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.

1. Introduction

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 relations 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, Wagner, Fudge, & Paulus, 2010; Kaye, Wierenga, Bailar, Simmonds, & Bischoff-Grethe, 2013; Kaye et al., 2009; O’Hara, Campbell, & Schmidt, 2015; Pietrini et al., 2011; Stefano et al., 2013; van...
neural differences to food cues between individuals with eating disorders, obese individuals, and healthy individuals (García-García, Narberhaus, 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; Papes, 2013; Papes & 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.

1.1. 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 A.1–A.4 in Appendix A 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.

1.2. 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.

1.3. 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 in Appendix A 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.
2. 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 Fig. 1A. Although Fig. 1A is adapted from the original Fig. 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 Fig. 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, & Andreas, 2003; Kringelbach, Stein, & van Hartevelt, 2012), and others suggesting a more caudal position in mid-insula (e.g., Simmons, Rapuano, Killman, 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, Wagner, 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 Fig. 1A illustrates, this circuit includes dorsal-lateral 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.

### 2.1. 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 et al. (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 decreased 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, Franzer, 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 et al. (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.

3. 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, 2016). 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 Fig. 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 & Yurgelun-Todd, 2005; Killgore et al., 2003; LaBar et al., 2001), animals (Holsen et al., 2005, 2006; Miller et al., 2007), dining-related utensils (Killgore & Yurgelun-Todd, 2005; Killgore et al., 2003), 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 A.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, Dziemidzik, 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, 2016).

Based on these findings, we propose that the network in Fig. 1B underlies the processing of visual food cues. As can be seen, this network is closely related to the eating network in Fig. 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 Fig. 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 Fig. 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 similar to the processing in actual eating (Fig. 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 (dIPFC), 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, Fig. 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 Fig. 1A and B, the only difference between these networks is the initial input into the system. When participants actually consume liquid food in a scanner (Fig. 1A), the input is through the mouth with no visual input. When participants process a visual food cue (Fig. 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.

3.1. The core eating network

The network for actual eating in Fig. 1A probably only becomes active during neuroimaging experiments when participants taste but don’t see liquid foods. In contrast, the network in Fig. 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 Fig. 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 Fig. 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 Fig. 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.

4. 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 Fig. 2A and B 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.

4.1. 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 et al., 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 & Yurgelun-Todd, 2005; Killgore et al., 2003).

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, midfrontal 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 A.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 A.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.

Fig. 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 Fig. 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 A.2 provides a complete list of experiments that have assessed the modulating influence of palatability on the processing of food pictures.

4.2. 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 (450–600 ms). 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 et al. (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- cueing 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: Stice et al., 2013; Uher et al., 2006).

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 et al. (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 et al. (2006), 24-h fasting was defined as the hunger state, whereas not having eaten for the previous 3 h was defined as the satiated state (“neither hungry nor acutely satiated”). Because some participants might be hungry after 3 h 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 afterward. 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 Pappas, 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.

Fig. 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 A.3 lists experiments that have assessed the modulating influences of hunger and satiety on the processing of food pictures.

Comparing Fig. 2B to A (and also Table A.3 to A.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.

5. Modulations of the core eating network associated with BMI

It is widely believed that an imbalance between 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 (Martore 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 decreased.

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.

5.1. 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.

5.2. 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 (lasting for 4–6 h), who ranged in weight from lean to obese. When participants were required to inhibit their impulses toward 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 dorsal 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 (anterior insula, striatum, 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 responsibility 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 et al., 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 D2 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.
5.3. 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, et al. (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.

5.4. 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 a meta-analysis showed lower insula activation). In addition, obese individuals sometimes show decreased neural activity in the dorsal control pathway (dIPFC), 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.

Fig. 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, Fig. 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 Fig. 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 A.4 lists experiments that compare brain responses to food cues or to actual food consumption in overweight/obese vs. normal weight individuals.

