Breaking Up Prolonged Sitting to Improve Cardiometabolic Risk: Dose–Response Analysis of a Randomized Crossover Trial

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ABSTRACT

DURAN, A. T., C. P. FRIEL, M. A. SERAFINI, I. ENSARI, Y. K. CHEUNG, and K. M. DIAZ. Breaking Up Prolonged Sitting to Improve Cardiometabolic Risk: Dose–Response Analysis of a Randomized Crossover Trial. *Med. Sci. Sports Exerc.*, Vol. 55, No. 5, pp. 847–855, 2023. **Purpose:** Sedentary time is ubiquitous in developed nations and is associated with deleterious health outcomes. Physical activity guidelines recommend reductions in sedentary time; however, quantitative guidelines that inform how often and how long sedentary time should be interrupted have not been provided. The purpose of this study was to examine the acute effects of multiple doses of a sedentary break intervention on cardiometabolic risk factors, concurrently evaluating efficacy of varying frequencies and durations of sedentary breaks. **Methods:** In a randomized crossover study, middle- and older-age adults ($n = 11$) completed the following 8-h conditions on five separate days: 1 uninterrupted sedentary (control) condition and four acute (experimental) trials that entailed different sedentary break frequency/duration combinations: every 30 min for 1 min, every 30 min for 5 min, every 60 min for 1 min, and every 60 min for 5 min. Sedentary breaks entailed light-intensity walking. Glucose and blood pressure (BP) were measured every 15 and 60 min, respectively. **Results:** Compared with control, glucose incremental area under the curve was significantly attenuated only for the every 30 min for 5-min dose (−11.8[4.7]; $P = 0.017$). All sedentary break doses yielded significant net decreases in systolic BP from baseline compared with control ($P < 0.05$). The largest reductions in systolic BP were observed for the every 60 min for 1 min (−5.2 [1.4] mm Hg) and every 30 min for 5 min (−4.3[1.4] mm Hg) doses. **Conclusions:** The present study provides important information concerning efficacious sedentary break doses. Higher-frequency and longer-duration breaks (every 30 min for 5 min) should be considered when targeting glycemic responses, whereas lower doses may be sufficient for BP lowering. **Key Words:** SEDENTARY BEHAVIOR, SITTING, PHYSICAL ACTIVITY, DOSE FINDING, GLUCOSE, BLOOD PRESSURE

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Technological advancements have led to an increasingly sedentary lifestyle in developed nations (1,2). Evidence has accumulated to indicate that sedentary behavior is strongly associated with incidence of cardiovascular disease and mortality, potentially independent of moderate-vigorous intensity physical activity (MVPA) (3). On the strength of this evidence, the second edition of the *Physical Activity Guidelines for Americans*, for the first time, advised that people would benefit from both increasing MVPA and reducing time spent sedentary (4). Several health agencies have similarly expanded their physical activity recommendations to now also advocate for reductions in sedentary time (5–12). Recommendations to "sit less, move more" are indicated for all age groups (13). However, these guidelines stop short of making specific recommendations about how to reduce sedentary time. The lack of specific recommendations is attributed to a dearth of empirical data to inform more quantitative guidelines (13). Accordingly, there is a critical research need for studies that compare different doses of reduced sedentary time on health outcomes to inform further development of evidence-based guidelines (13,14).

Accumulating sedentary time in prolonged, uninterrupted bouts (e.g., sitting for hours at a time) has emerged as potentially the most hazardous form of sedentary behavior (15–17). Accordingly, interrupting prolonged bouts with sedentary (or activity) breaks has been recommended by some health agencies as a viable strategy to offset the harms of sedentary behavior (5,9). Many experimental studies have demonstrated that regular sedentary breaks yield cardiometabolic benefit (18). However, the existing evidence base has yielded limited information to

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inform an efficacious sedentary break dose with respect to how often (break frequency) and for how long (break duration) sedentary time should be interrupted. For example, in a recent systematic review, only nine break frequency/duration combinations had been tested across all 44 identified studies; 6 of which used a frequency of breaks ≤30 min (i.e., every 20 min; a likely intolerable dose) (18). Existing studies have also provided limited dosing information (58% of studies tested a single dose; none tested >3 doses) and focused on a single element (e.g., manipulated frequency alone) while fixing the remaining elements (e.g., duration, type, intensity) (18). Such an approach is flawed as there may be more than one possible dose pair (frequency–duration) that is efficacious when considering combinations of sedentary break elements. For example, a study testing frequency at two doses (30 and 90 min) while fixing the duration (1 min) could find that a 30-min frequency, but not a 90-min frequency, yields cardiometabolic benefit and thus conclude that a 90-min frequency is not efficacious. However, had the duration of activity element also been varied; it is possible that a 90-min frequency is efficacious at certain durations (e.g., 5 or 10 min). Thus, studies that test multiple doses and take into account the multiple elements of a sedentary break (i.e., frequency and duration) are needed to inform optimal sedentary break dosing particularly as establishing a range of effective doses will be important for developing viable public health guidance that can accommodate most individuals.

