Nutrition 28 (2012) 341–343

Contents lists available at ScienceDirect

Nutrition

journal homepage: www.nutritionjrnl.com

Review

Further developments in the neurobiology of food and addiction: Update on the state of the science

Nicole M. Avena Ph.D. [a,b,*], Jessica A. Gold M.S. [c], Cindy Kroll A.B. [b], Mark S. Gold M.D. [a]

[a] Department of Psychiatry, University of Florida, College of Medicine, Gainesville, Florida, USA
[b] Psychology Department, Princeton University, Princeton, New Jersey, USA
[c] Yale University School of Medicine, New Haven, Connecticut, USA

ARTICLE INFO

Article history:
Received 11 March 2011
Accepted 20 March 2011

Keywords:
Addiction
Dopamine
Food intake
Obesity
Overeating

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 a new word, "globesity," 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 in and ameliorate the effects and decrease the incidence and medical consequences of globesity. One theory that has gained popularity in recent years, is based on the idea that an excessive intake of highly palatable foods shares similarities with the effects on brain and behavior that are seen with some drugs of abuse. Although this theory is not new, empirically-based translational research has only recently provided strong support for this hypothesis. In the present article, we review the present state of the science in this area and describe some newer clinical and preclinical works that shed light on innovative and interesting overlaps between excessivly palatable food intake and drug use.

Introduction

Obesity is a global epidemic affecting people's quality of life and national and international economies [1,2]. In 2004, the prevalence of obesity was at least 25% in 9 of the 50 United States; by 2010, this prevalence had increased to 36 states [3]. It is predicted that if current trends continue, 86.3% of Americans will be overweight or obese by 2030 [4].

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]. At 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, although surgical efforts have shown promise in reversing diabetes and other medical consequences of obesity, they have not increased longevity [7]. Therefore, although 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 decreasing the incidence of obesity has resulted in diverse ideas concerning 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 previous article [11] discussed the neurobiological mechanisms associated with addictive-like food consumption, the results of behavioral studies examining food addiction in humans and laboratory animals, and possible pharmacologic 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 pharmacologic treatments relating to food and drug use.

Funding was provided by the University of Florida Foundation (M.S.G.), USPHS grant DA-030123-01 (N.M.A.), and the National Eating Disorders Association (N.M.A.).

* Corresponding author. Tel.: 352-294-4935; fax: 609-259-3787.
E-mail address: navena@ufl.edu (N. M. Avena).

0899-9007/$ - see front matter © 2012 Elsevier Inc. All rights reserved.
doi:10.1016/j.nut.2011.11.002

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 on the contemporary understanding of the similarities between food and drug addictions. Until recently, most of the preclinical work on "food addiction" has 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 when precipitated by the opiate antagonist naloxone or during fasting, as previously 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." Although 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 with overeating sugar.

Other factors, such as whether 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 [20] 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. Similar to the effects of exposure to addictive drugs, rats receiving an 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 diets. Differentiating rats into obesity-prone (OP) and obesity-resistant 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 after a period of palatable food withdrawal. In addition, they noted a decrease in μ-opioid gene expression in the nucleus accumbens of the OP rats during the consummatory phase but not after withdrawal. Likewise, in another study, OP rats were not found to differ from obesity-resistant rats in the motivation for food pellets, measured by a progressive ratio break point, lever pressing, or response rate [22]. However, at 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 an increased susceptibility to addiction-like behaviors compared with obesity-resistant rats. It is also interesting to note that in rats preselected for saccharin preference (high versus low), proneness to bingeing appeared to be more pronounced in rats with a high-saccharin preference and proneness to withdrawal appeared to be more pronounced in rats with a low-saccharin preference [23]. However, intake escalation and somatic indices of withdrawal did 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 prone to binge-eating consumed significantly more palatable food and tolerated higher levels of foot shock for palatable food than rats considered resistant to binge-eating [24]. However, after undergoing periods of cyclic food restriction and refeeding, binge-resistant rats showed an increased tolerance of shock for palatable food. These findings are important because they suggest rats are willing to endure an adverse environment to obtain a palatable food and that the pattern of food intake can have dramatic effects on behavior.

