Dovepress

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

Joseph A Wonderlich[1,2]
Mariya Bershad[1,2]
Joanna E Steinglass[1,2]

[1]Department of Psychiatry, Columbia University Irving Medical Center, New York, NY, USA; [2]Department of Psychiatry, New York State Psychiatric Institute, New York, NY, USA

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

Correspondence: Joseph A Wonderlich
Department of Psychiatry, Columbia University Irving Medical Center, New York, NY, USA
Tel +1 646 774 6198
Email jaw2263@cumc.columbia.edu

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.

Disclosure

Dr Joanna E Steinglass reports mentoring grants from NIMH K24, during the conduct of the study; royalties from UpToDate, outside the submitted work. The authors report no other conflicts of interest in this work.

References

1. Wu J, Liu J, Li S, Ma H, Wang Y. Trends in the prevalence and disability-adjusted life years of eating disorders from 1990 to 2017: results from the Global Burden of Disease Study 2017. *Epidemiol Psychiatr Sci*. 2020;29. doi:10.1017/S2045796020001055
2. Association AP. *Diagnostic and Statistical Manual of Mental Disorders: DSM-5*. Washington, D.C: American Psychiatric Association; 2013.
3. Cassin SE, von Ranson KM. Personality and eating disorders: a decade in review. *Clin Psychol Rev*. 2005;25(7):895–916. doi:10.1016/j.cpr.2005.04.012
4. Wonderlich SA, Mitchell JE. Eating disorders and comorbidity: empirical, conceptual, and clinical implications. *Psychopharmacol Bull*. 1997;33(3):381.
5. Fairburn CG, Shafran R, Cooper Z. A cognitive behavioural theory of anorexia nervosa. *Behav Res Ther*. 1999;37(1):1–13. doi:10.1016/S0005-7967(98)00102-8
6. Colles SL, Dixon JB, O'brien PE. Loss of control is central to psychological disturbance associated with binge eating disorder. *Obesity*. 2008;16(3):608–614. doi:10.1038/oby.2007.99

7. Keski-Rahkonen A, Mustelin L. Epidemiology of eating disorders in Europe: prevalence, incidence, comorbidity, course, consequences, and risk factors. *Curr Opin Psychiatry.* 2016;29 (6):340–345. doi:10.1097/YCO.0000000000000278

8. Kessler RC, Berglund PA, Chiu WT, et al. The prevalence and correlates of binge eating disorder in the World Health Organization World Mental Health Surveys. *Biol Psychiatry.* 2013;73(9):904–914. doi:10.1016/j.biopsych.2012.11.020

9. Cavanagh JF, Frank MJ. Frontal theta as a mechanism for cognitive control. *Trends Cogn Sci.* 2014;18(8):414–421. doi:10.1016/j. tics.2014.04.012

10. Schuch S, Koch I. Mood states influence cognitive control: the case of conflict adaptation. *Psychol Res.* 2015;79(5):759–772. doi:10.1007/s00426-014-0602-4

11. Badre D. Defining an ontology of cognitive control requires attention to component interactions. *Top Cogn Sci.* 2011;3 (2):217–221. doi:10.1111/j.1756-8765.2011.01141.x

12. Miyake A, Friedman NP, Emerson MJ, Witzki AH, Howerter A, Wager TD. The unity and diversity of executive functions and their contributions to complex "frontal lobe" tasks: a latent variable analysis. *Cogn Psychol.* 2000;41(1):49–100. doi:10.1006/cogp.1999.0734

13. Bartholdy S, Dalton B, O'Daly OG, Campbell IC, Schmidt U. A systematic review of the relationship between eating, weight and inhibitory control using the stop signal task. *Neurosci Biobehav Rev.* 2016;64:35–62. doi:10.1016/j.neubiorev.2016.02.010

14. Miles S, Gnatt I, Phillipou A, Nedeljkovic M. Cognitive flexibility in acute anorexia nervosa and after recovery: a systematic review. *Clin Psychol Rev.* 2020;101905. doi:10.1016/j.cpr.2020.101905

