Background Inactivity Blunts Metabolic Adaptations to Intense Short-Term Training

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ABSTRACT

BURTON, H. M., A. S. WOLFE, E. VARDARLI, R. SATIROGLU, and E. F. COYLE. Background Inactivity Blunts Metabolic Adaptations to Intense Short-Term Training. *Med. Sci. Sports Exerc.*, Vol. 53, No. 9, pp. 1937–1944, 2021. **Purpose:** This study determined if the level of background physical inactivity (steps per day) influences the acute and short-term adaptations to intense aerobic training. **Methods:** Sixteen untrained participants (23.6 ± 1.7 yr) completed intense (80%–90% $\dot{V}O_{2peak}$) short-term training (5 bouts of exercise over 9 d) while taking either 4767 ± 377 steps per day (n = 8; low step) or 16,048 ± 725 steps per day (n = 8; high step). At baseline and after 1 d of acute exercise and then after the short-term training (posttraining), resting metabolic responses to a high-fat meal (i.e., plasma triglyceride concentration and fat oxidation) were assessed during a 6-h high-fat tolerance test. In addition, responses during submaximal exercise were recorded both before and after training during 15 min of cycling (~79% of pretraining $\dot{V}O_{2peak}$). **Results:** High step displayed a reduced incremental area under the curve for postprandial plasma triglyceride concentrations by 31% after acute exercise and by 27% after short-term training compared with baseline ($P < 0.05$). This was accompanied by increased whole-body fat oxidation (24% and 19%; $P < 0.05$). Furthermore, stress during submaximal exercise as reflected by heart rate, blood lactate, and deoxygenated hemoglobin were all reduced in high step ($P < 0.05$), indicating classic training responses. Despite completing the same training regimen, low step showed no significant improvements in postprandial fat metabolism or any markers of stress during submaximal exercise after training ($P > 0.05$). However, the two groups showed a similar 7% increase in $\dot{V}O_{2peak}$ ($P < 0.05$). **Conclusion:** When completing an intense short-term exercise training program, decreasing daily background steps from 16,000 to approximately 5000 steps per day blunts some of the classic cardiometabolic adaptations to training. The blunting might be more pronounced regarding metabolic factors (i.e., fat oxidation and blood lactate concentration) compared with cardiovascular factors (i.e., $\dot{V}O_{2peak}$). **Key Words:** EXERCISE, SEDENTARY, CARDIOVASCULAR, HYPERLIPIDEMIA, STEPS, EXERCISE RESISTANCE

Exercise induces acute and chronic adaptations in numerous bodily systems at the molecular, tissue, and organ level that usually improve whole-body function (1,2). Some adaptations manifest in hours, such as increased muscle lipoprotein lipase (LPL) activity (3), whereas others become apparent only after several weeks or longer of training (e.g., muscle capillarization or cardiac hypertrophy) (4–7).

Along these lines, we have reported a phenomenon termed "exercise resistance" to describe the inactivity-induced (e.g., low daily steps) lack of improvement in fat metabolism during the 16- to 22-h period after acute exercise (1 h of running) that normally elicits robust increases in fat oxidation and the postprandial lowering of plasma triglycerides (8,9). The condition that appears to elicit "exercise resistance" in this case is prior physical inactivity as judged by daily step counts of 5000 or less (10). It is possible that inactivity functions to prevent the normal increase in muscle LPL in the 4- to 20-h period after exercise, and this reduces the postprandial clearance of triglyceride from blood and reduces whole-body fat oxidation (3). This model of studying postprandial plasma triglycerides and whole-body fat oxidation has proven sensitive to acute changes in physical activity (11).

With the observation that acute inactivity impairs some adaptations to exercise, the present study sought to determine whether chronic inactivity impairs a broad range of whole-body adaptations after short-term intense aerobic training. A large part of the improvements with intense aerobic training occurs during the first 1–2 wk of training (12), and thus the present study used 5 bouts of training over a 9-d period. During this period, one group took a high number of background steps (e.g., ~16,000 steps per day) and another group took a low number of steps (e.g., ~5000 steps per day). Their adaptive responses were compared before and after the short-term training during cycling at a fixed absolute intensity as well as during $\dot{V}O_{2peak}$. Postprandial measures of fat metabolism were made at baseline and both the morning after the first training bout (acute) and the last training bout (chronic short-term training). It is our hypothesis that a low level of background physical activity (i.e., low steps per day) during the days of exercise training will attenuate some of the cardiovascular and metabolic adaptations that are normally realized with intense aerobic training.

