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Further Developments in the Neurobiology of Food and Addiction: Update on the State of the Science

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Abstract

Over the past three decades obesity has become a major public health crisis in the United States. The prevalence of obesity in the United States and in other parts of the World has led to the new word, globesity, now being used to describe the problem. As a result of this increased emphasis on understanding the causes and consequences of obesity, novel theories have stimulated new research aimed to prevent, intervene with, and ameliorate the effects and reduce the incidence and medical consequences of globesity. One theory that has gained popularity in recent years, which we described and analyzed in our previous paper *Neurobiology of Food Addiction*, is based on the idea that excessive intake of highly-palatable foods shares similarities with the effects on brain and behavior that are seen with some drugs of abuse. While this theory is not new, empirically-based translational research has only recently provided strong support for this hypothesis. In this article, we review the present state of the science in this area and describe a variety of newer clinical and preclinical works that shed light on innovative and interesting overlaps between excessive palatable food intake and drug use.

Keywords

Addiction; Dopamine; Food intake; Obesity; Overeating

Introduction

Obesity is a global epidemic affecting people's quality of life, as well as national and international economies [1, 2]. In 2004, the prevalence of obesity was 25% or greater in nine out of the fifty United States; by 2010 this prevalence had increased to thirty-six states [3]. It is predicted that if current trends continue, 86.3% of Americans will be overweight or obese by 2030 [4].

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To address this growing problem, there have been multiple efforts and diverse attempts to provide tools for individuals to lose weight and maintain a healthy body weight. Most recently, politicians and communities have promoted public weight loss campaigns aimed at stimulating physical activity and making healthy food choices [5, 6]. On the other end of the spectrum, some people have used bariatric and other surgical treatments to lose weight. It is too early to tell whether weight-loss campaigns have had an effect, but we do know that while surgical efforts have shown promise in reversing diabetes and other medical consequences of obesity, they have not increased longevity [7]. So, while prevention efforts and medical treatments have helped, but not reversed the obesity problem, clearly, there remains no cure for obesity [8].

The difficulty in treating and reducing the incidence of obesity has resulted in diverse ideas regarding its etiology and treatment. One theory that is gaining popularity is the idea that palatable foods may be “addictive,” in the way that is seen with drugs of abuse [9, 10]. In 2010, our article *Neurobiology of Food Addiction* [11] discussed the neurobiological mechanisms associated with addictive-like food consumption, results of behavioral studies examining food addiction in humans and laboratory animals, and possible pharmacological treatments. Since the publication of the article, a significant amount of new research has emerged on this topic, shedding light on unique and interesting overlaps between excessive palatable food intake and drug use. We have continued our work in this area and in separating the neurobiology of appetite from hedonic overeating [10, 12-17]. In the present article, we expand and update the status of the burgeoning field of food addiction by reviewing information on the neurobiology, theory, and pharmacological treatments relating to food and drug use.

Update on theoretical and neurobiological evidence of overlaps between food and addiction from animal models

Studies examining humans and laboratory animals have continued to expand upon the contemporary understanding of the similarities between food and drug addictions. Up until recently, the majority of the preclinical work on “food addiction” focused on animal models of sugar dependence [9]. However, more recent work has expanded to study the addictive potential of other palatable foods. It is interesting to note that not all palatable foods appear to be similar in their effect on the expression of behaviors common to addiction. A 2011 study by Bocarsly et al. [17] examined opiate-like withdrawal symptoms in rats given access to palatable fat-rich foods and control rats with access to chow. Rats with a fat-rich food did not show signs of opiate-like withdrawal, either when precipitated by the opiate antagonist naloxone or upon fasting, as had previously been shown with sugar [18, 19]. These findings of a lack of opiate-like withdrawal in response to overeating a fat-rich food highlight the importance of understanding the effects of specific nutrients on the behaviors associated with “food addiction.” While fat-rich food may impart addiction-like effects, the lack of opiate-like withdrawal suggests that brain opioid systems are differentially affected by overeating fat-rich foods compared to overeating sugar.

Other factors, such as whether or not the individual is obese or the presence of food variety, may be important in eliciting signs of “food addiction” [10]. For example, Johnson and Kenny (2010) examined addiction-like behaviors in rats given diets consisting of a variety of palatable, energy-dense food (a cafeteria-style diet) that typically results in obesity [20]. Similar to the effects of exposure to addictive drugs, rats receiving extended access to cafeteria food showed a disruption in the brain reward function, as determined by decreased striatal D2 signaling. The findings also showed that this diet resulted in weight gain and overeating, and suggested that extended access to palatable food propagates consumption.

