The effects of hormonal imbalance due to obesity on human behavior

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Rationale

Since rates of obesity are rising, it is important to assess the impact on human behavior, in order to fully understand individuals who are obese. There are multiple studies assessing the cause of obesity, but few address the impact of obesity on human behavior. In performing this literature review, my main goal of this paper was to assess how obesity may lead to changes in behavior. The reason I chose this topic is because, as a student studying physiology and psychology, I am interested in how the body employs certain physiological processes in order to maintain homeostasis. Furthermore, I am interested in how altering physiology can affect psychology. For obese individuals, the imbalance between energy spent and energy intake causes the body to alter its physiological processes.

This paper will analyze the mechanism causing obesity, the genetics of obesity, and common psychological effects that obesity is believed to play a role in. Obesity is a complex process resulting from the interaction of multiple physiological systems. Some common behaviors associated with energy imbalance are stress eating, self-esteem issues, and even depression. Through performing multiple literature searches, I have compiled many studies that provide explanations for how obesity affects behavior.

Introduction

A body mass index of above 30 km/m^3 is considered obese (Bell et al., 2005). Being overweight can lead to a variety of medical complications, decrease an individual's average lifespan, and cause psychological problems. To make matters worse, the issue is widely prevalent: nearly 1 in 3 American adults are classified as obese, and the trend is consistent worldwide (Flegal et al., 2002). Researchers believe that by 2030, 1.12 billion individuals will be

considered obese (Kelly, et al., 2008). In addition to the growth of industrialization, the social characteristics of the workforce have changed. In terms of the workforce, people are now more urbanized and develop a sedentary lifestyle. This type of lifestyle incorporates a larger caloric intake, while having a decrease in energy expense, and both of these factors eventually result in obesity unless physical activity is incorporated (Bell et al., 2005). When analyzing obesity, it is important to understand the implications of physiological and molecular processes.

How obesity arises

The physiological aspect of weight regulation includes the interplay between the circulatory, nervous, endocrine, and digestive systems. The hypothalamus obtains information about energy levels within the body from neurons, as well as from multiple hormones (Goldstone, 2006). The nuclei involved in neural and hormonal regulation are the ventro-medial, paraventricular, and arcuate nuclei. These three types of nuclei facilitate the recognition of signals involved in food intake and energy expenditure. Within the arcuate nucleus, there are two categories of neurons that are crucial for information integration: (1) the agouti-regulated protein (AGRP) and neuropeptide Y (NPY) neurons and (2) the pro-opiomelanocortin (POMC) and cocaine-and amphetamine regulated transcript (CART). Both ARGP and NPY neurons fall into the category of orexigenic neurons, meaning they promote food consumption and reduce energy depletion, while POMC and CART neurons are anorexigenic neurons, meaning they inhibit food consumption and increase energy depletion. This intricate antagonistic relationship is essential for the balance of food intake and energy expenditure.

Peripheral endocrine signals utilize the NPY/AGRP neurons and the POMC/CART neurons in a variety of ways. The role of insulin is to signal specific cells to take in glucose from the blood. Insulin has anorexigenic effects by stimulating the POMC/CART neurons, and

inhibiting the AGRP/NYP neurons; this allows the body to inhibit food consumption by increasing energy depletion through moving glucose into specific cells of the body. The hormone leptin also has anorexigenic effects. Leptin plays a role in the long-term regulation of adiposity by stimulating the leptin receptor (LEPR) on the POMC/CART neurons and inhibiting NPY/ARGP neurons by binding to the LEPR receptors, both actions resulting in food consumption inhibition. Peptide YY_{3-36} is another hormone that leads to a decrease in food intake by binding to the Y2R receptor on the NPY/ARGP neurons. The feeling of satiety is partly mediated by a gut hormone cholecystokinin (CCK). The hormone ghrelin has orexigenic effects, and is secreted by the stomach and duodenum of the small intestine to increase food consumption. Ghrelin binds to the GHSR receptor located on NPY/ARGP neurons. All of these signals are processed by the central arcuate nucleus and transmitted to downstream effector neurons.