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METHODS

Sixteen healthy and untrained male (n = 8) and female (n = 8) college-age participants were recruited and randomly assigned to two groups, each group with four males and four females. Both groups completed a training regimen administered under the supervision of the investigators. Outside of the exercise regimen, one group was physically active (n = 8), taking 16,048 ± 1390 steps per day (high step [HS]), and the other group was more sedentary (n = 8; more time seated), taking 4767 ± 871 steps per day (low step [LS]). Both groups were asked to refrain from any planned exercise outside the experimental design. The HS group was encouraged to spread their steps throughout the day by looking for opportunity to walk longer routes to their destinations. No jogging was performed. The LS group limited their walking to the minimum needed to get to destinations. Participants were given written and verbal description of all the procedures used in this study, and written informed consent was obtained. The Institutional Review Board of the University of Texas at Austin approved this study (ClinicalTrials.gov identifier: NCT03352063).

Experimental design. The experimental design consisted of 17 d with three distinct phases (see Fig. 1). Days 1–3 (baseline) consisted of pretraining measures. Days 4–14 (training) consisted of alternating days of training and rest days. The final 3 d, days 15–17 (posttraining), consisted of repeating measurements taken in the pretesting phase.

On the first day, participants visited the laboratory for a baseline high-fat tolerance test (HFTT). The second day was the determination of peak oxygen consumption while cycling ($\dot{V}O_{2peak}$). The following day, D3, participants completed a 15-min submaximal cycling test at 79% of $\dot{V}O_{2peak}$. On the third day, participants began wearing an activity monitor (activPAL; PAL Technologies, Glasgow, Scotland). Aside from showering, the activity monitor was worn continuously throughout the training phase.

The morning after the first bout of exercise training on the evening of day 6, another HFTT was performed on day 7 to evaluate responses to an acute bout of exercise. Participants continued the training regimen, exercising and resting on alternating days such that there were five exercise sessions and four rest days in this training phase. All exercise bouts were identical and consisted of a 20-min cycling bout at ~80% of the participant's baseline $\dot{V}O_{2peak}$ followed by 10 min of rest. Participants then completed two 5-min bouts at ~90% $\dot{V}O_{2peak}$ with 5-min rest intervals between each bout. This exercise prescription is in line with, or exceeds, the current physical activity guidelines published by the American Heart Association and the U.S. Department of Health and Human Services (Physical Activity Guidelines for Americans; 2018) (1,13).

In the posttraining phase, participants completed an HFTT the morning after the final bout of exercise. On D16, participants completed another 15-min submaximal exercise test at the same absolute work rate as the submaximal test during the pretesting at 80% of baseline $\dot{V}O_{2peak}$. On the final day, participants completed a posttraining $\dot{V}O_{2peak}$ test.

Dietary control. During the course of the study, participants were asked to eat to satiety, following a diet standard in macronutrient breakdown. Also, participants logged all food using the MyFitnessPal mobile application (MyFitnessPal, Inc.). Participants were asked to consume the same foods on the day before each HFTT. On the evening before the HFTT, participants were given a low-fat meal to consume as fat in the previous meal can affect the response to a high-fat test meal (14,15).

HFTT. On the morning of the HFTT, participants arrived at the laboratory after a 12-h fast. After resting for 5 min, an

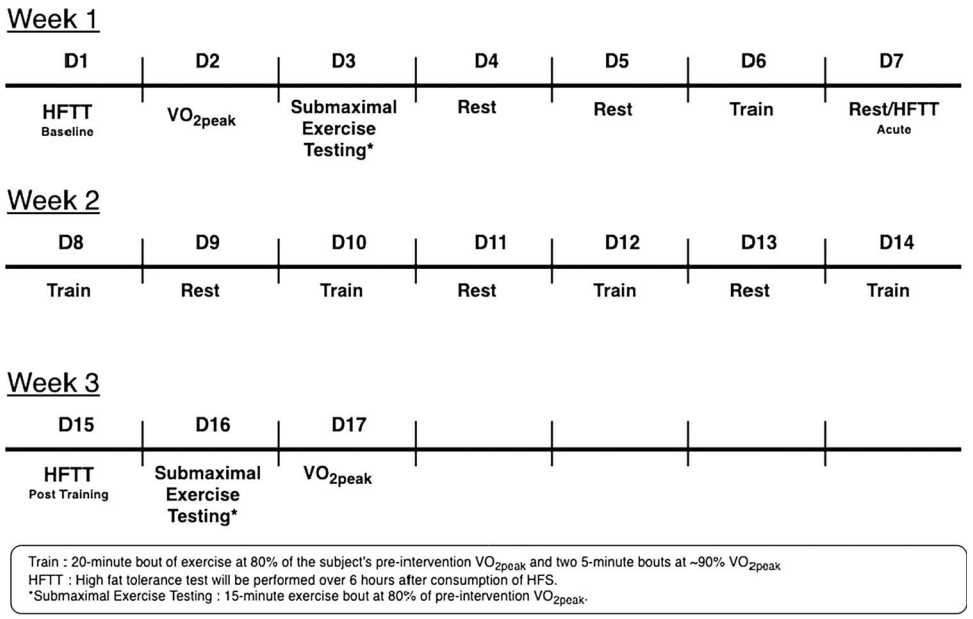

FIGURE 1—Study design. Participants were separated into two groups (high step or low step) and completed the same short-term exercise training regime with cardiovascular and metabolic testing pre- and posttraining. Subjects took their assigned step number on days 4–16.

intravenous catheter was inserted into an antecubital vein. A resting blood sample was taken, and 10 min later, the HFTT test meal consisting of melted ice cream and heavy cream, approximately 14.8 kcal·kg^{-1} (0.8 g, 1.2 g, and 0.2 g·kg^{-1} BW of carbohydrate, fat, and protein, respectively), was consumed in 5 min. Blood samples were then taken hourly for the next 6 h as the subject rested quietly in a comfortable chair.

