Leptin Level Lowers in Proportion to the Amount of Aerobic Work After Four Weeks of Training in Obesity

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Key words
- leptin
- insulin resistance
- obesity
- physical training
- anaerobic threshold

Abstract

Leptin values are higher in obesity. Physical exercise reduces fat mass (FM) and decreases leptin levels. Intensity of physical training seems to play a role in reducing circulating leptin. In 16 obese subjects (8 men and 8 women, age 38.6 ± 3.9 years, BMI 35.9 ± 1.8 kg/m^2), leptin was sampled before and after 4 weeks of controlled training. Eight subjects (4 men and 4 women) performed an aerobic training schedule (Group A), the remainders an aerobic training program with a bout of work beyond the anaerobic threshold (AT) (Group B). Training determined a reduction in leptin levels in both groups, which was significant in Group A (12.2 vs. 27.8 µg/l, $p < 0.05$), even when related to the change in FM (0.372 vs. 0.762 µg/l/kg, $p < 0.05$). FM decreased significantly in Group B when compared to Group A (–7.4 vs. –2.6 kg, respectively, $p < 0.001$). While in Group A the slight loss of FM was aggregated to a significant decrease in leptin levels, the opposite occurred in Group B. In Group A, leptin lowering was proportional to the amount of total work performed ($p < 0.001$, $R^2 = 0.89$). In obesity, a reduction is observed in leptin levels after short-term training, which is seemingly dissociated from concomitant decrease of FM. Aerobic training alone appears to be linked to a greater leptin reduction, which is well correlated with the amount of work performed.

received 20.05.2014
accepted 06.11.2014

Bibliography
DOI http://dx.doi.org/10.1055/s-0034-1395637
Published online: December 12, 2014
Horm Metab Res 2015; 47: 225–231

ISSN 0018-5043

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Introduction

Leptin is a hormone mainly secreted by adipocytes that works to regulate body weight and satiety [1]. Its levels in blood serum are higher in obese compared to lean subjects, but the significance of this difference on the development of obesity remains uncertain. In fact, the failure of the metabolic response to endogenous leptin in the setting of obesity, a condition also known as leptin resistance, is a question still open to debate [2].

Previous studies in different experimental conditions have pointed out that serum leptin may decrease in state of acidosis [3], elevated glucose uptake in the presence of lactate [4], and inhibition of glycolysis [5]. In contrast, a stressed leptin secretion by adipocytes has been shown after acute administration of growth hormone (GH) [6], glucose infusion [7], and acute infusion of glucosamine with an increase in leptin mRNA [8, 9].

Acute physical exercise promotes a decrease in plasma leptin levels in trained subjects, as observed 9 h after resistance exercise [10], or at the end of a moderately intense prolonged exercise in relation to energy expenditure [11]. In normal as well as in obese subjects, a period of prolonged physical training also promotes a decrease in leptin [12, 13].

Regular exercise is an important strategy in the management of obesity, together with hypocaloric diet and appropriate lifestyle. The aim of this study was to elucidate in obesity the behaviour of leptin after a comparable type of training at work loads of different intensity, that is: 1) after exclusively aerobic work, and 2) after aerobic work plus a bout of anaerobic work. On the basis of previous observations on GH and nonesterified fatty acids (NEFAs) [14, 15], we might presume different behaviours of leptin with regard to differences in quantity of physical training.

Subjects and Experimental Protocol

Among 50 initially screened patients admitted between January 2009 and December 2011 to Auxologic Italian Institute for workup of obesity and weight management program, 16 subjects (8

males and 8 females, age 38.6 ± 3.9, range 22–59 years, body mass index (BMI) 35.9 ± 1.8 kg/m^2, range 31–43) were enrolled and studied at the beginning and at the end of a 4-week inpatient period.

Exclusion criteria were smoking, physical inability, arterial hypertension, diabetes, or any other cardiovascular or metabolic disorder as well as thyroid and autoimmune disorders. Women were analysed during early follicular phase of the menstrual cycle. Anthropometric measures after voiding, EKG, routine blood and urine analysis were carried out to exclude medical illnesses. Bioimpedance analysis (BIA 101/S Akern, Florence, Italy) previously validated [16] to exclude fluid overload and fat mass (FM, kg) and fat-free mass (FFM, kg) was performed in each participant before and after the training period. A preliminary nocturnal O_2 saturation monitoring excluded the presence of significant periods of pathological low values in each participant.

