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A Core Eating Network and Its Modulations Underlie Diverse Eating Phenomena

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Abstract

We propose that a *core eating network* and its modulations account for much of what is currently known about the neural activity underlying a wide range of eating phenomena in humans (excluding homeostasis and related phenomena). The core eating network is closely adapted from a network that Kaye, Fudge, and Paulus (2009) proposed to explain the neurocircuitry of eating, including a ventral reward pathway and a dorsal control pathway. In a review across multiple literatures that focuses on experiments using functional Magnetic Resonance Imaging (fMRI), we first show that neural responses to food cues, such as food pictures, utilize the same *core eating network* as eating. Consistent with the theoretical perspective of grounded cognition, food cues activate eating simulations that produce reward predictions about a perceived food and potentially motivate its consumption. Reviewing additional literatures, we then illustrate how various factors modulate the core eating network, increasing and/or decreasing activity in subsets of its neural areas. These modulating factors include food significance (palatability, hunger), body mass index (BMI, overweight/obesity), eating disorders (anorexia nervosa, bulimia nervosa, binge eating), and various eating goals (losing weight, hedonic pleasure, healthy living). By viewing all these phenomena as modulating a core eating network, it becomes possible to understand how they are related to one another within this common theoretical framework. Finally, we discuss future directions for better establishing the core eating network, its modulations, and their implications for behavior.

Keywords: core eating network; food cues; grounded cognition; neuroimaging

Multiple research literatures have examined the neural responses to food cues and actual eating in a variety of different eating situations and populations. So far, however, no integrated theoretical account for all these eating-related phenomena exists. The primary aim of this article is to develop a theoretical framework that integrates the major findings across these literatures. As will become clear, this theoretical framework includes a core eating network, together with modulations of this network in different eating situations and populations. Importantly, our account primarily focuses on the higher level processing of food cues and their relation to eating, not addressing homeostasis and related processes (cf. Hege, Stingl, & Preissl, 2014).

Specifically, our theoretical framework aims to integrate the following phenomena: (1) high-level neural responses during eating; (2) neural responses to food cues in healthy individuals, (3) neural responses to food cues as palatability and hunger vary, (4) neural responses to food cues in overweight/obese individuals, (5) neural responses to food cues in individuals with eating disorders, and (6) neural responses to food

cues in populations with different eating-related goals, such as losing weight via dieting, pursuing hedonic pleasure from eating, and eating for a healthy life.

Many previous reviews and meta-analyses have addressed research in the individual areas just described. One review established brain areas associated with actual eating (Kaye, Fudge, & Paulus, 2009). Another review and meta-analysis established the brain areas that process food cues in healthy individuals (van der Laan, de Ridder, Viergever, & Smeets, 2011). Other reviews have investigated the neural bases of eating disorders, including anorexia nervosa, bulimia nervosa, and binge eating (e.g., Kaye et al., 2009; Kaye, Wagner, Fudge, & Paulus, 2010; Kaye, Wierenga, Bailer, Simmons, & Bischoff-Grethe, 2013; O'Hara, Campbell, & Schmidt, 2015; Pietrini et al., 2011; Stefano et al., 2013; van Kuyck et al., 2009; Zhu et al., 2012). A related review established neural differences to food cues between individuals with eating disorders, obese individuals, and healthy individuals (García-García et al., 2013). Another review focused on altered neural responses to both the anticipation and consumption of food in obesity (Stice, Spoor, Ng, & Zald, 2009). Finally, a meta-analysis focused on aberrant neural responses to food cues in obesity, showing both increased and reduced activations in various brain areas (Brooks, Cedernaes, & Schiöth, 2013). Again, however, no work has attempted to integrate the findings from these reviews and their related literatures into a comprehensive account.

Besides attempting to fill this gap, our theoretical framework establishes how the processing of food cues is related to actual eating. Establishing the neural systems that underlie actual eating is clearly important. Establishing the neural systems that underlie the processing of food cues is no less important, given the powerful roles that they play in motivating eating, especially unhealthy eating (Marteau, Hollands, & Fletcher, 2012). The perspective of grounded cognition offers a natural account of how food cues and actual eating are related: When encountering a food cue, a simulation of eating the cued food becomes active, with the simulation predicting the food's taste and reward value (e.g., Barsalou, 2008, 2010; Papies, 2013; Papies & Barsalou, 2015). To the extent that a simulation represents a food as tasty and rewarding, it potentially motivates the food's consumption. From this theoretical perspective, neural systems that underlie eating a food become active on encountering cues for it. As we will see, the empirical literatures that address eating and food cue processing strongly support this proposal.

Methodological considerations. The literatures that we review primarily address neural activity established from linear contrasts during functional Magnetic Resonance Imaging (fMRI), establishing brain areas for important food processing in contrast with nonfood stimuli as controls. Tables 1, 2, 3 and 4 present examples of the specific contrasts used. As will be seen, the controls used in a given contrast vary widely across phenomena. When considering food significance, for example, high-calorie foods are often contrasted with low-calorie foods, but when considering the effects of body mass index (BMI), obese individuals are contrasted with normal weight individuals, or BMI is viewed as a continuous variable.

For the purpose of this review, we assume (like most current researchers) that the brain areas active for a particular type of eating situation or population constitute a network, even though, technically speaking, network connectivity remains to be demonstrated formally. As described later, establishing these networks using functional connectivity, causal modeling, and related methods remains an important goal for future research.

At certain points in our review, findings from behavioral, event-related potential (ERP), and eye tracking paradigms are included to better understand a particular eating network and the behavior it produces. More detailed reviews of relevant findings from these paradigms are beyond the scope of this article, given that we focus primarily on the neural networks that underlie food cue processing as established in fMRI research. Nevertheless, it is important to bear in mind that other literatures are relevant for evaluating the issues we address as well.

Relations to other appetitive behaviors. Although we focus on brain areas associated with eating, some of these areas are also important in other appetitive behaviors. Some meta-analyses, for example, show that the amygdala, orbitofrontal cortex (OFC), and ventral striatum become active not only when processing food cues, but also when processing smoking cues (Tang, Fellows, Small, & Dagher, 2012) and other drug cues (García-García et al., 2014; Volkow, Wang, Fowler, Tomasi, & Baler, 2012; Volkow, Wang, Tomasi, & Baler, 2013). Nevertheless, the core eating network, as a whole, is unique for food, because it includes food-specific regions, such as regions responsible for gustatory processing and body image. Simon et al. (2015), for example, demonstrated that neural responses to food cues differ from those to monetary cues. Thus, the networks for eating and other appetitive phenomena differ, while sharing important overlapping regions.

Overview. In the next section, we first address the network that underlies normal eating, proposed originally by Kaye et al. (2009). We then address an important variant of this network related to processing food cues. Consistent with

the perspective of grounded cognition, the food cue network produces eating simulations in response to food cues that inform and motivate decisions to consume or not consume a cued food. Once we establish the networks for eating and processing food cues, we then define the core eating network as the network variant that processes visual food cues (for reasons presented later). We then describe how various factors modulate the activity of the core eating network, increasing and/or decreasing the activity of its neural areas. First, we address how two forms of food significance—palatability and hunger—modulate neural activity in the core eating network. Second, we address modulations that result as BMI increases in overweight and obese individuals. Third, we address modulations associated with the eating disorders of anorexia nervosa (AN), bulimia nervosa (BN), and binge eating disorder (BED). Fourth, we address modulations associated with the eating goals of weight loss, hedonic pleasure, and healthy living. For each modulation of the core eating network, we do not exhaustively review all relevant articles in the fMRI literature, but instead cover a selection that represents examples of relevant research. To provide a more complete overview, we include tables that list larger sets of relevant articles in each area.

Finally, we adopt the following strategy in evaluating our theoretical claims. First, we start with the assumption that the core eating network adapted from Kaye et al. (2009) underlies all of the eating phenomena we address. Second, as we review a particular literature on an eating situation or a specific population, we assess whether the relevant brain areas fall within the core eating network or not (in the large majority of cases they do). Third, in a bottom-up empirical manner, we use each literature addressed to develop an account of how the relevant eating situation or population modulates this network. What brain areas inside (or outside) the core eating network are affected by the eating situation or population, and how? Whereas we adopt the core eating network in an a priori manner, we develop modulations of it in an empirical manner based on each literature reviewed. Of general interest is whether existing areas of the core eating network can accommodate these modulations, or whether additional brain areas are necessary for explaining them. As we will see, the core eating network generally accommodates these modulations with a few relatively minor exceptions. As we will also see, however, modulation of a specific brain area doesn't always occur across experiments, and in a few cases is modulated in opposite directions (i.e., both higher activation and lower activation than normal across experiments). It follows that further research is necessary to establish the core eating network and its modulations more definitively, together with conditions that cause modulations to vary.

The Neural Network that Underlies Normal Eating

To establish the neural mechanisms that underlie actual eating, the majority of existing experiments have used a paradigm pioneered by Frank et al. (2003). In this paradigm, participants receive liquids such as milkshake through a tube in their mouth, thereby avoiding head movements caused by chewing behavior (problematic in fMRI experiments). Although liquid food consumption differs in important ways from normal eating, it can be used in fMRI experiments to study brain regions associated with taste, food reward, and appetite regulation, thereby helping establish the neural mechanisms of actual eating.

Based in part on research that used the methods just described, Kaye et al. (2009) proposed that the neurocircuitry of eating takes the form illustrated in Figure 1a. Although Figure 1a is adapted from the original Figure 3 in Kaye et al. (2009), it contains the same brain areas, connected with the same pathways, but presented in a manner that will later be useful for presenting modulations of this network. Kaye et al.'s account contains two important neurocircuits: the ventral neurocircuit, and the dorsal neurocircuit. We address each in turn.

First consider the *ventral neurocircuit* in Figure 1a. When someone tastes a (liquid) food, chemoreceptors on the tongue detect the taste and transmit the signal through the brainstem and thalamic taste centers to primary gustatory cortex, which lies in the insula and frontal operculum. The insula, consistent with its general role in interceptive awareness, underlies the interoceptive experience of taste. An important issue is how rostral vs. caudal the primary gustatory cortex is in the insula, with some articles suggesting a more rostral position in anterior insula (e.g., Kaye et al., 2009; Kringelbach, O'Doherty, Rolls, & Andrews, 2003; Kringelbach, Stein, & van Hartevelt, 2012), and others suggesting a more caudal position in mid-insula (e.g., Simmons, Rapuano, Kallman et al., 2013; Stice, Burger, & Yokum, 2013). In many experiments, taste activations further extend dorsally into the adjacent frontal operculum. In general, these taste regions play a central role in what Kaye et al. referred to as the *ventral (limbic) reward neurocircuit* for eating, through its connection with the amygdala, the ACC, and the OFC.

Moving along this circuit, the amygdala, in general, is believed to process the significance and

novelty of stimuli (e.g., Lindquist, Wager, Kober, Bliss-Moreau, & Barrett, 2012). In the context of eating, the amygdala similarly appears to process the attentional salience of food, increasing attention to relevant food cues and supporting impulses to consume the respective foods (e.g., Hoogeveen, Dalenberg, Renken, ter Horst, & Lorist, 2015; Kaye et al., 2009).

Much research demonstrates that the ACC, in general, plays a central role in a wide variety of autonomic and cognitive functions, such as response monitoring, reward anticipation, decision-making, and empathy (e.g., Botvinick, Cohen, & Carter, 2004). The ACC appears to play similar roles in the eating network (e.g., Kaye et al., 2009). In particular, ventral ACC (extending into ventromedial OFC) contributes to the affective significance of food (ventral reward pathway), whereas dorsal ACC contributes to conflict monitoring when multiple eating goals arise (dorsal control pathway).

Much research further indicates that the OFC represents the predicted value of a cued food in the ventral reward pathway (e.g., knowing that chocolate is likely to be rewarding). Similar to its role in predicting many other kinds of reward, the OFC is also central for predicting food reward (e.g., Rudebeck & Murray, 2014). As a result, the OFC plays central roles in the decision-making and emotion associated with food choice and eating (e.g., Murray, O'Doherty, & Schoenbaum, 2007).

Afferents from cortical structures in the ventral circuit project to the ventral striatum. Similar to its role in many other reward phenomena (e.g., O'Doherty, 2004), the ventral striatum represents positive reward for food, and also plays important roles in regulating homeostatic appetitive needs (Kringelbach, 2004).

Kaye et al. also present a second important circuit for eating, the *dorsal neurocircuit*. As Figure 1a illustrates, this circuit includes dorsolateral prefrontal cortex (dlPFC), which, in general, is responsible for motor planning, organization, regulation, and executive control (e.g., Miller, 2000). Clearly, such regulatory activity can be central to eating behavior, especially for regulating unhealthy eating impulses, for pursuing healthy eating goals, and for resolving conflicts about food choices. The dorsal circuit also includes parietal cortex, which, in general, is believed to play roles in integrating sensory information from various parts of the body, supporting quantitative processing, and executing actions through space during the manipulation of objects (e.g., Culham & Kanwisher, 2001). In eating, this area is associated with actions that control eating behavior, and with estimating the amount of food consumed. Parietal cortex, especially in somatosensory areas, also plays a role in body image, which can bear on food consumption and its long-term consequences, especially in eating disorders (Vocks et al., 2010). Together, dlPFC and parietal areas send signals to the dorsal striatum that implement cognitive control functions, such as inhibiting impulses and planning future actions. Finally, signals from both the ventral reward circuit and the dorsal control circuit can be integrated in various ways as they interact in parallel and sequentially, resulting, for example, in approach ('eat') behaviors or avoidance ('do not eat') behaviors.

Examples of research that established the eating network. In seminal work that established the brain areas associated with human eating in vivo, Frank et al. (2003) reported increased OFC activation in five healthy control women during receipt of glucose solution compared to receipt of artificial saliva. Similarly, Kringelbach, O'Doherty, Rolls, and Andrews (2003) reported increased activation in bilateral insula/operculum, the caudal OFC, and the ACC in healthy males as they consumed liquid foods compared to tasteless solutions. Additionally, Kringelbach et al. observed a significant decrease in OFC activity as liquid food was consumed to satiety, indicating that OFC plays an important role in representing the reward value of liquid food. Much subsequent work has similarly shown that, as a food becomes increasingly less rewarding (e.g., due to satiety), it produces less OFC activation.

Other factors also modulate neural responses in OFC and other reward regions when participants consume rewarding liquid food while being scanned (versus tasteless solution). As an individual's food addiction score increases, reward activations in lateral OFC actually decrease, while consuming milkshake compared to tasteless solution (Gearhardt et al., 2011). This counter-intuitive finding demonstrates that food addiction attenuates the reward value of food consumption. Conversely, anticipatory reward responses to food cues become stronger as food addiction scores increase. In other words, food addiction reduces the reward of actual eating, while increasing the reward associated with perceiving a food temptation.

Similar to individuals with food addiction, obese individuals exhibit decreased activation in reward regions during actual eating. In Stice, Spoor, Bohon, Veldhuizen, and Small (2008), obese adolescent girls showed increased activation in gustatory and somatosensory cortex, both to food cues and during actual consumption, but more importantly showed deceased reward activation in caudate nucleus during actual consumption (relative to lean adolescent girls). These results indicate that obese individuals anticipate highly

rewarding taste experiences when they see food cues, but do not find these foods as rewarding as do healthy individuals while eating. These seemingly paradoxical findings may, to some extent, explain why obese individuals often overeat. On the one hand, food cues are highly tempting; on the other, food consumption is not very rewarding. Thus, consuming larger amounts of food is necessary to achieve satisfying eating experiences.

In addition, various experiments have found that neural responses to liquid food consumption vary with the motivational states of hunger and satiety. When participants in Uher, Treasure, Heining, Brammer, and Campbell (2006) consumed chocolate milk or chicken broth in both fasted and satiated states, activations in the left anterior insula and frontal operculum to both foods were significantly stronger in the fasted state than in the satiated state. In a similar study, Stice, Burger, and Yokum (2013) found that the duration of acute calorie deprivation correlated positively with neural responses in the insula to the receipt of milkshake (compared with tasteless solution). Other experiments, however, have reported the opposite effect. Vocks, Herpertz, Rosenberger, Senf, and Gizewski (2011) found that the insula in healthy females showed a stronger response to the receipt of chocolate milk (versus water) in the satiated state than in the hunger state. In a somewhat different vein, AN patients showed stronger activation in the extrastriate body area (EBA) while eating in a satiated state than in hungry state (relative to healthy females), perhaps reflecting fear of weight gain in this population.

To sum up, neuroimaging research has established that the ventral pathway, especially the insula/frontal operculum and OFC, plays important roles in representing taste and reward, respectively, during the actual consumption of rewarding liquid food (versus tasteless solution). Although these experiments do not reveal increased activation to food consumption in all regions of the core eating network, they do so for areas associated with taste and reward.

One explanation for why other regions do not become active could potentially be related to the baseline conditions used in these imaging experiments. Specifically, consuming a tasteless solution may activate these other regions to the same level as when consuming liquid food, such that activations in these regions are subtracted out of the critical contrasts. In this manner, important areas associated with gustatory processing and cognitive control during eating may not reveal themselves in these particular experiments. Nevertheless, as Kaye et al. (2009) demonstrate, the important roles of these areas in actual eating behavior become evident in other paradigms. Although we have not yet addressed the dorsal pathway of the eating network in any detail, we do so in later sections that address the regulatory processing of food cues.

The Neural Network Associated with Processing Food Cues (Core Eating Network)

How the brain responds to food cues, especially in industrialized societies with abundant junk food and food marketing available widely, is important for understanding the neural mechanisms that underlie obesity and eating disorders (Marteau et al., 2012). Here, a "food cue" is any information associated with a particular kind of food that is capable of activating cognition about it (while not actually eating it). Such cues include, for example, pictures that represent the food, words that label the food, smells of the food, sounds of eating the food, etc. In their daily lives, people are frequently exposed to food pictures in the media, smells of food when passing by restaurants, the logos of restaurants that serve fast food, and many other sources of food information and signals. Because food cues are both ubiquitous and powerful, exploring neural responses to them is essential for understanding the mechanisms that motivate and regulate eating. Indeed, the large majority of the experiments reviewed in this article used food pictures to investigate neural activity related to eating, with a few that used food words.

