Impaired Regulation of Energy Intake in Old Age

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Introduction

Aging is associated with predictable alterations in body fat that are thought to have an important impact on health. From early adult life through middle age there is a substantial increase in body fat [1, 2], while after 65–70 years of age body fat typically decreases, even in healthy individuals [1, 2]. Unexplained weight loss becomes relatively common after the age of 65 [3, 4] and 30–50% of institutionalized elderly are reported to suffer from protein-energy malnutrition [3, 4]. This loss of body fat in later years is associated with several adverse factors including micronutrient deficiencies, frailty, increased hospital admission, an increased risk of disability from falls, delayed recovery from injury and premature death [5–8].

As reviewed elsewhere [9–12], negative energy balance resulting from low energy intake relative to total energy expenditure is suggested to be the usual cause of the loss of body fat in old age and, consistent with this suggestion, nationwide studies have suggested that low dietary energy intake is widespread even among healthy elderly adults [13]. However, the underlying determinants of low energy intake remain uncertain. There are several factors, such as reductions in the sensations of taste and smell, poor dentition, prescription medications, depression and social isolation that may possibly promote inadequate energy intake [14–17]. In addition, an impairment in the ability to regulate food intake, termed the ‘anorexia of aging’ [15], is speculated to be important. This chapter synthesizes recent results and reviews [9–12] on changes in the regulation of food intake in old age and the possible underlying mechanisms.
Impaired Regulation of Food Intake in the Elderly

To our knowledge, three peer-reviewed studies have examined the regulation of food intake in old age in humans [18–21]. Concerning the studies from our laboratory, Roberts et al. [18, 19] conducted overfeeding and underfeeding studies in 35 sedentary or moderately active young and elderly men. The study was a 77-day investigation that included a dietary intervention component. The subjects were required to sleep at the research center for the nights before four measurements of resting energy expenditure were made, but otherwise could reside at home. Subjects were provided with all food and caloric beverages (mimicking a typical American diet, containing 1.5 g/kg body weight of protein and 55% of non-protein energy from carbohydrate and 45% from fat) for the first 31 days of the study, and this was consumed either at the research center or at the subjects’ places of work or residence. During the first 10 days of the study, weight-maintenance energy requirements were established by simultaneous determinations of metabolizable energy intake and total energy expenditure determined using the doubly labeled water method [22, 23]. For the next 21 days, energy intake was either increased by 4.2 MJ/day \((n = 7 \text{ young men and } n = 9 \text{ elderly men})\) or decreased by 3.3 MJ/day \((n = 10 \text{ young men and } n = 9 \text{ elderly men})\). After this time, food in the form of a self-selection menu was provided for a further 10 days and the subjects were instructed to eat as much or as little as they required for normal satiation and not to try to compensate for weight change during the prior overfeeding/underfeeding component of the study. Following the end of this 10-day self-selection period, subjects lived at home and consumed their own food and were free to gain or lose weight as desired (only 1 subject reported any conscious effort to change body weight). Body weight and composition (by underwater weighing and \(\text{H}_{2}^{18}\text{O}\) dilution) were measured at intervals during the study to determine changes in weight and body energy content.

Both groups gained a similar amount of weight and fat during overfeeding (Fig. 1), but young men tended to lose all the excess weight following overfeeding while the weight of the elderly men did not decrease significantly (Fig. 1). This difference was apparently due to the fact that the young men significantly decreased their voluntary energy intake following overfeeding, while the energy intake of the elderly men did not decrease significantly and indeed remained elevated relative to their previous weight-maintenance requirement (Fig. 2). Comparable results were obtained in the underfeeding component of the study. As with overfeeding, there was a similar weight loss during underfeeding in the young and elderly subjects (Fig. 3). However, subsequently, young men gained back the weight lost during underfeeding while elderly men did not (Fig. 3). This difference was apparently due to the fact that the young men significantly increased their energy intake following...
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Fig. 1. Body weight change during 21 days of overfeeding and a subsequent 46-day period of ad libitum diet [18]. Values are mean ±SEM for young (■) and older (□) men. *p < 0.05 relative to the young men. Reprinted with permission from JAMA.

overfeeding, while the energy intake of the elderly men did not increase significantly and indeed remained somewhat depressed relative to their previous weight-maintenance requirement (Fig. 4).

