Breaking prolonged sitting reduces postprandial glycemia in healthy, normal-weight adults: a randomized crossover trial[1–3]

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ABSTRACT

Background: Sedentary behavior is a risk factor for cardiometabolic disease. Regularly interrupting sedentary behavior with activity breaks may lower this risk.

Objective: We compared the effects of prolonged sitting, continuous physical activity combined with prolonged sitting, and regular activity breaks on postprandial metabolism.

Design: Seventy adults participated in a randomized crossover study. The prolonged sitting intervention involved sitting for 9 h, the physical activity intervention involved walking for 30 min and then sitting, and the regular-activity-break intervention involved walking for 1 min 40 s every 30 min. Participants consumed a meal-replacement beverage at 60, 240, and 420 min.

Results: The plasma incremental area under the curve (iAUC) for insulin differed between interventions (overall $P < 0.001$). Regular activity breaks lowered values by 866.7 IU · L^{-1} · 9 h^{-1} (95% CI: 506.0, 1227.5 IU · L^{-1} · 9 h^{-1}; $P < 0.001$) when compared with prolonged sitting and by 542.0 IU · L^{-1} · 9 h^{-1} (95% CI: 179.9, 904.2 IU · L^{-1} · 9 h^{-1}; $P = 0.003$) when compared with physical activity. Plasma glucose iAUC also differed between interventions (overall $P < 0.001$). Regular activity breaks lowered values by 18.9 mmol · L^{-1} · 9 h^{-1} (95% CI: 10.0, 28.0 mmol · L^{-1} · 9 h^{-1}; $P < 0.001$) when compared with prolonged sitting and by 17.4 mmol · L^{-1} · 9 h^{-1} (95% CI: 8.4, 26.3 mmol · L^{-1} · 9 h^{-1}; $P < 0.001$) when compared with physical activity. Plasma triglyceride iAUC differed between interventions (overall $P = 0.023$). Physical activity lowered values by 6.3 mmol · L^{-1} · 9 h^{-1} (95% CI: 1.8, 10.7 mmol · L^{-1} · 9 h^{-1}; $P = 0.006$) when compared with regular activity breaks.

Conclusion: Regular activity breaks were more effective than continuous physical activity at decreasing postprandial glycemia and insulinemia in healthy, normal-weight adults. This trial was registered with the Australian New Zealand Clinical Trials registry as ACTRN12610000953033. *Am J Clin Nutr* 2013;98:358–66.

INTRODUCTION

Since the 1950s, there have been substantial increases in time spent engaged in sedentary behaviors such as television viewing and inactive forms of transportation (1). Time spent engaged in sedentary behaviors has been reported to be a risk factor for cardiovascular disease, type 2 diabetes (2), and all-cause mortality (2, 3). This association was still present among those participating in high levels of moderate-to-vigorous physical activity (4), which indicates that regular participation in high levels of physical activity does not fully protect against the risks associated with prolonged bouts of sedentary behavior. However, it appears that the pattern in which total sedentary time is accumulated may partially attenuate the negative effects of sedentary behavior. Results from 2 observational studies (5, 6) indicate that individuals who accumulate their sedentary time with longer uninterrupted bouts have a worse cardiovascular and metabolic risk factor profile than those whose total sedentary time is the same, but is regularly interrupted with bouts of predominantly light physical activity (5, 6).

Investigations have attempted to explain the metabolic processes responsible for the relations between sedentary behavior and risk factors for cardiovascular and metabolic disease. In young healthy men and women, 24 h of sedentary behavior resulted in dramatic increases in the amount of insulin required to clear a standardized glucose infusion (7). In rats, 12–240 h of immobilization caused marked reductions in lipoprotein lipase activity and triglyceride uptake, which returned to normal when rats were allowed to ambulate normally (8–11). From these observations, it is hypothesized that the influence of sedentary behavior on cardiovascular and metabolic risk may be mediated through the action of insulin, the upregulation of lipoprotein lipase activity, and triglyceride uptake. Measures of triglyceride (12, 13), glucose (14), and insulin (15) collected in the postprandial period have been shown to independently predict cardiovascular morbidity and mortality. This provides further support that interventions that lower postprandial glucose, insulin, and triglyceride concentrations may decease the risk of morbidity and mortality. Indeed, in a trial recently conducted in a small sample ($n = 19$) of overweight and obese participants, it was found that regularly interrupting sedentary behavior with short bouts of light- or moderate-intensity walking lowered postprandial glucose and insulin concentrations when compared with prolonged sitting (16). However, it is not known how

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[2] Supported by the University of Otago. Heinz-Watties (Hastings, New Zealand) provided the meal-replacement beverages used in this study.

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regularly interrupting sedentary behavior compares with a single continuous bout of physical activity in terms of lowering postprandial glucose and insulin concentrations. In addition, the effects on postprandial lipidemia of regularly interrupting sedentary behavior in comparison with prolonged sitting or continuous physical activity has not been investigated. Therefore, the primary aim of this study was to compare the effects of prolonged sitting, a single 30-min brisk walk followed by prolonged sitting, and sitting interrupted with regular short (1 min and 40 s) walks on postprandial glycemia, insulinemia, and lipidemia.