Postprandial substrate oxidation. During the HFTT, expired gas was collected for the determination of whole-body carbohydrate and fat oxidation. Participants rested for 10 min in a seated position, followed by 10 min of expired gas collection via meteorological balloons performed at 0, 2, 4, and 6 h. It has been previously demonstrated that inactivity reduces whole-body fat oxidation (16). Energy expenditure and substrate oxidation were calculated from oxygen consumption, carbon dioxide production, and RER. Substrate oxidation was calculated based on the methods of Frayn (17).

Peak oxygen consumption testing. During this procedure, participants breathed into a mouth piece (while wearing a nose clip), and their expired air was analyzed for O_2 and CO_2 concentration (Applied Electrochemistry, Models S-3A/I and CD-3A, respectively) while ventilation was measured via an inspiratory pneumotachometer (Hans Rudolph, Kansas City, MO). From this, participant's oxygen consumption was determined and their peak value ($\dot{V}O_{2peak}$) was identified. The intensity of exercise was increased every 1–2 min until they reached their maximal effort level and became fatigued. Volitional fatigue was associated with difficulty or inability to maintain cadence (>60 rpm) while cycling. The total length of the test was ~8–12 min, including a 4-min warm-up. Heart rate was also measured continuously from a strap worn around the chest (Suunto, Vantaa, Finland) and used as a validation method for obtaining $\dot{V}O_{2peak}$.

Submaximal exercise testing. Submaximal exercise testing was conducted on a cycle ergometer and consisted of a 15-min bout at an intensity of ~80% of $\dot{V}O_{2peak}$. Blood samples were taken from an indwelling venous catheter at the beginning and end of the 15-min submaximal exercise protocol to evaluate blood lactate responses. Heart rate and $\dot{V}O_2$ were measured continuously, as described above. Near-infrared spectroscopy (NIRS) (OxiplexTS; ISS Oximeter Model 95205, Champaign, IL) was used to measure deoxygenated hemoglobin (HHb) in the vastus lateralis during exercise, as a measure of physiological stress during submaximal testing. The NIRS data, collected between 9 and 10 min of the testing protocol, were recorded and averaged.

Biochemical analysis. For plasma triglyceride and glucose concentrations, all blood samples collected were immediately transferred to K2 EDTA collection tubes (BD Vacutainer, Franklin Lakes, NJ), centrifuged at 3000*g* for 15 min at 4°C. Plasma was then stored in separate aliquots at −80°C until later analysis. All measurements for each participant were performed in duplicate within the same analysis. Plasma triglyceride and glucose concentrations were measured by a spectrophotometric method using commercially available kits (Pointe Scientific, Inc., Canton, MI).

For blood lactate concentrations, blood samples were immediately deproteinized by placing it in 8% perchloric acid, and lactic acid levels were later measured on the supernatant. The enzymatic analysis was used to determine blood lactate concentration based on methods of Farrell et al. (18).

Statistical analysis. Descriptive statistics are reported as mean ± SE and compared using Student's *t*-test with Bonferroni correction ($\alpha = 0.05$). Differences in daily steps, maximal and submaximal exercise responses, postprandial responses, and incremental (AUC_I) and total (AUC_T) areas under the curve for concentrations of plasma triglyceride and glucose were determined by two-way ANOVA (treatment × time). Within-group differences in plasma triglyceride concentration and postprandial substrate oxidation were determined using repeated-measures two-way ANOVA (trial × time). Tukey's LSD was performed to determine whether statistical significance exists. All data were analyzed using GraphPad Prism 7 (GraphPad Software Inc., La Jolla, CA). The probability level for statistical significance was set at $P < 0.05$.

RESULTS

Participant characteristics. Participants' characteristics are described in Table 1. Participants were young, healthy, and untrained adults, and HS and LS had similar $\dot{V}O_{2peak}$ values. The two group's pretraining HR, blood lactate, and RPE during exercise at 79% $\dot{V}O_{2peak}$ were all similar.

Daily steps. As designed, HS took significantly more daily steps than the LS group (HS, 16,048 ± 725 steps per day, vs LS, 4767 ± 376; $P < 0.001$) over the 11-d period of short-term training (Fig. 2). On D7, individuals in HS took fewer steps because the HFTT on that day required sitting for 6 h.

