

Effects of intense cycling training on plasma leptin and adiponectin and its relation to insulin resistance

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Abstract

OBJECTIVE: Adiponectin, the most abundant protein secreted by white adipose tissue, is known for its involvement in insulin resistance (HOMA-R). The purpose of this investigation was to assess the effect of intense cycling training for six months on plasma concentrations of adiponectin and leptin and HOMA-R.

METHODS: Eight trained males non professional cyclists participated in this study. They completed two times maximal exercises separated by six months heavy cycling training. Blood samples were obtained before exercise, at the end and after 30 and 60 minutes of recovery.

RESULTS: Before training, adiponectin concentrations were not significantly altered after maximal exercise, but plasma leptin levels decreased significantly at the end of exercise (–21.42%, $p < 0.01$) and after 60 min of recovery (–21.18%, $p < 0.05$). After 6 months training, subjects exhibited a decreased in control leptin concentrations (–44.91%, $p < 0.05$) and in HOMA-R (–30.68%, $p < 0.05$) and showed delayed increase in adiponectin concentrations (after 30 min of recovery) (14.10%, $p < 0.01$).

CONCLUSIONS: Our results showed that adiponectin is sensitive to maximal exercise when realised after intense training and that six months heavy cycling training don't affect adiponectin concentrations, but decreases the synthesis of leptin and HOMA-R and improves aerobic capacity. Furthermore, it appears that after 6 months heavy chronic exercise adiponectin is not associated with aerobic capacity and/or insulin resistance and/or body composition modifications.

INTRODUCTION

Adipose tissue secretes multiple proteins known as adipocytokines that modulate various biological functions (Ronti *et al.* 2006). One of these adipocytokines is adiponectin (Scherer *et al.* 1995) which is the most abundant. Low circulating levels of adiponectin have been implicated in the development of insulin resistance (Yamamoto *et al.* 2004) and associated disorders such as obesity (Hara *et al.* 2003), dislipidemia (Saunders *et al.* 2012), type 2 diabetes (Lindsay *et al.* 2002) and cardiovascular diseases (Schulze *et al.* 2005). Adiponectin plays also an important role in glucose and lipid metabolism (Bouassida *et al.* 2010a). The response of plasma adiponectin concentration to acute and chronic exercise is limited and controversial (Bouassida *et al.* 2010b).

Further, evidence also suggests that an acute bout of vigorous aerobic exercise may result in a significant increase in plasma adiponectin levels in trained athletes, although this increase is not apparent until 30 minutes after the cessation of exercise (Jürimäe *et al.* 2005; Jürimäe *et al.* 2006). In contrast, immediately following the cessation of exercise, adiponectin levels are reported to be unchanged (Mansouri *et al.* 2011; Pop *et al.* 2010) or decreased (Numao *et al.* 2011; Gökbel *et al.* 2012).

Further, evidence also suggests that an acute bout of aerobic exercise at a moderate intensity has little or no impact on adiponectin levels in healthy, but untrained populations (Bouassida *et al.* 2010b).

It has been established that endurance training increases insulin sensitivity and causes improvements in insulin sensitivity. However, there is still controversy with regard to the effects of endurance training on adiponectin. For example, different authors have demonstrated no change (Plinta *et al.* 2011; Mansouri *et al.* 2011) or an increase (Saunders *et al.* 2012; Kelly *et al.* 2012) in adiponectin following different training protocols.

The purpose of the present study was to examine the effect of six months heavy cycling training on plasma adiponectin, leptin and insulin sensitivity during acute maximal exercise. We also sought to determine the effect of training on adiponectin and insulin resistance in trained cyclists subjects.

We hypothesized that adiponectin levels would be significantly increased following the acute maximal exercise after six months heavy cycling training. In this context, we want to confirm the results of Jürimäe *et al.* who indicated a delayed increase (after 30 min) in adiponectin concentration after heavy exercises performed by trained rowers. We also hypothesized that heavy chronic exercise would increase control adiponectin levels and decrease control leptin concentrations and insulin resistance.