Hypotheses on the genetics of obesity

There are a variety of hypotheses explaining the genetics of obesity (Walley et al., 2009). The *thrifty gene hypothesis* incorporates the idea that evolution has tuned our bodies to enhance weight gain during periods of food deprivation. When food deprivation is not present, weight gain ensues, because our finely tuned physiological processes have been programmed to prevent starvation rather than to regulate weight gain. One hypothesis arguing against the thrifty gene hypothesis is the *predation release hypothesis*, which argues that during the evolution of humans, obesity would have been selected against, because predators would have easily captured the more obese individuals. This hypothesis is partly based on the idea that famine alone was not a strong enough evolutionary force throughout human history to completely explain how obesity arises. Another important component of this debate is the *fetal programming hypothesis*, which

is based on the notion that fetal development is dependent on the mother. When the mother is over nourished or undernourished, a response will be present in the child. Often times, *the thrifty gene hypothesis* and the *fetal programming hypothesis* are grouped together, because they have certain components that are similar. A major distinction, however, is that the *fetal programming hypothesis* emphasizes the mother's nutritional status, rather than the genes contributed to the offspring. A newer idea for the cause of obesity is incorporated in the *sedentary lifestyle hypothesis*. The basis of this hypothesis is that throughout the last 50 years, the average lifestyle has reduced physical activity, while simultaneously increasing the consumption of higher calorie and fat foods. The theory proposes that metabolic enzymes could have a substantial role in predisposition to obesity. One theory that encompasses the variety of hypotheses of obesity is the *complex hypothesis*, which suggests that there is not a single genetic basis for obesity, but obesity is a consequence of multiple occurrences. It is important to realize that obesity is not caused by one factor and is not likely explained by just one hypothesis. Both genetic and environmental factors have a role in obesity.

Genetic components of obesity

These physiological pathways previously described are necessary for weight control and energy storage or removal. Therefore, the genes that regulate these physiological pathways are crucial for normal function. The progression of many severe early-onset forms of obesity is genetically determined (Bell et. al, 2005). Although scientists know that genes that control the physiological processes associated with obesity do exist, this avenue of research is not fully resolved. Genome-wide association studies (GWASs) and candidate gene studies have given researchers insight to which genes are involved in weight control. The first GWAS study identified that variation in introns of the fat mass and obesity-associated gene (FTO) in part

caused obesity (Frayling et al. 2007). The FTO gene is widely expressed throughout the brain and animal studies have provided evidence of high levels of expression throughout hypothalamic nuclei, which are critical for regulating energy balance (Walley et al, 2009). Genome wide studies have identified the genes involved in the physiological pathways of weight control, food intake, and energy storage/removal. Candidate gene studies have also been important to identifying which genes are associated with the homeostatic process of weight control.

The concept of energy balance is simple: energy intake from feeding must balance energy expenditure from physical activity, basal metabolism, and adaptive thermogenesis. However, the genetic contribution to energy imbalance leading to obesity is more complex. The genetic heritability of obesity is estimated to be around 40%, however, the mechanisms of heritability and implications to obesity are still being investigated (Price, 2002). Current research indicates that the heritable variance of obesity may be a product of allelic dominance, recessivity, and non-allelic gene interactions (Hager, et al 1998). For example, some genes are necessary to mediate the effects of others, as in the case of neuropeptide Y modulating the effects of leptin (Spiegelman and Flier, 2001). This is possible because both neuropeptide Y and leptin act on the paraventricular nuclei of the hypothalamus.

