Internet-delivered lifestyle physical activity intervention: limited inflammation and antioxidant capacity efficacy in overweight adults

Derek T. Smith,1,2 Lucas J. Carr,1,2 Chris Dorozynski,1 and Chirag Gomashe1

1Human Integrative Physiology Laboratory, Division of Kinesiology and Health, College of Health Sciences; and 2Department of Zoology and Physiology, College of Arts and Sciences, University of Wyoming, Laramie, Wyoming

Submitted 23 April 2008; accepted in final form 12 November 2008

MORE THAN 50% of the U.S. population is not meeting current physical activity (PA) recommendations (22), and ~25% engage in no leisure-time PA (63a) despite the known health benefits of leading a habitually physically active lifestyle (33, 65). Such health benefits have recently been highlighted in the American Heart Association and American College of Sports Medicine’s recommendations and their jointly sponsored Exercise Is Medicine initiative (22, 40, 67). Specifically, greater PA is known to prevent and reduce the risk of many cardiometabolic diseases (5, 10, 33). However, the underlying cardioprotective mechanisms of habitual exercise continue to be elucidated. Recent efforts have supported a PA-induced alleviation of oxidative stress and chronic low-grade inflammation as a possible mechanism for disease risk reduction (1, 20).

Imbalance between oxidative molecules and antioxidant capacity and proinflammatory and anti-inflammatory states are both associated with overweight and physical inactivity (18, 28, 46, 74). Proinflammatory cytokines and reactive oxygen species (ROS) from both visceral and accumulated subcutaneous fat compartments are implicated in increased cardiometabolic disease risk (17, 18). Conversely, PA is associated with elevations in anti-inflammatory cytokines (26, 43) and antioxidant enzyme capacity (16, 50), as well as diminished systemic inflammation (46) and oxidative stress (44), all of which support the cardioprotective actions of PA. However, the effects of chronic PA on basal levels of inflammation, oxidation, and antioxidant capacity biomarkers are still controversial (16, 19, 50), largely due to PA intensity disparities. Moreover, the majority of previous applied human research has focused primarily on the effects of moderate- to high-intensity exercise training and/or the effects of acute bouts of exercise. To our knowledge, only one study has included low (25% maximal oxygen consumption)-intensity PA (20), and no studies have investigated lifestyle-oriented PA intervention/programs, which are often of low intensity, focused on reducing physical inactivity, and gaining clinical- and wellness-based popularity in part due to the obesity epidemic (14).

Recently, significant research efforts have focused on the use of theory-based and Internet-delivered PA behavior change programs due to their 1) demonstrated efficacy; 2) potential delivery and reach to community/population levels; and 3) adoption feasibility and safety for diverse populations (overweight, elderly) necessitating low-intensity volume-based approaches to increasing PA (21, 39, 69). The Active Living Every Day (ALED; Human Kinetics) PA behavior change program is a theory-based [transtheoretical model (51) and social cognitive theory (2)] and commercially available program that has been shown to favorably increase self-reported PA (73) and aerobic fitness (15) when delivered in small-group face-to-face formats. An Internet-delivered version of ALED (ALED-I) is also commercially available, and through a randomized control trial, we recently demonstrated its efficacy in increasing objectively measured PA levels (pedometer) and decreasing central adiposity, triglycerides, and coronary risk ratio (CRR) over 16 wk in a group of sedentary and overweight adults (9).

The Task Force on Community Preventive Services strongly recommends theory-based and individually adapted and targeted health behavior-change programs for increasing PA in...
Community (63a). The ALED-I behavior change program adheres to these recommendations and has demonstrated efficacy in rural, geographically isolated populations devoid of PA resources more common to urban/metropolitan areas (9). However, the efficacy of this program and most other theoretically based programs, regardless of delivery method, has not been extended to physiological mechanisms (e.g., inflammation) etiologically pinned to cardiometabolic diseases. The present study is a preliminary investigation aimed at determining whether the 16-wk ALED-I PA behavior change program elicited further cardiometabolic disease protection through favorable modulation of biomarkers assessing inflammation, oxidation, and antioxidant capacity.