The purpose of this randomized crossover study was to examine the acute effects of multiple doses of a light-intensity walking-based sedentary break intervention on cardiometabolic risk factors among middle- and older-age adults, concurrently testing two sedentary break dose elements—break frequency and break duration. As the viability of a given sedentary break dose for implementation under real-world conditions will likely depend on whether it elicits psychological distress or excessive burden, the effects of the tested sedentary break doses on fatigue, mood, and cognitive performance were also evaluated.

METHODS

Study Population

Middle- and older-age adults (≥45 yr of age) without any preexisting chronic medical conditions were recruited from local community advertisements. Participants qualified for the study if they were sedentary for >8 $h \cdot d^{-1}$ and accumulated ≥50% of their sedentary time per day from prolonged (>30 min) sedentary bouts as determined by a 7-d accelerometer protocol. Participants were excluded if they had any of the following: mobility-limiting health condition, diagnosed chronic medical condition (including cardiovascular, renal, endocrine, neurologic, liver, and rheumatologic diseases), self-reported history of diabetes or dyslipidemia, use of medications or supplements known to influence glucose metabolism, current smoker, or self-reported exercise ≥3 $d \cdot wk^{-1}$. Participants were enrolled between November 2018 and March of 2020. The study was approved by Columbia University Medical Center's institutional review board. All participants provided informed consent.

Of 25 participants who attended a screening visit, 11 were randomized (see Supplemental Fig. 1, Supplemental Digital Content, CONSORT diagram, http://links.lww.com/MSS/C779). There were no dropouts after randomization. However, two participants were active in March of 2020 when the study was terminated due to the COVID-19 pandemic. Data from these participants are included in the present analysis. Thus, the analytic sample is comprised of 11 participants, nine of which completed all study visits and two with partial data. Because the study was prematurely terminated due to the COVID-19 pandemic, our planned enrollment (n = 17) was not achieved. The study was originally powered to detect a 23% reduction in the primary outcome (glucose incremental area under the curve [iAUC]) relative to control with 90% power (two-sided, $\alpha = 0.05$) based on a previous experimental study (19). *Post hoc* analysis showed that with a final analytic sample of n = 11, we had 80% power to detect a 31% reduction in glucose iAUC compared to control (two-sided, $\alpha = 0.05$); a reduction less than or comparable to those reported in other experimental studies (20–25).

Study Design

Participants completed five conditions, in random order, with a minimum 4-d washout period (maximum permitted washout was 14 d). The trial conditions consisted of one uninterrupted sedentary (control) condition and four acute (experimental) conditions that entailed different sedentary break frequency/duration combinations: (1) light-intensity walking every 30 min for 1 min, (2) light-intensity walking every 30 min for 5 min, (3) light-intensity walking every 60 min for 1 min, and (4) light-intensity walking every 60 min for 5 min. All trials were 8 h in duration. Before testing, participants completed a screening and familiarization session where anthropometrics were collected, participants were familiarized with treadmill walking and the continuous glucose monitor (CGM), and were instrumented with an activPAL accelerometer for 7-d monitoring to screen for habitual sedentary and physical activity levels (see Supplemental Methods, Supplemental Digital Content, http://links.lww.com/MSS/C779) (26).

Randomization

Participants completed the five trial conditions in a randomized order. A third party who was not involved with data collection assigned participants to their order of trial conditions using a computer-generated randomization code and sealed envelopes. Study personnel and participants were blinded to trial condition order up until commencement of the fourth trial visit, with personnel/participants informed of the trial condition for a given visit after baseline measures were obtained.

