EATING DISORDERS: ANOREXIA NERVOSA, BULIMIA NERVOSA, AND BINGE-EATING DISORDER

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Eating disorders (EDs), including anorexia nervosa (AN), bulimia nervosa (BN), and binge-eating disorder (BED), are serious psychiatric disorders that often first manifest in adolescence and are associated with dangerous medical complications, high rates of comorbid psychopathology, and significant psychosocial impairment (American Psychiatric Association, 2013). EDs affect approximately 1% to 3% of individuals and tend to be more common in girls and women, with only around 10% occurring in boys and men (Klein & Walsh, 2003), although improvements in the characterization of EDs in male individuals suggest this percentage may be much higher (Nagata et al., 2020). AN has the highest mortality rate of all psychiatric disorders and is the third most common chronic illness in female adolescents. AN is characterized by the restriction of energy intake leading to significantly low body weight, intense fear of gaining weight, and a marked disturbance in the experience of one's weight and shape (American Psychiatric Association, 2013). The fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-5*) includes two subtypes of AN: the binge-eating/purging subtype (AN-BP), defined by regular binge eating and/or purging, and the restricting subtype (AN-R), defined by the absence of binge-eating or purging symptoms. BN is characterized by recurrent cycles of binge eating, defined as the consumption of a large amount of food in a short time period that are often combined with a sense of loss of control over eating, and compensatory behavior (e.g., self-induced vomiting), as well as periods of dietary restraint, but individuals are not low weight (American Psychiatric Association, 2013). Individuals with BED, roughly 40% of whom are obese, engage in recurrent binge eating without compensatory behaviors (American Psychiatric Association, 2013).

The etiology of EDs is likely complex and poorly understood, which has hindered development of effective treatments. Less than 50% of treatment seekers with AN, BN, or BED achieve behavioral and/or psychological remission (Keel et al., 1999; van den Berg et al., 2019), resulting in a chronic relapsing and remitting course for many. Advances in our understanding of the pathophysiology of EDs are beginning to offer new targets of treatment that may help to improve treatment outcome. This chapter focuses primarily on neuropsychological and brain alterations in AN, BN, and BED. Due to limited studies of neurocognitive function, feeding disorders (e.g., pica, avoidant/restrictive food intake disorder, rumination disorder) are not discussed.

WHAT THE FIELD KNOWS

EDs are increasingly seen as neurobiologically based disorders, like all psychiatric conditions. This chapter reviews the currently accepted neuropsychological science supporting this notion.

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Risk, Etiological, and Neuropathological Factors

A growing body of research is beginning to establish genetic, personality, and brain-based factors that contribute to the onset and maintenance of eating disorders.

Genetic factors. AN, BN, and BED are complex heritable conditions that are influenced by a combination of genetic and environmental factors. Early family studies indicate an increased rate of EDs in first-degree relatives (Strober et al., 2000). For example, female individuals who have a relative with AN are 11 times more likely to develop AN than those without a relative with AN, and individuals with family members diagnosed with BN carry an increased risk of an ED and of BN in particular (Strober et al., 2000). Based on twin studies, heritability estimates for AN range from 48% to 74%; for BN, from 55% to 62%; and for BED, from 39% to 45% (Bulik et al., 2019; Steiger & Booij, 2020). AN and BN are strongly genetically correlated (0.46–0.79), as are bulimic behaviors and alcohol use disorder (0.33–0.61; Bulik et al., 2019).

Early candidate gene studies have not been replicated, although meta-analyses indicate serotonin (5-HT) genes may be involved in the etiology of AN (Baker et al., 2017). Recent genome-wide association studies in AN support a reconceptualization of AN as both a psychiatric and metabolic disorder and have identified multiple risk loci for AN that are positively associated with psychiatric disorders (e.g., obsessive–compulsive disorder, major depressive disorder, anxiety disorder, schizophrenia), personality traits (e.g., neuroticism), and physical activity and are negatively associated with metabolic, lipid, and anthropometric traits (e.g., glucose and lipid metabolism, Type 2 diabetes, fat mass, body mass index; Watson et al., 2019). Genome-wide association studies have also identified shared genetic liability in ED- and substance-use-related phenotypes (Baker et al., 2017; Munn-Chernoff et al., 2021). There are currently no published genome-wide association studies for BN or BED. Emerging evidence is beginning to support the role of epigenetic processes, which link environmental exposures such as malnutrition and life stresses (gestational, perinatal, childhood) to modifications in gene expression, in the etiology of EDs (Steiger & Booij, 2020).

Temperament risk factors. Individuals with AN and BN tend to share certain genetically determined temperament and personality traits, which often first occur in childhood before the onset of an ED and are thought to create or increase vulnerability to develop an ED. For example, individuals with AN and BN tend to have difficulties with emotional regulation and negative affect, characterized by increased trait anxiety, high incidence of comorbid anxiety disorders, elevated intolerance of uncertainty, and exaggerated harm avoidance, a temperament trait that contains elements of anxiety, inhibition, and inflexibility (Cassin & von Ranson, 2005; Wagner, Barbarich-Marsteller, et al., 2006). They also share traits including perfectionism, obsessionality, interoceptive deficits, and increased sensitivity to punishment (Harrison et al., 2010; Lilenfeld et al., 2006). These temperament and personality factors persist after recovery, further supporting the theory that these are stable traits associated with ED etiology (Wagner, Barbarich-Marsteller, et al., 2006). Recent research has begun to link these temperament factors to neuropsychological deficits commonly observed in EDs, as discussed next.

Brain alterations. Altered brain structure and function has been observed in AN, BN, and BED. Acutely ill individuals with AN exhibit significant morphometric alterations, including cerebral atrophy and enlarged ventricles; overall reduced gray and white matter structure; and variations in white matter integrity, particularly within frontoparietal, limbic, and cingulum tracts (Van den Eynde et al., 2012). Cross-sectional and a limited number of longitudinal studies, mainly in adults and after some degree of remission, tend to find reversal of some ill AN-related morphometric disturbances, such as cortical thinning, gyrification, and white matter microstructure changes (Bernardoni et al., 2016), although others report that these abnormalities may persist into remission (Castro-Fornieles et al., 2009; Wagner, Greer, et al., 2006). Structural changes have also been reported in BN, with evidence of decreased

inferior frontal gray matter and volume reductions within frontostriatal circuitry, including the caudate nucleus. Notably, reduced cortical thickness in frontoparietal regions (Berner, Stefan, et al., 2018) and greater deformations on the surface of subcortical structures (Berner, Wang, et al., 2019) in BN were associated with greater symptom severity.

EDs are also associated with functional disturbances in the dorsal frontostriatal circuits that support inhibitory control and in overlapping ventral circuits that support reward processing and reward-based learning, discussed in more detail later. Altered neurotransmitter function has been implicated in EDs, with considerable data showing that individuals with AN and BN have disturbances of dopamine (DA) and 5-HT systems (Kaye et al., 2009, 2013). Disturbances in DA are thought to contribute to altered reward processing, motivation to eat, and decision making, whereas alterations in 5-HT may be implicated in altered mood, impulsivity, and satiety in these EDs (Kaye et al., 2013).

In summary, recent pathogenic risk models for the onset and maintenance of EDs have begun to incorporate genetic liability, temperament factors, epigenetic influences, and neurocognitive and imaging findings within the context of adolescent development. For instance, models of AN tend to focus on the genetic, environmental (e.g., trauma, stress, messages regarding health and food), and neurobehavioral factors that contribute to weight loss and on the subsequent effects of low weight on brain and cognitive development that may exacerbate anxiety, cognitive inflexibility, and harm avoidance, serving to perpetuate the illness (Frank et al., 2019; Kaye et al., 2009; Olivo et al., 2019). Neurobiologically informed models of BN tend to focus on the balance between inhibitory or self-regulatory control and reward-based processing as instrumental to ED psychopathology and on state (e.g., negative mood) or personality-trait (e.g., negative urgency) influences that increase risk to engage in impulsive binge-eating and purging behaviors (Berner & Marsh, 2014; Pearson et al., 2014).

Neuropsychological Findings

In the past decade, clinical and empirical interest in neuropsychological functioning in EDs has substantially increased, with a growing body of research examining underlying neurocognitive processes that may contribute to their etiology and/or maintenance (Smith et al., 2018). However, despite this increased interest, most work has focused on AN, with more limited findings in BN and BED. Persistence of maladaptive ED behaviors (e.g., restricted eating, binge eating, purging) despite negative consequences suggests difficulty adapting behavior in response to the environment and implicates multiple aspects of cognition, including executive functions, attention, learning/memory, and sensory and perceptual processing. Each of these domains is discussed in this section.

Executive functioning. *Executive functioning* refers to the capacity to plan, organize, and monitor the execution of behaviors that are strategically directed in a goal-oriented manner. This section discusses research supporting the involvement of several components of executive functioning, including cognitive flexibility and set shifting, inhibitory control, decision making, and central coherence, in EDs.

Cognitive flexibility and set shifting. Set shifting refers to the ability to flexibly change thoughts or actions according to situational demands, which is critical for adaptive behavior. Cognitive rigidity and poor set shifting are widely considered components of a neurocognitive endophenotype of AN (Roberts et al., 2007; Smith et al., 2018) that may contribute to behavioral inflexibility, compulsive behaviors, and extreme dietary restriction. The Wisconsin Cart Sorting Test (WCST) and the Trail Making Test are the most commonly used tests to assess set shifting in EDs. A comprehensive meta-analysis of cross-sectional studies of set shifting in ill adolescents and adults (Wu et al., 2014) reported poor set shifting in all EDs compared with healthy controls (HC), with medium effect sizes (g = –0.51–0.53) in AN-R, BN, and BED but not in AN-BP (g = –0.18). There is currently little support for differences in set shifting among ED diagnostic groups (Smith et al., 2018). In AN, some evidence suggests greater deficits in set shifting in adults compared with adolescents (Westwood et al., 2016). Weight-restored and recovered AN samples show

more attenuated disturbances in set shifting than ill individuals (Fuglset, 2019), suggesting deficits may not fully resolve with symptom remittance. Notably, set-shifting deficits in AN appear independent of the rule learning and feedback sensitivity inherent in the WCST, as findings from two task-switching studies indicated inefficient set shifting in ill (Berner, Romero, et al., 2019) and recovered individuals with AN (King et al., 2019).