Further, Alsio et al. [21] examined the eating patterns of rats with extended access to high-fat and high-sugar (HFHS) diets. Differentiating rats into obesity-prone (OP) and obesity-resistant (OR) groups, they found that in the OP rats there was a decrease in the expression of D1 and D2 dopamine receptors in the nucleus accumbens during the consummatory phase, and also after a period of palatable food withdrawal. In addition, they noted a decrease in mu-opioid gene expression in the nucleus accumbens of the OP rats during the consummatory phase, but not following withdrawal. Likewise, in another study OP rats were not found to differ from OR rats in terms of motivation for food pellets, measured via progressive ratio break point, lever pressing or response rate [22]. Yet, upon discontinuation of the palatable diet, OP rats increased their motivation (i.e. craving) and showed evidence of increased anxiety levels. OP rats also showed a long-term dysregulation of feeding behavior that persisted when the animals were returned to a standard rodent chow diet. Collectively, these results suggest that rats identified as OP show brain changes and enhanced susceptibility to addiction-like behaviors compared with OR rats. It is also interesting to note that in rats pre-selected for saccharin preference (Hi-S vs. Lo-S), bingeing-proneness appears to be more pronounced in Hi-S rats and withdrawal-proneness among Lo-S rats [23]. Yet, intake escalation and somatic indices of withdrawal do not differ between the rat lines.

Other studies have focused on the intermittent availability of palatable food and how this may have a role in addiction-like behaviors. Rats classified as binge-eating prone consume significantly more palatable food and tolerate higher levels of footshock for palatable food than rats considered binge-eating resistant [24]. However, after undergoing periods of cyclic food restriction-refeeding, binge-resistant showed increased tolerance of shock for palatable food. These findings are important in that they suggest rats are willing to endure an adverse environment in order to obtain a palatable food, and that the pattern of food intake can have dramatic effects on behavior.

Newer research suggests that obesity affects not only the present generation, but also offspring. When pregnant rats are maintained on a highly-palatable diet, the offspring show changes in dopamine and opioid gene expression in reward-related brain regions [25]. Further, the offspring show an increased preference for sugar and fat. Reflecting on other studies showing that the cafeteria-style diet or a high-fat diet perturbs the mesolimbic reward pathway in adults [26] *in utero* exposure to a highly-palatable diet resulted in similar alterations in brain-reward functioning. These results may have implications for addiction to food that could be epigenetic in nature.

Update on theoretical and neurobiological evidence of overlaps between food and addiction from clinical studies

Basic and clinical research has found parallels between excessive food intake and drug addiction [14]. While the majority of the work linking excessive palatable food intake and addiction has come from laboratory animal models, more studies are emerging on this topic in clinical populations. The theoretical basis for food addiction in humans is founded on the fact that consumption of palatable food is regulated, in part, by the same brain regions that are activated in response to drugs of abuse. As such, the brain circuitry is in place for certain foods to have addictive potential. Modern-day foods might have reinforcing abilities similar to alcohol or other drugs of abuse. Further, earlier work in humans implicated a role for mesolimbic DA in the overlap between obesity and addiction; as with drug addicts, lower levels of D2 receptor availability are seen in obese humans [27].

“Food addiction” has been defined in humans in relation to the Diagnostic and Statistical Manual of Mental Disorders definition of substance dependence [28]. Gearhardt and

colleagues have developed the Yale Food Addiction Scale (YFAS) to analyze food dependence based on these criteria for substance abuse. Building upon their work in developing this scale, they have recently tested brain activation to food cues in patients with differing degrees of food addiction, specifically those signaling impending delivery of a chocolate milkshake vs. a tasteless control solution, and those consuming a chocolate milkshake vs. a tasteless solution [29]. The results showed an association between higher food addiction scores and increased activation of regions encoding motivation in response to food cues, such as the amygdala, anterior cingulate cortex, and orbital frontal cortex. Based on this information, it is concluded that addicted individuals are more likely to react to substance cues, and that the anticipation of a reward when a cue is noticed could contribute to compulsive eating.

In a related study, Stice and colleagues have assessed genetic factors that influence brain DA in humans in relation to neuroimaging [30]. They have shown that individuals with the DRD2 TaqIA A1 allele have weaker activation of the frontal operculum, lateral orbitofrontal cortex, and striatum in response to imagined intake of palatable foods, versus imagined intake of unpalatable foods or water, and the presence of these alleles predicted future increases in body mass. Thus, individuals may overeat to compensate for hypofunctioning in reward-related brain regions, and this may be more apparent in those with with genetic polymorphisms thought to attenuate DA signaling in this region.

Conclusion

It is expected that obesity will continue to be a threat to global health. While experts have worked to develop the hypothesis of palatable food as an addiction over the past 30 years, today research in laboratory animals and humans connecting food and drug addictions has supported a similar role of DA and opioid systems in both conditions. In recognizing these parallels, it is also necessary to understand their limitations. Some are cautious about the notion of “food addiction” because appetite and eating food is necessary to human survival, whereas drugs of abuse are not. However, while humans need food to survive, they do not need excessive amounts of highly-palatable combinations of foods, which seem to be common to our diets. While the science linking food and drug addiction is still relatively young, the emerging data collectively suggest that overlaps do exist in these behaviors, and this warrants further exploration and query. Further studies of “food addiction” in preclinical and clinical models will hopefully allow us to harness the information on the effects of maladaptive feeding behaviors and apply it to better understand how to reinforce healthy living, discover new treatments for overeating and obesity based on the addiction model, and answer questions regarding the types of foods that pose the greatest risk for addictive overeating.

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