Study Protocol

Participants abstained from caffeine, alcohol, vitamins/supplements, and exercise (e.g., no physical activity beyond

activities of daily living) for 48 h before study visits and maintained any medication regimen. On the date of study visits, participants arrived in the morning after an overnight fast (>8 h). After voiding, body weight was measured and participants were instrumented with study devices (heart rate monitor, blood pressure [BP] cuff). After instrumentation, participants completed 5 min of quiet rest in an upright chair. Thereafter, baseline measures were obtained. The trial commenced upon administration of a standardized breakfast (0 h), with the time taken to consume (<20 min per meal) in the first trial replicated in subsequent conditions. At 4.0 h, participants consumed a standardized lunch. Participants consumed water *ad libitum* during the first trial and were instructed to replicate the volume consumed in the subsequent trials. Meals were standardized between trials and were individualized to meet 33% of daily estimated energy requirements (27). The target macronutrient profile was 12% to 15% protein, 55% to 58% carbohydrate, and 29% to 31% fat.

Participants completed trials under direct supervision from research staff. Participants sat upright in an ergonomic chair throughout all trials, only rising from the chair to void. Lavatory visits were standardized. Participants were permitted to read, use their phone, or use a computer for work or leisure during study trials. The minimum and maximum doses for frequency and duration were selected based on the minimum/maximum doses that exhibited beneficial cardiometabolic effects in previous experimental studies (18,25,28). Although a frequency of every 20 min has been demonstrated to have beneficial cardiometabolic effects (19), this dose was deemed likely to have poor tolerability/uptake. Activity breaks entailed light walking on a treadmill at 2.0 mph (0% grade) in accordance with previous experimental studies (20,29). Walking was selected as the activity modality because, compared with other aerobic activities, it is a popular, familiar, convenient, and free form of activity that can be incorporated into almost every life setting (30). Activity intensity during walking breaks was monitored using heart rate (Polar V800) and rating of perceived exertion (RPE, Modified Borg 0–10 scale) (31).

Study Measures

The primary and secondary outcomes were glucose and BP, respectively. Exploratory measures included fatigue, mood, and cognitive performance which were assessed by visual analog scale, the Profile of Mood States (POMS) questionnaire, and the Symbol Digit Modalities Test (SDMT), respectively (see Supplemental Methods, Supplemental Digital Content, http://links.lww.com/MSS/C779). Supplemental Figure 2 (see Supplemental Digital Content, http://links.lww.com/MSS/C779) shows the collection time points.

Glucose. Glucose was measured using the Freestyle Libre Pro (Abbott, Alameda, CA), an interstitial CGM that is FDA-approved and validated for the estimation of blood glucose levels (32,33). Glucose levels are recorded by the device at 15-min intervals. The CGM was fixed over the deltoid area on the dominant arm >12 h before trial visits to account for acclimation of the CGM to the participant's body.

Blood pressure. Blood pressure was measured using an Omron HEM-791IT oscillometric BP monitor (Omron Healthcare Inc., Lake Forest, IL) and a standardized protocol (34). Measures were obtained by trained research staff using an appropriate sized cuff, on the nondominant arm, while participants were seated with back supported and feet flat on the floor. Participants rested their arm on a desk so that the cuff was at heart level. Blood pressure measures were obtained at baseline and every hour thereafter for each trial visit. Measurements were obtained before scheduled activity breaks.

Acceptability

Acceptability of the sedentary break frequency/duration dose combinations was evaluated using a four-item questionnaire with five-point Likert scale responses (see Supplemental Methods, Supplemental Digital Content, http://links.lww.com/MSS/C779).

Statistical Analyses

Glucose measures over each 8-h study visit were summarized using iAUC, which provided a single value for each participant-condition day. These endpoints were analyzed using linear mixed effect models to account for within-participant correlation; and the models were used to compare each sedentary break condition against the control condition. For secondary and exploratory outcomes (BP, fatigue, mood, and cognitive performance), the change from baseline were analyzed using linear mixed effect models with fixed effects including time and condition, and a random participant effect. Analyses were conducted using R version 4.1.2.

RESULTS

Participant Characteristics

Sociodemographic, anthropometric, biochemical, and accelerometer-derived participant characteristics are shown in Table 1. The mean age (standard deviation) was 57.0 (8.6) yr, 54.5% male, and 35.3% were Black. Participants were predominantly normoglycemic (90.9%, fasting glucose <100 mg·dL^{-1}), with n = 1 (9.1%) prediabetic (fasting glucose 100–125 mg·dL^{-1}). For BP levels, n = 5 (45.5%) were normotensive (BP <120/80 mm Hg and not on antihypertensive medication), n = 4 (36.3%) were prehypertensive (BP ≥120/80 and <140/90 mm Hg and not on antihypertensive medication), and n = 2 (18.2%) were hypertensive (BP ≥140/90 mm Hg or on antihypertensive medication).

