Chapter 5

The Brain, the Environment, and Human Obesity: An Evolutionary Perspective on the Difficulty with Maintaining Long-Term Weight Loss

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Abstract

The dramatic increase in obesity within one or two generations cannot possibly be due to a change in genetics. It is the processing, distribution, and availability of foods that have changed, not the brain. For most people, in the presence of pleasant tasting (high calorie) foods, the brain's reward circuitry overwhelms the satiety signals. For 2 million years, overeating (on the occasional basis when that was possible) had adaptive value, and it has only been since the rise of an omnipresent obesogenic environment that such behavior has become maladaptive, resulting in widespread obesity. Long-term weight loss is, at minimum, a two-part process: (1) initial weight loss and (2) relapse prevention. All weight loss programs (diet, pharmacology, or surgical) work in the short run, but none used alone have proven widely effective in the long term. After initial weight loss, relapse is common because until recently interventions failed to consider our evolutionary history and thus have underestimated the sensory/reward aspects of feeding behavior. Strongly heritable behavioral characteristics that differentiate obesity-prone individuals from others (e.g., food cue responsiveness, satiety responsiveness) have now been identified and can potentially be targeted to help people learn how to better interact with an obesogenic environment.

Keywords: obesity, brain satiety mechanisms, evolutionary pressures, heritable traits, obesogenic environment

1. Introduction: The brain and regulation of food intake

Up until at least 1973, the brain was believed to act much like a thermostat in its regulation of food intake and body weight. Hundreds of studies had shown that damage to the ventromedial

hypothalamus (VMH) resulted in hyperphagia and obesity in a wide variety of species including humans and that lesions of the adjacent lateral hypothalamus (LH) resulted in aphagia and weight loss [1]. Female rats with large VMH lesions frequently doubled their body weight within 30 days [2]. In 1954, Eliot Stellar used these two nuclei as the model example for his dual-center hypothesis for motivated behavior [3]. The LH was the "excitatory center," activation of which caused the organism to eat. Food intake provided some (unknown at that time) manner of glucostatic, lipostatic, and/or thermostatic feedback to the VMH, the "inhibitory center," which then inhibited the LH, resulting in cessation of feeding. The underlying principal was homeostasis, i.e., food intake decreased when body weight exceeded some stable state (set point) and increased when body weight fell below this set point (see [4] for a history of set point theory). The weight changes observed after lesions were generally attributed to a resetting of the set point [5].

So compelling was the evidence, and model, that the leading researchers of human obesity of that era directly compared obese humans to obese rats with VMH lesions [6–8]. Similarities in patterns of food intake, hyperreactivity to the sensory qualities of food (e.g., taste), and unwillingness to work for food were particularly noted. Researchers concluded that obese individuals had "a weak ventromedial hypothalamus" [6, p. 450] and that "the obesity of rats and men has a common physiological locus in the ventromedial hypothalamus" [8, p. 143].

The simplicity of the dual-center model was abandoned in the 1970s when, first, it was found that transection of the ventral noradrenergic bundle at the level of the midbrain resulted in overeating and obesity [9] and, second, when a few years later it was discovered that lesions of the hypothalamic paraventricular nucleus (PVN) also produced hyperphagia and obesity [10, 11]. The next 30 years of research (with lab rats) focused on the role of the PVN and arcuate nuclei [12] and circulating levels of leptin and insulin, hormones that are released in proportion to body fat content [13]. Mice that have mutations in the gene for leptin (ob/ob) become markedly obese [14]. Other brain structures were also found to play a role in the regulation of food intake and body weight, including the posterodorsal amygdala [15, 16]. The model had become more complex, but the underlying principal was still believed to be energy homeostasis [13, 17] and the related concept of set point (or settling point). Human obesity was explained, at least in part, as a malfunction of the system, e.g., resistance to leptin [18].

The studies with rats confined in small cages and fed a single standard lab chow diet have contributed greatly to our understanding of brain mechanisms regulating individual meal parameters [19], but how well do they explain regulation of body weight in free-living humans? The answer is not very well. Similar to lab rats, humans do not overeat when offered a bland diet ad libitum [20], but many researchers have noted that homeostatic controls appear to be absent in environments with an abundance of good-tasting foods [13, 18, 21–26]. In fact, in a long series of studies, de Castro and colleagues determined that only 14% of the variance in the daily food intake of free-living humans could be explained by brain homeostatic mechanisms [27]. As stated by Cameron and Doucet [21], "…when given a barrage of anorexigenic signals, humans still manage to overconsume even at gluttonous levels" (p. 183).

The prevalence of overweight and obese individuals in the United States has nearly tripled since 1980 [23]. One third of adults are overweight (BMI > 25 kg/m^2), and over one third more

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are clinically obese (BMI > 30 kg/m^2) [28]. Researchers have projected that at least 42–44% of Americans will be obese by 2030 [29, 30]. This is a substantial increase since 1960 when only about one in five Americans was overweight [31]. Any explanation for the regulation of body weight in humans must be able to account for this dramatic increase in obesity in just a few-decade time. It is highly unlikely that the modern obesity pandemic is due to recent pathology in genetics, metabolism, or the brain homeostatic (inhibitory) controls of feeding behavior [22]. Two thirds of the American population could not suddenly have become leptin resistant.