Chromosomal location of obesity genes

In order to fully understand the genetic source for obesity, genome-wide scans help determine the exact chromosomal location of genes involved in obesity. Hager et al. (1998) performed genome-wide scans on 158 families (n=514) that showed signs of obesity, based on their body mass index (BMI). A BMI of greater than 30 kg/m^2 is considered obese (Bell et al., 2005). One family member had a BMI of over 40 kg/m^2, and at least one other family member

had a BMI of over 27 kg/m^2. The individuals were genotyped for 380 microsatellite markers, and the distance between markers was estimated to be 9.1 ± 2.5 cM. A multipoint analysis indicated linkage in nine regions across the genome. One region in particular, an area on chromosome 10, showed an indication for linkage (Hager et al 1998). Genetic linkage refers to alleles located close together on a chromosome are inherited together during meiosis. Scanning for linkage is important because it will help determine the genes associated with obesity. Results showed a strong linkage on chromosome 2, due to the location of the proopiomelanocortin gene (POMC), which is important for the MC4R receptor within the paraventricular neurons of the hypothalamus. Strong linkage on chromosome 5 is more difficult to analyze, and the research suggests that the prevalence of linkage is due to both a large amount of candidate genes for obesity located on this chromosome as well as the widespread duplication that the chromosome undergoes. Furthermore, chromosomes 2 and 5 showed a connection with leptin serum levels (Hager et al 1998). Although chromosome 2 and chromosome 5 contain genes associated with obesity, the highest allele frequencies are correlated with chromosome 10, indicating that there is a major locus for obesity on chromosome 10 (Hager et al 1998). However, it is important to note that human obesity is a result of genetic and environmental influences. Dong et al (2003) conducted a study assessing the gene interactions on chromosomes 7, 10, and 20 and found evidence of genes within chromosomes 10 and 20 that increase susceptibility to human obesity. The occurrence of gene regions correlated with obesity within chromosome 10 have been confirmed by Price et al. (2001).

Importance of SIM-1

One crucial gene responsible for the overweight phenotype is the mammalian homolog of the *Drosophila* single-minded 1 gene (SIM1 in mammals). This gene is one of only six linked to

obesity resulting from a single-gene mutation, a fact documented by comparing obese individuals to lean individuals, where obese individuals showed a mutation within SIM1, while lean individuals showed no mutation in SIM1 (Ahituv et al, 2007). Haploinsufficiency of the gene has been connected to an increase in food intake, leading to obesity in both humans and mice (Holder et al, 2000). In mice with a heterozygous genotype for SIM1, while normal energy expenditure occurred, the mice failed to stimulate the paraventricular neurons (Kublaoui et al, 2008). The paraventricular neurons are essential for energy homeostasis. In a clinical study of a patient with haploinsufficiency of SIM1 gene, obesity was a result of the mutation. Since the patient only had one functional copy of the gene, the food intake was not regulated (Holder et al, 2000). The transcription target and/or the SIM1 gene itself is essential for the development of the supraoptic and paraventricular hypothalamic nuclei in mice. Holder and colleagues (2000) found that other genetic mutations typically associated with obesity, more specifically, the leptin gene, were not present in the genome-wide scan. These are important mechanisms of food intake and energy homeostasis.

The role of the MC4R receptor in energy homeostasis

Paraventricular neurons also contain the melanocortin-4 receptor (MC4R), which is part of the food intake regulation and energy homeostasis (Gale et al, 2004). The MC4R gene is activated by α-MSH hormone, which results from the breakdown of the prohormone proopiomelanocortin (POMC). However, as mentioned previously, a mutation within the POMC gene on chromosome 2 can occur. Mutations in the MC4R gene have similar effects to mutations in the SIM1 gene mentioned above, and monogenic obesity is the result of mutations within the MC4R gene in mice and humans (Vaisse, et al 1998). The results of the Holder et al. (2000) case study suggest that both the SIM1 and MC4R genes may play a physiological or

molecular role in controlling energy equilibrium and tall growth in this specific patient. Typically, normal growth is caused by the MC4R receptor, and inhibited by leptin deficiency. Since the patient had normal levels of leptin and a mutation within the SIM1 and MC4R genes, disruption of energy homeostasis and obesity was a result of the irregular genotype.