Sedentary Break Responses

All participants were able to complete the sedentary break dose protocols as prescribed. The average heart rate responses and RPE across all walking breaks are shown in Supplemental Table 1 (see Supplemental Digital Content, Perceived exertion and heart rate during activity break for each trial condition, http://links.lww.com/MSS/C779). On average, heart rate was higher for the 5-min duration doses (every 30 min and every

TABLE 1. Participant characteristics.

Variables	Mean (SD) or %
Age (yr)	57.0 (8.6)
Male (%)	54.5
Race and ethnicity (%)	
Non-Hispanic White	36.3
Non-Hispanic Black	36.3
Hispanic	18.2
Other	9.1
Education (%)	
High school/GED	18.2
Some college	27.3
College/graduate degree	54.5
Body mass index ($kg \cdot m^{-2}$)[a]	28.3 (6.1)
Body mass index category (%)[a]	
Normal weight	36.4
Overweight	27.2
Obese	36.4
Waist circumference (cm)	80.4 (13.1)
Systolic BP (mm Hg)[a]	113.7 (11.5)
Diastolic BP (mm Hg)[a]	76.2 (6.7)
Antihypertensive medication (%)	18.2
Fasting glucose ($mg \cdot dL^{-1}$)[a]	85.5 (10.2)
Prescribed energy intake (%)	
1600 kcal	9.1
1800 kcal	54.5
2000 kcal	27.3
2200 kcal	9.1
Accelerometer data	
Waking wear time ($min \cdot d^{-1}$)	1003.7 (97.5)
Sedentary time ($min \cdot d^{-1}$)	697.3 (103.7)
Standing time ($min \cdot d^{-1}$)	244.2 (106.8)
Stepping time ($min \cdot d^{-1}$)	62.4 (25.3)
Sedentary bouts ≥30 min (bouts per day)	6.8 (1.6)
Sedentary time from bouts ≥30 min ($min \cdot d^{-1}$)	467.4 (93.4)
Percent of sedentary time from bouts ≥30 min (%)	67.8 (13.0)

[a]Average of five baseline/fasting measures across five study visits.

60 min) compared with the 1-min duration doses, however these differences were not statistically significant.

Glucose and BP Responses

Glucose over time by trial condition and as a net iAUC compared with control are shown in Figure 1. Compared with the control condition, net glucose iAUC was significantly attenuated for the every 30 min for 5-min dose (mean, −11.8; SE, 4.7; $P = 0.017$). Attenuations were also observed for the other sedentary break doses, most notably for the every 30 min for 1-min dose (mean, −6.7; SE, 4.6; $P = 0.159$), but were not statistically significant.

BP over time by trial condition and as a net change from baseline compared with control are shown in Figure 2. All sedentary break doses yielded significant net decreases in systolic BP from baseline compared with the control condition ($P < 0.05$). The largest reductions in systolic BP were observed for the every 60 min for 1-min dose (mean, −5.2; SE, 1.4 mm Hg; $P < 0.001$), followed by the every 30 min for 5-min dose (mean, −4.3; SE, 1.4 mm Hg; $P = 0.003$). No significant effects were observed for diastolic BP. Detailed data shown in Figures 1 and 2, as well Cohen's *d* effect sizes, are shown in Supplemental Tables 2–4 (see Supplemental Digital Content, The effect of sedentary break conditions on change in glucose from baseline, on change in BP from baseline, and on glucose and BP compared to control condition, http://links.lww.com/MSS/C779).

Fatigue, Mood, and Cognitive Performance

Fatigue, mood, and cognitive performance over time by trial condition and as net changes from baseline compared with control are shown in Figure 3. All sedentary break doses yielded significant net decreases in fatigue from baseline compared with the control condition ($P < 0.05$), except the every 60 min for 1-min dose which trended toward, but was not statistically significant ($P = 0.050$). The largest reductions in fatigue were observed for the every 30 min for 5-min dose (mean, −5.8; SE, 2.1; $P = 0.006$) and every 60 min for 5-min dose (mean, −5.9; SE, 2.0; $P = 0.003$).

