

Bringing Homeostasis Back into Weight Control

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Abstract

Homeostasis is a well-known concept in physiology and medicine, and as obesity is becoming pandemic, homeostasis is finally emerging as a scientific interest in the field of weight control. However, instead of being incorporated into public health education the discoveries in weight homeostasis arise from a desire to find medical and surgical solutions to the problem of overweight. Energy homeostasis involves a myriad of biochemical forces aimed at keeping a balanced weight. Despite homeostatic forces both voluntary and automatic, many of the world's populace is storing excess energy. Standard interventions and education to curb the obesity epidemic acknowledge the effect of overriding "fullness" cues on weight gain and have focused on education that has people cutting back and eating healthy. Unfortunately, this may result in another disruption in homeostasis that could also result in excess weight. Ignoring either anorexigenic or orexigenic forces causes a disruption in homeostasis that may result in overcompensation. Because starvation is more of an immediate threat than obesity, the error in weight homeostasis is to preserve energy stores over leanness. Ignoring hunger cues can be as detrimental to maintaining leanness as ignoring fullness cues. Before resorting to artificial means to combat overcompensation, perhaps patient education could teach the value of tuning into homeostatic cues. Eating in this intuitive and intrinsic way may provide an effective and accessible means to stay healthy and avoid excessive weight gain.

Keywords: Weight Homeostasis; Energy Homeostasis; Weight Control; Intuitive Eating; Intrinsic Eating; Ghrelin; Leptin

Bringing Homeostasis back into Weight Control

Ironically, as dieting and eating healthy recommendations fail to curb the obesity epidemic [1-3] and patients are turning to medical and surgical remedies to rid themselves of excess fat, more and more is being discovered about weight homeostasis. Homeostasis is a force that works to keep internal balance within an organism. The word homeostasis comes from the Greek words "homeo", meaning similar, and "stasis", meaning to stand still [4]. The property of homeostasis is critical to all living organisms that require a stable, internal milieu. Unfortunately, with the obesity epidemic, balance is disappearing and excess fat appears to be prevailing. This phenomenon has resulted in a paradox where the physiologic forces curbing appetite are increasingly understood at the same time diets and eating healthy still prevail as remedies to combat excess fat [5,6].

Despite vast increases in what is known about the hunger and satiety forces keeping weight balanced, this knowledge has yet to be translated into health advice for the populace. Today, perhaps more than at any other time in history, homeostatic cues like hunger and fullness are needed to guide eating and curb weight gain. It is generally agreed upon that disrupting homeostasis by ignoring fullness cues will result in excess weight gain. What may not be common knowledge is that ignoring hunger cues may also result in excess weight gain. Going hungry disrupts homeostasis causing overcompensation that errs on the side of preventing starvation. Bringing homeostasis back into the concept of "weight control" can help avoid rebound and excessive weight gain that is seen today. Honoring hunger and fullness cues is a sustainable way to keep a balanced and healthy weight. This paper examines the role of restraint and deprivation in cyclic weight gain and ultimately excess weight. A case study* illustrating a real life example of restraint will be presented. The paper also includes a brief look at the physiologic and psychological forces involved in weight homeostasis. The paper will finish with a call to embrace the tuning in to homeostatic cues to maintain a healthy weight and prevent weight gain.

Weight Homeostasis

Whether it is weight, body temperature, or pH, there are many

physiologic actions at work to regulate life requiring conditions [7]. With pH, for example, either a too low blood pH or a too high pH can be fatal. The pH regulatory system either self corrects by excreting or retaining hydrogen ions, or spurs behavioral change in the host. Extra breaths may be necessary to increase pH. In the case of pH, all of these compensatory mechanisms are involuntary with the organism unaware of what it is doing to maintain a balance of acidity and alkalinity. Body temperature also involves involuntary responses, like shivering or limb cooling [8] but it may also require higher level thinking, including the seeking out of warmer or cooler environments [7].