15. Wierenga CE, Ely A, Bischoff-Grethe A, Bailer UF, Simmons AN, Kaye WH. Are extremes of consumption in eating disorders related to an altered balance between reward and inhibition? *Front Behav Neurosci.* 2014;8:410. doi:10.3389/fnbeh.2014.00410

16. Lilenfeld LRR, Wonderlich S, Riso LP, Crosby R, Mitchell J. Eating disorders and personality: a methodological and empirical review. *Clin Psychol Rev.* 2006;26(3):299–320. doi:10.1016/j. cpr.2005.10.003

17. Treasure J, Schmidt U. The cognitive-interpersonal maintenance model of anorexia nervosa revisited: a summary of the evidence for cognitive, socio-emotional and interpersonal predisposing and perpetuating factors. *J Eat Disord.* 2013;1(1):1–10. doi:10.1186/2050-2974-1-13

18. Lee JE, Namkoong K, Jung Y-C. Impaired prefrontal cognitive control over interference by food images in binge-eating disorder and bulimia nervosa. *Neurosci Lett.* 2017;651:95–101. doi:10.1016/j.neulet.2017.04.054

19. Svaldi J, Naumann E, Trentowska M, Schmitz F. General and food-specific inhibitory deficits in binge eating disorder. *Int J Eat Disord.* 2014;47(5):534–542. doi:10.1002/eat.22260

20. Marsh R, Steinglass JE, Gerber AJ, et al. Deficient activity in the neural systems that mediate self-regulatory control in bulimia nervosa. *Arch Gen Psychiatry.* 2009;66(1):51–63. doi:10.1001/archgenpsychiatry.2008.504

21. Lenartowicz A, Kalar DJ, Congdon E, Poldrack RA. Towards an ontology of cognitive control. *Top Cogn Sci.* 2010;2(4):678–692. doi:10.1111/j.1756-8765.2010.01100.x

22. Sabb FW, Bearden CE, Glahn DC, Parker DS, Freimer N, Bilder RM. A collaborative knowledge base for cognitive phenomics. *Mol Psychiatry.* 2008;13(4):350–360. doi:10.1038/sj.mp.4002124

23. Widge AS, Heilbronner SR, Hayden BY. Prefrontal cortex and cognitive control: new insights from human electrophysiology. *F1000Research.* 2019;8:1696. doi:10.12688/f1000research.20044.1

24. Wager TD, Davidson ML, Hughes BL, Lindquist MA, Ochsner KN. Prefrontal-subcortical pathways mediating successful emotion regulation. *Neuron.* 2008;59(6):1037–1050. doi:10.1016/j.neuron.2008.09.006

25. Ochsner KN, Gross JJ. The cognitive control of emotion. *Trends Cogn Sci.* 2005;9(5):242–249. doi:10.1016/j.tics.2005.03.010

26. Oberndorfer TA, Kaye WH, Simmons AN, Strigo IA, Matthews SC. Demand-specific alteration of medial prefrontal cortex response during an inhibition task in recovered anorexic women. *Int J Eat Disord.* 2011;44(1):1–8. doi:10.1002/eat.20750

27. Lock J, Garrett A, Beenhakker J, Reiss AL. Aberrant brain activation during a response inhibition task in adolescent eating disorder subtypes. *Am J Psychiatry.* 2011;168(1):55–64. doi:10.1176/appi.ajp.2010.10010056

28. Zastrow A, Kaiser S, Stippich C, et al. Neural correlates of impaired cognitive-behavioral flexibility in anorexia nervosa. *Am J Psychiatry.* 2009;166(5):608–616. doi:10.1176/appi.ajp.2008.08050775

29. Castro-Fornieles J, de la Serna E, Calvo A, et al. Functional MRI with a set-shifting task in adolescent anorexia nervosa: a cross-sectional and follow-up study. *Neuropsychologia.* 2019;131:1–8. doi:10.1016/j.neuropsychologia.2019.05.019

30. Skunde M, Walther S, Simon JJ, et al. Neural signature of behavioural inhibition in women with bulimia nervosa. *J Psychiatry Neurosc.* 2016;41(5):E69. doi:10.1503/jpn.150335