All doses significantly attenuated total mood disturbance scores compared with the control condition with the every 30 min for 5 min (mean, −4.7; SE, 1.4; $P = 0.001$) and every 60 min for 5 min (mean, −5.0; SE, 1.4; $P < 0.001$) yielding the greatest reductions. Results analyzing each POMS subscale (anger, confusion, depression, fatigue, tension, and vigor) are shown in Supplemental Figure 3 (see Supplemental Digital Content, The effect of sedentary break and control conditions on Profile of Mood subscales over time, http://links.lww.com/MSS/C779). Significant effects were observed for the fatigue, tension, and vigor subscales, with the most robust effects observed for the vigor subscale.

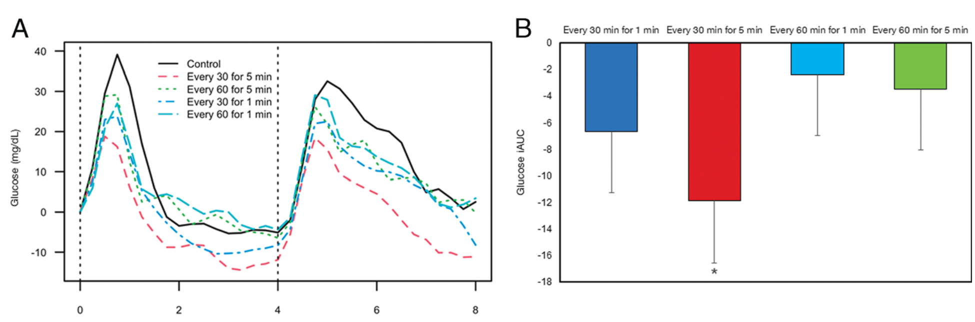

FIGURE 1—The effect of sedentary break and control conditions on glucose levels over time (A) and glucose expressed as net iAUC compared with the control condition (B). ***Vertical dashed line*** **in panel A indicates timing of breakfast (0 h) and lunch (4 h) meals. Data presented as mean change from baseline in panel A. Tabular data, including standard errors, are presented in Supplemental Table 2 (http://links.lww.com/MSS/C779). Data presented as mean glucose iAUC and standard error in panel B. *Significant difference from control condition ($P < 0.05$).**

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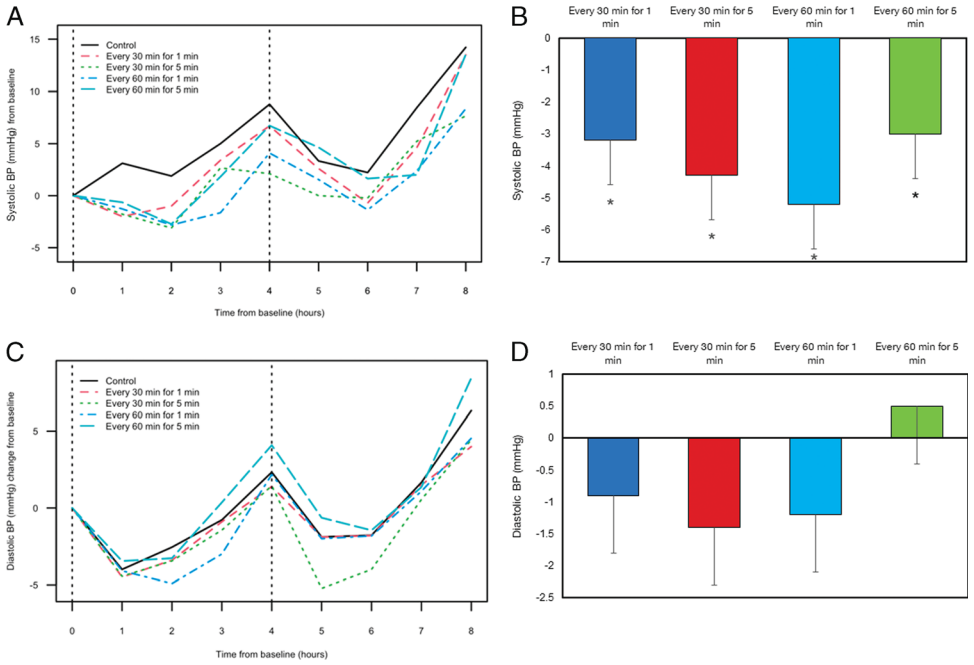

FIGURE 2—The effect of sedentary break and control conditions on BP levels over time (A [systolic] and C [diastolic]) and BP expressed as net change from baseline across the 8-h condition compared with the control condition (B [systolic] and D [diastolic]). *Vertical dashed line* in panels A and C indicates timing of breakfast (0 h) and lunch (4 h) meals. Data presented as mean change from baseline in panels A and C. Tabular data, including standard errors, are presented in Supplemental Table 2 (http://links.lww.com/MSS/C779). Data presented as mean net change in BP compared with control and standard error in panels B and D. *Significant difference from control condition ($P < 0.05$).