Weight homeostasis is more like temperature regulation. There are many involuntary compensatory reactions to keep a steady weight, neither gaining nor losing energy. To a greater degree however, the organism is constantly required to use higher level thinking in obtaining food (energy). In humans and many animals, despite higher level thinking in meal preparation, there are complex biochemicals and hormonal guides directing what and how much to eat [9-11]. Unfortunately, despite these internal "guides", a growing number of modern day humans have excessive amounts of stored energy. In other words, the balance of weight has shifted to excess. Eating nutrient rich foods beyond the point of fullness is generally recognized as one of the causes of the obesity epidemic [12]. In homeostatic terms this happens because the internal homeostasis cue of "fullness" is overridden, ignored, or misinterpreted. Certainly much of the research into the obesity epidemic has focused on overriding fullness cues in favor of overeating. However, this could underestimate the effect of ignoring hunger in rising weights.

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Case Study

Susan's* story

Susan is a 36 year old OR nurse. Her relationship to weight management began during her childhood while witnessing her mother's struggle with her own weight. While Susan sailed through childhood as a "skinny kid", her mother always seemed to be on a diet. Susan remembered the "ice cube milk shakes", the cottage cheese breakfasts, and the broiled turkey breast dinners that would guarantee the loss of a couple of pounds. Susan basically remembers her mother as an attractive brunette, who got progressively larger over the years. Her mother, a normal weight newlywed, a "pleasantly plump" mom had finally become an "obese" grandmother, diabetic and on insulin.

Susan's struggle

As a young adult Susan didn't worry too much about her weight. While she was not the skinny kid she had been, by watching the how much salad dressing and butter she used coupled with staying away from fast food, she managed to keep relatively slim into her adult years. However, with pregnancy, all restraint disappeared and nothing was off limits. She gained 60 pounds by the time her daughter was born and had only 25 of these pounds by the time her baby was eight months old.

Susan's slippery slope

When her daughter was eight months old, Susan went back to work in the OR. Her life was busier than ever she felt a nagging sense of failure at balancing career and motherhood. A baseline shift in her mood also had her longing for a boost to her feeling of accomplishment. Susan's sense of desperation was not helped by the fact that she could only fit into two outfits. She remembered how empowered her mother felt when the scale tipped just a little bit less than it had the week before. So Susan decided to "slim down". She decided to "be smart" and cut down on her carbs and fat, and increase the amount of lean protein. Not believing in "depression" or the use of psychotropic drugs, she sought weight control as a way to boost her mood. After a week of cutting calories by 15%, Susan anticipated feeling the same elation. She began "rewarding" herself by getting on the scale every two days or so to see if she had lost yet another pound. After a month of this she had "slimmed down" a full eight pounds. She got out some more of her prepregnancy clothes.

Susan's success?

Susan felt that sense of elation she had seen in her mother. She loved being able to wear her "before child" clothes. She loved the power it gave her. She decided to ramp it up. Still eating a low carb/low fat diet she now cut her portions down by 1/3. By month three she had lost 28 pounds. Many of her "slim" clothes were now too big.

Susan's trip down anorexia lane

Susan was noticing that she had a baseline hunger pretty much all the time. She realized she thought about food all the time. And while she only fantasized about coffee cake and lasagna, she meticulously prepared her sparse fare. What was this dieting doing to Susan's body? Little did Susan know, as she began to "get her weight back to a healthier level", that she was disturbing the delicate balance of weight homeostasis.