31. Hege MA, Stingl KT, Kullmann S, et al. Attentional impulsivity in binge eating disorder modulates response inhibition performance and frontal brain networks. *Int J Obes.* 2015;39 (2):353–360. doi:10.1038/ijo.2014.99

32. Kaye WH, Wagner A, Fudge JL, Paulus M. Neurocircuity of eating disorders. *Behav Neurobiol Eat Disord.* 2010:37–57.

33. O'Hara CB, Campbell IC, Schmidt U. A reward-centred model of anorexia nervosa: a focussed narrative review of the neurological and psychophysiological literature. *Neurosci Biobehav Rev.* 2015;52:131–152. doi:10.1016/j.neubiorev.2015.02.012

34. Kaye WH, Wierenga CE, Bailer UF, Simmons AN, Bischoff-Grethe A. Nothing tastes as good as skinny feels: the neurobiology of anorexia nervosa. *Trends Neurosci.* 2013;36(2):110–120. doi:10.1016/j.tins.2013.01.003

35. Scheurink AJW, Boersma GJ, Nergårdh R, Södersten P. Neurobiology of hyperactivity and reward: agreeable restlessness in anorexia nervosa. *Physiol Behav.* 2010;100(5):490–495. doi:10.1016/j.physbeh.2010.03.016

36. Lloyd EC, Steinglass JE. What can food-image tasks teach us about anorexia nervosa? A systematic review. *J Eat Disord.* 2018;6(1):1–18. doi:10.1186/s40337-018-0217-z

37. Gianini L, Foerde K, Walsh BT, Riegel M, Broft A, Steinglass JE. Negative affect, dietary restriction, and food choice in bulimia nervosa. *Eat Behav.* 2019;33:49–54. doi:10.1016/j.eatbeh.2019.03.003

38. Meule A, Küppers C, Harms L, et al. Food cue-induced craving in individuals with bulimia nervosa and binge-eating disorder. *PLoS One.* 2018;13(9):e0204151. doi:10.1371/journal.pone.0204151

39. Carter FA, Bulik CM, Lawson RH, Sullivan PF, Wilson JS. Effect of mood and food cues on body image in women with bulimia and controls. *Int J Eat Disord.* 1996;20(1):65–76. doi:10.1002/(SICI)1098-108X(199607)20:1<65::AID-EAT8>3.0.CO;2-2

40. Gizewski ER, Rosenberger C, De Greiff A, et al. Influence of satiety and subjective valence rating on cerebral activation patterns in response to visual stimulation with high-calorie stimuli among restrictive anorectic and control women. *Neuropsychobiology.* 2010;62 (3):182–192. doi:10.1159/000319360

41. Sanders N, Smeets PAM, van Elburg AA, et al. Altered food-cue processing in chronically ill and recovered women with anorexia nervosa. *Front Behav Neurosci.* 2015;9:46. doi:10.3389/fnbeh.2015.00046

42. Cowdrey FA, Park RJ, Harmer CJ, McCabe C. Increased neural processing of rewarding and aversive food stimuli in recovered anorexia nervosa. *Biol Psychiatry.* 2011;70(8):736–743. doi:10.1016/j.biopsych.2011.05.028

43. Holsen LM, Lawson EA, Blum J, et al. Food motivation circuitry hypoactivation related to hedonic and nonhedonic aspects of hunger and satiety in women with active anorexia nervosa and weight-restored women with anorexia nervosa. *J Psychiatry Neurosc*. 2012;37(5):322. doi:10.1503/jpn.110156

44. Bischoff-Grethe A, McCurdy D, Grenesko-Stevens E, et al. Altered brain response to reward and punishment in adolescents with anorexia nervosa. *Psychiatry Res Neuroimaging*. 2013;214 (3):331–340. doi:10.1016/j.pscychresns.2013.07.004

45. Decker JH, Figner B, Steinglass JE. On weight and waiting: delay discounting in anorexia nervosa pretreatment and posttreatment. *Biol Psychiatry*. 2015;78(9):606–614. doi:10.1016/j.biopsych.2014.12.016

