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Fuel oxidation at the walk-to-run-transition in humans

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Abstract

Multiple factors (including anthropometric, kinetic, mechanical, kinematic, perceptual, and energetic factors) are likely to play a role in the walk-to-run transition in humans. The primary purpose of the present study was to consider an additional factor, the metabolic fuel source. Indirect calorimetry was used to measure fuel oxidation, and perception of effort was recorded as 10 overnight-fasted adults locomoted on a level treadmill at speeds progressing from 1.56 to 2.46 m s^{-1} in increments of 0.11 m s^{-1} and 10.0 minutes under 3 conditions: (1) unconstrained choice of gait, (2) walking at all speeds, and (3) running at all speeds. The preferred transition speed was 2.08 ± 0.03 m s^{-1}. Gait transition from walking to running increased oxygen consumption rate, decreased the perception of effort, and decreased the rate of carbohydrate oxidation. We propose that, in an evolutionary context, gait transition, guided by the perception of effort, can be viewed as a carbohydrate-sparing strategy.

1. Introduction

Quadrupeds can adopt multiple terrestrial gait patterns, whereas natural bipedal gait patterns in humans are limited to walking and running. A preferred speed to transition from one gait to another is commonly observed in most mammalian species, including humans. In humans, preferred transition speed (PTS) from walking to running occurs within the delimited range of 1.8 to 2.2 m s^{-1} [1,2].

Factors other than physical limitations trigger human gait transition because walking at higher speeds and running at lower speeds than the PTS are well tolerated. Previous investigations of gait transition have explored anthropometric [3,4], kinetic [1,5], mechanical [6], kinematic [4,7], perceptual [2,8], and energetic [1,7,9-11] factors.

Locomotion across the speed range relevant to the PTS is dependent upon energy derived from the combustion of fat and carbohydrate, 2 fuels stored at vastly different levels. Because of the profound evolutionary implications regarding the need to defend the extremely limited carbohydrate stores of the human body [12-15], the primary purpose of the present study was to consider the potential role of metabolic fuel selection in the walk-to-run transition in humans.

From preferred walking speed up to PTS and beyond, the energy cost of walking (in kilocalories per kilometer per kilogram) steadily rises, revealing the right upward leg of this familiar U-shaped curve. In contrast, the energy cost of running remains relatively constant across this range of speed [1]. Prilutsky and Gregor [2] showed that summed lower extremity electromyography (EMG) conformed to this same pattern. Thus, they proposed that the steadily rising neural input to muscle and energy consumption required to increase walking speed toward PTS might elicit the transition to running, where the slope of these changes would flatten.

At the PTS, gait transition from walking to running increases the rate of energy expenditure [1,7,10,16], despite the reasonable, and perhaps more intuitive, prediction that it should have the opposite effect [9,11,17,18]. Moreover, this elevated energy cost is curiously attended by decreased perception of effort [2,8,10] and greater neural input into muscle as assessed from the summed EMG of active muscle [2]. These published observations present an interesting paradox: the walk-to-run transition increases energy expenditure and the apparent neural input into muscle, whereas it decreases the perception of effort.

This study was approved by the Institutional Review Board at Arizona State University, where the work was performed.

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During human walking, perception of effort can be largely explained by the rate of carbohydrate oxidation [15]. In contrast, fat oxidation does not contribute to the explained variance in perception of effort. Thus, during walking at least, central nervous system (CNS) activation of muscle to an energy turnover rate low enough to be supported by fat combustion is not sensed as effort. In contrast, the recruitment of carbohydrate fuel, which is required to support higher intensities, appears to be sensitively monitored as effort. We [15] previously proposed a simple model based on the connectivity property of metabolic control analysis [19], which suggests these outcomes. The evolutionary advantage provided by such a control system is obvious: a physically fit and lean human stores enough fat to support more than 1000 km of walking, whereas stored carbohydrate would support less than 50 km [15].

The purpose of the present study was to assess fuel oxidation across a range of speeds from less than to higher than the PTS in humans. On the basis of our previous findings and the evolutionary context in which they were interpreted [15], along with previous reports showing that the walk-to-run transition reduces the perception of effort [2,8], we predicted that the elevated energy expenditure required to transition from walking to running at the PTS would be quantitatively met by fat oxidation. Furthermore, we predicted that the gait change would provide a carbohydrate-sparing effect at speeds higher than the PTS.

