Synchronizing Gait with Cardiac Cycle Phase Alters Heart Rate Response during Running

KEREN CONSTANTINI¹, ABIGAIL S. L. STICKFORD², JEFFERY L. BLEICH³, PAUL D. MANNHEIMER³, BENJAMIN D. LEVINE⁴, and ROBERT F. CHAPMAN¹

¹Department of Kinesiology, Indiana University, Bloomington, IN; ²Appalachian State University, Boone, NC; ³Pulson, Inc, Palo Alto, CA; and ⁴Institute for Exercise and Environmental Medicine, Presbyterian Hospital of Dallas, University of Texas Southwestern Medical Center, Dallas, TX

ABSTRACT

CONSTANTINI, K., A. S. L. STICKFORD, J. L. BLEICH, P. D. MANNHEIMER, B. D. LEVINE, and R. F. CHAPMAN. Synchronizing Gait with Cardiac Cycle Phase Alters Heart Rate Response during Running. *Med. Sci. Sports Exerc.*, Vol. 50, No. 5, pp. 1046–1053, 2018. Timing foot strike to occur in synchrony with cardiac diastole may reduce left ventricular afterload and promote coronary and skeletal muscle perfusion. **Purpose**: This study aimed to assess heart rate (HR) and metabolic responses to running when foot strikes are timed to occur exclusively during 1) the systolic phase of the cardiac cycle or 2) the diastolic phase. **Methods**: Ten elite male distance runners performed a testing session on a treadmill at 4.72 m·s⁻¹ while matching their steps to an auditory tone and wearing a chest strap that transmitted accelerometer and ECG signals. Testing comprised eight prompted 3-min stages, where a real-time adaptive auditory tone guided subjects to step with each ECG R-wave (systolic stepping) or alternatively, at 45% of each R-R interval (diastolic stepping), followed by a 3-min unprompted control stage. Metabolic variables were measured continuously. **Results**: HR (P < 0.001) and minute ventilation (P < 0.001) were significantly lower during diastolic stepping compared with systolic stepping, whereas O₂ pulse (P < 0.001) was correspondingly significantly higher during diastolic stepping. **Conclusion**: Synchronizing foot strikes when running to the diastolic portion of the cardiac cycle results in a significantly reduced HR and minute ventilation compared with stepping during systole. This cardiac and ventilatory response to diastolic stepping may be beneficial to distance running performance. **Key Words:** CARDIAC–LOCOMOTOR COUPLING, DISTANCE RUNNING, GAIT, ATHLETES, COUNTERPULSATION

During dynamic, large muscle group exercise in humans, blood flow is produced by two opposing pumps. The heart provides the pressure head for blood flow to skeletal muscle, and contracting skeletal muscle pumps blood back to the heart. It has been proposed that synergy between these two pumps could provide cardiometabolic efficiencies that are beneficial for endurance exercise performance, particularly when cardiac and skeletal muscle contraction rates are equal (1,2). In fact, during rhythmic locomotion such as running, heart rate (HR), and step rate (SR) at steady state, submaximal workloads often naturally synchronize such that

Accepted for publication December 2017.

0195-9131/18/5005-1046/0

MEDICINE & SCIENCE IN SPORTS & EXERCISE_ ${\ensuremath{\mathbb R}}$

Copyright © 2017 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the American College of Sports Medicine. This is an openaccess article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

DOI: 10.1249/MSS.000000000001515

there is a constant ratio between the two rates (2-8), with the ratio in most competitive distance runners approaching one (i.e., a 1:1 correspondence between the rates). This phenomenon is termed cardiac–locomotor coupling and has been shown to exist mainly during running and to a smaller extent during walking and cycling (4,5,7). If cardiac and locomotor phase timing are optimally coordinated, it has been proposed that this coupling has the potential to improve hemodynamic efficiency and cardiovascular function during dynamic, rhythmic exercise and, therefore, be advantageous for endurance performance (2–4,6,9–11).

During running, arterial pressure is influenced by cardiac ejection as well as vertical movements of the body generating positive and negative inertial pressure waves in the aorta (12). In addition, several studies have shown fluctuations in skeletal intramuscular pressure within a gait cycle, as well as an increase in peak anterior tibial pressures as speed increases (4,13,14). The observed pattern of fluctuations is such that intramuscular pressure and blood inflow are intimately related to skeletal muscular force production. Thus, skeletal muscle contraction or relaxation can hinder or promote muscle blood flow, respectively (11,15). Physiologically, when the frequencies of HR and SR are close, but not equal, the relative timing of the heart and musculoskeletal pumps causes alternating periods of high and low pulse

APPLIED SCIENCES

Address for correspondence: Robert F. Chapman, Ph.D., 1025 E. 7th St, PH 112, Bloomington, IN 47405; E-mail: rfchapma@indiana.edu. Submitted for publication September 2017.

