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Review

Obesity as an addiction: Why do the obese eat more?

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ABSTRACT

The rising number of obese individuals on a global scale has led the scientific community to determine the causes for this disease. Besides over-consumption of high-caloric foods and/or endocrine dysfunction, food addiction has been found to be a major culprit for weight gain. Food addiction results from craving certain food or food-substances so as to obtain a state of heightened pleasure, energy or excitement. Major intervention is needed in curbing these cravings and suppressing the appetite to promote weight loss. Functional magnetic resonance imaging (fMRI) has been applied to study why obese individuals overeat. Introduction of this technology will serve as a means in paving the way for new weight loss drugs.

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Contents

1. Introduction

Obesity, as a world-wide problem, has posed a significant health threat to individuals. Obesity-linked health problems are numerous, including stroke, cardiovascular disease, diabetes mellitus, and increased risk for developing cancer [1]. The causes of obesity are multiple and troublesome to identify, and its etiology is not well explained. However, obesity is largely due to abnormal eating habits which is caused by excessive energy intake [2]. Under increasing pressure, the scientific community has been summoned to answer the question 'why do the obese eat so much?' Food addiction, as a potential decisive factor, emerges as a possible answer. Food addiction can be defined as a chronic, relapsing problem caused by various fundamental factors that encourage craving for food or food-substances so as to obtain a state of heightened pleasure, energy or excitement [3]. By analyzing the reasons why food addiction causes obesity, we hope our work benefits clinics and enlightens future research for novel weight loss drugs. Finally, functional magnetic resonance imaging (fMRI) has been applied to study why obese individuals overeat [4], and we also want to introduce

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this technology as a means to pave the way for new weight loss drugs.

2. Hunger and satiety signals

To eat is to achieve energy balance. The regulation of food intake is based on an intricate feedback system, which is controlled by hunger and satiety signals. The signals are generated in the brain itself and certain neurons in the hypothalamus are the targets of these signals [5]. Palatable food up-regulates the expression of hunger signals and satiety signals, while simultaneously blunting the response to satiety signals and activating the reward system. Most food addiction may be caused by the loss of control of neural signals, and also the impulsive and/or compulsive behavior, which results from environmental conditions and a psychological dependence on food [6].

3. High-fat and high-sugar foods environment

Currently, in developed countries and many developing countries such as China, the food industry has become savvy in exploiting foods of high quality and quantity, most of which are high-fat and high-sugar foods [7]. Access to these high-fat and high-sugar foods is easy, as more and more of them are now available in grocery stores, shops, schools, homes, and restaurants [8]. There was a 42% per capita increase in the consumption of added fats and a 162% increase for cheese. In contrast, consumption in fruits and vegetables only increased by 20% between 1970 and 2000 [9,10]. Cues for high-fat and high-sugar foods increase the likelihood of ingesting these foods, which leads to overeating and greater energy consumption [10]. Stice and his colleagues [11] claimed that there existed a relationship between the abnormalities in food reward to the risk for future weight gain, which would be stronger for participants in an unhealthy food environment. We may then suggest that diets high in concentrated fats and sugars are addictive substances.

4. Sugar and fat bingeing

Testing sugar addiction in rats is a good animal stimulation to ascertain why certain people crave sweets, and why it is difficult to wean themselves from such an eating behavior [12]. Sugar has been found to be an addictive substance since it releases dopamine (DA), a characteristic of addiction neurochemicals [13]. Rada and colleagues [14] found that the rats ate high-sugar food to release more DA in the nucleus accumbens (N_{AC}), which is parallel to the result of certain abused drugs. They also found that sugar-dependent rats had a delayed acetylcholine (Ach) response for satiety, imbibed more sugar, and released more DA than controls [14]. Using fMRI on human beings, Liu and his colleagues [15] demonstrated that the satiety signal in obese individuals was delayed, compared with normal individuals. At the same time, sugar craving as an example of food addiction makes the consumers improve their mood caused by a drop in serotonin levels [16].

High-fat foods are the major cue for the energy density of foods [17], and overeating of these foods is common in obese humans [18]. High-fat foods affect the satiety signal and drive eating behavior out of control [19]. At the same time, high-fat foods induce insulin resistance, which from the point of view of appetite regulation means suppressed satiety [20]. In one study [21], high-fat foods caused increased leptin expression and an increased body weight compared with a standard diet. It suggested that leptin was involved in the feedback control of fat intake, and high-fat foods led to an inability to respond to leptin [21].