As described earlier, one hypothesis about the brain areas that process food cues follows from theories of grounded cognition (e.g., Barsalou, 1999, 2008, 2009, 2010, in press). According to grounded cognition, the brain areas that represent an entity or event in actual experience also represent it conceptually in its absence. When thinking about a hammer, for example, the brain areas that become active are similar to the brain areas active when actually using a hammer (e.g., Martin, 2007). From this perspective, it follows that thinking about a food should be closely related to actually eating it. Specifically, the network of brain areas that becomes active on perceiving a food cue should be similar to the network active while actually consuming the food. In other words, the brain simulates actual eating experiences to anticipate likely eating experiences associated with perceived food cues (Papies, 2013; Papies & Barsalou, 2015). We demonstrate next that, based on accumulating evidence from neuroimaging studies, the neural network associated with processing food cues is indeed similar to the network for actual eating in Figure 1a. The overlap between the eating network and the related network that becomes active when

processing food cues supports the proposal that cognitive responses to food cues are grounded in actual eating experiences.

In Simmons, Martin, and Barsalou (2005), for example, participants viewed pictures of foods and buildings in a one-back visual matching task. Relative to the building pictures, food pictures activated a gustatory processing region (right insula/operculum) and a food reward area (left OFC), along with regions of visual cortex that represented food recognition and shape. This pattern indicates that brain areas associated with food taste and reward become active, not only during the tasting of actual foods, but also while viewing food pictures, consistent with the proposal that the processing of food cues is grounded in the same brain areas that underlie actual eating. As much other research has similarly found, food pictures activate similar brain regions as actual eating across many different tasks, and also when food pictures are compared to different kinds of nonfood pictures, including non-edible objects (Beaver et al., 2006; Führer, Zysset, & Stumvoll, 2008; Killgore et al., 2003; Killgore & Yurgelun-Todd, 2005; LaBar et al., 2001), animals (Holsen et al., 2005; Holsen et al., 2006; Miller et al., 2007), dining-related utensils (Killgore et al., 2003; Killgore & Yurgelun-Todd, 2005), and mixed categories of nonfood (Cornier, Von Kaenel, Bessesen, & Tregellas, 2007; Cornier et al., 2009; Davids et al., 2010; Rothemund et al., 2007; Santel, Baving, Krauel, Münte, & Rotte, 2006; Schur et al., 2009; St-Onge, Sy, Heymsfield, & Hirsch, 2005).

Table 1 summarizes experiments that have contrasted food pictures with nonfood pictures in healthy individuals to establish brain regions associated with processing food cues. In general, these regions include the inferior temporal gyrus and the fusiform gyrus (visual processing of foods), insula and frontal operculum (food taste), OFC (food reward), amygdala (food relevance), inferior frontal gyrus (eating behaviors), parietal cortex (body image), and striatum (food reward). In other words, the brain areas that become active when perceiving pictures of food overlap considerably with the brain areas that become active during actual eating. From the grounded perspective, these brain areas can be viewed as simulating the experience of what it would be like to consume the cued food across the visual, gustatory, and somatomotor modalities, and how rewarding it would be to do so.

Using activation likelihood estimation (ALE), van der Laan et al. (2011) performed a meta-analysis on 17 experiments that examined neural responses to food cues in healthy individuals. van der Laan et al. found that the most common brain regions activated in response to viewing food pictures were the bilateral posterior fusiform gyrus, the left middle insula, and the left lateral OFC. In research using non-picture cues, food-related words (Barros-Loscertales et al., 2012; Pelchat, Johnson, Chan, Valdez, & Ragland, 2004) and food-related odors (Bragulat et al., 2010; Eiler, Dzemidzic, Case, Considine, & Kareken, 2012) activated similar brain regions, demonstrating that a common distributed network processes food cues across different input modalities (pictures, words, and odors). In each case, food cues appear to activate the same ventral reward pathway, suggesting that different cues produce similar anticipatory responses. As Papies and Barsalou (2015) suggest, pattern completion inferences that result from cuing memories of previous eating situations may underlie the production of these simulations (also see Barsalou, in press).

Based on these findings, we propose that the network in Figure 1b underlies the processing of visual food cues. As can be seen, this network is closely related to the eating network in Figure 1a adapted from Kaye et al. (2009). In both figures, the same two basic pathways emphasized earlier are apparent: a ventral pathway for processing food reward, and a dorsal pathway for implementing cognitive control. Because we are not committed to the specific connections (arrows) between brain areas in the original Kaye et al. figure, we have replaced them in Figure 1b with more general relations, simply indicating the ventral and dorsal pathways (in all later figures as well). An additional reason for not including Kaye et al.'s original connections is that the literatures we review have little to say about their validity. By simplifying connections, our review best captures the findings that we review and does not go beyond them.

As Figure 1b illustrates, when a person perceives a visual food cue, (e.g., a picture of pizza), primary visual cortex performs early visual analysis of the cue, and then sends input to fusiform gyrus, where the pictured object is recognized. Following object recognition, processing of the food cue is essentially the same as in actual eating (Figure 1a). Information is transmitted to regions that process attention (amygdala), taste (insula/frontal operculum), and reward (OFC, ventral ACC, ventral striatum). In parallel, the dorsal control pathway, including dorsolateral prefrontal cortex (dlPFC), dorsal ACC, and parietal cortex, sends signals to the dorsal striatum and mediates cognitive control functions such as planning future consequences and restrained eating. These different sources of information about the food associated with the food cue are then integrated to produce an overall approach or avoidance tendency toward the anticipated food.

Thus, Figure 1b proposes that processing a

food cue activates the same basic network that is also involved in actual food consumption. As can be seen by comparing Figures 1a and 1b, the only difference between these networks is the initial input into the system. When participants actually consume liquid food in a scanner (Figure 1a), the input is through the mouth with no visual input. When participants process a visual food cue (Figure 1b), the input is only through the visual system, such that the primary visual cortex and fusiform gyrus become relevant.

Importantly, however, visual processing is relevant in most naturalistic situations when people actually eat food, because people typically see the food they're eating (unlike liquid foods consumed through tubes in scanning experiments). Thus the network for actual eating, in principle, should include the same basic visual processes associated with processing food cues. As a result of processing foods visually during actual eating, visual information should become active later when perceiving food cues that activate eating simulations.

The core eating network. The network for actual eating in Figure 1a probably only becomes active during neuroimaging experiments when participants taste but don't see liquid foods. In contrast, the network in Figure 1b tends to become active during the processing of both food cues and actual eating. As we just saw, this network becomes active when processing visual food cues. This network is also likely to become active when processing non-visual food cues (e.g., smells, words), not only simulating how a cued food would taste, but also how it would look. Finally, this network becomes active during actual eating, again because consumed foods are typically perceived visually. Thus, across all these different eating situations, the network in Figure 1b is likely to be active, with additional brain areas for other modalities becoming active when relevant (e.g., gustatory, olfactory, auditory). As we will also see in later sections, the network in Figure 1b tends to be active when visual food cues are encountered across a wide variety of additional eating situations and populations.

For all these reasons, we will refer to the network in Figure 1b as the *core eating network.* Because this network is likely to be active across all the eating phenomena just described, it appears to be the common denominator, with other brain areas complementing it as necessary.

Modulations of the Core Eating Network Associated with Food Significance

We next review how two important variables associated with food significance—palatability and hunger—modulate neural activity in the core eating network. As Figures 2a and 2b each illustrate (for palatability and hunger respectively), high food significance produces greater activation in regions of the ventral reward pathway relative to low food significance.

Palatability. To assess the neural effects of food palatability (typically correlated with calories and energy density), Beaver et al. (2006) contrasted neural responses to pictures of appetizing foods, disgusting foods, bland foods, and nonfood objects in healthy individuals. Compared to bland food pictures, appetizing food pictures increased neural activity in the ventral striatum, amygdala, midbrain, and ventral pallidum. Moreover, individual variation in trait reward sensitivity correlated positively with activation in these regions to images of appetizing food pictures. In other words, individuals with higher reward sensitivity showed stronger reward responses to pictures of palatable foods.

Many other experiments have similarly reported enhanced neural responses to high-calorie food pictures (versus low-calorie food pictures) in reward-related regions, including the striatum and hypothalamus (Cornier, Von Kaenel, Bessesen, & Tregellas, 2007; Goldstone et al., 2009; Passamonti et al., 2009; Schur et al., 2009), OFC (Goldstone et al., 2009), and amygdala (Goldstone et al., 2009; Passamonti et al., 2009). Interestingly, visual and motor regions can also become more active for high-calorie foods. Visual processing regions could become more active because of greater visual attention to attractive foods (Cornier et al., 2007; Passamonti et al., 2009; Schur et al., 2009), and the cerebellum could become more active due to anticipated motor activity (Killgore et al., 2003; Killgore & Yurgelun-Todd, 2005).

As found in a recent meta-analysis (van der Laan et al., 2011), the most common regions that respond more to high-calorie food pictures than to low-calorie ones in healthy individuals are the ventral striatum, hypothalamus, visual processing areas, mid-frontal gyrus, and cerebellum. Notably, not all regions along the ventral reward pathway of the core eating network consistently exhibit higher activations for high-calorie food pictures (e.g., Rothemund et al., 2007). In particular, the insula, OFC, amygdala, and ACC are not always more active for high-calorie food pictures, although sometimes they are (Table 2). A possible explanation is that the healthy individuals in different studies are in different hunger states that modulate neural activity in these regions (as Table 2 documents for experiments that included high-calorie vs. low-calorie food comparisons). As described shortly for hunger, people's motivational states moderate neural responses to food pictures substantially,

especially for high-calorie foods.

Figure 2a summarizes how highly palatable (high calorie) foods modulate neural activity in the core eating network. As the network components highlighted in red illustrate, highly palatable foods consistently increase neural activity in the ventral striatum and visual processing areas. As described earlier, however, palatable foods sometimes increase neural activity in other areas of the ventral reward pathway as well (also in experiments on hunger, as described shortly). In Figure 2a, areas in the ventral reward pathway that sometimes increase with palatability are partially highlighted in red (insula, OFC, amygdala, ACC).

Finally, palatability consistently increases neural activity in the hypothalamus (van der Laan et al., 2011). As described in the Discussion, brain areas outside the core eating network sometimes play central roles in eating phenomena, suggesting that the core eating network dynamically incorporates other brain areas under various conditions. Table 2 provides a complete list of experiments that have assessed the modulating influence of palatability on the processing of food pictures.

Hunger. Not only does palatability modulate ventral reward pathway activations to food pictures in healthy individuals, so do motivational states. As we will see, the ventral reward pathway becomes more active when people are hungry (presumably because hunger typically makes food consumption more rewarding). When assessing event-related potentials (ERP) to palatable food pictures, for example, Stockburger, Weike, Hamm, and Schupp (2008) and Stockburger, Schmälzle, Flaisch, Bublatzky, and Schupp (2009) found that hunger increased positive potentials initially over posterior sensory sites during the 170-310 ms post-stimulus time window, and later over parietal and frontal locations (450-600ms). In contrast, hunger vs. satiety did not modulate these ERPs to other non-food control images. Thus, hunger increased selective attention to food stimuli during processing stages related to focused attention and categorization.

These ERP results are consistent with related fMRI findings. LaBar et al. (2001), for example, compared brain activations to food pictures vs. tool pictures when healthy adults were in a hungry or satiated state. They found that food pictures, but not tool pictures, elicited greater activations in the amygdala, fusiform gyrus, and parahippocampal gyrus when participants were hungry than when they were satiated. Similarly, Führer, Zysset, and Stumvoll (2008) reported a significant interaction between motivational state (hunger or satiety) and type of visual picture (food or non-food) in the ACC, amygdala, OFC, and superior occipital sulcus. Using a directional-cuing attention paradigm, Mohanty, Gitelman, Small, and Mesulam (2008) found increased neural activity in the amygdala, parahippocampal gyrus, and peristriate cortex for food pictures relative to tool pictures, and more so when participants were hungry than when they were satiated. Consistent with the grounded cognition perspective, increased neural activity in the ventral reward pathway for food cues when participants are hungry mirrors the analogous ventral reward activations that can occur when participants are hungry during actual eating (as described earlier in the section on eating; Uher et al., 2006; Stice et al., 2013).

Results from normal weight children and adolescents closely parallel the findings in adults. In Holsen et al. (2005), healthy children and adolescents showed increased activation to food pictures relative to animal pictures in the amygdala, mPFC/OFC, and insula when they were hungry, but not when they were satiated.

A few experiments, however, have not observed stronger neural responses to food cues when participants are hungry. Perhaps measurement issues underlie these discrepancies. In Santel, Baving, Krauel, Münte, and Rotte (2006), hunger was assessed with self-reported hunger ratings. Because the relation of self-reported hunger to actual hunger may vary across individuals, it is possible that actual food deprivation was not measured accurately in this experiment. In Uher, Treasure, Heining, Brammer, and Campbell (2006), 24-hour fasting was defined as the hunger state, whereas not having eaten for the previous 3 hours was defined as the satiated state ("neither hungry nor acutely satiated"). Because some participants might be hungry after 3 hours of not eating, hunger again may not have been measured accurately.

Hunger not only elicits greater responses to food pictures (compared to nonfood pictures), but also enhances neural responses to high-calorie foods relative to low-calorie foods. Not only did Goldstone et al. (2009) find that hunger enhanced the subjective appeal of high-calorie foods, they further found that hunger increased neural activity to high-calorie food pictures over low-calorie food pictures in the ventral reward pathway (e.g., ventral striatum, amygdala, anterior insula, OFC). Siep et al. (2009) reported similar results in medial OFC, insula, fusiform gyrus, caudate, putamen, and posterior cingulate cortex. Interestingly, when the healthy females in this experiment were satiated, these regions showed stronger responses to low-calorie food pictures, perhaps indicating greater interest in healthy foods.

Because neuroendocrine factors are known

to modulate hunger and satiated states, some experiments have correlated neuroendocrine levels with neural responses to food pictures. Malik, McGlone, Bedrossian, and Dagher (2008), for example, assessed the effects of ghrelin administered intravenously to healthy volunteers, where ghrelin is a hormone that regulates appetite, increasing before a meal and decreasing afterwards. Malik et al. found that ghrelin levels correlated positively with subjective appetite, and also with neural activation to food cues in the anterior insula, OFC, amygdala, and striatum (also see Jakobsdottir, de Ruiter, Deijen, Veltman, & Drent, 2012; Kroemer et al., 2013).

To summarize, participants find food pictures more rewarding and salient when they are hungry than when satiated (also see Papies, Pronk, Keesman, & Barsalou, 2015). Specifically, hunger increases neural responses to food cues in regions of the ventral reward pathway, including the amygdala, insula, OFC, and ventral striatum. In a recent meta-analysis (van der Laan et al., 2011), the amygdala/parahippocampal gyrus and lateral OFC/ inferior frontal gyrus were consistently more active when participants were hungry than when satiated. Because these findings were only based on five studies, however, they should be interpreted with caution. As we have seen, other areas in the ventral reward pathway also become more active as participants view food pictures while hungry, including the insula and ventral striatum. Additionally, ERP experiments show that hunger can heighten attention to food cues, consistent with the greater activation of visual processing areas in fMRI experiments. Based on evidence from both fMRI and ERP experiments, it appears that regions of the ventral reward pathway, in general, often responds more strongly to food pictures when hungry than when satiated.

Figure 2b illustrates how hunger modulates the core eating network by enhancing attention and reward responses to food cues. Following van der Laan et al. (2011), the OFC and the amygdala consistently become more active during hunger, with other areas in the ventral reward pathway becoming more active on some occasions. Table 3 lists experiments that have assessed the modulating influences of hunger and satiety on the processing of food pictures.

Comparing Figure 2b to Figure 2a (and also Table 3 to Table 2), it appears that hunger modulates the core eating network somewhat more than does palatability. This makes sense, given that palatability can be viewed as a property of certain foods, such that they activate greater attention and reward responses than do other foods, whereas hunger raises food significance to another level, where all foods become more salient. And as we have also seen, palatability and hunger interact, with hunger amplifying the palatability effect, perhaps reflecting the importance of identifying high-caloric foods when hungry.

Modulations of the Core Eating Network Associated with BMI

It is widely believed that an imbalance in energy intake and energy expenditure is the fundamental cause of weight gain, with increased energy intake being especially problematic. In industrialized environments, exposure to food cues can be overwhelming, with abundant supplies of highly-rewarding high-calorie foods being readily available (Marteau et al., 2012). Thus, exploring the neural responses to food cues in overweight and obese individuals is important for establishing the underlying causes of overeating and for developing effective interventions.

Obese individuals, relative to normal weight individuals, often exhibit atypical neural activations to food cues both before meals and after. In Stoeckel et al. (2008), for example, obese women found high-calorie food cues more attractive than did lean women. Specifically, high-calorie food cues produced significantly higher activations in taste and reward areas for the obese participants, especially when they were hungry (e.g. OFC, amygdala, ventral striatum/nucleus accumbens, insula, ACC). Additionally, obese participants produced longer sustained neural activations in OFC, caudate, and ACC. This latter finding suggests that obese individuals show sustained responses in brain regions associated with reward and addiction even after eating, which may explain why they often overeat.

In Martin et al. (2010), obese individuals showed stronger neural responses to food pictures in ACC and mPFC before eating (relative to healthy weight controls), and in mPFC and caudate after eating, again suggesting stronger anticipatory responses to food cues both before and after eating. Furthermore, mPFC activations in obese individuals correlated positively with self-reported hunger before eating, whereas ACC activations decreased as self-reported disinhibition increased. Martin et al. concluded that as reward responses in ACC and mPFC increase, obese participants' ability to regulate their eating responses decreases.

Finally, Dimitropoulos, Tkach, Ho, and Kennedy (2012), examined neural responses to high-calorie foods, low-calorie foods, and nonfood pictures before and after eating in obese and normal weight individuals. Compared to normal weight individuals, obese individuals

showed lower activations in dlPFC to food pictures before eating but higher activations after eating (suggesting increased regulation when satiated). Obese individuals, compared to normal weight individuals, again showed greater activation in reward areas after eating to high-calorie food cues (e.g., OFC, ACC, caudate).

Thus, neural activity to food cues in overweight and obese adults differs considerably from the analogous neural activity in normal-weight adults. Obese adults, relative to normal-weight adults, exhibit higher neural activity in the ventral reward pathway both before and after eating.

Obesity in children. Research with children has found that obesity is associated with patterns of neural activity similar to those in obese adults. Bruce et al. (2010), for example, compared neural responses to food pictures between obese children and normal weight children in hungry and satiated states. Obese children, compared to normal weight children, exhibited less post-meal reduction of activation in OFC and nucleus accumbens. Obese children also exhibited stronger activation to food pictures in dlPFC when hungry, suggesting greater attempts at inhibitory control. Davids et al. (2010) reported similar results. Additionally, they found that stronger dlPFC activations were associated with low self-esteem in obese children, suggesting that these children required greater inhibitory control when attempting to regulate eating. In general, these experiments suggest that the patterns of neural processing associated with obesity begin early in life.

