

**REVIEW**

# The neurobiological reward system and binge eating: A critical systematic review of neuroimaging studies

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## Abstract

**Objective:** Changes in reward processing are hypothesized to play a role in the onset and maintenance of binge eating (BE). However, despite an increasing number of studies investigating the neurobiological reward system in individuals who binge eat, no comprehensive systematic review exists on this topic. Therefore, this review has the following objectives: (1) identify structural and functional changes in the brain reward system, either during rest or while performing a task; and (2) formulate directions for future research.

**Methods:** A search was conducted of articles published until March 31, 2022. Neuroimaging studies were eligible if they wanted to study the reward system and included a group of individuals who binge eat together with a comparator group. Their results were summarized in a narrative synthesis.

**Results:** A total of 58 articles were included. At rest, individuals who binge eat displayed a lower striatal dopamine release, a change in the volume of the striatum, frontal cortex, and insula, as well as a lower frontostriatal connectivity. While performing a task, there was a higher activity of the brain reward system when anticipating or receiving food, more model-free reinforcement learning, and more habitual behavior. Most studies only included one patient group, used general reward-related measures, and did not evaluate the impact of comorbidities, illness duration, race, or sex.

**Discussion:** Confirming previous hypotheses, this review finds structural and functional changes in the neurobiological reward system in BE. Future studies should compare disorders, use measures that are specific to BE, and investigate the impact of confounding factors.

**Public Significance Statement:** This systematic review finds that individuals who binge eat display structural and functional changes in the brain reward system. These changes could be related to a higher sensitivity to food, relying more on previous experiences when making decisions, and more habitual behavior. Future studies should use a task that is specific to binge eating, look across different patient groups, and investigate the impact of comorbidities, illness duration, race, and sex.

## Resumen

**Objetivo:** Se plantea la hipótesis de que los cambios en el procesamiento de la recompensa desempeñan un papel en el inicio y mantenimiento de los atracones (BE). Sin embargo, a pesar de un número creciente de estudios que investigan el

sistema de recompensa neurobiológica en individuos que comen en atracones, no existe una revisión sistemática exhaustiva sobre este tema. Por lo tanto, esta revisión tiene los siguientes objetivos: (1) identificar cambios estructurales y funcionales en el sistema de recompensa cerebral, ya sea en reposo o mientras se realiza una tarea; (2) formular direcciones para futuras investigaciones.

**Métodos:** Se realizó una búsqueda de artículos publicados hasta el 31 de marzo de 2022. Los estudios de neuroimagen eran elegibles si querían estudiar el sistema de recompensa e incluían a un grupo de individuos que comían en atracón junto con un grupo de comparación. Sus resultados se resumieron en una síntesis narrativa.

**Resultados:** Se incluyeron un total de 58 artículos. En reposo, los individuos que comen en atracón mostraron una menor liberación de dopamina estriatal, un cambio en el volumen del cuerpo estriado, la corteza frontal y la ínsula, así como una menor conectividad frontostriatal. Al realizar una tarea, hubo una mayor actividad del sistema de recompensa cerebral al anticipar o recibir alimentos, más aprendizaje de refuerzo sin modelos y un comportamiento más habitual. La mayoría de los estudios sólo incluyeron un grupo de pacientes, utilizaron medidas generales relacionadas con la recompensa y no evaluaron el impacto de las comorbilidades, la duración de la enfermedad, la raza o el sexo.

**Discusión:** Confirmando hipótesis anteriores, esta revisión encuentra cambios estructurales y funcionales del sistema de recompensa neurobiológica en BE. Los estudios futuros deben comparar los trastornos, utilizar medidas que sean específicas para el comer en atracones e investigar el impacto de los factores de confusión.

#### KEY WORDS

anorexia nervosa binge-eating/purgung type, binge eating, binge-eating disorder, bulimia nervosa, MRI, neuroimaging, PET, RDoC, reward processing

## 1 | INTRODUCTION

Binge eating (BE) is defined as eating an amount of food, within any 2-hour period, that is definitively larger than what most individuals would eat in a similar time period under similar circumstances combined with a feeling that one cannot stop eating or control how much one is eating (American Psychiatric Association, 2013). It is a pivotal symptom of several psychiatric disorders such as binge-eating disorder (BED), bulimia nervosa (BN), and anorexia nervosa binge/purge type (AN-BP) (American Psychiatric Association, 2013).

Changes in reward processing are thought to play an important role in the onset and maintenance of BE (Pearson et al., 2015). The acquired preparedness model hypothesizes that certain individuals acquire maladaptive expectancies about food because they display high-risk personality traits that influence reward learning (Combs et al., 2010). According to this model, Individuals who are more impulsive when negative affect is elevated could acquire the expectancy that impulsive actions such as BE alleviate negative affect. Separately, the incentive sensitization theory suggests that repeated BE episodes are themselves a maintaining factor for BE (Robinson & Berridge, 1993). This is because they are thought to sensitize the reward system to the anticipation of food, leading to a higher incentive salience (i.e., "wanting") (Robinson &

Berridge, 1993). However, repeated BE episodes could also cause habituation of the reward system to receiving food, leading to a lower responsiveness and necessitating the consumption of even larger amounts to elicit the same response (Berridge & Robinson, 2016).

Indeed, several studies find differences in monetary and food reward processing between individuals who binge eat and controls. They find that individuals who binge eat display a higher incentive salience for food, a steeper discounting of monetary rewards, and difficulties with reinforcement learning (Schaefer & Steinglass, 2021; Steinglass et al., 2019). These behavioral differences are thought to be the result of changes in the neurobiological reward system. Important brain regions for reward processing are the insula, the ventral striatum (VS) or nucleus accumbens (NAc), the dorsal striatum (DS) which consists of the caudate nucleus (CN) and putamen, the anterior cingulate cortex (ACC), the orbitofrontal cortex (OFC), the ventromedial PFC (vmPFC), and the dorsolateral PFC (dlPFC) (Schultz, 2015). However, investigating the neurobiological reward system can be challenging with studies often reporting difficult to interpret or even contradictory results (Zald & Treadway, 2017). One reason for these challenges could be the overall lack of uniformity and specificity in how reward processing is defined in neuroimaging research (Zald & Treadway, 2017). Therefore, to have more uniform definitions in neuroscience, the

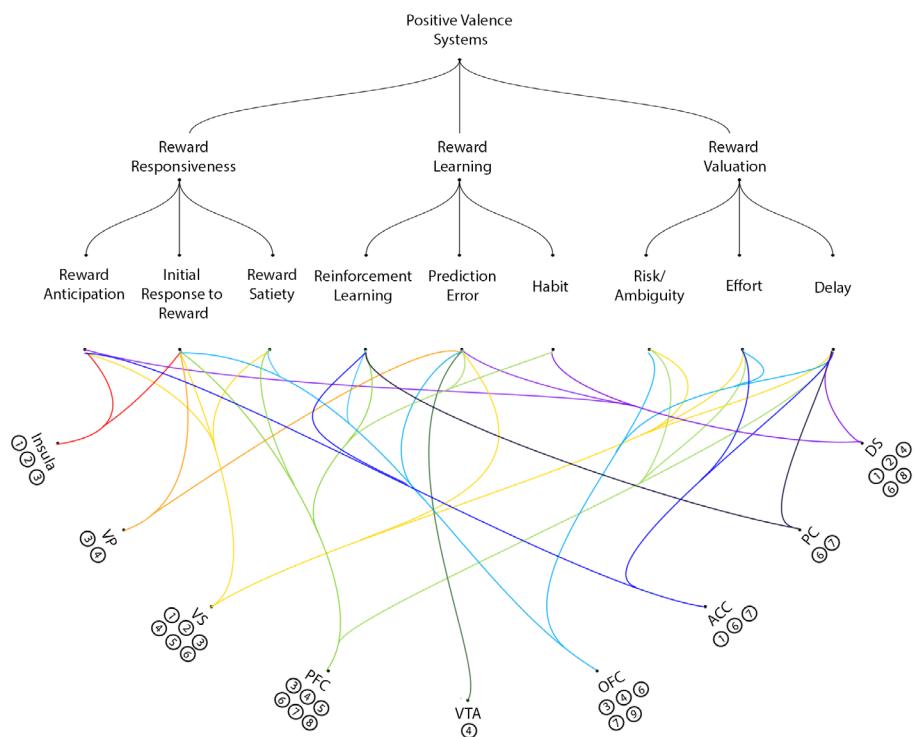
National Institute for Mental Health (NIMH) has developed the Research Domain Criteria (RDoC). In the RDoC framework, reward processing is subsumed under the positive valence systems which consist of three constructs and nine subconstructs (Insel et al., 2010). For a detailed overview of the positive valence systems, see Figure 1.