TABLE 1. Subject characteristics.

	Age (yr)	Height (m)	Mass (kg)	Primary Event	Personal Best Time (min:s)
1	25	1.79	64.2	Mile	3:58.5
2	23	1.80	68.0	1500 m	3:50.9
3	24	1.81	63.1	3000 m	7:51.6
4	23	1.66	64.3	Mile	4:05.7
5	23	1.79	59.4	Mile	3:58.9
6	25	1.79	68.3	Mile	3:58.5
7	25	1.69	57.9	1500 m	3:57.5
8	26	1.85	66.4	1500 m	3:48.2
9	19	1.84	65.7	3000 m	8:03.9
10	20	1.78	64.4	3000 m	8:08.1
Mean SD	23.3 2.3	1.78 0.05	64.2 3.3		

pressure that are observed as a so-called "beat phenomenon" in the runner's arterial pulse pressure (16). Specifically, when muscle relaxation is timed to occur during ventricular contraction and the subsequent peak in systolic pressure, blood flow into the exercising skeletal muscle is optimized (15) and cardiac afterload is reduced (4).

Previous studies have suggested that timing foot strikes and subsequent skeletal muscle contraction to occur consistently with cardiac diastole (i.e., between cardiac contractions) may reduce cardiac afterload, increase preload, and promote coronary and skeletal muscle perfusion (1,2,17,18). For example, O'Rourke (1) demonstrated that when lower body and cardiac pressure waves are 180° out of phase, systolic left ventricular pressure is reduced, possibly diminishing myocardial O2 demand, whereas diastolic pressure is augmented, likely enhancing myocardial blood flow and ventricular ejection. In addition, the HR response to running has been shown to vary with changes to the timing of foot strike and skeletal muscle contraction relative to the timing of the cardiac cycle (19), with lower HR when foot strike is timed to occur during diastole and a higher HR with foot strike during systole. However, these HR changes have only been shown to be instantaneous, leaving it unclear whether they are maintained over time or whether they are associated with any metabolic effects. If so, the effect could be positive for distance running performance; for example, in elite endurance athletes where very small changes in physiological outcomes can have quite large performance effects.

The aim of this study was to explore sustained HR changes, metabolic effects, and ventilatory responses associated with running when foot strikes are timed to occur consistently during either the systolic phase of the cardiac cycle or the diastolic phase in elite distance runners. If timing foot strike (i.e., skeletal muscle contraction and peak intramuscular pressure) to occur in synchrony with cardiac diastole reduces cardiac afterload and promotes coronary and skeletal muscle perfusion (1,2,17,18), such synchrony should produce a reduced HR response at a constant running velocity compared with stepping during systole-perhaps secondary to an increased stroke volume. Therefore, we hypothesized that 1) HR would be lower during diastolic relative to systolic stepping and 2) O_2 consumption $(\dot{V}O_2)$ would also be lower during diastolic, compared with systolic stepping, because of the presumed lower systolic blood pressure, cardiac afterload, and HR.

METHODS

Design and subjects. Ten elite male distance runners participated in this study. The subjects were collegiate and professional postcollegiate athletes and included three subjects who had run under 4 min in the mile. Subject characteristics, including personal best times for each runner in his main event, are presented in Table 1. Each subject visited the Human Performance Laboratory at Indiana University for a single testing session on a motor-driven treadmill (Model 18-72; Quinton, Bothell, WA). Subjects were instructed to refrain from caffeine and alcohol consumption for 24 h before testing. All subjects gave written informed consent to a protocol approved by the Institutional Review Board of Indiana University.

Study protocol. Figure 1 outlines the study protocol. Following a 5- to 10-min warm-up period on the treadmill at a self-selected pace, subjects were familiarized with the testing protocol and practiced matching their foot–ground contacts to an auditory tone while running. After a brief rest, this practice session was followed by an experimental session, during which the subjects ran on the treadmill at a constant speed of $4.72 \text{ m} \text{ s}^{-1}$ (5:40 min·mile⁻¹ pace). This pace was selected as it was slower than the subjects'

Study Protocol									
Condition	SS	DS	SS	DS	SS	DS	SS	DS	control
Pair #	1	L		2		3	4	1	
% R-R Interval	100	45	100	45	100	45	100	45	silent
Time (min)	3	3	3	3	3	3	3	3	3