**METHODS**

The reader is referred to Carr et al. (9) for a full description of the initial randomized control trial recruitment/enrollment process, power determination, and detailed descriptive data collection procedures from which this preliminary investigation stemmed. The initial randomized control trial achieved a power of 0.82 based on the primary outcome measure of PA (steps per day). Due to this a priori design, the present study does not achieve similar power with respect to the selected biomarker outcome measures but rather provides pilot evidence regarding the influence of a lifestyle-oriented and Internet-delivered PA behavior change program on selected biomarkers of inflammation, oxidation, and antioxidant capacity.

**Subjects.** Briefly, forty-one sedentary, overweight [body mass index (BMI) ≥ 25.0 kg/m²] adults (8 men, 33 women) were recruited and randomized to either the 16-wk Internet-delivered ALED-I PA intervention (n = 19; age = 40.4 ± 1.9 yr; BMI = 31.4 ± 1.1 kg/m²) or the delayed-intent-to-treat control condition (n = 22; age = 46.6 ± 1.3 yr; BMI = 31.0 ± 0.7 kg/m²). Descriptive, anthropometric, metabolic, and primary biomarker measures were assessed at baseline and following the 16-wk intervention period and were conducted 24–36 h following each participant’s most recent bout of PA. Participants randomized to the control condition maintained their present lifestyle throughout the duration of the 16-wk experimental period. Participants were nonsmokers, devoid of ambulatory/exercise limitations, and free of overt, complicated, or acute cardiovascular, metabolic, respiratory, or neurological diseases as assessed by medical history. Female participants were predominantly premenopausal (2 perimenopausal and 1 postmenopausal, surgical). None of the latter used any form of hormone replacement therapy, and three premenopausal women used oral contraception. All experimental protocols were approved by the Institutional Review Board for projects involving human subjects at the University of Wyoming, Laramie, WY, and randomized to either the 16-wk Internet-delivered ALED-I PA intervention and randomized to either the 16-wk Internet-delivered ALED-I PA intervention or the delayed intent-to-treat control condition (week 16 of the study in 28 participants (13 food diaries not complete or not returned) to characterize potential group differences and/or time course changes in micro- and macronutrient intake. Food diaries, which were analyzed using Nutritionist Pro software, are demonstrated to be reliable and valid (48) and are a practical and feasible measure in free-living adults (34).

**Metabolic and biomarker measurements.** In an attempt to remain consistent with previous best-practice profiling recommendations for characterization of the complex and interrelated effects of PA and overweight on oxidative and inflammatory homeostasis (12), six biomarkers, measurable in venous serum/plasma samples, were selected. These biomarkers included TNF-α, high-sensitivity C-reactive protein (CRP), myeloperoxidase (MPO), catalase (CAT), superoxide dismutase (SOD), and total antioxidant capacity (TAC), and all were measured at baseline and postintervention (16 wk). The biomarkers were selected based on existing evidence linking/implementing them with cardiometabolic diseases, overweight/obesity, and physical activity as follows. TNF-α is a proinflammatory cytokine produced by adipocytes (35), is inversely associated with PA (26), and is a predictor of cardiovascular disease outcomes (32). TNF-α was measured in plasma by sandwich ELISA (Alpco Diagnostics, Salem, NH). CRP is an acute-phase protein produced by the liver (47), is associated with cardiovascular disease (53), glycemic control (29), and overweight/obesity (70). CRP was measured by an outside clinical laboratory (LabCorp, Denver, CO) as previously reported (9). MPO is a peroxidase enzyme and biomarker of lipid peroxidation that is active in atherosclerotic lesions and predicts early risk of myocardial infarction (7). It is mechanistically linked to both inflammation and oxidation, catalyzing nitrilation of tyrosine residues during inflammation and contributing to depletion of endothelium-derived NO, respectively (24, 68), and was determined in plasma by ELISA (Alpco Diagnostics). SOD is a cytosolic, mitochondrial, and extracellular antioxidant enzyme that promotes the dismutation of superoxide anion to hydrogen peroxide and oxygen. In obesity models of aerobic exercise, elevated levels of SOD activity have been demonstrated (58). SOD enzymatic activity was measured in serum (Cayman Chemical, Ann Arbor, MI). CAT is a ubiquitous antioxidant enzyme found in most aerobic cells that catalyzes the decomposition of hydrogen peroxide to water and oxygen (50). Differences in CAT expression by extent of adiposity have been documented (59) but activity level responsiveness to exercise training is mixed (19). CAT activity was measured in serum (Cayman Chemical). TAC is a global measure of antioxidant capacity (enzymatic and nonenzymatic) measuring hydrogen peroxide quenching by available serum/plasma antioxidants (27). Greater abdominal adiposity is associated with lower TAC (11); however, the influence of exercise (physical activity) is mix (8, 45, 71). TAC was determined in serum by colorimetric assay (Alpco Diagnostics). All biomarkers were determined in duplicate, and the intra- and interassay coefficients of variation were 3.6% and 3.5% for TNF-α, 3.6% and 3.2% 96.6% and 8.8% for SOD, 10.7% and 10.2% for CAT, and 3.7% and 2.1% for TAC, respectively. Lipid/lipoprotein, glucose, and insulin concentrations were determined by an outside clinical laboratory (LabCorp) as previously reported (9). Insulin sensitivity and resistance were estimated using the inversely correlated homeostasis model assessment (HOMA-IR) and the quantitative insulin sensitivity check index (QUICK-I) (41, 55).
Blood samples were collected at the research laboratory in Laramie, WY, and a medical facility in Riverton, WY, according to standard phlebotomy techniques with minimal venostasis following an overnight fast (~10 h) with the exception of water consumption. An infection/inflammation questionnaire was administered to rule out underlying acute illness or infection before collection of 20 ml of blood between 6:00 A.M. and 9:00 A.M. into two vacutainer tubes containing either 0.081 ml 15% (K3) EDTA solution or clot activator. Samples were centrifuged at 4,000 rpm for 15 min, aliquoted, and frozen at −70° until biochemical analyses.