SUBJECTS AND METHODS

Subjects

Participants were recruited through the distribution of flyers and e-mails around the wider university campus (University of Otago, Dunedin, New Zealand). Eligible participants were 18–40 y of age, were nonsmokers, and did not have a history of diabetes, cardiovascular disease, or other medical conditions that prevented them from participating in physical activity or that affected lipid or carbohydrate metabolism, had a predominantly sedentary occupation and did not participate regularly in >2.5 h of physical activity per week. Participants were excluded from participation if they had a fasting blood glucose concentration >6.1 mmol/L; if fasting total cholesterol, LDL, or triglyceride concentrations were >50% above the New Zealand recommendations (6, 3, or 2.6 mmol/L, respectively); or if systolic or diastolic blood pressures were >140 and 90 mm Hg, respectively (**Figure 1**). A total of 70 participants [mean (±SD) age: 25.9 ± 5.3 y; BMI (in kg/m^2): 23.6 ± 4.0; **Table 1**], completed at least one experimental testing session and are included in the final analysis.

Study design

The study was a randomized crossover trial conducted in Dunedin, New Zealand, between February and October 2010. The University of Otago Human Ethics Committee approved the trial, and written informed consent was obtained from all participants before the screening procedures.

Preliminary testing

At least 7 d before participating in their initial intervention session, participants completed a maximal aerobic capacity assessment with the use of a modified version of the Bruce protocol (17) and a Stek 8020 treadmill. Starting at 3 km/h and 0% incline, increases in speed and incline were made every 3 min until a

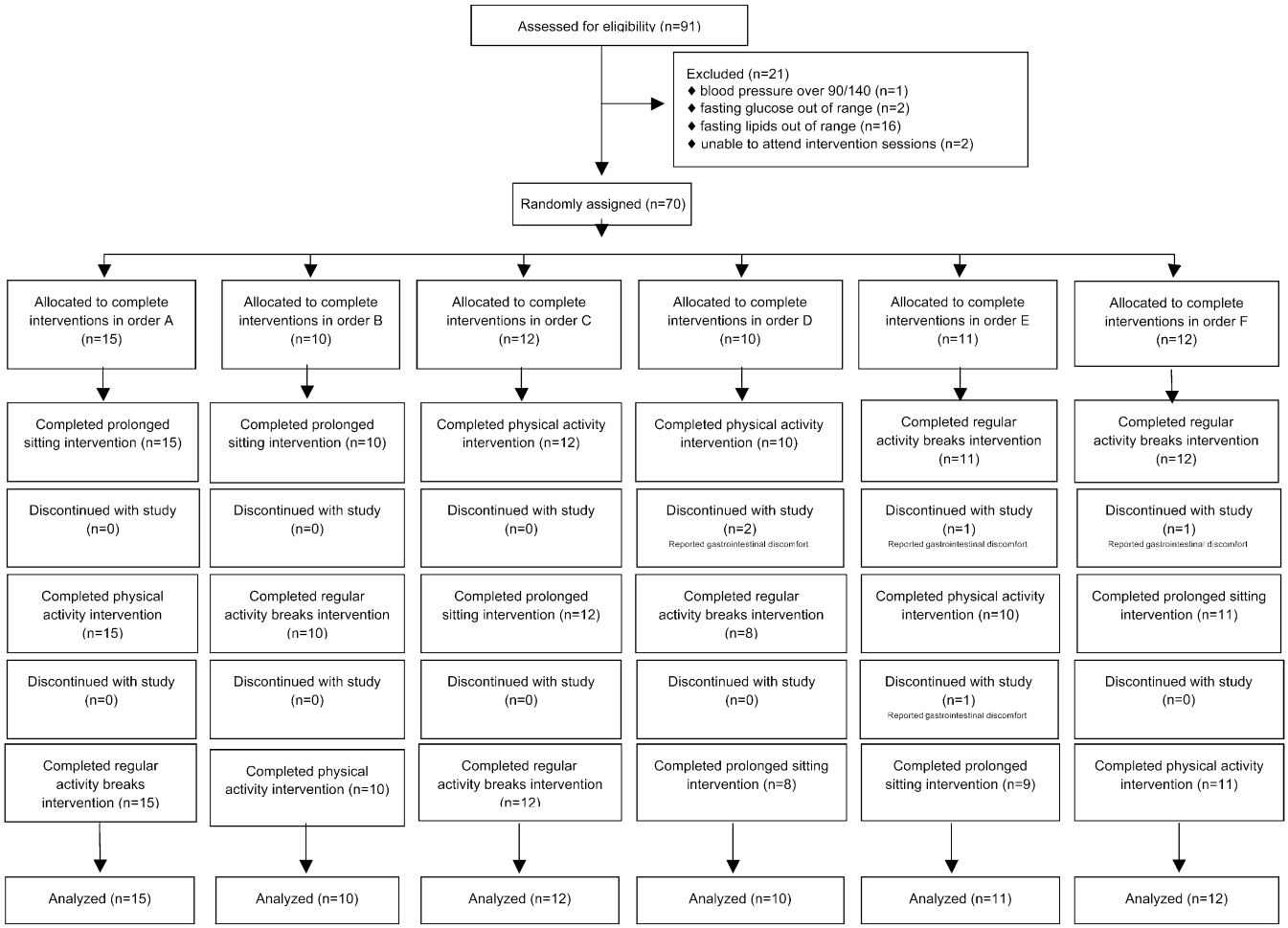

FIGURE 1. Participant flow diagram.