The protocol was approved by the Ethics Review Committee of the Institute and written informed consent was given by all the subjects before participation, in accordance with the Helsinki Declaration of the World Health Organization (1964, amended in 1975 and 1983) and with the Updated Ethical Standards in Sport and Exercise Science Research [17].

Body weight was stable in each subject for at least 3 months before enrollment. Prior to exercise testing, subjects were asked to restrain from strenuous activity for at least 24 h. Following an overnight fast, in the morning every subject performed a continuous incremental test on a Gould bicycle ergometer with power output increased by 20 Watt (at 60 rpm) every 4 min until the pedalling frequency could no longer be maintained despite verbal encouragement. Subsequently, everyone continued pedalling effortlessly for 2 min, and then stopped and remained in a sitting position for up to 30 min.

The Vmax 229 (Sensor Medics, Yorba Linda, CA, USA) gave continuous analysis of oxygen consumption (VO_2), CO_2 production (VCO_2), and ventilation (VE). Work capacity was assessed by the maximum work rate obtained together with the detected VO_2 max related to predicted VO_2 max [18], and ventilatory anaerobic threshold (AT) measured by the V-slope method [19]. Heart rate (HR) and EKG signals were recorded by a CASE 6.5 (GE Medical System Milwaukee, WI, USA), and oxyhaemoglobin saturation was controlled by a Radiometer percutaneous oxymeter every 20 s. Calibrations were performed prior to each test.

Sampling was carried out before the test from the antecubital vein of the right or left arm and analysed for determination of leptin (Linco's RIA; sensitivity, 0.5 µg/l; intra-assay CV, 8.3 %), nonesterified fatty acids (Randox Laboratories USA; sensitivity, 0.072 mmol/l; inter- and intra-assay CV, 4.5 and 4.74 %, respectively), insulin (Immulite 2000 Analyzer; Diagnostic Products Corp., Los Angeles, CA; sensitivity, 2 µlU/mL; inter-and intra-assay CV, 4.0 and 5.1 %, respectively), and glycaemia (Gem Premier 3000; Instrumentation Laboratory). In addition to absolute concentrations leptin was expressed as values normalised for fat mass ($leptin_{FM}$) both at the beginning and at the end of the study, and variations between these values ($leptin_{FM}$ after training/ $leptin_{FM}$ before training) as percent. The modified HOMA model was used to yield an estimate of insulin sensitivity and β-cell function from fasting plasma insulin and glucose concentration [20].

After the preliminary exercise testing, 8 subjects were considered for Group B; the others were considered for Group A and an effort was made to maintain an equal distribution between the 2 Groups as far as sex, age and BMI are concerned.

Group A performed an exclusively aerobic training (power output attaining 70 % of HR registered at AT: 30 min, 2 sessions daily, 6 days/week, 4 weeks). Group B performed a mixed training (aerobic part attaining 70 % of HR registered at AT: 25 min, followed by anaerobic part attaining 85 % of HR max: 5 min, 2 sessions daily, 6 days/week, 4 weeks). About Group B we reasoned that, in accordance with our previous experience, 5 min of work beyond anaerobic threshold could be performed by a great majority of obese subjects. Planning 5 min 2 times a day for 6 days/week for 4 weeks, a total amount of 4 h of anaerobic work would have been performed. This might represent a significant quantitative difference from aerobic work alone.

During the training period increments of power outputs were imposed in both groups in view of the actual reconditioning and the aforesaid HR were maintained as the reference standards. At the end of each training period, everyone underwent a conclusive ergospirometric test according to the same protocol setting as the entry test and sampling.

During the study every subjects observed a balanced diet (57 % carbohydrate, 25 % lipid, 18 % protein) corresponding to their basal metabolic rate determined by indirect calorimetry with a ventilated canopy (Vmax 229, Sensor Medics, Yorba Linda, CA, USA), and no strict dietary restriction was imposed.