The first construct, *reward responsiveness*, is divided into reward anticipation, the *initial response to a reward*, and *reward satiation*. *Reward anticipation* is defined as the hedonic response in anticipation of a future reward while the *initial response to a reward* concerns the hedonic response to receiving a reward (National Institute of Mental Health, 2021). *Reward satiation* is the increase (sensitization) or decrease (habituation) of the motivational value of a reward after repeated exposure (Schmid et al., 2015). The second construct, *reward learning* contains the subconstructs of *reinforcement learning*, *prediction errors*, and *habits*. *Reinforcement learning* consists of *model-free* and *model-based reinforcement learning*. In *model-free reinforcement learning*, decisions are made reflexively and are formed by previous *prediction errors* which are the difference between the predicted value of a reward and the perceived value of the reward when it is acquired (Watabe-Uchida et al., 2017). In *model-based reinforcement learning*, an internal model of the current reward and the environment is constructed to make decisions (Lee et al., 2012; O'Doherty et al., 2017). In turn, *habits* are defined as inflexible, unconscious, and automatic behaviors that are acquired slowly and are insensitive to the devaluation of rewards (Seger & Spiering, 2011). The third construct, *reward valuation*, refers to the attribution of subjective and motivational value (i.e., incentive salience) to a reward (Schultz, 2015). It is modulated by the *effort* needed to acquire the reward, the *delay* between the stimulus and the delivery of the reward, and the uncertainty (*risk/ambiguity*) of the reward (Schultz, 2015).

Each subconstruct is linked to several brain regions within the reward circuit and each brain region can be associated with a number of subconstructs. A representation of these connections can be seen in Figure 1. The relationship between RDoC subconstructs and brain regions can be studied with several methods. On the one hand, the connections can be investigated in the absence of a task. This makes it possible to investigate the organization of the neurobiological reward system at rest. These results can then be linked to changes in reward processing by relating them to reward-related measures. On the other hand, these connections can be explored with a task that makes it possible to directly link the neurobiological reward system to specific aspects of reward processing.

The number of studies investigating the neurobiological reward system in BE has been steadily increasing. Some of these studies have also been the topic of reviews (Bello & Hajnal, 2010; Collantoni et al., 2021; Donnelly et al., 2018; Frank, 2013; Gianni et al., 2020; Hartogsveld et al., 2022b; Hiluy et al., 2021; Kessler et al., 2016; Mele et al., 2020; Steward et al., 2018; Wonderlich et al., 2021; Yu et al., 2022). However, these reviews have often focused on specific brain reward pathways (e.g., dopamine transmission, brain activity, and functional connectivity) and have frequently lacked a clear theoretical framework. This means that there is still a need for a systematic review that uses a well-defined theoretical framework to comprehensively review structural and functional findings on the neurobiological reward system in BE. This systematic review aims to fill that gap. It will use the RDoC as a framework to critically interpret study findings and will only include only studies that have stated to investigate the reward system. Both studies reporting on results at rest as well as results related to a task will be discussed. Studies using a task will be subdivided according to the RDoC criteria in articles probing reward responsiveness, reward learning, and reward valuation. These results will then be used to formulate directions for future studies.

**FIGURE 1** Figure displaying the RDoC positive valence systems with its constructs and subconstructs. Based on previous literature, a non-exhaustive list of connections is illustrated between the subconstructs and several brain areas. Abbreviations: ACC, anterior cingulate cortex; DS, dorsal striatum; OFC, orbitofrontal cortex; PC, parietal cortex; PFC, prefrontal cortex; VP, ventral pallidum; VS, ventral striatum; VTA, ventral tegmental area. References: 1, Wilson et al., 2018; 2, Oldham et al., 2018; 3, Berridge & Robinson, 2016; 4, Watabe-Uchida et al., 2017; 5, De Luca, 2014; 6, Schultz, 2015; 7, O'Doherty et al., 2017; 8, Seger & Spiering, 2011; 9, Wallis, 2007



## 2 | METHODS

This systematic review was conducted according to the PRISMA guidelines and has been registered with the PROSPERO International Prospective Register of Systematic Reviews of the University of York (CRD42019133795 24) (Moher, 2015). A protocol was written based on the PRISMA-P statement and can be consulted with the following link: [https://www.crd.york.ac.uk/PROSPERO/display\\_record.php?RecordID=133795](https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=133795).

Deviations from the protocol can be consulted in the Supplementary Files.

### 2.1 | Eligibility criteria

To establish the criteria for this systematic review, the PICOS system was used (population, intervention/exposure, comparator, outcome, and study characteristics).

- **Population:** Studies were eligible if they were written in English, conducted with human participants, and investigated BE. For BE, the definition of the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) was used (American Psychiatric Association, 2013). No specific criteria concerning psychiatric disorders were implemented as BE can occur within a psychiatric disorder as well as on its own. Likewise, no specific criteria concerning age were used as BE is prevalent in all age groups (Goldschmidt et al., 2016; Micali et al., 2017; Mitchison et al., 2017; Smink et al., 2013).
- **Exposure:** No specific in- or exclusion criteria concerning participants were specified.
- **Comparator:** Studies needed to include either a group of healthy controls (HC) who did not meet the criteria for BE as comparator, or another group of individuals who binge eat (e.g., BN vs. HC or BN vs. BED).
- **Outcomes:** The primary outcomes were gray matter volume (GMV) or cortical thickness (CT) (regional and global) when using structural imaging modalities, activity or connectivity (regional or global, task-based or at rest) when using functional imaging modalities, brain neurochemistry (e.g., receptor, transporter or neurotransmitter availability) when using positron emission tomography, and diffusion metrics (e.g., fractional anisotropy and mean diffusivity) when using diffusion imaging.
- **Study characteristics:** Studies needed to be longitudinal or cross-sectional using neuroimaging techniques, with or without neuropsychological tasks, state that they want to study the reward system, and be published in peer-reviewed journals or be submitted as a preprint or dissertation. Only articles published or submitted before the March 31, 2022 were included.

### 2.2 | Search strategy

A literature search of all articles published up to March 31st, 2022 was conducted through Medline, Embase, and Web of Science. A gray

literature search was performed through PsyArXiv for preprints and ProQuest for dissertations. Three concepts were used in the search string: “binge eating,” “reward,” and “neuroimaging.” These concepts were transformed into Medical Subject Headings (MeSH), Emtree, and free-text terms. For the first concept “binge eating,” the MeSH terms “bulimia,” “bulimia nervosa,” and “binge-eating disorder” were used, as well as several free-text terms such as “binge eating” and “binge eating syndrome.” For the second concept “reward,” the MeSH terms “Reward,” “Reinforcement,” and “Motivation” were supplemented with free-text terms such as “instrumental learning” and “decision making”. For the third concept “neuroimaging,” MeSH terms such as “Positron-Emission Tomography” and “Magnetic resonance imaging” were used together with free-text terms such as “Functional MRI.” The full literature search strategy can be found in Supplementary Files.