TABLE 1
Participant characteristics at the time of enrollment

Characteristic	All (n = 70)
Female [n (%)]	42 (60)
Age (y)	25.9 ± 5.3[1]
Cardiovascular disease factors, fasting (mmol/L)	
Total cholesterol	4.3 ± 0.7
LDL cholesterol[2]	2.5 ± 0.7
HDL cholesterol	1.4 ± 0.5
Triglyceride	1.0 ± 0.4
Glucose	4.9 ± 0.5
Blood pressure (mm Hg)	
Systolic blood pressure	112.3 ± 10.2
Diastolic blood pressure	66.7 ± 6.9
Anthropometric measures	
Height (cm)	170.6 ± 9.7
Weight (kg)	68.0 ± 15.3
BMI (kg/m^2)	23.6 ± 4.0
Body fat (%)	23.3 ± 9.0
Waist circumference (cm)	76.0 ± 10.7
Hip circumference (cm)	99.7 ± 8.5
Waist-to-hip ratio	0.8 ± 0.1
Aerobic fitness	
Absolute maximal aerobic capacity (L/min)	3.0 ± 1.1
Relative maximal aerobic capacity (mL · kg^{-1} · min^{-1})	42.9 ± 10.3
Habitual physical activity (min/wk)	90 ± 42

[1] Mean ± SD (all such values).
[2] Calculated by using the Friedewald formula.

respiratory exchange ratio of 1.1 was recorded. Throughout the test, gas exchange was measured by using an online gas analysis system (Metalyzer II). The speed and incline estimated to elicit 60% maximal aerobic capacity was then determined by identifying the stage in the Bruce protocol at which 60% maximal aerobic capacity was reached. The speed and incline calculated to elicit 60% maximal aerobic capacity was used as the speed and incline in both the physical activity and regular-activity-break interventions.

Experimental protocol

Participants completed three 9-h interventions: *1*) prolonged sitting; *2*) physical activity, in which prolonged sitting was interrupted by a single continuous bout of physical activity; and *3*) regular activity breaks in which sitting was interrupted by 18 short bouts of activity. The sequence in which the participants received the 3 interventions was determined by random assignment. Each intervention was separated by a minimum of 6 d (median: 6 d; 25th and 75th percentiles: 6 and 13 d, respectively; 56% of periods between interventions were exactly 6 d) to allow participants to return to preintervention levels of all outcome measures. During the prolonged sitting intervention, participants sat continuously for 9 h, only moving from sitting to visit the bathroom when required. In the physical activity intervention, participants sat for 15 min, walked on the treadmill for 30 min, and then sat continuously for 8 h and 15 min. In the regular-activity-break intervention, participants performed the same amount of total activity as in the physical activity intervention, but did so by interrupting their sitting with eighteen 1-min 40-s bouts of brisk treadmill walking (total of 30 min) equally spaced over the 9-h period. The first short walk was performed 15 min after the beginning of the intervention. For each participant the treadmill was set at the same speed and incline for both the physical activity and regular-activity-break interventions. Measurement of gas exchange was conducted throughout all walking on the treadmill (Metalyzer II) to monitor exercise intensity. When sitting, participants were permitted to read, watch television, or work on a laptop computer.

Randomization

Participants were randomly assigned to complete the 3 interventions in 1 of 6 possible orders. The randomization sequence was created by MP using Stata software (version 11 for Mac; StataCorp) and concealed in sequentially numbered, brown sealed envelopes before participant enrollment in the study.

Standardization of prior diet and exercise

Participants were asked to avoid physical activity for 3 d before and abstain from the consumption of alcohol for 24 h before each intervention session. In the 24 h before their first intervention session, participants were asked to record everything they ate and drank. A copy of this record was given to participants who were then asked to consume the same foods and beverages in the 24 h preceding each of the 2 subsequent interventions. The intervention session only commenced if participants verified their compliance with both the physical activity and dietary-standardization protocols.

Test meals

Participants consumed a meal-replacement beverage (Complan; Heinz-Watties) at 1, 4, and 7 h during each 9-h testing session. Each meal-replacement beverage was consumed in <15 min and was prescribed to provide 0.46 g fat, 0.54 g protein, and 1.12 g carbohydrate per kg body mass. Participants consumed water ad libitum during the first intervention session, and the volume ingested was replicated in subsequent intervention sessions.