Plasma triglyceride and glucose concentrations during HFTT. In HS, at hours 1, 2, and 3 of the HFTT, TG concentrations were significantly lower in both acute and posttraining compared with baseline ($P < 0.05$) (Fig. 3A). In LS, no significant differences were found between trials at any time point for the 6-h TG excursion (Fig. 3B). Over the 6 h, plasma glucose excursion was not significantly different between trials at any time point, between or within either treatment group (data not shown). As such, plasma glucose AUC_T and AUC_I showed no significant effects within, or between either treatment groups ($P > 0.05$).

Total plasma triglyceride area under the curve responses. Calculated incremental area under the curve (AUC_I) and total area under the curve (AUC_T) for plasma

TABLE 1. Descriptive statistics of the two groups (i.e., high step and low step) at baseline (i.e., pretraining).

Physical Characteristics	HS (n = 8)	LS (n = 8)
M/F	4/4	4/4
Age (yr)	23.4 ± 2.0	23.8 ± 1.4
Height (cm)	166 ± 3	167 ± 3
Body mass (kg)	74.4 ± 5.9	72.6 ± 3.9
Body mass index (kg·m^{-2})	26.7 ± 1.9	25.9 ± 1.0

All data are reported as mean ± SE.

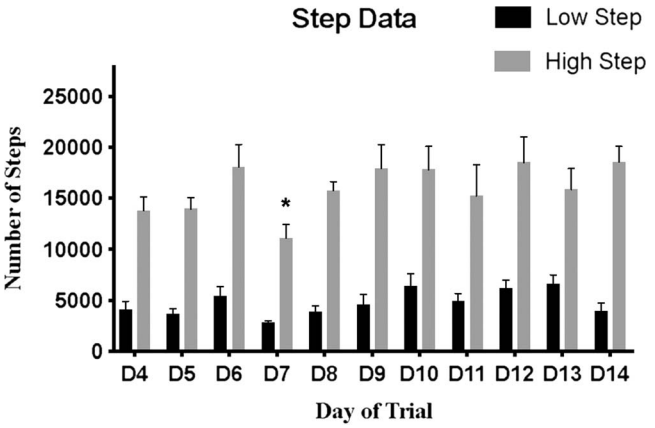

FIGURE 2—Daily steps were measured via activable activity monitor, attached on the participant's anterior thigh throughout each trial. Average daily step count for each group is presented for the 11-d intervention period (D4–D14). Average daily steps were significantly different between groups for every day measured ($P < 0.001$). *Significantly different from D12 and D14 within treatment group ($P < 0.05$).

TG are shown in Figure 4. In HS, both AUC_T and AUC_I were significantly ($P < 0.05$) reduced by 27%–31% in acute and posttraining time points, respectively, compared with baseline with no significant differences between acute and posttraining ($P > 0.05$). Within the LS group, no significant improvements in either AUC_T or AUC_I for plasma triglyceride were observed with acute or chronic training compared with baseline (Fig. 4).

Postprandial substrate oxidation. Resting oxidation calculations were limited to seven participants from each treatment group due to possible hyperventilation at rest. Within HS, RER values during the HFTT were reduced after both acute (0.79 ± 0.01) and posttraining (0.80 ± 0.01) compared with pretraining (0.83 ± 0.01, $P < 0.05$; Table 2). However, no significant reductions in RER were found within LS. Likewise, percent fat oxidation was significantly improved in HS ($P < 0.05$), whereas no significant improvements were seen within LS. More importantly, in HS, postprandial absolute fat oxidation (i.e., kcal/6 h) was higher by 24% in acute ($P < 0.05$) and 19% in posttraining ($P < 0.05$) compared with baseline. In LS, the 6%–7% increase in absolute fat oxidation was not a significant increase in baseline, acute, or posttraining ($P > 0.05$).

Exercise responses. Peak and submaximal exercise responses are summarized in Table 3. Peak oxygen consumption ($\dot{V}O_{2peak}$) increased significantly in both HS (i.e., 7.6%) and LS (i.e., 7.2%) from baseline to posttraining ($P < 0.05$). During submaximal exercise, oxygen consumption and workload were identical and remained at the absolute values representing 79% $\dot{V}O_{2peak}$ of the baseline values. Blood lactate concentration during submaximal exercise was high at baseline in both groups (i.e., >7 mM) and displayed a significant decrease in HS yet no reduction in LS. Baseline data showed no differences in submaximal HR, RPE, or RER between groups ($P > 0.05$). Posttraining testing revealed a significant reduction in submaximal HR (i.e., 12 bpm; $P < 0.05$) in HS compared with a 5-bpm and nonsignificant decrease in LS ($P > 0.05$). Furthermore, NIRS measurements showed that after training, muscle HHb was significantly lower than baseline within the HS group ($P < 0.05$). No significant decrease in HHb was found in LS pre- versus posttraining ($P > 0.05$). Regarding RPE, HS displayed a significant ($P < 0.01$) reduction posttraining, whereas the reduction in LS was close to but not quite at the level of statistical significance (i.e., $P = 0.07$).