FIGURE 1—The testing session included four pairs of prompted stepping phases (pair = 2×3 min). The signal to step was given either at the subject's R wave, i.e., 100% of the subject's RRI (systolic stepping [SS]) or 45% of R-R (diastolic stepping [DS]). The order of diastolic and systolic stepping within each pair was randomized and double blinded.

maximal steady-state or lactate threshold pace, based on their workout history, so that they could hold this pace comfortably for as long as 30 min with no cardiac drift. Treadmill grade was set between 0% and 2% before or during the initial unpaced warm-up period, as required to match each subject's HR more closely to their baseline SR, after which the grade was held constant throughout the study session.

The experimental session began with a short (<3 min) period of unpaced free stepping, immediately followed by 27 min of continuous running, divided into 9 \times 3 min stages. Throughout the first eight stages, subjects were asked to match their steps to an auditory tone that repeated at their real-time measured HR, guiding them to 3 min of either constant systolic or constant diastolic stepping. Systolic stepping was defined as step timing to occur at the subject's R-wave, and diastolic stepping was defined as step timing at 45% of the R-R interval (RRI). Each user experienced four identical sets of two paired stages-a systolic stepping stage followed by a diastolic stage or a diastolic stage followed by a systolic stepping stage. The eight-guided stages were followed by a 3-min control stage of unpaced free stepping (no beep tone). The order of the alternating diastolic and systolic stages was randomized among subjects in a balanced design but was kept constant within each individual (i.e., five of the subjects began with diastolic stepping and five with systolic stepping). All subjects and investigators were blinded to treatment conditions, except for a single investigator who monitored and ran the pacing software.

Gait cycle timing guidance. All subjects were fitted with a chest strap that generated both accelerometer and ECG signals (Zephyr BioHarness[™] 3; Medtronic/Zephyr Performance Systems, Annapolis, MD). These signals were logged internally into memory within the BioHarness, as well as transmitted wirelessly to a tablet computer (ASUS Nexus 7, Taipei, Taiwan) running real-time proprietary software (Pulson, Inc., Palo Alto, CA).

The software processed incoming raw signals to identify the timing relationship between the subject's ECG R-waves (signaling onset of systole) and the point when the accelerometer signal in the vertical plane crossed 1g in a positive direction during each gait cycle (signaling foot strike and the approximate timing of maximal skeletal muscle contraction). Step and R-wave time stamps were used to compute their relative phase (%RRI):

$$\% \text{RRI} = 100 (t_{\text{step}} - t_{\text{R-wave1}}) / (t_{\text{R-wave2}} - t_{\text{R-wave1}}),$$

where $t_{R-wave1}$ and $t_{R-wave2}$ refer to the times of two consecutive R-waves, and t_{step} refers to the time of the step that occurred between them. HR was computed from the RRI in the conventional manner. The software further generated a beep tone to audibly guide the user's step timing, which repeated nominally at the subject's HR. To lead the subject to the targeted diastolic or systolic step timing as defined by the protocol, the software made small adjustments to the beep prompt period continuously, based on the difference between the sensed step timing and the cardiac cycle timing

target during that stage. The tone prompt was played on a speaker loud enough to be easily heard by the subject running on the treadmill. Provided subjects maintained their general running rhythm with the metronome, the software adjustments would align their measured %RRI phase to the target value. Data from the software program (R-wave and step timing) were logged for later analysis.

Metabolic parameters. Ventilatory and metabolic variables were continuously measured and monitored during exercise using a computer-interfaced, open-circuit, indirect calorimetry system. A data acquisition control system (DASYLab 10.0, National Instruments, Norton, MA) sampling at 50 Hz was used to sample all dependent variables, with those values averaged over a 15-s period. Minute ventilation ($\dot{V}_{\rm E}$) was determined using a pneumotachograph (Series 3813/4813; Hans Rudolph, Shawnee, KS) on the inspired line. Subjects wore a facemask and breathed through a low-resistance, two-way valve (#2700, Hans Rudolph). A 5-L mixing chamber was used for the collection of expired gases. Fractional concentrations of O2 and CO2 were determined from dried expired gas, sampled at a rate of $300 \text{ mL} \cdot \text{min}^{-1}$, using separate O₂ and CO₂ analyzers (Ametek; Thermox Instruments, Pittsburgh, PA). Analyzers were calibrated before each test using commercially available gas mixtures within a physiological range. The dependent variables of $\dot{V}_{\rm E}$, $\dot{V}O_2$ and CO_2 production ($\dot{V}CO_2$) were averaged over 15-s epochs during exercise and converted to minute values, with $\dot{V}_{\rm E}$ corrected to BTPS and VO2 and VCO2 corrected to STPD. Oxygen pulse (O₂-P), an index of stroke volume, was estimated as five times the quotient of $\dot{V}O_2$ and HR (20).