No significant effects were observed for SDMT performance, albeit nonsignificant improvements in test performance were observed across all doses compared with the control condition. Detailed data shown in Figure 3 and Supplemental Figure 3 (see Supplemental Digital Content, The effect of sedentary break and control conditions on Profile of Mood subscales over time, http://links.lww.com/MSS/C779), as well as Cohen's *d* effect sizes, are shown in Supplemental Tables 5–8 (see Supplemental Digital Content, The effect of sedentary break conditions on change in fatigue, mood, and cognitive performance from baseline and compared with control condition; and the effect of sedentary break conditions on change in POMS subscale scores from baseline and compared with control condition, http://links.lww.com/MSS/C779).

Acceptability

Acceptability of the sedentary break frequency/duration dose combinations is shown in Supplemental Figure 4 (see Supplemental Digital Content, Acceptability of the sedentary break frequency/duration dose combinations, http://links.lww.com/MSS/C779). All doses were well tolerated with ≥80% of participants reporting a willingness to follow each dose long-term under real world conditions.

DISCUSSION

In this randomized crossover study among middle- and older-age adults, we tested the effects of multiple sedentary break doses on cardiometabolic risk factors—concurrently testing two sedentary break dose elements—break frequency and break duration. It was observed that only sedentary breaks that were high in frequency and duration (every 30 min for 5 min) yielded significant reductions in glucose relative to a control condition. Conversely, all tested sedentary break doses—both high and low frequency (every 30 min or every 60 min) and high and low duration (1 min or 5 min), yielded significant reductions in systolic BP. The elucidation of optimal sedentary break doses is of paramount concern as ongoing and future long-term randomized controlled trials bear the risk of being a waste of resources and time because the tested doses have potential of being inefficacious given that investigators must largely rely on a best-guess to select doses rather than using empirically derived evidence. Thus, the present study provides important information concerning efficacious sedentary break doses.

An important contribution of this work is our finding that high frequency sedentary breaks (every 30 min), but not low frequency (every 60 min), yielded reductions in glucose iAUC relative to a control condition. Although the effect of the sedentary break dose of every 30 min for 1 min did not reach statistical significance, it should be noted that the effect size was moderate (Cohen's $d = 0.49$). Nonetheless, our findings suggest that sedentary breaks every 60 min may not be an efficacious frequency for the lowering of glucose at a given sedentary break duration of 1 or 5 min; albeit further research is needed to determine if a higher sedentary break duration (i.e., 10 min) or intensity (i.e., moderate or vigorous) would yield stronger effects at this frequency. Our findings are consistent with a recent network meta-analysis, which identified

