

原著

# Increased plasma adiponectin after low-intensity exercise in middle-aged women

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## 中年女性の低強度運動による 血清アディポネクチン濃度の増加について

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### SUMMARY

We investigated the number of daily-walking steps and rate of changes in plasma adiponectin concentration in 27 middle-aged women (mean age: 55 ± 8 years) who participated in health promotion class. A significant positive correlation between the mean total number of daily steps and plasma adiponectin concentration ( $r = 0.416$ ,  $p < 0.01$ ) was found, and the participants who walked over 10,000 steps per day on average or who continuously walked over 2,000 steps per day showed a significant elevation of plasma adiponectin concentration as compared with the participants who walked less than 10,000 steps per day on average or who continuously walked less than 2,000 steps per day ( $p < 0.05$ ).

These findings indicate that even relatively low-intensity exercise may yield higher plasma adiponectin concentration.

### 要 旨

健康教室に参加した中年女性27名(平均年齢 55 ± 8歳)を対象に日常歩行歩数と血清アディポネクチン濃度の変化について検討を加えた。その結果、一日平均歩行総数と血清アディポネクチン濃度との間には、有意な正の相関が認められた( $r=0.416$ ,  $p<0.01$ )。また、一日平均歩行歩数10,000歩以上あるいは一日連続歩行2,000歩以上の者は、一日平均歩行歩数10,000歩未満あるいは、一日連続歩行2,000歩未満の者に比べて、有意に血清アディポネクチン濃度が上昇していた( $p<0.05$ )。以上は、比較的低強度の運動でも血清アディポネクチン濃度が上昇したことを示している。

**Key words:** the mean total number of daily-walking steps, aerobic exercise, plasma adiponectin concentration

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## INTRODUCTION

In recent years it has been demonstrated that adipocytes serve not only to store energy, but also to secrete various biologically active molecules called adipocytokines. One of these molecules is adiponectin, a 244-amino acid secretory protein that is the most abundant gene transcript 1 (apM1) product of a gene specific to human adipose tissue<sup>10)</sup>. According to several studies, insulin resistance<sup>9,11,19,20)</sup>, arteriosclerosis<sup>3,13,16)</sup>, and angiogenesis<sup>15)</sup> are significant factors of adiponectin secretion.

Decreased release of adiponectin in hypertrophied adipocyte and lipotrophy models, and increased release in small adipocytes<sup>11)</sup> have been reported. Thus, the accumulation of small adipocytes seems important for preventing or mitigating lifestyle-related diseases such as insulin resistance and arteriosclerosis. It has long been known that physical exercise causes adipocytes to decrease in size<sup>2)</sup>. According to the results from studies of the relation between physical exercise and plasma adiponectin concentrations in healthy people, it has likely appeared that plasma adiponectin concentrations increase with exercise performed for a fixed period or regularly<sup>4,8,12,18)</sup>. On the other hand, other studies have reported that adiponectin decreases<sup>7)</sup> or is unchanged<sup>5,20)</sup> with physical exercise<sup>17)</sup>. This lack of consistency in research findings may be related to the effects of exercise type, intensity, and duration.

In any case, further investigations to identify the increase in plasma adiponectin concentration through appropriate exercises are needed. Walking is a good form of exercise that most people can manage in daily life. It has been a focus of attention as an exercise that causes fatty-acid oxidation<sup>16)</sup> and effectively promotes aerobic energy metabolism even at low-intensity<sup>1)</sup>. To our knowledge, there have been no reported studies on the relation between adiponectin and the steps of low-intensity-walking per day. In the present study, we researched plasma adiponectin concentration and the total number of walking steps a day of the in the middle-aged women participating in the health promotion class, and examined the relation of them.

## SUBJECTS AND METHODS

The subjects were 27 women (age:  $55 \pm 8$  years) who participated in a 3-month health promotion class from October 2004 to December 2004. An average step of all participants was 76 cm. Their physical and physiological attributes are shown in Table 1.

Height, body weight, BMI ( $\text{kg}/\text{m}^2$ ), plasma adiponectin concentration, glucose, and insulin and HbA1C (%) were measured at the beginning and end of the study period. HOMA-IR was calculated from plasma glucose and plasma insulin levels ( $(\text{plasma glucose (mg/dL)} \times \text{plasma insulin (}\mu\text{U/mL)} \div 405)$ ).

During the experimental period, subjects had worn a pedometer (HJ-2000, Omron, Japan) at all times except when sleeping.

From the number of steps recorded each month, the mean total number of steps was calculated for both the total number of steps per day and the total number of steps at least 10 minutes of continuous-brisk walk at a pace of 60 steps per minute (about 45.6 m per minute, from the mean values for women with a mean age of 55 years) (Y. Yanagimoto, unpublished observations).