6. Modulations of the core eating network in eating disorders

6.1. 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 inordinate 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, Zeck, 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 dIPFC, whereas AN patients showed greater activation in dIPFC, 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 dIPFC 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

Fig. 4. Modulations of the core eating network from Fig. 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 (dIPFC) 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; dIPFC, dorsolateral prefrontal cortex. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)
produces binge eating, together with less regulatory processing than AN patients.

Finally, hunger and satiety modulate neural responses to food cues in AN. Santel et al. (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).

Fig. 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, 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).

Fig. 4B illustrates how BN modulates neural responses in the core eating network. Although relatively few articles address the neural bases of BN, Fig. 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.

6.2. 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).

Fig. 5A presents a modulation of the core eating network associated with BED. Similar to BN, relatively few articles address the neural bases of BED. Fig. 5A offers speculation about modulations of the core eating network during this disorder. As Fig. 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 Figs. 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

7. 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, 2016; 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.

7.1. 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 dIPFC 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 (medial frontal gyrus). Using near-infrared spectroscopy, Suda et al. (2010) found that dietary restraint correlated positively with activation in right fronto-temporal cortex.

Fig. 5B illustrates how the goal of dietary restraint modulates neural responses to food cues in the core eating network. As Fig. 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.

7.2. 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 in the up-
regulation condition (smell, taste, and texture), they exhibited
increased food craving and enhanced activation in the ventral
reward pathway (ventral striatum, ventral segmental area, ope-
culum, 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 et al., 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 area (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
participants were asked to regulate thinking about eating
sequences of eating high-calorie non-healthy foods. Relative to
participants to think of negative long-term health and social conse-
quences of focusing on long-term health. When partici-
pants 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 hedo-
nic impulses.

In a related experiment, Hollmann et al. (2012) asked partici-
pants to think of negative long-term health and social conse-
quences 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 inter-
vention over the course of seven weeks (1 h per week) in which
they practiced using cognitive reappraisal to increase the con-
sumption 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/ex-
pectation regions.

In a variety of related behavioral experiments, implicit cues
activating health goals effectively reduced consumption of
unhealthy foods in restrained eaters (Papies & Hanstra, 2010;
Papies, Potjes, Keesman, Schwingammer, & 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 differ-
tential 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 net-
work 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 modu-
late the core eating network to support situated action (cf.
Barsalou, 2003, 2016; 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, partici-
pants are asked to imagine the health consequences of consuming
a high-calorie food, they exhibit greater activity in the dorsal con-
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 reconfigur-
ing the core eating network in this manner occurs frequently,
and that such reconfigurations explain recruitment of areas out-
side the core eating network that we have seen throughout this
review.2

8. Discussion

This article, to our knowledge, is the first to integrate food-
related processing in the human brain across different eating sit-
uations 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 situa-
tions 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.

8.1. The ventral reward and dorsal control pathways

A consistent theme across eating phenomena is the impor-
tance of two processing streams within the core eating network:

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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.
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.

8.2. 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 (Papis, 2013; Papis & 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 Papis 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 important ways. As we saw earlier, high BMI individuals 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 dorsal control network is likely to also be critical for developing successful interventions.

9. 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 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. Additionally, understanding how the ventral reward and dorsal control pathways interact with homeostasis and related processes will be essential (e.g., Hege et al., 2014).

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, Jurado, et al., 2013; García-García, Narberhaus, et al., 2013; McFadden, Tregellas, Shott, & Frank, 2014; Stoeckel et al., 2009). 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.