Disrupting Homeostasis

Some of the mechanisms by which "too little" turns into "too much" are the physiologic and psychological responses to restrictive eating that

induce a "mayday response". Perhaps because starvation poses more of an immediate threat to survival than does obesity, weight homeostasis will tend to err on the side of retaining or recouping weight, versus shedding extra pounds. In spite of this, the majority of human kind prior to the 21st century used only internal cues to guide how much to eat and maintained a healthy "weight with precision" [11]. The fact that homeostatic forces to maintain weight are stronger than the forces to reduce weight does not negate the benefit of using internal cues as a way to maintain a healthy weight. Homeostasis exists to keep the organism alive when the balance is disturbed during times of famine (or dieting). Using internal cues to guide intake avoids disturbing homeostasis and "overcompensation to prevent starvation". Despite overcompensation driving excess fat stores, there are many biological forces on both sides of weight balance: orexigenic (or hunger factors) and anorexigenic (satiety factors). Above and beyond the physiology of homeostasis, the psyche is also instrumental in preventing starvation. Ultimately, because starvation is more of an immediate threat to survival than obesity, homeostatic friendly ways to keep a healthy weight must be considered.

Physiologic Forces in Homeostasis

Orexigenic forces

While many people rely on external cues to eat; the clock, lunchtime, the time the family sits down to eat, there are actually many internal cues telling us it is physically time to eat. In the central nervous system, neuropeptide Y and orexin are two hunger hormones increasing appetite and providing a cue to eat [13,14]. Ghrelin is another hunger hormone produced in the periphery. Ghrelin is considered to be a "meal starting" hormone [15,16]. Ghrelin is a hunger hormone produced by the gastric mucosa as soon as the stomach empties and food metabolism has begun [17-19]. Interestingly, ghrelin is the only known circulating "hunger hormone" among many satiety hormones and peptides [20,21].

Like other homeostasis hormones, ghrelin affects more than just appetite. As a growth hormone, ghrelin affects many other parts of the body, including the liver, heart, and central nervous system, specifically the hypothalamus [22-24]. Both sleep and cardiac health are improved with normal, fluctuating ghrelin levels [22]. The multiple ways in which ghrelin impacts health makes its suppression to achieve weight control less than desirable. Ideally, in normal weight individuals, ghrelin levels spike before eating and then immediately fall as soon as food is consumed [25]. In severely overweight individuals compared to normal weight individuals, ghrelin levels are lower overall with smaller spikes before meals and not as much of a reduction after eating [26,27]. Perhaps the lower ghrelin levels seen in overweight individuals demonstrate a homeostatic reaction to reduce energy intake. In the severely overweight, while still delivering a hunger signal, the reduced ghrelin signal may decrease appetite, thereby preventing excessive weight gain [28]. Consistent with overcompensation to prevent starvation, the reduced level of this hunger hormone does not appear to be sufficient to cause weight loss. And in genetically deficient individuals, an absence of ghrelin does not indicate an absence of appetite [29]. On the other hand, without this homeostasis response, it is unknown how much greater the weight gain would be.

Excess ghrelin

Normal spikes and dips of ghrelin corresponding to meals appear to be consistent with health and stable normal weights [16]. However, excessive ghrelin is associated with both negative health effects and

higher weights. Ghrelin can be abnormally elevated in response to energy loss or fasting, or as a genetic increase. In the genetic disease, Prader-Willi syndrome, high ghrelin levels are associated with morbid obesity [30,31]. It is also speculated that high ghrelin levels cause hyperphagia and excessive weight gain after dieting or fasting [18]. High ghrelin levels not only contribute to weight gain by excessive eating, but also by decreasing sympathetic nervous system tone specifically, decreasing metabolism overall, and promoting the synthesis of fat cells [15,30,32-34].

Implications for case study

The constant, low level hunger that is now a constant companion of Susan's, is in large part due to increases in ghrelin. Part of this increase results from energy deficit, and part may be due to Susan's restrained style of eating. In a study of young anorexic women (ANs) it was found that higher than normal ghrelin levels were associated with "restrained eating" though the ANs may have dampened awareness of their hunger [35]. Regardless of all the factors involved, she is no doubt succumbing to some of the side effects of excess ghrelin; decreased metabolism, and increased fat synthesis.

The longer Susan deprives herself of necessary energy, the greater ghrelin's compensation will be. Susan's initial weight loss has slowed, and she is also noticing that she must eat about a third less calories per day to maintain the same weight. This is largely due to "hibernation" state where energy is being conserved and very little energy is being expended [21,33,36].