Thus, in two separate protocols involving opposite, experimentally imposed changes in energy balance, older men had a substantial reduction in their ability to maintain a constant energy balance compared to young men. The fact that the same result was obtained under opposite experimental conditions (overfeeding and underfeeding) strongly indicates that the findings reveal a real difference between age groups, rather than being due to a difference explainable by experimental factors. When interpreting these results, it is important to recognize that periods of substantially positive and negative energy balance occur as a normal part of life. [24] Thus, the results obtained in these studies are directly relevant to the normal life pattern of older people. It is also noteworthy that the age-related changes in food intake were observed in healthy older men and women who reported having no problems with their appetite.

Rolls et al. [20] also investigated changes in the regulation of food intake with aging using a repeated-measures preload protocol in which young and
Fig. 2. Voluntary energy intake during a 10-day period following overfeeding in young and older men [18]. Values are means ±SEM in comparison with initial weight-maintenance energy requirements (---). The change in energy intake relative to initial weight-maintenance requirements were significantly different between the age groups (p = 0.006). Reprinted with permission from JAMA.
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**Fig. 3.** Body weight change during 21 days of underfeeding and a subsequent 46-day period of *ad libitum* diet [18]. Values are mean ±SEM for young (■) and older (□) men. **p < 0.001 relative to the young men. Reprinted with permission from JAMA.**

elderly subjects were required to consume yogurt preloads with different energy contents on different days, and the subsequent voluntary energy intake at lunch was monitored. In this study, young subjects accurately compensated for the preloads, and their total energy intake from the preload plus lunch was similar across days when preloads of different energy contents were consumed. In contrast, elderly subjects did not compensate significantly for the preloads, and in consequence consumed more total energy when high-energy preloads were administered.

We have additionally obtained more recent data [21] suggesting that elderly men and women experience less frequent hunger during negative energy balance than do young individuals. During a 6-week period in which energy intake was reduced by an average of 896 kcal/day relative to weight-maintenance energy intakes, older men and women (aged 64–78 years) reported less frequent hunger than healthy young subjects despite the fact that the reduction in energy intake represented a larger fraction of weight-maintenance energy requirements and resulted in significantly greater weight loss.
Impaired Regulation of Food Intake versus Other Factors

The studies summarized above indicate that there is a reduced ability to regulate energy intake in old age. However, rather than energy disregulation occurring independent of other factors, it is possible that weight loss (or weight gain) in older subjects may be caused by the combination of a reduction in
the ability to regulate food intake and other adverse events, rather than by any one factor individually. [18] For example, it may be difficult for older individuals to compensate subconsciously for normal day-to-day fluctuations in energy intake, leading to the potential for progressive weight change. Similarly, elderly individuals may have an impaired ability to regain weight after periods of weight loss precipitated by disease. In addition, factors that have previously been thought to cause anorexia and weight loss (such as illness requiring hospitalization, loss of teeth, reduction in sensations of taste and smell, and depression) may precipitate a long-term reduction in body weight only when the metabolic signals that drive adaptive variations in energy intake are absent or reduced, as they appear to be in older individuals. In support of this suggestion, an analysis of a national cohort indicated that depression is associated with weight gain in young adults but weight loss in the elderly [25].

**Metabolic Mechanisms**

There are several potential mechanisms that may explain a decreased ability to regulate food intake in old age, and further research is needed to determine which may be quantitatively important [9–11, 17, 21]. For example, as suggested elsewhere, nitric oxide is postulated to influence food intake through both central and peripheral mechanisms, and there is a decrease in messenger RNA for nitric oxide synthase with aging in older animals [17]. In addition, cholecystokinin and insulin have been suggested to contribute to satiety in humans, and the concentrations of postprandial values are increased in older subjects [26, 27]. Finally, low circulating glucose is thought to be one of the signals for hunger in young adults [28] and detection of hypoglycemia may be impaired in older individuals [29]. Even if glucose impairment is not quantitatively important, glucose may still be an important mediator of changes in the regulation of food intake with age. For example, we have recently shown that circulating glucose remains markedly elevated following consumption of large meals [30], a factor that would be predicted to prolong satiety and decrease subsequent food intake.