Appendix A

<table>
<thead>
<tr>
<th>Article (authors/year of publication)</th>
<th>Participants</th>
<th>Food stimuli</th>
<th>Nonfood stimuli</th>
<th>Task</th>
<th>Relevant results</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pictures</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beaver et al. (2006)</td>
<td>14 HC fasting for 2 h</td>
<td>Appetizing foods</td>
<td>Objects</td>
<td>Passively view pictures</td>
<td>OFC, posterior insula, precentral gyrus, parahippocampal gyrus, anterior STS, posterior STS, fusiform gyrus, cuneus, precuneus, vmPFC, dIPFC</td>
</tr>
<tr>
<td>Cornier et al. (2007) (eucaloric condition)</td>
<td>25 thin healthy adults overnight fasting</td>
<td>High hedonic foods</td>
<td>Objects (animals, trees, books, furniture, buildings)</td>
<td>Passively view pictures</td>
<td>Neutral &gt; object: insula, dIPFC</td>
</tr>
<tr>
<td>Cornier et al. (2009) (control group)</td>
<td>22 thin HC</td>
<td>Neutral hedonic foods</td>
<td>Objects (animals, trees, books, furniture, buildings)</td>
<td>Passively view pictures</td>
<td>Insula, inferior visual cortex, parietal cortex, postcentral cortex, OFC, IFG, MFG, ventral striatum, hippocampus, cingulate gyrus</td>
</tr>
<tr>
<td>Davids et al. (2010) (control group)</td>
<td>22 obese/overweight</td>
<td>Foods</td>
<td>Pleasant pictures (young animals, babies, etc.)</td>
<td>View pictures attentively</td>
<td>Inferior occipital gyrus, superior occipital gyrus, superior parietal gyrus, SMA, superior temporal pole, vIPFC, IFG, insula, putamen, amygdala, hippocampus</td>
</tr>
<tr>
<td>Führer et al. (2008)</td>
<td>12 healthy lean males &lt;1 h vs. &gt;4 h fasting</td>
<td>Foods</td>
<td>Nonfoods not related to hand–mouth action</td>
<td>Press a button for a target picture (image frame with no object)</td>
<td>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</td>
</tr>
<tr>
<td>Holsen et al. (2005)</td>
<td>9 healthy children and adolescents 4-h fasting vs. after meal</td>
<td>Foods</td>
<td>Animals</td>
<td>Remember images for memory task</td>
<td>Pre-meal: medial OFC, lateral OFC, medial frontal cortex, superior parietal cortex, cerebellum/fusiform</td>
</tr>
<tr>
<td>Holsen et al. (2006) (control group)</td>
<td>9 with PWS</td>
<td>Foods</td>
<td>Gaussian-blurred images</td>
<td>Remember images for memory task</td>
<td>Post-meal: STG, fusiform gyrus</td>
</tr>
<tr>
<td>Kilgore et al. (2003)</td>
<td>9 HC pre-meal (4-h fasting) vs. post-meal</td>
<td>High-calorie foods</td>
<td>Blurred control images</td>
<td>Remember images for memory task</td>
<td>Insula, amygdala/hippocampus, post-central gyrus, cerebellum, fusiform gyrus, inferior occipital gyrus, medial frontal gyrus, transverse temporal gyrus, STG, precuneus, posterior cingulate</td>
</tr>
<tr>
<td>Killgore and Yurgelun-Todd (2005)</td>
<td>8 female children &gt;1 h fasting</td>
<td>High-calorie foods</td>
<td>Nonedible dining-related utensils (e.g. forks)</td>
<td>Remember images for memory task</td>
<td>Fusiform gyrus, inferior occipital gyrus, inferior orbitofrontal gyrus, parahippocampal gyrus, supramarginal gyrus, MTC, IFG, thalamus, inferior parietal lobe, Rolandic operculum, STG, putamen</td>
</tr>
<tr>
<td>LaBar et al. (2001)</td>
<td>17 HC &gt;8 h fasting vs. 1 h fasting</td>
<td>Foods</td>
<td>Tools</td>
<td>Press a button when object blinks</td>
<td>Parahippocampal gyrus, fusiform gyrus, amygdala, extrastriate cortex, insula</td>
</tr>
<tr>
<td>Malik et al. (2008) (control group)</td>
<td>20 healthy males 3 h fasting</td>
<td>Foods</td>
<td>Gaussian-blurred objects</td>
<td>Focus attention on images</td>
<td>IPG/MFG, anterior insula, fusiform gyrus, inferior occipital gyrus, superior parietal lobule, vmPFC, subcallosal cingulate cortex, visual cortex</td>
</tr>
<tr>
<td>Miller et al., 2007</td>
<td>8 adults with PWS</td>
<td>Foods</td>
<td>Animals</td>
<td>Passively view pictures</td>
<td>Low-calorie &gt; control: ITG</td>
</tr>
<tr>
<td>Rothemund et al. (2007) (control group)</td>
<td>13 obese females 13 HC &gt;1.5 h fasting</td>
<td>High-calorie foods</td>
<td>Neutral control</td>
<td>Observe pictures attentively</td>
<td></td>
</tr>
</tbody>
</table>