Newer research has suggested that obesity affects not only the present generation but also offspring. When pregnant rats were maintained on a highly palatable diet, the offspring showed changes in dopamine and opioid gene expression in reward-related brain regions [25]. Further, the offspring showed 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]. Although most 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 an additive potential. Modern-day foods might have reinforcing abilities similar to alcohol or other drugs of abuse. Further, previous work in humans has implicated a role for mesolimbic dopamine in the overlap between obesity and addiction; as with drug addicts, lower levels of D2 receptor availability have been observed 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 et al. [29] developed the Yale Food Addiction Scale to analyze food dependence based on these criteria for substance abuse. Building on their work in developing this scale, they recently tested brain activation to food cues in patients with different degrees of food addiction, specifically during an impending delivery of a chocolate milkshake versus a tasteless control solution and during the consumption of a chocolate milkshake versus a tasteless solution [29]. The results showed an association between higher food addiction scores and an increased activation of regions encoding the motivation in response to food cues, such as the amygdala, anterior cingulate cortex, and orbital frontal cortex. Based on this information, it was 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 et al. [30] assessed the genetic factors that influence brain dopamine in humans in relation to neuroimaging. They found that individuals with the DRD2 *Taq*IA A1 allele have weaker activation of the frontal operculum, lateral orbitofrontal cortex, and striatum in response to the imagined intake of palatable foods versus the imagined intake of

unpalatable foods or water, and that 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 genetic polymorphisms thought to attenuate the dopamine signaling in this region.

Conclusion

It is expected that obesity will continue to be a threat to global health. Although experts have worked to develop the hypothesis of palatable food as an addiction over the previous 30 y, current research in laboratory animals and humans connecting food and drug addictions has supported a similar role for the dopamine and opioid systems in the two 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 are necessary to human survival, whereas drugs of abuse are not. However, although humans need food to survive, they do not need excessive amounts of highly palatable combinations of foods, which seem to be common to contemporary diets. Although 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 may 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 on the types of foods that pose the greatest risk for addictive overeating.

