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REVIEW

Exploring Neural Mechanisms Related to Cognitive Control, Reward, and Affect in Eating Disorders: A Narrative Review of FMRI Studies

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Abstract: Studies using functional magnetic resonance imaging (fMRI) have contributed to our understanding of possible neural abnormalities among individuals with eating disorders. Many of these studies have focused on three domains: 1) cognitive control, 2) reward processing, and 3) affective processing. This review attempts to summarize the recent fMRI findings across these domains among the most well-characterized eating disorders: anorexia nervosa (AN), bulimia nervosa (BN), and binge eating disorder (BED). Though the literature is a bit murky, a few major themes have emerged. Cognitive control systems are affected among individuals across eating disorder diagnoses, but effects seem least pronounced in AN. Specifically, individuals with all eating disorders appear to show decreased prefrontal activation during cognitive control, but there is less evidence in AN linking decreased prefrontal activation with behavior. There is some evidence that the reinforcing value of food is reduced in AN, but individuals with BN and BED show hyperactivation to rewarding food-related stimuli, suggesting the reinforcing value of food may be enhanced. However, more complex reward processing paradigms show that individuals with BN and BED exhibit hypoactivation to reward anticipation and provide mixed results with regards to reward receipt. There are fewer neuroimaging findings related to affective processing, yet behavioral findings suggest affective processing is important in understanding eating disorders. Though the extant literature is complicated, these studies represent a foundation from which to build and provide insight into potential neurobiological mechanisms that may contribute to the pathophysiology of eating disorders.

Keywords: anorexia nervosa, bulimia nervosa, binge eating disorder, neuroimaging, fMRI

Introduction

Eating disorders are serious psychiatric illnesses with a significant public health impact.[1] All eating disorders are characterized by a combination of disturbances in body image and maladaptive eating behaviors. The most well-characterized are anorexia nervosa (AN), bulimia nervosa (BN), and binge eating disorder (BED).[2] AN is defined, in part, by low body weight and can include either solely restrictive behaviors, or a combination of restriction and binge eating or purging. BN is defined by the presence of binge eating and compensatory behaviors (eg, vomiting), and BED includes binge eating without any compensatory behaviors. These disorders are complex, with myriad symptoms in addition to the defining symptoms, and often co-occur with other illnesses.[3,4] Mechanisms of these complex illnesses are likely multidimensional, and this is reflected in the variety of research

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approaches. Restriction of dietary intake is often considered a manifestation of self-control,[5] whereas binge eating is often thought to reflect loss of control,[6] making cognitive control a candidate mechanism. The maladaptive nature of behavior around food also raises questions about abnormal reward processing. The frequent co-occurrence of anxiety and mood disorders with eating disorders (up to 70% of the time for all eating disorders[7] and potentially higher for individuals with BN and BED[8]) has also generated hypotheses about possible disturbances in affective processing. Increasingly, neural correlates of eating disorder psychopathology have been identified.

This review focuses on neuroimaging across three inter-related neuropsychological constructs relevant to mechanisms of eating disorders: 1) cognitive control, 2) reward processing, and 3) affective processing. Cognitive control can modulate reward sensitivity, and cognitive control is also modulated by affect.[9,10] Complex psychiatric illnesses, like eating disorders, include inter-related thoughts, feelings, and behaviors, which is the basis for the cognitive-behavioral therapy treatment approach. While these are not the only relevant neurocognitive processes, these constructs merit understanding within the context of eating disorders. These neural networks are not entirely independent in terms of neuroanatomy, with some brain overlapping across circuits. Task-based fMRI studies offer useful information about each of these neurocognitive processes and how they function in patients with eating disorders. To date, most research has concentrated on AN, with less data available for BN and BED. The aim of this review is to consider pathways that may be fruitful for future research across eating disorders.