(continued on next page)
<table>
<thead>
<tr>
<th>Article (authors/year of publication)</th>
<th>Participants</th>
<th>Food stimuli</th>
<th>Nonfood stimuli</th>
<th>Task</th>
<th>Relevant results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Santel et al. (2006) (control group)</td>
<td>13 AN</td>
<td>High-calorie foods</td>
<td>Objects of use (tools, make-up items, pencils)</td>
<td>Rate pleasantness</td>
<td>1 h fasting: cuneus, middle occipital gyrus, inferior occipital gyrus</td>
</tr>
<tr>
<td>Schienle et al. (2009) (control group)</td>
<td>10 HC 12 h vs. 1 h fasting</td>
<td>High-calorie foods</td>
<td>Household articles</td>
<td>Passively view pictures</td>
<td>12 h fasting: lingual gyrus, fusiform gyrus, lingual gyrus, fusiform, insula, ACC, lateral OFC, medial OFC, amygdala, ventral striatum</td>
</tr>
<tr>
<td>Schur et al. (2009)</td>
<td>17 BED females 14 BN females 19 HC 17 overweight control overnight fasting</td>
<td>Disgusting foods</td>
<td>Nonfood stimuli</td>
<td>Remember images for memory task</td>
<td>Brainstem, hypothalamus, amygdala, inferior frontal, insula, striatum (putamen, nucleus accumbens), thalamus occipital lobe</td>
</tr>
<tr>
<td>Simmons et al. (2005)</td>
<td>9 HC</td>
<td>High-calorie foods</td>
<td>Locations</td>
<td>One-back task (same or different)</td>
<td>Insula, OFC/anterior cingulate, ITG, fusiform</td>
</tr>
<tr>
<td>St-Onge et al. (2005) (visual group)</td>
<td>12 HC &gt;12 h fasting</td>
<td>From high-calorie to low-calorie foods</td>
<td>Office supplies, plastic toys, dolls</td>
<td>Passively view pictures</td>
<td>Fusiform gyrus, lingual gyrus, angular gyrus, anterior insula, Posterior fusiform gyrus, inferior occipital gyrus, IFG/lateral OFC, middle insula cortex</td>
</tr>
<tr>
<td>Uher et al. (2006) (visual group)</td>
<td>18 HC 24 h vs. &lt;3 h food fasting</td>
<td>Pleasant and appetizing foods</td>
<td>Non-edible objects</td>
<td>Rate liking</td>
<td></td>
</tr>
<tr>
<td>van der Laan et al. (2011) (visual group)</td>
<td>Meta-analysis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Words**

<table>
<thead>
<tr>
<th>Articles (year)</th>
<th>Participants</th>
<th>Food stimuli</th>
<th>Nonfood stimuli</th>
<th>Task</th>
<th>Relevant results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barros-Loscertales et al. (2012)</td>
<td>59 native Spanish speakers</td>
<td>Taste-related words</td>
<td>Control words</td>
<td>Passive reading task</td>
<td>Insula, frontal operculum/lateral OFC, STG/ angular gyrus, posterior cingulate, precentral/ middle frontal gyrus, superior PFC, SFG/MFG, cuneus/precuneus, substantia nigra, subthalamic nucleus/thalamus</td>
</tr>
<tr>
<td>Pelchat et al. (2004)</td>
<td>20 HC 10 monotonous diet 10 normal diet</td>
<td>2 ‘really like’ foods</td>
<td>Monotonous foods</td>
<td>Think about the favorite version of the food</td>
<td>Monotonous diet group: fusiform gyrus, parahippocampal gyrus, amygdala, caudate nucleus, putamen, cingulate gyrus</td>
</tr>
</tbody>
</table>