METHODS

Participants

Eight healthy young males non professional cyclists were enrolled into this study before the beginning of the season (after one month and half holiday with no training or dietary restrictions). Their physical characteristics are shown in table 1. None of them smoked or drank alcohol or was taking any medication. Informed consent was obtained from all subjects and the study protocol that was in accordance with the principles of the Declaration of Helsinki 1975 (as revised in 1983). The study has been approved by the Ethical Committee of the University Hospital of Sousse, Tunisia.

Anthropometric measurements

Height was measured with a standing stadiometer and recorded with a precision of 0.1 cm. Body mass, percent body fat, fat mass and lean body mass were measured using bioelectrical impedance analysis (BEURER, Germany). Body mass index (BMI) was calculated using the standard formula: body mass in kilograms divided by height in meters squared ($\text{kg}\cdot\text{m}^{-2}$).

Experimental design

Participants performed an incremental exercise test to exhaustion on a calibrated cycle ergometer (Ergoline, Germany) to determine maximal oxygen consumption ($\dot{V}O_{2\text{max}}$). The test consisted in a 5 min warm-up followed by increments in power of one minute at 60 rpm until exhaustion. The loads during warm-up and increments were individually adjusted by taking into account the age, height and body mass of each subject (Wasserman *et al.* 1987). The analyzer was calibrated before the rest with the gases of known concentration. Validation of attainment of $\dot{V}O_{2\text{max}}$ satisfied two of the following four criteria: 1) an oxygen uptake plateau despite increasing exercise intensity, 2) respiratory exchange ratio ≥ 1.10 , 3) maximal heart rate within 10 beats.min⁻¹ of the age predicted maximal values (Tanaka *et al.* 2001) and 4) subject exhaustion.

Exercise sessions

These incremental exercises were carried out in Farhat Hached Hospital laboratory. Each subject performed them separated by a 6-months interval. A standardized breakfast (398 kcal) (Food Processor, version 8.3) was taken at 08:15 a.m. in the laboratory (the last meal taken by the subjects was at around 8:00 p.m. the day before and no other food or drink was taken until breakfast) just after the blood sampling (08:00 a.m.). The exercise started at 09:00 a.m.

The experiment was designed as follows:

- Maximal Exercise 1 (MEx1): This exercise was performed before the beginning of the preparation period.
- Maximal Exercise 2 (MEx2): This exercise was performed after six months cycling training.

Blood analysis

Blood samples were collected by venepuncture on 4 occasions: before the exercise control value (S1), at the end (S2), after 30 min (S3) and 60 min (S4). The same protocol was repeated after 6-months of heavy training.

The fasting blood samples (10 ml) were obtained from the antecubital vein with the subject in the upright position at 8:00 a.m. The plasma was separated and frozen at -80°C for later analysis.

Plasma adiponectin concentration was measured by immunoradiometric assay (Diagnostic Systems laboratories, USA intra-assay coefficient of variation (CV) was 2.6% and interassay CV was 3.7%). Plasma leptin concentration was determined by an immunoradiometric method (Immunotech, France, intra-assay CV was 3.3% and interassay CV was 4.8%). Glucose was measured using the hexokinase/glucose-6-phosphatase dehydrogenase method with a commercial kit (Boehringer, Mannheim, Germany). Plasma insulin concentration was estimated by a radioimmunoassay method (Immunotech, France, intra-assay CV was 2.8% and interassay CV was 5.3%). The insulin resistance index from fasting plasma insulin and plasma glucose levels was estimated using the homeostasis model assessment for insulin resistance (HOMA-R) and was calculated as described by Mathewes *et al.* (1985) $\{[\text{fasting insulin } (\mu\text{U/ml}) \times \text{fasting glucose } (\text{mmol/L})/22.5]\}^{(23)}$.

Hydration

To maintain optimal hydration, each subject drank three times the amount of 200 ml of water every 30 min: just before, after 10 and 40 min recovery.