Data processing. For all dependent variables, averages were taken from the last minute of exercise at each stage, where subjects were compliant with stepping criteria. Data were considered to be valid if mean within-subject diastolic stepping occurred at $45\% \pm 15\%$ RRI and mean within-subject systolic stepping occurred at $100\% \pm 15\%$ RRI (i.e., approximately concurrent with the R-wave). These values and tolerances were chosen based on data collected previously by authors JLB and PDM (unpublished) that evaluated HR response to stepping at a variety of targets in the RRI, wherein the %RRI at minimum HR (optimal timing) and the %RRI at maximum HR (least advantageous timing) were identified. The early diastolic target timing of 45% of the RRI is consistent with the timing of mechanical counterpulsation technologies used regularly in the clinical setting, including intra-aortic balloon counterpulsation, left ventricular assist device counterpulsation, and external counterpulsation (21-23). Optimal timing of the musculoskeletal pump during the gait cycle, similar to the preferred timing of clinical counterpulsation therapies, is immediately after aortic valve closure during the heart's pump cycle, when intra-aortic blood pressure first exceeds intra ventricular pressure (3).

Statistical analysis. Data were analyzed using R (24). A Shapiro–Wilk test was used, and all data were determined to be normally distributed; therefore, parametric tests were

used in all further analyses. Values presented are mean \pm SD unless otherwise stated. Differences in all dependent variables between diastolic stepping and systolic stepping were assessed using paired *t*-tests. Pearson correlations were calculated to evaluate relationships between diastolic and systolic stepping for selected dependent variables. For all tests, statistical significance was set at $P \leq 0.05$.

RESULTS

The 10 subjects each accurately timed their steps with the auditory tones throughout all of the timing prompted stages of the protocol (diastolic stepping, $45.1\% \pm 1.2\%$ RRI; systolic stepping, $100.2\% \pm 2.2\%$ RRI). Nine subjects completed four diastolic–systolic stepping pairs (a total of eight toned phases), and one subject completed two pairs, giving a total of 38 valid

diastolic–systolic stepping pairs for comparison. The HR and SR response of every step for the entire protocol of a typical subject can be seen in Figure 2A.

HR, SR, step length, and metabolic data are presented in Table 2. Group mean HR was significantly lower during diastolic compared with systolic stepping (P < 0.001; Fig. 3A). Because subjects were highly compliant with adhering to the auditory tone, SR data were effectively identical to HR in the prompted stages. To maintain constant running speed on the treadmill in both conditions, subjects had to adjust step length to match SR to any change in HR. As a result of the lower HR during diastolic stepping, step length was significantly greater during diastolic compared with systolic stepping (P < 0.001; Table 2). In addition, strong correlations were observed between diastolic and systolic stepping for HR, SR, and step length (P < 0.05, r = 0.95 for all comparisons; Fig. 4A–C).



FIGURE 2—A. Values for step timing as a percentage of the R-R interval (%RRI; *top panel*) and HR (*bottom panel—darker filled circles*) and step rate (SR; *bottom panel—lighter open circles*) recorded throughout a study session with a single subject. Each point represents an individual step. Horizontal bars represent mean values for HR at the end of each 3-min phase. SS, systolic stepping phase; DS, diastolic stepping phase. B. Individual step data as a percentage of the RRI (%RRI) for two subjects. Note that after the final paced phase, subject 6 continued stepping during diastole, although the final phase was silent, with no auditory tone to guide stepping. Similarly, subject 10 also stepped during diastole during the final, silent phase, despite no tone and being guided to systolic stepping in the phase prior.

TABLE 2. Treadmill running at 4.72 m·s⁻¹ (5:40 mile·min⁻¹).

