phenomenon is speculated to be peak intra-arterial pressure due to cardiac contraction occurring at the lowest phase of the intramuscular pressure cycle. Niizeki reported evidence for physiological CLS using computer-assisted bilateral thigh-cuff occlusion and suggested that CLS may be associated with the improved perfusion of exercising muscles[2)]. If CLS has the physiological significances described above, CLS has the potential to improve the exercise capacity of patients with cardiovascular diseases and thus may be useful in rehabilitation programs. However, the physiological significance of CLS for muscle blood perfusion during walking, running and cycling, which are usually performed in physical therapy, has not yet been clarified in healthy subjects. Therefore, we examined whether CLS has physiological significance for lower leg muscle blood perfusion during walking to obtain evidence of physiological CLS in healthy subjects.

SUBJECTS AND METHODS

Eleven healthy men (mean ± SD, height: 167.8 ± 4.5 cm, weight: 56.1 ± 5.0 kg, age: 21.3 ± 2.2 years) were included in this study after obtaining their informed consent. This study was approved by the Ethics Committee of Seirei Christopher University (approval number: 09008). Physical activity and alcohol and caffeinated beverage consumption were prohibited for 24 h before testing. Drinking and eating, except water, were also prohibited for 3 h before testing.

We determined each subject's treadmill load (treadmill speed and grade) at which their heart rate (HR) was maintained at approximately 120 beats/min (bpm). The target heart rate was derived from the 50–70% of estimated maximal heart rate, which is the 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), with gradually increasing treadmill speed within the range in 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

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achieved. Subjects walked at the determined treadmill speed and grade for at least 5 min to confirm appropriate load.

Subjects then rested for at least 15 min during which they were instrumented for data collection. Electrodes for electrocardiography (ECG), a foot switch sensor and a near-infrared spectroscopy (NIRS) probe were placed on the chest, right heel and posterior surface of the lower left leg, respectively. Thereafter, subjects were instructed to perform two treadmill protocols in a random order. In one, subjects walked at the frequency of their HR to induce cardiac-locomotor synchronization (CLS protocol). In the other, subjects walked at their preferred pace (free protocol). Both protocols were performed at the individual's predetermined treadmill load for 20 min. The first 10 min was the warm-up period, and it was followed by 10 min of measurement. As the treadmill load was fixed for each subject, the effort was identical in both protocols. Subjects rested in a sitting position for at least 15 min between protocols.

To achieve CLS in the CLS protocol, subjects walked at their predetermined load for 5 min and then for 5 min with a buzzer signal generated by an ECG monitor (Bedside monitor BSM-2400 series Life Scope 1, Nihon Kohden Corp., Tokyo, Japan). The buzzer sounded with each R wave to indicate HR. After their HR reached a steady state, they walked in synchrony with the buzzer signal for 10 min, and data was collected during this period. In the free protocol, subjects walked at their predetermined load for 10 min and then at their preferred pace for 10 min and data were collected during the latter 10-min walking period. Thus, identical treadmill loads and exercise times were established for both protocols.

The R-R interval (RRI) was measured continuously by surface ECG using standard bipolar leads (CM5). The ECG signal was amplified and band-pass filtered between 10–300 Hz to distinguish R waves of the QRS complex and to suppress movement artifacts. The ECG signal was digitised at s 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 measured by a foot switch sensor (Inline Foot Contact Sensor, Noraxon) on the right heel. The foot switch signal was collected at a sampling frequency of 1.5 kHz using a personal computer-based system (MyoResearch XP, Noraxon). As ECG and foot switch signals were recorded using separate computers, ECG and HCI recordings began at same time. In addition, a near infrared spectrophotometer (Omega Monitor; BOM-L1 TRW, Omega Wave, Tokyo, Japan) was used to monitor tissue oxygen saturation. The wavelengths measured were 780, 810 and 830 nm. Using these three wavelengths, it is possible to differentiate between oxygenated and deoxygenated haemoglobin. The sum of oxygenated and deoxygenated haemoglobin reflects the total amount of haemoglobin (total Hb), which can be interpreted as blood volume in the underlying tissue[3]. The NIRS signal is generally used with artery or venous occlusion to examine tissue blood flow and tissue metabolism[4, 5]. It was not possible to compress the subjects' lower extremities, because the focus of this study was muscle blood perfusion when CLS occurred during walking. Therefore, the index of muscle blood perfusion during walking was defined as total Hb only. Additionally, a free protocol was used to obtain reference data. A probe with a dedicated light-occluding holder was attached to the posterior surface of the lower left leg section with the greatest diameter with surgical tape and an elastic bandage. NIRS signals were stored on a personal computer.

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

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

where r and h are integers.

The synchronization index, λ, was calculated to quantify the strength of phase locking between the heartbeat and 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. λ was calculated from 60-point windows (approximately 30 s epochs) with a sliding window of 10 points. Mean λ was calculated as the average of the entire measurement period of each protocol. The fractional points were rounded down when points of relative phases were insufficient at the end of calculations. λ was restricted to $0 \leq \lambda \leq 1$, and a higher value indicates stronger phase locking between the two rhythms.

A surrogate data technique was also used to determine the probability of entrainment between the cardiac and locomotor rhythms[6]. The surrogate data were generated by randomly shuffling the original order of raw HCI data, while successive RRIs remained the same to create a new phase relationship between the two rhythms. The phase relationships between the heartbeat and locomotor activity rhythm were destroyed because of the random order of HCI. If two rhythms had an exact phase relationship, a relative phase similar to the original relative phase would occur in the surrogate data. The average λ value of original data was compared with that of surrogate data calculated from an identical observation window.