### 2.3 | Study selection

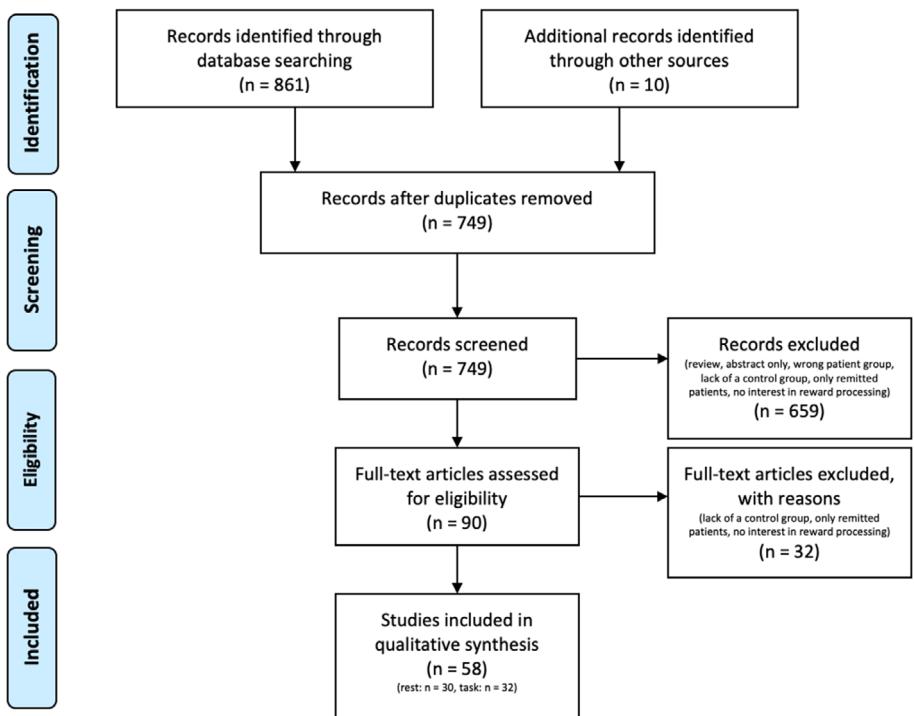
Relevant studies were selected by two researchers independently. The first researcher screened all titles and abstracts of the articles found using the search strategy. And the second researcher screened a randomly selected 25% of the abstracts to test the accuracy of the selection process. Inter-rater agreement between the two researchers was calculated using Cohen's kappa (Sim & Wright, 2005). Afterward, the same selection process was applied to the full articles and again, Cohen's kappa was calculated.

### 2.4 | Data extraction

The following information was extracted from all included articles: general information (article title, author, and year of publication), study characteristics (aim/objectives of the study and study design), study inclusion and exclusion criteria, participant characteristics (age, gender, race, ethnicity, socioeconomic status, disease characteristics, co-morbidities, number of participants in each characteristic category for intervention, and control), intervention (task performed and imaging modality), and results (relevant results to the objective of this review).

### 2.5 | Data analysis and risk of bias assessment

After data extraction, the risk of bias in each individual study was evaluated with an index based on the guidelines for neuroimaging research in patients with an eating disorder (Collantoni et al., 2021; Frank et al., 2018; Olivo et al., 2019). It includes 27 items that assess study design, participant characteristics, and analysis methods. Each item is given a score of 0, .5, or 1, which is then multiplied by the importance of the item (1: desirable, 2: strongly desirable, and 3: essential). These scores are then added up to generate a total score for each article ranging between 0 and 68.5. The index and its items can be found in the Supplementary Files. The first researcher scored all the articles and the second researcher scored a randomly selected 25% of the articles to assess the accuracy of the quality assessment.

**FIGURE 2** PRISMA flow diagram

Inter-rater agreement was evaluated by calculating the intraclass correlation coefficient. After quality assessment, a narrative synthesis of the articles was produced according to the Guidance on the Conduct of Narrative Synthesis in Systematic Reviews (Popay et al., 2016). A meta-analysis was not performed due to the widely different designs of the studies included in this review.

### 3 | RESULTS

#### 3.1 | Study selection

The search strategy yielded 58 articles which were included in this systematic review. The different phases of the review are represented in Figure 2. The inter-rater reliability for the screening of abstracts was “good” with a Cohen’s Kappa of .737. The inter-rater reliability for the screening of the full-text articles was “excellent” with a Cohen’s Kappa of .948. Both researchers agreed on the inclusion of 89% of the articles.

#### 3.2 | Study characteristics

Of the 58 articles in this review, 32 (55%) included a sample of patients with BN, 20 (34%) included a sample with BED, 2 (3%) included a mixed sample with BN or BED, 2 (3%) included a sample with AN-BP, and 9 (16%) included a sample of individuals who binge eat but do not meet the criteria for a specific disorder. Of the 20 studies that included patients with BED, 12 (60%) had an HC group with overweight or

obesity as comparator. Only eight (14%) studies included more than one sample with BE with only three (5%) studies comparing them. The total sample sizes varied between 18 and 575 with a median of 52. The mean age of all patient groups ranged from 9.9 to 49.4 years with a median of 25.74, while the mean age of HC ranged from 10.0 to 47.0 years with a median of 25.2. Most studies ( $n = 43$ , 74%) only included female participants. The majority of studies ( $n = 49$ , 84%) used magnetic resonance imaging (MRI), and the remaining studies ( $n = 9$ , 16%) used Positron emission tomography imaging (PET). Of these, 30 (52%) reported on results at rest and 32 (55%) reported task-based results. The quality scores for the articles ranged from 11.25 to 49 with a median score of 30. The inter-rater reliability for the quality assessment was “excellent” with an intraclass correlation of .91. Less than 10% of all articles mentioned recent weight changes or controlled for contraceptive use. Less than 20% considered race in their analyses, quantified exercise, mentioned treatment length, or controlled for cycle phase. A total of 25 (43%) studies reported the socioeconomic status (education:  $n = 24$  (41%), unemployment:  $n = 1$  (2%), and benefits:  $n = 1$  (2%)) of their participants and only 11 (19%) studies reported race or ethnicity.

#### 3.3 | Summary of findings

An overview of the different modalities, tasks, and outcomes can be found in Table 1. The findings concerning the neurobiological reward system at rest are summarized in Table 2 and Figure 3. The results of the studies using a task are summarized in Table 3 and Figure 4. A brief explanation of the methods and analysis techniques of the studies can be found in the Supplementary Materials.

**TABLE 1** Tasks (type and allocation to RDoC subconstructs), modalities, and outcomes of the studies included in this systematic review

Task	Positive valence systems		Reward learning				Reward valuation			Modality/Neural Assessment Approach
	Reward response Initial	Reward response Anticipation to Reward	Reward Satiation	Reinforcement Learning	Prediction Errors	Habits Ambiguity	Effort	Delay		
Rest	•									PET (D2/D3-receptor, presynaptic DA, CB1R, $\mu$ -opioid receptor, SERT, mGlu5 availability)
Food cue reactivity		•								fMRI (neural activity, functional and effective connectivity)
Food odor reactivity		•								fMRI (neural activity)
Monetary/Food incentive delay task		•								fMRI (neural activity)
Reward-guessing task	•		•							fMRI (neural activity)
Taste reactivity		•		•						fMRI (neural activity)
Spatial learning task		•			•					PET (DA-release)
Temporal difference model task				•	•					fMRI (neural activity)
Weather prediction task					•					fMRI (neural activity)
Two-step task						•				PET (correlation with SERT availability)
Reward-guided decision-making task						•				fMRI (neural activity)
Instrumental learning task						•				fMRI (neural activity)
Reversal learning task						•				MRS (correlation with myo-inositol, NAA, and glutamate levels)
Risky decision-making task						•				fMRI (correlation with resting-state functional connectivity)
Delay discounting task						•				PET (correlation with $\mu$ -opioid receptor availability)

Abbreviations: ASL, arterial spin labeling; CB1R, cannabinoid type 1 receptor; CBF, cerebral blood flow; CT, cortical thickness; DA, dopamine; DWI, diffusion-weighted imaging; fMRI, functional magnetic resonance imaging; GMV, gray matter volume; mGlu5, glutamate receptor 5; MRS, magnetic resonance spectroscopy; NAA, N-acetyl aspartate; PET, positron emission tomography; SERT, serotonin transporter.