Statistical analysis

ANOVA was employed to determine differences between groups and between pre- and post-training values with a statistical power at least higher than 70 % [21]. We used the least-squares criterion applying ANOVA to the regression model to calculate the straight-line multiple regression [22]. Values were expressed as mean ± SEM. A difference was considered statistically significant for $p < 0.05$.

Results

Group A consisted of 8 subjects (4 M, 4 F) with a mean age of 39.6 ± 3.7 years, Group B consisted of 8 subjects (4 M, 4F) with a mean age of 37.8 ± 4.1 years. Anthropometric data are summarised in **Table 1**. Basal BMI, weight and FM were not significantly different between the 2 groups (p = NS, p = 0.051, and p = NS, respectively), while height and FFM were significantly lower in Group A (p = 0.039 and p = 0.044, respectively) by 2 tailed analysis of variance (**Table 1**). Training did not significantly decrease body weight compared to baseline both in Group A (92 ± 8 kg vs. 89 ± 7 kg) and Group B (114 ± 8 kg vs. 107 ± 7 kg). Nevertheless, the decrease in FM resulted significantly higher in Group B compared with Group A (–7.4 ± 1.1 kg vs. –2.6 ± 0.8 kg,

Table 1 Anthropometric and functional data of the samples.

Variable†	Group A		Group B	
	Before training	After training	Before training	After training
Weight (kg)	92 ± 8	89 ± 7	114 ± 8	107 ± 7
Height (cm)	162 ± 4	–	176 ± 4	–
BMI (kg/m^2)	35 ± 2	34 ± 2	37 ± 2	35 ± 2
Fat-free mass (FFM) (kg)	53 ± 4	53 ± 4	68 ± 6	68 ± 6
Fat mass (FM) (kg)	39 ± 4	36 ± 3	46 ± 3	38 ± 3
Exercise peak (Watts)	95 ± 9	109 ± 10	125 ± 9	138 ± 10
Anaerobic threshold (AT) (Watts)	67 ± 6	76 ± 6	86 ± 7	94 ± 9

† Values are mean ± SEM. BMI: Body mass index

Table 2 Individual and mean variations in weight, FM, FFM, and leptin together with (leptin$_{FM}$ after/leptin$_{FM}$ before) percent in men and women of Group A and Group B.

Group A									
Males	**Weight (kg)**		**Fat mass (kg)**		**Fat-free mass (kg)**		**Leptin (µg/l)**		**(Leptin$_{FM}$ after/ leptin$_{FM}$ before) %**
	Before	**After**	**Before**	**After**	**Before**	**After**	**Before**	**After**	
1	117.4	113.0	38.3	34.2	79.1	78.8	63.0	6.2	–89.0
2	131.0	130.0	59.0	57.1	71.8	72.9	27.2	12.1	–54.0
3	79.7	76.1	35.7	33.7	44.0	42.4	25.4	16.7	–30.0
4	78.9	77.0	30.9	30.4	48.0	46.6	10.8	7.6	–28.6
mean ± SE	101.7 ± 13.2	99.0 ± 13.4	41.0 ± 6.2	38.8 ± 6.1	60.7 ± 8.7	60.0 ± 9.2	31.6 ± 11.1	10.6 ± 2.4	–50.4
		–2.7%		–5.4%		–1%		–66.5%	
Females									
5	76.5	73.6	30.6	26.4	45.9	47.2	10.3	6.4	–28.2
6	69.9	65.5	27.1	24.7	42.8	40.8	16.4	10.2	–31.8
7	82.2	80.0	37.1	35.2	45.2	44.8	35.4	14.8	–56.0
8	98.0	96.8	52.9	48.5	45.1	48.3	33.9	23.8	–23.4
mean ± SE	81.6 ± 6.0	79.0 ± 6.6	36.9 ± 5.7	33.7 ± 5.4	44.8 ± 0.7	45.3 ± 1.7	24.0 ± 6.3	13.8 ± 3.7	–34.9
		–3.2%		–8.7%		+1.3%		–42.5%	
Group B									
Males	**Before**	**After**	**Before**	**After**	**Before**	**After**	**Before**	**After**	
1	141.0	137.3	56.5	47.1	84.5	89.6	22.0	26.2	+44.0
2 *	147.3	139.1	50.3	44.8	97.0	93.7	9.1	3.7	(–54.0)
3	123.0	115.3	50.0	41.0	71.0	73.7	12.6	12.6	+21.8
4	98.6	94.3	36.2	31.3	62.4	62.4	48.5	26.8	–38.9
mean ± SE	127.5 ± 10.9	121.5 ± 10.6	48.2 ± 4.9	41.0 ± 3.5	78.7 ± 7.6	79.8 ± 7.2	23.1 ± 8.9	17.3 ± 5.6	(–6.8)
		–5.1%		–15.4%		0%		–21.1%	
Females									
5	100.7	96.1	51.8	44.2	48.9	51.3	29.1	27.0	+8.7
6	84.0	70.0	33.2	20.6	50.8	48.8	34.0	25.3	+19.9
7	106.8	100.6	53.1	47.0	53.7	53.0	32.4	22.9	–20.2
8	110.3	101.7	38.1	31.4	72.2	69.7	5.6	3.6	–21.8
mean ± SE	100.4 ± 5.8	92.1 ± 7.5	44.0 ± 5.0	35.8 ± 6.1	56.4 ± 5.4	55.7 ± 4.7	25.3 ± 6.6	19.7 ± 5.4	–3.4
		–8.3%		–18.6%		–1.3%		–22.2%	