One of Subject's groups, consisting of 12 women, walked average over 10,000 steps per day or walked average over 2,000 steps per day in continuous brisk walking, named HS group, and another group, consisting

of 15 women, walked average under 10,000 steps per day and walked average under 2,000 steps per day in continuous brisk walking, named LS group. The groups were then compared. The study was approved by the ethics committee of the Nagoya University Research Center of Health, Physical Fitness, and Sports.

## RESULTS

The rate of changes in all measured items at the beginning and end of the study period is shown in Table 1 for all subjects. No significant differences were seen in body weight, BMI, plasma insulin concentration, HOMA-IR, or HbA1C. However, the plasma adiponectin concentration, at the end of study, increased significantly ( $p < 0.005$ ), while the plasma glucose concentration decreased significantly ( $p < 0.05$ ).

Table 1. Changes in indicators before and after participation in health promotion class for all subjects.

	<b>before</b> <b>MEAN ± S. D.</b>	<b>after</b> <b>MEAN ± S. D.</b>	<b>P&lt;</b>
<b>Body weight (kg)</b>	<b>55.4 ± 5.9</b>	<b>56.0 ± 5.7</b>	<b>n. s.</b>
<b>BMI</b>	<b>23.6 ± 3.0</b>	<b>23.8 ± 3.0</b>	<b>n. s.</b>
<b>Plasma adiponectin concentration (μg/ ml)</b>	<b>10.7 ± 4.6</b>	<b>12.5 ± 5.9</b>	<b>0.004</b>
<b>Plasma glucose concentration (mg/ dl)</b>	<b>96.2 ± 10.8</b>	<b>80.1 ± 11.0</b>	<b>0.003</b>
<b>Plasma insulin concentration (μU/ ml)</b>	<b>5.9 ± 2.5</b>	<b>6.9 ± 4.0</b>	<b>n. s.</b>
<b>HOMA-IR</b>	<b>1.3 ± 0.3</b>	<b>1.6 ± 0.8</b>	<b>n. s.</b>
<b>HbA1C</b>	<b>5.4 ± 1.2</b>	<b>5.0 ± 0.6</b>	<b>n. s.</b>

(The unit of measurement, etc. are shown in the text.)

Next, a comparison between the HS and LS groups in rate of change for each measured item before and after the study period was made (Table 2). No significant differences were found between the groups in rate of changes in body weight, BMI, plasma insulin concentration, plasma glucose concentration, HOMA-IR, or HbA1C, but the change in plasma adiponectin concentration was significantly greater in the HS group than in the LS group ( $p < 0.05$ ).

Table 2. Rates of change in LS and HS groups before and after health promotion class.

	<b>LS group</b> <b>MEAN ± S. D.</b>	<b>HS group</b> <b>MEAN ± S. D.</b>	<b>P&lt;</b>
<b>Δ Body weight (kg)</b>	<b>1.01 ± 0.02</b>	<b>1.01 ± 0.02</b>	<b>n.s.</b>
<b>Δ BMI</b>	<b>1.01 ± 0.02</b>	<b>1.01 ± 0.05</b>	<b>n.s.</b>
<b>Δ Plasma adiponectin concentration (μg/ ml)</b>	<b>1.06 ± 0.16</b>	<b>1.23 ± 0.18</b>	<b>0.03</b>
<b>Δ Plasma glucose concentration (mg/ dl)</b>	<b>0.85 ± 0.12</b>	<b>0.83 ± 0.08</b>	<b>n.s.</b>
<b>Δ Plasma insulin concentration (μU/ ml)</b>	<b>1.12 ± 0.36</b>	<b>1.22 ± 0.53</b>	<b>n.s.</b>
<b>Δ HOMA-IR</b>	<b>1.25 ± 0.45</b>	<b>1.22 ± 0.54</b>	<b>n.s.</b>
<b>Δ HbA1C</b>	<b>1.01 ± 0.02</b>	<b>1.00 ± 0.02</b>	<b>n.s.</b>

(According to the results of pre-observational measurements between LS and HS, it is found that there is no significant difference in Body weight (kg)  $p < 0.7$ , BMI  $p < 0.9$ , Plasma adiponectin concentration  $\mu\text{g/ml}$   $p < 0.1$ , Plasma insulin concentration ( $\mu\text{g/ml}$ )  $p < 0.2$ , Homa-IR  $p < 0.2$ , and HbA1C (%)  $p < 0.09$ .)

A significant positive correlation was observed between plasma adiponectin concentration and mean total number of steps per day at the end of the study period (Fig. 1,  $r = 0.416$ ,  $p < 0.01$ ). A significant negative correlation was seen between plasma adiponectin concentration and HOMA-IR (Fig. 2,  $r = -0.608$ ,  $p < 0.003$ ).