46. King JA, Geisler D, Bernardoni F, et al. Altered neural efficiency of decision making during temporal reward discounting in anorexia nervosa. *J Am Acad Child Adolesc Psychiatry*. 2016;55 (11):972–979. doi:10.1016/j.jaac.2016.08.005

47. Doose A, King JA, Bernardoni F, et al. Strengthened default mode network activation during delay discounting in adolescents with anorexia nervosa after partial weight restoration: a Longitudinal fMRI Study. *J Clin Med*. 2020;9(4):900. doi:10.3390/jcm9040900

48. King JA, Bernardoni F, Geisler D, et al. Intact value-based decision-making during intertemporal choice in women with remitted anorexia nervosa? An fMRI study. *J Psychiatry Neurosc*. 2020;45(2):108. doi:10.1503/jpn.180252

49. Wierenga CE, Bischoff-Grethe A, Melrose AJ, et al. Hunger does not motivate reward in women remitted from anorexia nervosa. *Biol Psychiatry*. 2015;77(7):642–652. doi:10.1016/j.biopsych.2014.09.024

50. Berridge KC, Robinson TE. What is the role of dopamine in reward: hedonic impact, reward learning, or incentive salience? *Brain Res Rev*. 1998;28(3):309–369. doi:10.1016/S0165-0173(98) 00019-8

51. Steinglass JE, Foerde K. Reward system abnormalities in anorexia nervosa: navigating a path forward. *JAMA Psychiatry*. 2018;75(10):993–994. doi:10.1001/jamapsychiatry.2018.1924

52. Foerde K, Daw ND, Rufin T, Walsh BT, Shohamy D, Steinglass JE. Deficient goal-directed control in a population characterized by extreme goal pursuit. *J Cogn Neurosci*. 2021;33(3):463–481. doi:10.1162/jocn_a_01655

53. Shott ME, Filoteo JV, Jappe LM, et al. Altered implicit category learning in anorexia nervosa. *Neuropsychology*. 2012;26(2):191. doi:10.1037/a0026771

54. Garrison J, Erdeniz B, Done J. Prediction error in reinforcement learning: a meta-analysis of neuroimaging studies. *Neurosci Biobehav Rev*. 2013;37(7):1297–1310. doi:10.1016/j.neubiorev.2013.03.023

55. Frank GKW, Reynolds JR, Shott ME, et al. Anorexia nervosa and obesity are associated with opposite brain reward response. *Neuropsychopharmacology*. 2012;37(9):2031–2046. doi:10.1038/npp.2012.51

56. DeGuzman M, Shott ME, Yang TT, Riederer J, Frank GKW. Association of elevated reward prediction error response with weight gain in adolescent anorexia nervosa. *Am J Psychiatry*. 2017;174(6):557–565. doi:10.1176/appi.ajp.2016.16060671

57. Redcay E, Warnell KR. A social-interactive neuroscience approach to understanding the developing brain. *Adv Child Dev Behav*. 2018;54:1–44.

58. Via E, Soriano-Mas C, Sánchez I, et al. Abnormal social reward responses in anorexia nervosa: an fMRI study. *PLoS One*. 2015;10(7):e0133539. doi:10.1371/journal.pone.0133539

59. Dickinson A, Balleine B. The role of learning in the operation of motivational systems. In: Pashler H and Gallistel R, Eds. New York: Wiley: Stevens'handbook of experimental psychology: Learning, motivation, and emotion (3rd ed); 2002;3: 497–533).

60. Everitt BJ, Robbins TW. Neural systems of reinforcement for drug addiction: from actions to habits to compulsion. *Nat Neurosci*. 2005;8(11):1481–1489. doi:10.1038/nn1579

61. Everitt BJ, Robbins TW. Drug addiction: updating actions to habits to compulsions ten years on. *Annu Rev Psychol*. 2016;67:23–50. doi:10.1146/annurev-psych-122414-033457

62. Everitt BJ, Robbins TW. From the ventral to the dorsal striatum: devolving views of their roles in drug addiction. *Neurosci Biobehav Rev*. 2013;37(9):1946–1954. doi:10.1016/j.neubiorev.2013.02.010

