Long-term, Aerobic Training Increases Adiponectin Levels in Trained, Middle-aged Females more than in Comparable Males

Authors:
Pooja P Mujumdar¹
E-mail: pmujumdar@llu.edu
Penelope J Duerksen-Hughes¹
E-mail: pdhughes@llu.edu
Anthony F Firek²
E-mail: anthony.firek@va.gov
David A Hessinger¹
E-mail: dhessinger@llu.edu

Affiliations:
1. Division of Pharmacology, Department of Basic Sciences, School of Medicine, Loma Linda University, Loma Linda, California, USA
2. Section of Endocrinology, Department of Medicine, Jerry L. Pettis VA Medical Center, Loma Linda, California, USA

ABSTRACT

Both aerobic training and the adipokine, adiponectin (ADPN), increase insulin sensitivity. Because the metabolic effects of aerobic training and ADPN are similar, aerobic training has been proposed to increase ADPN, which has been generally confirmed. However, in separate studies physically active adolescent females showed higher ADPN levels than sedentary controls, but trained young males showed no increase in ADPN levels. Because no direct comparison of males and females has been provided and because physically fit middle-aged adults have been largely neglected from studies on the effects of exercise on ADPN levels, we hypothesized that long-term (6 months), progressive long-distance training would increase ADPN levels more in trained, middle-aged females than in comparably trained, middle-aged males. We recruited aerobically trained, normal-weight, middle-aged females (n=8) and males (n=10) to participate in a prescribed marathon training protocol progressing from 10 to 90 km (6 to 55 miles) per week over 6 months. We collected and stored fasting plasma samples and recorded body measurements at 0 (baseline) and 6 months. Stored samples were analyzed for insulin, glucose, and ADPN. ADPN increased significantly among females [from 18.37 ± 10.39 (mean ± SD) to 22.50 ± 9.87 µg/ml; P<0.05], but non-significantly among males (from 6.69 ± 4.47 to 8.10 ± 5.57 µg/ml; P=0.2). No significant reduction in insulin resistance or anthropometric measurements occurred in either group. Our findings suggest that long-term, progressive aerobic training produces greater increases in circulating ADPN levels in trained, middle-aged, normal-weight females than in comparably trained males.

KEY WORDS: adiponectin, exercise, human, intervention studies, sex differences
1. INTRODUCTION

Central obesity, characterized by increased visceral adipose mass, is on the rise in middle-aged men and women (Jurimae et al. 2009, Wang et al. 2008). Central obesity reduces insulin sensitivity and decreases the production of adiponectin (ADPN), an adipokine positively correlated with insulin sensitivity (Havel 2004). ADPN knockout mice on a high fat diet developed insulin resistance and coronary artery disease (Maeda et al. 2002), while ADPN over-expression improved insulin sensitivity (Shibata et al. 2004). Because ADPN levels negatively correlate with obesity, high blood pressure, type II diabetes, hyperlipidemia, and metabolic syndrome (Weiss et al. 2009), higher levels of ADPN may preserve insulin sensitivity in middle-aged men and women (Wang et al. 2008, Jurimae et al. 2009).

Aerobic exercise improves insulin sensitivity, blood pressure, lipoprotein profile, and metabolic and cardiovascular health (Das 2004, Tall 2002, Blair et al. 1989). Because some of the effects of aerobic exercise training and ADPN are similar, aerobic training has been shown by many to increase ADPN levels (Das 2004). Cross-sectional studies reported significantly higher ADPN levels in physically active versus sedentary adolescent females (Ischander et al. 2007, Gruodyte et al. 2010). However, long-term studies on young, elite male rowers showed no changes in ADPN levels (Jurimae, Purge, and Jurimae 2006, 2007). These studies indirectly suggest that ADPN levels increase more in physically active, young females than in physically active, young males. However, no study has yet directly compared the effect of long-term aerobic training on ADPN levels in physically trained, normal weight males and females. Despite the known effects of exercise in preventing the health problems in middle-aged populations, most studies on the benefits of long-term exercise have been conducted on young athletes (Ischander et al. 2007, Gruodyte et al. 2010, Jurimae, Purge, and Jurimae 2006, 2007) rather than middle-aged athletes. Because physically fit middle-aged adults have been largely omitted from studies on the effects of exercise on ADPN levels, we hypothesized that trained, normal-weight, middle-aged females would exhibit significantly greater increases in ADPN in response to long-term, progressive aerobic training than similarly trained, exercising middle-age males. To test our hypothesis, we compared the effects of a 6-month, progressive, marathon-training program on ADPN levels in trained male and female groups of similar age and baseline BMI. Consistent with our hypothesis, we found that ADPN levels increased significantly in trained, middle-aged females by the end of 6-month training, but not in comparable males. Such results, if confirmed by additional
studies, suggest that males and females benefit differently from aerobic fitness.