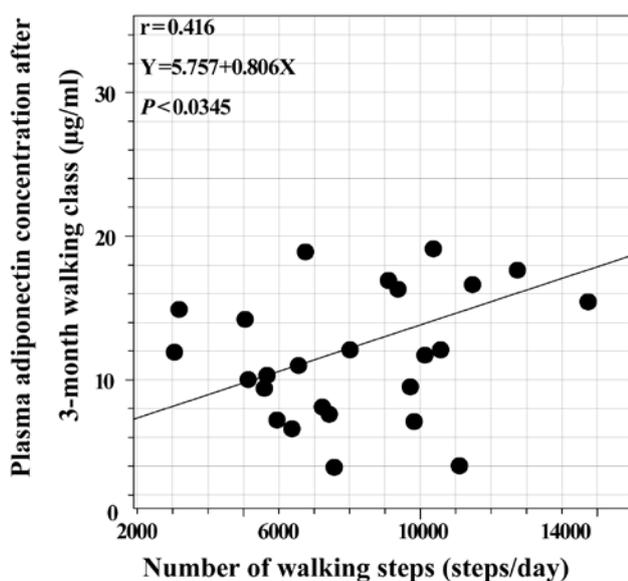


Fig.1. Relation between mean number of steps walked per day and post-health class plasma adiponectin concentration.

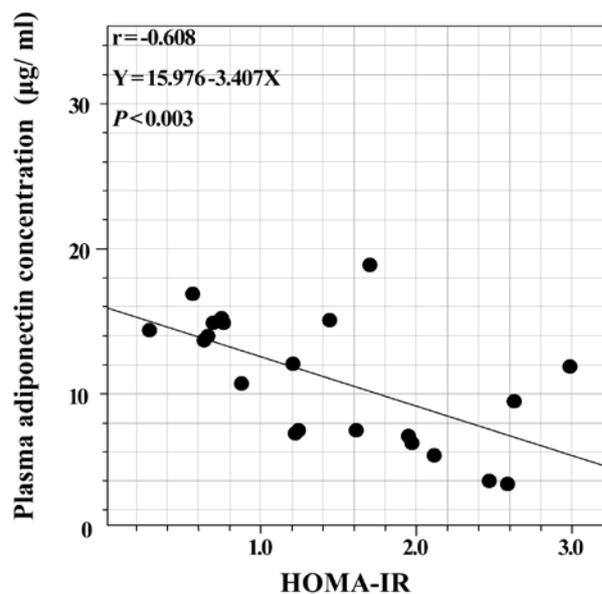


Fig.2. Relation between plasma adiponectin concentration and HOMA-IR.

## DISCUSSION

Various findings have indicated an association between adiponectin and insulin sensitivity. Maeda et al.<sup>10)</sup> reported an increase in adiponectin with the administration of thiazolidinediones (TZDs), known as insulin sensitizers. This suggests that increased adiponectin improves insulin sensitivity. Yamauchi et al.<sup>19)</sup> administered adiponectin directly to insulin-resistant mice and reported an improvement in insulin resistance. Hulver et al.<sup>7)</sup> found a negative correlation between plasma adiponectin and insulin levels. Kriketos et al.<sup>9)</sup> also reported a negative correlation between plasma adiponectin concentration and insulin resistance, while Yatagai et al.<sup>20)</sup> reported a positive correlation between insulin sensitivity and plasma adiponectin concentration.

In the present study, a significant negative correlation was found between plasma adiponectin concentration and HOMA-IR (Fig. 2,  $r = -0.608$ ,  $p < 0.01$ ). However, the concentration of plasma glucose concentration, which is closely related to plasma insulin concentration, decreased with exercise even though there was no significant change in its concentration. This result seems reasonable because the subjects in this study were healthy middle-aged women with no insulin resistance, so that plasma insulin concentration was maintained at a normal level.

On the other hand, there are multiple conflicting with reports as to the relation between adiponectin secretion and exercise. Some studies have found that plasma adiponectin concentration increase with exercise performed for a fixed-term-period or a regular exercise habit<sup>4,8,12,18)</sup>, whereas others have found no association<sup>5,7,20)</sup>. Fatouros et al.<sup>4)</sup> had males aged 65 to 78 years perform resistance exercise of varying intensities for a period of 6 months, and reported no change in plasma adiponectin concentration with low-intensity resistance training, but an increase in it with moderate-to-high resistance training.

Kriketos et al.<sup>9)</sup> reported finding that plasma adiponectin concentration increased significantly after 10 weeks of walking or jogging at an intensity of 55–70%  $Vo_{2max}$ . According to the same study, they reported

that plasma adiponectin concentration was negatively correlated with total body fat, central subcutaneous fat, and visceral fat mass. This seems to agree with the result of a report that the adiponectin concentration decreased in models of hypertrophied adipocytes and lipoatrophy, and increased in small adipocytes<sup>11)</sup>. These findings may suggest that hypertrophied adipocytes become smaller and there is increased release of adiponectin as a result of exercise. Tsukinoki et al.<sup>18)</sup> reported higher plasma adiponectin concentration in people who walked for about 1 hour twice a week than in those who did not.