Statistical analyses. All data, including physiological/dietary descriptors, PA, and biomarker outcome measures, were analyzed by two-way repeated-measures ANOVA (mixed model: group × time). ANOVA models for the specific measure of interest included the groups (control and intervention) and time (baseline and post-16 wk). Before these analyses and due to group differences in baseline age (attrition following randomization) (9), adjustment was made accordingly. Additionally, baseline TNF-α levels were different between groups, so the TNF-α model was adjusted for this baseline difference. Of the biomarker outcome measures, only TAC met the assumption of normality; thus TNF-α, high-sensitivity CRP, CAT, MPO, and SOD were log transformed before analyses and reported as such. When indicated by a significant F value (group × time interaction), post hoc procedures were performed (Tukey). Linear regression analysis was performed with the observed changes in PA (steps/day) and waist circumference (Δ = postintervention − baseline) as independent response variables and the observed changes in inflammatory and oxidation/antioxidative biomarkers (Δ = postintervention − baseline) as potential predictors. Statistical significance was set a priori at P < 0.05. All data are presented as means ± SE. (SigmaStat 3.11; 2004).

RESULTS

Descriptive and metabolic measures at baseline and postintervention for the control and interventions groups are provided in Table 1. At baseline, PA levels and most descriptive and metabolic measures were similar between groups (Table 1).

Table 1. Descriptive and physiological characteristics of participants (n = 41)