**TABLE 2** Results for the findings at rest. The table is organized based on the primary method and the first author name of each study

Article	Participants (n)	Age (mean, SD)	Age (range)	Race and ethnicity (n, %)	SES (mean, SD)	Sex ratio (F/M, %)	Modality	Main findings	Quality score
Martins et al., 2020	BN/BED: 25; HC: 23	BN/BED: 25.58 (6.31); HC: 23.6 (3.79)	NR	NR	RQF: BN: 4.88 (1.75) HC: 5.31 (1.67)	BED/BN/HC: 48/0, 100%	ASL & Structural MRI	- Patients with BN/ BED had a higher CBF in the PFC, OFC, right insula, ACC, ITG, and MTG - Patients with BN/BED had a lower GMV of the right pre- and postcentral gyrus, ITG, and MTG	305
Estella et al., 2020	BED: 17; HC-OB: 13; HC-NW: 17	BED: 33.82 (7.2); HC-OB: 38.03 (9.7); HC-NW: 34.70 (11.0)	NR	BED/HC-OB/ NW: 18-55 <sup>a</sup>	Education (years): BED: 14.12 (1.5); HC-OB: 14.53 (1.3); HC-NW: 14.07 (1.6)	BED/HC-NW/HC-OB: 37/0, 100%	Diffusion Weighted MRI	- Patients with BED had a higher FA than HC-OB in the forceps minor - Patients with BED had a higher AD than HC-OB in the superior longitudinal fasciculus, cortical tract, cingulum, corpus callosum body, and corpus callosum splenium - Patients with BED had a higher AD than HC-NW in the forceps minor, superior longitudinal fasciculus, inferior longitudinal fasciculus, anterior thalamic radiation, forceps major, inferior fronto-occipital fasciculus, and anterior thalamic radiation	32
Frank, Shott, Riederer, & Pryor, 2016	AN: 26; BN: 25; HC: 26	AN: 23.23 (5.26); BN: 24.64 (4.22); HC: 24.39 (3.49)	NR	NR	Education (years): AN: 14.39 (2.25); BN: 15.77 (3.09); HC: 16.52 (1.92)	AN/BN/HC: 77/0, 100%	Task-based fMRI where participants had to perform a temporal difference learning task & diffusion-weighted magnetic resonance imaging	- Patients with BN had a higher structural connectivity between the left insula and middle OFC, the ventral and dorsal anterior insula to the NAc and dorsal anterior insula, from the posterior insula to medial PFC, and between the inferior OFC and gyrus rectus and NAC, from the right posterior insula and medial OFC to NAc and from the dorsal anterior insula to the medial PFC. - Patients with BN had a lower structural connectivity from the left ventral anterior insula to inferior OFC and central nucleus of the amygdala and from the right amygdala basolateral nucleus to the NAc and dorsal anterior insula.	43.75
He et al., 2016	BN: 28; HC: 28	BN: 21.32 (6.11); HC: 20.61 (6.12)	BN: 14-46; HC: 12-40 <sup>a</sup>	NR	BN/HC: 56/0, 100%	Diffusion-weighted MRI	- Patients with BN had lower FA values and higher RD values in the forceps minor and major, superior longitudinal fasciculus, inferior fronto-occipital fasciculus, anterior thalamic radiation, corticospinal tract, uncinate fasciculus, and cingulum - In patients with BN, performance on the Stroop task was correlated negatively with FA scores in the forceps minor,	35.5	

(Continues)

TABLE 2 (Continued)

Article	Participants (n)	Age (mean, SD)	Age (range)	Race and ethnicity (n, %)	SES (mean, SD)	Sex ratio (F/M, %)	Modality	Quality score
Mettler et al., 2013	BN: 20; HC: 21	BN: 25.2 (5.3); HC: 27.5 (6.6)	NR	NR	NR	BN/HC: 41/0, 100%	Diffusion-weighted MRI & structural MRI	38/25
Wang et al., 2019	BN: 48; HC: 44	BN: 22.0 (3.4); HC: 23.1 (3.4)	NR	NR	Education (years): BN: 14.1 (1.9); HC: 14.6 (1.7)	BN/HC: 92/0, 100%	Diffusion-weighted MRI	32/25

left corticospinal tract, superior longitudinal fasciculus, right anterior thalamic radiation, and inferior fronto-occipital fasciculus while it correlated positively with RD values in the left corticospinal tract, inferior fronto-occipital fasciculus, and forceps major. The opposite was true in HC.

- Patients with BN had lower FA values in the corona radiata, anterior limb of the internal capsule, left corpus callosum, left inferior fronto-occipital fasciculus, left uncinate fasciculus, and the posterior limb of the internal capsule

- Patients with BN had higher ADC values in the corona radiata, anterior limb of the internal capsule, left corpus callosum, left uncinate fasciculus, and the posterior limb of the internal capsule

- There were no differences in GMV

left corticospinal tract, superior longitudinal fasciculus, right anterior thalamic radiation, and inferior fronto-occipital fasciculus while it correlated positively with RD values in the left corticospinal tract, inferior fronto-occipital fasciculus, and forceps major. The opposite was true in HC.

- Patients with BN had lower FA values in the corona radiata, anterior limb of the internal capsule, left corpus callosum, left uncinate fasciculus, and the posterior limb of the internal capsule

- Patients with BN had higher ADC values in the corona radiata, anterior limb of the internal capsule, left corpus callosum, left uncinate fasciculus, and the posterior limb of the internal capsule

- Patients with BN had a higher strength of the left superior OFC, left inferior temporal gyrus, left insula, left hippocampus, left PHG, and left thalamus but a lower nodal strength of the left ACC and right precuneus.

- Patients with BN had a higher betweenness in the left superior medial OFC, left ACC, left STG, left precuneus, right fusiform gyrus, left insula, left PHG, left putamen, right pallidum, left thalamus, and right amygdala but a lower betweenness in the right IFG, right superior OFC, left fusiform gyrus, and right insula

- Patients with BN had a higher local efficiency in the left superior OFC, left STG, left ITG, left superior temporal pole, left thalamus, and left amygdala but a lower local efficiency in the right precentral gyrus and right precuneus

- Patients with BN had more connections within the OFC, between the OFC and ACC, insula, CN, and thalamus. There were also more connections between the lateral temporal-occipital cortex and OFC and PHG. There were reduced connections between the IFG, insula, and lateral temporal cortex

TABLE 2 (Continued)

Article	Participants (n)	Age (mean, SD)	Age (range)	Race and ethnicity (n, %)	SES (mean, SD)	Sex ratio (F/M, %)	Modality	Main findings	Quality score
Broft et al., 2012	BN: 16; HC: 17	BN: 24.4 (5.1); HC: 24.9 (4.2)	NR	Race/Ethnicity: • BN: Caucasian (13, 81.3%), Mixed Caucasian (2, 12.5%), and Native American (1, 6.3%) • HC: Caucasian (7, 43.8%), Mixed Caucasian (4, 25.0%), Hispanic (2, 12.5%), and Asian (1, 6.3%)	NR	BN/HC: 33/0, 100%	PET with [ <sup>113</sup> C] raclopride with or without the administration of methylphenidate	- There were no differences in D2/D3-receptor availability at rest - Patients with BN had displayed a lower dopamine release in the anterior and posterior putamen	35.5
Ceccarini et al., 2016	AN: 14; BN: 16; FD: 12; OB: 12; HC: 26	FID: 29.3 (12.6); HC: 34.6 (15.3)	NR	NR	AN/BN/FD/OB/HC: 80/0, 100%	PET with [ <sup>18</sup> F]MK-9470	- There was a significant negative correlation between CB1R availability and log BM in the patient groups in the hypothalamus, pons, medulla, midbrain, NAc, CN, putamen, pallidum, OFC, insula, and amygdala	44	
Gérard et al., 2011	BN: 16; AN: 14; HC: 19	BN: 23.8 (7.1); AN: 20.5 (3.6); HC: 25.2 (98.5)	NR	NR	BN/AN/HC: 49/0, 100%	PET with [ <sup>18</sup> F]MK-9470	- There was a significantly higher CB1R availability in the bilateral insular cortex of patients with BN	32	
Mihov et al., 2020	BN: 15; HC: 15	BN: 29.3 (7.1); HC: 28.9 (6.7)	BN: 20– 44; HC: 18–44 <sup>b</sup>	NR	BN/HC: 30/0, 100%	PET with [ <sup>113</sup> C]ABP688.	- Patients with BN had a higher metabotropic glutamate receptor 5 distribution volume ratio in the ACC, straight gyrus, and subgenual PFC	15.75	
Majuri et al., 2016	BED: 7; Pathological Gambling: 15; HC: 17	BED: 49.43 (5.09); Pathological Gambling: 42.60 (11.81); HC: 43.29 (11.10)	NR	NR	BED: 7/0, 100%; Pathological Gambling: 7/8, 47%; HC: 9/8, 53%	PET with [ <sup>18</sup> F]fluorodopa and [ <sup>113</sup> C]carfentanil	- Patients with BED had a lower $\mu$ -receptor availability in the thalamus, NAc, hippocampus, PCC, isthmus of the PCC, PHG, frontal pole, pars orbitalis of the ventrolateral prefrontal cortex, lateral OFC, and ventrolateral PFC. - Patients with BED had a lower dopamine availability in the NAc, CN, and putamen	17	
Majuri et al., 2017	BED: 7; Pathological Gambling: 13; HC: 16	BED: 49.4 (5.1); Pathological Gambling: 43.0 (12.7); HC: 42.4 (10.8)	NR	NR	BED: 7/0, 100%; Pathological Gambling: 7/6, 54%; HC: 9/7, 56%	PET with [ <sup>113</sup> C]MADAM	- Patients with BED had a higher serotonin transporter availability in the bilateral superior and inferior parietal cortices and the bilateral lateral occipital cortex, but a lower availability in the NAc, ITGus, and lateral OFC	22.5	
Canna et al., 2017	BN: 13; AN: 15; HC: 16	BN/AN/HC: NR	BN/AN/ HC: 18– 45 <sup>b</sup>	NR	BN/AN/HC: 44/0, 100%	Resting-State fMRI & diffusion-weighted MRI & structural MRI	- Patients with BN had a lower voxel- mirrored homotopic connectivity in the OFC and DLPFC - There were no differences in GMV - There were no differences in FA value in the corpus callosum	28.5	