Blood collection protocol

Participants arrived at the clinic between 0730 and 0800 after an overnight fast of ≥10 h. The 9-h testing session began with the collection of a fasting blood sample. A total of 16 blood samples were collected from each participant. One sample was collected each hour between baseline and 9 h, and 6 additional samples were collected 30 and 45 min after the consumption of each meal-replacement beverage. Blood samples were collected by syringe from a venous cannula situated in the lower arm, and blood was transferred immediately to EDTA-containing tubes stored on ice. Samples were centrifuged (1500 × g for 15 min at 4°C) within 3 h of collection (18–20), and plasma was stored at −80°C for later analysis.

Physiologic measures

Heart rate was recorded (S725×; Polar Electro) every 5 s for the duration of the 9-h testing session, which provided a total of 6480 measurements. The volume of oxygen consumed and carbon dioxide produced was measured (Metalyser II) over 5 min

of steady state concentrations at baseline (after the participant had been sitting for ~15 min) and hourly, at rest, throughout each experimental intervention session. This provided 10 measurements of mean oxygen consumption and carbon dioxide production at steady state that were used to calculate the mean respiratory exchange ratio. Respiratory gases were also measured during each bout of treadmill walking to give the mean oxygen consumption and carbon dioxide production. These were used to calculate exercise intensity (percentage maximal aerobic capacity) for each of the 1-min 40-s walks in the regular-activity-break intervention and the 30-min walk in the physical activity intervention.

Analytic methods

Plasma triglyceride concentrations were measured by using the glycerol phosphate oxidase enzymatic method. Plasma glucose concentrations were measured by using the hexokinase enzymatic method. Kits and calibrators for analysis of glucose and triglycerides were from Roche Diagnostics, and the analysis was conducted on a Cobas Mira Plus analyzer. Plasma insulin concentrations were measured by using electrochemiluminescence methods on an Elecsys 2010, with kits and calibrators from Roche Diagnostics. All samples from the same participant were assayed in a single run. Intraassay CVs were 3.10% for glucose, 3.10% for triglycerides, and 2.63% for insulin.

Statistical analysis

Data were analyzed by using Stata software (version 11.0 for Mac; StataCorp). The primary outcome for this study was a difference in incremental AUCs (iAUCs) for triglyceride, glucose, and insulin between interventions.

With the use of the glucose, insulin, and triglyceride concentrations measured from each of the 16 time points across each intervention, iAUCs were computed by first calculating the total AUC with the trapezoid rule (which approximates the AUC by considering the areas between continuous time points to be trapezoid in shape; the areas of the individual trapezoids are then summed to provide the total AUC) and then subtracting the area from the baseline concentration over the 9-h period. This provided a single value for each outcome per participant-intervention combination. Differences in the proportions of the planned samples that were analyzed were compared across the 3 interventions by using chi-square tests for triglycerides, glucose, and insulin. The effects of the different interventions on the summary measures of glucose, insulin, and triglyceride iAUCs were evaluated by using a mixed-model regression (xtmixed command; StataCorp) (21) with the intervention being the predictor of interest, while age, sex, and BMI were controlled for (22–24). A random-participant effect was used to accommodate the clustering effects of 3 measures being included from each participant. Potential nonlinearities in associations with continuous predictors were assessed by using scatter plots of residuals compared with each predictor. Residuals from the models were also visually checked for approximately normal distributions and homoscedasticity over predictions. Substantial departures from the assumptions of the models were not observed; thus, log transformations were not required. Inclusion of the variables age, sex, and BMI in the model was determined a priori as each was previously associated with differences in postprandial responses (22–24).

Carryover effects were expected to be minimal because of the minimum 6-d washout period between consecutive interventions; the effects of physical activity on postprandial response have been shown to dissipate within 72 h (25). The presence of first-order carryover effects was, however, investigated for each outcome by adding a variable to the model that specified the previously performed intervention (including no previous intervention, so that this variable had 4 levels). First-order carryover effects were not found to be significant for glucose, insulin, or triglyceride iAUC responses (all $P > 0.771$); therefore, carryover effects were not included in the final models.

Period effects were not expected to bias the estimates of the intervention effects because of the balanced crossover design of the study. The presence of period effects for each outcome was, however, investigated by adding a variable to the model that specified the period in which it occurred (period 1, period 2, or period 3). Period effects were not found to be significant for glucose, insulin, or triglyceride iAUC responses (all $P > 0.060$) and thus were not included in the final model. Because period effects were almost statistically significant for glucose ($P = 0.060$), but not for insulin or triglyceride ($P > 0.10$), models for glucose were rerun with the period included as an additional predictor. However, the inclusion of period effects did not meaningfully affect the results (the intervention effect sizes all changed by <4% and statistical significance was unaffected); therefore, these results are not presented.

Summary measures of the resting respiratory exchange ratio and heart rate were computed by taking the mean of measurements collected across each intervention period ($n = 10$ for respiratory exchange ratio, $n = 6480$ for heart rate). This provided a single value for each outcome per participant-intervention combination. The effect of the interventions on the summary measures for respiratory exchange ratio and heart rate were again assessed by using a mixed-model regression, with the intervention being the predictor of interest, while age, sex, and BMI were controlled for and a random-participant effect was included to accommodate the repeated measures from the 3 interventions. Model diagnostics were performed as described above for iAUC outcomes. A natural log transformation was used on respiratory exchange ratio data because the residuals from the model showed a positive skew, which was improved by the transformation. Log transformations were not required for heart rate data.