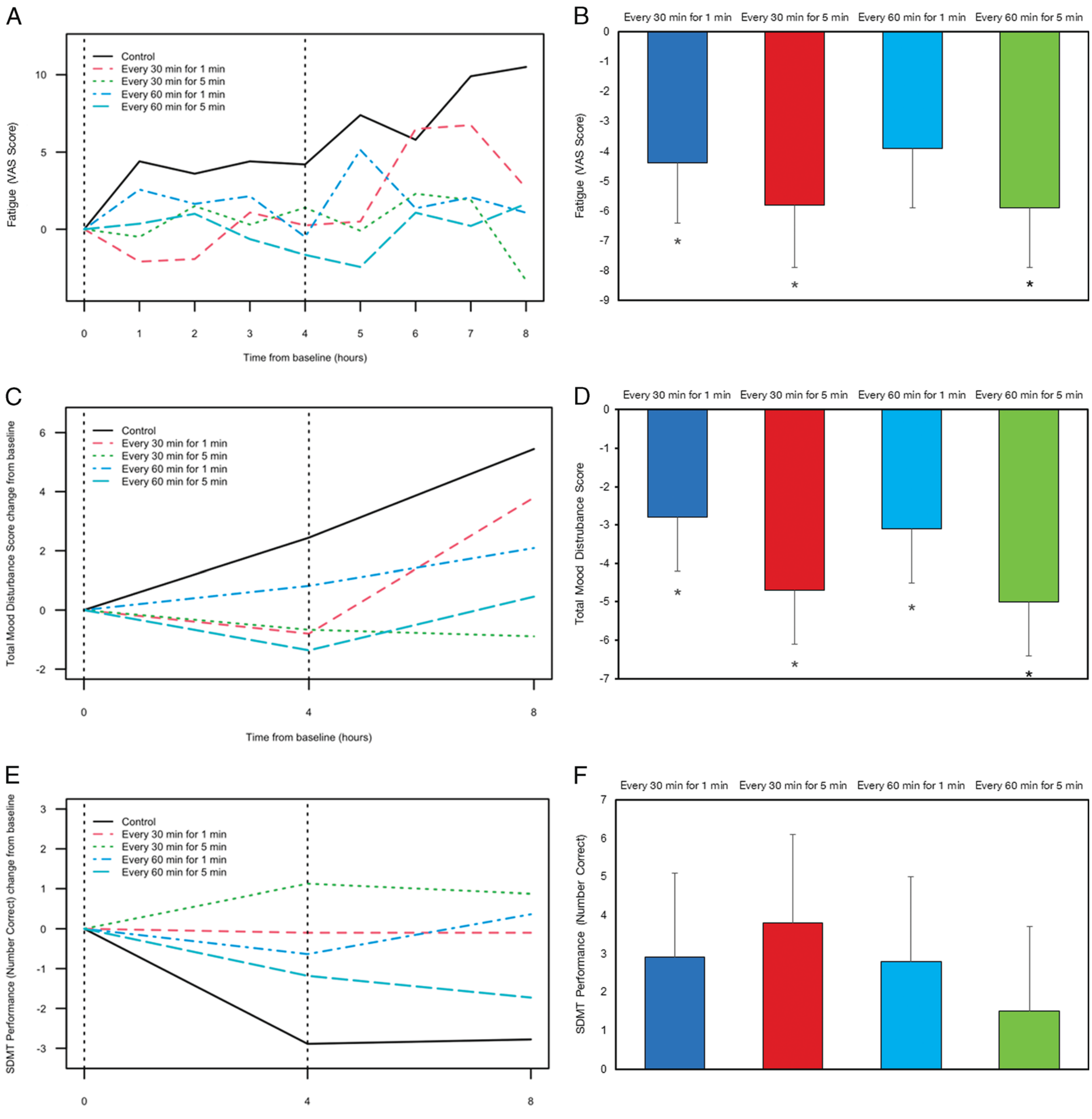

FIGURE 3—The effect of sedentary break and control conditions on fatigue, mood, and cognitive performance over time (A [fatigue], C [mood], and E [cognitive performance]) and fatigue, mood, and cognitive performance expressed as net change from baseline across the 8-h condition compared with the control condition (B [fatigue], D [mood], and F [cognitive performance]). ***Vertical dashed line*** **in panels A, C, and E indicates timing of breakfast (0 h) and lunch (4 h) meals. Data presented as mean change from baseline in panels A, C, and E. Tabular data, including standard errors, are presented in Supplemental Table 4 (http://links.lww.com/MSS/C779). Data presented as mean net change in outcome compared with control and standard error in panels B, D, and F. *Significant difference from control condition ($P < 0.05$).**

a sedentary break frequency of every 20 to 30 min as the optimal frequency for reducing postprandial glycemic responses (35). We extend upon this work and confirm the efficacy of the every 30 min sedentary break frequency within the context of a single study, which permits direct comparisons of dose under identical controlled laboratory settings. Our findings further underscore the need to evaluate combinations of sedentary breaks elements simultaneously (e.g., manipulating both frequency and duration) as fixing duration to 1 min and just testing two dose levels of frequency would have led to erroneous conclusions about sedentary break frequency.