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, dIPFC = dorsolateral prefrontal cortex, PCC = posterior cingulate cortex, STS = superior temporal sulcus, vmPFC = ventromedial prefrontal gyrus.
Table A.2
Articles that assessed the effect of palatability on neural responses to food cue pictures (palatable vs. non-palatable foods).

<table>
<thead>
<tr>
<th>Article (authors/year of publication)</th>
<th>Participants</th>
<th>Conditions</th>
<th>Task</th>
<th>Relevant results (high calorie foods &gt; low calorie foods)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beaver et al. (2006)</td>
<td>14 HC fasting for 2 h</td>
<td>Appetizing foods Low-calorie foods Non-food objects</td>
<td>Passively view pictures</td>
<td>Appetizing &gt; bland: ventral striatum, amygdala, midbrain, ventral pallidum</td>
</tr>
<tr>
<td>Cornier et al. (2007)</td>
<td>25 thin healthy adults overnight fasting</td>
<td>High hedonic foods Neutral nonfood objects</td>
<td>Passively view pictures</td>
<td>Premotor cortex, inferior visual cortex, hypothalamus, parietal cortex, hippocampus</td>
</tr>
<tr>
<td>Goldstone et al. (2009)</td>
<td>20 HC overnight fasting</td>
<td>High-calorie foods Low-calorie foods Non-food objects</td>
<td>Rate the appeal of each picture</td>
<td>Ventral striatum, amygdala, insula, medial and lateral OFC</td>
</tr>
<tr>
<td>Killgore et al. (2003)</td>
<td>13 healthy female &gt;1.5 h fasting</td>
<td>High-calorie foods Low-calorie foods Nonedible food-related stimuli</td>
<td>View and try to remember</td>
<td>SFG, thalamus, MTG, medulla, cerebellum, middle occipital gyrus</td>
</tr>
<tr>
<td>Killgore and Yurgelun-Todd (2005)</td>
<td>8 healthy female children adolescents &gt;1 h fasting</td>
<td>High-calorie foods Low-calorie foods Nonedible food-related stimuli</td>
<td>View and try to remember</td>
<td>Midline anterior cingulate gyrus, cerebellum, MTG, cerebellar crus</td>
</tr>
<tr>
<td>Passamonti et al. (2009)</td>
<td>21 HC ≥2 h fasting</td>
<td>Highly appetizing foods Bland foods</td>
<td>Indicate its position (L/R)</td>
<td>vACC, dIPFC, frontal pole, MTG, STG, PCC, ventral striatum, amygdala, extrastriate visual cortex</td>
</tr>
<tr>
<td>Rothemund et al. (2007)</td>
<td>13 obese and 13 HC females &gt;1.5 h fasting</td>
<td>High-calorie foods Low-calorie foods Eating-related stimuli Neural control items</td>
<td>View and try to remember</td>
<td>None in HC group</td>
</tr>
<tr>
<td>Schur et al. (2009)</td>
<td>10 healthy adult women 2–4 h after a meal</td>
<td>“Fattening” foods “Non-fattening” foods Non-food objects</td>
<td>View and try to remember</td>
<td>Brainstem, hypothalamus, amygdala, I FG, insula, striatum, thalamus, occipital pole Hypothalamus, ventral striatum, cerebellum, frontal middle gyrus, middle occipital gyrus, ITG</td>
</tr>
<tr>
<td>van der Laan et al. (2011)</td>
<td>Meta-analysis</td>
<td>Neutral control items</td>
<td>None in HC group</td>
<td></td>
</tr>
</tbody>
</table>

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

Table A.3
Articles that assessed the effect of hunger on neural responses to food cue pictures (hunger vs. satiety).