63. Graybiel AM. Habits, rituals, and the evaluative brain. *Annu Rev Neurosci*. 2008;31:359–387. doi:10.1146/annurev.neuro.29.051605.112851

64. Walsh BT. The enigmatic persistence of anorexia nervosa. *Am J Psychiatry*. 2013;170(5):477–484. doi:10.1176/appi.ajp.2012.12081074

65. Foerde K, Steinglass JE, Shohamy D, Walsh BT. Neural mechanisms supporting maladaptive food choices in anorexia nervosa. *Nat Neurosci*. 2015;18(11):1571–1573. doi:10.1038/nn.4136

66. Foerde K, Schebendach JE, Davis L, et al. Restrictive eating across a spectrum from healthy to unhealthy: behavioral and neural mechanisms. *Psychol Med*. 2020. 1–10. doi:10.1017/S0033291720003542

67. Steding J, Boehm I, King JA, et al. Goal-directed vs. habitual instrumental behavior during reward processing in anorexia nervosa: an fMRI study. *Sci Rep*. 2019;9(1):1–9. doi:10.1038/s41598-019-49884-6

68. Smith DG, Robbins TW. The neurobiological underpinnings of obesity and binge eating: a rationale for adopting the food addiction model. *Biol Psychiatry*. 2013;73(9):804–810. doi:10.1016/j.biopsych.2012.08.026

69. Michaelides M, Thanos PK, Volkow ND, Wang G-J. Dopamine-related frontostriatal abnormalities in obesity and binge-eating disorder: emerging evidence for developmental psychopathology. *Int Rev Psychiatry*. 2012;24(3):211–218. doi:10.3109/09540261.2012.679918

70. Schag K, Teufel M, Junne F, et al. Impulsivity in binge eating disorder: food cues elicit increased reward responses and disinhibition. *PLoS One*. 2013;8(10):e76542. doi:10.1371/journal.pone.0076542

71. Wu M, Brockmeyer T, Hartmann M, Skunde M, Herzog W, Friederich H-C. Reward-related decision making in eating and weight disorders: a systematic review and meta-analysis of the evidence from neuropsychological studies. *Neurosci Biobehav Rev*. 2016;61:177–196. doi:10.1016/j.neubiorev.2015.11.017

72. Boswell RG, Kober H. Food cue reactivity and craving predict eating and weight gain: a meta-analytic review. *Obes Rev*. 2016;17(2):159–177. doi:10.1111/obr.12354

73. Schienle A, Schäfer A, Hermann A, Vaitl D. Binge-eating disorder: reward sensitivity and brain activation to images of food. *Biol Psychiatry*. 2009;65(8):654–661. doi:10.1016/j.biopsych.2008.09.028

74. Weygandt M, Schaefer A, Schienle A, Haynes J. Diagnosing different binge-eating disorders based on reward-related brain activation patterns. *Hum Brain Mapp*. 2012;33(9):2135–2146. doi:10.1002/hbm.21345

75. Bohon C, Stice E. Reward abnormalities among women with full and subthreshold bulimia nervosa: a functional magnetic resonance imaging study. *Int J Eat Disord*. 2011;44(7):585–595. doi:10.1002/eat.20869

76. Balodis IM, Kober H, Worhunsky PD, et al. Monetary reward processing in obese individuals with and without binge eating disorder. *Biol Psychiatry*. 2013;73(9):877–886. doi:10.1016/j.biopsych.2013.01.014

77. Simon JJ, Skunde M, Walther S, Bendszus M, Herzog W, Friederich H-C. Neural signature of food reward processing in bulimic-type eating disorders. *Soc Cogn Affect Neurosci*. 2016;11 (9):1393–1401. doi:10.1093/scan/nsw049

78. Tamietto M, De Gelder B. Neural bases of the non-conscious perception of emotional signals. *Nat Rev Neurosci*. 2010;11 (10):697–709. doi:10.1038/nrn2889

79. Lavender JM, Wonderlich SA, Engel SG, Gordon KH, Kaye WH, Mitchell JE. Dimensions of emotion dysregulation in anorexia nervosa and bulimia nervosa: a conceptual review of the empirical literature. *Clin Psychol Rev*. 2015;40:111–122. doi:10.1016/j.cpr.2015.05.010

