INDIVIDUAL DIFFERENCES IN THE NEUROPHYSIOLOGY OF FOOD REWARD

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In 1983, Weingarten showed that conditioned cues elicit feeding in sated rats.[1] This finding is significant because it demonstrated that seemingly neutral cues, upon association with food presentation, can enhance feeding even in the absence of a physiological need. The experiment consisted of two phases. In the conditioning phase, rats were brought to an experimental cage while hungry and learned that when a buzzer was played, they could press a lever and receive food. Over time, the rats associated the buzzer with lever-pressing for food. On the experimental day, the rats were fed to satiety before they were brought to the experimental cage where food was freely available. Strikingly, playing the buzzer to the sated rats significantly increased their food intake. This effect, dubbed "cue-potentiated feeding," was later shown by Peter Holland, Michaela Gallagher, and Goricia Petrovich to depend on the integrity of neural fibers connecting the basolateral amygdala and lateral hypothalamus.

It is easy to think of anecdotal parallels of "cue-potentiated" feeding in humans. A passing dessert cart induces a sated individual who planned not to order dessert to succumb and order the triple chocolate fudge cake. However, not all people succumb to the dessert tray and not all people are becoming fat. Therefore, it stands to reason that individual differences in the neurophysiology of food reward may predispose some people to overeat. Despite a general agreement about this possibility, there is considerable debate over the nature of the individual differences. Some researches, somewhat influenced by the cue-potentiation effect, propose that heightened response to cues increases risk for overeating and obesity.[2] Other groups, however, hypothesize that obese individuals have a hypofunctioning reward circuitry, with overeating constituting an effort to compensate for this deficiency (Blum et al., 2000; Wang, Volkow, & Fowler, 2002). Yet another possibility is that food reward is multifaceted and that there is both hypo- and hyperactive brain responses. For example, consistent with the incentive-sensitization theory of drug addiction,[3] Raynor and Epstein propose that consummatory and anticipatory reward operate in tandem in the development of reinforcing value of food, but that over-repeated presentations of food, consummatory reward decreases (e.g., liking ratings), while anticipatory reward increases.[4]

Work in my laboratory has focused on characterizing and dissociating the neural circuits that respond to cues that predict the upcoming receipt of a food reward (i.e., respond during the anticipatory phase of food reward) from the circuits that preferentially respond to the receipt and ingestion of food (i.e., during the consummatory phase of food reward).[5] In our research with lean, healthy individuals, we have provided evidence for the existence of separable, although partially overlapping, brain circuits responsive to each phase of food reward processing. More recently, in collaboration with Eric Stice, Sonja Spoor, Elisa Epel, and David Kessler, we have inquired how neural response to predictive food cues and food receipt might vary as a function of body mass index (BMI), eating style, and the presence of the A1 allele of the DRD2 gene, which has been associated with increased BMI.[6] Three independent studies have been performed; one in adults at Yale and two in adolescent girls at the University of Oregon.

The data collected in all three studies show that there are significantly different responses to predictive food cues and to the receipt of food in lean vs. overweight/obese individuals. Most of these differences reflect heightened responses in individuals with higher BMI to cues and to receipt. For example, there is greater response in the insula, orbitofrontal cortex, hippocampus, and the amygdala to predictive food cues and to food receipt in high vs. low BMI. Also, there are some regions that show consistently lower responses as a function of BMI, such as the caudate nucleus, in which response to food receipt is inversely related to BMI.

It is important to notice, however, that the differential activations observed in obese vs. lean individuals could arise for a variety of factors. These differential responses could be accounted for, on one hand, by the metabolic/physiological alterations that usually accompany obesity; alternatively, differential activations also could be explained by the presence of particular behavioral traits—such as those influencing eating style—whose persistence will eventually lead to obesity. We have been engaged recently in trying to dissociate the contributions of behavioral traits to high-BMI specific brain activations from those related to body fat composition itself. In fact, in the dataset collected at Yale (N = 34), we have found that most of the brain response patterns previously associated with high BMI was enhanced in individuals self-reporting higher ratings of compulsive eating, cue responsiveness, disinhibition, and bingeing in comparison to individuals reporting lower ratings, even when the two groups were matched for BMI. This suggests that differences in eating style and food reward sensitivity, but not BMI or associated physiological factors, account for most of the BMI-dependent activations, a noticeable exception being the caudate nucleus. Conversely, when groups were matched for scores on the behavioral scales but differed in BMI, activity in the caudate nucleus was found to be inversely correlated with BMI. Notably, response in the caudate is inversely related to ratings of the perceived pleasantness of the food only in overweight subjects. This suggests that response in the caudate nucleus primarily reflects reduced consummatory food reward in obese subjects. We also have observed, in those subjects for whom genotyping was performed (dataset collected in Oregon), that the effect in the caudate is dependent on A1 allele status; that is, the relationship between caudate responses to food receipt and BMI depends on the presence of the A1 allele. Furthermore, the magnitude of the reduced response predicts weight gain at 1-year followup in subjects with the allele but not in those without the allele, while response in the hippocampus to predictive food cues predicts weight gain in the subjects irrespective of allele status.

Taken together, this research is consistent with the possibility that heightened food reward leads some people to overeat and that overeating results in decreases in food reward in a subset of these individuals who possess the A1 allele.

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