	Diastolic Stepping	Systolic Stepping
%RRI	45.1 ± 1.2	$100.2 \pm 2.2^{***}$
HR (bpm)	172.4 ± 6.3	$175.0 \pm 6.7^{***}$
Step rate (steps per minute)	172.4 ± 6.3	$175.0 \pm 6.7^{***}$
Step length (m per step)	1.65 ± 0.06	$1.62\pm0.06^{***}$
\dot{VO}_2 (mL·kg ⁻¹ ·min ⁻¹)	58.1 ± 2.8	$57.7 \pm 2.8^{\star}$
$\dot{V}_{\rm E}$ (L·min ⁻¹)	98.7 ± 12.3	$100.9 \pm 13.3**$
RER	0.93 ± 0.03	$0.94\pm0.03^{**}$
O ₂ -P (mL per beat)	$108.4~\pm~8.5$	$106.2\pm8.6^{***}$

Values are presented as mean \pm SD. VO₂, O₂ uptake; \dot{V}_{E} , expired minute ventilation; RER, respiratory exchange ratio; O₂-P, O₂ pulse. Significantly different from diastolic stepping: *P<0.05, **P<0.01, ***P<0.001.

 $\dot{V}_{\rm E}$ and RER were slightly but significantly lower (P < 0.001and P < 0.01, respectively), and $\dot{V}O_2$ was marginally yet significantly higher (P < 0.05) during diastolic compared with systolic stepping (Table 2, Fig. 3B-C). This directional outcome was observed in 73%, 64%, and 67% of pairs for $\dot{V}_{\rm E}$, RER, and VO₂, respectively (Fig. 4D-F). The mean change in \dot{VO}_2 of 0.4 mL·kg⁻¹·min⁻¹ or 0.7%, although statistically significant, is substantially less than the commonly reported typical error of the measure for steady-state, submaximal oxygen uptake (ranging from 2.3% to 5.4% [25,26]). Significant correlations existed between diastolic and systolic stepping for $\dot{V}_{\rm E}$, RER, and $\dot{\rm VO}_2$ (*P* < 0.001, *r* = 0.96, 0.89, and 0.94, respectively). O₂-P, an estimate of stroke volume, was significantly higher (P < 0.0001) during diastolic compared with systolic stepping, and there was a significant correlation for O_2 -P between the stepping conditions (P < 0.001, r = 0.98).

DISCUSSION

Primary findings. The primary finding of this study was that synchronizing foot strike with the diastolic phase of the cardiac cycle, as opposed to the systolic phase, significantly reduces HR during submaximal running and has specific metabolic effects in elite distance runners. This outcome held true for the group mean data, and the HR response was also apparent in nearly all diastolic–systolic stepping pairs compared (87%, or 34/38 of pairs). Our findings suggest that diastolic step timing provides a cardiac advantage that may be beneficial to elite distance running performance when compared with running with systolic step timing.

Cardiovascular response of synchronizing foot strike and cardiac cycle. It is well documented that coupling of cardiac and locomotor rhythms exists during running in humans (2,4,5,7,8), and this entrainment has been suggested to be favorable for physiological functions, such as augmented stroke volume during cardiac–locomotor synchronization (1,18). For example, data from Nomura et al. (19) suggest that cardiac contraction/ejection naturally varies to match muscle relaxation, resulting in a lengthening of the RRI. However, our data are novel for several reasons. Besides the elite nature of the cohort tested, this study appears to be the first to test the HR response specifically to guided stepping during diastole and systole for prolonged periods of time—not just an examination of the HR response to a periodic oscillation of stride rate (19) or a theoretical model (1).

The difference in HR response we observed between diastolic and systolic stepping could be explained by both central and peripheral mechanisms. Centrally, the synchronization of muscle contraction (foot strike phase) and cardiac relaxation/filling during diastolic stepping has been proposed to promote cardiac function by reducing afterload (reduced



FIGURE 3—HR (A), ventilation (B), and respiratory exchange ratio (C) as a function of stepping phase across all subjects. Values are presented as mean \pm SE. DS, diastolic stepping (*closed circles*); SS, systolic stepping (*open squares*). *Significant difference between conditions for all data, P < 0.001.



FIGURE 4—Relationship between systolic and diastolic stepping for HR (A), step rate (SR; B) and step length (SL; C) O_2 uptake ($\dot{V}O_2$; D), ventilation (\dot{V}_E ; E), and respiratory exchange ratio (RER; F) for individual pair comparisons. *Significant correlation, P < 0.05. Alike symbols represent an individual subject. Dashed line, line of identity; solid line, least squares regression.

systolic pressure from reduced backward wave augmentation) and improving coronary perfusion (increased diastolic pressure). In turn, this would manifest as a reduced HR response at a constant running velocity. Our results support this concept because there was a concurrent and significant decrease in HR and increase in O_2 -P as an estimation of stroke volume during diastolic step timing compared with systolic step timing.