2. METHODS

2.1 Subjects

We recruited subjects from a large (n ≈ 600) local running club to participate in a 6-month, progressive, marathon-training program. The Institutional Review Board of Loma Linda University approved the research protocol. We presented the objectives and procedures of the study to the club members and gave interested members an informed consent document explaining the procedures and risks and afforded opportunities to ask questions. Potential subjects signed the informed consent document before completing a screening questionnaire. Inclusion criteria were middle-aged males and females that have been training for and completing a minimum of one full-distance, competitive marathon (26.2 mi) per year for each of the past five years. Exclusion criteria were known cardiovascular, renal, hepatic, pulmonary, adrenal, pancreatic, thyroid, or pituitary disorder and smoking.

2.2 Demographic characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Trained Male (n=14)</th>
<th>Trained Female (n=10)</th>
<th>P$^5$</th>
</tr>
</thead>
<tbody>
<tr>
<td>age</td>
<td>51.5 ± 11.1</td>
<td>54.9 ± 10.6</td>
<td>NS</td>
</tr>
<tr>
<td>HT</td>
<td>1.77 ± 0.05</td>
<td>1.63 ± 0.09</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>WT</td>
<td>81.1 ± 12.8</td>
<td>63.3 ± 11.7</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>BMI</td>
<td>25.8 ± 3.7</td>
<td>23.9 ± 3.5</td>
<td>NS</td>
</tr>
<tr>
<td>BF</td>
<td>22.5 ± 6.4</td>
<td>28.2 ± 8.1</td>
<td>NS</td>
</tr>
<tr>
<td>WST</td>
<td>93.1 ± 11.6</td>
<td>80.0 ± 13.1</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>HIP</td>
<td>99.4 ± 7.7</td>
<td>98.9 ± 8.9</td>
<td>NS</td>
</tr>
<tr>
<td>WHR</td>
<td>0.94 ± 0.07</td>
<td>0.81 ± 0.09</td>
<td>&lt;0.005</td>
</tr>
</tbody>
</table>