Mean HR, mean step rate (SR) and total Hb in the lower left leg muscles were calculated over the final 10 min of each protocol to investigate the CLS physiological response. HR and SR were calculated using RRI data and HCI data, respectively.

Values are shown as mean ± standard deviations. In this study, CLS occurrence was defined as Δλ exceeding 0.3, where Δλ is the difference in λ between the CLS and free

protocols ($\lambda_{CLS} - \lambda_{free}$), because λ values show substantial individual variability even during CLS induction[7]. In subjects whose Δλ exceeded 0.3, λ values were compared between the two protocols using the paired t-test to determine whether phase synchronization occurred during the CLS protocol. In addition, the λ values of the original and surrogate data of both protocols were compared using the paired t-test to determine whether phase synchronization occurred by entrainment. For subjects whose Δλ exceeded 0.3, mean HR, mean SR and total Hb were compared between the two protocols using the paired t-test to examine the effect of CLS on muscle blood perfusion during walking. Furthermore, for all subjects, the relationship between Δλ and Δtotal Hb (%), calculated as the ratio between total Hb in the CLS and free protocol, using Pearson's product-moment correlation coefficients was investigated. All statistical analyses were performed using SPSS version 19 for Windows software (SPSS Japan, Inc., Tokyo, Japan). A value of $p < 0.05$ was considered statistically significant.

RESULTS

In 9 of 11 subjects, the difference in the synchronization index, λ, between the CLS and free protocol (Δλ) exceeded 0.3, indicating the occurrence of CLS during the CLS protocol in the majority of subjects. In subjects whose Δλ exceeded 0.3, the mean λ value was also significantly greater in the CLS protocol than in the free protocol (0.54 ± 0.16 vs. 0.06 ± 0.06, N = 9, $p < 0.05$) and that of the surrogate data (0.54 ± 0.16 vs. 0.24 ± 0.08, N = 9, $p < 0.05$), indicating that phase synchronization was the result of heartbeat entrainment by locomotor activity. In contrast, the mean λ value of the free protocol did not differ from that of the surrogate data (0.06 ± 0.06 vs. 0.05 ± 0.05, N = 9, not significant), indicating that phase synchronization did not occur in the free protocol.

In subjects whose Δλ exceeded 0.3, mean HR and mean SR did not differ significantly between the two protocols (mean HR: 122 ± 6.5 vs. 120 ± 7.1 beat/min, mean SR: 122 ± 6.3 vs. 124 ± 7.9 step/min, N = 9, not significant). However, despite the identical treadmill load of the two protocols, total Hb during the CLS protocol was significantly higher than that during the free protocol (17.8 ± 2.6 vs. 17.5 ± 2.7 10^4 pieces/mm^3, N = 9, $p < 0.05$). For all subjects, correlation analysis revealed a significant relationship between Δλ (range, 0.16–0.65) and Δtotal Hb (range, 98–104%) ($R = 0.64$, N = 11, $p < 0.05$).

DISCUSSION

The main finding of the present study was that total Hb in the lower leg muscles increased with the λ value during walking. Furthermore, the λ value of the CLS protocol was significantly greater than that of both the surrogate data and the free protocol, indicating that the difference in the physiological data between the two protocols possibly shows a physiological response when CLS occurs. The increased lower leg muscle blood perfusion during walking suggests that this entrainment can enhance exercise efficiency.

Total Hb increased significantly during the CLS protocol compared with that during the free protocol, despite the identical treadmill load. In addition, a positive correlation was observed between Δtotal Hb and Δλ, strongly suggesting a causal relationship between the increase in total Hb and CLS occurrence. A possible explanation for this is the occurrence of an optimal phase relationship between arterial and intramuscular pressures, leading to improved muscle blood perfusion. During locomotion, muscle contraction induces an elevation in intramuscular pressure and compresses the vascular bed, leading to cessation of perfusion[8]. Niizeki reported evidence of a physiological CLS using computer-assisted bilateral thigh-cuff occlusion to simulate intramuscular pressure changes during bipedal locomotion[2]. Alternating cuff occlusion at HR resulted in phase synchronization, and individual heart beats were unlikely to overlap with elevated cuff pressure. In addition, Kimura et al. suggested that CLS with an appropriate phase difference attenuates peripheral vascular resistance and systolic blood pressure while increasing stroke volume[9]. It is possible that there is a specific phase difference between cardiac systole and muscle contraction that confers peak leg arterial pressure during the lowest muscle capillary resistance. Thus, CLS may enhance the blood supply to active muscles.

Three limitations of the present study should be noted. First, the effect of respiratory rhythm on the relationship between cardiac and locomotor rhythms was not assessed. Respiration could indirectly influence the occurrence of CLS as respiratory sinus arrhythmia modulates the heartbeat through neural effects[10], and ventilation modulates venous return through movement of the diaphragm[11]. Second, changes in total Hb on the time scale of individual CLS events could not be assessed. As a result, the beat-by-beat CLS physiological response during exercise was unclear. Third, our sample only consisted of healthy young males. Additional studies are required to assess this relationship in other populations, such as patients with cardiovascular diseases who may benefit from CLS to improve the capacity for therapeutic exercise.

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