Continuous relations between BMI, neural responses to food cues, and weight gain. The differences between obese and lean individuals generalize further to correlational studies that use BMI as a continuous predictor of neural responses to food cues. Batterink, Yokum, and Stice (2010), for example, investigated neural responses during a go/no-go task with foods and non-foods in adolescent girls (fasting for 4-6h), who ranged in weight from lean to obese. When participants were required to inhibit their impulses towards appetizing food pictures, BMI correlated positively with behavioral impulsivity and negatively with neural activity in inhibitory regions (e.g., superior frontal gyrus, middle frontal gyrus, dlPFC, mPFC), suggesting that inhibitory processing of food cues decreases as BMI increases. Moreover, neural activity in the insula/frontal operculum to food images also correlated positively with BMI, suggesting that taste intensity increases with weight. In general, these results suggest that higher body weight is related to hyper-functioning of the ventral reward pathway and to hypo-functioning of the regulatory control pathway.

Similar patterns were found for another group of adolescent girls when they were hungry (Yokum, Ng, & Stice, 2011). In this experiment, BMI correlated positively with speeded responses to both appetizing and unappetizing food pictures (but not for neutral images). Additionally, BMI correlated positively with activations to food cues in regions associated with taste and reward (e.g., insula/ frontal operculum, OFC). Rothemund et al. (2007) reported similar results for female adults, with BMI again predicting neural activity to high-calorie food pictures in taste and reward areas (striatum, anterior insula, posterior cingulate, OFC). Interestingly, Killgore et al. (2013) found that the relationship between BMI and neural responses to food pictures only occurred for women but not for men, perhaps reflecting the heightened importance of body image for many women.

Neural responses to food cues also predict future weight gain and difficulties in regulating one's weight. For 35 adolescent girls ranging in weight from lean to obese, greater lateral OFC activation during initial attention to appetizing food cues predicted their one-year BMI increases (Yokum et al., 2011). A similar experiment with obese individuals reported stronger activations to high-calorie vs. control pictures in the ventral reward pathway (nucleus accumbens, ACC, insula), which were associated with less success in losing weight during a subsequent 12-week weight-loss treatment (Murdaugh, Cox, Cook, & Weller, 2012). Additionally, neural activity to high-calorie food pictures in the insula, putamen, fusiform gyrus, and hippocampus predicted the subsequent 9-month change in percent weight gain. Another experiment found that stronger neural activity in dlPFC to food pictures after a systematic diet program predicted long-term weight maintenance in obese individuals (Weygandt et al., 2015). Finally, Stice, Yokum, Blum, and Bohon (2010) found that women who gained weight over 6 months showed a reduction in striatal responses to the actual consumption of palatable food across this period, relative to weight-stable overweight/obese women. Together, these results show that higher responses to food cues in the ventral reward pathway and lower reward sensitivity to food while actually eating increase the risk for overeating. Furthermore, overeating may attenuate the responsivity of reward circuitry in a feedback process.

A recent meta-analysis that included ten experiments largely confirmed the results that we have reviewed thus far, finding that the ventral reward pathway tends to become more active during the processing of food cues as BMI increases (Brooks, Cedernaes, & Schiöth, 2013). Two additional findings of interest, however, also

emerged. First, high BMI was generally associated with lower activations in gustatory cortex (insula) during the processing of food cues, suggesting that high BMI may be associated with blunted taste responses. Second, high BMI was associated with lower dlPFC activations, suggesting less inhibitory control in response to food cues.

Abnormal leptin levels may also contribute to the strong reward responses that high BMI individuals exhibit to food cues, where leptin is a hormone associated with satiety. As leptin level increases, hunger normally decreases. In Grosshans et al. (2012), increasing BMI was not only associated with stronger ventral striatum responses to food cues, but also with increased leptin levels. Elevated leptin levels in obese participants suggest that dysfunctional processing of leptin contributes to their stronger reward responses. Although increasing leptin might be expected to decrease reward responses, it does not appear to do so in high BMI individuals.

Results from Wang et al. (2001) further implicate abnormal reward responses to food cues in high BMI individuals. As BMI increased, the availability of D_2 receptors in the striatum decreased, suggesting that high BMI individuals experience weak reward responses to food. Thus, high BMI individuals may overeat, not only because of their insensitivity to satiety signals, but because they experience weak rewards from eating, requiring more food to experience pleasure.

The relation between neural responses to food cues and actual eating in obesity. Finally, we address how neural responses to food cues in obese individuals differ from their neural responses during actual eating. In some research, obese individuals exhibit stronger responses to food cues in the ventral reward pathway, relative to lean adults, but exhibit weaker responses during actual food consumption. In Gearhardt et al. (2011), for example, higher food addiction scores correlated positively with neural activity in ACC, OFC and amygdala when processing food cues, but correlated negatively with neural activity in OFC during actual milkshake consumption. These patterns of neural activity in eating behavior are similar to those associated with drug dependence: Elevated reward responses to drug cues, accompanied by reduced reward responses to drug intake.

A similar pattern emerged in an experiment with adolescent girls. In Stice, Spoor, Bohon, Veldhuizen, and Small (2008), obese girls (relative to controls) exhibited greater activation in gustatory cortex (anterior and mid-insula, frontal operculum) and in somatosensory cortex (parietal operculum, rolandic operculum), both when anticipating milkshake consumption (to food cues) and during actual milkshake consumption (vs. tasteless solution). Conversely, however, the obese girls showed decreased activation in the caudate nucleus during actual consumption.

Some experiments, however, offer conflicting results. In Stice, Yokum, Burger, Epstein, and Small (2011), neural responses to actual food consumption were assessed in adolescents with high risk for obesity (as indicated by two obese or overweight parents) vs. low-risk children (as indicated by two lean parents). Although high- and low-risk adolescents did not differ in response to food cues that signaled food reward, high-risk children exhibited greater activation in the caudate, parietal operculum, and frontal operculum during actual food consumption. Stice et al. (2011) suggest that higher reward processing while eating during adolescence may eventually lead to overeating, which in turn, may produce blunted dopamine signaling in adulthood.

In Szalay et al. (2012), however, obese adults show enhanced neural activity in the ventral reward pathway during actual eating, not blunted responses. Specifically, obese individuals (relative to controls) exhibited stronger neural responses to three different liquid foods (compared to distilled water) across the insula, OFC, amygdala, ACC, nucleus accumbens, putamen, and pallidum. Viewing all the research in this area together, much remains to be learned about how obesity modulates increased vs. decreased neural activity in the ventral reward pathway, not only across development, but also in adulthood.

Finally, a clever experiment demonstrates how taste blunting to food cues might result from overeating. Cornier et al. (2009) found that after two-days of overeating, healthy individuals exhibited attenuated responses to food pictures (compared to nonfood pictures) in insula, hypothalamus, and visual cortex. Moreover, weight-reduced obese individuals exhibited less attenuation, suggesting that their responses in these areas may have already become somewhat blunted.

Summary. When exposed to food cues, high BMI individuals (at least women) tend to exhibit stronger neural responses in the ventral reward pathway, including, OFC, amygdala, ventral striatum, ACC, and insula (although the meta-analysis showed lower insula activation). In addition, obese individuals sometimes show decreased neural activity in the dorsal control pathway (dlPFC), although children and motivated adults can show increased activity. Furthermore, stronger responses in the ventral reward pathway predict future weight gain,

whereas stronger responses in the dorsal control pathway predict better weight maintenance after dieting. Similar patterns also occur for adolescents and children at risk for obesity, suggesting that the neural networks associated with obesity become established early in life.

Figure 3a illustrates how increasing BMI modulates neural responses to food cues in the core eating network. As just described, this modulation includes increased activation of the ventral reward pathway, although insula activation sometimes decreases, perhaps due to blunting. High BMI also tends to be associated with increased visual processing of food and with decreased use of the dorsal control pathway (although increased use occurs under various conditions noted).

Moving from food cues to actual eating, Figure 3b illustrates how increasing BMI modulates neural responses to actual eating in the core eating network. Depending on the experiment, obese individuals sometimes exhibit decreased activity in the ventral reward pathway during actual food consumption, and sometimes exhibit increased activity. Sometimes these differences appear related to development, exhibiting a shift from increased to decreased activity across childhood and adolescence. The ventral reward pathway in Figure 3b displays this ambiguity, illustrating the potential for both increases and decreases in the relevant brain areas. As we saw earlier, the relatively sparse findings in this area are quite mixed, with further research being necessary to reach any conclusions with confidence. Table 4 lists experiments that compare brain responses to food cues or to actual food consumption in overweight/obese vs. normal weight individuals.

Modulations of the Core Eating Network in Eating Disorders

Anorexia nervosa (AN) and bulimia nervosa (BN). In Western cultures, people often have access to abundant food resources. At the same time, people (especially women) are under strong social pressure to have a slim body. In AN and BN, striving for a lean body by restricting food intake becomes an important goal. AN is an eating disorder characterized by immoderate food restriction and irrational fear of weight gain, as well as distorted body perception. AN typically involves excessive weight loss by severely restricting food intake, and occurs more often in women than in men. BN is a related eating disorder characterized by consuming large amounts of food in a short amount of time (binging), followed by an attempt to rid oneself of consumed food (purging), typically by vomiting, by taking a laxative, diuretic, or stimulant, and/or by excessive exercise. Because maintaining a slim body shape is the goal in both AN and BN, these populations are likely to process food cues differently than do normal eaters.

In a modified dot-probe task that measured attentional focus, AN and BN patients, relative to controls, exhibited robust and reliable attentional biases toward eating-related and weight-related pictures (presented for 1000 ms), whereas attentional bias toward shape stimuli was less strong (Shafran, Lee, Cooper, Palmer, & Fairburn, 2007). In a recent meta-analysis, patients with eating disorders exhibited greater attentional bias to food stimuli than did controls (Brooks, Prince, Stahl, Campbell, & Treasure, 2011).

In an experiment that assessed ERPs to food pictures in AN, BN, and normal controls, Blechert, Feige, Joos, Zeeck, and Tuschen-Caffier (2011) reported a similar pattern. Whereas AN and BN patients exhibited enhanced processing for both high-calorie and low-calorie food pictures relative to neutral pictures, healthy controls only showed enhanced processing for high-calorie food pictures, suggesting that AN or BN patients have a generalized attentional bias for food cues. Using eye-tracking, Giel et al. (2011) reported a different pattern of visual attention. Whereas AN patients demonstrated no early vigilance to food pictures, they exhibited later avoidance. Moreover, the extent of avoidance was associated with the disorder's severity. This finding suggests that AN patients may initially perceive the incentive salience of food similar to healthy controls, but later avoid food cues to restrict eating.

When exposed to food cues in fMRI experiments, patients with AN or BN also exhibit a pattern of neural responses that differs from normal eaters. Brooks et al. (2011), for example, compared neural responses to food pictures (vs. non-food pictures) in AN patients, BN patients, and healthy controls. Relative to controls, BN patients showed greater neural activation to food pictures in visual cortex, insula, precentral gyrus, and dlPFC, whereas AN patients showed greater activation in dlPFC, cerebellum, and precuneus. In direct comparisons between BN and AN patients, BN patients exhibited greater activation in the insula, caudate, supplementary motor area, and superior temporal gyrus, while also showing significantly decreased activation in the parietal lobe and PCC. In a related experiment, Brooks et al. (2012) asked AN patients to think about eating the food shown in images. Relative to normal eaters, AN patients showed reduced activation in the bilateral cerebellar vermis (associated with feeding behavior), together with increased activation in dlPFC and visual cortex, again

suggesting greater control. In Sanders et al. (2015), AN patients did not show reduced activation in the ventral reward pathway, but did show increased activation in the dorsal control pathway. Together, these results suggest that patients with AN and BN both activate top-down cognitive control in response to food cues, but that BN patients are more likely to exhibit increased activation in reward and sensory-motor regions that produces binge eating, together with less regulatory processing than AN patients.

Finally, hunger and satiety modulate neural responses to food cues in AN. Santel, Baving, Krauel, Münte, and Rotte (2006), for example, asked AN patients and healthy controls to rate the pleasantness of visual food and nonfood stimuli while either in a hungry or satiated state. Relative to controls, AN patients generally rated food as less pleasant. When hungry, AN patients displayed weaker activation of right occipital cortex than healthy controls, suggesting that decreased attentional focus on food cues supports restrained eating. When satiated, AN patients showed decreased activation in left inferior parietal cortex relative to controls, suggesting decreased food-related somatosensory processing during satiety (perhaps related to body image).

Figure 4a illustrates how AN modulates neural responses in the core eating network. Based on both the behavioral and neuroimaging findings, AN patients can exhibit either enhanced or inhibited visual processing of food. They also exhibit decreased anticipation of how food tastes (lower insula activations), and typically show strong regulatory responses (higher dlPFC activations). Together, reductions in bottom-up appetitive processing with increases in top-down regulatory processing make food restriction possible (Kaye et al., 2009; Kaye et al., 2010; Van den Eynde & Treasure, 2009; van Kuyck et al., 2009; Zhu et al., 2012). Altered parietal functions have also been reported in AN patients, perhaps reflecting distorted body image (Kaye et al., 2006).

Figure 4b illustrates how BN modulates neural responses in the core eating network. Although relatively few articles address the neural bases of BN, Figure 4b offers speculation about modulations associated with this population. Based on existing behavioral and neural findings, BN patients generally exhibit enhanced attention to food and enhanced reward expectancy, perhaps associated with binge eating behavior. Similar to AN patients, BN patients also show increased attempts to regulate anticipatory responses to food, but not as much as AN patients.

Binge-eating disorder (BED). Another type of eating disorder, BED is characterized by recurrent binge episodes, together with impaired control over eating and subsequent distress. Unlike BN, in which inappropriate compensatory strategies (e.g. vomiting) are employed to counteract the effects of overeating, BED patients do not perform regular behaviors to counteract weight gain, such as purging. As a consequence, BED patients are often overweight or obese. In Schienle, Schäfer, Hermann, and Vaitl (2009), BED patients (relative to controls) reported enhanced reward sensitivity to food pictures (as indicated by the behavioral activation scale), further supported by stronger activations in mOFC that correlated positively with the self-reports.

Using multivariate pattern analysis (MVPA), Weygandt, Schaefer, Schienle, and Haynes (2012) found that patterns of neural activation in the right insula could discriminate between BED patients and normal controls (and also between BN patients and healthy controls). In addition, activation patterns in the right ventral striatum separated maximally between BED patients and overweight controls, whereas the left ventral striatum separated maximally between BED patients and BN patients. These results indicate that BED patients exhibit abnormal responses to food cues in the ventral reward pathway (insula and striatum). For BED patients, voxel-based morphometry (VBM) further revealed significant gray matter atrophy in the right ventral insula, striatum, and OFC. Because these patients perceive satiety but fail to translate satiety signals into appropriate behaviors, damage to the OFC-insular-striatal circuit could be associated with overeating behavior (Woolley et al., 2007).

Figure 5a presents a modulation of the core eating network associated with BED. Similar to BN, relatively few articles address the neural bases of BED. Figure 5a offers speculation about modulations of the core eating network during this disorder. As Figure 5a suggests, BED is associated with functional and structural changes in the ventral reward pathway, specifically, in the OFC, insula, and ventral striatum.

Across the panels for AN, BN, and BED in Figure 4 and 5, individuals with different eating disorders exhibit different neural responses to food cues. When individuals are trying to restrain food intake to achieve a slim body shape (AN and BN), enhanced activation in the dorsal control pathway plays a central role. When participants have the tendency to binge eat (BN and BED), they exhibit enhanced activation in the ventral reward pathway.[1]

Modulations of the Core Eating Network Associated with Eating Goals

Because cognition is highly dynamic—and the processing of food cues is no exception—we

expect that focusing on different eating goals should modulate the core eating network in myriad ways (cf. Barsalou, 2003, in press; Lebois, Wilson-Mendenhall, & Barsalou, 2015; Wilson-Mendenhall, Barrett, Simmons, & Barsalou, 2011). As eating goals change, the core eating network reconfigures itself dynamically to support them. In this next section, we briefly address three important eating goals: (1) Losing weight via dieting, (2) hedonic goals oriented toward experiencing immediate eating reward, (3) regulatory goals aimed at achieving long-term health.

Losing weight via dieting. Often people adopt dieting strategies when pursuing the goal of losing weight, attempting to reduce their caloric intake in an intentional and sustained manner (Wadden, Brownell, & Foster, 2002). Much research indicates that females with high scores on dietary (restrained eating) scales, relative to low scores, are at greater risk for future onset of binge eating, bulimic symptoms, and bulimic pathology (Stice & Agras, 1998; Stice, Davis, Miller, & Marti, 2008). For these reasons, restrained eaters are likely to exhibit hyperactivation of the ventral reward pathway to food and food cues. To assess this possibility, Burger and Stice (2011) examined the relationship between dietary restraint scores and neural responses during the receipt and anticipated receipt of chocolate milkshake, and also to food pictures. Although dietary restraint scores did not correlate with neural activity in response to anticipated receipt of milkshake or exposure to food pictures, restraint scores correlated positively with activations in right OFC and bilateral dlPFC in response to actual milkshake consumption.

In another experiment, Coletta et al. (2009) found that motivational states modulated neural responses to food pictures in restrained eaters. When fasted, restrained eaters reported less hunger than unrestrained eaters and showed activation only in the cerebellum when exposed to highly palatable food cues (relative to low-palatable cues). When satiated, however, restrained eaters found palatable food more appealing than did unrestrained eaters, and showed activations in areas associated with desire, expectation of reward, and inhibitory control. In Ely, Childress, Jagannathan, and Lowe (2014), dieters, when fasted, exhibited stronger responses to highly palatable food images (compared to moderately palatable food images) in the ventral reward pathway (amygdala, ventral striatum, ACC), and also higher activation in the dorsal control pathway (middle frontal gyrus). Using near-infrared spectroscopy, Suda et al. (2010) found that dietary restraint correlated positively with activation in right fronto-temporal cortex.

Figure 5b illustrates how the goal of dietary restraint modulates neural responses to food cues in the core eating network. As Figure 5b illustrates, dietary restraint is associated with enhanced activation in both the ventral reward pathway and the dorsal control pathway. On the one hand, restrained eaters find food more rewarding; on the other, they have the tendency to regulate their impulsivity toward food so that they can lose or maintain weight.