Inhibitory control. Inhibitory control involves the suppression of inappropriate or unwanted behavioral (e.g., motor) or cognitive responses and is critical in regulating behavior and emotions. EDs are thought to occur on an inhibition–disinhibition continuum, with restricting EDs (i.e., AN-R) characterized by excessive inhibitory control and bulimic-spectrum EDs (i.e., BN, BED) characterized by deficient inhibitory control and greater impulsivity (Cassin & von Ranson, 2005; Lilenfeld et al., 2006; Wierenga, Bischoff-Grethe, et al., 2014; Wierenga, Ely, et al., 2014). The most frequently used tasks of inhibitory control in EDs include tests of motor control (stop-signal task [SST], go/no-go task) and interference control (variations of the Stroop Color–Word Interference Test). Despite the hypothesized role of inhibitory control in food restriction, the majority of studies of inhibitory motor control have focused on individuals with bulimic-spectrum EDs, with converging evidence supporting motor inhibitory control deficits across a range of measures and some indication of stronger associations with proactive inhibition (e.g., SST) versus reactive inhibition (e.g., go/no-go; Smith et al., 2018). In contrast, evidence suggests that women with AN demonstrate greater proactive inhibition (via the go/no-go task) compared with HC (Bartholdy et al., 2017).

Research on cognitive inhibitory control is mixed. For instance, there is some support for a greater interference effect in individuals with AN versus HC, but this has been assessed primarily with modified Stroop tests that use symptom-specific food or body-shape words (Dobson & Dozois, 2004), raising the possibility that inhibitory control may be confounded with altered attention bias toward or away from disorder-specific stimuli (see later discussion). Similarly, cognitive inhibitory control deficits have also been observed in response to disorder-relevant stimuli, such as food/eating or body shape in bulimic-spectrum EDs (Kittel et al., 2015; Wu et al., 2013). No differences were observed between individuals remitted from AN and HC on the Delis–Kaplan Executive Function System (DKEFS) Color–Word Interference Test, although anxiety was associated with poorer performance only in the remitted AN group (Ely et al., 2016). Other studies have also reported no difference between performance of individuals with BN and HC on the Stroop Color–Word Interference Test (Darcy et al., 2012). These findings support the proposal that enhanced cognitive control in AN may underlie persistent dietary restriction, whereas dysregulated or reduced inhibitory control in BN may contribute to binge-eating behavior (Wierenga, Ely, et al., 2014).

Decision making. Decision making comprises multiple cognitive functions, including stimulus assessment, action selection and execution, and outcome appraisal. Dysfunctional value-based decision making is thought to contribute to EDs, given that ED symptoms and behaviors often reflect inconsistencies between actions and goals (e.g., binge eating despite desire to maintain or lose weight) or persistence of actions despite negative consequences (e.g., continued dietary restriction despite medical complications). Moreover, traits commonly observed in EDs, such as impulsivity, harm avoidance, and altered sensitivity to reward and punishment, likely affect cognitive appraisal and action selection and may underlie variability in the ability to forego immediate rewards (food) for long-term goals (weight loss). A meta-analysis of 82 neuropsychological studies provides evidence for altered reward-related decision making in AN, BN, and BED, with medium effect sizes for the differences between currently ill ED patients and HC (Hedges's $g = -0.49$; Wu et al., 2016). Decision making was found to be altered to similar degrees in all ED subtypes, although effect size differed by decision making task. Overall, decision making in adolescents appears to be less affected than in adults and appears to improve with recovery (Giannunzio et al., 2018).

Intertemporal-choice (e.g., delay discounting) paradigms and gambling tasks (e.g., the Iowa Gambling Task [IGT], Game of Dice Task) are the most commonly used assessments of decision making in EDs. Delay-discounting tasks require choosing between sooner smaller and larger later monetary rewards and assess one's ability to delay gratification. On delay-discounting tasks, individuals with AN generally tend to prefer larger later rewards when ill (Steinglass et al., 2012), although this appears to normalize with weight restoration (Decker et al., 2015) and remittance of symptoms (Bernardoni et al., 2020; Ritschel et al., 2015; Wierenga, Ely, et al., 2014). However, one recent study revealed higher risk aversion for gains in remitted AN (Bernardoni et al., 2020). In contrast, individuals with BN and BED tend to show greater temporal discounting (i.e., a preference for smaller sooner rewards; Kekic et al., 2016; Steward et al., 2017). These findings suggest enhanced inhibitory control, reduced impulsivity, and a greater capacity to delay reward in AN, which may explain the ability to resist immediate temptation and override hunger in the long-term pursuit of thinness. In contrast, increased rates of temporal discounting in BN may contribute to binge-eating and compensatory behaviors, symptoms that reflect preference for immediate over delayed rewards.

The IGT involves a series of trials requiring the selection of a card from one of four decks, two of which are advantageous (i.e., result in lower levels of net loss) and two of which are disadvantageous (i.e., result in higher levels of net loss). The index of decision making is commonly calculated as the number of advantageous choices minus the number of disadvantageous choices. A meta-analysis of IGT performance in AN, BN, and BED revealed significantly worse performance in all patient groups compared with HC, with medium to large effects (Hedges's *g* effect sizes of –0.72 in AN, –0.62 in BN, and –1.26 in BED; Guillaume et al., 2015). Restrictive AN patients perform worse than purging AN patients. Poor IGT performance in AN tends to be characterized by inhibition to risk taking or intolerance of uncertainty (Bodell et al., 2014; Giannunzio et al., 2018), although performance appears to improve with recovery (Bodell et al., 2014). These findings support the theory that altered general reward-related decision making is a salient neuropsychological factor across EDs in adulthood (Wu et al., 2016).

Central coherence. *Central coherence* refers to the degree of focus on details in processing and the global integration of this information. AN and BN are characterized by a detail-focused processing style, often called weak central coherence, which includes difficulties with understanding the context or seeing the bigger picture (Lang et al., 2014). Central coherence is most commonly studied using the Rey–Osterrieth Complex Figure. In comparison with HC, patients with current AN and BN tend to apply an inefficient strategy when copying the complex figure, characterized by a perceptual bias to detail and reduced global processing and thought to reflect inefficient higher level executive functioning abilities (Hamatani et al., 2018; Lang et al., 2016). Impaired central coherence has also been observed in some studies of remitted AN (Weinbach et al., 2017) but not others (Lang et al., 2016). Thus, weak central coherence or poor global processing is considered a potential etiologic or maintenance factor for AN and BN that may explain the tendency for individuals with EDs to excessively focus on individual details (e.g., body weight) as opposed to broader concepts (e.g., sense of self; Hamatani et al., 2018). There are few studies of central coherence in BED.

Attention bias. *Attention bias* refers to elevated attention toward or away from disorder-relevant or salient environmental stimuli. Attention bias has been implicated in EDs, given the characteristic preoccupation with weight, shape, and food (American Psychiatric Association, 2013). The two most commonly used cognitive methods of assessing attention bias in EDs are the modified Stroop test, which include ED-salient words (e.g., "fat"), and variants of the dot-probe task that assess hypervigilance (fixating toward) or avoidance (looking away) from salient or threatening stimuli. There is generally consistent evidence for an attention bias—as evidenced by longer color-naming durations reflecting greater interference—in ill and remitted individuals with AN and

BN to words related to food and/or body shape, with some reports of disorder-specific biases (i.e., greater interference for food- or body-related words in AN and for body- or weight-related words in BN; Kittel et al., 2015; Ralph-Nearman et al., 2019). Results of dot-probe tasks are mixed. As reviewed by Smith et al. (2018), a meta-analysis demonstrated attention bias away from positive eating- and shape-related stimuli and toward negative shape-related stimuli in individuals with AN and BN versus HC, whereas a systematic review concluded that differences exist between AN and BN, such that women with AN tend to avoid food as well as overweight bodies and women with BN tend to approach food and other body types (Ralph-Nearman et al., 2019). Attention toward food cues is also seen in BED (Aviram-Friedman et al., 2018).

Working memory. *Working memory* refers to the ability to temporarily hold and manipulate information in mind for use in executing behavior. Measures of working memory that are commonly applied to EDs include the spatial and digit span tasks and the *n*-back task. In general, although some evidence suggests working memory deficits across EDs, there are largely inconsistent results across studies comparing working memory in AN (Brooks et al., 2017), BN (Van den Eynde et al., 2011), and BED (Kittel et al., 2015), with substantial heterogeneity in types of measures and stimuli used. A recent meta-analysis found that individuals with BED show worse performance on working memory tasks compared with obese individuals without BED but did not provide definitive evidence of alterations in other aspects of executive functioning (Cury et al., 2020).

Learning and memory. Although deficient learning has been hypothesized to contribute to repeated engagement in disordered behavior and illness maintenance, relatively few studies on EDs have examined learning, with the majority of those studies involving AN and focused on explicit memory. Prior studies have demonstrated impaired verbal memory functioning in patients with AN for both immediate (Bayless et al., 2002) and delayed (Bayless et al., 2002; Oltra-Cucarella et al., 2015) verbal recall. In contrast, no difference in verbal list learning or recall was detected in women remitted from AN (Stedal et al., 2019). However, the remitted AN group made significantly more repetition errors and within-trial perseveration errors than HC, which is consistent with prior suggestions that verbal recall scores may be associated with basic cognitive abilities, such as processing speed and cognitive inhibition (Oltra-Cucarella et al., 2015), and may implicate inefficient learning in the cognitive phenotype of AN. Some evidence indicates worse implicit category learning in AN (Shott et al., 2012) and worse probabilistic classification learning in BN (i.e., weather prediction task; Labouliere et al., 2016). Individuals with AN demonstrated poorer learning from reward-based feedback and lower accuracy during recall on the acquired equivalence test before and after intensive weight restoration treatment, as compared with HC. Reduced learning from reward-based feedback was associated with longer illness duration and with greater ED symptom severity at baseline, which may contribute to difficulties in changing maladaptive behaviors (Foerde & Steinglass, 2017).