Leptin and leptin receptor

Of indisputable importance in the regulation of human obesity is the hormone leptin, regulated by the *OB* gene. Leptin acts to reduce body fat by controlling food consumption. Reed et al (1996) examined obesity in 78 families and mapped the *OB* gene in obese and lean family members. The researchers tested for the possibility of linkage disequilibrium of the OB gene region and frequent transmission from parent to an obese offspring, and concluded that linkage disequilibrium in the OB region was consistent with extreme obesity, thus the OB gene is linked.

The leptin receptor, Ob-Rb, is a cytokine receptor located primarily in the hypothalamus that utilizes kinases for signal transduction (Flier, 2004). Leptin administration has been shown to reduce body mass and decrease food intake by binding to the Ob-Rb receptor and causing a cascade of events in the hypothalamus (Flier, 2004). It has been shown that animals given leptin voluntarily consumed less food in addition to a change in metabolism (Halaas et al. 1995). As a result of the decreased food intake, the body mass of the subjects decreased, but the metabolic changes observed cannot be completely explained by leptin. In order to explore the mechanism of leptin, Soukas et al., 2000 utilized oligonucleotide microarrays on wild-type and *ob/ob* mice treated with leptin to relate the gene expression in adipose tissue of leptin deficient *ob/ob* and wild type mice. The gene expression in *ob/ob* white adipose tissue was drastically different from that in lean mice, providing evidence for leptin's role in obesity. Leptin deficiency, along with an *ob/ob* genotype, alters normal gene expression in adipose tissue of obese mice. Furthermore, a

shortage of leptin affects crucial genes regulating fatty acid biosynthesis (fatty acid synthase, FAS, in particular) (Kim and Spiegelman, 1998). The presence of FAS was decreased in white adipose tissues of obese mice compared to wild-type mice. FAS is crucial for catalyzing the reactions of the conversion of malonyl-CoA to fatty acids. If FAS is not present, fatty acids will not be created from glucose in the blood (Loftus et al. 2000). Further evidence of leptin's ability to decrease fat in adipocytes was provided by Frühbeck et al. (1997). Leptin has not only been found in adipocytes and the hypothalamus, but also in skeletal muscles and the stomach (Wang, et al.,1998). The effects of this hormone in these areas are not yet known, but further investigations could provide evidence for the physiological importance of leptin in these areas.

Although leptin does cause a decrease in food intake, obesity can still develop despite high leptin levels. To a certain degree, the body can develop leptin resistance (Coll et al, 2007). It is believed that leptin resistance evolved to allow for energy storage in times of high resources, in anticipation of times of less food availability (Neel, 1999). A mechanism of leptin resistance is the inability of leptin to freely cross the blood brain barrier, thus inability to reach the leptin receptor and elicit responses in the hypothalamus (Spiegelman and Flier, 2001). Researchers have tested and obtained support for this hypothesis by injecting leptin directly into the brain to suppress food intake, compared to injecting leptin into the peripheral route that did not result in food intake suppression (Van Heek et al. 1997). Leptin acts as a control over obesity, but has its limits. Since the role of leptin is to switch the body from a fasted to a fed state, it functions to control obesity (Considine et al. 1996). However, after an organism is obese for a long period of time, the organism loses sensitivity to leptin. Initially, leptin accomplishes its role by preventing the action of two orexigenic (appetite stimulant) peptides and promoting the action of two anorexigenic peptides by directly acting on arcuate neurons via the Ob-Rb receptor. (Spiegelman

and Flier, 2011).

The role of insulin

The primary role of insulin is to control blood glucose levels, which is crucial in regulating energy balance. Insulin cooperates with leptin to facilitate the role of leptin by acting as a regulator of leptin abundance within fat cells (Spiegelman and Flier, 2001). Further evidence for the link between leptin and insulin is that triglyceride accumulation in non-adipose tissue (more specifically muscle and liver tissues) is suppressed due to leptin receptor signaling, and this contributes to insulin resistance (Emanuelli et al., 2000). Furthermore, insulin levels decrease in the fasting state and increase in a fed state due to insulin's role as a glucose transport facilitator (Wood and Trayhurn, 2003). Although insulin is not the primary peripheral signal to the central nervous system to regulate energy balance, it does have a role in energy balance.