* The outlier value of leptin$_{FM}$ after/leptin$_{FM}$ in percent for the male subject 2 is given in parentheses

$p < 0.001$), even when corrected for difference in starting FM (–16.6% ± 3.0 vs. –7.1% ± 1.3, $p < 0.05$, respectively).

Table 2 shows the individual modifications of weight, FM, and FFM of both groups after training.

The total amount of physical work performed during the study period resulted significantly higher in Group B than in Group A (mean 6240 ± 510 Kjoules vs. 4270 ± 330 Kjoules, $p = 0.018$, respectively) (**Table 3**). After training periods, work capacity improved albeit not significantly both in Group A and Group B (**Table 1**).

Heart rate increased in both groups during exercise testing in accordance with the increase of work output either before and after the training period (**Table 3**), nevertheless after training females of Group A seem to evidence a more pronounced increase in correspondence of peak activity.

In **Table 4,5** are reported single session work outputs at the beginning of training and at the end of training in Group A and Group B as a whole and as a ratio to FFM, and, within brackets, the share of anaerobic work of each participant of Group B. In **Table 5**, with regard to the differences in FFM and performance between the 2 groups, we have added the calculated findings of simulated equal work outputs obtained by replacing the performed anaerobic shares of each subject with the hypothetical corresponding shares of aerobic work. It is possible to observe that the singular initial session performed by Group A and the initial simulated session of Group B do not differ when expressed as ratio to FFM (1.53 vs. 1.58 Kjoules/FFM, respectively).

Similarly, the total work performed by Group A does not significantly differ from both simulated and real total work performed by Group B (81.6 ± 4.2 vs. 82.6 ± 5.3 Kjoules/FFM and 81.6 ± 4.2 vs. 93.0 ± 5.5 Kjoules/FFM, respectively).

A decline in leptin levels, both when expressed as absolute values and in relation to FM, reached statistical significance only in Group A, while it decreased nonsignificantly in Group B (**Table 6**). Individual values of leptin before and after training and the variations between these values (leptin$_{FM}$ after training/leptin$_{FM}$ before training) as percent are reported in **Table 2**. In Group A, these findings were paralleled by a nonsignificant reduction of insulin levels after training, while these were unchanged in Group B (**Table 6**). Fasting plasma glucose was unmodified in either groups at the study end. After training HOMA2-B was significantly lower in Group A (**Table 6**). NEFA significantly decreased in Group A and significantly increased in Group B after training (**Table 6**).

In Group A, we found a linear inverse correlation between the total work performed and the ratio of leptin$_{FM}$ after training and leptin$_{FM}$ before training in percent ($R^2 = 0.89$) (**Fig. 1**) which remains significant even after the addition of NEFA and insulin variations (adjusted R^2 from 0.847 to 0.774). In Group B, after excluding one outlier (marked with * in **Fig. 1**), a linear direct correlation was documented ($R^2 = 0.88$). Positive values were

Table 3 Individual heart rate and work outputs (Kjoules) during exercise testing before and after the aerobic training period in men and women of Group A and the aerobic plus anaerobic training period of Group B.

