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Response to the letter to the editor by Chapelot

To the Editor,

Dr Chapelot makes interesting comments regarding our observation on energy adaptation to glucocorticoid-induced hyperleptinemia [1]. Indeed, plasma glucose levels increased modestly, especially during meal times, after hydrocortisone (HC) infusion, as was indicated in our article. In designing the study, we considered measures that would minimize the expected glucose excursions in response to glucocorticoid exposure. Infusing insulin to clamp plasma glucose was not an option because insulin is a leptin secretagogue [2,3]. On the other hand, fasting the study subjects to dampen glucose excursions was equally untenable because that would have abolished the leptin response to glucocorticoid [4,5].

It is thus possible, as argued by Dr Chapelot, that preprandial plasma glucose levels could have contributed to the modulation of food intake observed during HC infusion. It must be noted though that the data showing modulation of hunger by preprandial blood glucose levels are most persuasive in animal models [6]. Among humans, hyperphagia persists in patients with diabetes despite ambient hyperglycemia. The latter indicates that any inhibitory effect of plasma glucose levels on food intake in humans must be quite modest or easily overridden. As described in the article [1], the subjects in our study were approached repeatedly and offered meals and snacks ad libitum. The results obtained from such a study design may be quite different from one in which patients request meals in response to hunger. We regret that a subjective hunger scale was not administered to the subjects in our study, as that would have helped clarify whether food intake was in response to hunger or other cues. In addition, the point regarding macronutrient specificity is well noted.

Clearly, multiple behavioral, metabolic, neural, and peripheral factors are involved in the regulation of food intake in humans [7]. Circulating leptin levels and ambient glycemia are but two of these numerous regulatory factors.

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