All analyses were conducted by using a modified intention-to-treat principle, which meant that all 70 participants who were randomly assigned to a treatment order were included in the final model, subject to available data. Statistical significance was 2-sided and set at $P < 0.05$. Pairwise comparisons between interventions were only undertaken when the overall intervention effect was statistically significant. In such cases, reported pairwise comparison P values and CIs were unadjusted for multiple comparisons.

Sample size was determined to provide 80% power to detect a 0.5-SD difference in the summary measures of postprandial metabolism between any of the 3 interventions by using a 2-sided test with $\alpha = 0.05$ and without making any assumptions about the correlations between repeated measures on each participant. After 10% attrition was accounted for, 70 participants were required to be recruited for this study.

RESULTS

Of the 70 participants who were scheduled to participate, 5 individuals withdrew or were asked to withdraw after reporting gastrointestinal discomfort after the first or second day of testing (Figure 1). All 70 participants who underwent randomization to a treatment order were included in the final analysis. Participant characteristics at the time of recruitment are summarized in Table 1.

The percentage of maximal aerobic capacity achieved in the 30-min walk in the physical activity intervention was 15.0% (95% CI: 11.1, 18.8%; $P < 0.001$) higher than the average achieved across the 18 walks in the regular-activity-break intervention. The overall effect of intervention on mean heart rate achieved over the 9-h testing session was significant (overall $P < 0.001$). Compared with prolonged sitting, the average heart rate was 8 beats/min (95% CI: 4, 11; $P < 0.001$) higher in the physical activity intervention and 9 beats/min (95% CI: 5, 12 beats/min; $P < 0.001$) higher in the regular-activity-break intervention (**Table 2**). Mean heart rate did not differ between the physical activity and regular-activity-break interventions (difference: 0 beats/min; 95% CI: −4, 3 beats/min; $P = 0.608$). The overall effect of intervention on mean resting respiratory ratio achieved over the 9-h testing session was significant (overall $P = 0.040$). The mean resting respiratory exchange ratio over the 9-h testing session for the regular-activity-break intervention was 3% (95% CI: 1%, 6%; $P = 0.033$) greater than that for the prolonged sitting intervention and 3% (95% CI: 1%, 6%; $P = 0.025$) greater than that for the physical activity intervention (Table 2). No significant difference was found between the prolonged sitting and the physical activity interventions (difference: 0%; 95% CI: −2%, 3%; $P = 0.917$).

No significant differences in the total amount of carbohydrate, protein, fat, or energy provided from each of the meal-replacement beverages were found between interventions (all $P \geq 0.788$). The mean (±SEM) amounts of macronutrients provided by each meal-replacement beverage were 31.4 ± 6.6 g fat, 36.8 ± 7.7 g protein, 76.4 ± 16.1 g carbohydrate, and 741.6 ± 155.7 kcal energy.

Greater than 99% of all planned samples were obtained in such a way that triglyceride and glucose measurements could be made. Greater than 97% of all planned samples were obtained in such a way that valid insulin measurements could be made (the lower percentage was a result of the insulin assay being more sensitive to hemolysis). No significant differences in the proportion of planned samples that were obtained for triglyceride (chi-square, $P = 0.544$), glucose (chi-square, $P = 0.544$), or insulin (chi-square, $P = 0.969$) were found between the interventions.

Plasma glucose, insulin, and triglyceride concentrations over the 9-h testing sessions for the 3 interventions are shown in **Figure 2**, and the derived iAUC adjusted for age, sex, and BMI are shown in **Table 3**. The overall effect of intervention on plasma glucose iAUC was significant (overall $P < 0.001$). The regular-activity-break intervention lowered plasma glucose iAUC by 18.9 mmol · L^{-1} · 9 h^{-1} (95% CI: 10.0, 28.0 mmol · L^{-1} · 9 h^{-1}; $P < 0.001$) compared with the prolonged sitting intervention and by 17.4 18.9 mmol · L^{-1} · 9 h^{-1} (95% CI: 8.4, 26.3 mmol · L^{-1} · 9 h^{-1}; $P < 0.001$) compared with the physical activity intervention. The effects of the prolonged sitting and physical activity interventions on plasma glucose iAUC did not differ significantly (difference: 1.6 mmol · L^{-1} · 9 h^{-1}; 95% CI: −7.4, 10.6 mmol · L^{-1} · 9 h^{-1}; $P = 0.730$).

The overall effect of intervention on plasma insulin iAUC was significant (overall $P < 0.001$). The regular-activity-break intervention lowered plasma insulin iAUC by 866.7 IU · L^{-1} · 9 h^{-1} (95% CI: 506.0, 1227.5 IU · L^{-1} · 9 h^{-1}; $P < 0.001$) when compared with the prolonged sitting intervention and by 542.0 IU · L^{-1} · 9 h^{-1} (95% CI: 179.9, 904.2 IU · L^{-1} · 9 h^{-1}; $P = 0.003$) when compared with the physical activity intervention. The effects of the prolonged sitting and physical activity interventions on plasma insulin iAUC did not differ significantly (difference: 324.7 IU · L^{-1} · 9 h^{-1}; 95% CI: −38.0, 687.4 IU · L^{-1} · 9 h^{-1}; $P = 0.079$).

