Neurocognition: The Food–Brain Connection[1–4]

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ABSTRACT

This article summarizes presentations from "Neurocognition: The Food–Brain Connection" symposium held at the ASN Scientific Sessions and Annual Meeting at Experimental Biology 2014 in San Diego, CA on 28 April 2014. Presenters reviewed research from several disciplines, including neurobiology, neuropsychology, cognitive neuroscience, and nutrition, concerning the role of the brain in food-intake regulation, reward, and addiction. A transdisciplinary approach was taken to evaluate the state of the science regarding addiction models, as well as research gaps and future research necessary to understand neurocircuitry and pathways involved in food-intake control and behavior in humans. *Adv. Nutr. 5: 544–546, 2014.*

Obesity prevalence in the United States remains elevated in both pediatric and adult populations. Concern about obesity led to public policies designed to discourage excessive caloric intake, especially from foods high in calories, sugars, and fats. These palatable foods were speculated recently to have addictive properties. However, there are several new human studies that fueled debate regarding the role of the brain in eating behavior.

The objectives identified for the speakers were as follows: *1*) to introduce topics on relations between the brain and food-related behaviors; *2*) to discuss the quality of evidence; and *3*) to identify gaps in the literature and directions for future research.

The first speaker, Dr. Berridge, gave a presentation entitled "Food Reward and the Brain: Current Perspectives, Controversies, and Applications." He said that it has become clear that the brain does not differentiate between food homeostatic and reward circuitry. Indeed, limbic and hypothalamic systems interact intimately in many regulatory pathways.

The limbic system of the brain separates food reward into liking vs. wanting. Increases in "wanting" to eat can occur in the absence of increases in "liking" for the same food being eaten. Wanting without liking is similar to incentive sensitization in drug addiction. Wanting to eat more food (e.g., extremely focused pursuit and consumption of sugar pellets) without liking it more can be produced in animals in the laboratory by microinjections of dopamine into the nucleus accumbens and even by opioids in some accumbens subregions. Alternatively, opioid, endocannabinoid, or orexin stimulation of hedonic hotspots throughout the limbic system increase both liking and wanting. Both liking and wanting are also increased together by most natural hungers. Therefore, wanting and liking circuits work together to increase eating behavior.

Extremely obese humans have reduced amounts of dopamine receptors, especially D_2 receptors. However, whether this is the cause or consequence of obesity and overeating is unknown. The cause of the overeating may be more likely due to hyper-reactivity in dopamine-related limbic circuitry. This would be similar to incentive sensitization in drug addiction. Nevertheless, whether food addiction exists remains a compelling question.

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[2] The organizer has indicated that related reviews of this symposium will be submitted for publication in an upcoming issue of *Advances of Nutrition*.

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Dr. Avena's presentation, "Empirical Evidence Supporting the Construct of Food Addiction: A Focus on Animal Models," centered on what she termed hyperpalatable, ultra-processed foods that might overactivate brain circuits linked to the reinforcement of food intake and reward.

Although drugs of abuse act on brain systems that reinforce natural behaviors, overlapping brain regions are activated by palatable foods and drugs of abuse. Her research suggests that normal-weight rats consuming excess sugar and rats that become overweight on a cafeteria-style diet show alterations in the mesolimbic dopamine and other brain systems that are consistent with what would be seen in animals using drugs of abuse.

In humans, the Yale Food Addiction Scale was used ostensibly to measure addiction-like responses toward food. Several studies were conducted using this scale, and, depending on the specific population studied, different percentages of people meet the criteria of the scale for food addiction. For example, ~11% of a general population meets the criteria for food addiction, but 56% of those who are obese with comorbid binge-eating disorder (BED) meet the criteria of the scale for having food addiction. Subsequent studies identified neurocorrelates between food addiction scores and activation of brain reward areas in response to the receipt or a cue for food, which maps to rat study findings.

After presenting evidence for the *Diagnostic and Statistical Manual of Mental Disorders* criteria for substance dependence, when the substance of abuse is palatable food, Dr. Avena dispelled areas of controversy in the comparison of food and drug addiction and then summarized where the field currently stands: "This is really just the start of a better understanding of food reward and brain mechanisms associated with eating, and how they may or may not lead to addictive-like behaviors."

Dr. Ziauddeen's presentation, "Obesity and the Brain: How Convincing is the Addiction Model?", drew on research in humans on the role of the brain reward system and normal and abnormal eating behavior. He noted that the brain–environment interaction in obesity development is a complex picture and that food addiction may have a specific place in it, albeit a small one.

Drug addiction/dependence results from the combination of a drug and a susceptible individual over time. Indeed, 85% of people who use an addictive substance never develop dependence. In addition, food addiction may not be associated with obesity. In fact, if there is a food addiction, one might expect to see more obesity in individuals who have had the condition for longer.

Long-term prospective studies are needed to develop a comprehensive model of food addiction that includes an addictive agent and charts the interaction between that agent and a susceptible individual over time, leading to the development of the addiction. However, typical research is cross-sectional, building models based on circumstantial evidence.