Consumption of high-fat and high-sugar foods leads to down-regulation of DAD2 receptors and decreased DAD2 sensitivity [22]. According to Stice et al. [11], chronic intake of high-fat and high-sugar foods, which may result from hyper-responsivity of the gustatory and somatosensory cortices, leads to a blunted response in this region to the intake of palatable foods. In other words, food addiction causes the formation of pathological brain pathways.

5. Food addiction and shared brain pathways

It is known that eating disorders tend to be clustered with drug addiction in individuals, and common neural circuits are thought to underlie food and drug rewards, especially dopaminergic pathways. DA, the key neurotransmitter of addiction, plays a significant role in regulating the intake of food and reinforces the effects of food [23].

DAD2 receptors are mediators of reinforcement and compulsiveness, and obese subjects have lower levels of these receptors in the striatum [24]. DA agonists were once used to increase the portion size of meals and length of feeding, while long-term administration of DA increased body mass and feeding behavior [2]. According to Stice et al. [25], obese versus lean adolescents showed less activation in the dorsal striatum in response to food consumption with fMRI. The activation of the dorsal striatum showed a strong inverse relationship to the concurrent Body Mass Index (BMI) for those with the Taq1A A1 allele, and a weaker relation to BMI for those without this allele [25]. Meanwhile, there is similar evidence that addictive behaviors are associated with low expression of DAD2 receptors and blunted sensitivity of the reward circuitry to drugs and financial reward [25]. We speculate that obese individuals experience less subjective reward from food intake because they have fewer DAD2 receptors and lower DA signal transduction.

In addition, the common pathway for addiction involves the mesolimbic frontocortical dopamine (MFD) system, which is a reward pathway controlling eating behavior. Addictive behaviors cause the release of DA in the reward pathway, introducing almost immediate positive reinforcement [13]. Morris and his team [26] showed that the state of hunger can be influential on the memory of food-related stimuli in fasting individuals. Warren and Gold [6] found that the activity of the brain was regulated depending on the stimulus it received. For example, the right anterior orbitofrontal cortex (OFC) had a variable response to all stimuli despite hunger, while the right posterior OFC had different responses only with food-related stimuli during hunger. Thus, the posterior area was associated with general rewards, while the anterior part was associated with abstract and goal-oriented rewards [6]. These studies are critical to localize the areas of the brain that can be identified and used to treat obesity-related diseases such as Prader–Willi syndrome [13].

The prefrontal cortex (PFC) is a very important region to understand why obese subjects consume more food. The medial prefrontal cortex (MPFC), which integrates the sensory and visceral afferents, feeds back the signals to the hypothalamus and limbic areas, thus motivating individuals to behave in a manner intended to alleviate hunger [27]. This indicates that obese people have a less inhibited ability to cease eating than lean people do. The dorsomedial prefrontal cortex (DLPFC) participates in the inhibition of excessive emotion [27]. Heekeren et al. [4] proposed that the left DLPFC of the human brain may contain a general mechanism for integrating perceptual evidence for decision making. Gautier's group [28] observed that obese men and women had greater neuronal activity in the left DLPFC and less activity in the limbic and paralimbic areas than did lean men and women during the satiety state. They claimed that the DLPFC may play an important role in central regulation of eating behavior by sending inhibitory inputs

to orexigenic areas to suppress hunger and to terminate a feeding episode [28].

Metabolic factors and non-homeostatic signals also control motivational eating. Cravings for food in humans can be elicited by food cues and are often associated with hedonic overeating [29]. Similarly, the PFC regions may also participate in brain networks involved in cue-induced drug cravings, which are in need of additional studies to determine if the rat model parallels the role of the medial OFC in human appetite and cravings. Ventral areas within the rat PFC could represent a functional counterpart of the OFC in humans [30]. A human study [29] showed that in diet-restricted eaters, food cues elicited specific cravings for the cued food, as opposed to a general desire to partake in non-craved food. Most importantly, as the craving for the desired food increased, the restricted dieters consumed more of the cued food [29].

