Serum Leptin Levels in Male Marathon Athletes before and after the Marathon Run*

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ABSTRACT
Leptin is a hormone produced by the adipocytes to regulate food intake and energy expenditure at the hypothalamic level. It is commonly accepted that the main determinants of leptin secretion are the net amount of body fat and the mean size of adipocytes. On the contrary, important vectors of energy flux in the organism, such as food intake and energy expended on exercise, are not thought to be regulators of that secretion. To understand whether leptin is regulated by an acute energy expenditure such as strenuous exercise, 29 male athletes who had trained for marathon running were studied before and after a marathon run and compared with 22 nonobese, age-, sex-, and body mass index (BMI)-matched sedentary controls.

Controls and marathon athletes showed no differences in BMI or fat-free mass. Marathon runners showed a strong reduction in total fat mass (6.2 ± 0.4 kg; 9.1 ± 0.5% of body fat) compared with controls (12.3 ± 0.5 kg; 16.1 ± 0.5% of body fat; P < 0.05). This difference in body composition was paralleled by a mean serum leptin level that in marathonians (2.9 ± 0.2 μg/L) was significantly (P < 0.05) reduced compared with that in controls (5.1 ± 0.6 μg/L). It is remarkable that the ratio of leptin per kg body fat, showed a very good agreement between the two groups, 0.40 ± 0.04 μg/L·kg for controls and 0.46 ± 0.03 μg/L·kg for marathonians. In the two groups, leptin was correlated with both body weight, BMI, and fat mass (P < 0.001).

The marathon trajectory was the standard 42.195 km accomplished in an average time of 3 h, 17 min, 7 s, with a calculated energy expenditure of over 2800 Cal. After the marathon run, a water imbalance occurred, with a significant decrease in body weight and an increase in serum albumin. A significant (P < 0.05) reduction in leptin levels was observed after the run (2.6 ± 0.2 μg/L) compared with before (2.9 ± 0.2 μg/L), which was more relevant considering the relative hemococoncentration.

In conclusion, 1) compared with sedentary subjects, leptin levels are reduced in male marathon runners in parallel with the relevant reduction in total body fat; 2) expressed as a ratio of leptin per kg body fat, no differences were observed between marathonians and controls; and 3) after an energy expenditure of 2800 Cal in the marathon run, a reduction in leptin levels occurred. Strong changes in energy expenditure may regulate serum leptin levels in man. (J Clin Endocrinol Metab 83: 2376–2379, 1998)
those in matched controls, and 2) to observe the effect on leptin concentrations of the most intense model of exercise-mediated energy expenditure, i.e. a run of 42.195 km performed in less than 3.5 h (2800 Cal).

**Subjects and Methods**

The subjects of this study were 29 nonprofessional male athletes trained for marathon running who at the moment of the study were training at a high level. Their mean age was 37.1 ± 1.7 yr (range 22.0–51.3 yr), weight was 67.7 ± 1.0 kg, height was 168 ± 3 cm, and body mass index (BMI) was 23.9 ± 0.3. They were studied both the day before and after finishing a marathon run. As controls, 22 nonobese males with little exercise activity in the normal range for the Spanish population were studied. Their mean age was 37.6 ± 1.5 yr (range, 23.0–48.2 yr), weight was 75.6 ± 1.7 kg, height was 176 ± 0.1 cm, and BMI was 24.1 ± 0.4. They were selected on the basis of being sex, age, and BMI matched with the marathonians. None of the subjects presented actual or past history of endocrinological or metabolic disease. The study was approved by the hospital ethical committee, and informed consent was previously obtained from all participants.

Standing height was measured using a portable direct reading Harpenden stadiometer. Weight was determined by means of a calibrated electronic scale. The mean BMI, defined as weight in kilograms divided by the square of height in meters, was calculated. Fat mass was determined by tetrapolar bioelectrical impedance (Human-IM Scan, Ditosystem, Barcelona, Spain), measured at 50 kHz. Total body water was estimated using sex-specific equations (23, 24). Fat-free mass was assumed to have a hydration constant of 0.73 and was calculated using the formula: fat-free mass = total body water/0.73.

To prevent circadian variations, blood samples were obtained from the controls and the marathonians before and after running at the same time. Blood samples were always obtained after a light breakfast in the morning (1000–1200 h) using a standard venipuncture technique, and after clotting at 4°C, the serum was separated by centrifugation and was stored at −20°C until assay. Marathon runners were assessed both the day before and the day of the marathon after finishing the run. Controls were assessed once.

Serum leptin levels were measured in duplicate by RIA for leptin using commercial kits (Human Leptin RIA, Linco Research, St. Charles, MO). The limit of sensitivity was 0.5 μg/L; the intra assay coefficient of variation was 8.3%, and the interassay coefficient of variation was 6.2%. Plasma GH was measured by an immunoradiometric assay (BioMerieux, Madrid, Spain), with intraassay coefficients of variation of 5% and 5.6%, respectively, and interassay coefficients of variation of 6% (1.6 μg/L) and 4.4% (19.0 μg/L), respectively. Albumin was determined using an automatic analyzer (Cobas, F. Hoffman-La Roche Ltd., Basel, Switzerland). Samples from each patient were assayed at the same time.

**Results**

Compared with nonobese controls, marathon athletes presented no differences in BMI or fat-free mass. Furthermore, marathonians showed a strong reduction in the total fat mass (6.2 ± 0.4 kg; 9.1 ± 0.5% of body fat) compared with controls (12.3 ± 0.5 kg; 16.1 ± 0.5% of body fat; Fig. 1). This important difference in body composition was paralleled by the serum level of leptin found in marathonians (2.9 ± 0.2 μg/L), which was significantly (P < 0.05) reduced compared with that in controls (5.1 ± 0.6 μg/L). Interestingly, when leptin concentrations were calculated by each kilogram of body fat, a very good agreement was observed in the two groups (0.40 ± 0.04 μg/kg for controls and 0.46 ± 0.03 μg/kg for marathonians).