Exercise training

The training program comprised 3 periods:

- *Preparatory period (3 months):*
The objective for this period is built a good basic fitness level at least 500 km for 5 days/week. The intensity of the exercise is done at 55–60 $\dot{V}\text{O}_{2\text{max}}$ (which corresponds with 60–65% of the heart rate reserve (HRR)). The HRR describes the difference between the maximum heart rate (HR_{max}) and resting heart rate. $\text{HRR} = \text{HR}_{\text{max}} - \text{HR}_{\text{rest}}$. The training heart rate can now be calculated: $\text{Training HR} = (\% \text{intensity} \times \text{HRR}) + \text{Resting HR}$. The HR_{max} was controlled by a Sport-tester device (Vantage NV, Polar Electro, Kempele, Finland). The mileage of the long ride increases gradually by no more than 10–12% per week.
- *Transition or Competition preparation phase period (2 months):*
For this period, the cyclists performed 5days/week with an intensity above 80% HR_{max}
Monday: 2 hours with intervals, of which 45 minutes high intensity
Tuesday: recovery day, rest

Wednesday: 2 hours: 3×20 min endurance + 8× sprint (6 sec work and 3 min active pause)

Thursday: 11/2–2 hours with intervals, of which 40 minutes high intensity

Friday: day off

Saturday: 1 ½ hours: 3x20 min endurance + 6× sprint (8 sec work and 2 min active pause)

Sunday: up to 4 hours: 45 min combination of high intensity and fartlek.

- *Competition period (1 month):*

At the competition phase of training is marked by intensity 85–88% HR_{max}. The cyclists trained 3 days/week.

Monday: 2–3 hours with intervals, of which 30 minutes high intensity and 30 minutes endurance.

Tuesday: day off

Wednesday: 2–3 hours with intervals, of which 30 minutes high intensity and 30 minutes endurance.

Thursday: day off

Friday: up to 4 hours: 45 minutes combination of high intensity and fartlek.

Saturday: day off

Sunday: competition

Statistical analysis

Mean \pm standard deviation (SD) were calculated for all variables. Friedman two-way analysis was performed, relating exercises (MEx1 and MEx2) and time of sampling (S1 to S4). When this analysis revealed significant differences a Wilcoxon paired test was used to identify significant changes between S1 and S2 to S4 and a Mann-Whitney test for unpaired data was used to locate where significant differences existed between MEx1 and MEx2. Correlation between adiponectin, leptin, insulin, BMI, body weight, percent body fat, body fat mass, lean body mass, $\dot{V}\text{O}_{2\text{max}}$, PAP and HOMA-R was performed using the Spearman method. $p < 0.05$ was considered statistically significant.

RESULTS

Subject characteristics

Physical characteristics of the subjects before and after 6 months training are presented in Table 1. After the intervention, body mass, BMI, fat mass and percent body fat were significantly decreased ($p < 0.05$). Whereas, $\dot{V}\text{O}_{2\text{max}}$ and PAP increased significantly by 11.25% ($p < 0.05$) and by 6.58% ($p < 0.05$), respectively.

Hormonal and metabolic modifications

Before training, adiponectin concentrations were not significantly altered after maximal exercise, whereas plasma leptin concentrations decreased significantly at the end of exercise (-21.42% , $p < 0.01$) and after 60 min of recovery (-21.18% , $p < 0.05$) (Table 2, Figures 1 and 2). *After 6 months training*, subjects exhibited a delayed increase in adiponectin concentrations (after 30 min of

Tab. 1. Physical characteristics of subjects.

	Before	After 6 months
Age (Yr)		20.7±4.8
Height (cm)		1.79±0.06
Body mass (kg)	66.9±6.37	65.3±5.8*
BMI kg/m ²	20.7±1.3	19.9±1.1*
Body Fat (%)	7.8±1.4	7.5±1.0*
Body fat mass (kg)	5.3±1.3	4.9±1.0*
Lean body mass (kg)	31.1±1.7	32.3±3.1
$\dot{V}O_{2max}$ (ml/kg/min)	64.0±5.9	72.1±8.8*
PAP (w)	399±23.70	425±31.19*

Data are means (±SD). $\dot{V}O_{2max}$: Maximal oxygen consumption; PAP: Peak Aerobic Power. *P<0.05 Before vs after 6 months.

Table 2. Mean ± SD changes in plasma adiponectin, leptin and insulin concentrations and in HOMA-R before and after the two maximal exercises realised before and after 6 months cycling training.