2. Materials and methods

2.1. Subjects

Ten healthy adults (6 women and 4 men) with a mean age of 26.6 ± 5.7 years and body mass of 66.8 ± 3.9 kg participated in this study. All subjects were weight stable and free from any metabolic, cardiovascular, orthopedic, or neurologic disorders. By subjective report, all subjects were habitually consuming a diet in which no conscious effort was made to substantially modify the intake of any macronutrient. Individuals with a body mass index greater than 25 kg m^{-2} and a waist-to-hip ratio of greater than 0.94 for men or 0.82 for women were excluded from the study.

The nature, purpose, and potential risks of the study were explained to all participants; and written informed consent was obtained in accordance with procedures approved by the Institutional Review Board at Arizona State University. All testing was conducted in the Exercise and Sport Research Institute in the Department of Kinesiology at Arizona State University.

2.2. Protocol

The study consisted of 4 separate testing sessions. The initial session involved treadmill acclimation and determination of maximal oxygen consumption (V_{O_2}max). The V_{O_2}max was determined using a modified Astrand [20] protocol. Briefly, after walking at a comfortable speed to warm up, the subject ran on the treadmill at approximately 2.5 m s^{-1}, 0% grade. The grade was increased 2.5% every 2 minutes until maximal aerobic capacity was reached. Defining criteria for the attainment of V_{O_2}max were as follows: a peak or leveling off of the participants V_{O_2} with increased workload, a heart rate (HR) within 10 beats per minute of age-predicted HR maximum (220 − age in years), and/or a respiratory exchange ratio (RER) greater than 1.0.

For the subsequent 3 exercise sessions, subjects reported to the laboratory between 7:00 AM and 9:00 AM in an overnight-fasted (10-12 hours) state having had abstained from strenuous exercise, nicotine, and caffeine for the preceding 24 hours. An overnight fast was chosen because acute nutrition affects fuel selection [21,22], yet Knapik et al [23] demonstrated no significant fall in muscle glycogen even after 3 days of starvation. Subjects were fitted with a heart monitor (Polar, Lake Success, NY) and instrumented for the collection of expired air. Resting HR and gas exchange were measured while subjects stood quietly for 15 minutes. During exercise session 1, subjects were instructed to select the most comfortable gait (walking or running) as they ambulated on the treadmill. The initial speed was set at 1.56 m s^{-1} (3.5 mph), and it was increased by 0.11 m s^{-1} (0.25 mph) every 10 minutes. The speed at which the individual transitioned from a walk to a run and stayed running for a majority of the stage was defined as that individual's PTS. For session 2, subjects walked for 10 minutes each at treadmill speed increments of 0.11 m s^{-1} beginning at 1.56 m s^{-1}. The session was terminated at 2.46 m s^{-1} or when a speed was reached at which the subject was no longer able to walk. During exercise session 3, subjects ran at those speeds completed in session 2.

During all treadmill testing, subjects breathed through a 2-way nonrebreathing valve (Hans Rudolph, Kansas City, MO); and O_2 consumption and CO_2 production were measured continuously with a TrueMax 2000 metabolic cart (Parvo, Salt Lake City, UT). Expired air and HR data were collected during the last 2.0 minutes at each speed during both gait conditions. Borg's [24] 6 to 20 rating of perceived exertion (RPE) was also assessed at all speeds by having subjects point to the appropriate value during the last 2.0 minutes. These values were then transformed to a 0 to 10 scale [25]. Blood was collected from a fingertip prick during the last 1.0 minute of each trial for the assay of blood lactate (Lactate Pro; Arkray, Kyoto, Japan).

2.3. Gas exchange and energy expenditure

Net gas exchange was calculated by subtracting resting values from exercise values for each subject. The O_2 cost of transport (in milliliters of O_2 per kilogram per kilometer) was calculated as mass-specific O_2 consumption rate divided by walking speed. Because comparisons of walking and running were made at identical speeds, the O_2 cost calculation is somewhat redundant to V_{O_2} information. We

nevertheless report the O_2 cost values because they provide a more direct comparison to most existing literature.

Indirect calorimetry was used to estimate carbohydrate and fat oxidation at rest and during walking [26]. Protein oxidation was assumed to be negligible [27]. The RER was determined as the V_{CO_2}/V_{O_2} ratio. Energy expenditure rates were calculated from net V_{O_2} and V_{CO_2} values [26] and are reported as the rate of mass-specific caloric use above rest (in calories per kilogram per minute). At the mild exercise intensities studied, gross whole-body gas exchange includes relatively large contributions from noncontractile tissues such as the splanchnic bed and the CNS [28-31]. Thus, the net gas exchange above rest was calculated to estimate the fuel metabolism of skeletal muscle activated during locomotion.