Cognitive Control

Cognitive control is the ability to voluntarily coordinate behavior in order to achieve internal goals.[11,12] Clinical symptoms in AN are suggestive of excessive cognitive control (eg, obsessionality, perfectionism, and restrictive eating),[13] and some neuropsychological studies have found deficits in cognitive flexibility.[14] Yet, disparate findings across studies leave open questions about which aspects of cognitive control may be disturbed in AN.[15–17] Symptoms associated with BN and BED suggest greater impulsivity (eg, loss of control eating and common comorbidities with other impulse-related disorders like substance use disorders), and here the data do fairly consistently indicate response inhibition challenges.[18–20] Measurement of cognitive control commonly includes tasks that quantify the ability to switch between different sets of rules (ie, task switching) as well as tasks that require inhibition of a response (as described in tasks below).[11,21,22] Cognitive control neurocircuitry typically includes the prefrontal cortex (PFC), orbitofrontal cortex (OFC), and anterior cingulate cortex (ACC), as well as parietal cortex.[23–25]

Measurement of cognitive control during fMRI scanning has typically shown hypoactivation of frontoparietal networks among individuals with AN as compared with HC.[13,15,26,27] During a stop signal task, even though there is no evidence of behavioral differences between patients with AN and HC, data from several studies suggest decreased medial PFC activity during trials that require response inhibition.[13,26,27] During a set-shifting task (used to assess the ability to adapt as the rules for what constitutes a correct response change), adults with AN made more errors than HC and showed hypoactivation in frontostriatal circuits.[28] Among adolescents with AN, there were no set-shifting differences from HC, and neural findings indicated decreased activation in different regions than in the studies with adults (ie, occipital and temporal cortex and cerebellum).[29] While these studies hint at decreased neural activation during cognitive processing in AN, no specific mechanism associated with illness emerges.

In studies of BN, cognitive control has commonly been measured via response inhibition tasks (eg, go/no-go tasks). While these studies are consistent in behavioral findings that reflect impulsivity, the neuroimaging results have been mixed. In one study, only the most symptomatic individuals with BN differed from HC, with decreased activation in the dorsal striatum.[30] Interestingly, this study found no behavioral or neural group differences during a food-specific go/no-go task. However, individuals with BED performed worse than HC on the food version of the go/no-go task, and poorer task performance was associated with reduced activity in the prefrontal regions.[31]

In a study using the Simon Spatial Incompatibility Task to assess cognitive control, individuals with BN exhibited greater impulsivity than HC, responding faster and making more errors, with associated decreased neural activity in frontostriatal regions, including the dorsal striatum, PFC, and dorsal ACC.[20] When individuals with BN or BED completed a Stroop task with food images, the results showed greater activation of striatal regions compared to controls, but only individuals with BN showed greater activation in the premotor cortex.[18]

These studies generally show decreased behavioral inhibition among individuals with BN and BED and most, but not all, found associated decreases in neural activity. However, brain regions differed depending on the types of tasks used and the study populations.

Reward Processing

Reward processing encompasses a range of constructs, including responsivity (or sensitivity), learning, and reward-related decision-making. Among healthy individuals, reward is often studied using food and/or monetary stimuli. However, within eating disorders, assessing reward is often complicated because the reward value of food cannot be assumed. Reward processes are mediated by a broadly distributed brain system, including the ventral and dorsal striatum, amygdala, parietal cortex, PFC, OFC, ACC, and insula.[32]

Several reward-centered models of AN have been proposed, some suggesting that decreased reward responsiveness underlies aspects of psychopathology.[15,33–35] Individuals with AN do typically rate food as less pleasurable than healthy controls.[36] Food ratings among individuals with BN and BED are more mixed; in fact, some (but not all[37]) show that these groups rate high-fat, high-calorie food as more pleasurable than HC do.[38,39]

Several neuroimaging studies have found differences between individuals with AN and HC in the regions commonly considered in the reward system (eg, ventral striatum, OFC, insula, and ACC) in response to passive viewing of food-related or body-related visual stimuli. However, the direction of activation has not been consistent across studies.[40–43] Given that food images or receipt may not be viewed by an individual with AN as rewarding, some research aims to study reward systems with stimuli that are not illness-specific. This allows comparison with HC, and probes the system functioning in a general way. One study found that during a monetary guess task (ie, no learning component), individuals with AN did not differ notably from HC in reward system neural activation.[44] Several studies have examined reward via delay-discounting tasks, in which subjects are asked to choose between receipt of an immediate smaller amount of money or wait for a delayed larger amount. In one such study,[45] individuals with AN showed a preference for delayed rewards (over immediate rewards) compared with HC, and this was associated with decreased neural activity in the striatum and dorsal ACC. Another study,[46] using a slightly different delay-discounting task and with a younger population of AN, found no delay discounting differences between individuals with AN and HC and no group differences in the striatum, but did find group differences in the dorsal ACC, which were correlated with reward valuation. In two separate studies, there were no behavioral or neural differences between weight-restored AN and HC[47,48]. In a study comparing the effects of metabolic state on delay discounting in individuals who had remitted from AN compared with HCs, there were no group differences in task performance; the AN group did not show fed-versus-fasted neural differences and the HC group did.[49] Reward processes may be linked with cognitive control in that cognitive control may be part of forgoing an immediate reward.