Sensory processing. Body-image disturbance is a core feature of EDs and is thought to reflect deficits in sensory processing that underlie body perception. Although the majority of ED studies focus on visual body misperception (Cash & Deagle, 1997), emerging evidence suggests nonvisual sensory impairment in tactile/haptic, proprioceptive, and interoceptive (e.g., body-state feelings) domains of body perception as well (Gaudio et al., 2014). For example, women with current or remitted AN tend to demonstrate worse haptic reproduction abilities, have altered tactile perception, show impaired spatial orientation constancy (Gaudio et al., 2014), have difficulty distinguishing actual from anticipated sensations, and show decreases in interoceptive accuracy after eating (Khalsa et al., 2015). Women with current or remitted BN tend to show altered pain thresholds, sensitivity to gastric distention, and heartbeat-detection accuracy (Klabunde et al., 2013) relative to HC. Together, this supports a multisensory impairment of body perception in EDs that extends beyond visual processing (Gaudio et al., 2014).

Task-Related Functional Neuroimaging Findings

Coincident with the growing interest in neurocognitive function in EDs is the increasing application of functional magnetic resonance imaging (fMRI) to reveal the neural substrates corresponding to altered cognition and behavior in EDs. Similar to neurocognitive studies, neuroimaging studies in BN and BED are more limited than in AN (Berner & Marsh, 2014; Donnelly et al., 2018). Although neuroimaging studies have examined many of the same constructs (e.g., set shifting, inhibitory control, decision making), they have also extended examination to other disorder-relevant processes, such as reward and punishment sensitivity (including taste processing), reinforcement learning, and interoception. There is considerable overlap in the corticostriatal limbic and salience circuitry regulating these processes, and in general, neuroimaging studies have demonstrated altered frontostriatal and insula function in EDs.

Reward and punishment processing. A sizeable literature suggests alterations in basic reward processing in EDs (Keating et al., 2012; Lloyd & Steinglass, 2018; Wierenga, Bischoff-Grethe, et al., 2014). Neuroimaging studies in ill or remitted individuals with AN show relatively consistent increased anticipatory response in the anterior insula, striatum, and frontal regions to food and money cues and decreased limbic–striatal response to actual reward (pictures, taste; Cowdrey et al., 2011; Lloyd & Steinglass, 2018; Oberndorfer, Frank, et al., 2013; Oberndorfer, Simmons, et al., 2013). In contrast, in BN, food anticipation is associated with diminished prefrontal and insula activity (Bohon & Stice, 2011), whereas ill or remitted individuals with BN demonstrate increased striatal and insula reward response to pictures/tastes of food and monetary rewards (Ely et al., 2017; Monteleone et al., 2017; Oberndorfer, Frank, et al., 2013; Wierenga, Ely, et al., 2014). Individuals with BED also demonstrate greater medial orbitofrontal and ventral striatum response while viewing food pictures (Schienle et al., 2009) but have decreased ventral striatum activity during anticipation of monetary rewards/losses and diminished prefrontal cortex and insula activity during outcome processing (Balodis, Kober, et al., 2013).

There is also evidence that the modulation of brain response by hunger and satiety is altered in AN and BN. It is well-established that hunger increases reward responsivity in healthy individuals. In contrast, individuals remitted from AN have an abnormally reduced reward response to sucrose in the left ventral putamen and insula (Kaye et al., 2020) and to immediately available monetary reward in the left ventral striatum (Wierenga et al., 2015) when hungry compared with fed, suggesting that difficulty translating hunger signals into motivated action may promote food avoidance. Moreover, reduced reward response to taste (but not response to money) in the dorsal caudate when hungry was associated with elevated harm avoidance in individuals remitted from AN, suggesting a brain basis for biasing risk over reward. In contrast, women remitted from BN demonstrated elevated taste reward response in the amygdala, suggesting difficulty integrating interoceptive satiety signals to devalue reward. This may contribute to difficulty stopping eating once started (binge eating; Ely et al., 2017).

Emerging evidence suggests processing of aversive stimuli may also be disrupted in EDs. For example, individuals with an ED demonstrate elevated harm avoidance, aversion to novelty, intolerance of uncertainty, anxiety, and oversensitivity to punishment (Harrison et al., 2010), which may contribute to an altered response to negative feedback or a bias to avoid outcomes perceived as aversive. Neuroimaging studies support a neural dysfunction to loss, with an exaggerated (Bischoff-Grethe et al., 2013) or undifferentiated (Wagner et al., 2007) striatal response to monetary losses compared with wins in AN and decreased response to aversive taste in AN and BN (Monteleone et al., 2017). Less is known about aversive processing in BED.

Executive functioning. In general, fMRI studies of AN reveal increased activity within dorsolateral cognitive circuitry associated with set shifting (Garrett et al., 2014; Zastrow et al., 2009) and reduced medial and lateral prefrontal activation during error monitoring and motor inhibitory

control in AN (Oberndorfer et al., 2011; Wierenga, Bischoff-Grethe, et al., 2014), which is thought to reflect enhanced cognitive control and ability to sustain inhibition. In terms of decision making, results of fMRI studies using delay-discounting paradigms in AN are mixed, implicating both altered reward processing and executive control, with evidence of decreased striatal and anterior cingulate activation corresponding to less steep discount rates (e.g., preference for delayed over immediate reward; Decker et al., 2015), decreased lateral prefrontal and posterior parietal activation associated with faster choice behavior, and decreased dorsal anterior cingulate activation during difficult decision making (King et al., 2016) in acutely underweight AN, suggesting neural efficiency and habitual responding. We showed that women remitted from AN had decreased ventral striatal response to immediate reward and elevated dorsolateral prefrontal brain response during the act of decision making (Wierenga, Ely, et al., 2014). Using an innovative approach to examine disorder-relevant maladaptive decision making, Foerde and Steinglass (2015) reported that individuals with AN had elevated dorsal striatum activation during a food-choice task designed to capture restrictive caloric intake. The dorsal striatum is involved in action control and learned automatic behaviors, supporting the notion that maladaptive food choice reflects habitual behavior.

Less is known about the neural mechanisms of executive functioning in BN and BED. One compelling theory suggests that binge-eating behavior results from the failure to appropriately engage frontostriatal circuits, reflecting reduced inhibitory or self-regulatory control (Berner & Marsh, 2014; Donnelly et al., 2018). In support of this notion, adolescents and adults with BN have decreased brain response in frontostriatal circuitry during correct responding on incongruent trials on the Simon Spatial Incompatibility task, and in adults, this reduced frontostriatal response was associated with greater errors and faster response times, suggesting that reduced activation may underlie impulsivity and difficulties inhibiting behavior in BN (Marsh et al., 2009, 2011). Similarly, decreased activation in the ventromedial prefrontal cortex, inferior frontal gyrus, and insula was observed during Stroop test performance in individuals with BED and was associated with reduced dietary restraint (Balodis, Molina, et al., 2013), consistent with reduced self-regulation and impulse control.

Reinforcement learning. Rigid or inflexible behavior that persists despite negative consequences indicates deficient reinforcement learning. The core idea of reinforcement learning is that the rate of learning is driven by violations of expectations, or prediction error (PE), which are operationalized as the received outcome minus the expected outcome (Rescorla & Wagner, 1972). Learning from experience occurs through updating expectations about the outcome in proportion to PE so that the expected outcome converges to the actual outcome, resulting in a smaller PE. The majority of functional neuroimaging studies demonstrating altered learning in EDs have utilized Pavlovian reward conditioning and operant probabilistic reversal learning tasks. For example, during an associative learning task of conditioned visual stimuli and sucrose taste, ill and remitted adults with AN (Frank et al., 2012, 2016) show enhanced activation of neural circuits associated with reward learning (including the anterior ventral striatum, insula, and orbitofrontal cortex) to unexpected receipt or omission of taste stimuli (i.e., elevated PE response). Exaggerated response in reward circuitry to reward PE is thought to reflect altered DA-mediated reward processing, as unexpected rather than predictable stimulation is related to DA activation (Schultz, 2002). Notably, in AN, increased PE response in the caudate, orbitofrontal cortex, and insula has been associated with elevated anxiety and worse treatment outcome (DeGuzman et al., 2017). In contrast, reduced PE signals in frontostriatal neural circuitry during reward learning have been reported in BN (Frank et al., 2011), thought to reflect reduced motivational salience of, and attention to, reward-learning stimuli. This suggests that, in contrast to AN, BN may result in deficits in reward responding to food cues, which may in turn contribute to overeating or binge-eating behavior. Of note, potential group differences in learning rate were not assessed, as these studies modeled PE response using a fixed learning-rate parameter across all participants;

by holding learning rate constant, increased PE response may reflect an elevated surprise response rather than differences in learning per se.

During an operant probabilistic reversal learning task, ill and recovered individuals with AN show elevated lose–shift behavior, and on lose–shift trials, ill AN individuals show increased dorsal ACC activation compared with HC (Geisler et al., 2017), whereas recovered AN individuals show elevated activation in frontoparietal regions, consistent with the notion of excessive cognitive control and increased sensitivity to negative feedback (Ritschel et al., 2017). This excessive top-down regulatory control during learning appears to extend to disorder-relevant stimuli; during a food-cue acquisition and reversal learning task, adolescents with AN demonstrated elevated prefrontal activation during food-cue acquisition and its reversal compared with healthy peers, despite no behavioral differences in the ability to acquire or reverse the food-cue association, suggesting greater reliance on prefrontal regulatory networks to acquire and alter expectancies to food (Hildebrandt et al., 2018). Although research on reinforcement learning has focused primarily on reward-based learning, with less attention to learning from aversive or punishing experiences, a recent study using a feedback-learning task that required adaptation to changing reward contingencies revealed that, behaviorally, individuals with AN had an increased learning rate specifically after punishing feedback (Bernardoni et al., 2018) but did not differ from health controls in neural response for learning rate, expected value, or PE. However, following punishment feedback, AN demonstrated elevated posterior medial frontal cortex activation, suggesting neural substrates of feedback learning may be selectively altered for punishment in AN.