Group A									
	Heart rate before training				**Heart rate after training**				**Kjoules**
Males	**Rest**	**AT**	**Max**	**70% AT**	**Rest**	**AT**	**Max**	**70% AT**	
1	78	147	168	103	74	121	146	85	6048
2	80	138	168	97	87	142	176	99	5140
3	80	121	143	84	72	126	156	88	3326
4	85	132	154	92	81	129	150	90	3629
mean ± SE	81 ± 1	134 ± 5	158 ± 6	94 ± 4	78 ± 3	129 ± 4	157 ± 7	90 ± 3	4536 ± 641
% vs. rest		+66	+96	+16		+65	+100	+15	
Females									
4	80	128	148	89	86	138	168	96	3931
5	81	124	134	87	68	121	150	84	4234
6	65	129	147	90	75	126	146	88	4536
7	97	150	164	105	96	152	166	106	3326
mean ± SE	81 ± 6	133 ± 6	148 ± 6	93 ± 4	81 ± 6	134 ± 7	157 ± 6	93 ± 5	4007 ± 258
% vs. rest		+66	+86	+16		+66	+96	+16	

Group B											
	Heart rate before training					**Heart rate after training**					**Kjoules**
Males	**Rest**	**AT**	**Max**	**70% AT**	**85% Max**	**Rest**	**AT**	**max**	**70% AT**	**85% Max**	
1	71	120	152	84	129	71	116	148	81	126	7128
2	67	114	148	80	126	64	108	160	76	136	8878
3	82	121	152	85	129	81	127	158	89	134	7380
4	64	110	142	77	121	70	112	147	78	125	4997
mean ± SE	71 ± 4	116 ± 4	148 ± 2	81 ± 2	126 ± 2	71 ± 4	116 ± 4	153 ± 3	81 ± 3	130 ± 3	7096 ± 799
% vs. rest		+64	+110	+16	+71		+62	+116	+13	+83	
Females											
5	76	122	155	85	132	72	125	156	87	133	6257
6	77	120	150	84	127	76	122	152	85	129	4874
7	88	136	168	95	143	86	130	158	91	134	5249
8	82	135	163	94	139	84	133	171	93	145	5126
mean ± SE	81 ± 3	128 ± 4	159 ± 4	89 ± 3	135 ± 4	79 ± 3	127 ± 2	159 ± 4	89 ± 2	135 ± 3	5376 ± 304
% vs. rest		+59	+97	+11	+67		+61	+101	+13	+70	

AT: Anaerobic threshold

Table 4 Individual work performed at beginning and ending training of Group A.

Group A						
	Single session work outputs at the beginning of training			**Single session work outputs at the end of training**		
Males	**Watts**	**Kjoules**	**Kjoules/FFM**	**Watts**	**Kjoules**	**Kjoules/FFM**
1	2100	126.0	1.59	2100	126.0	1.58
2	1470	88.2	1.26	2100	126.0	1.75
3	1050	63.0	1.43	1260	75.6	1.78
4	1260	75.6	1.58	1260	75.6	1.62
mean ± SE	1470 ± 227	88.2 ± 13.6	1.47 ± 0.08	1680 ± 242	100.8 ± 14.5	1.68 ± 0.05
Females						
5	1260	75.6	1.61	1470	88.0	1.86
6	1260	75.6	1.77	1680	101.0	2.42
7	1260	75.6	1.64	1890	113.0	2.47
8	1050	63.0	1.35	1260	75.6	1.53
mean ± SE	1208 ± 53	72.5 ± 3.2	1.59 ± 0.09	1575 ± 136	94.4 ± 8.1	2.07 ± 0.23
Total mean ± SE	1339 ± 119	80.3 ± 7.1	**1.53 ± 0.06**	1627 ± 130	97.6 ± 7.8	1.88 ± 0.1

detected in correspondence to maximal training work outputs in 3 of 4 cases. When both groups were merged, such correlations were lost.