Hedonic and health goals. Siep et al. (2012) demonstrated the neural consequences of focusing on hedonic pleasure. When participants were asked to focus on the hedonic properties of highly palatable foods (smell, taste, and texture) in the up-regulation condition, they exhibited increased food craving and enhanced activation in the ventral reward pathway (ventral striatum, ventral tegmental area, operculum, insula, mOFC, and vmPFC). Similarly, in another experiment when participants were asked to think about their favorite version of a palatable food and to focus on its hedonic properties, the insula, caudate nucleus, and hippocampus responded strongly (Pelchat, Johnson, Chan, Valdez, & Ragland, 2004).

Conversely, when participants in Siep et al. (2012) were asked to suppress any thoughts about food palatability and food craving, they showed decreased neural activity in the ventral reward pathway (e.g. ventral striatum), together with enhanced activity in regulatory areas (e.g. dlPFC, anterior PFC). Similarly, in Giuliani, Mann, Tomiyama, and Berkman (2014), stronger neural responses in the dorsal control pathway occurred when participants were asked to regulate thinking about eating personally-craved foods (e.g. dlPFC, dorsal ACC, inferior frontal cortex). In Scharmüller, Übel, Ebner, and Schienle (2012), obese individuals (relative to controls) exhibited stronger dlPFC responses when asked to cognitively decrease the reward value of presented foods, suggesting greater efforts at appetite control.

Hare, Malmaud, and Rangel (2011) demonstrated the neural consequences of focusing on long-term health. When participants received exogenous cues that directed attention to food healthiness, they made healthier food choices. Furthermore, when cues associated with healthy eating goals were present, activations in vmPFC became more strongly correlated with food healthiness (relative to when no eating goal was primed). One interpretation of this finding is that vmPFC represents healthy eating goals that can override eating impulses in the ventral reward pathway. Hare et al. further found that dlPFC

modulated these vmPFC activations, suggesting that exogenous cues activate cognitive control areas of dlPFC, which in turn activate healthy eating goals in vmPFC, thereby reducing hedonic impulses.

In a related experiment, Hollmann et al. (2012) asked participants to think of negative long-term health and social consequences of eating high-calorie non-healthy foods. Relative to desiring these foods, thinking about the long-term consequences of consuming them produced stronger responses in brain areas associated with cognitive control and response inhibition (dlPFC, pre-supplementary motor areas, IFG, dorsal striatum, temporo-parietal junction; also regions in the ventral reward pathway, including anterior insula and bilateral OFC).

In Yokum and Stice (2013), participants were either asked to think about the long-term costs of eating unhealthy foods vs. the long-term benefits of not eating them. Both strategies increased activation in inhibitory regions (dlPFC, superior frontal gyrus), and reduced activation in attention and vision regions (precuneus, PCC). Interestingly, thinking of the long-term benefits of not eating appeared to increase inhibitory activity and to reduce attention activity more effectively than thinking about the long-term costs of eating.

In Stice et al. (2015), normal-weight adults received an intervention over the course of seven weeks (one hour per week) in which they practiced using cognitive reappraisal to increase the consumption of healthy foods and to reduce the consumption of high-calorie foods. Later, when participants viewed high calorie food pictures, they exhibited stronger neural activity in inhibitory control regions, accompanied by reduced activity in attention/expectation regions.

In a variety of related behavioral experiments, implicit cues activating health goals effectively reduced consumption of unhealthy foods in restrained eaters (Papies & Hamstra, 2010; Papies, Potjes, Keesman, Schwinghammer, & van Koningsbruggen, 2014; Papies & Veling, 2013). Notably, these health primes did not significantly change the behavior of non-restrained eaters. As Papies and Barsalou (2015) suggest, only restrained eaters have established previous memories of restrained eating available for health cues to prime. Because non-restrained eaters do not have these memories, health primes have no effect. Assessing the differential effects of primes between restrained and non-restrained eaters seems like a productive direction for future neuroimaging research.

In summary, the processing of food cues is dynamic, depending on a person's eating goals. Because so few studies exist in this area, we do not suggest systematic modulations of the core eating network at this point. Nevertheless, the implications of the work so far in this area are consistent with the general assumption of grounded cognition that different eating goals dynamically modulate the core eating network to support situated action (cf. Barsalou, 2003, in press; Lebois et al., 2015; Wilson-Mendenhall et al., 2011). When participants receive a food cue and are asked to imagine the reward value of the respective food, they exhibit greater activation in ventral reward pathway, which is likely to make them approach the food impulsively. When, however, participants are asked to imagine the health consequences of consuming a high-calorie food, they exhibit greater activity in the dorsal control pathway, which is likely to inhibit their desire for consuming the food.

As this literature further illustrates, the core eating network may recruit additional brain areas to achieve various eating goals. Specifically, we just saw that adopting a healthy eating goal tends to recruit mPFC, an area not in the core eating network, nor active in much of the literature we reviewed earlier (although it has been important in several experiments). Nevertheless, the mPFC appears to play central roles in mentalizing about health goals, and is thus recruited into the core eating network when health goals become relevant. We suspect that dynamically reconfiguring the core eating network in this manner occurs frequently, and that such reconfigurations explain recruitment of areas outside the core eating network that we have seen throughout this review.[2]

Discussion

This article, to our knowledge, is the first to integrate food-related processing in the human brain across different eating situations and populations into a single theoretical account. As we have seen, a core eating network adapted from Kaye et al. (2009), together with systematic modulations of this network observed in the literatures that we reviewed, explains different patterns of neural activity observed for different eating situations and populations. Across all these phenomena, the large majority of brain areas relevant to explaining each phenomenon fell within the core eating network, with modulations of specific areas distinguishing different phenomena from one another. Thus, the core eating network and its modulations provide insight into how all these phenomena are related and how they differ.

The ventral reward and dorsal control pathways. A consistent theme across eating phenomena is the importance of two processing streams within the core eating network: a ventral reward pathway, and a dorsal control pathway. As Kaye et al. (2009) proposed, the ventral pathway processes the taste, reward, significance, and affective value of food, whereas the dorsal

pathway regulates neural and behavioral responses to food and food cues, helping achieve various eating and health goals. As we have seen, these two pathways operate ubiquitously throughout various eating phenomena, sometimes alone (e.g., hedonic responses to food cues), and sometimes together (e.g., bulimia nervosa, restrained eating, achieving health goals). Given the prevalence of dual-process theories in psychology and neuroscience (Sherman, Gawronski, & Trope, 2014), it is not surprising that a dual-pathway framework underlies the core eating network.

Across the two pathways of the core eating network, various modulations appear to go a long way in explaining diverse eating phenomena. Increased use of the ventral reward pathway, for example, appears central for explaining effects of palatability, hunger, and BMI. Increased use of the dorsal control pathway appears central for explaining eating disorders, dietary restraint, and the pursuit of health goals. By viewing these phenomena within a common theoretical framework, it becomes possible to understand them better and see their relations to one another.

Implications for grounded cognition. Consistent with the perspective of grounded cognition, simulations of eating behavior underlie the processing of food cues. When people encounter a food cue, they simulate an experience of consuming the food, which can then motivate them to actually consume it (Papies, 2013; Papies & Barsalou, 2015). As much evidence indicates, these eating simulations activate taste and reward areas similar to those that become active during actual food consumption, as well as other areas associated with eating (e.g., Barros-Loscertales et al., 2012).

Across eating phenomena, eating simulations vary in systematic ways that have the potential to inform our understanding of these phenomena. When people are hungry, for example, they simulate the taste and reward value of foods more than when they are satiated (also see Papies et al., 2015). Similarly, when people encounter tasty unhealthy foods, they are more likely to simulate taste and reward than when they encounter less flavorful healthy foods. Individual differences in eating behavior also appear to affect eating simulations. As people's BMI increases, they are increasingly likely to simulate taste and reward, reflecting their greater interest in eating. Conversely, when people are anorexic, they are less likely to simulate taste and reward, thereby decreasing the likelihood that they will consume foods they encounter.

Interestingly, eating simulations can sometimes diverge from neural activity during food consumption in interesting and important ways. As we saw earlier, high BMI individiuals can exhibit relatively strong hedonic responses to food in anticipation of consuming it, while showing relatively weak hedonic responses during consumption (at least in some experiments). Thus, simulations do not rigidly track consumption, but can vary in important ways that reflect the cognitive and behavioral processes associated with a complex phenomenon, such as eating.

Finally, changing a person's eating simulations may play important roles in changing their eating behavior. For example, decreasing taste and reward simulations for unhealthy foods and increasing them for healthy foods could contribute to a healthier diet. Increasing food simulations in general could contribute to treating AN, whereas decreasing them could contribute to treating BN and BED. Because the networks that underlie a given person's eating simulations are likely to be highly entrenched, disabling and replacing them with new networks offers significant challenges. Finding effective ways to develop and strengthen regulatory pathways in the dorsol control network is likely to also be critical for developing successful interventions.

Future directions. It is important to address the potential roles of additional brain areas outside the core eating network. Although the core eating network generally appears to underlie diverse eating phenomena, other brain areas undoubtedly become important as well. Under various conditions, additional brain regions areas are recruited that add functionality to the core eating network as required. As we saw when people process cues for highly palatable foods, the hypothalamus tends to be active. As we saw when people pursue healthy eating, the mPFC can be recruited to help process health goals, thereby overcoming hedonic impulses. As Simmons, Rapuano, Ingeholm, et al., (2013) show, the ventral pallidum plays important roles in making reward inferences about food. Understanding how the core eating network reconfigures itself dynamically across different situations by recruiting additional neural resources is an important topic for future research.

Finally, only a few studies to date have explored the functional connectivity of the core eating network during rest and eating-related tasks (Boehm et al., 2014; García-García et al., 2013; Stoeckel et al., 2009; McFadden, Tregellas, Shott, & Frank, 2014). Thus, another important direction for future research is to more thoroughly examine the functional connectivity of food networks across the eating situations and populations reviewed here.

As BMI| increases, for example, does functional connectivity become relatively higher in the ventral reward pathway than in the dorsal control pathway? Direct evidence for functional (and perhaps anatomical) connectivity is essential for establishing greater confidence regarding the

presence of the ventral and dorsal pathways reviewed here. To the extent that such pathways are central for eating, connectivity between the relevant brain areas in each should be strong. Furthermore, connectivity strength should vary systematically across different eating situations and populations in ways that our accounts of these phenomena anticipate. To the extent that these networks can be better established and better understood, it should become increasingly possible to develop interventions that disrupt dysfunctional connectivity and train healthier connectivity.

References

Barros-Loscertales, A., Gonzalez, J., Pulvermuller, F., Ventura-Campos, N., Bustamante, J. C., Costumero, V., … Avila, C. (2012). Reading salt activates gustatory brain regions: fMRI evidence for semantic grounding in a novel sensory modality. *Cerebral Cortex*, *22*, 2554–2563.

Barsalou, L. W. (1999). Perceptual symbol systems. *Behavioral and Brain Sciences*, *22*, 577–660.

Barsalou, L. W. (2003). Situated simulation in the human conceptual system. *Language and Cognitive Processes*, *18*, 513–562.

Barsalou, L. W. (2008). Grounded cognition. *Annual Review of Psychology*, *59*, 617–645.

Barsalou, L. W. (2009). Simulation, situated conceptualization, and prediction. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *364*, 1281–1289.

Barsalou, L.W. (2010). Grounded cognition: Past, present, and future. *Topics in Cognitive Science, 2*, 716-724.

Barsalou, L. W. (in press). Situated conceptualization: Theory and application. In Y. Coello & M. H. Fischer, *Foundations of embodied cognition*. East Sussex: Psychology Press.

Batterink, L., Yokum, S., & Stice, E. (2010). Body mass correlates inversely with inhibitory control in response to food among adolescent girls: An fMRI study. *NeuroImage*, *52*, 1696–1703.

Batty, G. D., Shipley, M. J., Jarrett, R. J., Breeze, E., Marmot, M. G., & Smith, G. D. (2005). Obesity and overweight in relation to organ-specific cancer mortality in London (UK): findings from the original Whitehall study. *International Journal of Obesity*, *29*, 1267–1274.

Beaver, J. D., Lawrence, A. D., van Ditzhuijzen, J., Davis, M. H., Woods, A., & Calder, A. J. (2006). Individual differences in reward drive predict neural responses to images of food. *Journal of Neuroscience*, *26*, 5160–5166.

Blechert, J., Feige, B., Joos, A., Zeeck, A., & Tuschen-Caffier, B. (2011). Electrocortical processing of food and emotional pictures in anorexia nervosa and bulimia nervosa: *Psychosomatic Medicine*, *73*, 415–421.

Boehm, I., Geisler, D., King, J. A., Ritschel, F., Seidel, M., Deza Araujo, Y., … Ehrlich, S. (2014). Increased resting state functional connectivity in the fronto-parietal and default mode network in anorexia nervosa. *Frontiers in Behavioral Neuroscience*, *8*:346.

Botvinick, M. M., Cohen, J. D., & Carter, C. S. (2004). Conflict monitoring and anterior cingulate cortex: an update. *Trends in Cognitive Sciences*, *8*, 539–546.

Bragulat, V., Dzemidzic, M., Bruno, C., Cox, C. A., Talavage, T., Considine, R. V., & Kareken, D. A. (2010). Food-related odor probes of brain reward circuits during hunger: A pilot fMRI study. *Obesity*, *18*, 1566–1571.

Brooks, S. J., Cedernaes, J., & Schiöth, H. B. (2013). Increased prefrontal and parahippocampal activation with reduced dorsolateral prefrontal and insular cortex activation to food images in obesity: A meta-analysis of fMRI studies. *PLoS ONE*, *8*, e60393.

Brooks, S. J., O′Daly, O. G., Uher, R., Friederich, H. C., Giampietro, V., Brammer, M., … Campbell, I. C. (2011). Differential neural responses to food images in women with bulimia versus anorexia Nervosa. *PLoS ONE*, *6*, e22259.

Brooks, S. J., O'Daly, O., Uher, R., Friederich, H. C., Giampietro, V., Brammer, M., … Campbell, I. C. (2012). Thinking about eating food activates visual cortex with reduced bilateral cerebellar activation in females with anorexia nervosa: An fMRI study. *PLoS ONE*, *7*, e34000.

Brooks, S., Prince, A., Stahl, D., Campbell, I. C., & Treasure, J. (2011). A systematic review and meta-analysis of cognitive bias to food stimuli in people with disordered eating behaviour. *Clinical Psychology Review*, *31*, 37–51.

Bruce, A. S., Holsen, L. M., Chambers, R. J., Martin, L. E., Brooks, W. M., Zarcone, J. R., … Savage, C. R. (2010). Obese children show hyperactivation to food pictures in brain networks linked to motivation, reward and cognitive control. *International Journal of Obesity*, *34*, 1494–1500.

Burger, K. S., & Stice, E. (2011). Relation of dietary restraint scores to activation of reward-related brain regions in response to food intake, anticipated intake, and food pictures. *NeuroImage*, *55*, 233–239.

Coletta, M., Platek, S., Mohamed, F. B., van Steenburgh, J. J., Green, D., & Lowe, M. R. (2009). Brain activation in restrained and unrestrained eaters: An fMRI study. *Journal of Abnormal Psychology*, *118*, 598–609.

Cornier, M. A., Salzberg, A. K., Endly, D. C., Bessesen, D. H., Rojas, D. C., & Tregellas, J. R. (2009). The effects of overfeeding on the neuronal response to visual food cues in thin and reduced-obese Individuals. *PLoS ONE*, *4*, e6310.

Cornier, M. A., Von Kaenel, S. S., Bessesen, D. H., & Tregellas, J. R. (2007). Effects of overfeeding on the neuronal response to visual food cues. *The American Journal of Clinical Nutrition*, *86*, 965–971.

Culham, J. C., & Kanwisher, N. G. (2001). Neuroimaging of cognitive functions in human parietal cortex. *Current Opinion in Neurobiology*, *11*, 157–163.

Davids, S., Lauffer, H., Thoms, K., Jagdhuhn, M.,

Hirschfeld, H., Domin, M., … Lotze, M. (2010). Increased dorsolateral prefrontal cortex activation in obese children during observation of food stimuli. *International Journal of Obesity*, *34*, 94–104.

Dimitropoulos, A., Tkach, J., Ho, A., & Kennedy, J. (2012). Greater corticolimbic activation to high-calorie food cues after eating in obese vs. normal-weight adults. *Appetite*, *58*, 303–312.

Eiler, W. J. A., Dzemidzic, M., Case, K. R., Considine, R. V., & Kareken, D. A. (2012). Correlation between ventromedial prefrontal cortex activation to food aromas and cue-driven eating: An fMRI study. *Chemosensory Perception*, *5*, 27–36.

Ely, A. V., Childress, A. R., Jagannathan, K., & Lowe, M. R. (2014). Differential reward response to palatable food cues in past and current dieters: A fMRI study. *Obesity*, *22*, E38–E45.

Frank, G. K., Kaye, W. H., Carter, C. S., Brooks, S., May, C., Fissell, K., & Stenger, V. A. (2003). The evaluation of brain activity in response to taste stimuli—a pilot study and method for central taste activation as assessed by event-related fMRI. *Journal of Neuroscience Methods*, *131*, 99–105.

Führer, D., Zysset, S., & Stumvoll, M. (2008). Brain activity in hunger and satiety: An exploratory visually stimulated fMRI study. *Obesity*, *16*, 945–950.

García-García, I., Horstmann, A., Jurado, M. A., Garolera, M., Chaudhry, S. J., Margulies, D. S., … Neumann, J. (2014). Reward processing in obesity, substance addiction and non-substance addiction: Obesity, addictions and reward. *Obesity Reviews*, *15*, 853–869.

García-García, I., Jurado, M. Á., Garolera, M., Segura, B., Sala-Llonch, R., Marqués-Iturria, I., … Junqué, C. (2013). Alterations of the salience network in obesity: A resting-state fMRI study: Salience network and obesity. *Human Brain Mapping*, *34*, 2786–2797.

García-García, I., Narberhaus, A., Marqués-Iturria, I., Garolera, M., Răduoi, A., Segura, B., … Jurado, M. A. (2013). Neural responses to visual food cues: Insights from functional magnetic resonance imaging. *European Eating Disorders Review*, *21*, 89–98.

Gearhardt, A. N., Yokum, S., Orr, P. T., Stice, E., Corbin, W. R., & Brownell, K. D. (2011). Neural correlates of food addiction. *Archives of General Psychiatry*, *68*, 808.

Giel, K. E., Friederich, H.-C., Teufel, M., Hautzinger, M., Enck, P., & Zipfel, S. (2011). Attentional processing of food pictures in individuals with anorexia nervosa—an eye-tracking study. *Biological Psychiatry*, *69*, 661–667.