6. Intervention

Treatment of obesity includes a combination of diet, exercise, behavior modification, and sometimes weight loss drugs. In some cases of severe obesity, gastrointestinal surgery may be recommended. Based on the hypothesis of food addiction, we believe that improving eating habits is an efficient way to lose weight and maintain weight. Ways of managing eating behaviors include: maintaining a highly controlled eating environment and food regimen with strict, consistent and reinforced rules with a low-calorie diet of 1200–1500 calories a day for women and 1500–1800 calories a day for men [31].

Another way of treating obesity is by weight loss drugs. There are two kinds of drugs that can reduce weight. One type is a fat absorption inhibitor. Xenical is the only example of this type of treatment approved for use in the U.S. Xenical works by blocking about 30% of dietary fat from being absorbed. Another type, the most available weight-loss medication, is an "appetite suppressant," which acts on the central nervous system. Lorcaserin, a new weight-loss drug, is a selective 5-HT2C receptor agonist. The activation of 5-HT2C receptors in the hypothalamus is supposed to activate pro-opiomelanocortin (POMC) production and consequently promote weight loss through a satiety signal. A 5-HT2C receptor agonist regulates appetite behavior through the serotonin system [13]. Two other investigational obesity drugs targeting the DA reward system are Contrave and Quexa. Contrave is a combination of two approved drugs – bupropion and naltrexone. Both drugs have individually shown some evidence of effective weight loss, and the combination is expected to have a synergistic effect [32]. Quexa consists of two prescription drugs, phentermine and topiramate. Phentermine has been used for years to fight obesity and has worked well. Topiramate has been used as an anti-convulsant, such as with epilepsy patients. Although topiramate has not been approved, nor really researched on as a weight loss drug, it is claimed to have caused weight loss in people as a side effect [13].

Recently, pharmacological MRI (phMRI) studies are making a significant contribution to our understanding of drug effects on brain systems. phMRI studies could further investigate the mechanisms of drug actions in the brain–on a systems level to establish novel pharmacodynamic measures of drug action [33]. This technology used in animals has already provided extensive physiological data. For instance, Dodd et al. [34] utilized phMRI in rats to study how the brain responds to 2-deoxy-D-glucose (2-DG), the glucose analogue, which is an inhibitor of glycolysis. At the same time, phMRI has been applied to clinical studies to evaluate certain drug actions. In one fMRI study [35], they found that sibutramine, an anti-obesity drug, modulates the hypothalamic response which has impact on both weight and subsequently measured ad libitum eating. Therefore, we plan to adopt this technology to discover new weight loss drugs and evaluate their drug actions.

Besides pharmaceutical means, other forms of intervention are necessary for middle-aged women who gain more weight than their younger counterparts, especially for post-partum women. There are many factors that contribute to obesity in women. However, changing eating habits is the preferred method [36]. As a pregnancy progresses, a woman's caloric intake tends to increase, because the growing fetus requires more nutrients. With appetite increasing accordingly, they would tend to choose to consume high-fat and high-sugar foods. After birth and when breast feeding has ceased, if food intake does not decrease by then, those extra calories can contribute to extra fat storage. Smith and his colleagues [37] claimed that the lifestyle of women should be managed closely during pregnancy and the post-partum period, which includes physical activity, healthy eating and emotional well-being. Eating behavior is the most important aspect. During pregnancy, quantities of high-fat and high-sugar foods should be controlled in a structured eating environment. High-protein foods are far more beneficial for them [38]. Therefore, lifestyle intervention keeps food addiction at bay especially in adult women.

7. Conclusions

In sum, much progress has been made toward fully understanding hunger and satiety signals, the high-fat and high-sugar foods environment, sugar and fat bingeing and pathological brain pathways; this assists us in understanding obesity as an addiction and what causes obese individuals to overeat. Food addiction as a leading cause for obesity is being more widely accepted by more researchers. Currently, the high-fat and high-sugar foods environment that surrounds most societies is more like to attract individuals to consume them. At the same time, high-fat and high-sugar foods as a form of food addiction allow consumers to overeat and absorb more calories, which lead to obesity in the end. Hence, in order to lose weight and maintain weight, creating a highly controlled eating environment and food regimen become necessary. In this review, we analyzed why obese individuals consume more calories and why this results in pathological brain pathways. Thus, using phMRI we could research new weight-loss drugs and establish their drug actions.

Contributors

Karen M. von Deneen-researched, composed, edited and submitted final manuscript.

Yijun Liu-researched and composed initial manuscript.

Competing interest

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