Abbreviation key: age (yr); HT, height (m); WT, total body weight (kg); BMI, body mass index (kg/m²); BF, total body fat (%); WST, waist circumference (cm); HIP, hip circumference (cm); WHR, waist-to-hip ratio; NS, not significant; P$, significance between Trained Male and Trained Female groups by independent t-test.
Table II. Physical characteristics and blood analytes in trained male and female groups at the baseline (0 months) and end (6 months).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Time</th>
<th>Trained Male (n=10)</th>
<th>Trained Female (n=8)</th>
<th>P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>age</td>
<td>0 mo</td>
<td>50.9 ± 11.5</td>
<td>58.8 ± 6.3</td>
<td>NS</td>
</tr>
<tr>
<td>HT</td>
<td>0 mo</td>
<td>1.75 ± 0.03</td>
<td>1.61 ± 0.08</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>WT</td>
<td>0 mo</td>
<td>75.8 ± 9.6</td>
<td>63.4 ± 11.8</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>6 mo</td>
<td>75.4 ± 9.9</td>
<td>64.4 ± 12.6</td>
<td>0.06</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>NS</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>0 mo</td>
<td>24.9 ± 3.0</td>
<td>24.4 ± 3.5</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>6 mo</td>
<td>24.7 ± 3.1</td>
<td>24.8 ± 3.8</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>NS</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>BF</td>
<td>0 mo</td>
<td>19.3 ± 7.7</td>
<td>30.9 ± 11.2</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>6 mo</td>
<td>19.2 ± 7.7</td>
<td>30.1 ± 8.1</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>NS</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>WST</td>
<td>0 mo</td>
<td>86.7 ± 11.4</td>
<td>80.4 ± 14.1</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>6 mo</td>
<td>86.4 ± 11.2</td>
<td>79.5 ± 10.7</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>NS</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>HIP</td>
<td>0 mo</td>
<td>93.5 ± 11.3</td>
<td>99.1 ± 8.7</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>6 mo</td>
<td>93.0 ± 12.4</td>
<td>98.5 ± 9.3</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>NS</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>WHR</td>
<td>0 mo</td>
<td>0.93 ± 0.10</td>
<td>0.81 ± 0.10</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>6 mo</td>
<td>0.93 ± 0.09</td>
<td>0.81 ± 0.07</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>NS</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>ADPN$_{LT}$</td>
<td>0 mo</td>
<td>6.69 ± 4.47</td>
<td>18.37 ± 10.39</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td></td>
<td>6 mo</td>
<td>8.10 ± 5.57</td>
<td>22.50 ± 9.87</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>NS</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>FPI</td>
<td>0 mo</td>
<td>5.69 ± 2.62</td>
<td>4.99 ± 3.63</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>6 mo</td>
<td>4.97 ± 2.94</td>
<td>5.11 ± 3.22</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>NS</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>FPG</td>
<td>0 mo</td>
<td>101.4 ± 30.2</td>
<td>101.7 ± 12.1</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>6 mo</td>
<td>97.9 ± 15.2</td>
<td>95.6 ± 17.4</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>NS</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>0 mo</td>
<td>1.43 ± 0.73</td>
<td>1.28 ± 1.00</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>6 mo</td>
<td>1.23 ± 0.79</td>
<td>1.25 ± 0.90</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>NS</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation key: age (yr); HT, height (m); WT, total body weight (kg); BMI, body mass index (kg/m2); BF, total body fat (%); WST, waist circumference (cm); HIP, hip circumference (cm); WHR, waist-to-hip ratio; ADPN, plasma total adiponectin (µg/ml); FPI, fasting plasma insulin (µU/ml); FPG, fasting plasma glucose (mg/dl); HOMA-IR, HOmeostasis Model Assessment of Insulin Resistance; NS, not significant; LT, tests were conducted on log transformed variable; P, significance within Trained Male and Trained Female groups by a paired t-test; P$, significance between Trained Male and Trained Female groups by independent t-test.
We separated the subjects into two groups by gender: trained males and trained females. The male and female cohorts were similar in mean age and mean BMI (Table I). Subjects were not restricted to a particular ethnic group, but the proportion of Caucasians to non-Caucasians in the completing cohorts of the study were similar with 80.0% and 87.5%, being Caucasians in the male and female groups, respectively. During the 6 months of progressive training, four trained males withdrew due to training-related injuries, whereas two of the trained females dropped out (compare Tables I and II). Several specific factors contributed to the relatively small sample size of our study. These were (i) the inclusion of only middle-aged, multi-year trained subjects and (ii) the exclusion of potential subjects on prescription medicines known to influence ADPN levels. However, the sample sizes of our two study groups were similar to those of other long-term exercise-intervention study cohorts (Jurimae, Purge, and Jurimae 2006, 2007).

We included postmenopausal females both on (n=3) and not on (n=4) hormone replacement therapy (HRT) because ADPN levels have been reported to not differ between postmenopausal women on HRT and those not on HRT (Sieminska et al. 2005). We also included a peri-menopausal female (age 53 years) on oral contraceptive (OC) because ADPN levels in females are reported to be stable throughout the menstrual cycle (Kleiblova, Springer, and Haluzik 2006, Jurimae et al. 2010) and unaffected by the use of OCs (Jurimae et al. 2010). Female participants on oral contraceptives or HRT continued to use these throughout the study.