The *energetically optimal transition speed* (EOTS) has been defined as the speed at which "metabolism" is equal under the 2 gaits of interest [32]. We calculated EOTS with respect to both O_2 consumption and energy expenditure rates; thus, we report both an "O_2 EOTS" and an "energy EOTS." In each case, the EOTS was estimated based on the point of intersection of the data under the conditions of walking and running.

2.4. Data analysis

Means and standard deviations were calculated to describe subject demographics. For data analysis, walk data represent an average of data collected during the transition session (exercise session 1) and the walking session (exercise session 2), and run data represent an average of data collected during the transition session and the running session (exercise session 3). This was done to account for the slight day-to-day variation in metabolic measurements. After screening the data for normality and homogeneity of variance, 2 × 2 × 5 (gait × sex × speed) repeated-measures analyses of variance were used to compare O_2 cost of transport, O_2 consumption rate, energy expenditure rate, and net carbohydrate and fat oxidation rates between gaits, between sexes, and across speeds. Because we were primarily interested in between-gait differences, post hoc tests (paired t tests at the points of interest) were performed in the presence of a significant main effect of gait or a significant gait × speed interaction, but not in the presence of a significant main effect of speed. Bonferroni corrections for multiple comparisons were made to reduce the chance of a type 1 error. $P < .05$ was used to determine significance.

3. Results

The mean PTS was 2.08 ± 0.03 m s^{-1}. Table 1 reports subject information, gas exchange, fuel oxidation, HR, and RPE at PTS and speeds less than (indicated by negative numbers) and higher than (indicated by positive numbers) the PTS for walking and running. Metabolic rates and RERs at rest were similar to those typical of 12-hour–fasted individuals [33,34]. Mean V_{O_2}max was 43.8 ± 5.0 mL kg^{-1} min^{-1}, which is 82% of the predicted value for a 67-kg mammal [35]. All subjects fell into the 50th to 75th percentile for age and sex mass-specific V_{O_2}max [36]. Main effects for sex were not significant.

3.1. Perception of effort

Of the 10 subjects, 6 subjects transitioned from a walk to a run at 2.01 m s^{-1} and 4 at 2.12 m s^{-1}. This transition was associated with a conservation of effort. At speeds less than the PTS, RPE was similar between the walking and running conditions. However, at speeds higher than the PTS, RPE was greater when walking compared with running (Fig. 1).

3.2. Preferred transition speed and oxygen consumption

Net mass-specific V_{O_2} rose linearly with speed during walking and running (Fig. 2). Running V_{O_2} exceeded that of

Table 1
Metabolic response to walking and running on a level motor-driven treadmill at speeds normalized to PTS

Speed	V_{O_2}	V_{CO_2}	RER	J_{cho}	J_{fat}	RPE	HR
(m s^{-1})	(mL min^{-1} kg^{-1})			(cal min^{-1} kg^{-1})			
Walking							
−0.11	15.5 ± 0.7	13.4 ± 0.7	0.865 ± 0.010	43.1 ± 3.9	32.2 ± 2.1	3.9 ± 0.7	128.8 ± 10.6
−0.22	18.9 ±1.0	16.5 ± 1.0	0.869 ± 0.012	54.1 ± 5.6	38.1 ± 2.8	5.1 ± 0.8	138.2 ± 11.6
PTS	21.6 ± 1.1	19.2 ± 1.1	0.884 ± 0.013	67.6 ± 6.5	38.2 ± 3.6	6.0 ± 0.9	153.4 ± 11.3
+0.11	25.1 ± 1.2	22.8 ± 1.3	0.906 ± 0.016	88.3 ± 9.3	35.7 ± 5.7	7.1 ± 0.8	166.1 ± 10.4
+0.22	27.2 ± 1.2	25.3 ± 1.4	0.930 ± 0.023	106.3 ± 32.4	28.7 ± 8.9	7.5 ± 0.7	167.0 ± 13.6
Running							
−0.11	20.9 ± 0.7	18.2 ± 0.6	0.872 ± 0.008	60.0 ± 3.5	41.8 ± 3.2	3.4 ± 0.2	131.4 ± 9.5
−0.22	22.6 ±0.9	19.4 ±0.8	0.859 ± 0.008	60.1 ± 4.2	49.5 ± 3.3	4.6 ± 0.4	141.8 ± 8.6
PTS	24.3 ± 0.8	21.0 ± 0.8	0.864 ± 0.010	67.1 ± 5.8	51.1 ± 3.7	4.9 ± 0.7	151.8 ± 9.0
+0.11	26.0 ± 0.8	22.4 ± 0.8	0.863 ± 0.012	70.9 ± 6.3	55.0 ± 4.7	5.2 ± 0.7	160.7 ± 8.9
+0.22	26.7 ± 0.8	23.0 ± 0.7	0.863 ± 0.016	72.7 ± 7.3	57.2 ± 7.8	5.3 ± 0.7	158.8 ± 12.2