DISCUSSION

It is well known that acute and chronic exercises stimulate molecular and systemic adaptations that generally improve physiological function with a half time of 10–12 d (12,19,20). However, it has more recently been found that there are some background conditions or cellular environments that seem to counteract potential adaptations (e.g., hyperglycemia or inactivity) (7–9). The present study has shown that the background of physical inactivity in LS (<5000 steps per day) restrained or prevented some classic physiological improvements after

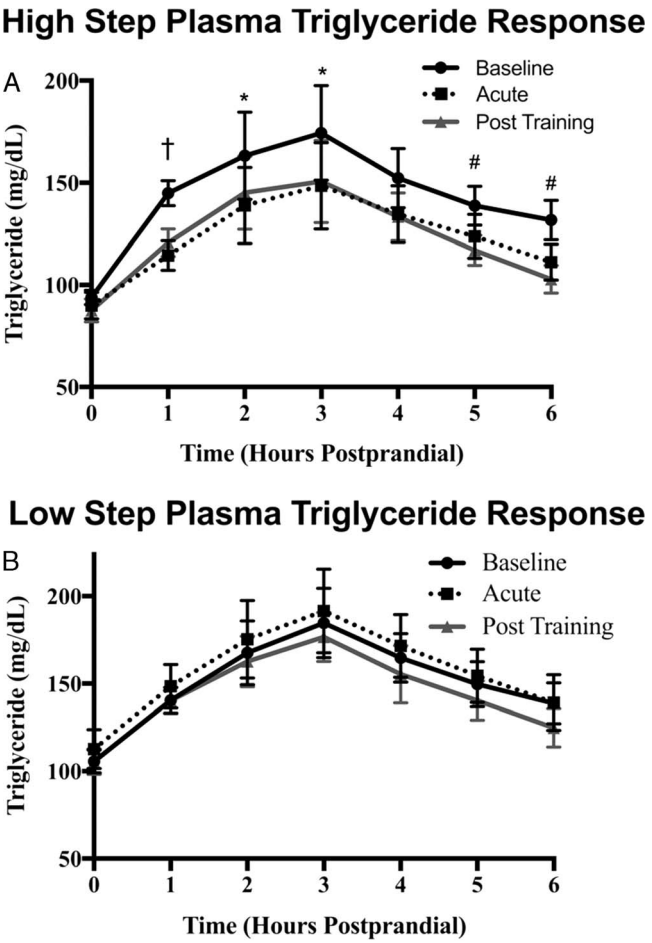

FIGURE 3—Temporal responses of plasma triglyceride concentrations for HS (A) and LS (B) treatments during the HFTT at baseline, after a single bout of exercise (Acute), and after 5 training bouts over the 9 d of training (posttraining). *Acute significantly different from baseline $P < 0.05$. † Acute and posttraining significantly different from baseline, $P < 0.01$. # Posttraining significantly different from baseline, $P < 0.05$. Data are reported as mean ± SE.

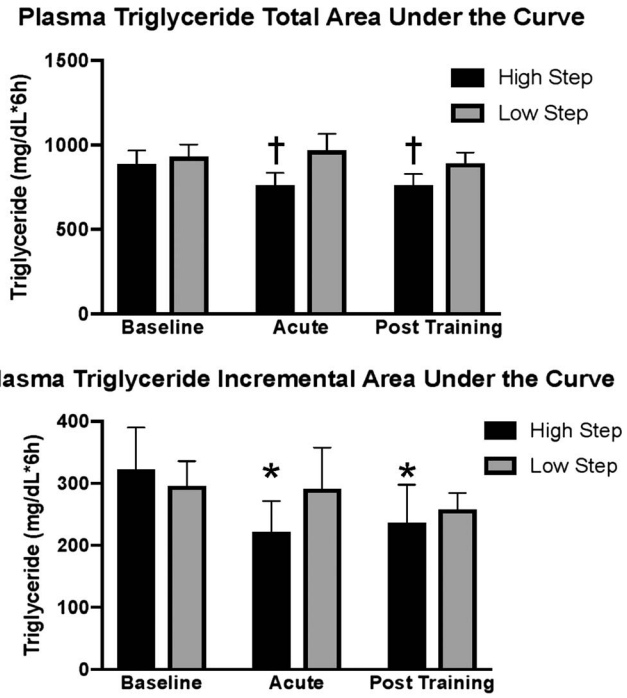

FIGURE 4—Total and incremental areas under the curve of plasma triglyceride concentration during HFTT at baseline, after a single bout of exercise (acute), and after 5 training bouts over the 9 d of training (posttraining). *Significantly different from baseline within treatment group, $P < 0.05$. †Significantly different from baseline within treatment group, $P < 0.01$. Data are reported as mean ± SE.

short-duration high-intensity aerobic training in terms of heart rate reduction, blood lactate reduction, and improved muscle oxygenation, all during submaximal exercise at a given absolute intensity (79% baseline $\dot{V}O_{2peak}$). In HS, all of these factors improved significantly ($P < 0.05$), yet in LS, none of these factors improved significantly. The only factor that improved significantly and equally in LS and HS was $\dot{V}O_{2peak}$ (i.e., 7%; $P < 0.05$).