Interoception. *Interoception*, or the detection and integration of signals relating to the body (e.g., taste, hunger, pain, heartbeat, respiration, touch), gives rise to emotions, critically determines one's experience of the body, and organizes behavior to meet one's physiological needs (Khalsa & Lapidus, 2016). A growing literature suggests an important role of the experience of the body in the emergence and maintenance of EDs (Badoud & Tsakiris, 2017; Khalsa & Lapidus, 2016; Klabunde et al., 2013), with impairments in interoception representing a transdiagnostic feature of EDs hypothesized to be related to disrupted interoceptive neural processing (Martin et al., 2019). The insula is a hub for interoception, and accumulating evidence suggests disturbances in anterior and middorsal insula function in ill and remitted individual with AN (Bischoff-Grethe et al., 2018; Kerr et al., 2016; Oberndorfer, Simmons, et al., 2013; Wagner et al., 2008). Individuals remitted from AN have also demonstrated a mismatch between insula and corticolimbic response to anticipation and receipt of pleasant touch (anticipation < receipt; Bischoff-Grethe et al., 2018), prolonged aversive breathing restriction (anticipation < receipt; Berner, Simmons, et al., 2018), and thermal heat pain (anticipation > receipt; Strigo et al., 2013) compared with HC, whereas individuals remitted from BN demonstrate greater anticipatory response to touch (Wierenga et al., 2020) and aversive breathing (Berner, Simmons, et al., 2019), with no difference in receipt. The observed mismatch between subjective experiences and objective brain response in EDs points to abnormal integration and, possibly, disconnection between reported, expected, and actual interoceptive states (Khalsa et al., 2015), although further work is needed to replicate these findings.

Summary

Growing evidence indicates that EDs, including AN, BN, and BED, are heritable disorders that are characterized by altered neurocognition and corticostriatal neural function. Multiple cognitive functions have been implicated in EDs, most notably altered executive functions (e.g., set shifting, cognitive flexibility, decision making, inhibitory control, central coherence). Neuroimaging studies have implicated altered reward and punishment processing, inhibitory control, decision making, reinforcement learning, and interoception in EDs, corresponding broadly to altered corticostriatal neural circuit function. Together fMRI studies support the hypothesis that EDs reflect an altered balance between inhibitory or self-regulatory control and reward-based processing, with AN characterized by enhanced higher order inhibitory function and

reduced reward motivation, corresponding to the ability to inhibit consummatory drives, and BN/BED characterized by reduced inhibitory control and increased reward motivation, corresponding to lowered ability to self-regulate and control impulses that may increase one's vulnerability to overeat.

ACCEPTED SCIENCE

- Eating disorders (EDs), including anorexia nervosa, bulimia nervosa, and binge-eating disorder, are brain- and biologically based heritable disorders.
- Pathogenic models of EDs include contributions of genes, temperament, environment, and neurocognitive function in the development and maintenance of EDs.
- Neurocognitive and neuroimaging studies have identified altered reward and punishment processing, inhibitory control, decision making, reinforcement learning, and interoception in EDs, corresponding to altered corticostriatal neural circuit function.
- Excessive underconsumption or overconsumption of food characteristic of EDs is thought to reflect an altered balance of reward and inhibitory control.

QUESTIONS AND CONTROVERSIES

Despite the important scientific advances in our understanding of EDs over the past few decades, many remaining questions must be answered to move the field toward a better mechanistic understanding of the pathophysiology of EDs.

Can Computational Modeling of Cognition Better Elucidate Neurocognitive Alterations in EDs?

Despite documented neurocognitive alterations in EDs, their underlying mechanisms remain largely unknown. The application of mathematical models of cognition may elucidate latent variables or component processes underlying cognitive test performance that can provide fundamental insights into the mechanisms of disordered behavior. Although computational modeling approaches have been more commonly used in fMRI studies (as described previously; see also Bernardoni et al., 2018; Frank et al., 2016), a few behavioral studies demonstrate the utility of this approach to examine mechanisms underlying altered learning and decision making in EDs. For example, by applying a computation model (Competition Between Verbal and Implicit Systems), Filoteo et al. (2014) simulated hyperlearning observed in AN by increasing the model parameter that represents sensitivity to negative feedback (δ parameter), whereas the deficit in set shifting was simulated by altering the parameters that represent changes in rule selection and flexibility (λ and γ parameters, respectively). These simulations suggest that alterations in sensitivity to negative feedback, rule-selection deficits, and inflexibility can affect category learning and set shifting in AN.

Can the Identification of Dimensional Constructs Underlying ED Symptoms and Their Neural Correlates Improve Our Mechanistic Understanding of EDs?

Overlapping symptoms, along with significant diagnostic crossover (e.g., from AN to BN) over the course of one's illness (Eddy et al., 2008), suggest shared features that are not well captured by current categorical *DSM-5* diagnostic approaches. The heterogeneity in behavior and weight in EDs suggests that both shared and distinct mechanisms may underlie symptoms across individuals with an ED. Focusing instead on the cognitive and neural processes that may promote significant dietary restriction in the presence/absence of binge eating/purging, and/or objectively low weight, rather than focusing solely on group differences, could improve mechanistic understanding of ED pathophysiology and inform better diagnostic subgrouping and clinical prediction.

Differentiating Between Illness State- and Trait-Related Alterations Remains a Challenge for the ED Field

Identifying cause and effect between pathological eating behavior and the impact of malnutrition on neural and cognitive processes in EDs remains a

major methodological question in the absence of prospective studies. Unlike most other psychiatric disorders, EDs involve significant physiological sequelae corresponding to illness state that can confound characterization of the neuropsychological manifestation of the illness. Malnutrition is associated with changes in brain structure (e.g., reduced gray matter, altered white matter integrity) and profound metabolic, electrolyte, and endocrine disturbances. Diet and weight can influence DA and 5-HT metabolism (Kaye et al., 2013). Commonly used strategies to avoid confounding effects of abnormal nutritional status have included characterizing behavioral traits that occur in childhood prior to the onset of an ED and studying individuals who have recovered from an ED, although it remains unclear whether altered findings reflect premorbid traits or scars from the illness. Moreover, there is no standard definition of recovery, resulting in considerable variability in the degree and length of weight restoration and/or resolution of cognitive and behavioral symptoms across studies. Studying patients when currently ill allows for a better ability to associate cognitive and brain disturbances with active symptomatology, and comparisons to findings in remitted individuals may help to clarify state- versus trait-based similarities and differences. However, studies of ill EDs must account for additional disease-specific confounds, such as medication, pubertal status, menstrual-cycle phase and/or hormonal levels, illness chronicity, weight history, comorbid psychopathology, and so on that could influence results, and differences in these variables often make cross-study comparisons difficult.

Longitudinal Designs Are Critically Needed to Understand the Trajectory of ED Psychopathology

The recovery process of EDs is poorly understood. Although about 50% of affected individuals will eventually normalize weight and nutrition (Keel et al., 1999; van den Berg et al., 2019), the other 50% tend to have persistent, chronic symptoms. Diagnostic crossover is also common, with one study reporting 73% of participants with an intake *DSM-IV* diagnosis of AN experienced diagnostic crossover over 7 years: 49% crossed over between the AN subtypes, and 34% crossed over from AN to BN, calling into question the validity of subtype classifications (Eddy et al., 2008). Elucidating the relationship of neurocognitive factors with symptom maintenance, diagnostic migration, and relapse or remission over time is critical to differentiate between cognitive processes that are maintenance factors, simple correlates, or consequences of illness.

The Effects of EDs on Neurodevelopment Are Poorly Understood

Most ED studies focus on adults, yet ED symptoms typically first manifest in early to middle adolescence (Klein & Walsh, 2003). Little is known about how extremes in eating behavior affect the regular course of brain development in adolescents. Pathogenic models posit delayed brain maturation in AN and BN (Berner & Marsh, 2014; Olivo et al., 2019), although few studies of neurodevelopment focus on EDs, making it difficult to determine whether adolescents with EDs are neurodevelopmentally delayed with respect to their healthy peers. For example, abnormal maturation of either dorsal frontostriatal circuits supporting self-regulatory control and/or ventral striatal circuits supporting reward-based learning could underlie inhibitory control and motivational deficits in AN and BN. Moreover, years of malnutrition may produce permanent or long-term alterations as white matter continues to develop into early adulthood. Regression to prepubertal status due to severe malnutrition may confer added vulnerability. Although cross-sectional studies can provide preliminary evidence of altered brain development, longitudinal studies are needed to determine whether disordered eating affects neural maturation and whether neurodevelopmental stage or trajectory may differ by symptom severity or ED subtype.

There Is Insufficient Inclusivity in ED Research

In recent decades, the field has recognized that EDs affect individuals across demographic categories, with studies consistently demonstrating EDs are experienced by individuals from diverse races and ethnicities (Franko et al., 2007), socioeconomic

backgrounds (Gard & Freeman, 1996), genders (Nagata et al., 2020), and stages across the lifespan (Brandsma, 2007). However, many research studies fail to include a representative sample. For instance, male individuals are typically excluded from the majority of imaging research studies on AN and BN, as these EDs among men and boys are relatively rare (less than 10% in clinical settings; see also Klein & Walsh, 2003) and have a different clinical presentation, which would introduce a confound if included. As a result, the degree to which existing neurocognitive and neuroimaging findings generalize to men and boys and other underrepresented groups is not well understood.

QUESTIONS AND CONTROVERSIES SUMMARY

- Can computational modeling of cognition better elucidate neurocognitive alterations in eating disorders (EDs)?
- Can the identification of dimensional constructs underlying ED symptoms and their neural correlates improve our mechanistic understanding and classification of EDs?
- How can a better understanding of the trajectory of ED psychopathology inform neurodevelopmental changes and predict clinical outcome?
- How can state versus trait influences be better differentiated to inform cause and effect in EDs?

CONCLUSION

Research into the neurocognitive and brain bases of ED is in its infancy. Future research is needed to identify dimensional neurocognitive mechanisms underlying symptom heterogeneity in EDs, determine the trajectory of ED psychopathology to inform state versus trait influences, and elucidate the impact of EDs on neurodevelopment. Advancing our understanding of neurocognitive constructs that underlie eating pathology and predict symptom change will improve diagnostic classification, identify novel therapeutic targets, and drive innovative treatment development for these often chronic and sometimes deadly disorders.