Neuropeptide Y

Neuropeptide Y (NPY) is another mechanism for regulating energy balance, and is widely expressed throughout the nervous system. NPY acts through G-coupled protein receptors in the PVN neurons to control energy equilibrium (Spiegelman and Flier, 2001). Studies have shown that animals lacking NPY have normal body weight and have normal feeding habits, but NPY deficiency enhances obesity in mice with the *ob/ob* genotype. This provides evidence for the role of NPY in facilitating the full response of leptin deficiency (Erickson et al, 1996).

The genetics of obesity are being pieced together quickly, and scientific knowledge about the genetic factors contributing to obesity is expanding. What is causing the rise in prevalence of obesity? The susceptibility for obesity has been present for a long time, so the rise in cases of

obesity is likely due to a changing environment, such as the increased availability of food and changing food composition, in addition to a less active lifestyle. The mechanism for weight control requires energy intake to balance energy expenditure and when this balance is not met, obesity arises. Further evidence for complex causes of obesity is provided by low frequency of mutations within genes, so obesity cannot be linked to genetic factors alone.

Hormone imbalance leading to behavioral changes

Another component of obesity, besides genetic predisposition or mutations, is the environment that contributes to the psyche of an individual. There are multiple effects of obesity on human behavior. Multiple studies have attempted to determine the effect of obesity on behavioral components, and what exactly is causing behavioral deviations.

The mechanism of stress eating

One topic of investigation is stress eating. The stress response is a crucial mechanism for maintaining allostasis. The body's reaction to stress is meant to be beneficial, but it can lead to dramatic changes in an individual's physiology, psychology, and behavior. The stress response is mediated by the hypothalamus-pituitary-adrenal (HPA) axis. Corticotropin-releasing hormone (CRH) within the PVN initiates the stress response, and ACTH is secreted from the anterior pituitary (Cohen, 2000). ACTH stimulates the zona fasciculate within the adrenal cortex to release cortisol. The presence of cortisol initiates the negative-feedback mechanism of the HPA axis, and cortisol is no longer secreted (Jacobson and Sapolsky, 2001). The negative feedback mechanism is crucial for individuals to maintain a healthy physiological state because a prolonged stress response has adverse effects on the organism. Typically, the stress response decreases blood flow to areas that are not necessary for movement, which induces appetite

suppression, as epinephrine induces the 'fight or flight' response (Sherwood, 2001). During the 'fight or flight response', non-essential processes are down regulated, while processes essential for avoiding the stressor are enhanced. Throughout this short term stressor, digestion is deemed as a non-essential process. However, exposure to a long term stressor has been shown to enhance food consumption (Oliver et al 2000). This is mostly a result of the hyperactivation of the HPA axis, resulting in high cortisol levels (Torres and Nowson, 2007). It is important to realize the relationship that both cortisol and CRH have on feeding behavior. Since cortisol is a steroid hormone, it has a longer half-life since it is a steroid hormone, and therefore has longer effects on appetite. CRH, on the other hand, is a peptide hormone, so it has a short half-life, and therefore has immediate effects on appetite.

Adam and Epel (2007) researched the effect of two different stressors, threat stressors and challenge stressors, on eating. The hypothesis was that a more controllable stressor, the challenge stressor, would not have as large of an effect on eating when compared to threat stressors. A threat stressor typically encompasses a situation in which an individual had little control, and characteristics of defeat, embarrassment, or fear are felt by the individual present. A challenge stressor typically involves a challenging, but controllable situation, and the individual feels as though they have the resources to cope with the stressor. Previous research has shown that increased levels of glucocorticoids often cause an increase in calorie consumption (Tataranni et al, 1996). A high response to stress results in higher cortisol levels, and this could explain why stress eating and food cravings occur. Furthermore, higher cortisol levels also lead to amplified visceral fat accumulation, because areas composed of visceral fat have a high prevalence of glucocorticoid receptors compared to other regions of the body (Djurhuus, et al 2002).