We have previously reported that postprandial fat metabolism is improved (i.e., lower postprandial plasma triglyceride concentration and higher fat oxidation) acutely the day after a 1-h bout of running when daily step count is high, whereas it does not improve if step count is low and sitting time is long (8,9). This agrees with the present findings, and we have termed this phenomenon by which inactivity impairs acute adaptation as "exercise resistance" (16). In the present study, postprandial fat metabolism was measured at baseline (pretraining)

TABLE 3. Physiological responses to maximal and submaximal exercise testing.

	High Step		Low Step	
	Baseline	Posttraining	Baseline	Posttraining
Absolute $\dot{V}O_{2peak}$ ($L \cdot min^{-1}$)	2.51 ± 0.3	2.70 ± 0.2**	2.35 ± 0.2 7	2.52 ± 0.3*
Relative $\dot{V}O_{2peak}$ ($mL \cdot kg^{-1} \cdot min^{-1}$)	34.1 ± 3.3	36.9 ± 3.6**	32.2 ± 2.9	34.5 ± 3.3*
Submaximal $\dot{V}O_2$ ($L \cdot min^{-1}$)	1.98 ± 0.7	1.98 ± 0.9	1.87 ± 0.6	1.88 ± 0.2
Heart rate (bpm)	181 ± 5	169 ± 4**	181 ± 5	176 ± 4
HHb (AU)	21.7 ± 4.6	20.1 ± 4.1*	21.1 ± 6.5	22.1 ± 6.3
Blood lactate (mmol)	7.6 ± 0.8	6.7 ± 0.8*	7.2 ± 0.3	7.2 ± 0.4
RPE	15.6 ± 0.8	13.7 ± 0.5 *	15.7 ± 0.4	14.5 ± 0.6***
Submaximal work rate (W)	135 ± 19	135 ± 19	126 ± 15	126 ± 15

All data are reported as mean ± SE.
*Significantly different from baseline (i.e., pretraining) within treatment group, $P < 0.05$.
**Significantly different from baseline (i.e., pretraining) within treatment group, $P < 0.01$.
***Compared with baseline within treatment group, $P = 0.07$.

and again after one bout of training and then also after five bouts of short-term training. In HS, the magnitude of improvement was the same after one bout of acute training or five bouts regarding the improvement of the postprandial plasma TG response and increased fat oxidation. However, in LS, either after one bout of acute exercise or five bouts of short-term training, there was a failure to significantly improve the postprandial plasma TG response or increase fat oxidation compared with baseline. The similar improvement that occurred in fat metabolism in HS after one and five bouts of training suggests that improvements are derived from the last bout of exercise and do not appear to accumulate with continued training, at least in the short term. This agrees with previous observations suggesting no additive effect of exercise bouts for further improvement of postprandial triglycerides on consecutive days (21,22). The fact that fat metabolism remained at baseline levels in LS after one or five bouts of training suggests that whatever is causing "exercise resistance" does not lessen with more short-term training when steps per day remain low.

Exercise has been a well-documented method to attenuate the rise in postprandial lipemia (23–27) and prevent long-term impairment to cardiovascular health and function (28–30). However, recent epidemiological evidence suggests that exercise training may not reduce the incidence of disease and other morbidities, and even death, in people who spend a large amount of time sitting (31,32). Despite well-established (1,15) guidelines and recommendations, exercise performed in accordance with these recommendations (e.g., 30 $min \cdot d^{-1}$ of vigorous intensity exercise) may not be sufficient to overcome the detrimental metabolic effects of long periods of background inactivity and sedentary time (16). From the

TABLE 2. Overall postprandial substrate oxidation during the HFTT at baseline (pretraining), after a single bout of exercise (acute), and after 5 training bouts over the 9 d of training period (posttraining).

	High Step			Low Step		
	Baseline	Acute	Posttraining	Baseline	Acute	Posttraining
RER	0.83 ± 0.01	0.79 ± 0.01*	0.80 ± 0.01*	0.83 ± 0.01	0.82 ± 0.01	0.81 ± 0.01
Fat oxidation (%)	58.5 ± 3.18	70.7 ± 2.32*	67.3 ± 2.10*	57.7 ± 3.89	62.6 ± 2.81	63.9 ± 2.57
Fat oxidation (kcal/6 h)	310 ± 18	384 ± 25*	369 ± 16.*	330 ± 37	352 ± 43	351 ± 29
CHO oxidation (%)	41.5 ± 3.2	29.3 ± 2.3*	32.7 ± 2.1*	42.3 ± 3.9	37.4 ± 2.8	36.1 ± 2.6
CHO oxidation (kcal/6 h)	217 ± 19	158 ± 12	181 ± 14	234 ± 22	204 ± 11	201 ± 23
Total energy expenditure (kcal/6 h)	527 ± 19	542 ± 26	550 ± 19	564 ± 40	555 ± 45	552 ± 4