<table>
<thead>
<tr>
<th>Article (authors/year of publication)</th>
<th>Participants</th>
<th>Conditions</th>
<th>Task</th>
<th>Relevant interaction results (hunger vs. satiety) × (foods vs. nonfoods)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Führer et al. (2008)</td>
<td>12 healthy lean males 14-h fasted vs. 1 h</td>
<td>Foods Nonfoods</td>
<td>Press a button on seeing an image frame with no object</td>
<td>ACC, superior occipital sulcus, pregenual cingulate cortex, amygdala, subcallosal gyrus, lateral OFC</td>
</tr>
<tr>
<td>Goldstone et al. (2009)</td>
<td>20 HC overnight fasted vs. 1.6 h fasted</td>
<td>High-calorie foods Low-calorie foods Non-food household objects Gaussian blurred images</td>
<td>Rate how ‘appealing’</td>
<td>High-calorie &gt; low-calorie when fasted but not when fed: ventral-striatum, amygdala, insula, medial and lateral OFC</td>
</tr>
<tr>
<td>Holsen et al. (2005)</td>
<td>9 healthy children and adolescents 4-h fasted vs. after meal</td>
<td>Foods Animals Gaussian blurred images</td>
<td>View and try to remember</td>
<td>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</td>
</tr>
<tr>
<td>Jakobsdottir et al. (2012)</td>
<td>15 healthy males 12-h fasted vs. 1 h</td>
<td>Foods Nonfoods</td>
<td>Judge indoor or outdoor</td>
<td>Fusiform gyrus, IFG, thalamus, Rolandic operculum, ACC, amygdala</td>
</tr>
<tr>
<td>Kroemer et al. (2013)</td>
<td>26 HC overnight fasted vs. post-cortical load</td>
<td>High palatable foods Scrambled pictures</td>
<td>Rate appetite after each block</td>
<td>Parahippocampal gyrus, fusiform gyrus, amygdala</td>
</tr>
<tr>
<td>LaBar et al. (2001)</td>
<td>17 healthy adults &gt;8 h fasted vs. 1 h after meal</td>
<td>Foods Tools Gaussian blurred objects</td>
<td>Press a button when object blinks</td>
<td></td>
</tr>
<tr>
<td>Mohanty et al. (2008)</td>
<td>9 healthy adults &gt;8 h fasted vs. &lt;1 h fasted</td>
<td>Foods Tools High-calorie foods Objects of use</td>
<td>Indicate target or foil</td>
<td>Amygdala, posterior cingulate, parahippocampal gyrus, peristriate cortex, brainstem</td>
</tr>
<tr>
<td>Santel et al. (2006)</td>
<td>13 AN females</td>
<td>10 control female self-report hunger scores</td>
<td>Rate pleasantness</td>
<td>HC group, none</td>
</tr>
<tr>
<td>Siep et al. (2009)</td>
<td>12 healthy females 18-h fasted vs. after meal</td>
<td>High-calorie foods Low-calorie foods Neutral objects</td>
<td>Rate liking</td>
<td>Medial OFC, insula, PCC, fusiform gyrus, caudate putamen</td>
</tr>
<tr>
<td>Uher et al. (2006)</td>
<td>18 HC 23-h fasted vs. 3 h fasted</td>
<td>Foods Non-edible objects</td>
<td>Rate “how do you like the picture?”</td>
<td>None</td>
</tr>
<tr>
<td>van der Laan et al. (2011) meta-analysis</td>
<td></td>
<td></td>
<td></td>
<td>Liberal threshold: bilateral fusiform gyrus</td>
</tr>
</tbody>
</table>

