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## Changes of serum leptin and endocrine and metabolic parameters after 7 days of energy restriction in men and women.

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#### Abstract

Circulating leptin decreases during fasting in rodents and humans; however, the mechanism of the decrease is unknown. The aim of this study was to examine the relationship between decrements of serum leptin concentrations and changes of hormonal (insulin and cortisol) and metabolic (glucose, ketones, and fatty acids) parameters involved in the metabolic adaptation to energy restriction in normal-weight humans. Because there are marked gender differences in circulating leptin, both men and women were studied. The body mass index (BMI), percent body fat (% body fat), and serum leptin, insulin, cortisol, glucose, beta-hydroxybutyrate, (BOHB), and nonesterified fatty acids (NEFA) were determined in 11 men and 13 women (age, 20 to 41 years; BMI, 21.2 to 26.8 kg/m<sup>2</sup>) before and during 7 days of energy restriction (-68% +/- 1% of daily energy requirements). Weight loss averaged about 4% in both men and women. Leptin in men was 3.7 +/- 0.5 and decreased to 2.1 +/- 0.4 ng/mL (percent change [%delta], -36% +/- 6.0%, P < .0005) during restriction. Concurrently, insulin decreased from 7.2 +/- 0.6 to 1.8 +/- 0.3 microU/mL (%delta, -74% +/- 4%, P < .0001). In contrast, leptin was higher in women before (16.2 +/- 1.9 ng/mL) and after (6.0 +/- 0.8 ng/mL) restriction and decreased more than in men (%delta, -61% +/- 4%, P < .02 v men), whereas the decrease of insulin in women was less than in men: 10.1 +/- 1.9 to 6.1 +/- 1.0 microU/mL (%delta, -31% +/- 9%, P < .0025; P < .0005 v men), perhaps because glucose decreased less in women than in men. Overall, the changes of leptin during fasting were independently correlated with the changes of glucose (r = .53, P < .007), NEFA (r = .53, P < .01), and BOHB (r = .65, P < .001). In addition, the change of leptin correlated with a combined index of the parameters that reflect decreased glucose availability and increased lipolysis ([delta]glucose + [delta]insulin + [delta]NEFA)/3, r = .73, P < .0001) or a combined index of parameters that would be expected to limit glucose uptake by adipocytes ([delta]glucose + [delta]insulin + [delta]cortisol)/3, r = .48, P < .02). We conclude that there are significant differences between men and women in the responses of leptin and insulin to energy restriction. Furthermore, decreases of circulating leptin during negative energy balance are related to changes of endocrine and metabolic parameters, suggesting that leptin secretion may be regulated by alterations of adipocyte glucose and lipid metabolism, ie, decreased glucose uptake and metabolism and increased lipolysis.

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