Net mass-specific whole body V_{O_2} and V_{CO_2} are reported as milliliters per minute per kilogram. Respiratory exchange ratio is the V_{CO_2}/V_{O_2} ratio. Net whole-body carbohydrate (J_{cho}) and fat (J_{fat}) oxidation rates are reported as calories per minute per kilogram. Rating of perceived exertion are data reported on a 0 to 10 scale. All data represent stable values observed from minute 8.0 to 10.0 at each speed. Data (except HR) are net values (gross − rest values), expressed as means ± SEM; n = 10.

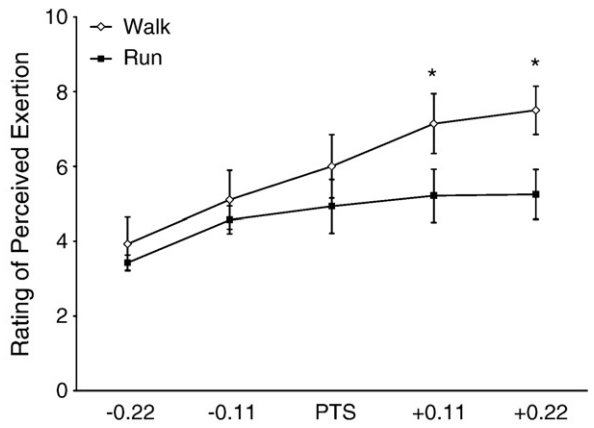

Fig. 1. Borg's converted (0-10) RPE across speeds normalized to PTS. The RPE associated with walking exceeded that of running at speeds higher than the PTS. All values are means ± SEM. *Significant differences between gaits at a given speed.

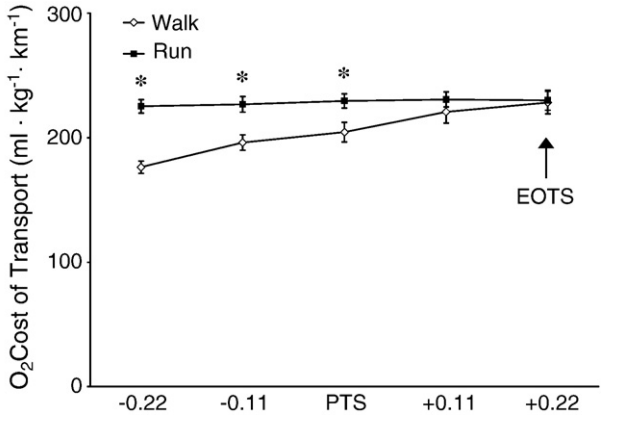

Fig. 3. The O_2 cost of transport, reported as milliliters of O_2 required to move 1 kg of body mass for 1 km, across speeds normalized to PTS. Note that these data represent the ascending limb of the classic U-shaped curve observed during locomotion, as very low speeds are not represented here. The arrow indicates that the EOTS as predicted by O_2 cost of transport occurs at the PTS ±0.22 m s^{-1}. All values are means ± SEM. *Significant differences between gaits at a given speed.

walking at speeds less than or equal to the PTS. The O_2 cost of transport rose across speeds during walking (ie, the ascending limb of the classic U-shaped curve above the preferred walking speed), but was essentially constant across speeds during running (Fig. 3).

As with V_{O_2}, O_2 cost of transport during running exceeded that during walking at and less than the PTS. At the PTS, the O_2 cost of transport running was 12% higher than that of walking (229.6 ± 5.7 and 204.5 ± 7.9 mL km^{-1} kg^{-1}, respectively). The EOTS of O_2 cost of transport occurred at 0.22 m s^{-1} higher than the PTS.

3.3. Preferred transition speed and total energy

Total energy expenditure rose across speeds and was higher in running conditions than in walking conditions at speeds less than or equal to the PTS (Fig. 4). However, it revealed a slightly different pattern from that seen with O_2 cost of transport because the measurement of aerobic energy production includes not just O_2 consumption but also CO_2 production. Whereas the EOTS for O_2 occurred at ±0.22 m s^{-1} (Fig. 3), the energy EOTS occurred at ± 0.11 m s^{-1} (Fig. 4). Indeed, the difference between these 2 estimates of the optimal transition speed reflects the markedly greater fractional contribution of carbohydrate to the fuel supply during walking compared with that during running (see below and Fig. 6).