While Susan's ghrelin levels increase, her ability to fight the intense hunger may give way to overeating and rebound weight with preferential fat gain [25,26]. A recent study of mice showed that when obese mice were put on a weight loss diet they regained the lost weight quickly and substantially. Furthermore, once the regain occurred the amount of expended energy never returned to the levels witnessed prior to the compensated obese state [36].

Susan is experiences the effects of prolonged dieting, and is falling victim to the mechanisms that could cause the rebound weight gain seen in dieters [37]. Going hungry appears to disrupt the homeostasis of ghrelin causing the individual to not only recoup the lost calories, but be better at creating fat cells, and more efficient at storing calories.

Anorexigenic Forces

There are three ways in which satiety is perceived. One way is passive, in other words, when the stomach fills and hunger hormone levels drop, hunger decreases and satiety is experienced as the absence of hunger [38]. Another way is through the stretching of the stomach neurons as the stomach gets full [39]. Stomach muscles stretch triggering afferent neurons that then send signals to the brain to [39].

Fullness is also perceived through a variety of peptides, proteins, and hormones. For example, as soon as the stomach fills and metabolism of food has begun, peptide YY is secreted [28,40]. Peptide YY, also known as PY36-336, or PYY, is a circulating enzyme that communicates satiety to the central nervous system [41]. PYY sends a signal to the hypothalamus 'turning off' orexigenic hormones like neuropeptide Y and orexigen [13,42]. These biochemical responses point to a system that resists hyperphagia and calls for limited quantities of food. This effect occurs after every meal, with the signal lessening as the stomach empties. Causing PYY to be continually infused however, does not continue to cause a feeling of fullness. In studies of rodents receiving continuous infusions of PYY, initial food intake decreases but does not

continue [43]. While "fullness" hormones like PYY have a physiologic effect of limiting weight, with unnatural and prolonged levels, it appears the default is to "turn off" fullness cues. This phenomenon also supports the "overcompensation to prevent starvation" hypothesis where weight homeostasis protects energy stores over protecting leanness.

Leptin

Leptin was originally thought to be a long term "satiety" hormone [44-47]. A biochemical produced by fat cells, leptin communicates the number of peripheral fat cells to the central nervous system: the higher the level of leptin the lower the levels of hunger hormones [13,48,49]. In this way, in a well-nourished body with adequate fat stores, appetite will be reduced [50,51]. Given this normal physiology, the view that homeostasis exists to keep an individual at a balanced weight is supported.

When leptin levels are low (low amounts of stored energy), a "starvation" response is elicited [51] including many of the responses seen with high ghrelin levels: hyperphagia, decreased thermogenesis, and decreased sympathetic energy expenditure [12]. When this homeostatic response leads to a rise in leptin levels, appetite is suppressed [49]. With extra fat, energy expenditure increases and thyroid function also rises in energy recouping states [12,48,52]. This compensatory increase in metabolism once again causes leptin levels to fall. Responding to low leptin levels in this way prevents succumbing to starvation, leading to the conclusion that weight homeostasis involving leptin not only communicates energy status that limits hunger but works to "defend against loss of adiposity" in times of deprivation [36].

Leptin excess

The kind of leptin sensitivity illustrated above means that the amount of stored energy is communicated to the CNS and hunger hormones, including neuropeptide Y and orexigen are suppressed. Sustained high levels of leptin, as seen in prolonged overweight states, do not appear to trigger the same increase in energy expenditure and fat cell lipolysis [46,53]. This finding has led researchers to conclude that the CNS can become resistant to leptin [54].