Reward learning is the capacity to predict rewarding events based upon previously rewarding experiences.[50] A few studies have identified reward learning abnormalities in AN.[51–53] One neural marker associated with reward learning is prediction error, which refers to the neural correlates of omission of an expected reward (and its inverse).[54] Two studies of individuals with AN found increased activity in reward circuits for both taste-related stimuli[55] and monetary stimuli,[56] suggesting heightened prediction error.

Social stimuli can also be rewarding and engage reward circuitry.[57] Few studies have examined the neural response to social rewards across eating disorders. In the one study using fMRI scanning[58] social acceptance in an experimental paradigm was associated with decreased activation in the dorsomedial prefrontal cortex among individuals with AN compared with HC.

Habit learning also relates to reward processes. Habit formation occurs when reinforcement learning is repeated: a stimulus (or, cue) leads to a behavior, which is initially reinforced by the receipt of a rewarding outcome; with sufficient repetition, the behavior becomes closely tied to the stimulus and relatively insensitive to the value of the outcome.[59] Habit formation is associated with a shift from ventral to dorsal frontostriatal circuits.[60–63] The habit-centered model of AN proposes that food restriction, the salient behavioral disturbance in AN, may become habitual over time, shifting from ventral to dorsal frontostriatal control, and making it highly entrenched and resistant to change.[64] Two studies of individuals with AN have shown that decisions about food choice were associated with dorsal striatum activity among individuals with AN significantly more than for HC.[65,66] These findings are consistent with, though not evidence of, the possibility that

habit formation underlies restrictive food intake in AN. Habit formation, and the behavioral and neural mechanisms that underlie habit, have been relatively understudied in eating disorders. One neuroimaging study attempted to measure habitual responding by examining whether individuals with AN expended energy in pursuit of an outcome (monetary reward) when HC did not (when the value decreased) by using an instrumental motivation task, similar to the momentary incentive delay task, during fMRI scanning.[67] The results suggested that some patients were more goal-oriented whereas others were more habitual, and the goal-oriented subgroup showed greater mOFC activation during reward anticipation compared to habit subgroup, who showed no mOFC activation during reward anticipation.

Some have proposed that binge eating in both BN and BED is mediated by hyperactivity of reward regions of the brain, coupled with less activation of the cognitive control networks as discussed in the previous section.[68] Studies using visual food cue paradigms to assess reward responsiveness in BN and BED have shown increased neural activation in reward-related regions of the brain in response to images of highly palatable food.[69–72] A few studies have also compared responses to images of food across BED, BN, and HCs who were either normal weight or overweight/obese. One study[73] found that individuals with BED showed greater medial OFC response to visual food stimuli compared to all other groups, while individuals with BN showed greater insula and ACC response to food images than all other groups. However, another study[74] demonstrated that individuals with BED, as compared with obese HC, showed increased activity in the insula, but not the OFC, when looking at food images.

While the previously mentioned studies suggest heightened reward-related activity in BN and BED, several studies have shown individuals with BN and BED exhibit hypoactivation in reward-related regions of the brain when anticipating reward. No group differences were observed during monetary reward trials. Individuals with BN exhibited hypoactivation in the right anterior insula in response to the anticipation of taste receipt of a chocolate milkshake compared to HC, and hypoactivation in the left middle frontal gyrus, right posterior insula, right precentral gyrus, and right dorsal insula in response to consumption.[75] One study[76] examined reward processing in BED using a monetary incentive delay task and found that individuals with BED displayed reduced ventrostriatal activity during reward anticipation and reduced PFC and insula activity during reward receipt, as compared with obese controls. However, when individuals with BN and BED completed both a monetary incentive delay task and a food version (in which points could be used toward snacks following the scan), both groups exhibited reduced brain activation in the posterior cingulate cortex during the anticipation of food and increased activity in the medial OFC, medial PFC, and posterior cingulate cortex during the receipt of snack.[77]

The neurobiological findings regarding reward-processing in BN and BED are inconsistent in their pattern of results and, in certain studies, contradictory. This may be due to methodological differences (eg, food vs monetary stimuli; visual food-cue paradigms vs decision-making tasks) as well as differences in the diagnostic groups included in the study.