KEY REFERENCES

Berner, L. A., & Marsh, R. (2014). Frontostriatal circuits and the development of bulimia nervosa. *Frontiers in Behavioral Neuroscience*, *8*, Article 395. https://doi.org/10.3389/fnbeh.2014.00395

Donnelly, B., Touyz, S., Hay, P., Burton, A., Russell, J., & Caterson, I. (2018). Neuroimaging in bulimia nervosa and binge eating disorder: A systematic review. *Journal of Eating Disorders*, *6*(1), Article 3. https://doi.org/10.1186/s40337-018-0187-1

Kaye, W. H., Wierenga, C. E., Bailer, U. F., Simmons, A. N., & Bischoff-Grethe, A. (2013). Nothing tastes as good as skinny feels: The neurobiology of anorexia nervosa. *Trends in Neuroscience*, *36*(2), 110–120. https://doi.org/10.1016/j.tins.2013.01.003

Smith, K. E., Mason, T. B., Johnson, J. S., Lavender, J. M., & Wonderlich, S. A. (2018). A systematic review of reviews of neurocognitive functioning in eating disorders: The state-of-the-literature and future directions. *International Journal of Eating Disorders*, *51*(8), 798–821. https://doi.org/10.1002/eat.22929

Watson, H. J., Yilmaz, Z., Thornton, L. M., Hübel, C., Coleman, J. R. I., Gaspar, H. A., Bryois, J., Hinney, A., Leppä, V. M., Mattheisen, M., Medland, S. E., Ripke, S., Yao, S., Giusti-Rodríguez, P., Hanscombe, K. B., Purves, K. L., Adan, R. A. H., Alfredsson, L., Ando, T., . . . Bulik, C. M. (2019). Genome-wide association study identifies eight risk loci and implicates metabo-psychiatric origins for anorexia nervosa. *Nature Genetics*, *51*(8), 1207–1214. https://doi.org/10.1038/s41588-019-0439-2

References

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). https://doi.org/10.1176/appi.books.9780890425596

Aspen, V., Darcy, A. M., & Lock, J. (2013). A review of attention biases in women with eating disorders. *Cognition and Emotion*, *27*(5), 820–838. https://doi.org/10.1080/02699931.2012.749777

Aviram-Friedman, R., Astbury, N., Ochner, C. N., Contento, I., & Geliebter, A. (2018). Neurobiological evidence for attention bias to food, emotional dysregulation, disinhibition and deficient somatosensory awareness in obesity with binge eating disorder. *Physiology & Behavior*, *184*, 122–128. https://doi.org/10.1016/j.physbeh.2017.11.003

Badoud, D., & Tsakiris, M. (2017). From the body's viscera to the body's image: Is there a link between interoception and body image concerns?

Neuroscience and Biobehavioral Reviews, *77*, 237–246. https://doi.org/10.1016/j.neubiorev.2017.03.017

Baker, J. H., Schaumberg, K., & Munn-Chernoff, M. A. (2017). Genetics of anorexia nervosa. *Current Psychiatry Reports*, *19*(11), Article 84. https://doi.org/10.1007/s11920-017-0842-2

Balodis, I. M., Kober, H., Worhunsky, P. D., White, M. A., Stevens, M. C., Pearlson, G. D., Sinha, R., Grilo, C. M., & Potenza, M. N. (2013). Monetary reward processing in obese individuals with and without binge eating disorder. *Biological Psychiatry*, *73*(9), 877–886. https://doi.org/10.1016/j.biopsych.2013.01.014

Balodis, I. M., Molina, N. D., Kober, H., Worhunsky, P. D., White, M. A., Rajita Sinha., Grilo, C. M., & Potenza, M. N. (2013). Divergent neural substrates of inhibitory control in binge eating disorder relative to other manifestations of obesity. *Obesity*, *21*(2), 367–377. https://doi.org/10.1002/oby.20068

Bartholdy, S., Rennalls, S. J., Jacques, C., Danby, H., Campbell, I. C., Schmidt, U., & O'Daly, O. G. (2017). Proactive and reactive inhibitory control in eating disorders. *Psychiatry Research*, *255*, 432–440. https://doi.org/10.1016/j.psychres.2017.06.073

Bayless, J. D., Kanz, J. E., Moser, D. J., McDowell, B. D., Bowers, W. A., Andersen, A. E., & Paulsen, J. S. (2002). Neuropsychological characteristics of patients in a hospital-based eating disorder program. *Annals of Clinical Psychiatry*, *14*(4), 203–207. https://doi.org/10.3109/10401230209147458

Bernardoni, F., Bernhardt, N., Pooseh, S., King, J. A., Geisler, D., Ritschel, F., Boehm, I., Seidel, M., Roessner, V., Smolka, M. N., & Ehrlich, S. (2020). Metabolic state and value-based decision-making in acute and recovered female patients with anorexia nervosa. *Journal of Psychiatry & Neuroscience*, *45*(4), 253–261. https://doi.org/10.1503/jpn.190031

Bernardoni, F., Geisler, D., King, J. A., Javadi, A. H., Ritschel, F., Murr, J., Reiter, A. M. F., Rössner, V., Smolka, M. N., Kiebel, S., & Ehrlich, S. (2018). Altered medial frontal feedback learning signals in anorexia nervosa. *Biological Psychiatry*, *83*(3), 235–243. https://doi.org/10.1016/j.biopsych.2017.07.024

Bernardoni, F., King, J. A., Geisler, D., Stein, E., Jaite, C., Nätsch, D., Tam, F. I., Boehm, I., Seidel, M., Roessner, V., & Ehrlich, S. (2016). Weight restoration therapy rapidly reverses cortical thinning in anorexia nervosa: A longitudinal study. *NeuroImage*, *130*, 214–222. https://doi.org/10.1016/j.neuroimage.2016.02.003

Berner, L. A., & Marsh, R. (2014). Frontostriatal circuits and the development of bulimia nervosa. *Frontiers in Behavioral Neuroscience*, *8*, Article 395. https://doi.org/10.3389/fnbeh.2014.00395

Berner, L. A., Romero, E. M., Reilly, E. E., Lavender, J. M., Kaye, W. H., & Wierenga, C. E. (2019). Task-switching inefficiencies in currently ill, but not remitted anorexia nervosa. *International Journal of Eating Disorders*, *52*(11), 1316–1321. https://doi.org/10.1002/eat.23175

Berner, L. A., Simmons, A. N., Wierenga, C. E., Bischoff-Grethe, A., Paulus, M. P., Bailer, U. F., Ely, A. V., & Kaye, W. H. (2018). Altered interoceptive activation before, during, and after aversive breathing load in women remitted from anorexia nervosa. *Psychological Medicine*, *48*(1), 142–154. https://doi.org/10.1017/S0033291717001635

Berner, L. A., Simmons, A. N., Wierenga, C. E., Bischoff-Grethe, A., Paulus, M. P., Bailer, U. F., & Kaye, W. H. (2019). Altered anticipation and processing of aversive interoceptive experience among women remitted from bulimia nervosa. *Neuropsychopharmacology*, *44*(7), 1265–1273. https://doi.org/10.1038/s41386-019-0361-4

Berner, L. A., Stefan, M., Lee, S., Wang, Z., Terranova, K., Attia, E., & Marsh, R. (2018). Altered cortical thickness and attentional deficits in adolescent girls and women with bulimia nervosa. *Journal of Psychiatry & Neuroscience*, *43*(3), 151–160. https://doi.org/10.1503/jpn.170070

Berner, L. A., Wang, Z., Stefan, M., Lee, S., Huo, Z., Cyr, M., & Marsh, R. (2019). Subcortical shape abnormalities in bulimia nervosa. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *4*(12), 1070–1079. https://doi.org/10.1016/j.bpsc.2018.12.011

Bischoff-Grethe, A., McCurdy, D., Grenesko-Stevens, E., Irvine, L. E., Wagner, A., Yau, W.-Y., Fennema-Notestine, C., Wierenga, C. E., Fudge, J. L., Delgado, M. R., & Kaye, W. H. (2013). Altered brain response to reward and punishment in adolescents with anorexia nervosa. *Psychiatry Research*, *214*(3), 331–340. https://doi.org/10.1016/j.pscychresns.2013.07.004

Bischoff-Grethe, A., Wierenga, C. E., Berner, L. A., Simmons, A. N., Bailer, U., Paulus, M. P., & Kaye, W. H. (2018). Neural hypersensitivity to pleasant touch in women remitted from anorexia nervosa. *Translational Psychiatry*, *8*(1), Article 161. https://doi.org/10.1038/s41398-018-0218-3

Bodell, L. P., Keel, P. K., Brumm, M. C., Akubuiro, A., Caballero, J., Tranel, D., Hodis, B., & McCormick, L. M. (2014). Longitudinal examination of decision-making performance in anorexia nervosa: Before and after weight restoration. *Journal of Psychiatric Research*, *56*, 150–157. https://doi.org/10.1016/j.jpsychires.2014.05.015

Bohon, C., & Stice, E. (2011). Reward abnormalities among women with full and subthreshold bulimia nervosa: A functional magnetic resonance imaging study. *International Journal of Eating Disorders*, *44*(7), 585–595. https://doi.org/10.1002/eat.20869

Brandsma, L. (2007). Eating disorders across the lifespan. *Journal of Women & Aging*, *19*(1–2), 155–172. https://doi.org/10.1300/J074v19n01_10

Brooks, S. J., Funk, S. G., Young, S. Y., & Schiöth, H. B. (2017). The role of working memory for cognitive control in anorexia nervosa versus substance use disorder. *Frontiers in Psychology*, *8*, Article 1651. https://doi.org/10.3389/fpsyg.2017.01651

Bulik, C. M., Blake, L., & Austin, J. (2019). Genetics of eating disorders: What the clinician needs to know. *Psychiatric Clinics of North America*, *42*(1), 59–73. https://doi.org/10.1016/j.psc.2018.10.007

Cash, T. F., & Deagle, E. A., III. (1997). The nature and extent of body-image disturbances in anorexia nervosa and bulimia nervosa: A meta-analysis. *International Journal of Eating Disorders*, *22*(2), 107–126. https://doi.org/10.1002/(SICI)1098-108X(199709)22:2<107::AID-EAT1>3.0.CO;2-J

Cassin, S. E., & von Ranson, K. M. (2005). Personality and eating disorders: A decade in review. *Clinical Psychology Review*, *25*(7), 895–916. https://doi.org/10.1016/j.cpr.2005.04.012

Castro-Fornieles, J., Bargalló, N., Lázaro, L., Andrés, S., Falcon, C., Plana, M. T., & Junqué, C. (2009). A cross-sectional and follow-up voxel-based morphometric MRI study in adolescent anorexia nervosa. *Journal of Psychiatric Research*, *43*(3), 331–340. https://doi.org/10.1016/j.jpsychires.2008.03.013