The overall effect of intervention on plasma triglyceride iAUC was significant (overall $P = 0.023$).The effects of the physical activity and regular-activity-break interventions on plasma triglyceride iAUC did not differ significantly from the effects of the prolonged sitting intervention. The mean difference in iAUC between the physical activity intervention and the prolonged sitting intervention was 3.8 mmol · L^{-1} · 9 h^{-1} (95% CI: −0.7, 8.3 mmol · L^{-1} · 9 h^{-1}; $P = 0.098$) and between the regular-activity-break and prolonged sitting interventions was 2.4 mmol · L^{-1} · 9 h^{-1} (95% CI: −2.0, 6.9 mmol · L^{-1} · 9 h^{-1}; $P = 0.284$). The physical activity intervention lowered the plasma triglyceride

TABLE 2
Physiologic responses during the prolonged sitting, physical activity, and regular-activity-break interventions measured in 70 healthy participants[1]

Physiologic measures	Prolonged sitting ($n = 65$)	Physical activity ($n = 68$)	Regular activity breaks ($n = 68$)	P
Percentage of maximal aerobic capacity achieved during activity	NA[2]	60.5 (57.9, 63.2)[3]	45.6 (42.8, 48.4)	<0.001
Mean heart rate (beats/min)[4]	77.0 (74.6, 79.4)	84.7 (82.3, 87.2)[5]	85.6 (83.2, 88.0)[5]	<0.001
Mean resting respiratory exchange ratio[6]	0.90 (0.88, 0.92)	0.90 (0.88, 0.92)	0.93 (0.91, 0.95)[7,8]	0.040

[1] All values are adjusted means of covariates (95% CIs) and were compared by using mixed models adjusted for age, sex, and BMI. In the prolonged sitting intervention, participants sat for 9 h; in the physical activity intervention, participants walked on the treadmill continuously for 30 min at 60% of maximal aerobic capacity in the morning and sat for 8.5 h; and in the regular-activity-break intervention, participants walked on the treadmill for 1 min 40 s every 30 min over the 9-h intervention period.
[2] Not applicable.
[3] Significantly different from regular activity breaks, $P < 0.001$.
[4] Mean of measurements collected every 5 min over the 9-h testing session.
[5] Significantly different from prolonged sitting, $P < 0.001$.
[6] Mean of 5-min steady state measurements collected hourly, while the subjects were sitting, over the 9-h testing session.
[7] Significantly different from prolonged sitting, $P = 0.033$.
[8] Significantly different from physical activity, $P = 0.025$.

