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Is Leptin a stress related peptide?

To the editor — Licinio and colleagues reported an inverse relationship between plasma leptin levels and the activity of the hypothalamic-pituitary-adrenal (HPA) axis[1], adding to evidence that leptin suppresses the activity of this axis[1,2]. Since animation of the HPA axis is important during critical illness, the question arises whether leptin is involved in the acute stress response in humans. Our recent preliminary findings in critically ill patients suggest it is.

Leptin, as well as ACTH and cortisol levels, were determined every 4 hours in seven critically ill patients (five females, two males) fulfilling the criteria of acute sepsis, during the first 24 hours after admission to our intensive care unit. Average Body Mass Index (BMI) was 24.1 ±1.1. Twenty-four hour mean ± SE leptin levels were 8.3 ±1.5 ng/ml and 8 am levels were 11.1 ±4.0 ng/ml. In all patients there was a significant fall in nocturnal leptin levels with a nadir at 1 am (5.9 ±3.0 ng/ml). Leptin levels were 20-30% lower during the night than during the day (see figure). In the same patients we observed a paradoxical increase of nocturnal ACTH and cortisol concentrations. This is in complete contrast with the data from normal lean or obese individuals who show decreased HPA-axis activity and increased leptin levels at night.[1,3] Licinio and colleagues reported that *in vivo* the HPA-axis does not influence leptin level. However, it has been shown recently that leptin inhibits the response of the HPA-axis to acute stress in mice[5]. Therefore, in our critically ill patients, the increased nocturnal cortisol and ACTH levels may be a consequence rather than a cause of falling leptin levels. In any case, it becomes evident that the inverse relationship between the two systems reported by Licinio *et al*, is acutely regulated in disease.

All patients demonstrated nocturnal leptin decline independently of gender or BMI and leptin levels do not seem to respond to short-term changes in diet composition or feeding[4]. Therefore, this rapid adaptation of circadian leptin concentrations in critically ill patients appears to be part of an acute stress response. Falling leptin levels may therefore be a critical signal for a neuroendocrine response suggesting that leptin is not only an adipostatic hormone, whose function it is to prevent obesity, but also a stress-related hormone which is potentially crucial for survival.

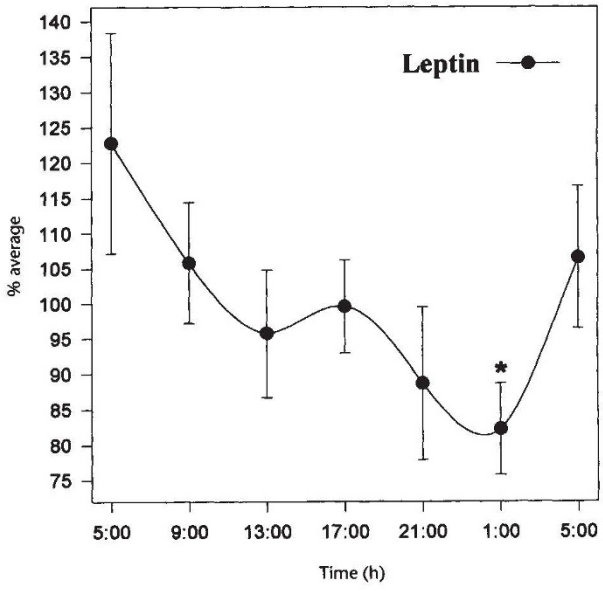

Fig 1 24 hour profile of plasma leptin concentration in seven critically ill patients (mean ± SE). Leptin levels are expressed as variability defined as a percentage of individual 24 hour averages, using the formula: variability at time t = (hormone level at time t/24-h individual average level)x100. Values were analyzed by ANOVA followed by Dunnett's test. * Asterisk indicates that leptin levels are statistically different from those at 5 am ($p < 0.05$). The nocturnal decrease occurred in all critically ill patients.

STEFAN R. BORNSTEIN
Department of Internal Medicine III
University of Leipzig, Germany
Current address: NIH, NICHD
Building 10, Room 10N262
Bethesda, MD 20892, USA

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