Our finding that all tested sedentary break doses yielded significant reductions in systolic BP provides critical dosing information that is largely void in the literature with respect to BP as the target outcome. A recent meta-analysis of 22 identified studies showed that sedentary breaks yielded significant effects on systolic BP (36). However, a minimally effective dose was largely not discernible. Our findings importantly highlight that breaking up prolonged sitting even at a low dose (every 60 min for 1 min) is enough to elicit BP reductions; suggestive that the documented elevations in BP elicited by prolonged sitting can be readily offset. Physiologically, prolonged

sitting exerts acute mechanical effects that may increase BP (37). The seated posture creates bends/constrictions in blood vessels of the lower limbs, eliciting decreased and turbulent blood flow. As a result of insufficient muscle contraction, the seated posture also yields increased hydrostatic pressure and reduced venous return, causing lower limb blood pooling. These hemodynamic conditions occur within 30–60 min of continuous sitting (38), resulting in increases in peripheral resistance. Although the present study did not evaluate underlying mechanisms, they nonetheless are suggestive that short, relatively infrequent sedentary breaks are sufficient to mitigate the BP increases incurred with prolonged sitting. Notably, the observed reductions in systolic BP (~3 to 5 mm Hg) are comparable to the acute and chronic BP lowering effects of aerobic exercise (39,40), a recommended first-level therapy for hypertension treatment (41), and are clinically meaningful as it would yield a ~ 13% to 15% reduction in risk of cardiovascular disease if sustained (42).

A sedentary break dose may be physiologically effective, but, if few want to follow it, then its public health relevance is questionable. Evaluation of dose acceptability and constructs that could influence uptake/compliance thus are key considerations for dose selection. Consistent with the principle of psychological hedonism, people tend to repeat behaviors that feel good and avoid behaviors that feel bad (43). When applied to physical activity, those who experience a positive affective response to physical activity are more likely to repeat it in the future (44). In the present study, all doses had high levels of acceptability (based on subjective responses to acceptability questionnaire). Furthermore, we demonstrate that the doses with a 5-min break duration (at either 30 or 60 min frequencies) yielded significant reductions in both fatigue and mood disturbances, the latter which was largely driven by increases in feelings of vigor. Although reductions in fatigue and mood disturbances for the 1-min break duration doses approached or were statistically significant, the observed reductions were less robust relative to the doses which used a 5-min break duration. Thus, longer break durations should be considered as a means to elicit more positive affective responses and ultimately maximize uptake. Future studies testing the feasibility of varying sedentary break doses under real world conditions are needed.

Strengths of this study include the randomized, crossover experimental design, testing of four sedentary break doses with manipulation of multiple elements of a sedentary break (frequency and duration), and collection of glucose measures at a high frequency interval (every 15 min) via use of CGM. Several limitations, however, should be noted. First, the acute nature of the study precludes generalization to chronic or long-term effects. However, it should be acknowledged that the treatment of chronic diseases, such as diabetes and hypertension is predicated on the acute management of risk factors via medications. Further, treatment guidelines endorse aerobic exercise all days of the week (and no more than 2 d between sessions) which is premised on the acute-physical activity mediated improvements in BP and glycemic control (12,41). Thus, it must be considered that the acute effects of sedentary breaks (rather than chronic) most closely reflect conventional pharmacologic treatment practices and are clinically relevant. Second, although the controlled laboratory nature of the study permits elucidating the "pure" efficacy of a given dose by controlling for confounders and assurance of compliance, the generalizability of the study findings to free-living conditions is not clear. Third, the study sample size was relatively small. Although the sample was sufficient to detect significant differences across tested outcomes, it is nonetheless difficult to generalize the study findings beyond the specific recruited study sample. Finally, the intensity and activity type of the tested sedentary break doses were fixed to light-intensity walking. We cannot rule out the possibility that the tested doses would yield differential effects with MVPA or a different activity type (i.e., muscle strengthening activity). Nonetheless, light-intensity walking was selected as it is more generalizable to everyday home, work, or social settings.

CONCLUSIONS

In conclusion, this randomized crossover study provides continued evidence that breaking up prolonged sitting with regular bouts of light intensity physical activity reduces glucose and BP in middle- and older-age adults; supportive of the concept that regularly breaking up sedentary time may be an important adjunct to existing physical activity and disease prevention/treatment guidelines. Importantly, our findings provide key dosing information necessary for the development of evidence-based quantitative guidelines that describe how often and for how long sedentary breaks should be taken when using light-intensity, aerobic-based sedentary breaks. To ensure efficacious and tolerated doses are used in future trials, higher frequency and longer duration breaks (every 30 min for 5 min) should be considered when targeting glycemic responses, whereas lower doses may be sufficient for BP lowering.

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Conflicts of Interest: The authors have no conflicts of interest to disclose. The results of the study are presented clearly, honestly, and without fabrication, or inappropriate data manipulation. The results of this study do not constitute endorsement by the American College of Sports Medicine.

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