Affective Processing

Affective processing refers to the ways that stimuli produce emotions and shape behavior.[78] Emotions are functionally associated with a variety of eating disorder behaviors across diagnostic categories.[79] Several studies have shown that increases in negative affect (a broad construct that includes anxiety, sadness, fear, anger, guilt and shame, and other unpleasant emotions) precede disordered eating behaviors, across eating disorder diagnoses.[80–83] Additionally, research has suggested that acute changes in mood can modulate both cognitive control and the salience of reward.[84,85] The neural circuitry involved in affective processing is complex, and still not fully understood. Affective neuroscience initially focused on the limbic system (ie, amygdala, anterior insula, anterior ventral striatum, and ventral regions of the ACC); however, more recently some have suggested that affective processing extends more broadly to include ventromedial and dorsolateral PFC and OFC.[23,79,87]

To date, neuroimaging studies of affective processing in eating disorders have examined fearful responses to disorder-specific stimuli, responses to emotion faces, and the induction of specific emotions and their impact on task performance. With regard to fearful responses to disorder-specific stimuli, several studies have shown increased activation in the amygdala in response to food in AN compared with HC, as well as decreased neural activation in reward regions.[88–90] This has often been interpreted as indicative of increased fearful responses to food. While food-cue paradigms are commonly considered to be related to reward in individuals with BN and BED, one study found that

individuals with BN had higher fear and disgust ratings than HC in response to visual food cues, associated with decreased activation of the ACC.[91] While the result from this study do not show increased amygdalar activation, the decrease in ACC activation is similar to the previously mentioned studies in AN.[88–90]

Other studies have examined social cues to examine affective processing.[86,92] A study of response to happy and sad facial expressions found no differences between individuals who had remitted from AN and HCs.[92] However, another study[93] showed that when the emotion on the face differed from the emotion written in a word across the face, individuals who had recovered from AN showed decreased activation in the amygdala, hippocampus and basal ganglia compared to HC. When presented with negatively valenced words, individuals with AN did not differ from HC in the rating of unpleasantness of the words, but showed increased activation in the OFC, dorsolateral PFC, and medial PFC.[94]

Acute stress is commonly associated with negative affect, and both have been linked with eating pathology, including binge eating and purging.[80,95–100] Among HC, negative affect is generally associated with activation in limbic systems; yet, stress has been associated with a dampening of the expected negative affect-related activation.[101–104] To examine whether stress has the same effect in BN, two studies have examined the effect of acute stress on passive viewing of visual food cues (instead of response to emotions).[100,105] In both studies, participants viewed both food and neutral images, completed the Trier Social Stress Test, and then viewed the stimuli again. One study[105] found that after the stressor, HC showed increased neural activation in the parietal cortex and the cerebellum. Yet, individuals with BN showed decreased activation in these regions. In a second component of this study, the procedure was conducted in a different sample of individuals with BN (no HC) and decreased neural activation to food cues following stress was seen in similar regions of the parietal cortex and in the cerebellum. A separate study[100] of individuals with BN (no HC) found within-person decreases in activity in the amygdala, ACC, and ventromedial PFC, in response to food cues following a social stress test. While the data are limited, they suggest differences between groups in neural responses to stress.

A novel fMRI approach examines how neural response to emotionally salient stimuli in the lab environment are associated with naturalistic assessment of eating disorder behavior, mood, or cognition, using an ecological momentary assessment (EMA). EMA assesses individuals' experiences, behaviors, and moods as they occur during daily life.[106] One study among individuals with AN and HC presented stimuli with positive and negative valence during fMRI scanning and gave the instruction to actively downregulate any emotions that arose. Differences in BOLD response in the ventral striatum on passive viewing trials and emotion regulation trials were calculated for each individual. Following the scan, the participants responded to EMA prompts about body-related rumination and negative affect several times a day for two weeks. While there were no overall group differences in activation during the task, reduced within-person ventral striatum activity associated with regulating emotions was correlated with increased negative affect and greater occurrence of body-related rumination throughout the two weeks following the scan among individuals with AN and not HC.[107]

