Sugar Addiction and Obesity Research at Princeton

BY CLARE MARTIN ’21

We all experience sweet cravings from time to time, but what happens when these cravings exceed the scope of normal behavior? When do they qualify as symptoms of an addiction?

Former Professor of Psychology and faculty member in the Princeton Neuroscience Institute (PNI) Bart Hoebel set about answering these types of questions over a decade ago, and his findings have since then made waves in the psychology, neuroscience, and nutrition fields. His passing in 2011 left a deep void in PNI and the walls beyond Princeton. Although the students he mentored have gone on to pursue areas related to the food addiction hypothesis he proposed, no professor has carried on Hoebel’s research at Princeton.

Hoebel is best known for his research on food addiction, and in particular, for his development of an animal model for sugar addiction. While neuroscience technology has advanced dramatically in recent years, neuroimaging techniques, such as fMRIs and PET scans, can only tell us so much about the complex brain of a human, making animals with functionally similar brains useful for learning about humans’ feeding and eating behaviors. Before Hoebel’s research, however, no animal model existed for food addiction.

According to an article published in the Yale Journal of Biology and Medicine, food addiction research is not a new concept. In fact, addiction to chocolate made its way into scientific discussion as early as the 19th century. The term “food addiction” was finally coined in the 1950s, while Hoebel was majoring in Psychology at Harvard. During his undergraduate years, Hoebel studied the brain’s involvement in the control of eating and satiety, serving as a research assistant to B. F. Skinner, a world-renowned psychologist who developed the theory of behaviorism and the classical psychology technique of operant conditioning. In 1962, Hoebel obtained his Ph.D. in physiological psychology at the University of Pennsylvania.

After completing his studies, Hoebel...
produced nearly 200 research articles. And although Hoebel joined Princeton’s faculty in 1963, his research into sugar addiction did not begin until nearly 2000. Up until then, his research generally dealt with feeding and weight regulation, hyperphagia (excessive eating) and obesity, drug-induced eating behavior, in vivo microdialysis of dopamine and serotonin, and the relationship between feeding and the brain’s reward pathway. While Hoebel’s early research focused mostly on the brain chemistry of food-related interactions, the research topics on which he published in the 2000s placed a greater emphasis on the behavior behind food addiction in the rats he studied. Hoebel and his colleagues’ development of a rodent model for sugar addiction and sugar and fat was critical for food addiction research in the 2000s. It laid the groundwork for current advancements in food addiction animal modeling, including the discovery of a substance abuse drug, GS 455534, that mitigates the addictive-like food behavior in rats—research to which Hoebel contributed but did not live to see published.

Dr. Nicole Avena, who received her PhD in Psychology from Princeton in 2006, worked closely with Hoebel as both a graduate student and a postdoctoral fellow. She recalls the adversity they faced in addressing the research question of whether sugar may be categorized as an addictive substance: “This whole idea of sugar addiction was so radical at the time. … Other scientists kind of thought it was silly to be studying food addiction.” In 2008, Avena, Hoebel, and Pedro Rada—a visiting medical professor from Venezuela—co-authored the groundbreaking article “Evidence for sugar addiction: Behavioral and neurochemical effects of intermittent, excessive sugar intake.”

To provide convincing evidence for the sugar-drug hypothesis, the three researchers amassed findings from previous studies involving rats as the animal model. In this model, the experimental group of rats were allowed to feed on regular chow and a solution of sugar water during a 12-hour window each day for a month, after which they “learn[ed] to drink the sugar solution copiously, especially when it first [became] available each day.” This period of “intermittent sugar access,” as the researchers called it, gave rise to behaviors one might observe in a human addicted to an abused substance: binging, withdrawal, craving, and sensitization, or “increased locomotion in response to repeated administrations of a drug.”