References

[1] Lobstein T. Prevalence and costs of obesity. Medicine 2011;39:11–3.
[2] Cecchini M, Sassi F, Lauer JA, Lee YY, Guajardo-Barron V, Chisholm D. Tackling of unhealthy diets, physical inactivity, and obesity: health effects and cost-effectiveness. Lancet 2010;376:1775–84.
[3] Centers for Disease Control and Prevention. U.S. obesity trends. 2011. Available at: http://www.cdc.gov/obesity/data/trends.html. Accessed August 3, 2011.
[4] Wang Y, Beydoun MA, Liang L, Caballero B, Kumanyika SK. Will all Americans become overweight or obese? Estimating the progression and cost of the US obesity epidemic. Obesity (Silver Spring) 2008;16:2323–30.
[5] USDA. Let's move. Learn the facts. 2011. Available at: http://www.letsmove.gov/learn-facts/epidemic-childhood-obesity. Accessed August 3, 2011.
[6] Khan LK, Sobush K, Keener D, Goodman K, Lowry A, Kakietek J, et al. Recommended community strategies and measurements to prevent obesity in the United States. MMWR Recomm Rep 2009;58(RR-7):1–26.
[7] Maciejewski ML, Livingston EH, Smith VA, Kavee AL, Kahwati LC, Henderson WG, et al. Survival among high-risk patients after bariatric surgery. JAMA 2011;305:2419–26.
[8] Geloneze B, Mancini MC, Coutinho W. Obesity: knowledge, care, and commitment, but not yet cure. Arq Bras Endocrinol Metabol 2009;53:117–9.
[9] Avena NM, Rada P, Hoebel BG. Evidence for sugar addiction: behavioral and neurochemical effects of intermittent, excessive sugar intake. Neurosci Biobehav Rev 2008;32:20–39.
[10] Avena NM, Gold MS. Variety and hyperpalatability: are they promoting addictive overeating? Am J Clin Nutr 2011;94:367–8.
[11] Blumenthal DM, Gold MS. Neurobiology of food addiction. Curr Opin Clin Nutr Metab Care 2010;13:359–65.
[12] Avena NM, Gold MS. Food and addiction—sugars, fats and hedonic overeating. Addiction 2011;106:1214–5.
[13] Avena NM. The study of food addiction using animal models of binge eating. Appetite 2010;55:734–7.
[14] Gold MS. From bedside to bench and back again: a 30-year saga. Physiol Behav 2011;104:157–61.
[15] Gold MS, Graham NA. Food addiction and obesity treatment development. Curr Pharm Des 2011;17:1126–7.
[16] Corwin RL, Avena NM, Boggiano MM. Feeding and reward: perspectives from three rat models of binge eating. Physiol Behav 2011;104:87–97.
[17] Bocarsly ME, Berner LA, Hoebel BG, Avena NM. Rats that binge eat fat-rich food do not show somatic signs or anxiety associated with opiate-like withdrawal: implications for nutrient-specific food addiction behaviors. Physiol Behav 2011;105:865–72.
[18] Avena NM, Bocarsly ME, Rada P, Kim A, Hoebel BG. After daily bingeing on a sucrose solution, food deprivation induces anxiety and accumbens dopamine/acetylcholine imbalance. Physiol Behav 2008;94:309–15.
[19] Colantuoni C, Rada P, McCarthy J, Patten C, Avena NM, Chadeayne A, et al. Evidence that intermittent, excessive sugar intake causes endogenous opioid dependence. Obes Res 2002;10:478–88.
[20] Johnson PM, Kenny PJ. Dopamine D2 receptors in addiction-like reward dysfunction and compulsive eating in obese rats. Nat Neurosci 2010;13:635–41.
[21] Alsio J, Olszewski PK, Norback AH, Gunnarsson ZE, Levine AS, Pickering C, et al. Dopamine D1 receptor gene expression decreases in the nucleus accumbens upon long-term exposure to palatable food and differs depending on diet-induced obesity phenotype in rats. Neuroscience 2010;171:779–87.
[22] Pickering C, Alsio J, Hulting AL, Schioth HB. Withdrawal from free-choice high-fat high-sugar diet induces craving only in obesity-prone animals. Psychopharmacology 2009;204:431–43.
[23] Yakovenko V, Speidel ER, Chapman CD, Dess NK. Food dependence in rats selectively bred for low versus high saccharin intake: implications for "food addiction". Appetite 2011;57:397–400.
[24] Oswald KD, Murdaugh DL, King VL, Boggiano MM. Motivation for palatable food despite consequences in an animal model of binge eating. Int J Eat Disord 2011;44:203–11.
[25] Vucetic Z, Kimmel J, Totoki K, Hollenbeck E, Reyes TM. Maternal high-fat diet alters methylation and gene expression of dopamine and opioid-related genes. Endocrinology 2010;151:4756–64.
[26] Geiger BM, Haburcak M, Avena NM, Moyer MC, Hoebel BG, Pothos EN. Deficits of mesolimbic dopamine neurotransmission in rat dietary obesity. Neuroscience 2009;159:1193–9.
[27] Wang GJ, Volkow ND, Thanos PK, Fowler JS. Similarity between obesity and drug addiction as assessed by neurofunctional imaging: a concept review. J Addict Dis 2004;23:39–53.
[28] Gearhardt AN, Corbin WR, Brownell KD. Food addiction: an examination of the diagnostic criteria for dependence. J Addict Med 2009;3:1–7.
[29] Gearhardt AN, Yokum S, Orr PT, Stice E, Corbin WR, Brownell KD. Neural correlates of food addiction. Arch Gen Psychiatry 2011;68:808–16.
[30] Stice E, Spoor S, Bohon C, Small DM. Relation between obesity and blunted striatal response to food is moderated by TaqIA A1 allele. Science 2008;322:449–52.