Giuliani, N. R., Mann, T., Tomiyama, A. J., & Berkman, E. T. (2014). Neural systems underlying the reappraisal of personally craved foods. *Journal of Cognitive Neuroscience*, *26*, 1390–1402.

Goldstone, A. P., Prechtl de Hernandez, C. G., Beaver, J. D., Muhammed, K., Croese, C., Bell, G., … Bell, J. D. (2009). Fasting biases brain reward systems towards high-calorie foods. *European Journal of Neuroscience*, *30*, 1625–1635.

Grosshans, M., Vollmert, C., Vollstädt-Klein, S., Tost, H., Leber, S., Bach, P., … Kiefer, F. (2012). Association of leptin with food cue–induced activation in human reward pathways. *Archives of General Psychiatry*, *69*, 529–537.

Hare, T. A., Malmaud, J., & Rangel, A. (2011). Focusing attention on the health aspects of foods changes value signals in vmPFC and improves dietary choice. *Journal of Neuroscience, 31*, 11077–11087.

Hege, M.A., Stingl, K.T., & Preissl, H. (2014). Food meets brain. *Magnoencephelography*, 901-920.

Holsen, L. M., Zarcone, J. R., Brooks, W. M., Butler, M. G., Thompson, T. I., Ahluwalia, J. S., … Savage, C. R. (2006). Neural mechanisms underlying hyperphagia in Prader-Willi syndrome. *Obesity*, *14*, 1028–1037.

Holsen, L. M., Zarcone, J. R., Thompson, T. I., Brooks, W. M., Anderson, M. F., Ahluwalia, J. S., … Savage, C. R. (2005). Neural mechanisms underlying food motivation in children and adolescents. *Neuroimage*, *27*, 669–676.

Hoogeveen, H. R., Dalenberg, J. R., Renken, R. J., ter Horst, G. J., & Lorist, M. M. (2015). Neural processing of basic tastes in healthy young and older adults — an fMRI study. *NeuroImage, 119*, 1–12.

Jakobsdottir, S., de Ruiter, M., Deijen, J. B., Veltman, D. J., & Drent, M. L. (2012). Brain activation by visual food-related stimuli and correlations with metabolic and hormonal parameters: A fMRI study. *The Open Neuroendocrinology Journal*, *5*, 5–12.

Kaye, W. H., Fudge, J. L., & Paulus, M. (2009). New insights into symptoms and neurocircuit function of anorexia nervosa. *Nature Reviews Neuroscience*, *10*, 573–584.

Kaye, W. H., Wagner, A., Frank, G., Bailer, U. F., Wonderlich, S., Mitchell, J. E., … Steiger, H. (2006). Review of brain imaging in anorexia and bulimia nervosa. *Annual Review of Eating Disorders: Part*, *2*, 113–129.

Kaye, W. H., Wagner, A., Fudge, J. L., & Paulus, M. (2010). Neurocircuity of eating disorders. In R. A. H. Adan & W. H. Kaye (Eds.), *Behavioral Neurobiology of Eating Disorders* (Vol. 6, pp. 37–57). Berlin, Heidelberg: Springer Berlin Heidelberg.

Kaye, W. H., Wierenga, C. E., Bailer, U. F., Simmons, A. N., & Bischoff-Grethe, A. (2013). Nothing tastes as good as skinny feels: the neurobiology of anorexia nervosa. *Trends in Neurosciences*, *36*, 110–120.

Killgore, W. D. S., Weber, M., Schwab, Z. J., Kipman, M., DelDonno, S. R., Webb, C. A., & Rauch, S. L. (2013). Cortico-limbic responsiveness to high-calorie food images predicts weight status among women. *International Journal of Obesity*, *37*, 1435–1442.

Killgore, W. D. S., & Yurgelun-Todd, D. A. (2005). Developmental changes in the functional brain responses of adolescents to images of high and

low-calorie foods. *Developmental Psychobiology*, *47*, 377–397.
Killgore, W. D. ., Young, A. D., Femia, L. A., Bogorodzki, P., Rogowska, J., & Yurgelun-Todd, D. A. (2003). Cortical and limbic activation during viewing of high- versus low-calorie foods. *NeuroImage*, *19*, 1381–1394.
Kringelbach, M. L. (2004). Food for thought: hedonic experience beyond homeostasis in the human brain. *Neuroscience*, *126*, 807-819.
Kringelbach, M. L., O'Doherty, J., Rolls, E. T., & Andrews, C. (2003). Activation of the human orbitofrontal cortex to a liquid food stimulus is correlated with its subjective pleasantness. *Cerebral Cortex*, *13*, 1064–1071.
Kringelbach, M. L., Stein, A., & van Hartevelt, T. J. (2012). The functional human neuroanatomy of food pleasure cycles. *Physiology & behavior*, *106*, 307-316.
Kroemer, N. B., Krebs, L., Kobiella, A., Grimm, O., Pilhatsch, M., Bidlingmaier, M., … Smolka, M. N. (2013). Fasting levels of ghrelin covary with the brain response to food pictures. *Addiction Biology*, *18*, 855–862.
LaBar, K. S., Gitelman, D. R., Parrish, T. B., Kim, Y.-H., Nobre, A. C., & Mesulam, M. M. (2001). Hunger selectively modulates corticolimbic activation to food stimuli in humans. *Behavioral Neuroscience*, *115*, 493–500.
Lebois, L. A. M., Wilson-Mendenhall, C. D., & Barsalou, L. W. (2015). Are automatic conceptual cores the gold standard of semantic processing? The context-dependence of spatial meaning in grounded congruency effects. *Cognitive Science, 39,* 1764-1801.
Lindquist, K. A., Wager, T. D., Kober, H., Bliss-Moreau, E., & Barrett, L. F. (2012). The brain basis of emotion: A meta-analytic review. *Behavioral and Brain Sciences*, *35*, 121–143.
Malik, S., McGlone, F., Bedrossian, D., & Dagher, A. (2008). Ghrelin modulates brain activity in areas that control appetitive behavior. *Cell Metabolism*, *7*, 400-409.
Marteau, T. M., Hollands, G. J., & Fletcher, P. C. (2012). Changing human behavior to prevent disease: the importance of targeting automatic processes. *Science (New York, N.Y.)*, *337*, 1492–1495.
Martin, A. (2007). The representation of object concepts in the brain. *Annual Review of Psychology, 58*, 25–45.
Martin, L. E., Holsen, L. M., Chambers, R. J., Bruce, A. S., Brooks, W. M., Zarcone, J. R., … Savage, C. R. (2010). Neural mechanisms associated with food motivation in obese and healthy weight adults. *Obesity*, *18*, 254–260.
McFadden, K., Tregellas, J., Shott, M., & Frank, G. (2014). Reduced salience and default mode network activity in women with anorexia nervosa. *Journal of Psychiatry & Neuroscience*, *39*, 178–188.
Miller, E. K. (2000). The prefontral cortex and cognitive control. *Nature Reviews Neuroscience*, *1*, 59–65.
Miller, J. L., James, G. A., Goldstone, A. P., Couch, J. A., He, G., Driscoll, D. J., & Liu, Y. (2007). Enhanced activation of reward mediating prefrontal regions in response to food stimuli in Prader-Willi syndrome. *Journal of Neurology, Neurosurgery & Psychiatry*, *78*, 615–619.
Mohanty, A., Gitelman, D. R., Small, D. M., & Mesulam, M. M. (2008). The spatial attention network interacts with limbic and monoaminergic systems to modulate motivation-induced attention shifts. *Cerebral Cortex*, *18*, 2604–2613.
Murdaugh, D. L., Cox, J. E., Cook, E. W., & Weller, R. E. (2012). fMRI reactivity to high-calorie food pictures predicts short- and long-term outcome in a weight-loss program. *NeuroImage*, *59*, 2709–2721.
Murray, E. A., O'Doherty, J. P., & Schoenbaum, G. (2007). What we know and do not know about the functions of the orbitofrontal cortex after 20 years of cross-species studies. *Journal of Neuroscience*, *27*, 8166–8169.
O'Doherty, J. (2004). Dissociable roles of ventral and dorsal striatum in instrumental conditioning. *Science*, *304*, 452–454.
O'Hara, C. B., Campbell, I. C., & Schmidt, U. (2015). A reward-centred model of anorexia nervosa: A focussed narrative review of the neurological and psychophysiological literature. *Neuroscience & Biobehavioral Reviews, 52*, 131–152.
Papies, E. K. (2013). Tempting food words activate eating simulations. *Frontiers in Psychology*, *4*, 1–12.
Papies, E. K., & Barsalou, L. W. (2015). Grounding desire and motivated behavior: A theoretical framework and review of empirical evidence. In W. Hofmann & L. F. Nordgren, *The psychology of desire* (pp. 36-60). New York: Guilford Press.
Papies, E. K., & Hamstra, P. (2010). Goal priming and eating behavior: Enhancing self-regulation by environmental cues. *Health Psychology*, *29*, 384–388.
Papies, E. K., Potjes, I., Keesman, M., Schwinghammer, S., & van Koningsbruggen, G. M. (2014). Using health primes to reduce unhealthy snack purchases among overweight consumers in a grocery store. *International Journal of Obesity*, *38*, 597–602.
Papies, E.K., Pronk, T.M., Keesman, M., & Barsalou, L.W. (2015). The benefits of simply observing: Mindful attention modulates the link between motivation and behavior. *Journal of Personality and Social Psychology, 108*, 148-170.
Papies, E. K., & Veling, H. (2013). Healthy dining. Subtle diet reminders at the point of purchase increase low-calorie food choices among both chronic and current dieters. *Appetite*, *61*, 1–7.
Passamonti, L., Rowe, J. B., Schwarzbauer, C., Ewbank, M. P., von dem Hagen, E., & Calder, A. J. (2009). Personality predicts the brain's response to viewing appetizing foods: The neural basis of a risk factor for overeating. *Journal of Neuroscience*, *29*, 43–51.
Pelchat, M. L., Johnson, A., Chan, R., Valdez, J., & Ragland, J. D. (2004). Images of desire: food-craving activation during fMRI. *NeuroImage*, *23*, 1486–1493.

Pietrini, F., Castellini, G., Ricca, V., Polito, C., Pupi, A., & Faravelli, C. (2011). Functional neuroimaging in anorexia nervosa: A clinical approach. *European Psychiatry*, *26*, 176–182.

Rothemund, Y., Preuschhof, C., Bohner, G., Bauknecht, H.-C., Klingebiel, R., Flor, H., & Klapp, B. F. (2007). Differential activation of the dorsal striatum by high-calorie visual food stimuli in obese individuals. *NeuroImage*, *37*, 410–421.

Rudebeck, P. H., & Murray, E. A. (2014). The Orbitofrontal Oracle: Cortical mechanisms for the prediction and evaluation of specific behavioral outcomes. *Neuron*, *84*, 1143–1156.

Sanders, N., Smeets, P. A. M., van Elburg, A. A., Danner, U. N., van Meer, F., Hoek, H. W., & Adan, R. A. H. (2015). Altered food-cue processing in chronically ill and recovered women with anorexia nervosa. *Frontiers in Behavioral Neuroscience*, *9*, 46.

Santel, S., Baving, L., Krauel, K., Münte, T. F., & Rotte, M. (2006). Hunger and satiety in anorexia nervosa: fMRI during cognitive processing of food pictures. *Brain Research*, *1114*, 138–148.

Scharmüller, W., Übel, S., Ebner, F., & Schienle, A. (2012). Appetite regulation during food cue exposure: A comparison of normal-weight and obese women. *Neuroscience Letters*, *518*, 106–110.

Schienle, A., Schäfer, A., Hermann, A., & Vaitl, D. (2009). Binge-eating disorder: Reward sensitivity and brain activation to images of food. *Biological Psychiatry*, *65*, 654–661.

Schur, E. A., Kleinhans, N. M., Goldberg, J., Buchwald, D., Schwartz, M. W., & Maravilla, K. (2009). Activation in brain energy regulation and reward centers by food cues varies with choice of visual stimulus. *International Journal of Obesity*, *33*, 653–661.

Shafran, R., Lee, M., Cooper, Z., Palmer, R. L., & Fairburn, C. G. (2007). Attentional bias in eating disorders. *International Journal of Eating Disorders*, *40*, 369–380.

Sherman, J. W., Gawronski, B., & Trope, Y. (2014). *Dual-process theories of the social mind*. New York: The Guilford Press.

Siep, N., Roefs, A., Roebroeck, A., Havermans, R., Bonte, M., & Jansen, A. (2012). Fighting food temptations: The modulating effects of short-term cognitive reappraisal, suppression and up-regulation on mesocorticolimbic activity related to appetitive motivation. *NeuroImage*, *60*, 213–220.

Siep, N., Roefs, A., Roebroeck, A., Havermans, R., Bonte, M. L., & Jansen, A. (2009). Hunger is the best spice: An fMRI study of the effects of attention, hunger and calorie content on food reward processing in the amygdala and orbitofrontal cortex. *Behavioural Brain Research*, *198*, 149–158.

Simmons, W. K., Martin, A., & Barsalou, L. W. (2005). Pictures of appetizing foods activate gustatory cortices for taste and reward. *Cerebral Cortex*, *15*, 1602–1608.

Simmons, W. K., Rapuano, K. M., Ingeholm, J. E., Avery, J., Kallman, S., Hall, K. D., & Martin, A. (2013). The ventral pallidum and orbitofrontal cortex support food pleasantness inferences. *Brain Structure and Function*.

Simmons, W. K., Rapuano, K. M., Kallman, S. J., Ingeholm, J. E., Miller, B., Gotts, S. J., … Martin, A. (2013). Category-specific integration of homeostatic signals in caudal but not rostral human insula. *Nature Neuroscience*, *16*, 1551–1552.

Simon, J. J., Skunde, M., Wu, M., Schnell, K., Herpertz, S. C., Bendszus, M., … Friederich, H. C. (2015). Neural dissociation of food- and money-related reward processing using an abstract incentive delay task. *Social Cognitive and Affective Neuroscience*.

Stefano, G. B., Ptáček, R., Kuželová, H., Mantione, K. J., Raboch, J., Papezova, H., & Kream. (2013). Convergent dysregulation of frontal cortical cognitive and reward systems in eating disorders. *Medical Science Monitor*, *19*, 353–358.

Stice, E., & Agras, W. S. (1998). Predicting onset and cessation of bulimic behaviors during adolescence: A longitudinal grouping analysis. *Behavior therapy*, *29*, 257-276.

Stice, E., Burger, K., & Yokum, S. (2013). Caloric deprivation increases responsivity of attention and reward brain regions to intake, anticipated intake, and images of palatable foods. *NeuroImage*, *67*, 322–330.

Stice, E., Davis, K., Miller, N. P., & Marti, C. N. (2008). Fasting increases risk for onset of binge eating and bulimic pathology: A 5-year prospective study. *Journal of Abnormal Psychology*, *117*, 941–946.

Stice, E., Spoor, S., Bohon, C., Veldhuizen, M. G., & Small, D. M. (2008). Relation of reward from food intake and anticipated food intake to obesity: A functional magnetic resonance imaging study. *Journal of Abnormal Psychology*, *117*, 924–935.

Stice, E., Spoor, S., Ng, J., & Zald, D. H. (2009). Relation of obesity to consummatory and anticipatory food reward. *Physiology & Behavior*, *97*, 551–560.

Stice, E., Yokum, S., Blum, K., & Bohon, C. (2010). Weight gain is associated with reduced striatal response to palatable food. *Journal of Neuroscience*, *30*, 13105–13109.

Stice, E., Yokum, S., Burger, K., Rohde, P., Shaw, H., & Gau, J. M. (2015). A pilot randomized trial of a cognitive reappraisal obesity prevention program. *Physiology & Behavior*, *138*, 124–132.

Stice, E., Yokum, S., Burger, K. S., Epstein, L. H., & Small, D. M. (2011). Youth at risk for obesity show greater activation of striatal and somatosensory regions to food. *Journal of Neuroscience*, *31*, 4360–4366.

Stockburger, J., Schmälzle, R., Flaisch, T., Bublatzky, F., & Schupp, H. T. (2009). The impact of hunger on food cue processing: an event-related brain potential study. *Neuroimage*, *47*, 1819–1829.