(Continues)

TABLE 2 (Continued)

Article	Participants (n)	Age (mean, SD)	Age (range)	Race and ethnicity (n, %)	SES (mean, SD)	Sex ratio (F/M, %)	Modality	Quality score
Haynos et al., 2021	BED: 27; HC: 21	BED: 32.27 (8.54); HC: 30.90 (7.99)	NR	NR	Education (years): BED: 14.61 (2.09); HC: 14.75 (1.84)	BED: 24/3, 88.9%; HC: 21/0, 100%	Resting-State fMRI	- Patients with BN had lower inter-hemispheric spectral coherence values in the dlPFC and OFC 30
Murray, Alba et al., 2022	BED: 58; HC: 68	BED: 9.90 (0.60); HC: 10.03 (0.63) <sup>a</sup>	BED/HC: 9-10 <sup>a</sup>	Race: • BED: White (30, 52%), Black (14, 24%), Mixed (8, 14%), Other (4, 7%), do not know (2, 3%) • HC: White (42, 62%), Black (6, 9%), Asian (4, 6%) Mixed (9, 13%), other (5, 7%), do not know (2, 3%) Ethnicity: • BED: Hispanic (15, 26%), Non-Hispanic (43, 74%) • HC: Hispanic (15, 22%), Non-Hispanic (53, 78%)	NR	- BED: 28/30, 48.2% - HC: 36/32, 52.9%	Resting-State fMRI	- Patients with BED displayed the following changes in functional connectivity. There was a lower connectivity between the amygdala and the dlPFC, PCC, SFG, and temporal lobe. There was a lower connectivity between the OFC and PCC, ACC, dlPFC, and vmPFC. There was a lower functional connectivity between the ACC and OFC, SFG, parahippocampal gyrus, and inferior temporal gyrus. There was a lower functional connectivity between the dlPFC and the OFC, middle temporal gyrus, SFG, and IFG.
Stoprya et al., 2019	BED: 27; BN: 29; HC-OB: 28; HC-NW: 30	BED: 38.39 (13.0); BN: 27.45 (10.5); HC-OB: 39.40 (10.48); HC-NW: 26.86 (6.59)	NR	NR	Education (years): BED: 12.04 (1.76); BN: 12.66 (1.40); HC-OB: 12.00 (2.02); HC-NW: 12.73 (0.83)	BN/BED/HC-NW/HC-OB: OB: 114/0, 100%	Resting-State fMRI	- In the salience network, patients with BED or BN had a lower functional connectivity of the anterior part of the dorsal cingulate cortex. Also, patients with BED had a higher connectivity in the posterior part of the dorsal cingulate cortex than patients with BN - In the default-mode network, patients with BN had a higher connectivity in the dorsal medial PFC than HC-NW and patients with BED. Also, patients with BED had a lower connectivity in the dorsal medial PFC than HC-OB. Patients with BN also had a higher connectivity in the lateral ventromedial PFC compared to HC-NW

TABLE 2 (Continued)

Article	Participants (n)	Age (mean, SD)	Age (range)	Race and ethnicity (n, %)	SES (mean, SD)	Sex ratio (F/M, %)	Modality	Quality score
Wang et al., 2017	BN:48; HC:45	BN:22.0 (3.4); HC: 23.1 (3.4)	BN/NR	HC:16-30 <sup>a</sup>	Education (years): BN: 14.1 (1.9); HC: 14.6 (1.7)	BN/HC: 93/0, 100%	Resting-state fMRI	<ul style="list-style-type: none"> <li>- In the executive network, patients with BN had a higher connectivity in the right MFC and angular gyrus than patients with BED. The combined eating disorders group had a lower connectivity in the inferior parietal cortex than the combined controls</li> <li>- Patients with BED had a higher functional connectivity between the dorsal ACC and the right cerebellum and right lingual gyrus compared to HC-OB. Compared to patients with BN, they also had a higher functional connectivity between the dorsal ACC and pre- and postcentral gyrus but a lower connectivity between the dorsal ACC and bilateral retrosplenial cortex</li> </ul>
Wang et al., 2020	BN:51; HC: 53	BN/HC:NR	BN/NR	HC:16-30 <sup>a</sup>	Education (years): BN: 13.9 (2.2); HC: 14.2 (1.7)	BN/HC: 104/0, 100%	Resting-State fMRI	<ul style="list-style-type: none"> <li>- Patients with BN displayed more local clustering and a longer path length</li> <li>- Patients with BN had a higher nodal strength in the left precentral gyrus, right postcentral gyrus, bilateral superior occipital cortex, bilateral middle occipital cortex, left cuneus, bilateral lingual gyrus, and right inferior temporal gyrus and right precuneus, but a lower nodal strength in the right middle OFC, left olfactory cortex, left hippocampus, bilateral PHG left insula, left amygdala, left putamen, and left thalamus</li> <li>- Patients with BN displayed a higher connectivity in the primary sensorimotor, unimodal association, and heteromodal association systems and a lower connectivity in subcortical, limbic, and paralimbic regions</li> </ul>

(Continues)

TABLE 2 (Continued)