In the present study, plasma adiponectin concentrations in all subjects were significantly higher at the end of the study period than at the beginning. Thus, the findings of this study appear to be the same results as previous studies of Fatourus et al.<sup>4)</sup>, Kriketos et al.<sup>9)</sup>, and Tsukinoki et al.<sup>18)</sup>. Moreover, in our study the increase rate was significantly greater in the HS group than in the LS group, and a significant positive correlation was found with the mean total number of steps normally walked per day (Fig.1,  $r = 0.416$ ,  $p < 0.034$ ) and the mean total number of brisk walking steps ( $r = 0.541$ ,  $p < 0.0043$ ). Even though there have been a number of reports with opposite results<sup>5,7,20)</sup> from the ones of our study, the study indicates that adiponectin concentrations increase even with low-intensity exercise if the amount of exercise is increased.

In addition, Yatagai et al.<sup>20)</sup> had 12 healthy male subjects aged 18-33 years perform exercise at a lactate threshold level of intensity on an ergometer for 1 hour per day, 5 days per week for 6 weeks. Therefore, he found no increase in plasma adiponectin even though there was an improvement in plasma glucose concentration. According to his study, there was no significant correlation between insulin sensitivity in the case of exercise and increase in plasma adiponectin concentration. Moreover, Hulver et al.<sup>7)</sup> had healthy male and female subjects with a mean age of 51 years perform treadmill, running, and stair-climbing exercise at an intensity of 65-80% peak  $VO_2$  consumption 4 days per week for 6 weeks. They found no relation with adiponectin amounts even though insulin resistance improved. Furthermore, Marcell et al.<sup>12)</sup> divided 51 males and females with a mean age of 45 years into 2 groups, and over 16 weeks had one group walk and jog at a moderate intensity (3.5 METs) for 30 minutes per day, 5 days per week, and the other group do aerobic exercise at an intensity of 80-90% peak  $VO_2$  consumption (4-6 METs). As the result of his study, comparison of the groups revealed that body fat and BMI decreased in both groups. Moreover, adiponectin increased somewhat in both groups, but the difference between the groups was not statistically significant ( $p < 0.09$ ). With regard to these results, there may have been a problem in the exercise intensity settings. Additionally, Hara et al.<sup>5)</sup> had obese young people perform endurance and resistance training for 5 months, but reported finding no increase in plasma adiponectin concentrations.

Consideration of these differences in terms of the present study, exercise intensity, and type of exercise suggests that continuation of low-intensity aerobic exercise may be related to increased release of adiponectin. In the present study, for example, walking more than 10,000 total steps per day at a normal pace or 2,000 steps per day briskly (the HS group) was correlated with adiponectin elevation and most of the walking in this group was done at a low-intensity of 2.2-3 METs<sup>6)</sup>. This intensity is low compared with the high speed of 76 m per minute that Adachi et al.<sup>1)</sup> indicated for the fat-burning rate. However, the results of a study by Jurimae et al.<sup>8)</sup>, trained boat athletes performed a rowing ergometer test for a maximum of 6,000 m (20 min: approx. 1,200.8 m), showed no change in the post-exercise adiponectin concentration compared with the pre-exercise level when no adjustment was made for change in venous plasma volume. A significant

increase in post-exercise adiponectin concentration was found, however, when adjustment was made for change in plasma volume. There was no change in leptin or insulin level in either condition. Considering this, although plasma volume was not measured in the present study, the change appeared in adiponectin but not in insulin level may have been found because blood was collected with the subjects at rest. No significant changes in plasma volume were observed with light exercise even when performed every day.

According to the study of Fatouros et al.<sup>4)</sup>, an increase in plasma adiponectin concentration was confirmed in moderate to high intensity training groups. However, the exercise in their study was resistance training rather than aerobic exercise such as walking. Ouchi et al.<sup>15)</sup> surmised that adiponectin stimulated AMP-activated protein kinase (AMPK), which accelerates sugar transport with muscle contraction, and increased the sugar transport of working muscle.

Further studies are necessary to confirm the types and intensity of exercise with which, if done regularly, adiponectin concentrations increase. In the present study, we found that in middle-aged women plasma adiponectin concentrations can be increased with walking of more than 10,000 steps per day and or more than 2,000 steps per day in brisk walking.

## CONCLUSION

According to this study, the significant positive correlation between the mean total number of daily steps and plasma adiponectin concentration was found. The findings indicate that even relatively low-intensity exercise can contribute effectively to plasma adiponectin secretion; therefore, the daily-walking exercise in the middle-aged women is relatively important to increase in plasma adiponectin concentration.

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