**Biobehavioral and Social Factors**

Factors such as reductions in the sensations of taste and smell, poor dentition, prescribed medications and depression have also been suggested to promote inadequate energy intake leading to weight loss [14–17]. Two additional factors that may promote low energy intake in old age are eating alone and reduced dietary variety.

Concerning eating alone, de Castro and de Castro [31] reported that less energy is eaten at meals taken alone than at meals eaten in company, with
the difference in energy intake between the two situations being a substantial 30%. Even after excluding individuals who ate alone, the number of individuals present at a meal correlated with energy intake in that study. Although such data are generally used to suggest that social eating is disadvantageous because it promotes overeating and obesity, the opposite (namely that eating alone leads to undereating and weight loss) may be an equally important interpretation. This observation is also especially noteworthy when it is considered that humans are a gregarious animal species, and naturally eat in social groups. This is directly relevant to the issue of low energy intake in older populations, because bereavement and functional disabilities limit social contact [32]. Thus, an increased frequency of eating alone may be one of the factors contributing to low energy intake in older adults. Furthermore, there is a positive association between the frequency of eating restaurant food and body fatness [33] and for reasons of social isolation and functional disabilities, older adults may eat out less frequently. The combination of these different observations and findings suggests a potentially important role for reductions in social meals and eating out in the low energy intake and body weight loss of older adults. Variety has been studied in both animal models and humans as a determinant of energy intake and body fatness. Studies in laboratory rats, cats and hamsters have shown that energy intake is greater when a variety of foods is provided compared to when only a single food is provided [34, 35] and rats also have greater body fat and body fat gain when fed a variety of foods compared to when only a single food is fed [36, 37]. Numerous single-meal studies in humans also show increased energy intake associated with increased dietary variety [35, 38], and we recently demonstrated a long-term association between dietary variety and both energy intake from individual food groups and body fatness in healthy adult men and women [34], using 6-month dietary intake reports from a food frequency questionnaire and accurate measurements of body fatness by underwater weighing. In multiple regression analysis controlled for age and sex, dietary variety within individual food groups was positively related to energy intake from that food group, as shown in Figure 5. In addition, dietary variety from a combined group of sweets, snacks, condiments, entrees and carbohydrates was positively associated with body fatness and in the same model dietary variety from vegetables was negatively associated with body fatness.

Although the study of McCrory et al. [34] did not specifically examine the effects of age in that study, the results are relevant to aging because some studies suggest that dietary variety may decrease in old age [39, 40], and a recent abstract reported that dietary variety was a strong predictor of energy intake within a population of frail elders in a nursing home [41]. The underlying reason for why dietary variety decreases with age is not known, but factors such as poverty and living alone may be important. In addition, Rolls and McDermott [42] demonstrated that older adults have
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Fig. 5. Energy intake per day from 8 food groups in relation to the dietary variety within each group [34]. Values are individual data points for 71 subjects. Note that the y axis values differ for each graph. Reprinted with permission from the American Journal of Clinical Nutrition.
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reduced ‘sensory specific satiety’, a term used to describe the phenomenon of declining pleasantness of food as it is consumed. In that study, the adolescent and young adult subjects responded in the expected manner to a yogurt preload (i.e. decreased desire to eat yogurt but not other offered foods). However, older subjects did not respond and in fact reported an equivalent desire to eat yogurt and other test foods after the preload. Although necessarily short-term, these data suggest that older adults may lack the normal patterns of sensory specific satiety that encourage wide dietary variety, and thus provide a potential explanation for the reported reduction in dietary variety in old age [39, 40]. One implication of these findings and observations is that an intentional increase in dietary variety may help counterbalance the tendency to reduce energy intake in association with decreased variety in old age, and thus could help prevent or reverse weight loss associated with the anorexia of aging.