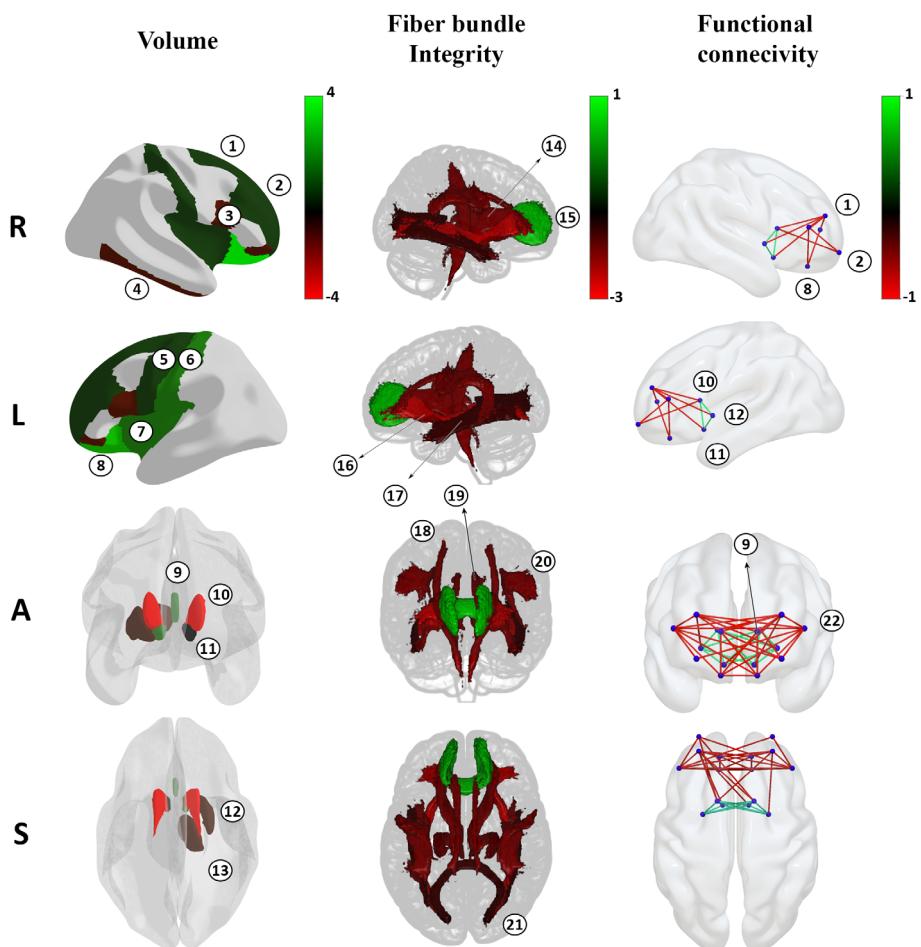
Article	Participants (n)	Age (mean, SD)	Age (range)	Race and ethnicity (n, %)	SES (mean, SD)	Sex ratio (F/M, %)	Modality	Quality score
Westwater et al., 2022	AN-bp: 22; BN: 33; HC: 30	AN-bp: 24.6 (4.7); BN: 23.6 (3.9); HC: 23.9 (3.5)	NR	Race: • AN-bp: White (19.86%), Asian (2.9%), Mixed (1.5%) • BN: White (27.83%), Asian (3.9%), Mixed (3.9%) • HC: White (21.70%), Asian (3.10%), Black (2.67%) Mixed (2, 6.7%), Other (2, 6.7)	NR	AN-bp/BN/HC: 85/0, 100%	Single photon magnetic resonance spectroscopy	- Putamen and the other striatal nuclei and thalamus, a higher negative connectivity with the bilateral primary sensorimotor and occipital, as well as a lower negative connectivity with the MFG, SFG, and parietal cortex - There were lower levels of myo-inositol and NAA in the inferior left PFC in patients with AN-bp, but not in patients with BN. There were no differences in glutamate levels. - Myo-inositol and NAA concentrations were negatively associated with eating disorder and depressive symptoms scores in the BN group.
Abdo et al., 2020	BE: 54; HC: 413	BE: 48.7 (18.6); HC: 47.0 (19.4)	BE/HC: 18-85 <sup>b</sup>	NR	NR	BE: 35/19, 65%; HC: 271/142, 66%	Structural MRI	13.75
Amianto et al., 2013	BN: 13; AN: 17; HC: 14	BN: 22 (3); AN: 20 (4); HC: 24 (3)	NR	NR	NR	BN/AN/HC: 44/0, 100%	Structural MRI	29.75
Berner et al., 2019	BN: 62; HC: 65	BN: 18.8 (4.0); HC: 19.3 (5.7)	NR	NR	NR	BN/HC: 127/0, 100%	Structural MRI	30.75
Coutinho et al., 2014	BN: 21; HC: 20	BN: 31.57 (8.27); HC: 30.90 (8.79)	NR	NR	Education (years): BN: 13.0 (4.51); HC: 15.8 (3.22)	BN/HC: 41/0, 100%	Structural MRI	31.75
Cyr et al., 2017	BN: 33; HC: 28	BN: 16.5 (1.5); HC: 16.2 (2.1)	NR	NR	NR	BN/HC: 61/0, 100%	Structural MRI	29.75
Frank et al., 2013	AN-ill: 19; AN-recovered: 24; BN: 20; HC: 24	AN-ill: 23.2 (5.8); AN-recovered: 30.3 (8.1); BN: 25.2 (5.3); HC: 27.4 (6.3)	NR	NR	Education (years): AN-ill: 14.5 (2.4); AN-recovered: 16.9 (2.7); BN: 16.0 (3.0); HC: 16.6 (2.1)	AN-ill/AN-recovered/BN/HC: 78/0, 100%	Structural MRI	42.75

TABLE 2 (Continued)

Article	Participants (n)	Age (mean, SD)	Age (range)	Race and ethnicity (n, %)	SES (mean, SD)	Sex ratio (F/M, %)	Modality	Quality score
Murray, Duval et al., 2022	BED: 71; HC: 74	BED: 9.92 (0.633); HC: 10.03 (0.647)	BED/HC: 9-10 <sup>a</sup>	Race: • BED: White (32, 45%), Black (16, 23%), Mixed (17, 24%). Other (4, 5%), Do not know (3, 3%) • HC: White (45, 61%), Black (8, 11%), Asian (5, 7%), Mixed (9, 12%). Other (4, 6%), Do not know (2, 3%)	NR	BED: 33/38, 46.5%; HC: 36/38, 51.4%	Structural MRI	- Patients with BED had a higher GMV of the dlPFC, MFG, SFG, ACC, OFC, middle temporal gyrus, and postcentral gyrus. - Higher behavioral approach scores were associated with a lower GMV of the dlPFC, SFG, and OFC
Schäfer et al., 2010	BED: 17; BN: 14; HC: 19	BED: 26.4 (6.4); BN: 23.1 (3.8); HC: 22.3 (2.6)	NR	NR	Education (years): BED: 13.0 (1.5); BN: 12.7 (0.8); HC: 13.2 (0.9)	BED/BN/HC: 50/0, 100%/ (0.8); HC: 13.2 (0.9)	Structural MRI	- Patients with BN had a higher GMV of the medial and lateral OFC, ventral and dorsal striatum than patients with BED. - Patients with BN had a higher GMV of the medial OFC and VS than HC
Turan et al., 2021	BED: 25; HC-OB: 25; HC-NW: 27	BED: 15.04 (1.79); HC-OB: 14.64 (1.73); HC-NW: 14.59 (1.39)	NR	NR	NR	BED: 17/18, 68%; HC-OB: 16/19, 68%; HC-NW: 19/19, 70.3%	Structural MRI	- Patients with BED had a larger GMV of the medial OFC. - Serum leptin levels were positively correlated with GMV in the medial OFC, right lateral OFC, and left ACC
Voon et al., 2015	BED: 20; HC-OB: 20	BED: 43.95 (9.47); HC-OB: 44.70 (10.12)	NR	NR	NR	BED: 12/18, 60%; HC-OB: 9/11, 45%	Structural MRI	- Patients with BED had a lower volume of the left NAC, left lateral OFC, bilateral medial OFC, and bilateral CN.
Zhang et al., 2021	BE: 115; HC: 460	All participants were scanned at 14, 16, and 18 years	BE/HC: 14-18 <sup>a</sup>	NR	NR	BE: 91/24, 79.1%; HC: 364/96, 79.1%	Structural MRI	- A higher GMV of the right putamen and globus pallidus at age 14 were related to binge eating at ages 16 and 18. - A lower GMV of the medial OFC, gyrus rectus, dlPFC, ACC, and middle cingulate cortex was associated with purging at ages 16 and 18.

Abbreviations: ACC, anterior cingulate cortex; AD, axial diffusivity; ADC, apparent diffusion coefficient; AN, anorexia nervosa; ASI, arterial spin labeling; BE, binge eating; BED, binge-eating disorder; BN, bulimia nervosa; CB1R, type 1 cannabinoid receptor; CBF, cerebral blood flow; DLPPC, dorsolateral prefrontal cortex; FA, fractional anisotropy; FD, functional dyspepsia; fMRI, functional magnetic resonance imaging; HC, healthy controls; IFG, inferior frontal gyrus; ITG, inferior temporal gyrus; GMV, gray matter volume; M, male; MFG, middle frontal gyrus; MR, magnetic resonance imaging; MTG, middle temporal gyrus; NAC, nucleus accumbens; NR, Not reported; NW, normal weight; OB, obese; OFC, orbitofrontal cortex; PCC, posterior cingulate gyrus; PET, positron emission tomography; PFC, prefrontal cortex; PHG, parahippocampal gyrus; RD, radial diffusivity; RQF, Regulated Qualifications Framework; SD, standard deviation; SES, socioeconomic status; STG, superior temporal gyrus.

<sup>a</sup>age range stated in the protocol.  
<sup>b</sup>Page range of the actual participants.