Leptin resistance at first glance may argue against viable weight homeostasis, with excess fat leading to excess fat. However, keeping in mind that the default in weight homeostasis is to resist starvation, the phenomenon of leptin insensitivity in the overweight may not be so counterintuitive. A similar kind of resistance to the fullness signal of PYY is seen with prolonged infusion [55]. Unfortunately, in leptin resistance the CNS cannot receive the communication, negatively impacting the health of the severely overweight person. Unable to receive leptin signals, the central nervous system of the leptin resistant individual responds much the same way as someone truly deficient in fat cells; through compensatory overeating and reducing the amount of energy expended [54,56].

When looking at physiologic changes during weight loss, contradictory forces appear to be at work. In the initial period of weight loss, leptin sensitivity increases helping to facilitate weight loss [12]. However, because low leptin levels induce a "starvation response", hyperphagia, decreased sympathetic tone, decreased thyroid, and overall decreased metabolism soon follows causing rebound weight gain. [12,57-60].

Ultimately, leptin works to curb appetite when neither hunger or fullness cues are overridden. Both overeating and undereating appear to reduce this effect long term.

Implications for case study

In our case study, in the beginning stages of Sue's weight loss, Sue continued to lose weight with relative ease as her sensitivity to leptin and insulin increased. Interestingly, it is the evidence showing that even modest weight loss can improve both leptin and insulin sensitivity that may now be working against Sue [12,35,61,62]. As her improved insulin sensitivity is helping transform glucose into adipocytes. Weight regain in rodents may be facilitated in part by the ease at which glucose is turned into fat cells [36].

With high ghrelin levels, low leptin levels, and increased insulin sensitivity, Susan is at increased risk of gaining excess fat. To avoid the negative effects of preferential fat gain, she must continue to eat extremely low amounts of food and calories. If unable to sustain the weight loss, she runs the risk of not only excessive weight gain but also excess fat gain, especially visceral adiposity [63]. When Susan can no longer fight the forces of lipogenesis, "hibernation" like metabolism, and constant hunger, she can expect to gain back a disproportionate amount of weight in the way of fat, and gain it back rapidly.

Psychological Forces

The psyche resists restraint. Restraint calls for inhibition of a need or desire. Psychological research has found that "inhibition" is followed by "disinhibition". In a landmark study of chocolate eaters, restrained eaters were found to consume more of this "forbidden" food than non-restrained eaters [64]. This disinhibition response appears to be the psyche's version of "overcompensation to prevent starvation" that is seen in the physiology of weight homeostasis. Interestingly, the psyche may also influence the body's homeostatic forces. In a recent study looking at ghrelin levels, Schur and colleagues (2008) found them to be higher among restrained eaters than their non-restrained counterpart, irrespective of weight loss. From a psychological perspective, restraint requires inhibition. From a psychological standpoint, inhibition is ultimately overridden by disinhibition [65].

Restraint has also been found to be a risk factor for excessive weight or weight gain in a number of studies. Two prospective, long term studies on weight control [66,67] found that adolescent girls who ate in a restrained manner weighed more than their unrestrained counterparts at the end of five years. These and other studies are leading to a growing consensus that restraint cannot be maintained and will eventually lead to weight gain [2,66-69].

Overriding hunger cues with restraint is emerging as a reason for the failure of dieting to result in long-term weight loss. While in the short term, weight loss restores leptin sensitivity, improves glucose tolerance, and reduces triglycerides [61] long term studies do not support resisting homeostatic cues [66,67,69]. It appears that obesity factors are at work even without extreme energy deprivation. While the evidence is inconclusive regarding the pros and cons of restrictive eating, there are recent studies suggesting that restrictive eaters weigh more than non-restrictive eaters [69].

A restrained psyche like its somatic counterpart, eventually succumbs to disinhibition, the psyche's version of "overcompensation to prevent starvation".

Case study implications

Susan has managed to inhibit her need for food for more than a year. She is thinner, has less energy, is cold intolerant with sluggish bowels, dry skin and hair. In addition to experiencing changes in her physical state, her thinking processes have also changed dramatically.