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post 16-wk intervention</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Control Group (n = 22)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, yr</td>
<td>46.6±1.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Predicted V02peak, ml·kg⁻¹·min⁻¹</td>
<td>29.6±1.3</td>
<td>33.5±1.4†</td>
<td>0.01</td>
</tr>
<tr>
<td>Physical activity, steps/day</td>
<td>6,826±509</td>
<td>7,156±540</td>
<td>0.50</td>
</tr>
<tr>
<td>Systolic BP, mmHg</td>
<td>125±3</td>
<td>123±2</td>
<td></td>
</tr>
<tr>
<td>Diastolic BP, mmHg</td>
<td>77±2</td>
<td>78±1</td>
<td>0.59</td>
</tr>
<tr>
<td>Waist circumference, cm²</td>
<td>99.2±2.2</td>
<td>99.8±2.1†</td>
<td>0.66</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>31.0±0.7</td>
<td>31.0±0.8</td>
<td>0.89</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>85.6±2.8</td>
<td>85.5±3.0</td>
<td>0.85</td>
</tr>
<tr>
<td>Body fat, %</td>
<td>43.6±1.4</td>
<td>44.7±1.6†</td>
<td>0.03</td>
</tr>
<tr>
<td>%Lean mass</td>
<td>56.4±1.4</td>
<td>55.3±1.6†</td>
<td>0.03</td>
</tr>
<tr>
<td>Total cholesterol, mg/dl</td>
<td>188±8.1</td>
<td>182±7.2*</td>
<td>0.27</td>
</tr>
<tr>
<td>LDL, mg/dl</td>
<td>110±7</td>
<td>107±6</td>
<td>0.36</td>
</tr>
<tr>
<td>Triglycerides, mg/dl</td>
<td>51±3</td>
<td>51±3</td>
<td>0.63</td>
</tr>
<tr>
<td>Fasting glucose, mg/dl</td>
<td>123±12</td>
<td>103±11</td>
<td>0.06</td>
</tr>
<tr>
<td>Fasting insulin, µIU/ml</td>
<td>94±3</td>
<td>94±2</td>
<td>0.69</td>
</tr>
<tr>
<td>HOMA-I</td>
<td>6.9±1.1</td>
<td>9.4±1.1</td>
<td>0.61</td>
</tr>
<tr>
<td>QUICK-I</td>
<td>3.4±0.1</td>
<td>3.4±0.1†</td>
<td>0.76</td>
</tr>
<tr>
<td>Coronary risk ratio</td>
<td>3.9±0.2</td>
<td>3.8±0.2</td>
<td>0.18</td>
</tr>
<tr>
<td>Reynold’s risk score (model B)</td>
<td>1.3±0.2</td>
<td>1.2±0.1*</td>
<td>0.32</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post 16-wk intervention</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ALED-I Group (n = 19)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, yr</td>
<td>40.4±1.9*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Predicted V02peak, ml·kg⁻¹·min⁻¹</td>
<td>34.9±1.9*</td>
<td>37.8±2.2†</td>
<td>0.01</td>
</tr>
<tr>
<td>Physical activity, steps/day</td>
<td>7,223±469</td>
<td>8,627±554†</td>
<td>0.01</td>
</tr>
<tr>
<td>Systolic BP, mmHg</td>
<td>122±2</td>
<td>124±3</td>
<td>0.50</td>
</tr>
<tr>
<td>Diastolic BP, mmHg</td>
<td>79±2</td>
<td>78±2</td>
<td>0.94</td>
</tr>
<tr>
<td>Waist circumference, cm²</td>
<td>100.6±2.4*</td>
<td>96.6±2.7†</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>31.4±1.1</td>
<td>31.2±1.1</td>
<td>0.44</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>89.6±3.8</td>
<td>89.3±3.9</td>
<td>0.75</td>
</tr>
<tr>
<td>Body fat, %</td>
<td>44.3±1.8</td>
<td>44.2±2.0</td>
<td>0.67</td>
</tr>
<tr>
<td>%Lean mass</td>
<td>55.6±1.8</td>
<td>55.8±2.0</td>
<td>0.67</td>
</tr>
<tr>
<td>Total cholesterol, mg/dl</td>
<td>207±11</td>
<td>197±11</td>
<td>0.27</td>
</tr>
<tr>
<td>LDL, mg/dl</td>
<td>124±10</td>
<td>120±9</td>
<td>0.63</td>
</tr>
<tr>
<td>Triglycerides, mg/dl</td>
<td>45±2</td>
<td>46±3</td>
<td>0.48</td>
</tr>
<tr>
<td>Fasting glucose, mg/dl</td>
<td>168±13*</td>
<td>148±18†</td>
<td>0.10</td>
</tr>
<tr>
<td>Fasting insulin, µIU/ml</td>
<td>93±2</td>
<td>94±2</td>
<td>0.78</td>
</tr>
<tr>
<td>HOMA-I</td>
<td>10.5±1.4</td>
<td>9.3±1.2</td>
<td>0.51</td>
</tr>
<tr>
<td>QUICK-I</td>
<td>2.5±0.4</td>
<td>2.2±0.3†</td>
<td>0.53</td>
</tr>
<tr>
<td>Coronary risk ratio</td>
<td>3.2±0.2</td>
<td>3.4±0.1†</td>
<td>0.23</td>
</tr>
<tr>
<td>Reynold’s risk score (model B)</td>
<td>4.8±0.3*</td>
<td>4.5±0.3‡</td>
<td>0.14</td>
</tr>
</tbody>
</table>

Values are means ± SE. ALED-I, Active Living Every Day-Internet; V02peak, peak oxygen consumption; BP, blood pressure; BMI, body mass index; LDL, low-density lipoprotein; HDL, high-density lipoprotein; HOMA, homeostatic model assessment; QUICK-I, quantitative insulin-sensitivity check index.