		Blood sampling			
		CV S1	0 min S2	30 min S3	60 min S4
Adiponectin µg/ml	Before	7.41±3.20	7.54±3.19	8.14±3.21	7.57±3.73
	After 6 months	5.53±2.12	5.54±2.10	6.31±2.09**	5.44±2.13
Leptin ng/ml	Before	8.26±4.85	6.49±4.59**	7.54±4.87	6.51±4.35**
	After 6 months	4.55±2.54+	5.09±3.01	4.36±1.75	4.34±2.17
Insulin µU/ml	Before	10.26±5.34	4.86±1.13*	6.19±5.79	4.05±2.52*
	After 6 months	11.94±7.18	6.44±2.73*	4.71±2.62*	2.37±0.90**
HOMA-R	Before		0.88±0.22		
	After 6 months		0.61±0.16+		

HOMA-R: Homeostasis model assessment for insulin resistance; S: Sampling point; CV: Control value. *p<0.05; **p<0.01 CV vs other samplings. +p<0.05 Before vs after 6 months.

recovery) (14.10%, p<0.01) and decreased control leptin concentrations (-44.91%, p<0.05) (Table 2, Figure 1, 2). HOMA-R was significantly reduced by 30.68%, p<0.05 following the 6 months cycling training.

Correlations

At rest, adiponectin levels during the second maximal exercise was only related to rest insulin concentrations (r=0.89, p<0.05).

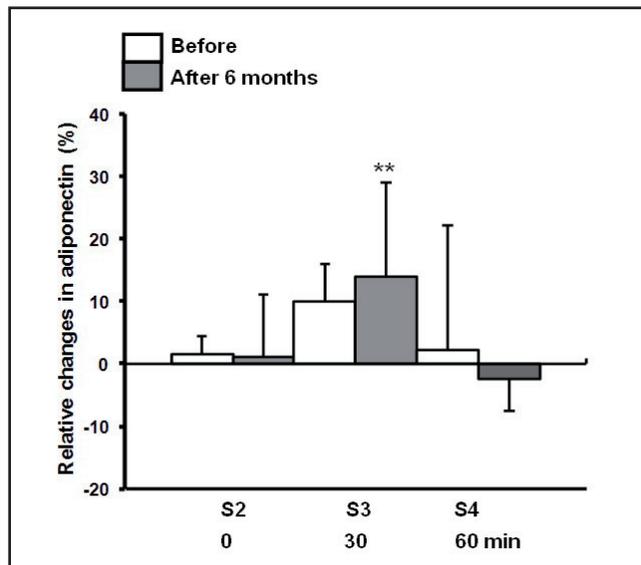


Fig. 1. Relative changes in serum levels of adiponectin before and after 6 months cycling training. Data are presented as percentage changes in relation to baseline values. **p<0.01 vs baseline.

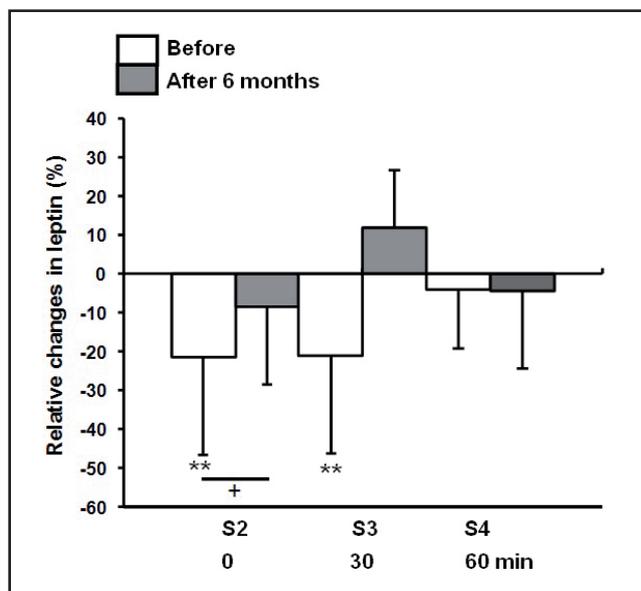


Fig. 2. Relative changes in serum levels of leptin before and after 6 months cycling training. Data are presented as percentage changes in relation to baseline values. **p<0.01 vs baseline. #p<0.05 before vs after 6 months training.