The paper also references the findings of an experiment that Avena and Hoebel published in 2003, in which after one week of sensitization to amphetamine, the rats demonstrated hyperactive behavior when they tasted a 10 percent sucrose solution. Research that Avena, Hoebel, and three other authors published in 2004 on the ability of sugar to serve as a gateway drug to alcohol provided additional evidence for the “gateway effect” seen with traditional substances of abuse, further supporting the researchers’ claim that sugar is an addictive substance. In addition, Rada, Avena, and Hoebel cited a paper they co-authored in 2005 as providing some of the most compelling evidence for sugar behaving more like a drug than regular food in their particular animal model. Through this research, they demonstrated that dopamine levels in extracellular brain fluid, as measured via in vivo microdialysis, did not attenuate after three weeks for rats on the daily intermittent sugar diet, while dopamine levels did attenuate for the three control groups—a group placed on a daily intermittent chow diet, a group permitted to feed on sugar and chow ad libitum, and a group fed sugar for just 1 hour on day 1 and on day 21.

At the time of the article’s release a decade ago, the idea that sugar dependency could resemble traditional drug addiction aroused controversy among academics, as few empirical studies existed that dealt with food addiction. According to Dr. Miriam Bocarsly, who worked in Hoebel’s lab as an undergraduate and graduate student at Princeton, Hoebel kickstarted further development in the field of food addiction. “I think he really trail-blazed and established the field and gave it some credibility,” she says, although admitting that the concept of sugar addiction faces

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High-fructose corn syrup might be critically implicated in the obesity epidemic our society faces. Currently, the Diagnostic and Statistical Manual of Mental Disorders (DSM), a handbook that medical professionals consult in diagnosing psychological disorders, does not recognize food addiction in its list of official disorders. Yet the recent recognition of gambling as a behavioral addiction has Bocarsly feeling optimistic about future revisions to the handbook. “I think it’s really awesome they’ve added behavioral addiction to the DSM, because that kind of paves the way for, for example, food addiction in the future, and I think it’s a step in the right direction, but I think they’re still looking for some more research to flesh out the story there,” she says.

As a graduate student at Princeton, Bocarsly teamed up with Hoebel, Avena, and an undergraduate student, Elyse Powell, to produce a complementary finding to the 2008 study’s linkage between sugar and substance abuse behavior, although this time from the perspective of obesity. In one of a set of multiple experiments, the researchers compared various health metrics—weight gain, body fat, and triglyceride levels—in rats fed sugar water with these same metrics in rats fed high-fructose corn syrup. They observed that the rats placed on the high-fructose corn syrup diet gained much more weight than the sugar-fed rats, despite controlling for overall caloric intake. Based on the results of this and another experiment, Hoebel and his co-authors concluded that high-fructose corn syrup might be critically implicated in the obesity epidemic our society faces.

In addition to achieving great success as a research scientist, Hoebel developed a reputation among students and colleagues as a gifted teacher and amiable person. Bocarsly attests to the confidence that Hoebel instilled in her, as well as the balanced role he played as a mentor. “He found this really sweet spot where he gave you just enough freedom that you really felt like you could own something,” she says, “but enough mentoring so that you didn’t feel like you were just flapping in the breeze, trying to figure out which way to go.”

Avena remembers her mentor’s infectious attitude toward research. “He spoke about his research with such passion and enthusiasm and made it sound so fun,” she recalls. According to Avena, she and Hoebel were able to accomplish a significant amount of work together during her doctorate years, in part due to the number of undergraduates eager to assist them in their research efforts. “We had almost an army of undergrads that would be working on these projects. Lots of people wanted to do their JP or thesis with Professor Hoebel,” she explains, noting that “he was just such a fun person to work with.”

Hoebel’s scientific influence survives not only in the pages of scientific journals, but also in the students whom he mentored over the years. According to Bocarsly, Hoebel equipped her with a mindset that has aided her in current research efforts. “There’s a lot of pressure these days with new techniques that are coming out in neuroscience to use the flashiest techniques, and my mentality that I’ve been going forward with now, and I think a lot of this is just based on having been trained by Bart, is I want to ask complicated questions that use straightforward techniques, like the things Bart taught me, rather than asking surface questions with flashy techniques,” she says.

Looking back on her experience collaborating with Hoebel on food addiction research at Princeton, Avena praises her mentor for his influence on the trajectory of her career and for the invaluable lessons he taught her in the lab about how to conduct and critique a study and how to maintain a strong work ethic. She also admires Hoebel for the lessons he taught her outside of the laboratory setting. “He also had an interesting work-life balance, too. He always made time for his family, [and] he was very welcoming in terms of always having students over to his house,” she says, adding, “He was a great mentor and an even better friend.”

REFERENCES


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