Data are reported as mean ± SE.
*Significantly different from baseline ($P < 0.05$).

present study, it appears that taking only approximately 5000 steps per day may not be sufficient physical activity, at least to maintain healthy postprandial fat metabolism and also metabolic responsiveness to short-term training. As mentioned below, we have recently observed that a healthy postprandial response regarding fat metabolism is seen when taking approximately 8500 steps per day and that taking 5000 step per day or lower is insufficient (10). We were not aware of those results at the time the present study was implemented, and we chose ~16,000 steps per day for the HS group to ensure an adequate stimulus. However, it is possible that 8500 steps per day might have been sufficient to elicit the classic training response observed in the HS group. Further investigation is warranted.

Evidence has emerged that prolonged inactivity and sedentary time may impede or eliminate some positive effects classically associated with acute exercise (8,16,33). Kim et al. (16) found that people who sat for >14 $h \cdot d^{-1}$ did not show the "classic" attenuation of postprandial lipemia and increased fat oxidation on the day after exercise (i.e., 1 h running at 67% $\dot{V}O_{2max}$) when step count was low (i.e., <1675 steps per day) (9,34). This was confirmed by Akins et al. (8) who also observed that 1 h of running failed to improve postprandial metabolism in people who sat for prolonged periods and took ~4000 steps per day. Some studies suggest that breaking up sedentary time, independent of total time in moderate to vigorous physical activity, may be able to attenuate postprandial increases in plasma TG concentration and insulin at least if activity is increased during that postprandial measurements are made (33–36). This makes sense from the perspective that contracting muscle increases plasma glucose and triglyceride uptake. Our approach has been to measure postprandial metabolism using an HFTT beginning the morning after inactivity/exercise, with the premise that cellular adaptations will be manifest during the 14- to 18-h period after activity/exercise. We have recently shown that breaking up prolonged sitting with hourly bouts of 4-s cycle sprints (5×) prevents the next day's impairment of fat metabolism due to inactivity (37). This observation agrees with the idea that "exercise resistance" is caused by the accumulation of a product generated by inactivity and which can be inhibited by hourly bouts of high-intensity cycling performed in 4-s bouts. We also recently reported that a healthy postprandial response to a high-fat meal occurs when taking 8500 or more steps per day, whereas taking 2500 or 5000 steps per day is equally insufficient for improving fat metabolism the day after acute exercise (10). Our present findings in HS (i.e., 16,048 steps per day) and LS (i.e., 4767 steps per day) agree with these observations.

Important comparisons in the present study were made during exercise at a constant absolute intensity (i.e., 79% of baseline $\dot{V}O_{2peak}$), whereas sensitive measures of cardiometabolic adaptations were reflected in the magnitude of reductions in heart rate, blood lactate, HHb concentrations, and RPE (Table 3). Although all four of these measures were significantly reduced ($P < 0.05$) in HS, thus displaying the classic pattern of improved aerobic metabolism, none of the four measures were improved significantly in LS. The heart rate responses during submaximal exercise were interesting in that HS displayed a 12-bpm reduction in heart rate ($P < 0.01$) whereas LS had a nonsignificant 5-bpm reduction in heart rate ($P = 0.08$) (Table 3). It is possible that with more subjects, the 5-bpm reduction in LS might become statistically significant. Given that LS increased their $\dot{V}O_{2peak}$ by ~7%, it would be expected that submaximal heart rate would be reduced to some extent, but under these conditions, it was relatively small.

A significant limitation of the present study is that baseline measures of steps per day were not made in these subjects, adding uncertainty as to how much the LS and HS regimes differed from the subject's normal activity. The normal range of steps per day for college students has been reported as ~7,000–11,000 (38), and we have recently reported that normal activity was ~10,500 steps per day in a cohort similar to the present subjects (10). Therefore, LS is assumed to have reduced daily steps by approximately 5000, whereas HS probably increased daily steps by approximately 5000. This raises the possibility that LS might have experienced a detraining effect and/or HS experienced a training effect from the alterations in steps per day during the 9-d training period. We cannot discount that possibility. However, it seems unlikely for two reasons. First, normal walking for active young healthy college-age individuals is performed at such low intensity (20%–25% $\dot{V}O_{2max}$) that the metabolic and cardiovascular stress is very low (39). Meta-analyses suggest that healthy college-age individuals can raise or lower their steps, in our case by 5000 per day, without altering $\dot{V}O_{2max}$ (40,41). Second, and more directly, the $\dot{V}O_{2peak}$ results of the present study suggest little influence of daily step count on causing adaptations. Both the LS and the HS groups performed the same training, and despite the estimated 5000 steps per day decrease and increase in walking, respectively, both groups displayed the same 7% increase in $\dot{V}O_{2peak}$. $\dot{V}O_{2peak}$ posttraining would be expected to be different in LS versus HS given their more than threefold difference in steps per day. These observations again suggest that increased steps per day seemed to have little influence, in these subjects, on the positive cardiovascular adaptations to training. However, when step count (i.e., physical activity) becomes too low (<8500 steps per day) (10), "exercise resistance" impairs metabolic adaptations but has little influence on $\dot{V}O_{2peak}$.