We have looked for any multiple correlation between leptin variations and the tested variables in both groups (Kjoules performed, FFM, NEFA, insulin, and glucose), finding no significant correlation among them.

Discussion

In this study, we looked at leptin dynamics in 2 groups of obese subjects after a short period of physical training at different work out-puts. The interest in leptin secretion is due to the effect of this hormone on satiety control in which it plays an important role, together with other adipokines, as well as pan-

Table 5 Individual work performed at beginning and ending training of Group B and simulated data of aerobic work instead of aerobic plus anaerobic work.

Group B									
Males	Single session work outputs at the beginning of training			Simulated aerobic single session work-outputs at the beginning of training			Single session work outputs at the end of training		
	Watts (>AT)	Kjoules (>AT)	Kjoules/ FFM (>AT)	Watts	Kjoules	Kjoules/FFM	Watts (>AT)	Kjoules (>AT)	Kjoules/ FFM (>AT)
1	2345 (595)	141 (36)	1.65 (0.42)	2100	126	1.47	2605 (680)	156.3 (40.8)	1.74 (0.45)
2 *	2865 (765)	172 (46)	1.75 (0.46)	2520	151	1.54	3300 (850)	198.0 (51.0)	2.11 (0.54)
3	2345 (595)	141 (36)	1.93 (0.49)	2100	126	1.73	2780 (680)	166.8 (40.8)	2.23 (0.55)
4	1735 (510)	104 (31)	1.64 (0.48)	1470	88	1.39	1735 (510)	104.1 (30.6)	1.67 (0.49)
mean ± SE	2323 ± 231	139 ± 14	1.74 ± 0.07	2048 ± 216	123 ± 13	1.53 ± 0.07	2705 ± 325	156 ± 20	1.94 ± 0.14
	(616 ± 53)	(37 ± 3)	(0.46 ± 0.02)				(689 ± 69)	(41 ± 4)	(0.51 ± 0.02)
Females									
5	2085 (510)	125 (31)	2.50 (0.61)	1890	113	2.27	2260 (510)	135.6 (30.6)	2.64 (0.60)
6	1475 (425)	89 (26)	1.70 (0.49)	1260	76	1.45	1910 (510)	114.6 (30.6)	2.29 (0.61)
7	1735 (510)	104 (31)	1.90 (0.56)	1470	88	1.61	1910 (510)	114.6 (30.6)	2.16 (0.58)
8	1650 (425)	99 (26)	1.36 (0.35)	1470	88	1.21	1910 (510)	114.6 (30.6)	1.62 (0.43)
mean ± SE	1736 ± 128	104 ± 8	1.87 ± 0.24	1523 ± 132	91 ± 8	1.64 ± 0.23	1998 ± 88	120 ± 5	2.18 ± 0.21
	(468 ± 25)	28 ± 2	(0.5 ± 0.06)				(510)	(31)	(0.56 ± 0.04)
Total mean ± SE	2029 ± 165	122 ± 10	1.8 ± 0.12	1785 ± 154	107 ± 9	**1.58 ± 0.11**	2301 ± 194	138 ± 12	2.01 ± 0.13
	(542 ± 39)	(33 ± 2)	(0.48 ± 0.03)				(595 ± 45)	(36 ± 3)	(0.53 ± 0.02)

Work beyond anaerobic threshold (AT) are shown in parentheses

Table 6 Measured indexes before and after training in the 2 groups.

		Group A			Group B		
Variable†	Training	Mean	SE	p-Value *	Mean	SE	p-Value *
VO_2max (ml/min/kg)	Before	18.0 (78%)	1.3		18.8 (76%)	1.7	
	After	19.6 (80%)	1.4	NS	20.1 (78%)	1.8	NS
VO_2AT (ml/min/kg)	Before	11.9	1.2		12.1	1.5	
	After	12.8	1.3	NS	14.0	1.6	NS
Leptin (µg/l)	Before	27.8	6.1		24.2	5.2	
	After	12.2	2.1	0.04	18.5	3.6	NS
$Leptin_{FM}$ (µg/l/kg)	Before	0.76	0.1		0.52	0.1	
	After	0.37	0.1	0.039	0.44	0.1	NS
Insulin (pmol/l)	Before	65.2	5.1		72.1	11.8	
	After	57.8	7.0	NS	73.0	7.1	NS
Glucose (mmol/l)	Before	4.89	0.5		4.93	0.2	
	After	5.07	0.3	NS	4.79	0.3	NS
HOMA2-B	Before	112.1	4.6		118.9	11.0	
	After	90.6	4.9	0.015	134.5	14.3	NS
NEFA (mmol/l)	Before	680	84		510	43	
	After	480	57	0.05	702	81	0.018

