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## The potential role of protein leverage in the US obesity epidemic

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#### Abstract

The protein leverage model of obesity posits that decreasing the protein fraction of the diet leads to compensatory increases in total energy intake in an attempt to maintain a target amount of absolute protein consumed. The resulting increased energy intake thereby causes weight gain. According to food balance sheets published by the Food and Agriculture Organization of the United Nations, while the absolute protein content of the US food supply has increased since the early 1970s the fraction of available calories from protein has decreased by ~1% due to greater increases in available carbohydrate and fat. Counterintuitively, even such a small decrease in the protein fraction of the food supply has the potential to result in relatively large increases in energy intake according to the protein leverage model. Therefore, while the protein leverage effect is unlikely to fully explain the obesity epidemic, its potential contribution should not be ignored.

Higher protein diets can assist with weight loss by sparing fat-free mass while increasing both satiety and energy expenditure (1). Conversely, lower protein diets might be expected to promote weight gain and obesity. Indeed, the protein leverage model of obesity (2) posits that decreasing the protein fraction of the diet leads to compensatory increases in total energy intake in an attempt to maintain a target amount of absolute protein intake. Increased energy intake thereby results in weight gain.

The protein leverage model is intriguing, but questions remain about the validity of the concept in human nutrition. For example, it is unclear why studies investigating three levels of dietary protein have not reproducibly found significant changes in energy intake across all protein groups as would be required to achieve a similar target absolute level of protein intake across diets. Specifically, two experimental studies in humans failed to detect increased energy intake when a low protein diet with 5% of total energy as protein was compared to a moderate 15% protein diet (4, 5). As a result, the low protein diet led to a substantial reduction in absolute protein intake. In those same studies, the higher protein diet with 30% of total energy as protein led to decreased energy intake, but this was insufficient to prevent an increase in absolute protein intake compared to the moderate protein diet.

In contrast, other studies have failed to detect decreases in energy intake with high protein diets. For example, a 25% protein diet resulted in energy intake similar to a moderate 15% protein diet whereas a 10% protein diet was found to increase energy intake compared to a

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moderate 15% protein diet, but insufficiently to prevent a drop in absolute protein intake (3). Another study found a significant negative correlation between percent dietary protein and energy intake when adults who had recovered from marasmus or kwashiorkor were randomized to diets with 10%, 15%, and 25% of energy as protein, but absolute protein intake was positively correlated with the dietary protein fraction indicating incomplete protein leverage (6). Similarly, a small study lasting a few days detected significant energy intake effects of varying dietary protein from 10% to 25% of total calories in a way that attenuated, but did not prevent, absolute changes in protein intake (7). Therefore, even if protein leverage is a real phenomenon in humans, the degree of leverage is probably incomplete.

For these reasons, along with the observation that the absolute amount of protein in the US food supply (as determined by national food balance sheets published by the Food and Agriculture Organization of the United Nations) has increased over the past several decades, I recently argued that the protein leverage model was an unlikely contributor to the rise in US obesity prevalence (8). However, I failed to appreciate the potential importance of the seemingly small ~1% dilution of protein availability as a fraction of total available calories in the US food supply due to greater absolute increases in carbohydrate and fat. After all, how could such a tiny decrease in the proportion of available calories as protein possibly be meaningful?

To quantitatively investigate this issue, I derived how protein leverage could affect the relationship between total energy intake, I, absolute protein energy intake, P, and the fraction of total energy as protein, p. By definition: P=Ip and deviations, dP, from baseline protein energy intake are given by the differential form:

$$dP = Idp + pdI$$

The following equation is a simple representation of the protein leverage concept:

$$dP = (1 - L)Idp$$

The extent of protein leverage, L, varies between no protein leverage (L=0) whereby changing the protein fraction of total energy by dp results in a passive change in absolute protein energy intake of dP=Idp. Alternatively, perfect protein leverage (L=1) results in no change in absolute protein energy intake: dP=0. Combining the above equations to eliminate dP results in the following differential equation relating I and p:

$$\frac{dI}{I} = -L\frac{dp}{p}$$

Integrating both sides gives:

$$\ln(I) = -L \times \ln(p) + C$$

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where C is the integration constant. Exponentiating both sides results in the following power-law solution:

 $I = K p^{-L}$ 

where the constant  $K = \exp(C)$  is determined by the baseline energy intake (assumed to be 2500 kcal/d corresponding to a physical activity level of ~1.6) at the baseline protein energy fraction (assumed to be 12.8%).

Figure 1A plots the relationship between the protein fraction of the diet and the energy intake predicted for two different assumptions about the degree of protein leverage. Interestingly, perfect protein leverage (L=1) predicts that very small decreases in the fraction of available protein calories since the early 1970s leads to a substantial ~200 kcal/d increase in energy intake that could easily be accommodated by the observed ~600–800 kcal/d increase in total US food supply daily per capita calories.

Figures 1B and 1C illustrate that an average  $\sim 250-300$  kcal/d increase in per capita energy intake was required to generate the observed increase in mean adult body weight as estimated by a validated mathematical model of human body weight dynamics (10). The difference between the  $\sim 600-800$  kcal/d increase in food supply calories and the  $\sim 250-300$  kcal/d increase in energy intake indicates progressive increases in food lost or wasted along the supply chain (9).

Assuming perfect protein leverage to accommodate the dilution of protein in the food supply, the predicted increase in total energy intake was found to potentially explain about two-thirds of the observed rise in mean adult body weight as shown in Figure 1C. Furthermore, even partial protein leverage (L=0.5 which is similar to that suggested by Gosby et al. (11)) may have contributed about one-third of the observed average adult weight gain during the US obesity epidemic.

Therefore, contrary to my previous conclusion (8), even partial protein leverage could potentially play an important role in obesity that should not be ignored. More research is required to better understand the validity of the protein leverage model in humans and to clarify its relationship to the well-known mechanisms by which dietary protein influences body weight and composition (1).

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#### Figure 1.

A) Increases in available calories in the US food supply since 1973 as a function of the protein fraction in the food supply (•) as reported by the food balance sheets published by the Food and Agriculture Organization of the United Nations (FAO) (http://www.fao.org/faostat/en/#data/FBS). The solid and dotted curves show the increase in energy intake associated with the decreased protein fraction of the food supply as predicted by the protein leverage model assuming perfect leverage (L=1) or modest leverage (L=0.5), respectively. B) Time course of the average adult energy intake changes as predicted by a validated mathematical model of human body weight dynamics (•) to fully explain the observed average weight changes as well as the increases in energy intake predicted by the protein leverage model. C) Observed average adult weight changes (•) according to the National

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Health and Nutrition Examination Survey (NHANES) and the predicted weight changes due to the increasing energy intake according to the protein leverage model.

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