*Statistical level within group (baseline to postintervention). †n = 32 (18 control; 14 ALED-I). *Female participants only. *P < 0.05 compared with baseline in control group. †P < 0.05 compared with baseline within same group. ‡P < 0.05, between-group comparison vs. postintervention in the control group.

For the control and ALED-I groups no significant main effect (group × time interaction) was found for CRP (P = 0.9), CAT (P = 0.5), MPO (P = 0.6), SOD (P = 0.8), or TAC (P = 0.5), and thus they were similar at baseline and 16 wk (Table 2). Within the intervention group, TNF-α declined significantly after adjustment for baseline group differences (F: 8.74; P < 0.01; Fig. 1); however, this reduction was not significantly different from the control group (P = 0.29). No change in TNF-α was evident in the control group after 16 wk (P = 0.41). For CAT, sufficient sample volume was only available on 32 of the 41 participants (14 intervention and 19 control...
participants); thus statistical analysis was performed on this subgroup of participants whose descriptive characteristics did not differ from that of the total sample (n = 41). Neither change in PA nor waist circumference was significantly associated with change in any of the measured inflammation, oxidation, or antioxidant biomarkers.

Following completion of the 16-wk experimental period, significant between-group differences were present for reported time (h/wk) spent in moderate-intensity activities (P = 0.01; Table 3). In both groups, greater than 54% of time was reportedly spent in light activities. Contrasting changes were observed in the two groups following the 16-wk experimental period. Time spent in moderate activities increased in the control group but decreased in the intervention group, and time spent in light-intensity activities increased in the intervention group (P = 0.055) and decreased in the control group (Table 3). There were no significant associations between change in intensity of activity, light or moderate, and changes in TNF-α. Analyses of 3-day food diaries in 28 of the 41 participants revealed no baseline or 16-wk between-group differences or within-group differences in any of the measured micro- or macronutrients. Table 2 shows that macronutrient intake was similar between groups ranging from 46–50% carbohydrate, 33–37% fat, and 16–18% protein. Importantly, potential sources of exogenous dietary antioxidants remained constant throughout the 16-wk study in both groups (Table 2).

**DISCUSSION**

The aim of this preliminary study was to determine whether previously demonstrated improvements in PA resulting from an Internet-delivered lifestyle-oriented PA behavior change program also elicited favorable improvements in inflammation, oxidation, and antioxidant capacity in sedentary overweight adults. Consistent with profiling recommendations (12), several biomarkers associated with PA, obesity, and cardiometabolic diseases were measured, including TNF-α, CRP, CAT, SOD, MPO, and TAC. The PA intervention resulted in favorable modification of only one inflammatory biomarker, TNF-α, and this improvement was not significantly different from the control condition. With the exception of TNF-α, these largely null findings are not entirely surprising due to the lifestyle-oriented volume-based approach of the ALED-I PA behavior change program that is devoid of individualized PA intensity prescription. The popularity and use of lifestyle-oriented Internet-delivered PA programs is increasing (39, 69); to our knowledge, this is the first study to expand the efficacy testing of such a program to disease-related physiological mechanisms such as inflammation and antioxidant capacity. The observed benefit of increased PA volume on TNF-α extends previous

![Fig. 1. TNF-α levels for control and Active Living Every Day-Internet (ALED-I) groups at baseline and postintervention (n = 41). *P < 0.01 compared with baseline in same group.](image-url)
The observed improvement in TNF-α is complementary to findings from previous cross-sectional (1) and moderate- to higher-intensity PA intervention studies (26, 61). Adipose tissue has been identified as a major source for circulating TNF-α (25), and a positive relation between inflammation and excess adiposity has been reported (49). Combined with increased adiposity as a consequence of leading a sedentary lifestyle (36), the 4% reduction in central adiposity and the 19% increase in PA likely contribute, at least in part, to explaining the reduced TNF-α concentrations in the ALED-I group. It is important to highlight that the associations between change in adiposity or PA and TNF-α were weak and insignificant, which has also been reported previously (52). The absence of change in TNF-α in the nonactive control group is supportive of the well-documented deleterious changes in body composition due to a sedentary lifestyle (6) and the corresponding deleterious changes in body composition (central adiposity, increased percent body fat, and reduced lean tissue mass) that occurred in the control participants over a relatively short period of time (9). Whether the small but statistically significant increase in percent body fat observed in the control group represents a clinically significant concern is arguable. Nonetheless, the observed increase in percent body fat occurred over a short time frame (16 wk) and if extrapolated over a longer duration, would likely achieve clinical significance should such sedentary lifestyles be maintained.