† Values are mean ± SEM. NS: Not significant

* By two-tailed analysis of variance

Theoretical values in percent are given in parentheses

creatic and gut hormones. In obesity, serum leptin levels are higher than in lean subjects and this divergence is not translated into an early satiety during the meal. Furthermore, leptin has been shown to be involved in vascular smooth muscle cells function and plaque formation [23].

In the management of obesity, physical training is an absolute priority together with hypocaloric diet. Nevertheless, debate exists on type of training and intensity of exercise required to accomplish such purpose.

We evaluated in 2 groups of obese subjects the effects of 2 exercise training (aerobic alone vs. aerobic with a bout of anaerobic work, 5 min at 85% of HRmax) performed during a 4-week period. The total amount of work was significantly different when expressed as Kjoules, but similar when related to FFM.

The differences between aerobic and anaerobic work are considerable. In fact, aerobic work requires an amount of energy compatible with the kinetics of the refurnishing process and ATP is restored by means of oxidative mechanisms consuming oxygen and utilizing the body stores of carbohydrates and fats as substrate. In such case, physical exercise can be maintained for several minutes in a steady-state condition. Alternatively, anaerobic work outbalances the capability of the mechanisms for energy restoration so that it may be supported for a limited period by the ATP sources at muscular level. These differences involve different dynamics in some chemical endogenous mediators which play a role in metabolism during and after physical exercise, like lactic acid, catecholamines, GH, and others.

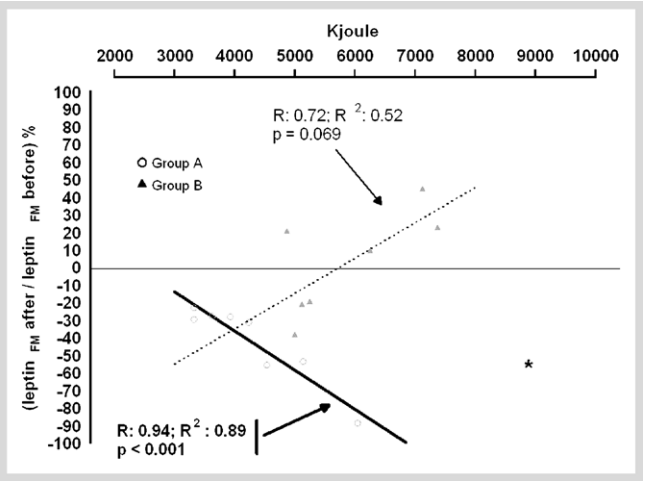

Fig. 1 Linear regression of the ratio of $leptin_{FM}$ after training and $leptin_{FM}$ before training in percent vs. total amount of performed work, in both groups. * Outlier of group B.

Our previous comparative studies between different models of physical training demonstrated that the addition of single bouts of exercise beyond the AT to aerobic activity may evoke a significant measurable GH responsiveness in obesity when exercise intensity exceeds AT [14]. Therefore, the higher levels in GH and catecholamines beyond AT [14,24] involve an increased lipolytic activity and a more evident FM loss [15]. Aerobic plus anaerobic work does not improve glucose metabolism and increases circulating NEFA [15].

Data from the literature suggest that physical exercise reduces serum leptin after a single training at moderate intensity and long duration in normal subjects [9], as well as after prolonged periods of activity at different intensities in sedentary overweight and obese men [11], and in women after intensive swimming training [25]. The decrease of leptin after these long periods of training has been associated to the loss of FM by the authors.