Stockburger, J., Weike, A. I., Hamm, A. O., & Schupp, H. T. (2008). Deprivation selectively

modulates brain potentials to food pictures. *Behavioral Neuroscience*, *122*, 936–942.
Stoeckel, L. E., Kim, J., Weller, R. E., Cox, J. E., Cook, E. W., & Horwitz, B. (2009). Effective connectivity of a reward network in obese women. *Brain Research Bulletin*, *79*, 388–395.
Stoeckel, L. E., Weller, R. E., Cook, E. W., Twieg, D. B., Knowlton, R. C., & Cox, J. E. (2008). Widespread reward-system activation in obese women in response to pictures of high-calorie foods. *NeuroImage*, *41*, 636–647.
St-Onge, M. P., Sy, M., Heymsfield, S. B., & Hirsch, J. (2005). Human cortical specialization for food: a functional magnetic resonance imaging investigation. *The Journal of Nutrition*, *135*, 1014–1018.
Suda, M., Uehara, T., Fukuda, M., Sato, T., Kameyama, M., & Mikuni, M. (2010). Dieting tendency and eating behavior problems in eating disorder correlate with right frontotemporal and left orbitofrontal cortex: A near-infrared spectroscopy study. *Journal of Psychiatric Research*, *44*, 547–555.
Szalay, C., Aradi, M., Schwarcz, A., Orsi, G., Perlaki, G., Németh, L., … Karadi, Z. (2012). Gustatory perception alterations in obesity: An fMRI study. *Brain Research*, *1473*, 131–140.
Tang, D. W., Fellows, L. K., Small, D. M., & Dagher, A. (2012). Food and drug cues activate similar brain regions: a meta-analysis of functional MRI studies. *Physiology & behavior*, *106*, 317-324.
Uher, R., Treasure, J., Heining, M., Brammer, M. J., & Campbell, I. C. (2006). Cerebral processing of food-related stimuli: Effects of fasting and gender. *Behavioural Brain Research*, *169*, 111–119.
Van den Eynde, F., & Treasure, J. (2009). Neuroimaging in eating disorders and obesity: Implications for research. *Child and Adolescent Psychiatric Clinics of North America*, *18*, 95–115.
Van der Laan, L. N., de Ridder, D. T. D., Viergever, M. A., & Smeets, P. A. M. (2011). The first taste is always with the eyes: A meta-analysis on the neural correlates of processing visual food cues. *NeuroImage*, *55*, 296–303.
Van Kuyck, K., Gérard, N., Laere, K. V., Casteels, C., Pieters, G., Gabriëls, L., & Nuttin, B. (2009). Towards a neurocircuitry in anorexia nervosa: Evidence from functional neuroimaging studies. *Journal of Psychiatric Research*, *43*, 1133–1145.
Vocks, S., Busch, M., Grönemeyer, D., Schulte, D., Herpertz, S., & Suchan, B. (2010). Neural correlates of viewing photographs of one's own body and another woman's body in anorexia and bulimia nervosa: an fMRI study. *Journal of psychiatry & neuroscience: JPN*, *35*, 163.
Vocks, S., Herpertz, S., Rosenberger, C., Senf, W., & Gizewski, E. R. (2011). Effects of gustatory stimulation on brain activity during hunger and satiety in females with restricting-type anorexia nervosa: An fMRI study. *Journal of Psychiatric Research*, *45*, 395–403.
Volkow, N. D., Wang, G. J., Fowler, J. S., Tomasi, D., & Baler, R. (2012). Food and drug reward: overlapping circuits in human obesity and addiction. In *Brain imaging in behavioral neuroscience* (pp. 1–24). Springer.
Volkow, N. D., Wang, G.-J., Tomasi, D., & Baler, R. D. (2013). Obesity and addiction: neurobiological overlaps: Overlaps between drug and food addiction. *Obesity Reviews*, *14*, 2–18.
Wadden, T. A., Brownell, K. D., & Foster, G. D. (2002). Obesity: Responding to the global epidemic. *Journal of Consulting and Clinical Psychology*, *70*, 510–525.
Wang, G. J., Volkow, N. D., Logan, J., Pappas, N. R., Wong, C. T., Zhu, W., … Fowler, J. S. (2001). Brain dopamine and obesity. *The Lancet*, *357*, 354–357.
Weygandt, M., Mai, K., Dommes, E., Ritter, K., Leupelt, V., Spranger, J., & Haynes, J. D. (2015). Impulse control in the dorsolateral prefrontal cortex counteracts post-diet weight regain in obesity. *NeuroImage*.
Weygandt, M., Schaefer, A., Schienle, A., & Haynes, J. D. (2012). Diagnosing different binge-eating disorders based on reward-related brain activation patterns. *Human Brain Mapping*, *33*, 2135–2146.
Wilson-Mendenhall, C. D., Barrett, L. F., Simmons, W. K., & Barsalou, L. W. (2011). Grounding emotion in situated conceptualization. *Neuropsychologia*, *49*, 1105–1127.
Woolley, J. D., Gorno-Tempini, M. L., Seeley, W. W., Rankin, K., Lee, S. S., Matthews, B. R., & Miller, B. L. (2007). Binge eating is associated with right orbitofrontal-insular-striatal atrophy in frontotemporal dementia. *Neurology*, *69*, 1424–1433.
Yokum, S., Ng, J., & Stice, E. (2011). Attentional bias to food images associated with elevated weight and future weight gain: An fMRI study. *Obesity*, *19*, 1775–1783.
Yokum, S., & Stice, E. (2013). Cognitive regulation of food craving: effects of three cognitive reappraisal strategies on neural response to palatable foods. *International Journal of Obesity*, *37*, 1565–1570.
Zhu, Y., Hu, X., Wang, J., Chen, J., Guo, Q., Li, C., & Enck, P. (2012). Processing of food, body and emotional stimuli in anorexia nervosa: A systematic review and meta-analysis of functional magnetic resonance imaging studies. *European Eating Disorders Review*, *20*, 439–450.

Figure Captions

Figure 1. Panel A: The neurocircuitry of eating, adapted from Figure 3 of Kaye et al. (2009). Our adaptation contains the same neural areas as Kaye et al.'s figure, with the same connections between them (although we ascribe slightly different roles to the areas, as indicated in red). Unlike Figure 3 in Kaye et al. (2009), our adaptation explicitly indicates the ventral reward pathway and the dorsal control pathway central in their account. Please see the text for discussion of how these pathways operate. **Panel B:** The *core eating network* that, with various modulations, underlies a wide variety of eating phenomena to be reviewed. Whereas the eating network in Panel A is specialized for gustatory sensing in neuroimaging taste experiments, the core eating network in Panel B assumes that visual processing typically occurs across eating phenomena (even when foods are tasted, smelled, and/or heard), making this the core network. The core eating network is also the network typically operative when visual food cues are encountered, as in many neuroimaging experiments that examine the neural bases of the eating phenomena reviewed. In Figure 1b, the original connections between brain areas in Figure 1a (from Kaye et al.'s (2009) Figure 3) have been removed, given that these connections are not relevant for our review, nor are we committed to them. These original pathways have been replaced with one arrow that represents processing along the ventral reward pathway, and a second arrow that represents processing along the dorsal control pathway. OFC, orbitofrontal cortex; ACC, anterior cingulate cortex; dlPFC, dorsolateral prefrontal cortex; NTS, nucleus tractus solitarii.

Figure 2. Modulations of the core eating network from Figure 1b as a function of food significance (palatability and hunger). **Panel A:** Modulation of the core eating network in response to highly palatable foods (i.e., food that tend to high-calorie and energy-dense) relative to less palatable foods. **Panel B:** Modulation of the core eating network in response to hunger relative to satiety. As both panels illustrate, food significance tends to associated with stronger neural responses in the ventral reward pathway. Fully red boxes indicate relatively consistent increases in activation across experiments; half red boxes indicate less consistent increases in activation. OFC, orbitofrontal cortex; ACC, anterior cingulate cortex; dlPFC, dorsolateral prefrontal cortex.

Figure 3. Modulations of the core eating network from Figure 1b as a function of increasing BMI (Body Mass Index). **Panel A:** Modulation of the core eating network in response to food cues as BMI increases from low to high body weight. Increasing BMI tends to be associated with increased neural activity in the ventral reward pathway to food cues (fully red boxes), although neural responses in the insula do not always increase and are sometimes blunted (half-red half-blue box). Increasing BMI has also been associated with modulations of dlPFC activity, including both stronger and weaker responses in different experiments (half-red half-blue box). **Panel B:** Modulation of the core eating network during actual eating as BMI increases from low to high body weight. Increasing BMI has been associated with changes in the ventral reward pathway during eating, sometimes taking the form of stronger responses and sometimes taking the form of blunted responses (half-red half-blue boxes). OFC, orbitofrontal cortex; ACC, anterior cingulate cortex; dlPFC, dorsolateral prefrontal cortex.

Figure 4. Modulations of the core eating network from Figure 1b in two eating disorders. **Panel A:** Modulation of the core eating network in anorexia nervosa (AN) relative to normal eaters. Neural responses in the dorsal control pathway often increase to regulate eating (dlPFC) based on body image (parietal). Some experiments further report decreased responses in the ventral reward pathway (half-blue box). Early in the processing of visual food cues, visual activity increases; later in processing, visual activity decreases (half-red half-blue boxes). **Panel B:** Modulation of the core eating network in bulimia nervosa (BN) relative to normal eaters. Neural responses in BN are similar to those in AN, exhibiting increased

regulatory processing in the dorsal control pathway. BN differs in also being associated with increased neural responses in the ventral reward pathway and also in visual processing. OFC, orbitofrontal cortex; ACC, anterior cingulate cortex; dlPFC, dorsolateral prefrontal cortex.

Figure 5. Modulations of the core eating network from Figure 1b in two additional eating phenomena. **Panel A:** Modulation of the core eating network in binge eating disorder (BED) relative to normal eaters. Neural responses in the ventral reward pathway tend to increase, illustrating greater interest in food consumption. Unlike AN and BN, neural responses in the dorsal control pathway do not increase, indicating less interest in regulating food intake. **Panel B:** Modulation of the core eating network in restrained eating (dieting) relative to normal eaters. Like BED, neural responses in the ventral reward pathway again tend to increase. Unlike BED, neural responses in the dorsal control pathway also increase, demonstrating an interest in regulating interest in food and food intake.

Footnotes

[1] Because the number of articles relevant to this section is relatively small, all the ones that we know of are reviewed here, thereby making a table listing all the research in the area unnecessary.

[2] Because the number of articles relevant to this section is again relatively small, all the ones that we know of are reviewed here, thereby making a table listing all the research in the area unnecessary.

Table 1

Articles that assessed neural responses to food cues (foods vs. nonfoods).

Article (authors/year of publication)	Participants	Food stimuli	Nonfood stimuli	Task	Relevant results (foods >nonfoods)
Pictures					
Beaver et al., 2006	14 HC fasting for 2h	appetizing foods disgusting foods bland foods	objects	passively view pictures	OFC, posterior insula, precentral gyrus, parahippocampal gyrus, anterior STS, posterior STS fusiform gyrus, cuneus, precuneus, vmPFC, dlPFC
Cornier et al., 2007 (eucaloric condition)	25 thin healthy adults overnight fasting	high hedonic foods neutral hedonic foods	objects (animals, trees, books, furniture, buildings)	passively view pictures	neutral > object: insula, dlPFC
Cornier et al., 2009 (control group)	22 thin HC 19 reduced-obese adults, overnight fasting	high hedonic foods neutral hedonic foods	objects (animals, trees, books, furniture, buildings)	passively view pictures	insula, inferior visual cortex, parietal cortex, postcentral cortex, OFC, IFG, MFG, ventral striatum, hippocampus, cingulate gyrus
Davids et al., 2009 (control group)	22 obese/overweight 22 control children <2h or >2h fasting	foods	pleasant pictures (young animals, babies, etc.) neutral pictures (landscapes, buildings, work-related situations)	view pictures attentively	inferior occipital gyrus, superior occipital gyrus, superior parietal gyrus, SMA, superior temporal pole, vlPFC, IFG, insula, putamen, amygdala, hippocampus
Fuhrer et al., 2008	12 healthy lean males 1-h vs. 14-h fasting	foods	nonfoods not related to hand-mouth action	press a button for a target picture (image frame with no object)	anterior midprefrontal gyrus, inferior parietal lobe, cingulate cortex, PCC, ACC, insula, thalamus, cerebellum, posterior superior frontal sulcus, superior parietal lobe, posterior temporal gyrus, anterior midfrontal gyrus, posterior middle temporal gyrus, accumbens
Holsen et al., 2005	9 healthy children and adolescents 4-h fasting vs. after meal	foods	animals Gaussian-blurred images	remember images for memory task	pre-meal: medial OFC, lateral OFC, medial frontal cortex, superior parietal cortex, cerebellum/fusiform post-meal: STG, fusiform gyrus
Holsen et al., 2006 (control group)	9 with PWS 9 HC pre-meal (4-h fasting) vs. post-meal	foods	animals blurred control images	remember images for memory task	pre-meal: lateral OFC, posterior OFC, medial PFC, fusiform gyrus, STG, inferior parietal lobule, post-meal: posterior OFC, fusiform gyrus/cerebellum

Killgore et al., 2003	13 healthy women >1.5 h fasting	high-calorie foods low-calorie foods	nonedible dining-related utensils (e.g. forks)	remember images for memory task	insula, amygdala/hippocampus, post-central gyrus, cerebellum, fusiform gyrus, inferior occipital gyrus, medial frontal gyrus, transverse temporal gyrus, STG, precuneus, posterior cingulate
Killgore et al., 2005b	8 female children >1h fasting	high-calorie foods low-calorie foods	nonedible dining-related utensils (e.g. forks)	remember images for memory task	fusiform gyrus, inferior occipital gyrus, inferior orbitofrontal gyrus, parahippocampal gyrus, supramarginal gyrus, MTG, IFG, thalamus, inferior parietal lobe, rolandic operculum, STG, putamen
LaBar et al., 2001b	17 HC >8h fasting vs. 1h fasting	foods	tools Gaussian-blurred objects	press a button when object blinks	parahippocampal gyrus, fusiform gyrus, amygdala, extrastriate cortex, insula
Malik et al., 2008 (control group)	20 healthy males 3h fasting	foods	scenery	focus attention on images	IFG/MFG, anterior insula, fusiform gyrus, inferior occipital gyrus, superior parietal lobule
Miller et al., 2007	8 adults with PWS 8 HC (control group)	foods	animals tools	passively view pictures	vmPFC, subcallosal cingulate cortex, visual cortex
Rothemund et al., 2007 (control group)	13 obese females 13 HC >1.5h fasting	high-calorie foods low-calorie foods	eating-related utensils neutral control	observe pictures attentively	low-calorie>control: ITG
Santel et al., 2006 (control group)	13 AN 10 HC 12 h vs. 1 h fasting	high-calorie foods	objects of use (tools, make-up items, pencils)	rate pleasantness	1h fasting: cuneus, middle occipital gyrus, inferior occipital gyrus 12h fasting: lingual gyrus, fusiform gyrus
Schienle et al., 2009 (control group)	17 BED females 14 BN females 19 HC 17 overweight control overnight fasting	high-calorie foods disgusting foods	household articles	passively view pictures	lingual gyrus, IFG, insula, ACC, lateral OFC, medial OFC, amygdala, ventral striatum
Schur et al., 2009	10 healthy women 2-4h fasted	'fattening" foods 'nonfattening' foods	not food-related objects (furniture, electronics, tools, household items)	remember images for memory task	brainstem, hypothalamus, amygdala, inferior frontal, insula, striatum(putamen, nucleus accumbens), thalamus occipital lobe
Simmons et al., 2005	9 HC	high-calorie foods	locations	one-back task (same or different)	insula, OFC, OFC/anterior cingulate, ITG, fusiform
St-Onge et al., 2005 (visual group)	12 HC >12h fasting	from high-calorie to low-calorie foods	office supplies, plastic toys, dolls	passively view pictures	cingulate gyrus, hippocampus/parahippocampal gyrus STG, insula, insula/caudate

Uher et al., 2006 (visual group)	18 HC 24h vs. <3h food fasting	pleasant and appetizing foods	non-edible objects	rate liking	fusiform gyrus, lingual gyrus, angular gyrus, anterior insula
van der Laan et al., 2012	meta-analysis				posterior fusiform gyrus, inferior occipital gyrus, IFG/lateral OFC, middle insula cortex
Words					
Barros-Loscertales et al., 2012	59 native Spanish speakers	taste-related words	control words	passive reading task	insula, forntal operculum/lateral OFC, STG/angular gyrus, posterior cingulate, precentral/middle frontal gyrus, superior PFC, SFG/MFG, cuneus/precuneus, substantia nigra, subthalamic nucleus/thalamus
Pelchat et al., 2004	20 HC 10 monotonous diet 10 normal diet	2 'really like' foods	monotonous foods	think about the favorite version of the food	monotonous diet group: fusiform gyrus, parahippocampal gyrus, amygdala, caudate nucleus, putamen, cingulate gyrus

HC = healthy controls, PWS= Prader-Willi syndrome, AN = anorexia nervosa, BED = binge eating disorder

BN = bulimia nervosa

ACC = anterior cingulate cortex; OFC = orbitofrontal cortex; IFG = inferior frontal gyrus, MFG = middle frontal gyrus, SFG = superior frontal gyrus, ITG = inferior temporal gyrus,

MTG = middle temporal gyrus, STG = superior temporal gyrus, PFC = prefrontal cortex, dlPFC = dorsolateral prefrontal cortex, PCC = posterior cingulate cortex

STS = superior temporal sulcus, vmPFC = ventromedial prefrontal gyrus

Table 2

Articles that assessed the effect of palatability on neural responses to food cue pictures (palatable vs. non-palatable foods).

Article (authors/year of publication)	**Participants**	**Conditions**	**Task**	**Relevant results** (high calorie foods > low calorie foods)
Beaver et al., 2006	14 HC fasting for 2h	appetizing foods disgusting foods bland foods nonfood objects	passively view pictures	appetizing > bland: ventral striatum, amygdala, midbrain, ventral pallidum
Cornier et al., 2007	25 thin healthy adults overnight fasting	high hedonic foods neutral hedonic foods neutral nonfood objects	passively view pictures	premotor cortex, inferior visual cortex, hypothalamus, parietal cortex, hippocampus
Goldstone et al., 2009	20 HC overnight fasting	high-calorie foods low-calorie foods non-food objects	rate the appeal of each picture	ventral striatum, amygdala, insula, medial and lateral OFC
Killgore et al., 2003	13 healthy female >1.5 h fasting	high-calorie foods low-calorie foods nonedible food-related utensils	view and try to remember	SFG, thalamus, MTG, medulla, cerebellum, middle occipital gyrus
Killgore et al., 2005b	8 healthy female children adolescents >1h fasting	high-calorie foods low-calorie foods nonedible food-related utensils	view and try to remember	midline anterior cingulate gyrus, cerebellum, MTG, cerebellar crus
Passamonti et al., 2009	21 HC ≥ 2h fasting	highly appetizing foods bland foods	indicate its position (L/R)	vACC, dlPFC, frontal pole, MTG, STG, PCC, ventral striatum, amygdala, extrastriate visual cortex
Rothemund et al., 2007	13 obese and 13 HC females >1.5h fasting	high-calorie foods low-calorie foods eating-related utensils neutral control items	view and try to remember	none in HC group
Schur et al., 2009	10 healthy adult women 2-4h after a meal	“fattening” foods “non-fattening” foods non-food objects	view and try to remember	brainstem, hypothalamus, amygdala, IFG, insula, striatum, thalamus, occipital pole

van der Laan et al., 2012 (meta-analysis)	hypothalamus, ventral striatum, cerebellum, frontal middle gyrus, middle occipital gyrus, ITG

HC = healthy controls

ACC = anterior cingulate cortex; OFC = orbitofrontal cortex; IFG = inferior frontal gyrus, SFG = superior frontal gyrus, ITG = inferior temporal gyrus, MTG = middle temporal gyrus,

STG = superior temporal gyrus, vACC = ventral anterior cingulate cortex , dlPFC = dorsolateral prefrontal cortex, PCC = posterior cingulate cortex

Table 3

Articles that assessed the effect of hunger on neural responses to food cue pictures (hunger vs. satiety).