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>
<thead>
<tr>
<th>Article (authors/year of publication)</th>
<th>Participants</th>
<th>Conditions</th>
<th>Hunger</th>
<th>Satiety</th>
<th>Results (obese &gt; HC, or BMI positively correlated with brain activity) × (foods &gt; nonfoods)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Food pictures: High BMI vs. low BMI groups</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Bruce et al. (2010)</td>
<td>10 obese children, 10 healthy children</td>
<td>Foods</td>
<td>4-h fasting</td>
<td>Post-meal</td>
<td>Pre-meal: SFG, MFG, IFG, OFC</td>
</tr>
<tr>
<td>Davids et al. (2010)</td>
<td>22 obese children, 22 healthy children</td>
<td>Foods</td>
<td>In each group 15 were tested &gt;2 h after meal</td>
<td>dlPFC</td>
<td></td>
</tr>
<tr>
<td>Dimitropoulos et al. (2012)</td>
<td>22 obese/overweight, 16 HC</td>
<td>High-calorie foods</td>
<td>5–8 h fasting</td>
<td>dlPFC, OFC, SFG, temporal, entorhinal cortex, STG, cerebellum-anterior lobe</td>
<td></td>
</tr>
<tr>
<td>Martin et al. (2010)</td>
<td>10 obese adults, 10 HC</td>
<td>Foods</td>
<td>4-h fasting</td>
<td>Post-meal: obese &lt; HC: dlPFC, precentral gyrus, cingulate</td>
<td></td>
</tr>
<tr>
<td>Stoeckel et al. (2008)</td>
<td>12 obese women, 12 HC women</td>
<td>Sweet and salty</td>
<td>8–9 h fasting</td>
<td>High-calorie &gt; car: medial OFC, lateral OFC, ACC,insula, NAck, amygdala, ventral pallidum, hippocampus, putamen</td>
<td></td>
</tr>
<tr>
<td><strong>Food pictures: Continuous BMI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Batterink et al. (2010)</td>
<td>29 adolescent girls from lean to obese</td>
<td>Vegetables (go trial)</td>
<td>4–6 h fasting</td>
<td>Orientation to appetizing food: mid insula, frontal operculum, anterior insula/frontal operculum, parietal operculum/cerebellum, brainstem</td>
<td></td>
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<tr>
<td>Grosshans et al. (2012)</td>
<td>21 obese individuals, 23 HC</td>
<td>Salty high-calorie foods</td>
<td>6 h fasting</td>
<td>Positive correlation (no-go &gt; fixation): temporal and frontal operculuminsula</td>
<td></td>
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<tr>
<td>Rothemund et al. (2007)</td>
<td>13 obese females, 13 HC</td>
<td>Low-calorie foods</td>
<td>1.5 h fasting</td>
<td>High-calorie condition: putamen, caudate body, anterior insula, caudatum, PCC, postcentral gyrus, lateral OFC, lateral globus pallidus</td>
<td></td>
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<tr>
<td>Yokum et al. (2011)</td>
<td>35 adolescent girls from lean to obese</td>
<td>Least appetizing foods</td>
<td>4–6 h fasting</td>
<td>Orientation to appetizing food: mid insula, frontal operculum, anterior insula/frontal operculum, lateral OFC</td>
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<tr>
<td><strong>Receipt of food</strong></td>
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<tr>
<td>Gearhardt et al. (2011)</td>
<td>39 young women from lean to obese (15 high food addiction)</td>
<td>Picture of milkshake/water</td>
<td>Food addiction score correlated positively with cues: ACC, medial OFC, amygdala</td>
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<tr>
<td>Stice, Davis, et al. (2008), Stice, Spoor, et al. (2008)</td>
<td>33 girls from lean to obese</td>
<td>Anticipated receipt of milkshake</td>
<td>4-h fasting</td>
<td>High &gt; low food addiction (cue): dlPFC, caudate</td>
<td></td>
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<tr>
<td>Stice et al. (2011)</td>
<td>60 lean adolescents, 35/60 of high-risk of obesity</td>
<td>Anticipated receipt of food or monetary reward</td>
<td>4–6 h fasting</td>
<td>High-risk &gt; low-risk (receipt of food): caudate, frontal operculum, parietal operculum</td>
<td></td>
</tr>
</tbody>
</table>

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.