Cowdrey, F. A., Park, R. J., Harmer, C. J., & McCabe, C. (2011). Increased neural processing of rewarding and aversive food stimuli in recovered anorexia nervosa. *Biological Psychiatry*, *70*(8), 736–743. https://doi.org/10.1016/j.biopsych.2011.05.028

Cury, M. E. G., Berberian, A., Scarpato, B. S., Kerr-Gaffney, J., Santos, F. H., & Claudino, A. M. (2020). Scrutinizing domains of executive function in binge eating disorder: A systematic review and meta-analysis. *Frontiers in Psychiatry*, *11*, Article 288. https://doi.org/10.3389/fpsyt.2020.00288

Darcy, A. M., Fitzpatrick, K. K., Colborn, D., Manasse, S., Datta, N., Aspen, V., Shields, C. S., Le Grange, D., & Lock, J. (2012). Set-shifting among adolescents with bulimic spectrum eating disorders. *Psychosomatic Medicine*, *74*(8), 869–872. https://doi.org/10.1097/PSY.0b013e31826af636

Decker, J. H., Figner, B., & Steinglass, J. E. (2015). On weight and waiting: Delay discounting in anorexia nervosa pretreatment and posttreatment. *Biological Psychiatry*, *78*(9), 606–614. https://doi.org/10.1016/j.biopsych.2014.12.016

DeGuzman, M., Shott, M. E., Yang, T. T., Riederer, J., & Frank, G. K. W. (2017). Association of elevated reward prediction error response with weight gain in adolescent anorexia nervosa. *American Journal of Psychiatry*, *174*(6), 557–565. https://doi.org/10.1176/appi.ajp.2016.16060671

Dobson, K. S., & Dozois, D. J. (2004). Attentional biases in eating disorders: A meta-analytic review of Stroop performance. *Clinical Psychology Review*, *23*(8), 1001–1022. https://doi.org/10.1016/j.cpr.2003.09.004

Donnelly, B., Touyz, S., Hay, P., Burton, A., Russell, J., & Caterson, I. (2018). Neuroimaging in bulimia nervosa and binge eating disorder: A systematic review. *Journal of Eating Disorders*, *6*(1), Article 3. https://doi.org/10.1186/s40337-018-0187-1

Eddy, K. T., Dorer, D. J., Franko, D. L., Tahilani, K., Thompson-Brenner, H., & Herzog, D. B. (2008). Diagnostic crossover in anorexia nervosa and bulimia nervosa: Implications for *DSM-V*. *American Journal of Psychiatry*, *165*(2), 245–250. https://doi.org/10.1176/appi.ajp.2007.07060951

Ely, A. V., Wierenga, C. E., Bischoff-Grethe, A., Bailer, U. F., Berner, L. A., Fudge, J. L., Paulus, M. P., & Kaye, W. H. (2017). Response in taste circuitry is not modulated by hunger and satiety in women remitted from bulimia nervosa. *Journal of Abnormal Psychology*, *126*(5), 519–530. https://doi.org/10.1037/abn0000218

Ely, A. V., Wierenga, C. E., & Kaye, W. H. (2016). Anxiety impacts cognitive inhibition in remitted anorexia nervosa. *European Eating Disorders Review*, *24*(4), 347–351. https://doi.org/10.1002/erv.2451

Filoteo, J. V., Paul, E. J., Ashby, F. G., Frank, G. K., Helie, S., Rockwell, R., Bischoff-Grethe, A., Wierenga, C., & Kaye, W. H. (2014). Simulating category learning and set shifting deficits in patients weight-restored from anorexia nervosa. *Neuropsychology*, *28*(5), 741–751. https://doi.org/10.1037/neu0000055

Foerde, K., & Steinglass, J. E. (2017). Decreased feedback learning in anorexia nervosa persists after weight restoration. *International Journal of Eating Disorders*, *50*(4), 415–423. https://doi.org/10.1002/eat.22709

Foerde, K., Steinglass, J. E., Shohamy, D., & Walsh, B. T. (2015). Neural mechanisms supporting maladaptive food choices in anorexia nervosa. *Nature Neuroscience*, *18*(11), 1571–1573. https://doi.org/10.1038/nn.4136

Frank, G. K. W., Collier, S., Shott, M. E., & O'Reilly, R. C. (2016). Prediction error and somatosensory insula activation in women recovered from anorexia nervosa. *Journal of Psychiatry & Neuroscience*, *41*(5), 304–311. https://doi.org/10.1503/jpn.150103

Frank, G. K. W., DeGuzman, M. C., & Shott, M. E. (2019). Motivation to eat and not to eat—The psycho-biological conflict in anorexia nervosa. *Physiology & Behavior*, *206*, 185–190. https://doi.org/10.1016/j.physbeh.2019.04.007

Frank, G. K. W., Reynolds, J. R., Shott, M. E., Jappe, L., Yang, T. T., Tregellas, J. R., & O'Reilly, R. C. (2012). Anorexia nervosa and obesity are associated with opposite brain reward response. *Neuropsychopharmacology*, *37*(9), 2031–2046. https://doi.org/10.1038/npp.2012.51

Frank, G. K. W., Reynolds, J. R., Shott, M. E., & O'Reilly, R. C. (2011). Altered temporal difference learning in bulimia nervosa. *Biological Psychiatry*, *70*(8), 728–735. https://doi.org/10.1016/j.biopsych.2011.05.011

Franko, D. L., Becker, A. E., Thomas, J. J., & Herzog, D. B. (2007). Cross-ethnic differences in eating disorder symptoms and related distress. *International Journal of Eating Disorders*, *40*(2), 156–164. https://doi.org/10.1002/eat.20341

Fuglset, T. S. (2019). Set-shifting, central coherence and decision-making in individuals recovered from anorexia nervosa: A systematic review. *Journal of Eating Disorders*, *7*(1), Article 22. https://doi.org/10.1186/s40337-019-0251-5

Gard, M. C., & Freeman, C. P. (1996). The dismantling of a myth: A review of eating disorders and socioeconomic status. *International Journal of Eating Disorders*, *20*(1), 1–12. https://doi.org/10.1002/(SICI)1098-108X(199607)20:1<1::AID-EAT1>3.0.CO;2-M

Garrett, A. S., Lock, J., Datta, N., Beenhaker, J., Kesler, S. R., & Reiss, A. L. (2014). Predicting clinical outcome using brain activation associated with set-shifting and central coherence skills in anorexia nervosa. *Journal of Psychiatric Research*, *57*, 26–33. https://doi.org/10.1016/j.jpsychires.2014.06.013

Gaudio, S., Brooks, S. J., & Riva, G. (2014). Nonvisual multisensory impairment of body perception in anorexia nervosa: A systematic review of neuropsychological studies. *PLOS ONE*, *9*(10), Article e110087. https://doi.org/10.1371/journal.pone.0110087

Geisler, D., Ritschel, F., King, J. A., Bernardoni, F., Seidel, M., Boehm, I., Runge, F., Goschke, T., Roessner, V., Smolka, M. N., & Ehrlich, S. (2017). Increased anterior cingulate cortex response precedes behavioural adaptation in anorexia nervosa. *Scientific Reports*, *7*(1), Article 42066. https://doi.org/10.1038/srep42066

Giannunzio, V., Degortes, D., Tenconi, E., Collantoni, E., Solmi, M., Santonastaso, P., & Favaro, A. (2018). Decision-making impairment in anorexia nervosa: New insights into the role of age and decision-making style. *European Eating Disorders Review*, *26*(4), 302–314. https://doi.org/10.1002/erv.2595

Guillaume, S., Gorwood, P., Jollant, F., Van den Eynde, F., Courtet, P., & Richard-Devantoy, S. (2015). Impaired decision-making in symptomatic anorexia and bulimia nervosa patients: A meta-analysis. *Psychological Medicine*, *45*(16), 3377–3391. https://doi.org/10.1017/S003329171500152X

Hamatani, S., Tomotake, M., Takeda, T., Kameoka, N., Kawabata, M., Kubo, H., Ohta, M., Tada, Y., Tomioka, Y., Watanabe, S., Inoshita, M., Kinoshita, M., & Ohmori, T. (2018). Impaired central coherence in patients with anorexia nervosa. *Psychiatry Research*, *259*, 77–80. https://doi.org/10.1016/j.psychres.2017.09.086

Harrison, A., O'Brien, N., Lopez, C., & Treasure, J. (2010). Sensitivity to reward and punishment in eating disorders. *Psychiatry Research*, *177*(1–2), 1–11. https://doi.org/10.1016/j.psychres.2009.06.010

Hildebrandt, T., Schulz, K., Schiller, D., Heywood, A., Goodman, W., & Sysko, R. (2018). Evidence of prefrontal hyperactivation to food-cue reversal learning in adolescents with anorexia nervosa. *Behaviour Research and Therapy*, *111*, 36–43. https://doi.org/10.1016/j.brat.2018.08.006

Kaye, W. H., Fudge, J. L., & Paulus, M. (2009). New insights into symptoms and neurocircuit function of anorexia nervosa. *Nature Reviews Neuroscience*, *10*(8), 573–584. https://doi.org/10.1038/nrn2682

Kaye, W. H., Wierenga, C. E., Bailer, U. F., Simmons, A. N., & Bischoff-Grethe, A. (2013). Nothing tastes as good as skinny feels: The neurobiology of anorexia nervosa. *Trends in Neuroscience*, *36*(2), 110–120. https://doi.org/10.1016/j.tins.2013.01.003

Kaye, W. H., Wierenga, C. E., Bischoff-Grethe, A., Berner, L. A., Ely, A. V., Bailer, U. F., Paulus, M. P., & Fudge, J. L. (2020). Neural insensitivity to the effects of hunger in women remitted from anorexia nervosa. *American Journal of Psychiatry*, *177*(7), 601–610. https://doi.org/10.1176/appi.ajp.2019.19030261

Keating, C., Tilbrook, A. J., Rossell, S. L., Enticott, P. G., & Fitzgerald, P. B. (2012). Reward processing in anorexia nervosa. *Neuropsychologia*, *50*(5), 567–575. https://doi.org/10.1016/j.neuropsychologia.2012.01.036

Keel, P. K., Mitchell, J. E., Miller, K. B., Davis, T. L., & Crow, S. J. (1999). Long-term outcome of bulimia nervosa. *Archives of General Psychiatry*, *56*(1), 63–69. https://doi.org/10.1001/archpsyc.56.1.63