Studies have shown support for the relationship between chronic stress and obesity. Epel et al. (2001) researched the effect of stressors on caloric intake in women. The results showed a statistically significant increase in caloric intake in women with higher cortisol levels. The women who responded more to the stressor also seemed to consume more sweet foods than the women who did not respond as much to the stressor. The main finding of this study is that the cortisol response could partly determine which individuals are more likely to consume more calories in response to stress, and which individuals consume less food after stress. It is important to note that cortisol levels do not cause an increase in eating. Instead, the interactions between cortisol and other energy regulating hormones is responsible for the variation in eating behavior in response to stress.

Energy homeostasis is controlled by multiple hormone actions and interactions. The relationship between cortisol and insulin is influenced by stress, and is just one example of the multiple hormone interactions crucial for energy balance. Lambillotte et al., (1997) revealed that, in mice, cortisol directly prevents insulin secretion from beta cells of the pancreas in mice. Furthermore, cortisol impairs the ability of insulin to move GLUT-4 to the surface of the muscle cell. These inhibitory actions of cortisol eventually lead to insulin resistance in mice. Research has also shown that when insulin and high cortisol levels are present, lipid mobilization is inhibited, and this promotes fat accumulation by inhibiting lipolysis (Martinez-Botas et al., 2000). An increase in visceral fat exacerbates obesity because excess visceral fat supplies a higher amount of intracellular glucocorticoids.

Another important hormonal interaction for the regulation of energy is the relationship between cortisol and leptin. It has been established that the main role of leptin is to decrease food intake. In a study involving rat subjects, the amount of leptin sensitivity was decreased

when glucocorticoid levels increased (Zakrzewska et al., 1997). When the rats were given a larger dosage of exogenous glucocorticoids, the rats overate, despite high levels of leptin. This finding suggests that high glucocorticoid levels could make it more likely for individuals to develop leptin resistance, which would eventually cause obesity phenotypes.

Stress eating is not the only psychological and physiological interaction in association with obesity phenotypes. Various psychological studies have attempted to explore the effect of obesity on certain behavioral characteristics. One point of interest is between obesity and body image.

The contribution of obesity on body image

The impact of obesity on an individual's psychology is composed of physical as well as social processes. The physical processes of weight gain include increased cortisol release and changes in neurotransmitters, which affect body image. The social processes associated with obesity are often negative. Some common personality traits often suggested as associated with obese individuals are: laziness, incompetency, emotional instability, and sloppiness (Puhl, et. Al, 2001). If these personality traits are common stereotypes against obese individuals, it is likely the individual consciously realizes the negative stereotypes, and internalizes this negative stigma.

This social process has a negative impact on an individual's self-esteem. There are four main contributors to negative self-perception: social comparison, sociocultural, negative verbalization, and maturational status (Thompson, 2002). Furthermore, research suggests that body image is a cognitive realization, rather than solely physical (Schwartz and Brownell, 2003). Body dissatisfaction is a strong predictor of other risk factors (Leon, et. al 1993). Cash et al (1990) measured perception of body image in three groups of individuals: participants who were

currently overweight, formerly overweight, and never overweight. Researchers found that the individuals who were formerly overweight could not reach the same positive body image as an individual who had never experienced being overweight (Cash et al., 1990). This 'phantom fat' example provides evidence for the idea that although the physical stigma associated with obesity is visually gone when an individual loses weight, the negative stigma associated with their previous obesity can remain with the individual and affect the individual mentally.

Schwartz and Brownell (2004) explain an alternative view to the psychological distress associated with obesity. They argue that negative body image is typically associated with other signs of psychological distress, and that individuals who have psychological distress due to body image are in a fragile psychological state to begin with. They point out that the individuals would be more likely to lose weight and improve their physical health if their mental health improved as well. Although one might place more importance on negative physical health due to obesity, negative psychological distress can contribute to overall poor health as well.