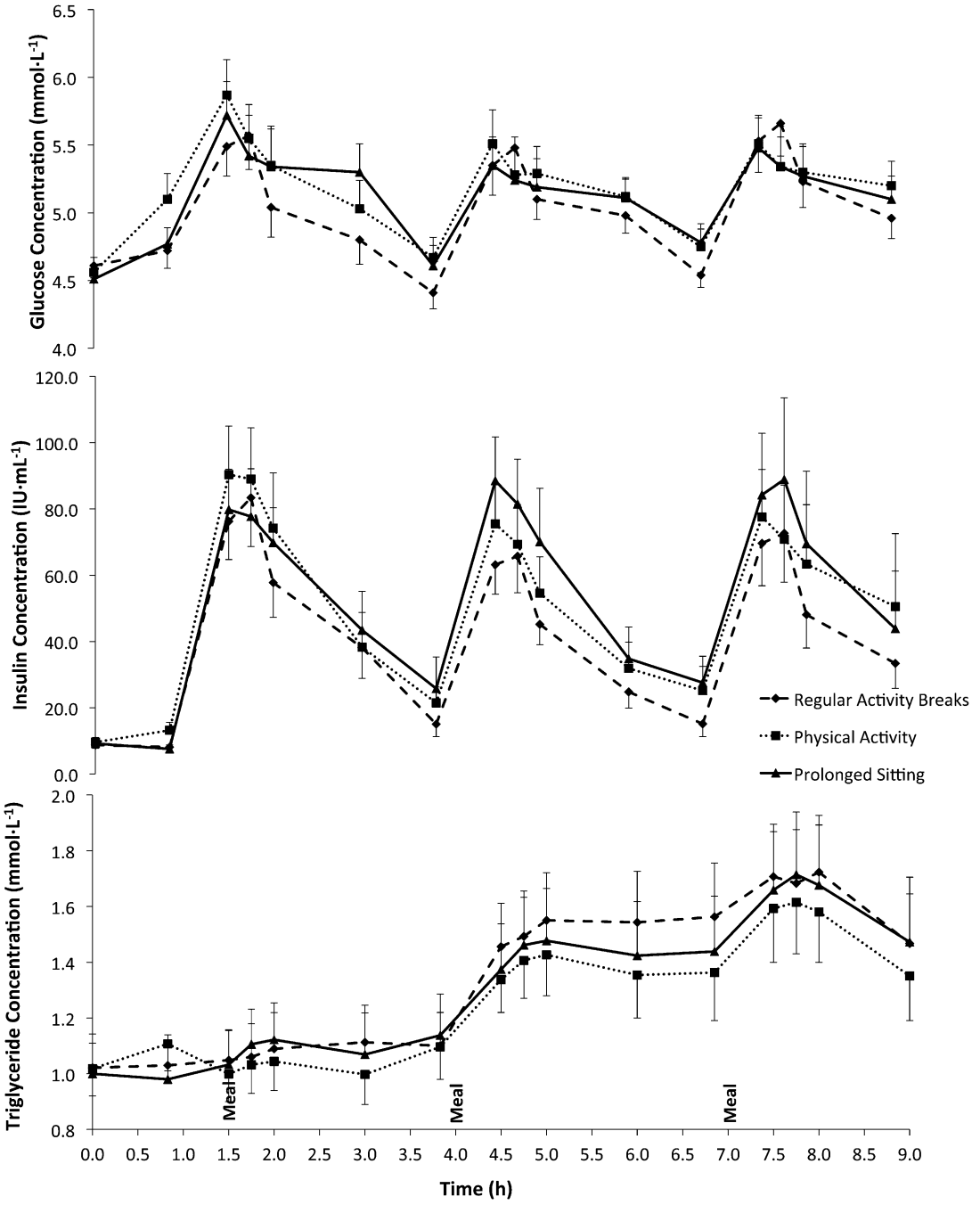

FIGURE 2. Mean (95% CI) plasma glucose, insulin, and triglyceride concentrations measured over a 9-h period during the prolonged sitting, physical activity, and regular-activity-break interventions measured in 70 healthy participants.

iAUC by 6.3 mmol · L^{-1} · 9 h^{-1} (95% CI: 1.8, 10.7 mmol · L^{-1} · 9 h^{-1}; $P = 0.006$) when compared with the regular-activity-break intervention.

DISCUSSION

The results of the current study showed that regularly breaking prolonged sitting with short (1 min 40 s) bouts of activity is more effective than a single continuous (30 min) bout of physical activity at lowering postprandial glucose and insulin concentrations in healthy, normal-weight adults. Observational evidence indicates that sedentary behaviors such as sitting are associated with type 2 diabetes (2), cardiovascular disease, and all-cause mortality (3). In addition, regularly interrupting periods of prolonged sitting have been associated with favorable metabolic risk profiles (5, 6), including lower 2-h plasma glucose concentrations (5). Our results extend these observations by providing strong experimental evidence that regularly breaking sedentary behavior has immediate and positive effects on postprandial glucose and insulin concentrations, which are not seen after a single bout of continuous physical activity.

The 37% reduction in plasma glucose iAUC and the 18% reduction in plasma insulin iAUC observed when regular activity breaks were compared with continuous physical activity is a novel

TABLE 3
Nine-hour plasma triglyceride, insulin, and glucose incremental AUC responses during the prolonged sitting, physical activity, and regular-activity-break interventions measured in 70 healthy participants[1]

iAUC	Prolonged sitting (n = 65)	Physical activity (n = 68)	Regular activity breaks (n = 68)	P
Glucose (mmol · L^{-1} · 9 h^{-1})	48.8 (40.7, 57.0)	47.2 (39.1, 55.4)	29.9 (21.8, 38.0)[2,3]	<0.001
Insulin (IU · L^{-1} · 9 h^{-1})	3337.0 (2783.4, 3890.6)	3012.3 (2460.5, 3564.1)	2470.3 (1919.6, 3021.0)[2,4]	<0.001
Triglyceride (mmol · L^{-1} · 9 h^{-1})	24.0 (19.3, 28.6)	20.1 (15.6, 24.7)[5]	26.4 (21.8, 31.0)	0.023

[1] All values are adjusted means of covariates (95% CIs) and were compared by using mixed models adjusted for age, sex, and BMI. In the prolonged sitting intervention, participants sat for 9 h; in the physical activity intervention, participants walked on the treadmill continuously for 30 min at 60% of maximal aerobic capacity in the morning and sat for 8.5 h; and in the regular-activity-break intervention, participants walked on the treadmill for 1 min 40 s every 30 min over the 9-h intervention period.
[2] Significantly different from prolonged sitting, $P < 0.001$.
[3,4] Significantly different from physical activity: [3]$P < 0.001$, [4]$P = 0.003$.
[5] Significantly different from regular activity breaks, $P = 0.006$.

finding. The reductions of both plasma glucose iAUC (by 39%) and plasma insulin iAUC (by 26%) with the regular activity breaks, in comparison with prolonged sitting, are slightly greater in magnitude those observed when slightly longer activity breaks (2 min) were performed every 20 min over a 5-h period in overweight and obese individuals (16). The duration and intensity of activity in the physical activity intervention were chosen to comply with physical activity guidelines, which typically recommend 30 min of moderate-to-vigorous physical activity daily (26). However, the lack of a difference in insulin and glucose responses between the physical activity and prolonged sitting interventions may have occurred because the exercise was of insufficient duration and intensity. Reductions in postprandial glycemia and insulinemia were observed when physical activity of a higher intensity or longer duration was compared with inactivity (27).