Peripherally, several studies indicate that skeletal muscle blood flow is impaired during peak intramuscular pressure (2,6,15). Specifically, during muscle contraction, a complete absence of flow or even negative (i.e., retrograde) flow occurs as intramuscular pressure peaks (9,17). This likely explains the findings of Niizeki (10), who suggested that ventricular systole and the subsequent increase in systolic blood pressure result in enhanced blood flow to the thigh muscles only when intramuscular pressure is reduced, whereas elevated intramuscular pressure is associated with blunted blood flow. Although that study used bilateral dynamic thigh cuff

occlusion rather than an actual muscular contraction-relaxation cycle, their results demonstrate the importance of timing ventricular systole and peripheral relaxation on a beat-by-beat basis to maximize blood flow to the exercising muscles (10). During systolic stepping in our study, the foot strike phase of the gait cycle, corresponding to muscle contraction and peak intramuscular pressure, was manipulated to occur simultaneously with systole, when peak arterial pressure occurs. If this type of synchronization of forward and backward pressure waves increased systolic arterial pressure in the periphery (proximal to the exercising skeletal muscle) as well as cardiac afterload, we would expect a reduction in stroke volume (1,6-8), as suggested by lower O₂-P values during systolic stepping, compared with diastolic stepping. However, these suggested mechanisms would need to be confirmed by direct measure of arterial pressures during diastolic and systolic stepping during running.

Metabolic effects of synchronizing foot strike and cardiac cycle. It is important to note that the mean difference we observed in VO2 between systolic and diastolic conditions (0.4 mL·kg⁻¹·min⁻¹ or 0.7%) is far less than the reported typical error of the measure for submaximal \dot{VO}_2 , which ranges from 2.3% to as high as 5.4% (25,26). From a magnitude-based inference perspective, this would be seen as a "trivial" outcome (27) with no practical difference between conditions. We had hypothesized that VO₂ would be lower during diastolic stepping in response to lower myocardial energy requirements (i.e., decreased HR and afterload), and our failure to observe a reduction in $\dot{V}O_2$ may be a result of minor increases in the biomechanical cost of running during diastolic stepping. That is, the significant increase in step length required to match SR to HR may have offset a portion of potential reduction in cardiac and respiratory muscle metabolic cost. It has been demonstrated that VO2 increases when subjects are asked to voluntarily increase or decrease step frequency compared with preferred step frequency (28,29). Hunter and Smith (29) demonstrated a $1.7 \text{-mL·kg}^{-1} \text{min}^{-1}$ (3.7%) increase in VO2 when well-trained runners were asked to acutely increase stride frequency by 4% over their preferred stride frequency and a 1.9-mL·kg⁻¹·min⁻¹ (4.1%) increase in VO2 when decreasing stride frequency by 4% from preferred stride frequency. Applying their regression model results to our subjects predicts an outcome that closely matches our observed differences in diastolic and systolic stepping (a 0.4-mL·kg⁻¹·min⁻¹ difference in $\dot{V}O_2$ with a 1.7% difference in SR between conditions).

A secondary finding of this study was that $\dot{V}_{\rm E}$ was also marginally but significantly lower during diastolic stepping compared with systolic stepping (Figs. 3 and 4). To the best of our knowledge, this study is the first to assess metabolic changes other than $\dot{\rm VO}_2$ during cardiac–locomotor coupling. Specifically, $\dot{V}_{\rm E}$ was ~2.2 L·min⁻¹ (~2.4%) higher during systolic compared with diastolic stepping. One possible explanation for this finding could be related to respiratory– locomotor coupling: elite athletes have been shown to entrain stepping and respiratory rates (30), and therefore the reduced $\dot{V}_{\rm E}$ during diastolic stepping could be a related to the lower SR and a subsequent reduction in respiratory rate during this condition (rather than a reduced metabolic demand).

Implications for exercise performance. Our finding that HR and $\dot{V}_{\rm E}$ were significantly lower when foot strike and diastole were synchronized, although the subjects were running at the same pace in both conditions, may influence distance running performance. It is important to remember that in elite endurance athletes, such as the subjects employed in this study, even small changes in physiological parameters can have large influences on performance outcomes. For example, a reduction in HR when stepping during diastole for a given exercise task would allow a distance runner to run at a given pace but be further away from maximal HR as compared with systolic stepping. As the HR response to running is historically known to be linear at submaximal workloads (31) and using HR versus velocity data from our laboratory on a similarly elite cohort of professional distance runners (32), a 2.6-bpm change in HR at a submaximal workload is equivalent to a change in velocity of $0.09 \text{ m} \cdot \text{s}^{-1}$. For our elite cohort, running at the testing speed of 4.72 $\text{m}\cdot\text{s}^{-1}$ is slightly slower than their projected marathon pace (4.72 m s⁻¹ = 5:40 per mile or 2:28:27 marathon pace). A velocity change of $0.09 \text{ m} \cdot \text{s}^{-1}$ extrapolated over an entire marathon (42.2 km) corresponds to a 172-s difference in finishing time, a magnitude that has tremendous performance implications.