3.4. Fuel oxidation

Fat oxidation was higher during running compared with walking at all speeds (Fig. 5A). Carbohydrate oxidation rates progressively rose across speeds during walking (Fig.

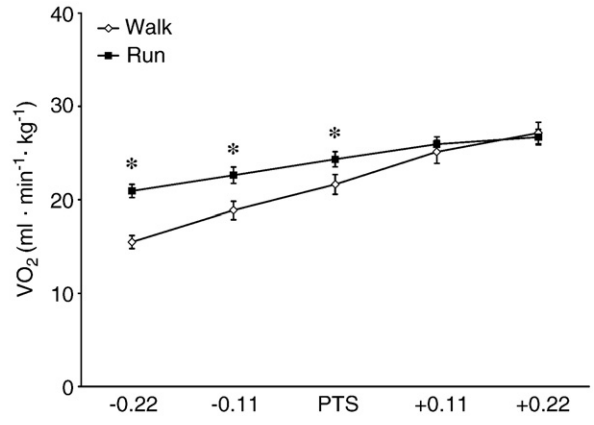

Fig. 2. Net mass-specific V_{O_2} across walking speeds normalized to PTS. The equations of the lines for walking and running are as follows: $y = 2.96x \pm 12.79$, $R2 = 0.99$, and $y = 1.49x \pm 19.65$, $R2 = 0.98$, respectively. All values are means ± SEM. *Significant differences between gaits at a given speed.

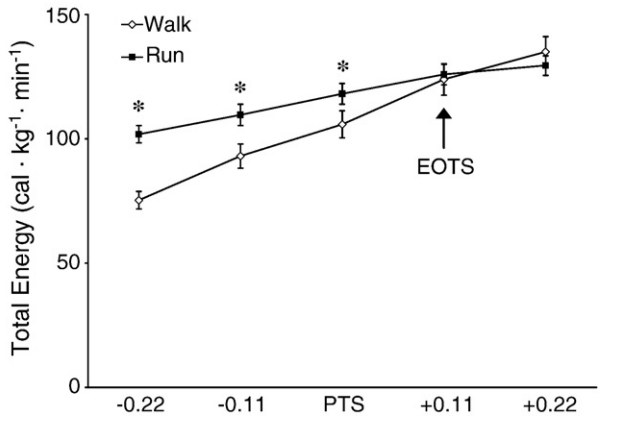

Fig. 4. Total energy across speeds normalized to PTS. The arrow indicates that the EOTS as predicted by total energy occurs at the PTS ±0.11 m s^{-1}. All values are means ± SEM. *Significant differences between gaits at a given speed.