Article (authors/year of publication)	**Participants**	**Conditions**	**Task**	**Relevant interaction results** (hunger vs. satiety) X (foods vs. nonfoods)
Führer et al., 2008	12 healthy lean males 14-h fasted vs. 1h	foods nonfoods	press a button on seeing an image frame with no object	ACC, superior occipital sulcus, pregenual cingulate cortex, amygdala, subcallosal gyrus, lateral OFC
Goldstone et al., 2009	20 HC overnight fasted vs. 1.6h fasted	high-calorie foods low-calorie foods non-food household objects Gaussian blurred images	rate how 'appealing'	high-calorie>low-calorie when fasted but not when fed: ventral-striatum, amygdala, insula, medial and lateral OFC
Holsen et al., 2005	9 healthy children and adolescents 4-h fasted vs. after meal	foods animals Gaussian blurred images	view and try to remember	amygdala, medial and lateral OFC, MFC, insula, basal operculum, parahippocampal gyrus, cingulate gyrus, fusiform gyrus, IFG, SFG, ITG, globus pallidus, postcentral gyrus, precentral gyrus, cerebellum
Jakobsdottir et al., 2012	15 healthy males 12-h fasted vs. 1h	foods nonfoods	judge indoor or outdoor	amygdala, fusiform gyrus, occipital cortex
Kroemer et al., 2012	26 HC overnight fasted vs. post-caloric load	high palatable foods scrambled pictures	rate appetite after each block	fusiform gyrus, IFG, thalamus, rolandic operculum, ACC, amygdala
LaBar et al., 2001	17 healthy adults >8h fasted vs. 1h after meal	foods tools Gaussian blurred objects	press a button when object blinks	parahippocampal gyrus, fusiform gyrus, amygdala
Mohanty et al., 2008	9 healthy adults >8h fasted vs. <1h fasted	foods tools	indicate target or foil	amygdala, posterior cingulate, parahippocampal gyrus, peristriate cortex, brainstem
Santel et al., 2006	13 AN females 10 control female self-report hunger scores	high-calorie foods objects of use	rate pleasantness	HC group, None
Siep et al., 2009	12 healthy females 18-h fasted vs. after meal	high calorie foods low calorie foods neutral objecst	rate liking	medial OFC, insula, PCC fusiform gyrus, caudate putamen

Uher et al., 2006	18 HC 23-h fasted vs. 3h fasted	foods non-edible objects	rate “how do you like the picture?”	None liberal threshold: bilateral fusiform gyrus
van der Laan et al., 2012 meta-analysis				parahippocampal gyrus, amygdala, IFG, lateral OFC

HC = healthy controls

IFG = inferior frontal gyrus, SFG = superior frontal gyrus, ITG = inferior temporal gyrus, ACC = anterior cingulate cortex, OFC = orbitofrontal cortex, MFG = middle frontal gyrus,

PCC = posterior cingulate cortex

Table 4

Articles that assessed the effect of BMI on neural responses to food cue pictures vs. actual eating (high BMI vs. low BMI).

Article (authors/year of publication)	**Participants**	**Conditions**	**Hunger**	**Satiety**	**Results** (obese > HC, or BMI positively correlated with brain activity) X (foods > nonfoods)
Food pictures: High BMI vs. low BMI groups					
Bruce et al., 2010	10 obese children 10 healthy children	foods animals Gaussian-blurred images	4-h fasting	post-meal	pre-meal: SFG, MFG, IFG post-meal: OFC
Davids et al., 2009	22 obese children 22 healthy children	foods pleasant pictures neutral pictures	in each group 15 were tested >2h fasting	in each group 7 were tested 2h after meal	dlPFC obese < HC: middle occipital gyrus, fusiform gyrus, ACC, caudate, hippocampus, parahippocampal gyrus, thalamus
Dimitropoulos et al., 2012	22obese/overweight 16HC	high-calorie foods low-calorie foods objects	5-8h fasting 3-7h fasting	post-meal	pre-meal: anterior PFC, post-meal: dlPFC, OFC, SFG, temporal.entorhinal cortex, STG, cerebellum-anterior lobe pre-meal: obese <HC: dlPFC, precentral gyrus, cingulate
Martin et al., 2009	10 obese adults 10 HC	foods animals Gaussian-blurred images	4-h fasting	post-meal	pre-meal: MPFC, medial frontal gyrus, MFG, ACC, IFG, cingulate, fusiform gyrus, cuneus, STG, MTG, occipital gyrus, cerebellum, brainstem pre-meal: obese<HC: STG, planum temporale post-meal: medial PFC, SFG, caudate, MTG, STG, hippocampus, precuneus
Stoeckel et al., 2008	12 obese women 12HC women	sweet and salty high-calorie foods low-calorie foods cars	8-9h fasting		high-calorie>car: medial OFC, lateral OFC, medial PFC, ACC, insula, NAc, amygdala, ventral pallidum, hippocampus, putamen high-calorie>car (obese< HC): medial PFC low-calorie>car: caudate, putamen low-calorie>car (obese<HC): lateral OFC, medial OFC, ACC

Food pictures: Continuous BMI				
Batterink et al., 2010	29 adolescent girls from lean to obese	vegetables (go trial) desserts (no-go trial)	4-6h fasting	negative correlation (no-go>fixation): SFG, MFG, vlPFC, medial PFC, OFC positive correlation (no-go>fixation): temporal and frontal operculum/insula
Grosshans et al., 2012	21 obese individuals 23 HC	salty high-calorie foods sweet high-calorie foods low-calorie foods	6h fasting	ROI analysis: ventral striatum
Rothemund et al., 2007	13 obese females 13 HC	high-calorie foods low-calorie foods eating-relateds neutral control s	1.5h fasting	high-calorie condition: putamen, caudate body, anterior insula, claustrum, PCC, postcentral gyrus, lateral OFC, lateral globus pallidus
Yokum et al., 2011	35 adolescent girls from lean to obese	appetizing foods least appetizing foods glass of water	4-6h fasting	orientation to appetizing food: mid insula, frontal operculum, anterior insula/frontal operculum, lateral OFC orientation to unappetizing food: vlPFC, frontal operculum, superior parietal lobe
Receipt of food				
Gearhardt et al., 2011	39 young women from lean to obese (15 high food addiction) 11 low food addiction)	picture of milkshake/water liquid milkshake/water		food addiction score correlated positively with cues: ACC, medial OFC, amygdala high>low food addiction (cue): dlPFC, caudate high<low food addiction (receipt): lateral OFC
Stice et al., 2008	33 girls from lean to obese	anticipated vs. actual receipt of milkshake	4-h fasting	anticipatory food reward (positive correlation): ventrolatereal PFC, dlPFC, temporal operculum receipt of food: insula/frontoparietal operculum, parietal operculum, caudate nucleus
Stice et al., 2011	60 lean adolescents 35/60 of high-risk of obesity	receipt vs. anticipated receipt of food reward or monetary reward	4-6h fasting	high-risk>low-risk (receipt of food): caudate, frontal operculum parietal operculum

HC = healthy controls

IFG = inferior frontal gyrus, OFC = orbitofrontal cortex, ACC = anterior cingulate cortex, PFC = prefrontal cortex, dlPFC = dorsolateral prefrontal cortex, SFG = superior frontal gyrus,

MFG = middle frontal gyrus, STG = superior temporal gyrus, MTG = middle temporal gyrus, NAc = nucleus accumbens/ventral striatum, PCC = posterior cingulate cortex

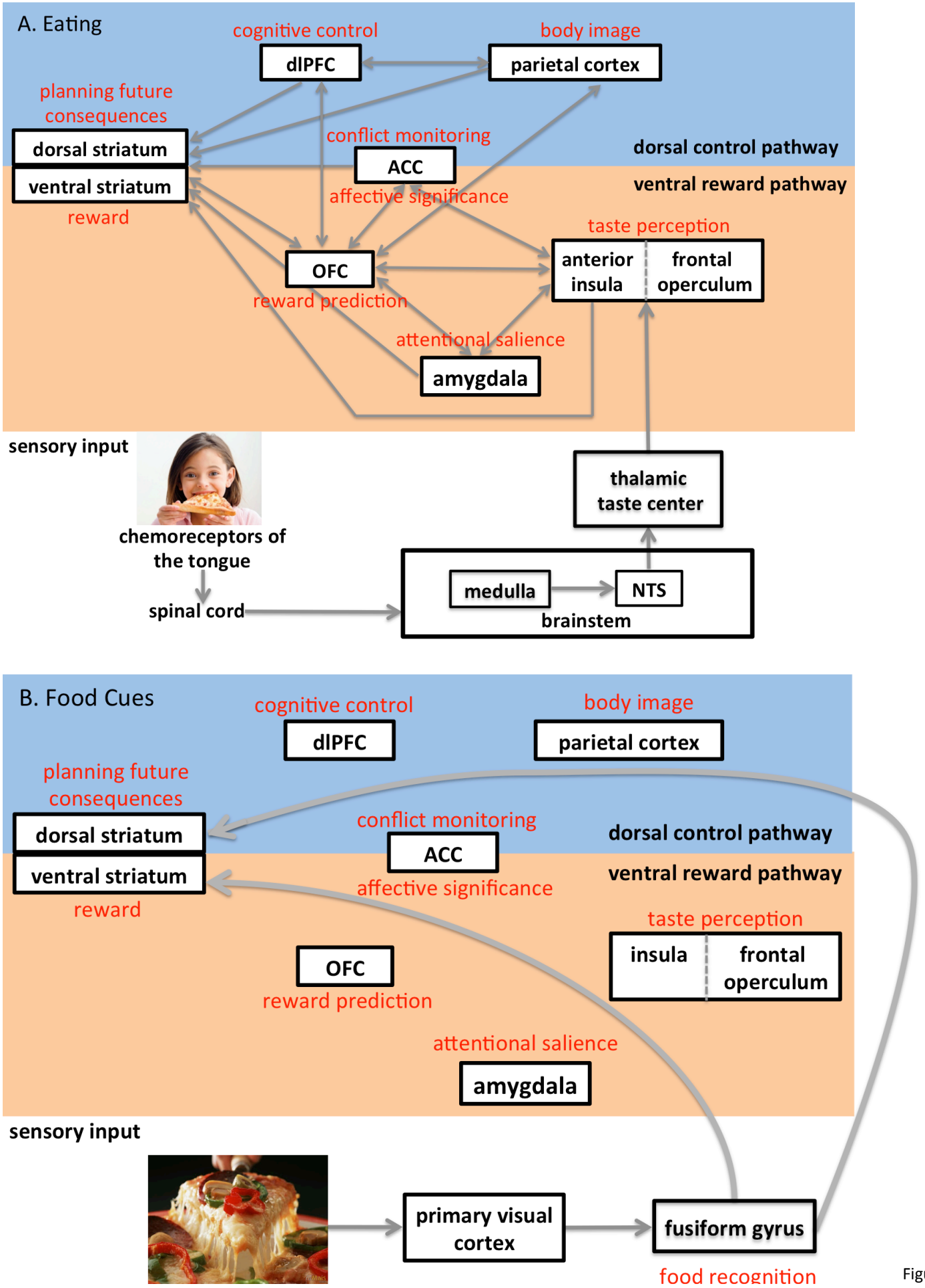
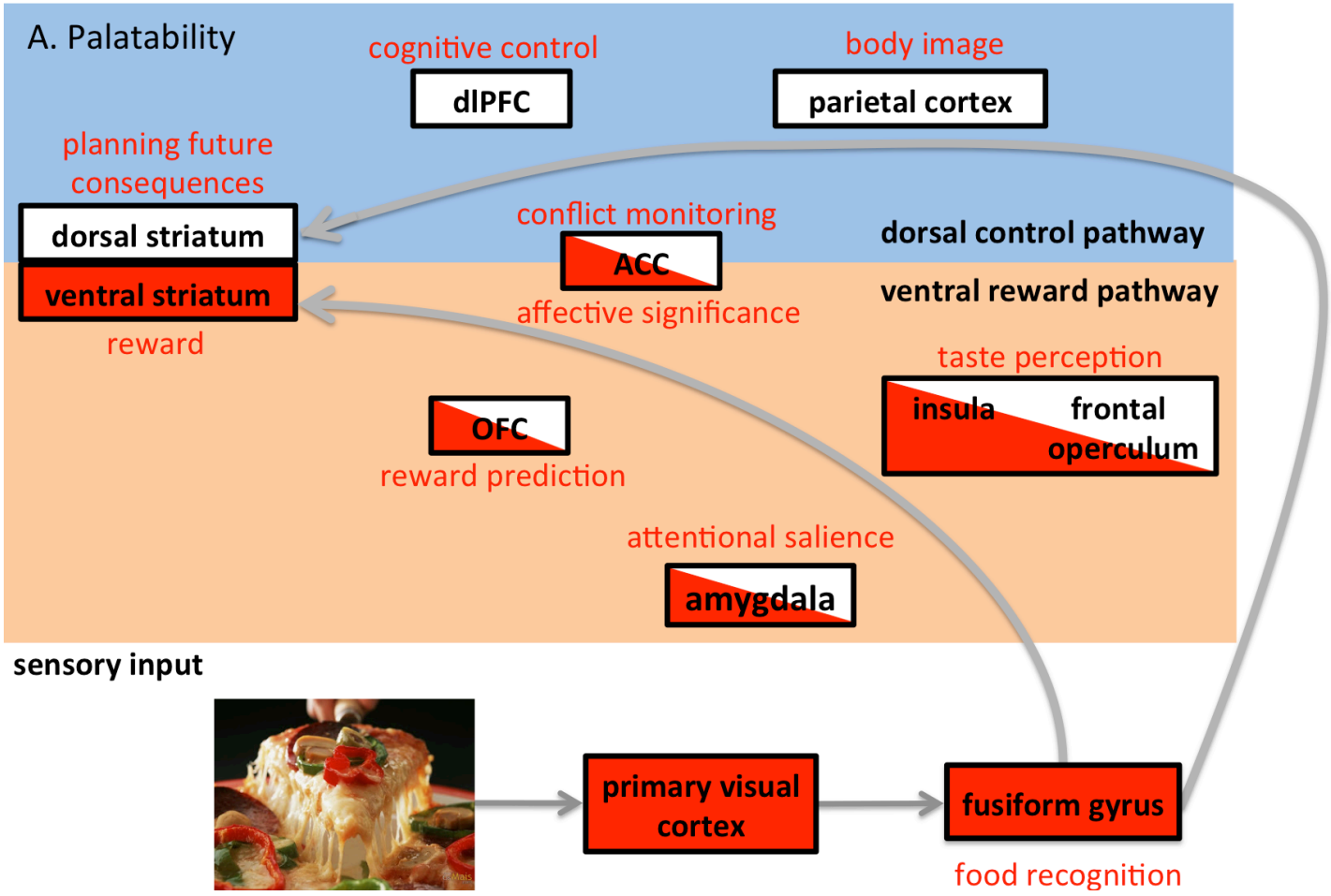

A. Eating
cognitive control
dlPFC
body image
parietal cortex
planning future consequences
dorsal striatum
ventral striatum
reward
conflict monitoring
ACC
affective significance
dorsal control pathway
ventral reward pathway
taste perception
anterior insula
frontal operculum
OFC
reward prediction
attentional salience
amygdala
sensory input
chemoreceptors of the tongue
spinal cord
thalamic taste center
medulla
NTS
brainstem
B. Food Cues
cognitive control
dlPFC
body image
parietal cortex
planning future consequences
dorsal striatum
ventral striatum
reward
conflict monitoring
ACC
affective significance
dorsal control pathway
ventral reward pathway
taste perception
insula
frontal operculum
OFC
reward prediction
attentional salience
amygdala
sensory input
primary visual cortex
fusiform gyrus
food recognition

Figure 1


A. Palatability
cognitive control
dlPFC
body image
parietal cortex
planning future consequences
dorsal striatum
ventral striatum
reward
conflict monitoring
ACC
affective significance
dorsal control pathway
ventral reward pathway
taste perception
insula
frontal operculum
OFC
reward prediction
attentional salience
amygdala
sensory input
primary visual cortex
fusiform gyrus
food recognition