Two studies of individuals with BN have administered fMRI with an acute stress manipulation as well as EMA (these studies did not have a healthy comparison group).[85,100] Participants viewed pictures of high-fat, high-calorie foods and non-food images before and after the Trier Social Stress Test during fMRI scanning. Following the scan, participants completed two weeks of EMA, assessing mood, stress, and eating disorder behaviors several times a day. In one study,[79] greater within-person decreases of activation in the amygdala and vmPFC were associated with greater increases in negative affect before binge eating and greater decreases in negative affect after binge eating. The second study[94] used the same paradigm and measured the trajectory of stress (not mood) during EMA. Here, greater within-person decreases in ACC and dlPFC activation when observing food cues following stress were associated with a significantly steeper trajectory of stress before binge eating and sharper decreases in stress following binge eating. These studies, though small in sample size and lacking control groups, suggest a useful approach for linking neuroimaging findings with real-life behaviors.

The neurobiology of affective processing in eating disorders is understudied. The limited available data do suggest differences in neural activity in the limbic system and more broadly across eating disorders during affective processing tasks. Given the clear relevance of emotion with maladaptive eating behavior, it will be important to leverage advances in affective neuroscience as they progress.

Conclusion

The existing literature examining the neurobiological correlates of cognitive control, reward processing, and affective processing in eating disorders is confusing, and at times conflicting. Nonetheless, these studies represent a foundation from which to build.

Though the literature can seem a bit murky, a few themes emerge within each domain. First, cognitive control systems are affected among individuals with eating disorders. Specifically, individuals with BN and BED show decreased prefrontal activation during cognitive control tasks and when presented with rewards or food-related stimuli. Individuals with AN also show decreased prefrontal activation; however, brain-behavior links are less robust. With regards to reward, there is evidence that the reinforcing value of food is reduced in AN, with decreased activity in reward networks as compared with HC across reward-processing tasks. Individuals with BN and BED typically experience hyperactivation to rewarding food-related stimuli. However, given that the visual appearance of food often predicts food consumption in day-to-day life, it is possible the presentation of visual food stimuli may be associated with reward anticipation in populations with BN and BED due to previous reinforcement. Though, paradigms which have examined differences in reward anticipation and receipt mostly suggest individuals with BN and BED exhibit hypoactivation to reward anticipation and provide mixed results with regards to reward receipt. Differences in results based on the paradigm used highlights the need for further examination of reward processing, specifically reward anticipation, in BN and BED. And finally, with regard to affective processing, while repeated behavioral findings suggest affective processing is important in understanding eating disorders, there is less clarity regarding the neural correlates of affective processing across eating disorders. Across all neuroimaging research, links with psychopathology and behavioral disturbances are lacking.

A few useful paths forward may include: 1) using a cognitive neuroscience framework to more carefully constrain experimental tasks and thereby associated neural mechanisms (ie, less emphasis on passive viewing);[51] 2) transparency and consistency in brain imaging research in eating disorders to increase rigor and reproducibility;[108] 3) using paradigms that directly link to salient eating disorder characteristics (eg, meal studies), including (but not limited to) maladaptive eating behaviors (ie, restrictive intake, binge eating, purging);[109] 4) relating neuroimaging paradigms to behavior in the environment. One noteworthy approach to reconcile and improve our understanding of the neurobiology of eating disorders is the integration of fMRI and EMA, which have shown that neurobiological correlates of mood and stress do predict or moderate real-time mood and stress surrounding eating disorder behaviors in the natural environment.

Common limitations in these studies included small sample sizes, with a few notable exceptions.[66,110] Challenges in combining studies, or drawing robust inferences, come from the differences in task designs and in participant samples (combining acutely ill and remitted patients), as well as challenges in differentiating discrete neural systems. Also, many of the studies summarized throughout this review do not link neuroimaging results to specific eating disorder behaviors, making it difficult to draw behavioral inferences based on neural activity. Only a select few studies have attempted to assess the ecological validity of neuroimaging studies with methodological approaches like laboratory measures of actual eating and EMA following a scan. A greater push to link brain and behavior will help to clarify the potential underlying mechanism of these complex, longstanding disorders.

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