The marathon distance was the standard length of 42.195 km performed in an average time of 3 h, 17 min, 7 s (range, 2 h, 28 min, 00 s to 3 h, 53 min, 52 s). The calculated energy expenditure in the marathon run was over 2800 Cal (25). When marathonians were analyzed after the marathon run, it was evident that a water imbalance had occurred despite their free access to water at regular intervals. In fact, a significant (P < 0.05) decrement in body weight was observed together with an increase in serum albumin concentration (4.9 ± 0.06 ηL vs. 5.6 ± 0.09 mg/dL; P < 0.05; Fig. 1). Similarly, an increase in GH values was observed, an expected change after intense exercise (26), without changes in insulin-like growth factor I (data not shown). After the marathon run, a significant decrease (P < 0.05) was observed in serum leptin (2.6 ± 0.2 μg/L) compared with that before the run (2.9 ± 0.2 μg/L), a value more relevant considering the relative hemoconcentration that occurs.

When individual leptin values were analyzed (Fig. 2), a good correlation was observed in each of the 2 groups between leptin and BMI, body weight, and total fat mass (all P < 0.001). Interestingly, a very good correlation was observed between leptin and total fat mass in the marathonians. On the contrary, in the control subjects, a considerable dispersion in leptin levels was observed for any fat mass value.
A line was evident (Fig. 3), and in 17 subjects a reduction in leptin levels was observed.

**Discussion**

The extraordinary conservation of the leptin molecule through species suggests that it played a key role in metabolism throughout the evolution. Leptin should be viewed as a hormone that in man regulated the neuroendocrine adaptations to fasting and the fluxes of energy in a world characterized by food shortage and enhanced energy expenditure (27, 28). Although both short term fasting and physical exercise led after some days to a reduction in serum leptin levels, no acute changes in leptin have been reported after either food intake or physical exercise. To understand the role of acute energy expenditure in nonfasting subjects, in the present work a group of trained marathon runners was studied before and after the marathon run, with blood samples obtained at similar times of the day to avoid changes due to circadian variations (29, 30).

Athletes trained for marathon running underwent a very complex and systematic training over several years that led to profound changes in body composition, with the net result of a total fat mass near half that in normal controls. As observed in this work, a strong reduction in leptin levels paralleled the reduction in body fat, as previously observed in other athletes (20, 22). A good correlation in each group was observed for leptin with BMI, body weight, and total fat mass, again confirming in this selected population that the main determinant of circulating leptin concentrations is the amount of adipose tissue in the individual even when the amount of this tissue is severely reduced. Interestingly, the correlation of leptin with total fat mass or BMI was very good in marathonians, whereas a high dispersion was found in the sedentary controls. It appears that with higher amounts of fat deposits, other factors regulating leptin secretion are operative, and the expected stoichiometry between adipocyte mass and leptin values becomes less strict. Interestingly, if leptin values are expressed as the ratio per kg body fat, no difference between sedentary controls and runners was observed, suggesting that this index might be of utility in further studies on leptin.

The marathon run is suitable to study the role of energy expenditure per se on leptin regulation. First of all, runners are not in a fasting state, because limited food and water intake are allowed at precise times both before and during the run. Second, it is the most strenuous type of exercise that an individual may accomplish, with more than 42 km normally run in less than 3.5 h and with a net energy expenditure of over 2800 Cal (31, 32). This means that in a short period of time the runner would have expended as much energy as in 24 h of a very active day. In the present work, the high energy expenditure in a short time was accompanied by a significant reduction in serum leptin levels. Although sta-
tistically significant, we are very cautious about the biological meaning of small differences in leptin such as those reported here before and after the marathon run. The only reason to reinforce the relevance of the figures is the hemoconcentration that occurs after the run (33), a fact that should enhance and never reduce the serum concentration of all circulating proteins with a long half-life such as leptin. The marathon is an exercise of such intensity that only perfectly trained individuals are able to participate and finish it. Thus, the athletes studied here were under a normal training schedule and well into energy balance before the run. The relevant state of negative energy balance induced by the run may well be the cause of the observed marathon-mediated leptin decline.

An exercise-mediated reduction in leptin values has been observed in previous reports, but without reaching statistical significance (22, 34). There is no clear explanation for these controversial results, but in a previous report about long distance runners (22) leptin values were corrected by applying a mathematical formula for hemoconcentration (35). Considering that changes in leptin are small, and hemoconcentration is not a finely measurable variable, the effects of two uncertainties may have been summed. There is no proof at the moment that such small changes in leptin levels may have a biological meaning, or what hormonal or metabolite signals are implicated in this reduction (17, 36, 37). However, the present report shows that a high level energy expenditure may acutely regulate serum leptin levels in man, and although scarce, these changes would become very relevant if the individual is in an environment requiring repetitive vigorous exercise.

In conclusion, 1) compared with matched sedentary subjects, leptin levels are reduced in male marathon runners in parallel with the strong reduction in total body fat; 2) expressed as the ratio of leptin per kg body fat, no differences were observed between marathoniands and controls; and 3) after an energy expenditure of 2800 Cal in the marathon run, a significant reduction in leptin levels occurred. Strong changes in energy expenditure may acutely regulate serum leptin levels in man.

Acknowledgments

The expert technical assistance of Ms. Mary Lage is gratefully acknowledged. The voluntary participation of the marathon team Grupo 10 and of Drs. A. Prada and M. Nieto from the Instituto de Deportes del Ayuntamiento de Sevilla, Spain, is gratefully acknowledged.

References