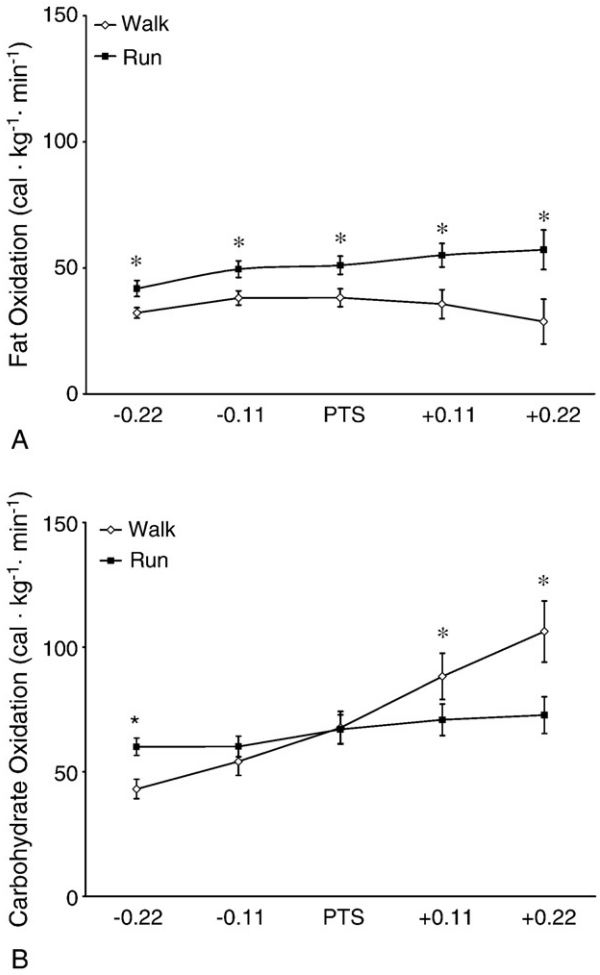

Fig. 5. Net fuel oxidation rates, calculated by subtracting resting V_{O_2} and V_{CO_2} from the corresponding steady-state values, across speeds normalized to PTS. These net V_{O_2} and V_{CO_2} values were then inserted into the equations of Frayn [26] to estimate carbohydrate and fat oxidation rates of skeletal muscle activated to support locomotion. A, Net fat oxidation rates during running exceeded those of walking at each speed. The lack of rise of net fat oxidation rates with walking suggests that almost all of the extra energy to walk at speeds higher than the PTS is met by increasing carbohydrate utilization. B, Net carbohydrate oxidation rates were essentially identical in walking and running. Continuing to walk at speeds higher than the PTS demanded increasingly higher carbohydrate oxidation rates. All values are means ± SEM. *Significant differences between gaits at a given speed. CHO indicates carbohydrate.

5B). At the PTS, the carbohydrate oxidation rate of walking was essentially identical to that of running (67.7 ± 6.5 and 67.1 ± 5.8 cal kg^{-1} min^{-1}, respectively). Thus, when subjects were allowed to transition from walking to running at PTS, all of the additional energy was provided by fat oxidation. Whereas walking at speeds higher than the PTS demanded increasingly higher carbohydrate oxidation rates, running at these same speeds elicited no change in carbohydrate demand (Fig. 5B). Thus, as speed of locomotion increased to higher than the PTS, walking, compared with running, became increasingly more dependent upon carbohydrate oxidation.

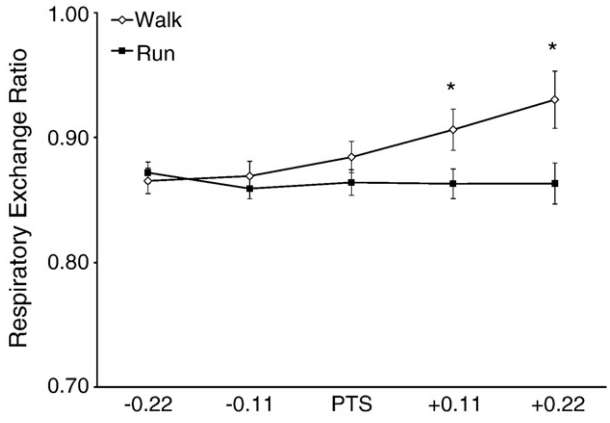

Fig. 6. Respiratory exchange ratio across speeds normalized to PTS. The RER associated with walking exceeded that of running at speeds higher than the PTS. All values are means ± SEM. *Significant differences between gaits at a given speed.

Respiratory exchange ratio was essentially constant during running across speeds (Fig. 6). This result indicates that although the overall rate of energy expenditure was generally higher during running, the relative contribution of carbohydrate to the fuel supply during running was steady. In marked contrast, during walking, RER (thus, relative carbohydrate dependence) rose with increasing speed and exceeded running at speeds higher than the PTS (Fig. 6).

Lactate concentrations, which were measured in blood samples collected during the last 2.0 minutes of each 10.0-minute speed increment, suggested that gas exchange provided reliable estimates of whole-body fuel oxidation during both walking and running. For both walking and running protocols, treadmill speed was increased progressively. During walking, in order from the lowest to the highest speed, the mean ± SEM blood lactate concentrations (in millimoles per liter) were 2.19 ± 0.31, 2.66 ± 0.29, 3.31 ± 0.52, 3.18 ± 1.61, and 3.88 ± 0.70. Paired *t* tests revealed no differences in blood lactate from any given 10-minute increment to the next increment in the sequence. In fact, a comparison of all means in the entire walking lactate data set without α correction revealed only one "significant" difference, between the lowest (PTS −0.22 m s^{-1}) and the highest speed (PTS ± 0.22 m s^{-1}), blood collections separated by 50 minutes of walking. During the running protocol, blood lactate was essentially constant. Again, in order from lowest to highest speed, the values were 2.90 ± 0.60, 2.50 ± 0.30, 2.41 ± 0.35, 2.69 ± 0.50, and 2.97 ± 0.48 mmol/L. Overall, these data provide confidence that the acid-base stability assumptions of indirect calorimetry were met.

4. Discussion

In the present study, the mean PTS was 2.08 ± 0.03 m s^{-1}. Consistent with previous literature [1,4], no sex differences were observed. Preferred transition speed occurred at speeds

less than the EOTS when the EOTS was expressed as either the O_2 cost of transport (Fig. 2) or the total energy expenditure rate (Fig. 3). These results corroborate several previous reports [1,7,10,16], which have shown that the change in metabolic rate elicited by the walk-to-run transition is opposite to the direction predicted by the least energy hypothesis. These many published observations and our corroboration of them, inspire the following question: why does the CNS adopt a gait that requires more energy?