2.3 Training Protocol

All subjects followed the same progressive training protocol for 6 months, which is described in detail elsewhere (Mujumdar et al. 2011). The Sunday distance increased linearly at an average rate of 1.16 km/week from 3.2 to 32.2 km (2 to 20 miles) over a period of 6 months. Weekday and total weekly distances increased non-linearly during the first 8 weeks and thereafter increased linearly until the end of 6 months (Figure 1). We monitored adherence to the prescribed training protocol using self-reported daily running logs, which we collected each Sunday. Subjects remained in the same pace group throughout the study. We instructed subjects to maintain their pre-intervention dietary habits during the course of the study. Although dietary intakes were not monitored, subjects reported no changes in their dietary habits.
**Figure 1.** Time course of long-term, progressive training protocol. Total weekly distance (□) is the sum of weekday distance (○) and Sunday distance (△). Anthropometric data and blood samples were collected at baseline (0 months) and 6 months as indicated by arrows.

### 2.4 Biochemical measurements

Biochemical measurements are described in detail elsewhere (Mujumdar et al. 2011). Briefly, we collected fasting blood samples from the median cubital vein on Sundays, immediately before the start of the 3.2- and 32.2-km (2- and 20-mile), long-run distances corresponding to 0 and 6 months, respectively. We collected plasma by centrifugation, separated plasma samples into 0.5 ml aliquots, and immediately stored them at -80°C until analyzed. We used spectrophotometric, sandwich ELISA-based assays for fasting total plasma ADPN (mg/ml; EZHADPN-61K, LINCO Research, St. Charles, MO) and for fasting plasma insulin (FPI; µU/ml; EZHI-14K, LINCOResearch) and the glucose oxidase procedure (2810-1, Eagle Diagnostics, De Soto, TX) for fasting plasma glucose (FPG; mg/dl). We calculated the HOmeostasis Model Assessment of Insulin Resistance (HOMA-IR) scores using the following equation (Matthews et al. 1985):

\[
\text{HOMA-IR} = \frac{\text{FPI} \times \text{FPG}}{(\text{mg/dl})/18}/22.5
\]
2.5 Anthropometric measurements

Qualified personnel measured and recorded height (HT, m), body weight (WT, kg), total body fat (BF, %), waist circumference (WST, cm) and hip circumference (HIP, cm) as previously described (Mujumdar et al. 2011). We took measurements at 0 and 6 months between 6-7 AM on the same day as the blood draw immediately before the long run on Sunday. We calculated waist-to-hip ratio (WHR) and body mass index (BMI) from the measurements. Height (m) was measured at baseline (0 mo) using a stadiometer. We measured total body fat on standard adult mode (non-athlete mode) using bioelectrical impedance (model BF-679, TANITA Corporation, Arlington Heights, IL). All measurements were obtained in duplicate, recorded, and averaged.

2.6 Statistical Analyses

We used the Statistical Package for Social Sciences (version 17.0) for Windows (SPSS, Inc., Chicago, IL) to perform all statistical analyses. We considered the results statistically significant if a two-tailed P-value was less than or equal to 0.05. We used histograms and the Kolmogorov-Smirnov test for normality to determine whether the variables for the study groups were normally distributed. We log transformed and reassessed the variables that were not normally distributed. We used an independent t-test to assess each dependent variable between the study groups separately for each data collection point (i.e. 0-months baseline and 6 months). We also used an independent t-test to assess percent changes in the variables between the groups. We used a paired t-test to assess the difference in each dependent variable separately for each group. We used G*Power (version 3.0.10 for Windows XP) for power calculations (Erdfelder, Faul, and Buchner 1996).