Evidence for food addiction to date includes the following: *1*) the clinical overlap between drug addiction and BED/obesity; *2*) familial co-occurrence of obesity/BED and substance use disorders; and *3*) neuroscientific evidence. Many issues surrounding the concept of human food addiction need to be addressed. The addictive agents are not always clearly identified. The clinical overlap is unconvincing, and evidence from animal models does not translate well beyond the laboratory. Receptor and neuroimaging studies in humans are inconsistent. Despite this, comparisons and superficial similarities are noted with drugs, and these are misleading. According to Dr. Ziauddeen, "At present there is little evidence to support a human food addiction syndrome."

Dr. Alonso-Alonso agreed, noting that, beyond extreme phenotypes related to the BED spectrum, there is limited evidence for food addiction in humans. In his presentation, "Beyond Food Reward: Broadening the Picture, Cognitive Influences," he summarized key issues in the food addiction model and discussed the importance of cognition as a moderator of responses to food reward.

Human fMRI studies indicate that palatable foods activate reward-related brain regions similar to other sources of pleasure in healthy individuals and drugs of abuse in the case of addicts. The majority of research focused on the identification of similarities, but recent studies comparing brain changes associated with drug addiction vs. obesity and eating disorders suggest that these overlaps are incomplete.

Dr. Alonso-Alonso reviewed several shortcomings in the use of functional neuroimaging in this field, including the following: *1*) the impossibility to diagnose addiction on the basis of these data because addiction relies on the subjective experience of an individual; and *2*) the limited external validity of the method.

Unlike laboratory rodents, humans live in a complex food environment that calls for >200 food-related decisions per day. These decisions rely on cognitive resources and, typically, the ability to balance immediate gratification against delayed reward on health or body image. Cognition influences rewarding responses to food via top-down mechanisms that are particularly developed in humans. Dr. Alonso-Alonso mentioned potential strategies to promote healthy eating via enhancement of cognitive control with interventions based on physical activity, meditation, neuromodulation, or drugs. He highlighted recent research suggesting that certain foods and nutrients potentially strengthen the status of brain regions underlying cognitive control, such as the lateral prefrontal cortex.

According to Dr. Alonso-Alonso, there is a need for integrated research to understand the interplay and relative contribution of 3 key factors underlying response to food reward: *1*) the food itself, including the impact of different food types, nutrients, doses, thresholds, and patterns of consumption; *2*) individual characteristics, such as genetic influences and phenotypes that can predispose or protect from overeating; and *3*) the context, which refers to situational factors, personal attitudes toward food, and social norms, cultural values, and other environmental contributors.

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The presentation also covered implications for treatment associated with the food-addiction model. Dr. Alonso-Alonso provided examples from past research in obesity to illustrate that abstinence may not be an adequate solution to reduce overeating and obesity in the general population. Additionally, numerous studies in the treatment of eating disorders concluded that, rather than advocating rigid dietary restrictions, the focus should be on addressing underlying issues and managing relations with food. There is also the potential for adverse unintentional consequences of defining food as addictive, including increased food-related anxiety and risk of reinforcing the overeating cycle.

The final presentation, by Dr. Allison, was "Neurocognition: The Food–Brain Connection—Methodologic and Epistemologic Considerations." He addressed questions pertaining to the following: *1*) determining appropriate research designs and how to do them well; and *2*) defining food addiction. He lauded previous speakers for not just showing data but for considering its relevance: "This is a fairly new level of sophistication in the conversation about food addiction, and the first step toward a scientifically meaningful definition of addiction."

An issue in the neuroscientific study of obesity is being "blinded by the light" of new technology. He cited the value of good experimental design principles and advised researchers to take a deep breath and ask themselves some questions when they evaluate studies, such as "Would I be convinced of this conclusion if it only showed a bar graph instead of brain images, and, if not, why do the pictures somehow make it seem like there's something more here?" "No matter what approach is used," said Dr. Allison, "we still need to correct multiple comparisons and publish the corrected results. We still need to stay grounded in the principles of sound investigation."

He noted the value in considering differences between experimental conditions and reality and encouraged that outcomes be accurately presented to the media. Topics such as obesity and addiction draw great media attention. "By putting accuracy-reducing spin in abstracts, press releases will almost always pick it up, as will the news," he said, adding that scientists need to be aware of their own complicity in misleading the public.

Other issues covered included skepticism about tools, such as the Yale Food Addiction Scale. "These approaches have been shown to be reliable and therefore measure something." he said, "The question is what." He emphasized the need to ensure that questions are meaningful, sample sizes are adequate, designs are valid, analyses are done properly, and results are interpreted fairly. "New technologies like functional magnetic resonance imaging may seem magical," he said, "but they're not magic and do not change the fundamental logic and statistics of experimental design." Importantly, only with an objective and logically coherent definition of what it means for a thing to be addictive can we ask whether food is addictive. He noted that *Diagnostic and Statistical Manual of Mental Disorders* definitions are intended to determine whether specific persons are addicted to specific things and not whether specific things can, in general, be judged to be addictive or not.

In summary, speakers evaluated the knowledge of the neurocircuitry and pathway physiology for food intake, addiction, and overlap with neurocognition. Whereas pathways of food addiction were well demonstrated in animal studies, the challenges that arise when translating animal addiction models to humans were acknowledged. The speakers evaluated research on brain reward systems and food intake and underscored the need to stay grounded in the basics of sound experimental design and data analyses. All presenters agreed that the study of the food–brain connection has some way to go before science develops a meaningful definition of food addiction.

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