Neural Reward, Energy Homeostasis, and Addiction-like Compulsive Eating

By Emily Latorraca and Stacey Reiss

To say that obesity is caused by merely consuming too many calories is like saying that the only cause of the American Revolution was the Boston Tea Party.

~ Adelle Davis (American nutritionist and author, 1904-1974)

Introduction

Obesity is quickly becoming a pandemic. In the United States alone, 65% of adults are overweight, and at least 30% of adults are clinically obese (Heindel and Saal, 2009). While many public health programs focus on decreasing energy intake and increasing energy expenditure, it is clear that simply concentrating on these two aspects is not effective. Obesity as a chronic disease is the result of a complex interplay of nature and nurture, along with epigenetic alterations.

Obesity is no longer viewed as the result of a lack of willpower. In fact, for the past

half-century, some have even proposed that sugar and other palatable foods can be addictive (Avena et al., 2008). Such an idea has merit if one considers the symptoms of binge eating and obesity. First of all, similar to cocaine or heroin, eating highly palatable foods like chocolate produces feelings of reward, and therefore, positive reinforcement. Rats will lever press for electrical stimulation of the dopaminergic reward circuitry or for drug administration despite adverse consequences: an electric foot shock. Likewise, those who engage in binge eating are generally obese and know that such behavior is detrimental to their health. They continue to overeat despite discomfort and outright public discrimination.

In light of the evidence of hedonic mechanisms underlying obesity, dopamine is a likely target of study. This catecholamine regulates many reward-related behaviors through the dopaminergic pathway from the ventral tegmental area to the nucleus accumbens. We consider two recent articles that study dopaminergic signaling and feeding behavior. The Kim et al. paper in *The Journal of Biological Chemistry* examines D2R-/- knockout mice and the role of the D2R in energy balance. The Johnson and Kenny paper from *Nature Neuroscience* explores the effects of a high-fat diet on brain reward circuitry, again in terms of D2Rs, though in a different region of the brain. Before reading through the papers, it is helpful to learn about the historical context of the study of regulation of feeding behavior. Other relevant papers are listed below. Click on the titles for a brief description of a key figure from that article. Once you have read through the annotations of the highlighted articles, click on the link below to read a comparison/ synthesis of the two articles as well as a brief note about future implications.

Click here for the historical background surrounding the controversy.

Highlighted Papers

Author(s)	Year	Title	Publication Information	Link
Epstein, D.H. and Shaham, Y.	2010	Cheesecake-eating rats and the question of food addiction	Nature Neuroscience 13(5): 529-531	PDF
Johnson, P.M. and Kenny, P.J.	2010	Dopamine D2 receptors in addiction-like reward dysfunction and compulsive eating in obese rats	Nature Neuroscience 13(5): 635-641	PDF
Kim, K.S. et al.	2010	Enhanced Hypothalamic Leptin Signaling in Mice Lacking Dopamine D2 Receptors	J. Biol. Chem. 285(12): 8905-8917	PDF

N.B. The article by Epstein and Shaham is a concise summary of the Johnson and Kenny article.

Historical Background Papers

Author(s)	Year	Title	Publication Information	Link
Campfield, L.A. et al.	1995	Recombinant Mouse OB Protein: Evidence for a Peripheral Signal Linking Adiposity and Central Neural Networks	Science 269: 546-549	PDF
Coleman, D.L.	1973	Effects of Parabiosis of Obese with Diabetes and Normal Mice	Diabetologia 9: 294-298	PDF
Hetherington, A.W. and Ranson, S.W.	1942	The Relation of Various Hypothalamic Lesions to Adiposity in the Rat	J. Comp. Neur. 76: 475-499	PDF
Olds, J. and Milner, P.	1954	Positive Reinforcement Produced by Electrical Stimulation of Septal Area and Other Regions of Rat Brain	J. Comp. Physiol. Psychol. 47: 419-27	PDF

Recommended Original Research

Click on the titles of these articles to read about one particular figure and its relevance to our research.

Author(s)	Year	Title	Publication Information	Link
Farooqi, I.S. et al.	2007	Leptin Regulates Striatal Regions and Human Eating Behavior	Science 317: 1355	PDF
Geiger, B.M. et al.	2009	Deficits of Mesolimic Dopamine Neurotransmission in Rat Dietary Obesity	Neuroscience 159: 1193-1199	PDF
Huang, X.F. et al.	2006	Dopamine transporter and D2 receptor binding densities in mice prone or resistant to chronic high fat diet-induced obesity	Behavioural Brain Research 175: 415-419	PDF
Stice, E. et al.	2010	Weight Gain is Associated with Reduced Striatal Response to Palatable Food	The Journal of Neuroscience 30(39): 13105-13109	PDF
Zhou, Q.Y. and Palmiter, R.D.	1995	Dopamine-Deficient Mice Are Severely Hypoactive, Adipsic, and Aphagic	Cell 83: 1197-1209	PDF

Recommended Review Articles / Commentaries

Author(s)	Year	Title	Publication Information	Link
Avena, N.M., Rada, P., Hoebel, B.G.	2008	Evidence for sugar addiction: behavioral and neurochemical effects of intermittent, excessive sugar intake.	Neurosci Biobehav Rev 32(1): 20-39	PDF
Heindel, J.J. and vom Saal, F.S.	2009	Role of nutrition and environmental endocrine disrupting chemicals during the perinatal period on the aetiology of obesity	Mol Cell Endocrinol 304(1-2): 90-6	PDF
Noble, E.P.	2000	Addiction and its reward process through polymorphisms of the D2 dopamine receptor gene	Eur Psychiatry 15: 79-89	PDF
Pijl, H.	2003	Reduced dopaminergic tone in hypothalamic neural circuits	Eur Jour Pharm 480: 125-131	PDF
Volkow, N.D. and Wise, R.A.	2005	How can drug addiction help us understand obesity?	Nature Neuroscience 8(5): 555-560	PDF
Zheng, H. and Berthoud, H.R.	2007	Eating for pleasure or calories	Current Opinions in Pharmacology 7: 607-612	PDF

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