3. RESULTS

3.1 Subject compliance

We enrolled subjects meeting the inclusion and exclusion criteria. Cohort sizes at each stage of the study are diagramed in Figure 2. Of the original 27 enrolled subjects, retention among trained male and trained female subjects was the same (66.7%). We carried out data analyses on a total of 18 subjects (i.e. males = 10; females = 8) who completed the 6-month training and provided complete data sets at baseline (0 months) and 6 months.
3.2 Adiponectin levels

The levels of ADPN increased at the end of 6 months of training in both the male and female groups, but significantly only among the females (Figure 3). The mean paired difference in ADPN level (paired t-test) was lower among the males (1.41 ± 2.52; 95% CI of the difference, 3.21 – 0.40) than among the females (4.13 ± 3.21; 95% CI of the difference, 6.81 – 1.45). In the female group ADPN levels at the baseline (0 months) and at the end of 6 months of training were three-fold higher than in the male group (Table II).

However, the percent increases in ADPN (∆ADPN%) were not significantly different between males (22.0 ± 43.4%; median, 11.4%) and females (38.7 ± 53.2%; median, 18.8%).
Figure 3. Plasma adiponectin levels at baseline and at end of 6 months aerobic training in groups identified by gender. Increase in adiponectin levels (mean ± SEM) between baseline (0 months, open bars) and end (6 months, filled bars) was significant in trained females, but not trained males, as determined by a paired t-test. Asterisk (*) indicates P<0.05. Sample sizes of each group are indicated in parentheses.

3.3 Insulin, glucose, and HOMA-IR score

Trained male and female groups exhibited similar fasting plasma insulin (FPI) and fasting plasma glucose (FPG) levels and similar HOMA-IR scores both at baseline and at the end of the study (Table II). Furthermore, FPI and FPG levels and HOMA-IR scores did not change by the end of the 6 months of training within either group.

3.4 Anthropometric measurements

The trained males had higher body weight (WT) than females. The difference was significant at the baseline, but non-significant at the end of the 6-month training. The male and female groups exhibited similar BMI, waist circumference (WST), and hip circumference (HIP) measurements at the baseline and at the end of 6 months of training. The females had significantly higher body fat (BF) and lower waist-to-hip ratio (WHR) compared to males at the baseline and at the end of 6 months of training. (Table II).

Both males and females exhibited negligible and non-significant reductions in
mean WST and HIP, and negligible increases in mean WHR and BF. Additionally, males exhibited negligible reductions in WT and BMI, whereas females exhibited negligible increases in WT and BMI (Table II).

4. DISCUSSION

In the present study, we compared the effects of long-term, progressive aerobic training on adiponectin (ADPN) levels in trained male and female marathoners who were middle- aged and normal-weight. Few exercise interventions measuring changes in ADPN levels have been conducted on middle-aged athletes. Because previous studies have mostly focused on trained, single-gender cohorts, the influence of gender on exercise-induced changes in ADPN has not been adequately addressed. Our results show that long-term, progressive aerobic training of 6 month duration increases circulating levels of ADPN to a greater extent in trained, middle-aged females than in similarly trained males.

4.1 Effects of gender

Females, in general, exhibit higher ADPN levels than males (Sun et al. 2009). In our previous study on untrained, middle-aged subjects undergoing 6-month, progressive aerobic training, ADPN levels in females were slightly higher both at baseline and at 6 months compared to males, and both males and females showed significant and similar increases in ADPN levels (Mujumdar et al. 2011). However, in the present study on trained, middle-aged marathoners, the male-female differences in ADPN levels at baseline and at 6 months were significantly larger with the trained females exhibiting ADPN levels about three times higher than the comparably trained males. In addition, our 6-month, aerobic protocol increased ADPN significantly in trained females (P<0.05), but non-significantly (P=0.19) in trained males. This is similar to a 6-month study showing no significant increases in ADPN levels among young, trained male rowers (Jurimae, Purge, and Jurimae 2007).