Collectively, the TNF-α findings for both groups may be important as TNF-α is a moderately strong predictor of future coronary events (54) and appears to be a primary instigator of insulin resistance and dyslipidemia (46), but several important considerations exist. The Internet-delivered PA intervention reduced triglyceride concentrations, but improvements in insulin resistance, sensitivity, and fasting insulin and glucose concentrations were absent. The lack of intervention-induced changes in these metabolic parameters may be due to 1) the relatively normal metabolic profile of these overweight adults, 2) the relatively short observation duration, and 3) the low-intensity nature of the volume-focused intervention. Moreover, the TNF-α findings are potentially confounded by largely unexplainable baseline differences between the groups. At baseline, both groups were similar in most physical and physiological descriptors with exception of age, CRR, triglycerides, and waist circumference. Although not statistically significant, the intervention group also had fasting insulin concentrations that were ~35% greater than the control group and were more insulin resistant (HOMA). A positive association between TNF-α and triglyceride concentrations and insulin resistance has been documented (60), which may help explain the higher baseline TNF-α levels in the ALED-I group. Likewise, the postintervention reduction in triglyceride levels may have contributed, similarly, to the significant reduction in TNF-α; however, the association between change in TNF-α and change in triglycerides was insignificant ($P = 0.79$). While our findings are encouraging, in context of an efficacious public health PA strategy that may also elicit improvements in TNF-α and subsequently cardiometabolic disease risk, the aforementioned limitations, small sample size, and attrition rate inherent within this preliminary investigation necessitate cautious interpretation.

The lifestyle-oriented PA behavior change program and its favorable PA and central adiposity effects did not significantly influence any other inflammation, oxidation, or antioxidant biomarkers. In addition to small sample size, other explanations for these largely null findings exist, namely intensity of PA. First, TAC is stratified from low to high capacity (1a) where TAC less than 280 μmol/l is considered low antioxidative capacity, 280 to 320 μmol/l is moderate antioxidative capacity, and greater than 320 μmol/l is high antioxidative capacity. In this relatively healthy sample of overweight and sedentary adults, baseline TAC levels for both groups were in the moderate antioxidative capacity range. Thus a greater dose (volume and intensity) of PA may be necessary to elicit favorable change in the already moderate antioxidative capacity levels as has been documented by others using greater exercise training doses (8). Second, with respect to CAT activity, no significant change was observed (+14%; $P = 0.07$) following the PA intervention, which is contrary to previous reports of exercise-induced increases in skeletal muscle (37), erythrocyte (42) and mRNA (19) CAT activity. Diminished antioxidant defense has been documented in overweight populations compared with normal weight counterparts such that overweight adults possess lower tissue levels of available antioxidant vitamins (β-carotene and vitamin C), antioxidant enzymes (SOD and glutathione peroxidase), and thiol-containing molecules (63). It is speculated that the antioxidant enzyme defense system in overweight individuals may be impaired or simply unable to overcome elevated levels of oxidation, further augmenting inflammation and leading to increased cardiometabolic disease risk (28). Based on the trend toward elevated CAT activity in this group of overweight adults, it may be worthwhile to consider modification of the Internet-delivered PA behavior change program to include more individualized attention to increasing intensity in conjunction with the increase in PA volume. This modification, which is not unrealistic, may serve to augment the beneficial effect of the Internet-delivered program on other disease-related biomarkers in addition to CAT activity.