Conclusions

Several lines of evidence suggest that elderly adults have an impaired ability to regulate food intake accurately. This regulatory loss may be an important factor in the unexplained weight loss that is common in older adults. As a practical measure, regular monitoring of body weight may help older individuals and their caretakers to detect and prevent unintentional weight loss. However, further work is needed to examine both biological and psychological determinants of impaired energy regulation in old age. In addition, studies are needed to explore the question of whether manipulating dietary variety may be a useful tool in the therapeutic management of the anorexia of aging.

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References


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Discussion

Dr. Bunout: In Chile in old people with really poor intakes, we try to devise methods of supplementing their food. In the light of your studies on taste changes, what do you think would be the best strategy for supplementing elderly people: giving a greater variety of foods, the same foods with different tastes, supplements as different snacks during the day or as one snack?

Dr. Roberts: I don’t have the data to answer that question at present.

Dr. Payette: When we increase food variety don’t you think that we automatically increase the amount of food we eat and also the amount of energy we eat? Can you distinguish between the effects of increased energy intake and of increased variety?

Dr. Roberts: From the data we have we can’t make that distinction at this time, but I agree it is an important issue.

Dr. Roubenoff: In the underfeeding/refeeding studies you showed earlier, do you have any data on regional body composition changes? Are older people more likely to regain fat in the abdomen?

Dr. Roberts: We have no statistically significant findings on regional changes.

Dr. Rosenberg: If there is a set point for energy regulation and if that set point becomes weaker or is lost in older people, what is the current thinking about the location of that loss of adaptation? What part of the stomach, or of the brain, or of the spinal cord is thought to be different in that regard, or is it an endocrinologic problem?

Dr. Roberts: We are no further forward in finding out where the set point is or what the genetic mechanisms may be. For a while everybody thought that circulating leptin
was the set point, but if you feed people leptin it has a trivial effect on body weight. There are a lot of possible candidates.

**Dr. Rosenberg:** Are there changes in leptin with age?

**Dr. Roberts:** Certainly, because there are parallel changes in body fat. Leptin just tracks body fat and it may be very responsive to underfeeding in general. Whether it is differentially responsive to underfeeding close to your set point versus underfeeding far from your set point, we don’t know. Much of the research energy on the genetic markers of energy regulation has gone into animal studies. This is a shame because we have a lot of genetic markers of obesity in animals now, and virtually none of them seem to have any relevance to human obesity!

**Dr. Morley:** A paper from the Dutch group earlier this year in the *Journal of Gerontology* showed that food enhancers would actually increase the amount of food intake. This is the first time that anyone has managed to show that over a long period of time, and I think it is a key point in relation to the data you were presenting.

In relation to appetite control, fundamentally I think that there are multiple controllers of the set point. That has always been the problem. Certainly our studies suggest that a change in adaptive relaxation with aging, getting food to the antrum more quickly and perhaps to the duodenum, makes a big difference, so that would be a stomach change. In older men, leptin does not parallel fat changes; it is testosterone dependent and it has been shown that testosterone can decrease leptin separately from fat. That is probably the reason for the increase in anorexia that you see physiologically in men, because testosterone goes down and the leptin levels go up. In our longitudinal study we have shown that the higher the histamin level the greater the weight loss in healthy older men who eat less. This may not happen in every culture, and that could be very important; we see cultural differences in food intake which may be relevant to aging, but no one has looked at that. The animal studies and some of our own studies certainly suggest there are differences in both central and peripheral neurotransmitters and in gastrointestinal hormones. So I think the reality is that there are many things put together that produce the change, and that is why it is so difficult to come out with a single answer.

**Dr. Planas:** Have you found differences in appetite control behavior between men and women? When we studied appetite control in relation to anxiety about hospitalization we found big differences between men and women: in men, their anxiety caused them to eat less, but that did not occur in women. I would be interested to know what differences you have found between men and women.

**Dr. Roberts:** I believe that ultimately we may find big differences between men and women, but right now there are not enough data to look at this in any great depth.

**Dr. Vazquez:** Several epidemiological studies have shown that old people prefer carbohydrate foods and dislike proteins, especially meat proteins. Is there any biological explanation for this rejection of protein foods?

**Dr. Roberts:** I don’t know of one, but it’s an important issue.