Finally, if diastolic stepping is truly advantageous for exercise performance, we wondered if there is any natural tendency for elite runners to step diastolically without prompting. We observed that 3 of the 10 subjects stepped accurately at the diastolic target timing ($45\% \pm 15\%$ RRI) during a substantial portion of their final, unprompted (silent) control period (e.g., see Fig. 2B). In one of those cases, the subject was guided to systolic step timing during the final prompted period but naturally reverted to stepping during diastole when the auditory prompt was removed. By comparison, none of the subjects stepped at a consistent systolic phase during the free stepping control stages. These anecdotal observations are also consistent with the findings of earlier authors, including Niizeki (10), which suggested that the heart automatically adjusts its timing, when HR = SR, to prevent ventricular systole from coinciding with maximal peripheral skeletal muscle contraction.

LIMITATIONS

We did not measure continuous arterial pressures, which may have been helpful in providing insight into the mechanisms behind the observed differences between diastolic and systolic stepping in this study. Measures such as skeletal muscle oxygenation, blood lactate concentration, cardiac output, and regional blood flow or skeletal muscle oxygenation (via near-infrared spectroscopy) could help identify whether the differences in HR and metabolic variables are due to central or peripheral mechanisms. Lastly, our subjects were all healthy young accomplished endurance athletes. The effects of synchronizing step timing with HR in patients with cardiovascular disease are unknown and deserving of further study.

CONCLUSION

In conclusion, HR during running is lower when synchronizing foot strike to occur during diastole compared with systole, presumably as a result of an increase in stroke volume and/or possibly enhanced coronary and skeletal muscle perfusion. Furthermore, such diastolic synchronization of the heart and step rates is associated with reduced

REFERENCES

- 1. O'Rourke M, Avolio A. Improved cardiovascular performance with optimal entrainment between heart rate and step rate during running in humans. *Coron Artery Dis.* 1992;3(9):863–9.
- O'Rourke M, Avolio A, Stelliou V, Young J, Gallagher D. The rhythm of running: can the heart join in? *Aust N Z J Med.* 1993; 23(6):708–10.
- Donville JE, Doherty TJ, Kirby RL, Gupta SK, Eastwood BJ, MacLeod DA. Effect of cardiac–locomotor coupling on the metabolic efficiency of pedalling. *Can J Appl Physiol.* 1993;18(4):379–91.
- Kirby RL, Nugent ST, Marlow RW, MacLeod DA, Marble AE. Coupling of cardiac and locomotor rhythms. *J Appl Physiol (1985)*. 1989;66(1):323–9.
- Niizeki K, Kawahara K, Miyamoto Y. Interaction among cardiac, respiratory, and locomotor rhythms during cardiolocomotor synchronization. J Appl Physiol (1985). 1993;75(4):1815–21.
- Nomura K, Takei Y, Yanagida Y. Analysing entrainment of cardiac and locomotor rhythms in humans using the surrogate data technique. *Eur J Appl Physiol*. 2001;84(5):373–8.
- Nomura K, Takei Y, Yanagida Y. Comparison of cardiolocomotor synchronization during running and cycling. *Eur J Appl Physiol.* 2003;89(3–4):221–9.
- Phillips B, Jin Y. Effect of adaptive paced cardiolocomotor synchronization during running: a preliminary study. J Sports Sci Med. 2013;12(3):381–7.
- Lutjemeier BJ, Miura A, Scheuermann BW, Koga S, Townsend DK, Barstow TJ. Muscle contraction-blood flow interactions during upright knee extension exercise in humans. *J Appl Physiol* (1985). 2005;98(4):1575–83.
- Niizeki K. Intramuscular pressure-induced inhibition of cardiac contraction: implications for cardiac–locomotor synchronization. *Am J Physiol Regul Integr Comp Physiol*. 2005;288(3):R645–50.
- 11. Walløe L, Wesche J. Time course and magnitude of blood flow changes in the human quadriceps muscles during and following rhythmic exercise. *J Physiol.* 1988;405(1):257–73.
- Nichols W, O'Rourke M, Vlachopoulos C. McDonald's Blood Flow in Arteries: Theoretical, Experimental and Clinical Principles. 6th ed. Boca Raton (FL): CRC Press; 2011. p. 768.
- Ballard RE, Watenpaugh DE, Breit GA, Murthy G, Holley DC, Hargens AR. Leg intramuscular pressures during locomotion in humans. *J Appl Physiol (1985)*. 1998;84(6):1976–81.
- McDermott A, Marble A, Yabsley R, Phillips MB. Monitoring dynamic anterior compartment pressures during exercise: a new technique using the STIC catheter. *Am J Sports Med.* 1982; 10(2):83–9.
- Rådegran G, Saltin B. Muscle blood flow at onset of dynamic exercise in humans. *Am J Physiol*. 1998;274(1):H314–22.
- Palatini P, Mos L, Mormino P, et al. Blood pressure changes during running in humans: the "beat" phenomenon. *J Appl Physiol* (1985). 1989;67(1):52–9.