Kekic, M., Bartholdy, S., Cheng, J., McClelland, J., Boysen, E., Musiat, P., O'Daly, O. G., Campbell, I. C., & Schmidt, U. (2016). Increased temporal discounting in bulimia nervosa. *International Journal of Eating Disorders*, *49*(12), 1077–1081. https://doi.org/10.1002/eat.22571

Kerr, K. L., Moseman, S. E., Avery, J. A., Bodurka, J., Zucker, N. L., & Simmons, W. K. (2016). Altered insula activity during visceral interoception in weight-restored patients with anorexia nervosa. *Neuropsychopharmacology*, *41*(2), 521–528. https://doi.org/10.1038/npp.2015.174

Khalsa, S. S., Craske, M. G., Li, W., Vangala, S., Strober, M., & Feusner, J. D. (2015). Altered interoceptive awareness in anorexia nervosa: Effects of meal

anticipation, consumption and bodily arousal. *International Journal of Eating Disorders*, *48*(7), 889–897. https://doi.org/10.1002/eat.22387

Khalsa, S. S., & Lapidus, R. C. (2016). Can interoception improve the pragmatic search for biomarkers in psychiatry? *Frontiers in Psychiatry*, *7*, Article 121. https://doi.org/10.3389/fpsyt.2016.00121

King, J. A., Geisler, D., Bernardoni, F., Ritschel, F., Böhm, I., Seidel, M., Mennigen, E., Ripke, S., Smolka, M. N., Roessner, V., & Ehrlich, S. (2016). Altered neural efficiency of decision making during temporal reward discounting in anorexia nervosa. *Journal of the American Academy of Child & Adolescent Psychiatry*, *55*(11), 972–979. https://doi.org/10.1016/j.jaac.2016.08.005

King, J. A., Korb, F. M., Vettermann, R., Ritschel, F., Egner, T., & Ehrlich, S. (2019). Cognitive overcontrol as a trait marker in anorexia nervosa? Aberrant task- and response-set switching in remitted patients. *Journal of Abnormal Psychology*, *128*(8), 806–812. https://doi.org/10.1037/abn0000476

Kittel, R., Brauhardt, A., & Hilbert, A. (2015). Cognitive and emotional functioning in binge-eating disorder: A systematic review. *International Journal of Eating Disorders*, *48*(6), 535–554. https://doi.org/10.1002/eat.22419

Klabunde, M., Acheson, D. T., Boutelle, K. N., Matthews, S. C., & Kaye, W. H. (2013). Interoceptive sensitivity deficits in women recovered from bulimia nervosa. *Eating Behaviors*, *14*(4), 488–492. https://doi.org/10.1016/j.eatbeh.2013.08.002

Klein, D. A., & Walsh, B. T. (2003). Eating disorders. *International Review of Psychiatry*, *15*(3), 205–216. https://doi.org/10.1080/0954026031000136839

Labouliere, C. D., Terranova, K., Steinglass, J., & Marsh, R. (2016). Implicit learning on a probabilistic classification task in adults and adolescents with bulimia nervosa. *Journal of Psychiatric Research*, *77*, 35–41. https://doi.org/10.1016/j.jpsychires.2016.02.004

Lang, K., Lopez, C., Stahl, D., Tchanturia, K., & Treasure, J. (2014). Central coherence in eating disorders: An updated systematic review and meta-analysis. *World Journal of Biological Psychiatry*, *15*(8), 586–598. https://doi.org/10.3109/15622975.2014.909606

Lang, K., Roberts, M., Harrison, A., Lopez, C., Goddard, E., Khondoker, M., Treasure, J., & Tchanturia, K. (2016). Central coherence in eating disorders: A synthesis of studies using the Rey Osterrieth Complex Figure Test. *PLOS ONE*, *11*(11), Article e0165467. https://doi.org/10.1371/journal.pone.0165467

Lilenfeld, L. R., Wonderlich, S., Riso, L. P., Crosby, R., & Mitchell, J. (2006). Eating disorders and personality: A methodological and empirical review. *Clinical Psychology Review*, *26*(3), 299–320. https://doi.org/10.1016/j.cpr.2005.10.003

Lloyd, E. C., & Steinglass, J. E. (2018). What can food-image tasks teach us about anorexia nervosa? A systematic review. *Journal of Eating Disorders*, *6*(1), Article 31. https://doi.org/10.1186/s40337-018-0217-z

Marsh, R., Horga, G., Wang, Z., Wang, P., Klahr, K. W., Berner, L. A., Walsh, B. T., & Peterson, B. S. (2011). An FMRI study of self-regulatory control and conflict resolution in adolescents with bulimia nervosa. *American Journal of Psychiatry*, *168*(11), 1210–1220. https://doi.org/10.1176/appi.ajp.2011.11010094

Marsh, R., Steinglass, J. E., Gerber, A. J., Graziano O'Leary, K., Wang, Z., Murphy, D., Walsh, B. T., & Peterson, B. S. (2009). Deficient activity in the neural systems that mediate self-regulatory control in bulimia nervosa. *Archives of General Psychiatry*, *66*(1), 51–63. https://doi.org/10.1001/archgenpsychiatry.2008.504

Martin, E., Dourish, C. T., Rotshtein, P., Spetter, M. S., & Higgs, S. (2019). Interoception and disordered eating: A systematic review. *Neuroscience and Biobehavioral Reviews*, *107*, 166–191. https://doi.org/10.1016/j.neubiorev.2019.08.020

Monteleone, A. M., Monteleone, P., Esposito, F., Prinster, A., Volpe, U., Cantone, E., Pellegrino, F., Canna, A., Milano, W., Aiello, M., Di Salle, F., & Maj, M. (2017). Altered processing of rewarding and aversive basic taste stimuli in symptomatic women with anorexia nervosa and bulimia nervosa: An fMRI study. *Journal of Psychiatric Research*, *90*, 94–101. https://doi.org/10.1016/j.jpsychires.2017.02.013

Munn-Chernoff, M. A., Johnson, E. C., Chou, Y. L., Coleman, J. R. I., Thornton, L. M., Walters, R. K., Yilmaz, Z., Baker, J. H., Hübel, C., Gordon, S., Medland, S. E., Watson, H. J., Gaspar, H. A., Bryois, J., Hinney, A., Leppä, V. M., Mattheisen, M., Ripke, S., Yao, S., . . . Agrawal, A. (2021). Shared genetic risk between eating disorder- and substance-use-related phenotypes: Evidence from genome-wide association studies. *Addiction Biology*, *26*(1), Article e12880. https://doi.org/10.1111/adb.12880

Nagata, J. M., Ganson, K. T., & Murray, S. B. (2020). Eating disorders in adolescent boys and young men: An update. *Current Opinion in Pediatrics*, *32*(4), 476–481. https://doi.org/10.1097/MOP.0000000000000911

Oberndorfer, T. A., Frank, G. K., Simmons, A. N., Wagner, A., McCurdy, D., Fudge, J. L., Yang, T. T., Paulus, M. P., & Kaye, W. H. (2013). Altered insula response to sweet taste processing after recovery from anorexia and bulimia nervosa. *American Journal of Psychiatry*, *170*(10), 1143–1151. https://doi.org/10.1176/appi.ajp.2013.11111745

Oberndorfer, T. A., Kaye, W. H., Simmons, A. N., Strigo, I. A., & Matthews, S. C. (2011). Demand-specific alteration of medial prefrontal cortex response

during an inhibition task in recovered anorexic women. *International Journal of Eating Disorders*, *44*(1), 1–8. https://doi.org/10.1002/eat.20750

Oberndorfer, T. A., Simmons, A., McCurdy, D., Strigo, I., Matthews, S., Yang, T., Irvine, Z., & Kaye, W. (2013). Greater anterior insula activation during anticipation of food images in women recovered from anorexia nervosa versus controls. *Psychiatry Research*, *214*(2), 132–141. https://doi.org/10.1016/j.pscychresns.2013.06.010

Olivo, G., Gaudio, S., & Schiöth, H. B. (2019). Brain and cognitive development in adolescents with anorexia nervosa: A systematic review of fMRI studies. *Nutrients*, *11*(8), Article 1907. https://doi.org/10.3390/nu11081907

Oltra-Cucarella, J., Rojo Moreno, L., Arribas Sáiz, P., Sanguesa García, C., Latorre Paniagua, P., Hidalgo Muñoz, E., & Rojo Bofill, L. (2015). Impaired executive functioning influences verbal memory in anorexia nervosa. *Eating Behaviors*, *16*, 47–53. https://doi.org/10.1016/j.eatbeh.2014.10.013

Pearson, C. M., Riley, E. N., Davis, H. A., & Smith, G. T. (2014). Two pathways toward impulsive action: An integrative risk model for bulimic behavior in youth. *Journal of Child Psychology and Psychiatry*, *55*(8), 852–864. https://doi.org/10.1111/jcpp.12214

Ralph-Nearman, C., Achee, M., Lapidus, R., Stewart, J. L., & Filik, R. (2019). A systematic and methodological review of attentional biases in eating disorders: Food, body, and perfectionism. *Brain and Behavior*, *9*(12), Article e01458. https://doi.org/10.1002/brb3.1458

Rescorla, R. A., & Wagner, A. R. (1972). A theory of Pavlovian conditioning: Variations in the effectiveness of reinforcement and non-reinforcement. In A. H. Black & W. F. Prokasy (Eds.), *Classical conditioning II: Current research and theory* (pp. 64–99). Appleton Century Crofts.