The within-subject design of the present study revealed that essentially all of the extra energy required to transition from walking to running was provided by lipid oxidation, irrespective of sex. During moderate-intensity cycling exercise at matched percentages of $V_{O_2}max$, women demonstrate greater relative dependence on lipid oxidation [37,38]. However, because women have lower $V_{O_2}max$, these same data show that sex-related differences in fuel selection disappear at identical mass-specific V_{O_2} (in milliliters of O_2 per minute per kilogram body mass). Because neither locomotion O_2 economy nor PTS is influenced by sex [1,4], our observation of no sex effect on substrate utilization agrees with the expected outcome.

Our findings also confirm that the walk-to-run transition reduces the perception of effort [2,8,10]. Prilutsky and Gregor [2] reported that transition from walking to running increased summed muscle EMG. The paradox described above is restated here: although metabolic rate and neural input to muscle rose at the PTS, the sense of effort fell. The paradox may be partly explained by Fig. 6. Respiratory exchange ratio reflects the relative contribution of fat and carbohydrate to total energy; it thus roughly approximates the fraction of the neural input into muscle that is activating fat-supported energy turnover vs the fraction activating carbohydrate-dependent metabolism. Irrespective of gait, increasing locomotion speed demands increased neural activation of muscle and metabolic rate. Fig. 6 reveals that gait transition allows a greater fraction of the additional energy metabolism to be provided by fat oxidation.

Previously, we demonstrated that fat oxidation accounts for none of the perception of effort during walking; in contrast, a strong coupling of carbohydrate oxidation and perception of effort was identified [15]. Our current results also indicate that perception of effort closely tracks the rate of carbohydrate oxidation regardless of gait pattern. We propose (Fig. 7) that walking at preferred speed elicits essentially no sense of effort because the neural input into muscle stimulates an adenosine triphosphate (ATP) turnover rate that can be supported by mitochondrial fat oxidation, resulting in a contractile output proportional to the neural input ("matched input-output"). However, as speed increases, the higher O_2 consumption rate and, particularly, the emerging requirement for carbohydrate to supplement the fuel supply together require stimulation from increased concentrations of their activators, adenosine diphosphate (ADP), adenosine monophosphate, and Pi [39-43]. In turn, this decline in energy status exerts inhibitory influence on

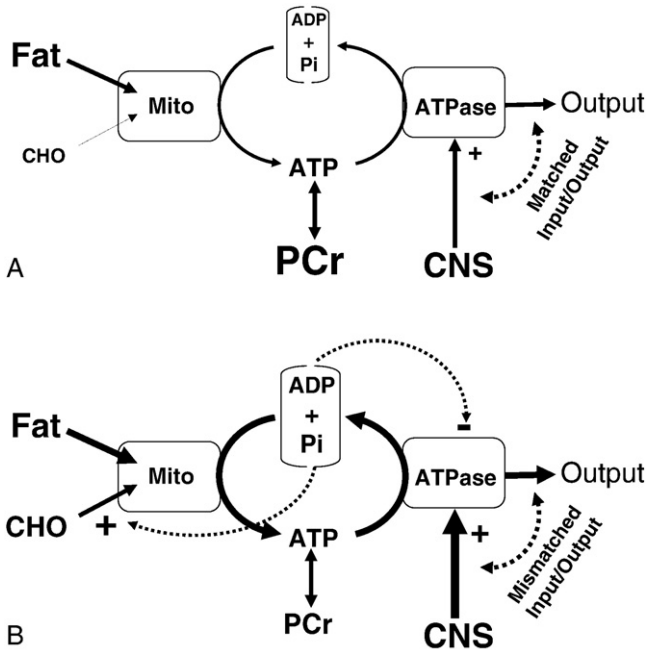

Fig. 7. A model of cellular ATP turnover in overnight-fasted muscle cells based on the connectivity property of metabolic control analysis [46]. A, Note the low ATP turnover of walking at preferred speed. The CNS activation of cellular ATP breakdown by ATPase is matched by mitochondrial ATP production with minimal perturbation to cellular energy state (free [ADP] and [Pi] rise very little from rest values). In this case, mitochondrial capacity for fat oxidation is catalytically competent to match the entire ATP demand; and what little glycolytic flux occurs requires no significant stimulation from a decline in cytosolic energy phosphate status. B, Higher speeds necessitate greater CNS drive, which increases the ATP turnover rate. Now the decline in cellular energy state required to stimulate both additional O_2 consumption and, particularly, the glycolytic pathway may simultaneously exert inhibitory influence on sites of ATP utilization and thus functional output. The mismatch in CNS input compared with functional (contractile) output may be sensed by the CNS as effort, which might be a cue to change gait. Brackets around ADP ± P_i denote that it is the concerted action of changes in the energy phosphate pool associated with declining ATP free energy that activates glycolysis and inhibits ATP-using processes. See text for further discussion.