**FIGURE 3** Representation of the results concerning volume, fiber bundle integrity, and functional connectivity (in the frontal cortex and striatum). The results are shown on a scale representing the number of studies that found a lower or higher volume, integrity, or connectivity in individuals who binge eat. Numbers: 1, superior frontal gyrus; 2, middle frontal gyrus; 3, inferior frontal gyrus; 4, inferior temporal gyrus; 5, precentral gyrus; 6, postcentral gyrus; 7, insula; 8, orbitofrontal cortex; 9, anterior cingulate cortex; 10, caudate nucleus; 11, nucleus accumbens; 12, putamen; 13, thalamus; 14, anterior thalamic radiation; 15, forceps minor; 16, inferior longitudinal fasciculus; 17, inferior fronto-occipital fasciculus; 18, corticospinal tract; 19, cingulum; 20, superior longitudinal fasciculus; 21, forceps major; 22, dorsolateral prefrontal cortex. Abbreviations: A, anterior; L, left; R, right; S, superior

### 3.3.1 | Rest

#### Neurochemistry

A total of six PET studies investigated the neurochemistry of the reward system at rest. A sample of patients with BN was included in four (67%) studies and a sample of patients with BED was included in two (33%) studies. Of these, two (33%) investigated the dopaminergic system, two (33%) the endocannabinoid system, one (17%) the serotoninergic system, one (17%) the endogenous opioid system, and one (17%) the glutamatergic system. The studies that investigated the dopaminergic system found no difference in striatal D<sub>2/3</sub> receptor availability, but they did find that BE is related to a reduction in striatal dopamine transmission (Broft et al., 2012; Majuri et al., 2016). They reported that patients with BED had lower levels of presynaptic dopamine in the NAc, CN, and putamen and that patients with BN displayed less dopamine release in the putamen (Broft et al., 2012; Majuri et al., 2016). Furthermore, patients with BN who displayed less dopamine release in the putamen had higher BE frequencies (Broft et al., 2012). For the endocannabinoid system, patients with BN had a higher cannabinoid type 1 receptor (CB1R) availability in the insular cortex (Gérard et al., 2011). However, this was also found in the AN group and was associated with a lower BMI and a higher drive for thinness (Ceccarini et al., 2016; Gérard et al., 2011). This led the authors to suggest that the higher CB1R

availability is not related to BE but to other factors such as restrictive eating. More specifically, they suggest that a lower endocannabinoid activity due to a restrictive eating pattern could lead to an upregulation of the CB1R. The studies that investigated the other neurotransmitter systems pointed to a disturbance in striatal and orbitofrontal neurotransmission with a lower μ-opioid receptor and serotonin transporter availability in patients with BED and a higher glutamate receptor 5 distribution volume ratio in patients with BN (Majuri et al., 2016; Majuri et al., 2017; Mihov et al., 2020). However, this was not associated with any clinical measures. Summarized, the studies using PET point to a link between BE and a lower striatal dopaminergic transmission at rest. Changes in other neurotransmitter systems have been found as well, but their relation to BE is less certain.

#### Volume

Overall, 14 articles assessed GMV or CT. A sample of patients with BN was included in eight (57%) studies, a sample with BED in four (29%) studies, a mixed BN/BED sample in one (7%) study, and a sample of individuals who binge eat in two (14%) studies. Most studies used voxel-based morphometry (VBM;  $n = 11$  studies, 79%) while others used surface-based morphometry (SBM;  $n = 2$ , 14%) or a manual segmentation technique ( $n = 1$ , 7%). Across the samples, the studies found a lower volume of the CN ( $n = 4$  studies, 29%) as well as a

**TABLE 3** Results for the findings during a task. The table is organized alphabetically based on the name of the first author of each study

Article	Participants (n)	Age (mean, SD)	Age (range)	Race and ethnicity (n, %)	SES (mean, SD of n, %)	Sex ratio (F/M, %)	Modality/task	Main findings	Quality score
Balodis et al., 2013	BED:19; HC-OB: 19; HC-NW 19	BED:43.7 (12.7); HC-OB:38.3 (7.5); HC-NW 34.8 (10.7)	NR	Race: • BED: • Caucasian (14, 73.7%), African American (3, 15.8%), Native American (2, 10.5%) • HC-OB: • Caucasian (12, 63.2%), African American (7, 36.8%), Native American (1, 10.5%) • HC-NW: • Caucasian (13, 68.4%), African American (5, 31.6%), Mixed (1, 5.3%), Asian (1, 5.3%) Ethnicity: • BED: Hispanic (1, 5.3%), Non-Hispanic (18, 94.7%) • HC-OB: Hispanic (1, 5.3%), Non-Hispanic (18, 94.7%) • HC-NW: Hispanic (1, 5.3%), Non-Hispanic (18, 94.7%)	NR	BED: 14/5, 64.2%; HC-OB: 10/9, 52.6%; HC-NW 10/9, 52.6%	Task-based fMRI where participants had to perform a monetary incentive delay task	- During reward anticipation, patients with BED had a higher activation of the dorsal CN, MFG, insula, claustrum, and left cingulate gyrus, but a lower activation of the dorsal medial frontal gyrus compared to HC-NW. Compared to HC-OB, Patients with BED had a lower activation of the lentiform nucleus, ventral striatum, hypothalamus, thalamus, CN, putamen, midbrain red nucleus, MFG, SFG, right insula, STG, left precentral gyrus, and left IFG - During the receipt of rewards, patients with BED had a lower activation of the STG, insula, cingulate gyrus, PCC, left inferior parietal lobule, left MTG, ventral striatum, CN, left postcentral gyrus, left precuneus, left cuneus, superior/middle occipital gyrus, culmen, ACC, right IFG, right claustrum, and MFG. Compared to HC-OB, patients with BED had a lower activation of the insula, lentiform nucleus, PHG, cuneus, thalamus, STG, right precentral gyrus, right IFG, right MFG, right ACC, VS, and CN	15.25

(Continues)

TABLE 3 (Continued)

Article	Participants (n)	Age (mean, SD)	Age (range)	Race and ethnicity (n, %)	SES (mean, SD of n, %)	Sex ratio (F/M, %)	Modality/task	Main findings	Quality score
Bodell et al., 2018	BE age 16: 29; HC age 16: 93; BE age 18: 28; HC age 18: 94 (Of those who denied BE at 16, 13 endorsed BE at 18)	All participants were scanned at 16 years and completed annual assessments to 18 years.	BE/HC: 16-18 <sup>a</sup>	Race: • BE/HC: Black (80, 65%), Caucasian (33, 26.8%), Multi-race (10, 8.1%)	Receipt of public assistance: BE/HC age 16: 53, 43.1%	BE age 16/BE age 18: 112/0, 100%	Task-based fMRI where participants had to perform a card-guessing task	- There were no differences in brain activity during reward anticipation - During the receipt of rewards, individuals who BE had a greater activation of the CN	16
Bohon & Stice, 2011	BN: 13; HC: 13	Total 20: 3 (1.87) (no data available per subgroup)	NR	Race/Ethnicity: • BN/HC: Caucasian (80%), Asian (12%), African American (4%), Hispanic (4%)	BN	BN/HC: 26/0, 100%	Task-based fMRI where participants were presented with 2 visual cues (a milkshake or a glass of water). Following 60% of the picture cues, a milkshake/tasteless solution was delivered. For the remaining 40% of the pictures, no milkshake/tasteless solution was delivered	- The pleasantness ratings of the chocolate milkshake and tasteless solution did not differ between the groups - There were no significant differences between the groups when anticipating or receiving the chocolate milkshake	20.5
Bohon & Stice, 2012	BN: 13; HC: 13	Total 20: 3 (1.87) (no data available per subgroup)	NR	Race/Ethnicity: • BN/HC: Caucasian (80%), Asian (12%), African American (4%), Hispanic (4%)	BN	BN/HC: 26/0, 100%	Task-based fMRI where participants were presented with 2 visual cues (a milkshake or a glass of water). Following 60% of the picture cues, a milkshake/tasteless solution was delivered. For the remaining 40% of the pictures, no milkshake/tasteless solution was delivered	- Patients with BN, but not HC, showed a positive correlation between negative affect and brain activity in the putamen, CN, and pallidum when anticipating the receipt of the chocolate milkshake - There was a higher functional connectivity among the amygdala, left insula, and left putamen during the anticipation of the chocolate milkshake in patients with BN. However, this connectivity was lower during the receipt of the milkshake	20.5

TABLE 3 (Continued)