Our study seems to point out the following considerations. In the obese subjects of this study, leptin decreases after a period of training of 4 weeks together with FM, and intensity of work seems to condition the behaviour of both FM and leptin. In fact, aerobic exercise promotes a slight FM loss together with a significant lowering of leptin, while aerobic exercise associated to a bout of work beyond AT promotes a more important FM loss without a significant reduction of leptin, even when adjusted to the loss in FM.

Some factors are able to contrast the extent of leptin reduction linked to physical stress. One of these could be GH, whose ability to increase serum leptin has been demonstrated in GH deficient subjects [6] and whose increase has been shown in obesity during a progressive working test after training with bouts of work beyond AT [14]. The appreciable lowering in FM together with the increased values of NEFA after training in Group B seems to be in agreement with a high, consistent mobilisation of lipids which probably exceeds their dynamic utilisation, linked to the enhanced GH response [15].

Another factor involved herein might be represented by the increase in intracellular products from glucose metabolism caused by the stress from bouts of work beyond AT [8] in absence of improvement in insulin sensitivity for glucose. Hexosamine biosynthesis, a relatively minor branch of glycolysis, has been observed to regulate leptin production in rodent as well as in human adipose tissue [8]. In fact, culturing human subcutaneous adipocytes with glucosamine, a relevant increase in leptin release has been detected [26]. Although causal relationships have not been established, numerous studies have shown a correlation between increased hexosamine biosynthesis pathway and insulin resistance [27,28].

Moreover, data from McClain [8] are consistent with a role for muscular tissue in the production of leptin. The higher FFM of our Group B may be in agreement with its leptin behaviour.

In our opinion, of some interest may be the linear correlation between the total amount of work performed during the 4-week period and the variations after training of $leptin_{FM}$ ($leptin_{FM}$ after training/$leptin_{FM}$ before training) as percent, evident in Group A.

In Group B, the percentages of variation after training of $leptin_{FM}$ ($leptin_{FM}$ after training/$leptin_{FM}$ before training) demonstrated an increasing trend and corresponded in 3 cases to the highest total performances. This might be related to the hypothesised increase of hexosamines (which stimulate leptin production) probably linked to anaerobic metabolism and to the increased production of GH as above mentioned. In these cases, the highest secretions of hexosamines and GH probably overpower the decrease of leptin due to exercise. The heavier FFM of Group B (consistent with a role for muscular tissue in the production of leptin) [9] might be a further factor.

The data of Group A may confirm the relevance of the quantity of work performed, but only aerobic work, in lowering serum leptin and may represent a predictive index in a program for controlling FM loss, and probably an improvement of satiety with exercise at low intensity.

Some caveats have to be considered as potential limitations of this study, such as the lack of measure of satiety collected before and after workout, the absence of measures of subcutaneous and visceral adiposity, with the former being a greater source of circulating leptin than the latter adipose compartment, and the limited number of analysed subjects.

Notwithstanding these limits, we think that the following conclusions may be allowed.

Physical training, in the absence of dietary restrictions, decreases leptin over-secretion and FM in obese individuals. The decrease of leptin levels is seemingly conditioned by the intensity and type of work, while appearing dissociated from the amount of FM lost during training. After aerobic training, there is a lower FM loss than that obtained after aerobic plus anaerobic exercise. The significant reduction in leptin levels, when related to the variation of FM, correlates with the amount of aerobic work performed, that is, greater the amount of aerobic work performed, stronger the decrement in leptin secretion (**Fig. 1**).

The opposite correlation in Group B appears to be less interesting, where the increased amount of total work performed corresponded to a lower magnitude in the reduction of leptin. Taken together, our current observations seem to confirm that the approach to antiobesity strategies by means of physical training should contemplate the opportunity to initially prescribe a period of work at aerobic and anaerobic intensity to get a significant reduction of FM, subsequently followed by sessions of aerobic work alone so as to improve FM loss, ameliorate the metabolic profile, reduce lower circulating leptin, and likely to improve satiety control. Nevertheless, a more extended study concerning the behaviour of leptin after aerobic and aerobic plus anaerobic training is desirable to confirm our data.

Acknowledgements

The authors wish to thank Dr. Gillian Walker for kindly supervising the text.

Conflict of Interest

The authors declare that they have no conflicts of interest in the authorship or publication of this contribution.

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