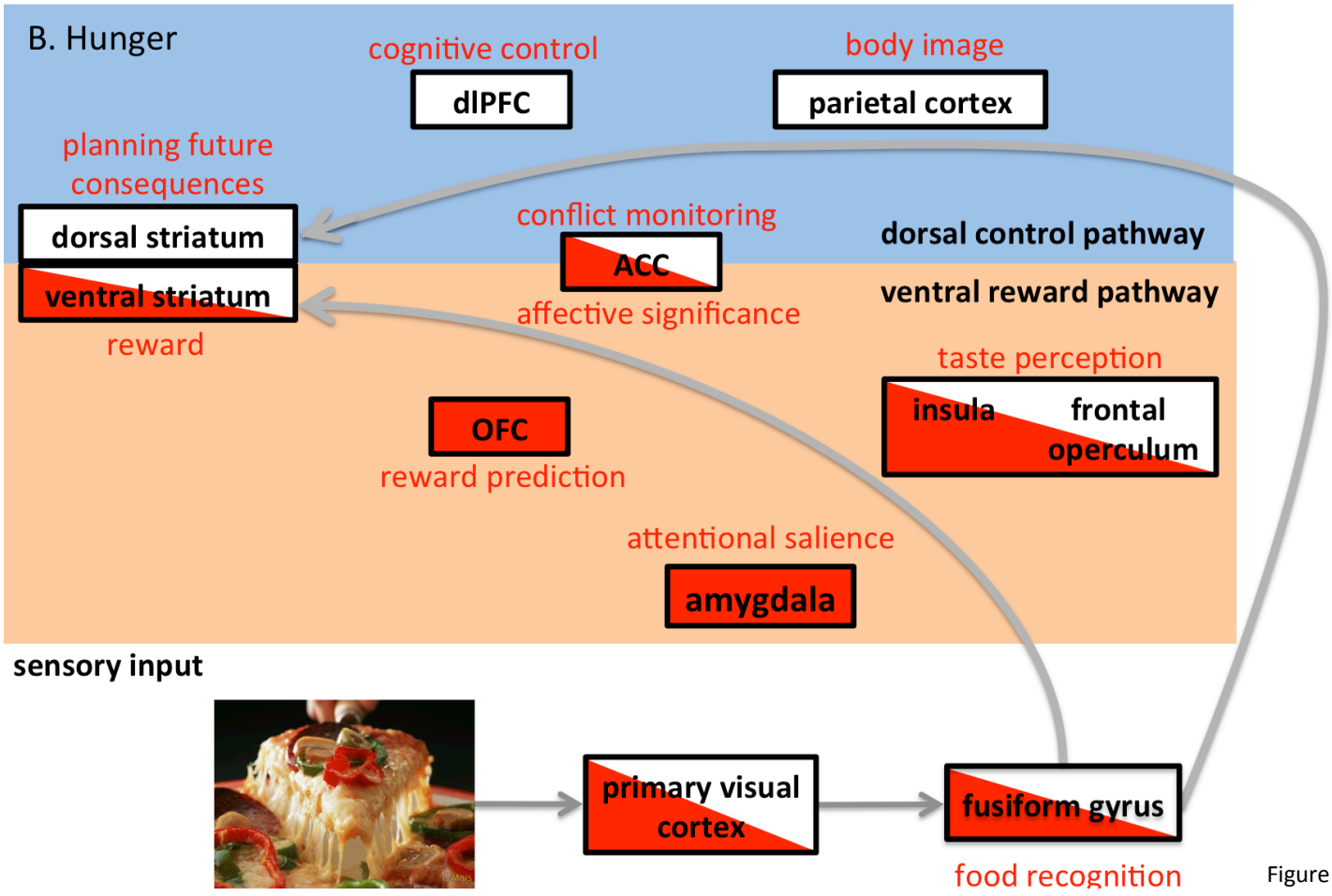
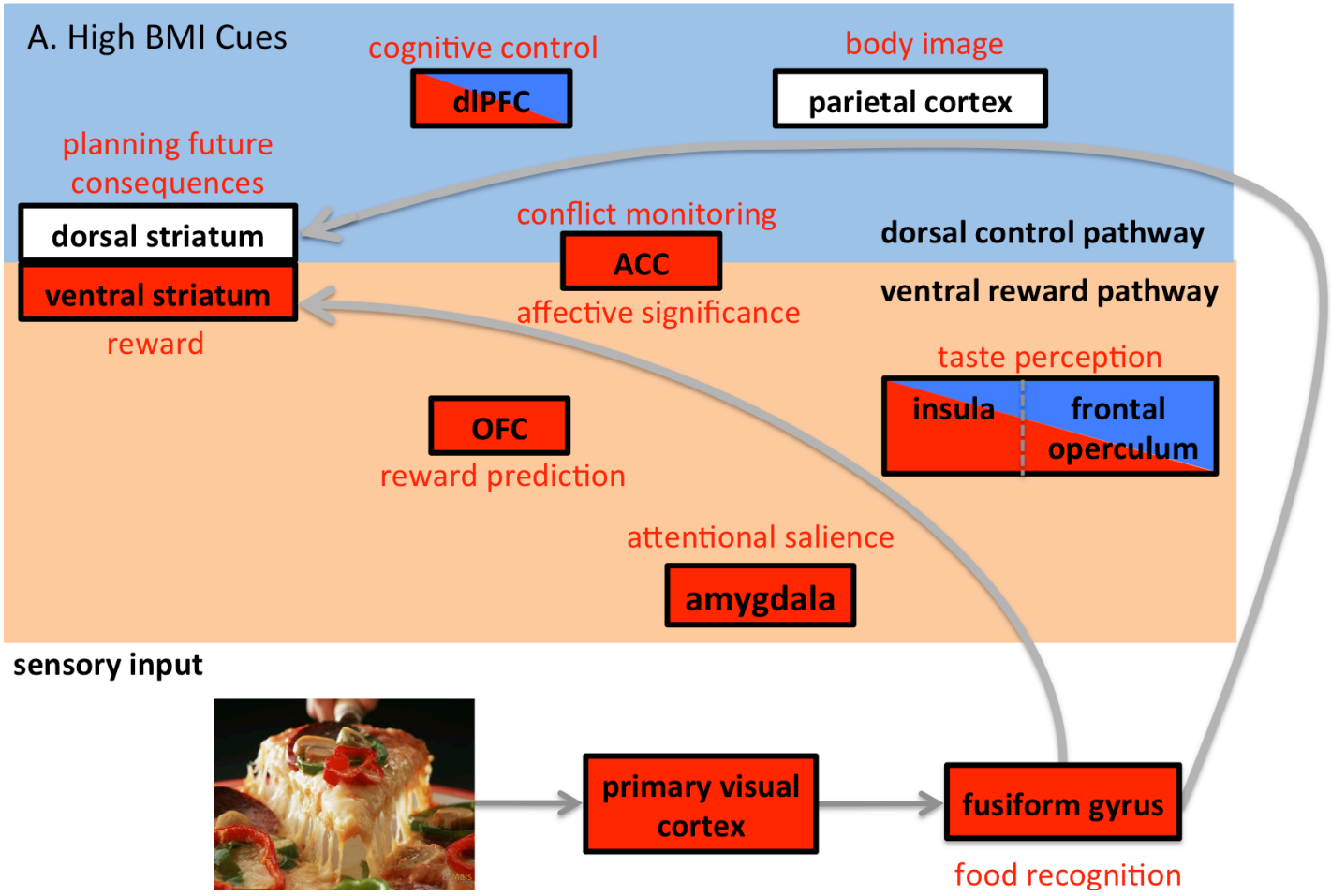

B. Hunger
cognitive control
dlPFC
body image
parietal cortex
planning future consequences
dorsal striatum
ventral striatum
reward
conflict monitoring
ACC
affective significance
dorsal control pathway
ventral reward pathway
taste perception
insula
frontal operculum
OFC
reward prediction
attentional salience
amygdala
sensory input
primary visual cortex
fusiform gyrus
food recognition

Figure 2


A. High BMI Cues
cognitive control
dlPFC
body image
parietal cortex
planning future consequences
dorsal striatum
conflict monitoring
ACC
dorsal control pathway
ventral striatum
affective significance
ventral reward pathway
reward
taste perception
insula
frontal operculum
OFC
reward prediction
attentional salience
amygdala
sensory input
primary visual cortex
fusiform gyrus
food recognition

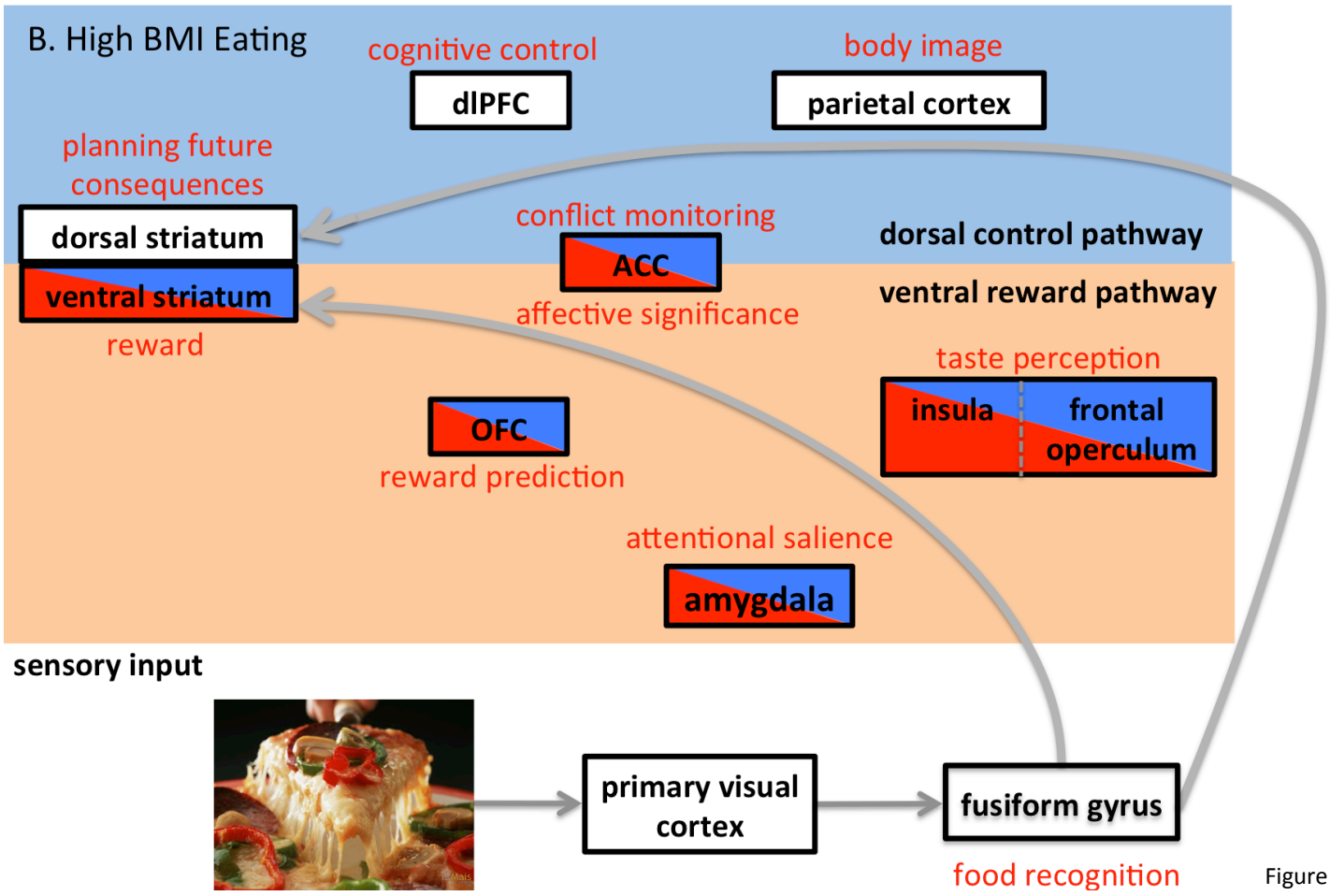

B. High BMI Eating
cognitive control
dlPFC
body image
parietal cortex
planning future consequences
dorsal striatum
conflict monitoring
ACC
dorsal control pathway
ventral striatum
affective significance
ventral reward pathway
reward
taste perception
insula
frontal operculum
OFC
reward prediction
attentional salience
amygdala
sensory input
primary visual cortex
fusiform gyrus
food recognition

Figure 3

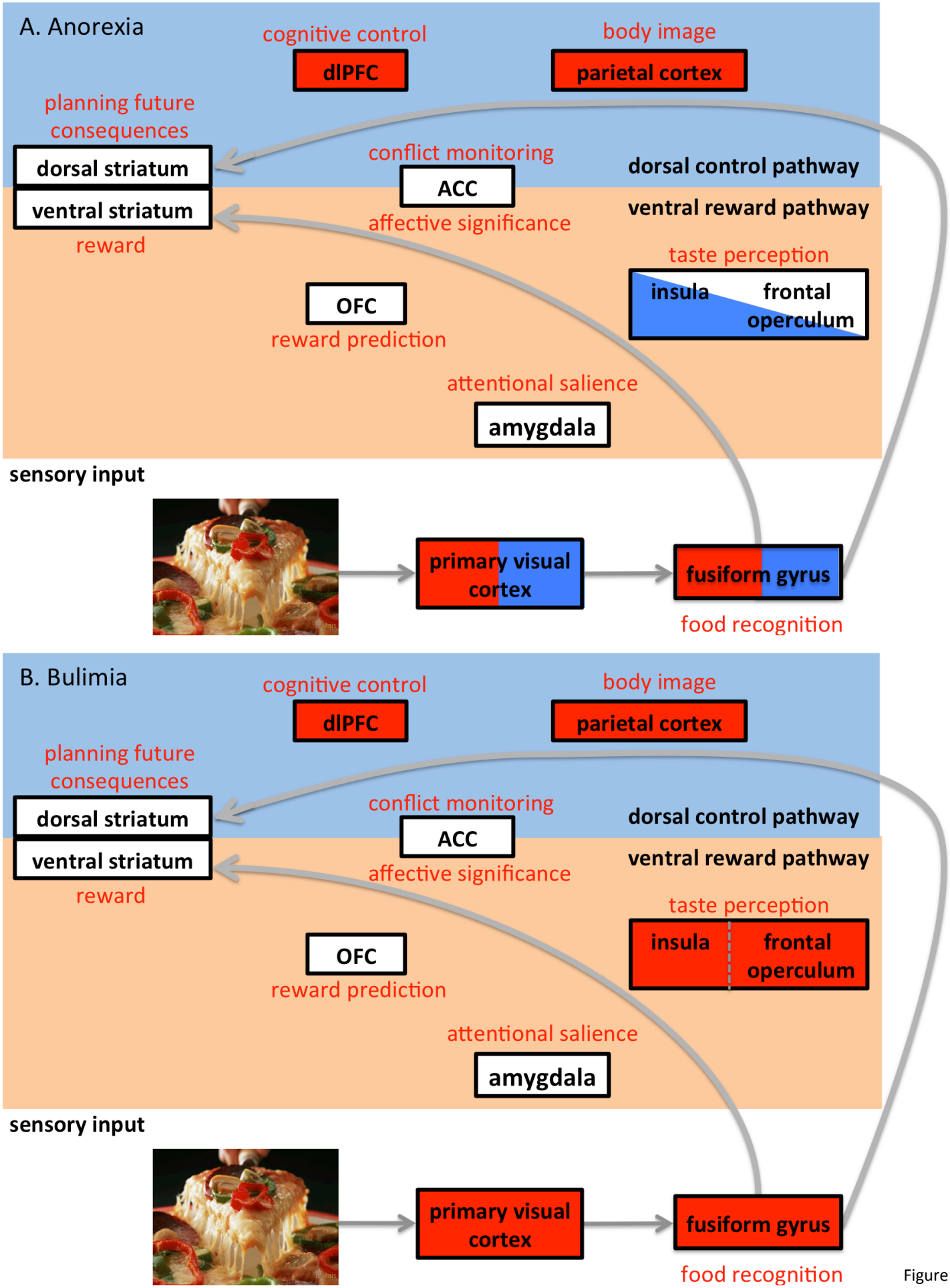

A. Anorexia
cognitive control
dlPFC
body image
parietal cortex
planning future consequences
dorsal striatum
ventral striatum
reward
conflict monitoring
ACC
affective significance
dorsal control pathway
ventral reward pathway
taste perception
insula
frontal operculum
OFC
reward prediction
attentional salience
amygdala
sensory input
primary visual cortex
fusiform gyrus
food recognition
B. Bulimia
cognitive control
dlPFC
body image
parietal cortex
planning future consequences
dorsal striatum
ventral striatum
reward
conflict monitoring
ACC
affective significance
dorsal control pathway
ventral reward pathway
taste perception
insula
frontal operculum
OFC
reward prediction
attentional salience
amygdala
sensory input
primary visual cortex
fusiform gyrus
food recognition

Figure 4

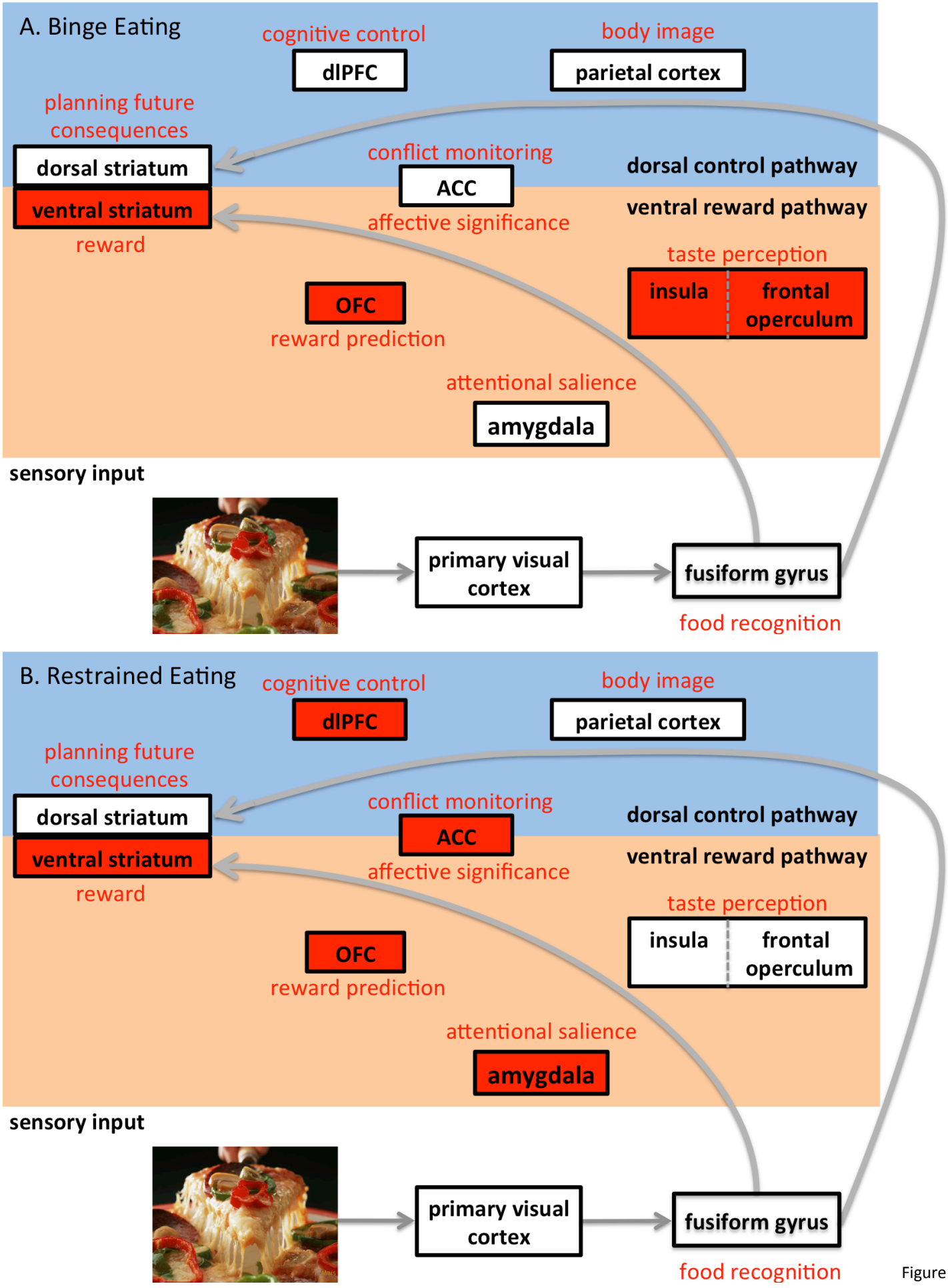

A. Binge Eating
cognitive control
dlPFC
body image
parietal cortex
planning future consequences
dorsal striatum
ventral striatum
reward
conflict monitoring
ACC
affective significance
dorsal control pathway
ventral reward pathway
taste perception
insula
frontal operculum
OFC
reward prediction
attentional salience
amygdala
sensory input
primary visual cortex
fusiform gyrus
food recognition
B. Restrained Eating
cognitive control
dlPFC
body image
parietal cortex
planning future consequences
dorsal striatum
ventral striatum
reward
conflict monitoring
ACC
affective significance
dorsal control pathway
ventral reward pathway
taste perception
insula
frontal operculum
OFC
reward prediction
attentional salience
amygdala
sensory input
primary visual cortex
fusiform gyrus
food recognition

Figure 5