In actuality, the brain is reacting to present-day environmental stimuli exactly in the manner in which it evolved during 2 million years of environmental selective pressures since the appearance of the genus *Homo* [23]. Considerable evidence has accrued that in obesity-prone individuals, it is the reward circuitry of the brain, not the hypothalamic homeostatic nuclei, that developed during human evolution which control feeding behavior when there is an abundance of good-tasting foods [21]. As expected, initial brain fMRI studies found activation of hypothalamic nuclei in response to changes in glucose and insulin levels [32–34]. However, more recent brain fMRI studies also reveal hyperactivation of the cortico-limbic-striatal structures in the reward circuitry of obese children and adults in response to pleasant food stimuli (see Refs. [35–37] for reviews). Genetically obesity-prone children display hyperactivation of the reward circuitry before they become obese [38, 39]. Previously obese adults who have dieted and lost their excess weight continue to show hyperactivity in the reward circuits in response to food [40]. It must be noted that brain fMRI studies of obesity are still in their initial stages, and attempts to identify the specific reward circuitry associated with obesity are inconsistent [37].

One thing is certain: the brain's reward circuitry is not homeostatic, i.e., there is no upper-level body weight set point at which it shuts down [41]. In short, the brain developed as an organ attracted to energy-dense rewards. For many people, the sensory/reward aspects of food simply overwhelm the homeostatic satiety signals [18, 23].

2. The environment and obesity

Until about 8000 BC, all humans lived in small nomadic, hunter-gatherer tribes [42, 43]. King [23] has reviewed the anthropological research showing that for the previous 2 million years, there were certainly periods (short and/or prolonged) of food shortages. It would have been advantageous to store energy as fat to survive periods of deprivation and have energy to hunt and thus, when food was plentiful, to consume more calories than was required just to satisfy short-term inter-meal deficits in energy [21, 25, 44]. In a restricted environment, this would have resulted, at most, in a moderately overweight phenotype.

In short, the modern societal practice of "three meals plus snacks every day is abnormal from an evolutionary perspective" [45, p. 16,647]. Interestingly, recent research has shown that intermittent fasting not only reduces body weight [45–48] but improves clinical health indicators [45, 47, 48] and may reduce processes leading to diseases such as diabetes, heart disease, and certain cancers [45, 47].

What has changed is not the brain, but the environment [23, 26]. The anthropological record reveals that the switch from hunting-gathering to farming as the primary source of food (with a greater reliance on carbohydrates than lean meat) began 10,000 years ago [49, 50]. The use of salt (and probably herbs and spices) to flavor foods dates back to at least the Bronze Age [51], but sugar was not widely available until the 1500s [52]. However, it was the industrialization of the food supply (i.e., the processing and distribution of food) in the last half of the twentieth century that has had the most dramatic impact on how today's humans eat [26, 53, 54].

The availability of high-calorie foods (e.g., carbohydrates and fats) has markedly increased in the United States since the 1970s [55]. One of the most obvious changes that began in the 1970s, at about the same time as the prevalence of obesity began to rapidly increase, was the proliferation of fast-food restaurants. McDonald's opened in 1955, had 1000 restaurants in 1968, and today has over 36,000 restaurants in over 100 countries. Burger King opened in 1954, had 275 restaurants in 1967, and today has 13,000 restaurants in 79 countries. Wendy's opened in 1969 and today has over 6850 restaurants. Similarly, today, Kentucky Fried Chicken has over 19,400 restaurants, Pizza Hut over 11,000, Taco Bell over 6500, Arby's over 3300, Chick-fil-A over 1950, and Church's Chicken nearly 1700 restaurants. Most of them have drive-up windows. Altogether, sales at the US fast-food restaurants increased from $16.2 billion in 1975 to about $110 billion by 2004 [56] with a corresponding increase in American's proportional consumption of calories in the form sweetened drinks and such foods as cheeseburgers and pizza [57, 58]. Add to fast-food restaurants an increase in cafeteria and full-menu restaurants, convenience stores, and dispensing machines, and the end result is an obesogenic environment: a high density of high-calorie food sources that require little energy expenditure for consumers to access.

Numerous studies have found a positive association between the geographical density of fast-food restaurants and prevalence of obesity [59–64] or obesity and the frequency with which individuals eat at restaurants [65–70; see also 71]. Compared to normal-weight persons, overweight and obese individuals consume larger meals when eating away from home [72]. Many studies have also found that when groups of people move from areas of the world where the prevalence of obesity is low to an obesogenic environment (e.g., the United States), they gain weight and eventually display the same prevalence of obesity as is found among those who were born in the obesogenic environment [73; see 24 for a review]. Freshman students often gain excess weight during the first few weeks of attending college [74]. One third of American adults may not (yet) be overweight, but many of them live in areas (e.g., very rural) that are not obesogenic.