The absence of individualized PA intensity prescription in the commercially available Internet-delivered ALED PA behavior change program is a limitation rooted in necessary safety considerations related to initiating nonmedically supervised PA programs in sedentary populations and plausibly contributed to our null findings for CRP, CAT, MPO, SOD, and TAC. We employed a self-report measure to quantify PA intensity in an effort to identify relations between PA intensity and improvements in the selected biomarkers. The increase in volume of PA for the ALED-I group includes an increase of ~1 h/day spent in low-intensity activities (4% increase from baseline to 16 wk) and a reduction of ~41 min/day spent in moderate-intensity activities. While these changes may seem counterintuitive in the ALED-I group, they are aligned with self-reported changes in PA intensity perception that accompany improved aerobic fitness, body composition, and energy costs of PA. Specifically, activities once perceived as moderate intensity were perceived as lower intensity after 16 wk of becoming more physically active. As with the change in
volume of PA, neither time spent in light activities nor moderate activities were associated with change in TNF-α. However, from a public health perspective, the observed effects of a modest increase in volume of low-intensity PA may have important implications as segments of the population, such as the overweight, elderly, or diseased, may be unable to achieve the current PA duration and intensity recommendations (23, 66).

Interpretation of our findings should be considered in the context of this preliminary investigation’s strengths and limitations. As addressed previously, the small attrition-related sample size is a limitation that likely influenced several of our findings such as CAT activity; however, this attrition is consistent with other Internet-delivered PA intervention studies (69). Acknowledging total attrition (postrandomization) at 51% (9), a strength of the study is maintenance of relatively similar metabolic and physical characteristics between the groups, protecting against other confounding variables such as hypertension or insulin resistance. None of the selected biomarkers assessed protein expression, and a direct measure of oxidative stress (e.g., lipid peroxidation) would have been informative. Assessment of 8-hydroxydeoxyguanosine (8-OHdG) was attempted (27) but unsuccessful due to technical issues with the ELISA kit and lack of available serum/plasma sample for repeat analysis. Participants were fasted, but alcohol consumption was not withheld more than 10 h before blood collection. Of the 28 participants submitting food diaries, only 3 reported alcohol consumption in the week before blood collection (2 at baseline and 1 at 16 wk). Three premenopausal women using hormone-based oral contraception were included in the final analyses as their exclusion did not alter any conclusions for the biomarker outcome measures, but the influence of hormone-based therapy is acknowledged (62, 72).

Of the 28 participants submitting food diaries, only 3 reported alcohol consumption in the week before blood collection (2 at baseline and 1 at 16 wk). Three premenopausal women using hormone-based oral contraception were included in the final analyses as their exclusion did not alter any conclusions for the biomarker outcome measures, but the influence of hormone-based therapy is acknowledged (62, 72).

The sample was predominantly female (81%) and ethically homogeneous (Caucasian). All of these limit the overall generalizability of our preliminary findings. The evidence demonstrating increased PA levels, reduced central adiposity, and reduced TNF-α do substantiate the potential efficacy of this Internet-delivered PA behavior change program. Due to the significant reach of Internet-delivered programs combined with high Internet use for health information, which continues to grow (38), the target populations for this type of PA intervention may only be limited by Internet access. The individualized nature of the ALED-I program, its emphasis on walking modes of activity and activities of daily living and individualized nature of the ALED-I program, its emphasis on walking modes of activity and activities of daily living and adoption by overweight adults make it well suited for populations without access to PA promotion resources and venues more common in urban/metropolitan areas, specifically rural populations that may be geographically isolated.

Recommendations and conclusions. With escalating use and attention to Internet-delivered and theory-based PA programs, such as ALED-I-to-increase population PA levels, larger more robust trials are necessary to clearly elucidate the dose response of PA on inflammation, oxidative stress, and antioxidant capacity. Specifically, inclusion of more direct and objective measures of PA intensity (accelerometry) to clarify the minimum volume-intensity dose of PA necessary to achieve health benefits may be necessary. The consequences of a sedentary lifestyle are well-documented and include increased risk for cardiometabolic diseases (6) which may be mediated by an imbalance between oxidative and antioxidative as well as pro-inflammatory and anti-inflammatory mechanisms. Our findings indicate that modest improvements in daily low-intensity PA as a result of a 16-wk Internet-delivered PA intervention may restore some of this balance through reduced TNF-α in overweight adults.

ACKNOWLEDGMENTS

We thank Christy Lohof, Mandolyn Vendela, Jill Korenke, Kevin Bretting, Dr. Jamie Broomfield, Dr. Todd Barbee, and Debbie McClure for contributions to these projects. We also thank our participants.

Data were collected at the Human Integrative Physiology Laboratory at the University of Wyoming in Laramie, WY, and a medical clinic in Riverton, WY.

GRANTS

This project was supported by National Institutes of Health Grant P20-RR-016474.

REFERENCES