There is optimistic research for improving body image. The idea of cognitive-behavioral therapy has been shown to improve body image in obese women (Rosen et al., 1995). This therapy does not focus on weight loss, but on changing the mentality surrounding obesity. Women who participated in this study showed an improvement in self-esteem without losing weight. Other forms of therapy include wellness programs. This type of therapy is focused on healthy eating and social support for obese individuals. Bacon et al. (2002) followed participants throughout a wellness program, and one year after the beginning of the program. The researchers found that body image had significantly improved. Both the cognitive-behavioral therapy and wellness approach to improving body image show that self-perception can increase without weight loss.

The relationship between stress eating and increased cortisol levels made me think about how negative body image could be incorporated into this process. To my knowledge, no study has investigated my hypothesis that a positive feedback mechanism could partly explain this relationship. As mentioned earlier, research shows that stress eating is partly due to an increase in cortisol levels. Also, negative body image is typically seen in individuals who view themselves as fat. So, it could be possible that stress causes an increase in caloric intake, which results in a negative body image, and this negative body image causes internal stress in the individual, which leads to stress eating again. This positive feedback mechanism could be used to explain how obesity evolves over an individual's life. Obesity is a gradual process, and is explained through genetics, environment, and psychology. The possible positive feedback mechanism in obese individuals is similar to addictive behavior in individuals who abuse drugs.

Obesity and depression

Obesity is shown to have a relationship with other psychological disorders, such as depression. Obesity-depression comorbidity may be a result of individuals who are more depressed at baseline (Stunkard et al., 2003), so it is important to assess the starting levels of depression when conducting studies investigating obesity and depression levels. Pine et al. (2001) described a positive connection between children with depression and adult BMI taken 10–15 years later. Other studies have shown that the occurrence of depression is higher in obese individuals than in the general population (Evans, et al 2005).

The linkage between obesity and depression is not completely clear; does obesity influence the likelihood of being depressed, or do depressive symptoms increase the likelihood of becoming obese? One idea is that depressed individuals have a distorted physiological

response to stress, which promotes an unhealthy lifestyle that ultimately results in obesity (Bornstein et al., 2006). The alternative mechanism is that a continuous negative body image due to obesity results in the development of depression (Luppino et al., 2010). Luppino and colleagues (2010) found that obese individuals had a 55% higher risk of forming symptoms of depression. Their study showed that depressed individuals had a 58% higher risk of developing an obese phenotype. These results indicate that there are bidirectional associations between obesity and depression. Hasler et al. (2003) studied mood disorders in nearly 600 young adults until they reached the age of 40. Nearly 19% of the participants were overweight, and researchers found a positive association of atypical depression in these participants. Although studies have shown positive associations between obesity and psychological disorders, the relationship between obesity and depression is still obscure (McElroy et al., 2004). On the other hand, it is important to not oversimplify the issue.

Some depressed patients also suffer from high cortisol levels, which as stated earlier, can lead to an increase in caloric intake (Brown et al., 2004). A higher cortisol level would translate to a chronic stressor, which activates the HPA axis. Chronic stress has been found to increase caloric intake, which could eventually lead to obesity. Most research conducted on depressed patients has been based on studies measuring basal HPA activity (Halbreich et al., 1985), and tests meant to assess the negative feedback mechanism of the HPA axis (Carroll et al., 1981). One explanation for higher susceptibility of people with depression to increased cortisol levels is the lower number of glucocorticoid receptors and decreased receptor sensitivity (Huizenga et al., 2000).

It is difficult to provide a concise effect of obesity on differing human behaviors because there are multiple causes of obesity, and numerous consequences from obesity from individual to

individual. The interplay between physiology and psychology has slowly begun to be realized, but many details need to be uncovered. Researchers have thoroughly studied various hormones and their role in regulating energy homeostasis. The effects of these hormones are seen throughout the body, and the next step for researchers is to determine what occurs within the brain to contribute to behavioral responses to obesity.

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