Previously trained, aerobically exercising females derive proportionately more of their expended energy from free fatty acid oxidation than males (Carter, Rennie, and Tarnopolsky 2001, Horton et al. 1998). ADPN expression positively correlates with hormone-sensitive lipase activity in females (Bullo, Salas-Salvado, and Garcia-Lorda 2005), which regulates lipolysis in adipose tissue. Thus, we suggest that our observation of trained exercising females exhibiting higher levels and greater increases in ADPN than comparably trained males may be metabolically linked to the greater capacity of aerobically trained female to mobilize and use free fatty acids during aerobic exercise.
4.2 Effects of training history

When comparing ADPN levels between untrained subjects from our previous study (Mujumdar et al. 2011) and trained subjects from our current study, the baseline ADPN levels in the trained males were not higher than those in the untrained males (Mujumdar et al. 2011). However, the baseline ADPN levels in the trained females were twice those in the untrained females (Mujumdar et al. 2011). Because of differences in mean age, BMI, and ethnicity between the cohorts of these two studies, we cannot directly compare untrained and trained subjects of the same gender. However, our present and previous findings (Mujumdar et al. 2011) and that of others (Gruodyte et al. 2010, Ischander et al. 2007, Jurimae, Purge, and Jurimae 2006, 2007) suggest that several years of prior aerobic training may increase ADPN levels much more in trained females than in trained males.

4.3 Effects of insulin resistance

Aerobic training lowers resting levels of insulin (Jurimae, Purge, and Jurimae 2006). However, we did not expect the 6-month training protocol to produce significant increases in insulin sensitivity because our subjects already were trained and exhibited HOMA-IR scores indicative of healthy insulin sensitivity. In fact, we did not observe any changes in insulin sensitivity following 6 months of training. Our findings suggest that exercise-induced increases in ADPN can occur without measurable reduction in HOMA-IR scores in trained males and females.

4.4 Effects of body measurement changes

Because our subjects of the present study were trained marathoners, we did not expect the 6-month aerobic training to produce significant changes in body measurements, nor did we observe any. Likewise, elite male rowers also showed no changes in body weight in response to 6-month training (Jurimae, Purge, and Jurimae 2007). Weight loss has been considered by some to be a necessary correlate to increased ADPN levels (Esposito et al. 2003, Hulver et al. 2002, Boudou et al. 2003, Madsen et al. 2008). However, studies using long-term aerobic training have reported increases in ADPN levels without weight loss in untrained (Ring-Dimitriou et al. 2006, Weiss et al. 2006, Mujumdar et al. 2011) and trained subjects (Jurimae, Purge, and Jurimae 2006, 2007). These and our current findings with trained subjects suggest that weight loss is not necessary for exercise-induced increases in ADPN.

5. CONCLUSIONS

We conclude that 6-month, progressive, aerobic training increases circulating ADPN
levels in multi-year trained females to a larger extent than in similarly trained males. To our knowledge, our findings are the first to directly show that trained females benefit more than comparably trained males in terms of increased ADPN levels induced by continued long-term training. In addition, we find that exercise-induced increases in ADPN levels can occur in the absence of changes in insulin-sensitivity or weight loss in previously trained individuals. Comparing our current findings with those of our previous study on untrained subjects and that of others, it appears that males show little to no increase in ADPN levels beyond what occurs during the first 6 months of progressive training.

However, in middle-aged females, ADPN levels increase beyond 6 months of marathon training provided that aerobic conditioning continues.

ACKNOWLEDGEMENTS
We thank: Bobby Thomas, M.B.B.S for supervising the blood draw sessions; Grenith Zimmerman, Ph.D. and Khaled Bahjri, M.D. M.P.H. for statistical advice; Glyne U. Thortington, Ph.D. for processing blood samples; the Board of Directors of the Lopers Club for permitting us to recruit subjects for the study; and the members of the Lopers Club for serving as subjects.

FUNDING
This research was supported by intramural grants 0316-6720 and 0316-6987 from Loma Linda University School of Medicine.

DECLARATION OF INTEREST
The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.
REFERENCES


Long-term, aerobic training increases adiponectin levels in trained, middle-aged females more than in comparable males.


Tall, A. R. 2002. "Exercise to reduce cardiovascular risk--how much is enough?"