80. Crowther JH, Sanftner J, Bonifazi DZ, Shepherd KL. The role of daily hassles in binge eating. *Int J Eat Disord*. 2001;29 (4):449–454. doi:10.1002/eat.1041

81. Harrison A, Sullivan S, Tchanturia K, Treasure J. Emotional functioning in eating disorders: attentional bias, emotion recognition and emotion regulation. *Psychol Med*. 2010;40 (11):1887–1897. doi:10.1017/S0033291710000036

82. Svaldi J, Griepenstroh J, Tuschen-Caffier B, Ehring T. Emotion regulation deficits in eating disorders: a marker of eating pathology or general psychopathology? *Psychiatry Res*. 2012;197(1–2):103–111. doi:10.1016/j.psychres.2011.11.009

83. Wildes JE, Marcus MD, Bright AC, Dapelo MM. Emotion and eating disorder symptoms in patients with anorexia nervosa: an experimental study. *Int J Eat Disord*. 2012;45(7):876–882. doi:10.1002/eat.22020

84. West R, Choi P, Travers S. The influence of negative affect on the neural correlates of cognitive control. *Int J Psychophysiol*. 2010;76(2):107–117. doi:10.1016/j.ijpsycho.2010.03.002

85. Wonderlich JA, Breithaupt L, Thompson JC, Crosby RD, Engel SG, Fischer S. The impact of neural responses to food cues following stress on trajectories of negative and positive affect and binge eating in daily life. *J Psychiatr Res*. 2018;102:14–22. doi:10.1016/j.jpsychires.2018.03.005

86. O'Neill M, Schultz W. Risk prediction error coding in orbitofrontal neurons. *J Neurosci*. 2013;33(40):15810–15814. doi:10.1523/JNEUROSCI.4236-12.2013

87. Phelps EA, Lempert KM, Sokol-Hessner P. Emotion and decision making: multiple modulatory neural circuits. *Annu Rev Neurosci*. 2014;37:263–287. doi:10.1146/annurev-neuro-071013-014119

88. Joos AAB, Saum B, van Elst LT, et al. Amygdala hyperreactivity in restrictive anorexia nervosa. *Psychiatry Res Neuroimaging*. 2011;191(3):189–195. doi:10.1016/j.pscychresns.2010.11.008

89. Zhu Y, Hu X, Wang J, et al. Processing of food, body and emotional stimuli in anorexia nervosa: a systematic review and meta-analysis of functional magnetic resonance imaging studies. *Eur Eat Disord Rev*. 2012;20(6):439–450. doi:10.1002/erv.2197

90. Vocks S, Herpertz S, Rosenberger C, Senf W, Gizewski ER. Effects of gustatory stimulation on brain activity during hunger and satiety in females with restricting-type anorexia nervosa: an fMRI study. *J Psychiatr Res*. 2011;45(3):395–403. doi:10.1016/j.jpsychires.2010.07.012

91. Joos AAB, Saum B, Zeeck A, et al. Frontocingular dysfunction in bulimia nervosa when confronted with disease-specific stimuli. *Eur Eat Disord Rev*. 2011;19(5):447–453. doi:10.1002/erv.1150

92. Cowdrey FA, Harmer CJ, Park RJ, McCabe C. Neural responses to emotional faces in women recovered from anorexia nervosa. *Psychiatry Res Neuroimaging*. 2012;201(3):190–195. doi:10.1016/j.pscychresns.2011.08.009

93. Bang L, Rø Ø, Endestad T. Amygdala alterations during an emotional conflict task in women recovered from anorexia nervosa. *Psychiatry Res Neuroimaging*. 2016;248:126–133. doi:10.1016/j.pscychresns.2015.12.008

94. Miyake Y, Okamoto Y, Onoda K, Shirao N, Okamoto Y, Yamawaki S. Brain activation during the perception of stressful word stimuli concerning interpersonal relationships in anorexia nervosa patients with high degrees of alexithymia in an fMRI paradigm. *Psychiatry Res Neuroimaging*. 2012;201(2):113–119. doi:10.1016/j.pscychresns.2011.07.014