Ritschel, F., Geisler, D., King, J. A., Bernardoni, F., Seidel, M., Boehm, I., Vettermann, R., Biemann, R., Roessner, V., Smolka, M. N., & Ehrlich, S. (2017). Neural correlates of altered feedback learning in women recovered from anorexia nervosa. *Scientific Reports*, *7*(1), Article 5421. https://doi.org/10.1038/s41598-017-04761-y

Ritschel, F., King, J. A., Geisler, D., Flohr, L., Neidel, F., Boehm, I., Seidel, M., Zwipp, J., Ripke, S., Smolka, M. N., Roessner, V., & Ehrlich, S. (2015). Temporal delay discounting in acutely ill and weight-recovered patients with anorexia nervosa. *Psychological Medicine*, *45*(6), 1229–1239. https://doi.org/10.1017/S0033291714002311

Roberts, M. E., Tchanturia, K., Stahl, D., Southgate, L., & Treasure, J. (2007). A systematic review and meta-analysis of set-shifting ability in eating disorders. *Psychological Medicine*, *37*(8), 1075–1084. https://doi.org/10.1017/S0033291707009877

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

Schultz, W. (2002). Getting formal with dopamine and reward. *Neuron*, *36*(2), 241–263. https://doi.org/10.1016/S0896-6273(02)00967-4

Shott, M. E., Filoteo, J. V., Jappe, L. M., Pryor, T., Maddox, W. T., Rollin, M. D., Hagman, J. O., & Frank, G. K. (2012). Altered implicit category learning in anorexia nervosa. *Neuropsychology*, *26*(2), 191–201. https://doi.org/10.1037/a0026771

Smith, K. E., Mason, T. B., Johnson, J. S., Lavender, J. M., & Wonderlich, S. A. (2018). A systematic review of reviews of neurocognitive functioning in eating disorders: The state-of-the-literature and future directions. *International Journal of Eating Disorders*, *51*(8), 798–821. https://doi.org/10.1002/eat.22929

Stedal, K., Ely, A. V., Kurniadi, N., Lopez, E., Kaye, W. H., & Wierenga, C. E. (2019). A process approach to verbal memory assessment: Exploratory evidence of inefficient learning in women remitted from anorexia nervosa. *Journal of Clinical and Experimental Neuropsychology*, *41*(6), 653–663. https://doi.org/10.1080/13803395.2019.1610160

Steiger, H., & Booij, L. (2020). Eating disorders, heredity and environmental activation: Getting epigenetic concepts into practice. *Journal of Clinical Medicine*, *9*(5), Article 1332. https://doi.org/10.3390/jcm9051332

Steinglass, J. E., Figner, B., Berkowitz, S., Simpson, H. B., Weber, E. U., & Walsh, B. T. (2012). Increased capacity to delay reward in anorexia nervosa. *Journal of the International Neuropsychological Society*, *18*(4), 773–780. https://doi.org/10.1017/S1355617712000446

Steward, T., Mestre-Bach, G., Vintró-Alcaraz, C., Agüera, Z., Jiménez-Murcia, S., Granero, R., & Fernández-Aranda, F. (2017). Delay discounting of reward and impulsivity in eating disorders: From anorexia nervosa to binge eating disorder. *European Eating Disorders Review*, *25*(6), 601–606. https://doi.org/10.1002/erv.2543

Strigo, I. A., Matthews, S. C., Simmons, A. N., Oberndorfer, T., Klabunde, M., Reinhardt, L. E., & Kaye, W. H. (2013). Altered insula activation during pain anticipation in individuals recovered from anorexia nervosa: Evidence of interoceptive dysregulation. *International Journal of Eating Disorders*, *46*(1), 23–33. https://doi.org/10.1002/eat.22045

Strober, M., Freeman, R., Lampert, C., Diamond, J., & Kaye, W. (2000). Controlled family study of anorexia nervosa and bulimia nervosa: Evidence of shared liability and transmission of partial syndromes.

American Journal of Psychiatry, *157*(3), 393–401. https://doi.org/10.1176/appi.ajp.157.3.393

van den Berg, E., Houtzager, L., de Vos, J., Daemen, I., Katsaragaki, G., Karyotaki, E., Cuijpers, P., & Dekker, J. (2019). Meta-analysis on the efficacy of psychological treatments for anorexia nervosa. *European Eating Disorders Review*, *27*(4), 331–351. https://doi.org/10.1002/erv.2683

Van den Eynde, F., Guillaume, S., Broadbent, H., Stahl, D., Campbell, I. C., Schmidt, U., & Tchanturia, K. (2011). Neurocognition in bulimic eating disorders: A systematic review. *Acta Psychiatrica Scandinavica*, *124*(2), 120–140. https://doi.org/10.1111/j.1600-0447.2011.01701.x

Van den Eynde, F., Suda, M., Broadbent, H., Guillaume, S., Van den Eynde, M., Steiger, H., Israel, M., Berlim, M., Giampietro, V., Simmons, A., Treasure, J., Campbell, I., & Schmidt, U. (2012). Structural magnetic resonance imaging in eating disorders: A systematic review of voxel-based morphometry studies. *European Eating Disorders Review*, *20*(2), 94–105. https://doi.org/10.1002/erv.1163

Wagner, A., Aizenstein, H., Mazurkewicz, L., Fudge, J., Frank, G. K., Putnam, K., Bailer, U. F., Fischer, L., & Kaye, W. H. (2008). Altered insula response to taste stimuli in individuals recovered from restricting-type anorexia nervosa. *Neuropsychopharmacology*, *33*(3), 513–523. https://doi.org/10.1038/sj.npp.1301443

Wagner, A., Aizenstein, H., Venkatraman, V. K., Fudge, J., May, J. C., Mazurkewicz, L., Frank, G. K., Bailer, U. F., Fischer, L., Nguyen, V., Carter, C., Putnam, K., & Kaye, W. H. (2007). Altered reward processing in women recovered from anorexia nervosa. *American Journal of Psychiatry*, *164*(12), 1842–1849. https://doi.org/10.1176/appi.ajp.2007.07040575

Wagner, A., Barbarich-Marsteller, N. C., Frank, G. K., Bailer, U. F., Wonderlich, S. A., Crosby, R. D., Henry, S. E., Vogel, V., Plotnicov, K., McConaha, C., & Kaye, W. H. (2006). Personality traits after recovery from eating disorders: Do subtypes differ? *International Journal of Eating Disorders*, *39*(4), 276–284. https://doi.org/10.1002/eat.20251

Wagner, A., Greer, P., Bailer, U. F., Frank, G. K., Henry, S. E., Putnam, K., Meltzer, C. C., Ziolko, S. K., Hoge, J., McConaha, C., & Kaye, W. H. (2006). Normal brain tissue volumes after long-term recovery in anorexia and bulimia nervosa. *Biological Psychiatry*, *59*(3), 291–293. https://doi.org/10.1016/j.biopsych.2005.06.014

Watson, H. J., Yilmaz, Z., Thornton, L. M., Hübel, C., Coleman, J. R. I., Gaspar, H. A., Bryois, J., Hinney, A., Leppä, V. M., Mattheisen, M., Medland, S. E., Ripke, S., Yao, S., Giusti-Rodríguez, P., Hanscombe, K. B., Purves, K. L., Adan, R. A. H., Alfredsson, L., Ando, T., . . . Bulik, C. M. (2019). Genome-wide association study identifies eight risk loci and implicates metabo-psychiatric origins for anorexia nervosa. *Nature Genetics*, *51*(8), 1207–1214. https://doi.org/10.1038/s41588-019-0439-2

Weinbach, N., Perry, A., Sher, H., Lock, J. D., & Henik, A. (2017). Weak central coherence in weight-restored adolescent anorexia nervosa: Characteristics and remediation. *International Journal of Eating Disorders*, *50*(8), 924–932. https://doi.org/10.1002/eat.22711

Westwood, H., Stahl, D., Mandy, W., & Tchanturia, K. (2016). The set-shifting profiles of anorexia nervosa and autism spectrum disorder using the Wisconsin Card Sorting Test: A systematic review and meta-analysis. *Psychological Medicine*, *46*(9), 1809–1827. https://doi.org/10.1017/S0033291716000581

Wierenga, C. E., Bischoff-Grethe, A., Berner, L. A., Simmons, A. N., Bailer, U., Paulus, M. P., & Kaye, W. H. (2020). Increased anticipatory brain response to pleasant touch in women remitted from bulimia nervosa. *Translational Psychiatry*, *10*(1), Article 236. https://doi.org/10.1038/s41398-020-00916-0

Wierenga, C. E., Bischoff-Grethe, A., Melrose, A. J., Grenesko-Stevens, E., Irvine, Z., Wagner, A., Simmons, A., Matthews, S., Yau, W. Y., Fennema-Notestine, C., & Kaye, W. H. (2014). Altered BOLD response during inhibitory and error processing in adolescents with anorexia nervosa. *PLOS ONE*, *9*(3), Article e92017. https://doi.org/10.1371/journal.pone.0092017

Wierenga, C. E., Bischoff-Grethe, A., Melrose, A. J., Irvine, Z., Torres, L., Bailer, U. F., Simmons, A., Fudge, J. L., McClure, S. M., Ely, A., & Kaye, W. H. (2015). Hunger does not motivate reward in women remitted from anorexia nervosa. *Biological Psychiatry*, *77*(7), 642–652. https://doi.org/10.1016/j.biopsych.2014.09.024

Wierenga, C. E., Ely, A., Bischoff-Grethe, A., Bailer, U. F., Simmons, A. N., & Kaye, W. H. (2014). Are extremes of consumption in eating disorders related to an altered balance between reward and inhibition? *Frontiers in Behavioral Neuroscience*, *8*, Article 410. https://doi.org/10.3389/fnbeh.2014.00410

Wu, M., Brockmeyer, T., Hartmann, M., Skunde, M., Herzog, W., & Friederich, H. C. (2014). Set-shifting ability across the spectrum of eating disorders and in overweight and obesity: A systematic review and meta-analysis. *Psychological Medicine*, *44*(16), 3365–3385. https://doi.org/10.1017/S0033291714000294

Wu, M., Brockmeyer, T., Hartmann, M., Skunde, M., Herzog, W., & Friederich, H. C. (2016). Reward-related decision making in eating and weight disorders: A systematic review and meta-analysis of the evidence from neuropsychological studies. *Neuroscience and Biobehavioral Reviews*, *61*, 177–196. https://doi.org/10.1016/j.neubiorev.2015.11.017

Wu, M., Hartmann, M., Skunde, M., Herzog, W., & Friederich, H. C. (2013). Inhibitory control in

bulimic-type eating disorders: A systematic review and meta-analysis. *PLOS ONE*, *8*(12), Article e83412. https://doi.org/10.1371/journal.pone.0083412

Zastrow, A., Kaiser, S., Stippich, C., Walther, S., Herzog, W., Tchanturia, K., Belger, A., Weisbrod, M., Treasure, J., & Friederich, H. C. (2009). Neural correlates of impaired cognitive-behavioral flexibility in anorexia nervosa. *American Journal of Psychiatry*, *166*(5), 608–616. https://doi.org/10.1176/appi.ajp.2008.08050775