The exact mechanism by which regular activity breaks reduce glucose and insulin responses is not clear. We proposed that the increases in carbohydrate oxidation with regular activity breaks, as indicated by the higher respiratory exchange ratio, stimulated an increased clearance of glucose from the bloodstream. The frequent nature of the short bouts of activity may have maintained an increased permeability of muscle cells to glucose (28). An alternative, or perhaps simultaneous mechanism, may have been that frequently performed light activity maintains glucose transporter type 4 in a position in the cell where it can be readily recruited to the cell surface in response to a minimal amount of activity (29).

Long-term glycemic control (based on glycated hemoglobin) has been associated with a decreased risk of developing diabetes (30) along with a decreased risk of developing diabetes-related complications and cardiovascular disease in those who already have diabetes (31). A simple nonpharmacologic aid that reduces postprandial glycemia on a daily basis is paramount to obtaining optimal long-term glycemic control. The results of the current study indicate that individuals who have occupations, which require them to sit for long periods, will reduce postprandial glycemia by regularly getting out of their chair and briskly walking up and down the corridor outside their office. Therefore, changes in the physical and social landscape of the work environment may be required to provide individuals opportunities to regularly break periods of prolonged sitting. Examples may include the following: moving the printer a distance away from those who use it frequently, installing software that prompts computer users to take regular breaks, or encouraging those who work in the same building to converse with colleagues face to face rather than on the phone or by e-mail. These easily achievable suggestions would encourage regular activity and improve health; however, the ramifications of these changes on work productivity and psychosocial well-being will need to be investigated.

In our study, physical activity induced a nonsignificant reduction in plasma triglyceride iAUCs compared with prolonged sitting. Lower postprandial plasma triglyceride iAUCs after both continuous and intermittent physical activity when compared with inactivity have been reported previously (32–34); however, in most cases, a reduction in triglyceride iAUC was only reported when postprandial measurement occurred 12–16 h after completion of exercise. Our results indicate that physical activity–induced reductions in postprandial lipidemia do not occur during the 8 h after 30 min of continuous exercise. Greater triglyceride responses observed in the regular-activity-break intervention may have been because of reduced insulin concentrations inducing a reduction in lipoprotein lipase activity in adipose tissue (35). In contrast, the trend toward a lower triglyceride concentration in the physical activity intervention (as compared with the regular-activity-break intervention) may have been a result of a small exercise-induced upregulation of lipoprotein lipase activity in muscle tissue.

Consideration should be given to the following aspects of the method that may have influenced the outcomes of the study. A liquid meal replacement was used to ensure accurate standardization of macronutrient delivery by body mass to each participant. It is unlikely that the metabolic effects of regular activity breaks would be limited to the consumption of liquid meals. Ideally, however, postprandial responses would be measured after consumption of foods regularly consumed by the target population.

The short duration of walking in the regular-activity-break intervention did not allow accurate measurement of the intensity of activity with indirect calorimetry. However, the average heart rate results indicated that the amount of absolute work did not differ between the physical activity and regular-activity-break interventions. Whereas not all participants completed the study, only 6% of possible data were missing because of dropouts, and this was not considered likely to have affected the results in any meaningful way.

We observed a reduction in glucose and insulin concentrations over a 9-h period. To determine whether these metabolic effects translate into lasting health benefits, long-term studies

investigating the effects of regular activity breaks are required to determine their direct effect on cardiovascular and metabolic disease outcomes. In addition, this study measured the effects of performing 1 min 40 s of brisk walking every 30 min. Further research is required to determine the optimal duration and frequency of activity breaks that will result in the greatest improvements in glycemic control. The crossover design, appropriate sample size, and high participant retention are among the strengths of our study. We chose a level of activity for the physical activity intervention that met current physical activity guidelines and has proven health benefits (26). However, the pattern of physical activity in the regular-activity-break intervention, while accumulating to a total of 30 min, did not meet current physical activity guidelines, which specify that individual bouts of activity must be ≥10 min in duration (26). The direct comparison of these 2 patterns of activity makes this study the first to provide evidence that regular activity breaks impart acute metabolic benefits that a single bout of continuous physical activity does not. Given these positive metabolic effects observed in healthy participants, it seems prudent that physicians consider providing prescriptive advice to all patients—both healthy and at risk of cardiovascular and metabolic disease—to regularly break periods of prolonged sitting with brief bouts of activity. We do not recommend that regular brief bouts of activity replace or displace the importance of engaging in longer bouts of physical activity. Rather, we propose that modifications to public health guidelines be considered that recommend regularly breaking periods of prolonged sitting supplementary to regularly participating in longer and more intense bouts of physical activity.

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