95. Smyth JM, Wonderlich SA, Heron KE, et al. Daily and momentary mood and stress are associated with binge eating and vomiting in bulimia nervosa patients in the natural environment. *J Consult Clin Psychol*. 2007;75(4):629–638. doi:10.1037/0022-006X.75.4.629

96. Freeman LMY, Gil KM. Daily stress, coping, and dietary restraint in binge eating. *Int J Eat Disord*. 2004;36(2):204–212. doi:10.1002/eat.20012

97. O'Connor DB, Jones F, Conner M, McMillan B, Ferguson E. Effects of daily hassles and eating style on eating behavior. *Health Psychol*. 2008;27(1 Suppl):S20–31. doi:10.1037/0278-6133.27.1.S20

98. Goldschmidt AB, Wonderlich SA, Crosby RD, et al. Ecological momentary assessment of stressful events and negative affect in bulimia nervosa. *J Consult Clin Psychol*. 2014;82(1):30–39. doi:10.1037/a0034974

99. Roemmich JN, Lambiase MJ, Lobarinas CL, Balantekin KN. Interactive effects of dietary restraint and adiposity on stress-induced eating and the food choice of children. *Eat Behav*. 2011;12(4):309–312. doi:10.1016/j.eatbeh.2011.07.003

100. Fischer S, Breithaupt L, Wonderlich J, et al. Impact of the neural correlates of stress and cue reactivity on stress related binge eating in the natural environment. *J Psychiatr Res*. 2017;92:15–23. doi:10.1016/j.jpsychires.2017.03.017

101. Arnsten AFT. Stress weakens prefrontal networks: molecular insults to higher cognition. *Nat Neurosci*. 2015;18(10):1376. doi:10.1038/nn.4087

102. Soares JM, Sampaio A, Ferreira LM, et al. Stress impact on resting state brain networks. *PLoS One*. 2013;8(6):e66500. doi:10.1371/journal.pone.0066500

103. Dedovic K, Duchesne A, Andrews J, Engert V, Pruessner JC. The brain and the stress axis: the neural correlates of cortisol regulation in response to stress. *Neuroimage*. 2009;47(3):864–871. doi:10.1016/j.neuroimage.2009.05.074

104. Nieuwenhuizen AG, Rutters F. The hypothalamic-pituitary-adrenal-axis in the regulation of energy balance. *Physiol Behav*. 2008;94(2):169–177. doi:10.1016/j.physbeh.2007.12.011

105. Collins B, Breithaupt L, McDowell JE, Miller LS, Thompson J, Fischer S. The impact of acute stress on the neural processing of food cues in bulimia nervosa: replication in two samples. *J Abnorm Psychol*. 2017;126(5):540–551. doi:10.1037/abn0000242

106. Burke LE, Shiffman S, Music E, et al. Ecological momentary assessment in behavioral research: addressing technological and human participant challenges. *J Med Internet Res*. 2017;19(3): e77. doi:10.2196/jmir.7138

107. Seidel M, King JA, Ritschel F, et al. The real-life costs of emotion regulation in anorexia nervosa: a combined ecological momentary assessment and fMRI study. *Transl Psychiatry*. 2018;8(1):1–11. doi:10.1038/s41398-017-0004-7

108. Frank GKW, Favaro A, Marsh R, Ehrlich S, Lawson EA. Toward valid and reliable brain imaging results in eating disorders. *Int J Eat Disord*. 2018;51(3):250–261. doi:10.1002/eat.22829

109. Walsh BT. The importance of eating behavior in eating disorders. *Physiol Behav*. 2011;104(4):525–529. doi:10.1016/j.physbeh.2011.05.007

110. Frank GKW, DeGuzman MC, Shott ME, Laudenslager ML, Rossi B, Pryor T. Association of brain reward learning response with harm avoidance, weight gain, and hypothalamic effective connectivity in adolescent anorexia nervosa. *JAMA Psychiatry*. 2018;75(10):1071–1080. doi:10.1001/jamapsychiatry.2018.2151