ventilation. Taken together, the cardiac and ventilatory advantages observed with diastolic stepping may be beneficial to distance running performance.

This study was funded by a grant from Pulson, Inc.

Jeffrey L. Bleich and Paul D. Mannheimer both have an ownership interest in Pulson, Inc. Pulson developed and markets the proprietary software platform that guided the subjects to coordinate gait cycle timing to cardiac phase. No other conflicts of interest, financial or otherwise, are declared by the authors. The results of the present study do not constitute endorsement by the American College of Sports Medicine. The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.

- Râdegran G. Ultrasound Doppler estimates of femoral artery blood flow during dynamic knee extensor exercise in humans. *J Appl Physiol*. 1997;83(4):1383–8.
- Zhang D, Celler BG, Lovell NH. The effect of heartbeatsynchronised running on the cardiovascular system. In: *Proceedings* of the Second Joint EMBS/BMES Conference. Houston (TX): IEEE; 2002. pp. 1295–6.
- Nomura K, Takei Y, Yoshida M, Yanagida Y. Phase-dependent chronotropic response of the heart during running in humans. *Eur J Appl Physiol.* 2006;97(2):240–7.
- Whipp BJ, Higgenbotham MB, Cobb FC. Estimating exercise stroke volume from asymptotic oxygen pulse in humans. *J Appl Physiol (1985)*. 1996;81(6):2674–9.
- Werner D, Hui J, Kropp J, Daniel W. Pneumatische externe Gegenpulsation-Therapieoption bei Angina pectoris. Z Für Kardiologie. 1998;87(14):s193–8.
- Taguchi I, Ogawa K, Kanaya T, Matsuda R, Kuga H, Nakatsugawa M. Effects of enhanced external counterpulsation on hemodynamics and its mechanism. *Circ J.* 2004;68(11):1030–4.
- Capoccia M, Bowles C, Pepper J, Banner N, Simon A. Evidence of clinical efficacy of counterpulsation therapy methods. *Heart Fail Rev.* 2015;20(3):323–35.
- R Core Team. R: A Language and Environment for Statistical Computing [Internet]. Vienna (Austria): R Foundation for Statistical Computing; 2014. Available from: http://www.R-project.org/.
- 25. Lamberts RP, Swart J, Woolrich RW, Noakes TD, Lambert MI. Measurement error associated with performance testing in welltrained cyclists: application to the precision of monitoring changes in training status. *Int SportMed J.* 2009;10(1):33–44.
- Achten J, Jeukendrup AE. Maximal fat oxidation during exercise in trained men. *Int J Sports Med.* 2003;24(8):603–8.
- Hopkins WG, Batterham AM. Error rates, decisive outcomes and publication bias with several inferential methods. *Sports Med.* 2016;46(10):1563–73.
- Cavanagh PR, Williams KR. The effect of stride length variation on oxygen uptake during distance running. *Med Sci Sports Exerc*. 1981;14(1):30–5.
- Hunter I, Smith GA. Preferred and optimal stride frequency, stiffness and economy: changes with fatigue during a 1-h highintensity run. *Eur J Appl Physiol*. 2007;100(6):653–61.
- Bramble DM, Carrier DR. Running and breathing in mammals. Science. 1983;219(4582):251–6.
- Astrand PO, Ryhming I. A nomogram for calculation of aerobic capacity (physical fitness) from pulse rate during sub-maximal work. *J Appl Physiol.* 1954;7(2):218–21.
- Chapman RF, Stager JM, Tanner DA, Stray-Gundersen J, Levine BD. Impairment of 3000-m run time at altitude is influenced by arterial oxyhemoglobin saturation. *Med Sci Sports Exerc.* 2011; 43(9):1649–56.