Basal adiponectin concentration was not related (p>0.05) to body mass (r=-0.56 MEx1; r=0.11 MEx2), BMI (r=-0.30 MEx1; r=-0.07), percent body fat (r=-0.38 MZEx1; r=-0.02 MEx2), fat mass (r=-0.36 MEx1; r=-0.04 MEx2), lean body mass (r=0.57 MEx1; r=0.02 MEx2), $\dot{V}O_{2max}$ (r=-0.14 MEx1; r=-0.46 MEx2), PAP (r=-0.14 MEx1; r=-0.59 MEx2), insulin (r=-0.29 MEx1), leptin (r=-0.15 MEx1; r=-0.29 MEx2), or HOMA-R (r=0.50 MEx1; r=0.73 MEx2) values.

DISCUSSION

The main findings of the present study were that: *Before training*, we failed to demonstrate significant changes in adiponectin concentrations after maximal exercise but, we showed a decrease in leptin concentrations. *After 6 months training*, we indicated a delayed increase in adiponectin concentrations after maximal exercise, a lower HOMA-R and control leptin concentrations and an increased aerobic capacity.

Adiponectin response to acute and chronic exercise

Our results support our first hypothesis and suggest that an acute bout of maximal exercise when realised by trained cyclists results in a significant delayed increase in plasma adiponectin levels.

Thus, we are the third study that shows a delayed increase (after 30 min) in adiponectin concentration after intense exercises performed by trained athletes. Indeed, trained rowers experienced a significant increase in adiponectin levels 30 min post 6.5 km rowing exercise at individual anaerobic threshold (Jürimäe *et al.* 2006) and post maximal 6 km rowing (Jürimäe *et al.* 2005). These authors attributed the delayed increase in adiponectin concentrations to the effects of short-term strenuous exercises realized when all major muscle parts are involved, such as rowing in highly trained subjects. Kelly *et al.* (2012) and Saunders *et al.* (2012) indicated also an increase in adiponectin concentrations after seven consecutive days of vigorous exercise in obese adults and after both acute and short-term aerobic exercise result in abdominally obese men, respectively. On the other hand, plasma adiponectin remained unchanged after 1) long-term moderate aerobic exercise in young female handball and basketball players (Magkos *et al.* 2010), 2) high intensity resistance exercise performed by trained and untrained subjects (Mansouri *et al.* 2011) and 3) single bout of moderate-intensity endurance exercise in healthy men and women (Magkos *et al.* 2010).

In contrast to our second hypothesis, we didn't demonstrate an increase in control adiponectin levels after the training in spite of the small modifications in body composition and aerobic capacity. Our results are in good agreement with previous exercise training studies showing no change in basal adiponectin levels after 12 weeks endurance or resistance training despite an improvement of maximal oxygen consumption and a significant decrease in body fat percentage (Ahmadi-zad *et al.* 2007). Several studies have shown that smaller decreases in the BMI do not result in any significant changes in adiponectin concentrations (Ryan *et al.* 2003; Mousavinasab *et al.* 2005). On the other hand, there are some reports indicating that considerable weight loss produces a significant increase in adiponectin levels (Yang *et al.* 2002 ; Esposito *et al.* 2003). Therefore, we presume that we did not observe any significant changes in adiponectin levels in our study

because the weight loss produced by exercise training was too subtle.

Potential mechanisms

Although insulin levels have been suggested to play a role in acute changes in adiponectin levels (Fasshauer *et al.* 2002 ; Jürimäe *et al.* 2005), it seem unlikely to explain the increase in adiponectin observed in the present study. In the present study, adiponectin levels were elevated above baseline only after 30 min recovery, while insulin levels were reduced in all time points for both exercises (immediately following exercises). This suggests that changes in insulin levels are not the primary mediator of the observed change in adiponectin levels. The mechanisms linking adiponectin to insulin are less unclear and further studies are necessary to clarify why in certain case adiponectin remains stable in spite of hypoinsulinemia. Further studies are needed to determine the mechanisms which intervene in the regulation of the synthesis and the release of adiponectin after the exercise and why this response is delayed.