As with any genetic trait (e.g., height), there is diversity, and some people are more obesity prone than others [18, 75–77]. Obese individuals are less responsive to homeostatic satiety mechanisms [76–78] and are much more responsive to external feeding stimuli than are normal-weight people [7, 24, 27, 77, 79]. The latter includes not only the taste and texture of food but also social cues (e.g., number of others eating, the sight of and variety of foods, portion size, time of day). Compared to others, obese individuals have a strong tendency to discount delayed food rewards in favor of immediate rewards [80–83].

Studies with twins reveal that appetite (responsiveness to food cues) and satiety responsiveness are highly heritable behavioral characteristics [27, 76, 77, 79], as is cognitive restraint,

which is generally less for obese individuals [27, 84, 85]. These heritable behavioral characteristics emerge early in life [76], and while they do not cause obesity directly, they result in individuals being more susceptible to overeating in an obesogenic environment [18, 77, 86]. Not everyone has these heritable traits, but based on the obesity statistics, a large majority of humans do have them. At present, at least 32 genetic loci associated with BMI have been identified [87].

In summary, obesity is the result of interaction between genetic risks and the environment. The brain reward circuitry that evolved during 2 million years of our hunter-gatherer ancestry has resulted in many humans being more responsive to environmental food stimuli than they are to caloric/homeostatic stimuli [7, 21, 23, 24, 27, 75–77]. In the words of one group of researchers, humans have "fat brains [and] greedy genes" [79].

3. Interventions to reduce obesity

As the prevalence of obesity has increased, the number and variety of weight loss programs have increased almost exponentially. Using the key terms "obesity," "humans," and "weight loss," Medline indicates 67 publications in the time period 1965–1974 and 13,904 publications from 2006 to 2015. Today, Americans spend over $60 billion a year on attempts to lose weight [88]. The medical cost of treating adult obesity in the United States is between $147 and $210 billion per year [30].

All diets work—in the short run. They may differ in the types of food recommended to eat, but when fewer calories are consumed than expended, the result is weight loss. Most overweight and obese individuals have successfully dieted for a few weeks and many for a few months, but in the long run, the success rate of behavioral therapies alone has proven to be very modest at best. Most dieting individuals do not maintain their weight loss [89, 90]. This was first noted nearly 60 years ago:

"Most obese patients will not remain in treatment. Of those who do remain in treatment, most will not lose significant poundage, and of those who do lose weight, most would regain it promptly" [91, p. 87].

Results with pharmacologic treatment of obesity alone have proven equally disappointing [92–94]—individuals achieve meaningful weight loss only when the medication is accompanied by additional lifestyle interventions [95] and maintain the weight loss (usually modest) only as long as they remain on the drugs [96]. Mean excess weight loss for extremely obese individuals who have undergone bariatric surgery is only about 50% ([97]; see [98, 99] for reviews), with many others losing substantially less weight (see [100] for a review), and still others eventually regaining much of their excess weight [101]. (Note: the author is not underestimating the health benefits of a 50% loss of excess weight.)

Long-term weight loss is, at minimum, a two-part process: (1) initial weight loss and (2) relapse prevention. The relapse rate is high because it is normal for the evolved brain's reward circuitry to direct humans to overeat when good-tasting/high-calorie foods are available [23]. Regard-

less of how weight loss is initially achieved (diet, pharmacology, and/or surgical intervention), sending the client back into an omnipresent obesogenic environment with a few behavioral-cognitive instructions (e.g., counting calories; monitoring carbohydrates, fats, and portion size; eating slowly; more exercise) has not worked long term for most people [89–91, 101].

For many individuals who have recently lost weight, relapse prevention will mean, in part, learning how to reduce food cue responsiveness [76]. Obese individuals are more easily tempted by pleasant-tasting food when it is easily available than are lean individuals [8], an aspect of the greater responsiveness to external stimuli. Today, the obesogenic environment is omnipresent—in the workplace, in schools, throughout the community, and in the media. Weight-loss interventions have failed because, historically, they have put the responsibility almost exclusively on the individual. In 2012, the Institute of Medicine [102] concluded that government, industry, the community, the media, and medicine must be part of a multifaceted approach (e.g., an increase in social marketing, as was done with smoking) to help individuals address how to limit and deal with an ever-increasing obesogenic environment [22, 26, 88, 103–105].

4. Conclusions

In free-living humans living in an obesogenic environment, there is little evidence in support of an upper limit set point around which body weight is regulated in a homeostatic fashion. For most people, the brain's reward circuitry plays the dominant role in feeding behavior. Living in a restricted environment with periods of food deprivation, it was necessary for survival for *Homo erectus* and *Homo sapiens* to consume as much pleasant-tasting food as possible when it was available. Only recently have high-calorie foods become widely available, but the brain still responds to pleasant-tasting foods in a manner that was adaptive for the hunter-gatherers that existed in our ancestral past. After excess weight loss, relapse is high because the brain's normal response is to direct humans to overeat in the presence of an abundance of foods. For obesity interventions to be successful, long-term strategies, both individual and collective, need to better address relapse prevention, and an important component of this must include how to limit and interact with an obesogenic environment.

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