ATP breakdown at the ATPase [19], resulting in "mismatched input-output" (Fig. 7B). We propose that the mismatch could provide a mechanism to alert the CNS of declining energy status in muscle and the recruitment of carbohydrate into the fuel supply.

The signal that links nervous system input to myosin ATPase within myocytes is Ca^{2+} release. Another parameter of metabolic control analysis, the "partitioned response coefficient," quantifies the extent to which an external effector (like Ca^{2+}) controls energy turnover in muscle. Jeneson [44] used this approach to show that neural control of muscle energy turnover is degraded as the intensity approaches the level where carbohydrate begins to make a large contribution to the fuel supply.

The evolutionary basis of this proposed model is that it would provide a mechanism by which the CNS might sense when the myocellular free energy of ATP hydrolysis

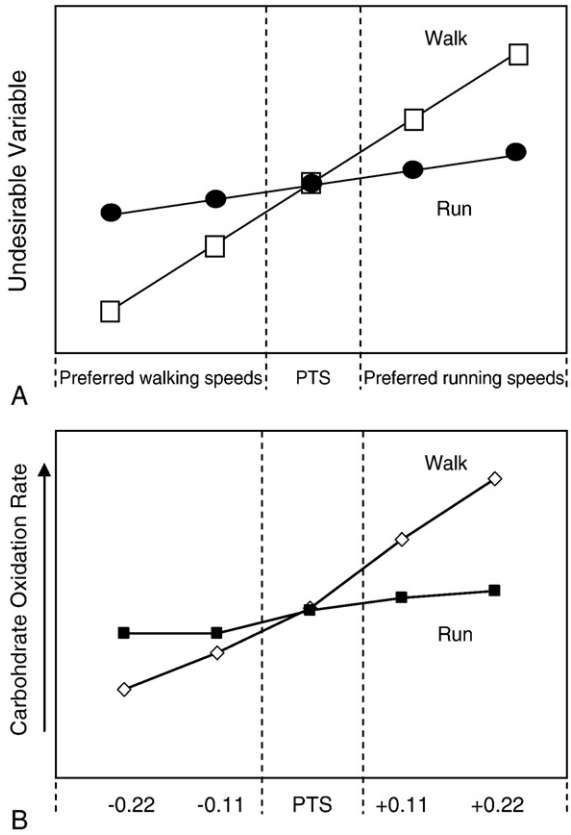

Fig. 8. Changes in an undesirable variable that can trigger the walk-to-run transition. A, Changes in a hypothetical undesirable variable can trigger the walk-to-run transition (reproduced from Prilutsky and Gregor [2], Fig. 6). "As walking speed increases and the magnitude of a variable during walking exceeds that during running … the walk-run transition occurs…." B, Changes in net carbohydrate oxidation rates closely resemble those modeled by Prilutsky and Gregor [2]. As walking speed increases, the rate of carbohydrate oxidation increases and exceed that during running at speeds higher than the PTS.

(ΔG_{ATP}) begins to be challenged [19] and thus the glycolytic pathway is activated [41,45]. During routine locomotion, the discomfort of effort might avert profligate depletion of carbohydrate, the fuel that is in very limited supply, is the primary fuel of the CNS, and is the only fuel capable of supporting burst activity.

Prilutsky and Gregor [2] suggested that in order "to find a trigger for the walk-run transition, one might search for a certain undesirable variable that becomes larger during walking than during running as locomotion speed increases beyond the preferred transition speed and is reduced by switching from walking to running" (Fig. 8A). Importantly, the superimposition of our carbohydrate oxidation data on their model yields a nearly perfect fit (Fig. 8B).

In summary, our results corroborate many previous reports [1,7,10,16] that refute the "least energy hypothesis" as an explanation for spontaneous walk-to-run transitions in humans. In the present study, gait transition resulted in increased energy expenditure, decreased sense of effort, and decreased rates of carbohydrate oxidation. We propose that rising carbohydrate oxidation reflects a falling energy state in active muscle, which may inhibit ATP utilization sites and create a discrepancy between motor input and contractile output. The resulting input-output mismatch, perceived as effort, might guide the CNS to adopt the gait that minimizes carbohydrate depletion. Further work is needed to characterize the complete afferent-efferent control loop underlying perception of effort with appropriate changes in motor commands.

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