Insulin resistance and adiponectin

In the present study, 6 months of heavy cycling training improved insulin resistance by 30.68% ($p < 0.05$). The relationship between adiponectin, insulin resistance and chronic exercise seems complicated and three models exist: 1) like our results, adiponectinemia stable and decreased insulin resistance (Ahmadi-zad *et al.* 2007), 2) hyperadiponectinemia and stable insulin resistance (Mujumdar *et al.* 2011) and 3) hyperadiponectinemia and decreased insulin resistance (Moghadasi *et al.* 2012). Several mechanisms have been proposed to be responsible for the increases in insulin sensitivity after exercise training (Ebeling *et al.* 1993; Dela *et al.* 1994). These include increased post-receptor insulin signalling (Dela *et al.* 1993), increased glucose transporter protein and mRNA (Dela *et al.* 1994), increased activity of glycogen synthetases and hexokinase (Ebeling *et al.* 1993) and increased muscle glucose delivery.

Leptin response to acute and chronic exercise

Another interesting finding of this study was that plasma leptin was significantly decreased at the end of the first exercise (-21.42% , $p < 0.01$) and after 60 min of recovery (-21.18% , $p < 0.05$).

Leptin concentrations significantly decreased following 1) 20 min at 80% of peak aerobic power (PAP) in overweight males (Bouassida *et al.* 2010a), 2) 6.5 km rowing at the individual anaerobic threshold in college level male rowers (Jürimäe *et al.* 2007) and 3) 90-min rowing at 70–75% of $\dot{V}O_{2max}$ in trained rowers (Des-gorges *et al.* 2004). On the other hand, Bouassida *et al.* (2010a); Kyriazis *et al.* (2007) and Olive & Miller (2001) showed that leptin concentrations were not altered after respectively, 20 min at 60% of PAP in overweight males, 60 min at 60% of $\dot{V}O_{2max}$ in obese men and 1 hour at 60% of $\dot{V}O_{2max}$ in trained subjects.

The decrease in leptin concentrations after the first maximal exercise can be explained by the total work output that was done during this exercise was beyond the threshold reduction in energy availability that must be reached to alter the leptin concentration (Bouassida *et al.* 2010a). But, the same energy expenditure was done during the second exercise after which we didn't found reduction in leptin. We speculate that lower control leptin concentration observed after training prevent us to note decline in leptin.

Following this study, we pointed out that interestingly, after 6 months trained subjects exhibited decreased control leptin concentrations (-44.91% , $p < 0.05$) with decreased body weight, BMI and body fat mass.

Several previous studies established that leptin concentrations were lower after 2 weeks of high-volume training in trained rowers (Rämson *et al.* 2012) and after 3 months aerobic training in preparation for the match season (Plinta *et al.* 2011). These declines in circulating leptin levels occur without body weight changes. Similar to our results, Huskoren *et al.* (2010) suggested that 8 weeks military training altered leptin and BMI. On the other hand, Ara *et al.* (2006) reported that 6 weeks resistance training did not effect leptin concentrations.

We suggest that weight and body fat loss combined with improved insulin sensitivity noted after 6-months of training cycling decreases control leptin concentrations.

The present study has several strengths and limitations which warrant mention. As mentioned previously, the present analysis focused only on adiponectin, leptin and insulin concentrations, rather than looking at concentrations of specific hormones that can modulate adiponectin concentrations such as interleukin-6, tumor necrosis factor and catecholamine (Chen *et al.* 2011; Schulpis *et al.* 2005). The current study also focused exclusively on a relatively trained group of non professional cyclists, and thus our findings may not translate to other individuals with ages or phenotypes different from those of participants in the current sample.

In conclusion, our results showed that adiponectin is sensitive to maximal exercise when realised after intense training and that six months heavy cycling training don't affect adiponectin concentrations, but decreases leptin and HOMA-R and improves aerobic capacity. Furthermore, it appears that after 6 months heavy chronic exercise adiponectin is not associated with aerobic capacity and/or insulin resistance and/or body composition modifications.

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