The present study provides no direct information as to the possible mechanism by which reducing steps and being more inactive prevents exercise and training induced improvements in postprandial lipemia and fat oxidation as well as preventing cardiometabolic improvements during submaximal exercise. One theory is that inactivity reduces muscle LPL activity (8). It has been observed that 6 h of hindlimb immobilization in rats resulted in an increase in thioredoxin interacting protein expression and mRNA and that this may interfere with the stimulation of various proteins involved with metabolism such as LPL (42). Another factor that is influenced by inactivity is GPIHBP1, which is LPL's partner for inserting it into the capillary endothelium (43). Although the mechanisms remain

unclear, it might be that inactivity causes a series of cellular events that are distinct from the positive molecular stimuli of aerobic exercise (e.g., PGC-1α) (44). In other words, inactivity is not simply a lack of exercise. It is possible that the inactivity of the LS group triggered cellular events that made them less responsive to the metabolic stimuli of aerobic training, except $\dot{V}O_{2peak}$.

There has been debate regarding why some people do not display much adaptation to aerobic training. One argument is that they are "physiological nonresponders" for unknown, possibly genetic reasons (45). The other argument is that the training is not sufficiently intense (46). The present training was equally intense in LS and HS, but LS showed little adaptation in variables that are related to muscle metabolism such as postprandial lipemia, fat oxidation, blood lactate concentration, muscle deoxygenation, and RPE during exercise. Therefore, the present observations favor the idea that a nonresponse to training, at least during submaximal exercise and involving metabolic factors, could in some circumstances be due to high background inactivity (i.e., low activity). This case has been recently made for chronic hyperglycemia as a potential negative regulator of aerobic adaptation, in part, via glucose-mediated modifications of the extracellular matrix, impaired vascularization, and aberrant mechanical signaling in the muscle (7). The observation that LS showed no statistically significant improvements in measures of stress during submaximal exercise should be considered in light of the training being only 5 intense bouts over 9 d. Therefore, it should not be assumed that subjects taking LS (<5000 steps per day) will not improve metabolic factors during submaximal exercise after weeks or months of training.

However, one adaptation to training that was not impaired in LS was their 7% increase in $\dot{V}O_{2peak}$. Aerobic training usually increases $\dot{V}O_{2peak}$ because of combinations of cardiovascular factors such as increased stroke volume and/or blood volume and muscle metabolic factors such as increased mitochondria and a-vO_2 difference. It is possible that cardiovascular factors were not as responsive to inactivity in LS as were the muscle metabolic factors.

Although Kim et al. (16) and one other study (8) also induced "exercise resistance" by reducing daily steps to <2000 and <4000 steps per day, respectively, and used the same HFTT testing procedures, these previous observations were limited to acute exercise bouts. In both of these studies, a 1-h bout of exercise at ~65% $\dot{V}O_{2peak}$ failed to improve postprandial metabolic responses when activity and steps per day were low. The lowering of postprandial triglycerides the day after exercise is a typical response, at least in subjects not limiting steps per day (23,25–27). The present design emphasizes the consequences of daily physical inactivity beyond responses to a single bout of acute exercise and into a paradigm of short-term aerobic training. Indeed, epidemiological studies are documenting that people who meet current exercise recommendations (e.g., 150–300 min·wk^{-1} of "moderate to vigorous physical activity") (1) may not realize the reduced risk of CVD potentially associated with meeting guidelines if these individuals are also inactive for the remainder of the day (32,47,48). It seems that in this interplay, prolonged inactivity reduces the potency of the stimulus provided by at least short-term exercise training (8,16,33). The findings from this investigation provide evidence explaining, in part, the observations reported in previous epidemiological studies that have found some individuals who are meeting published guidelines for exercise training but not realizing the reduced risk of CVD in association with a low background of physical activity (i.e., high inactivity) (16,32,47,49,50).

In conclusion, these data indicate that during a period of short-term intense aerobic training, 11 d of background inactivity from a daily step reduction (i.e., LS; <5000 steps per day) prevents improvements in postprandial lipemia and fat oxidation seen when step count is high (i.e., HS; 16,000 steps per day). Furthermore, reducing steps to approximately 5000 steps per day prevented some classic whole-body training adaptations during submaximal exercise from being manifested such as a significant reduction in HR, blood lactate, muscle deoxygenation, and RPE. All of these measures showed significant improvement when background steps were high but displayed no significant improvement when background steps were low. The only measure that increased equally (i.e., 7%; $P < 0.05$) with the short-term intense training in HS and LS was $\dot{V}O_{2peak}$.

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