While she is competent at her job, and enjoys the time she spends with her daughter, she has trouble being "in the moment" as her mind is fixated on food. She is constantly thinking about how to prepare her "healthy food", how to eat in a way that minimizes her hunger, and most of all she finds herself fantasizing about forbidden food.

When Susan eventually experiences "disinhibition" and goes from famine to feasting she can expect to gain back more weight than before she began her diet. She can also expect to gain more visceral adiposity and have a worse metabolic profile [61,63]. Ultimately she can expect worse health and earlier mortality with each bout of cyclic weight gain [70].

Implications

There are two competing conclusions to be drawn when looking at homeostasis and weight control. Based on current recommendations for weight control, the most pervasive conclusion appears to be that the human body cannot be trusted and that cognitive restraint must be used to prevent or treat obesity (us preventive task force; Wright The implication is that tuning into homeostatic cues like hunger and fullness either results in excess weight gain or fails to regain a healthy weight.

There are several phenomena "supporting" this conclusion. The "leptin resistant" phenomenon, whereby excess weight apparently leads to excess weight by "causing" leptin resistance, at first glance, does not support the role of weight homeostasis in alleviating the obesity epidemic. However, the reason why individuals most benefitting from decreased appetite caused by leptin signaling would be unable to receive the signal remains a mystery. With a few orexigenic signals and many anorexigenic signals working to preserve balance, the question arises, "why would extra fat lead to extra fat"? A biochemical perspective may help make sense of leptin resistance. Maybe it's not fat per se that is begetting fat, but rather a biochemical change that could occur in either fasting or feasting states. For example, elevated levels of free fatty acids might impair leptin sensitivity regardless of adipocyte concentration [71]. Interestingly, free fatty acids can abound in both energy deficient states as well as in nutrient rich environments. Free fatty acids are a byproduct of lipolysis, an event that occurs in prolonged fasting and starvation [72,73]. Recent research in mice points to fasting as interfering with ability of the leptin signal to reach the CNS [55]. Other research has also shown that low leptin levels might trigger weight gain in insulin resistant Pima Indians [74]. Whether this is a consequence of high glycemic intake or a byproduct of fatty acids, either excessive nutrition or insufficient nutrition may lead to leptin resistance. Unfortunately, the "lose weight" to recoup leptin sensitivity strategy decreases leptin levels and increases ghrelin levels, resulting in a "hunger response". This homeostatic response in turn causes decreased energy expenditure and increased food intake which leads to weight regain.

There appears to be no fast and easy remedy for excess weight gain. While in the short term, rapid weight loss can reverse even more effectively than medicine some of the metabolic compensations that work to keep weight on [76], in the long term, overcompensation kicks in and rebound weight gain ensues in the majority of cases [68,69,77]. The particular affinity our post industrialized world has for extreme and precise calorie counting measures to lose weight eventually and unfortunately results in overcompensation to prevent starvation.

The conclusion proposed in this paper is that excess weight gain occurs when fullness cues are overridden or hunger cues are ignored. Any disruption in homeostasis risks unleashing a cascade of

physiologic forces aimed at preserving energy stores. This means that while it may be relatively easy to lose weight initially, regaining lost weight over time is often inevitable [69,77,78]. This finding has in turn led to increased investigation into medical and surgical weight loss [79], leading to a simultaneous and ironic side effect of a better understanding of weight homeostasis [outland].

If weight education could focus on tuning into both hunger and fullness cues rather than decreasing calories, perhaps some of the excess weight gain could be prevented [75]. All humans were born with the ability to eat intrinsically [80]. The current trend in infant feeding [81] and eating disorder treatment [82] uses homeostatic friendly ways to guide consumption. A growing number of commercial and therapeutic treatments are also helping train chronic dieters to eat in this innately oriented way [83-88]. Tuning into homeostatic cues avoids overriding fullness and eating too much as well as ignore hunger and initially eating too little only to overcompensate at a later date. Eating in an “Intuitive” or “intrinsic” way may be a low cost, easily accessible and effective way to ease and prevent obesity in at least a portion of the population.

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