Article	Participants (n)	Age (mean, SD)	Age (range)	Race and ethnicity (n, %)	SES (mean, SD of n, %)	Sex ratio (F/M, %)	Modality/task	Main findings	Quality score
Brooks et al., 2011	AN-restrictive: 11; AN-binge/purge: 7; BN: 8; HC: 24	AN-restrictive: 26 (7.2); AN-binge/purge: 25 (6.6); BN: 25 (7.1); HC: 26 (9.5)	AN-restrictive/AN-binge/purge/BN: 16-50*	NR	Education (years): AN-restrictive: 8 (4); AN-binge/purge: 8 (3); BN: 12.5 (6.3); HC: 12 (6.5)	AN/BN/HC: 50/0, 100%	Task-based fMRI where participants were shown photographs of food as well as non-food items and were asked to imagine eating the food items and to imagine using the non-food items	- Patients with BN had a lower activation of the bilateral STG, insula, and left visual cortex	37.5
Celone et al., 2011	BE: 18; HC: 19	BE: 20.67 (2.10); HC: 20.42 (1.95)	NR	NR	Education (years): BE: 14.26 (1.70); HC: 14.74 (1.66)	BE/HC: 37/0, 100%	Task-based fMRI where participants had to perform a weather prediction task	- There were no differences in learning - Individuals who BE had a higher activation of the right CN, bilateral DLPFC, right precuneus, right ACC, and left putamen - Individuals who BE also showed greater increases in activity of the right ventrolateral PFC, bilateral DLPFC, ACC, and precuneus over the duration of the task while HC showed decreases in activity in the bilateral hippocampus, ACC, left MFG, left retrosplenial cortex, and right precuneus	23
Cyr et al., 2016	BN: 27; HC: 27	BN: 16.6 (1.5); HC: 16.3 (2.1)	NR	Race/Ethnicity: • BN: • Caucasian (16, 59.3%), Hispanic (7, 25.9%), Asian (3, 11.1%), Other (1, 3.7%) • HC: • Caucasian (9, 33.3%), African American (4, 14.8%), Hispanic (9, 33.3%), Asian (4, 14.8%), Other (1, 3.7)	NR	BN/HC: 54/0, 100%	Task-based fMRI where participants had to navigate an 8-arm radial maze in order to find rewards	- There were no significant group differences in learning between the groups - Patient with BN activated the IFG in both the learning and the control condition, whereas HC only activated the IFG in the learning condition - Opposite to HC, patients with BN displayed a deactivation of the	34.5

(Continues)

TABLE 3 (Continued)

Article	Participants (n)	Age (mean, SD)	Race and ethnicity (n, %)	SES (mean, SD of n, %)	Sex ratio (F/M, %)	Modality/task	Main findings	Quality score
Frank et al., 2011	BN: 23; HC: 20	BN: 25.2 (5.3); HC: 27.2 (6.4)	NR	NR	BN/HC: 43/0, 100%	Task-based fMRI where participants had to perform a temporal difference model task	- There were no differences in sweetness and pleasantness ratings - Patients with BN had reduced response activation for unexpected presentations of sucrose and reduced deactivation for unexpected omission of sucrose in the ventral putamen, insula, and OFC. - For the temporal difference model, patients with BN had a lower activation of the bilateral putamen, amygdala, insula, and OFC	38
Frank, Shott, Keffler, & Cormier, 2016	BN: 20; AN-ill: 21; AN-recovered: 19; HC-OB: 19; HC-NW: 27	BN: 25.2 (5.3); AN-ill: 22.9 (6.1); AN-recovered: 27.0 (5.3); HC-OB: 28.2 (8.1); HC-NW: 26.2 (7.0)	NR	NR	AN-ill/AN-recovered/ BN/HC-OB/HC-NW: 106/0, 100%	Task-based fMRI where participants had to perform a temporal difference model task	- There was no difference in classification accuracy between the groups when classifying the sucrose v. no solution or artificial saliva v. no solution. There was also no difference in classification accuracy when classifying sucrose v. artificial saliva between patients with BN and HC - Classification between sucrose vs. no solution	30.5

TABLE 3 (Continued)

Article	Participants (n)	Age (mean, SD)	Age (range)	Race and ethnicity (n, %)	SES (mean, SD of n, %)	Sex ratio (F/M, %)	Modality/task	Main findings	Quality score
Frank, Shott, AN: 26; BN: 25; HC: 26 Riederer &, 2016	AN: 23.23 (5.26); BN: 24.64 (4.22); HC: 24.39 (3.49)	NR	NR	Education (years): AN: 14.39 (2.25); BN: 15.77 (3.09); HC: 16.52 (1.92)	AN/BN/HC: 76/0, 100%	Task-based fMRI where participants had to perform a temporal difference learning task and diffusion-weighted Magnetic Resonance Imaging	- Patients with BN did not have an effective connectivity pattern between the hypothalamus and the central striatum. Patients with BN had an effective connectivity from the ACC to the VS and then to the hypothalamus, from the substantia nigra to the thalamus, from the ACC to the medial OFC, from the left from ventral anterior insula to inferior OFC, middle to inferior OFC, and from the dorsal to ventral anterior insula.	- Patients with BN did not have an effective connectivity pattern between the hypothalamus and the central striatum. Patients with BN had an effective connectivity from the ACC to the VS and then to the hypothalamus, from the substantia nigra to the thalamus, from the ACC to the medial OFC, from the left from ventral anterior insula to inferior OFC, middle to inferior OFC, and from the dorsal to ventral anterior insula.	43.75
Frank et al., 2021	BN: 56; BED: 16; BE: 34; AN: 91; HC: 120	BN: 23.52 (4.65); BED: 28.60 (7.39); BE: 22.10 (5.92); AN: 21.85 (5.82); HC: 25.15 (4.95)	NR	NR	BN/BED/BE/AN/HC: 317/0, 100%	Task-based fMRI where participants had to perform a temporal difference model task	- Prediction error responses in the left ventral anterior insula and left NAC were related to BMI and binge-eating frequency across all eating disorder groups. - There was an effective connectivity pattern from the VS to the hypothalamus across the eating disorder groups and this was correlated with bulimia symptoms.	- Prediction error responses in the left ventral anterior insula and left NAC were related to BMI and binge-eating frequency across all eating disorder groups. - There was an effective connectivity pattern from the VS to the hypothalamus across the eating disorder groups and this was correlated with bulimia symptoms.	49
Gellebter et al., 2006	BE-OB: 5; BE-NW: 5; HC-OB: 5; HC-NW: 5	BE-OB: 23.4; (2.5); BE-NW: 20.8 (1.6); HC-OB: 21.2 (8); HC-NW: 21.2 (.8)	NR	BE-OB/BE-NW/HC-OB/HC-NW: 20/0, 100%	Task-based fMRI where participants were presented with visual and auditory stimuli representative of	- There were no differences in hunger, liking, and desire to eat scores	- There were no differences in hunger, liking, and desire to eat scores	24.5	

(Continues)

TABLE 3 (Continued)

Article	Participants (n)	Age (mean, SD)	Race and ethnicity (n, %)	SES (mean, SD of n, %)	Sex ratio (F/M, %)	Modality/task	Main findings	Quality score
Gellebter et al., 2016	BE = 10 (5 NW, 5 OB); HC = 10 (5 NW, 5 OB)	BE: 22.1 (2.3); HC: 21.3 (6)	BE-OB/BE-NW/HC-OB/HC-NW: 20-27 <sup>b</sup>	NR	BE/HC: 20/0, 100%	Task-based fMRI where participants were presented with visual and auditory stimuli representative of binge-type foods, non-binge-type foods, and neutral non-food stimuli	- All five BE-OB displayed an activation in the right precentral gyrus and premotor area for binge food stimuli. Four of these showed activations of the right precentral gyrus, IFG, left lingual, and fusiform gyrus for non-binge foods - Four of five BE-NW displayed activation of the left inferior occipital gyrus and the right GL for non-binge foods	13.5
Hartogsveld et al., 2022a	BED: 38; HC: 38	BED: 26.11 (6.49) HC: 23.84 (4.35)	BED: 20-49; HC: 18-33 <sup>b</sup>	NR	BED: 29/9, 76%; HC: 32/6, 84	Task-based fMRI where participants were needed to perform an instrumental learning task before and after stress induction	- There were no differences in hunger, liking, and desire to eat scores - When comparing high- vs. low-energy-dense food, individuals who BE had a higher activation of the dorsal ACC	22

TABLE 3 (Continued)

Article	Participants (n)	Age (mean, SD)	Age (range)	Race and ethnicity (n, %)	SES (mean, SD of n, %)	Sex ratio (F/M, %)	Modality/task	Main findings	Quality score
Haynos et al., 2021	BE: 27; HC: 21	BED: 32.27 (8.54); HC: 30.90 (7.99)	NR	Education (years): BED: 14.61 (2.09); HC: 14.75 (1.84)	BED: 24/3, 88.9%; HC: 21/0, 100%	Resting-State fMRI. Separately, participants had to perform a reversal learning task.	- Individuals with a lower connectivity between the NAc and SFG displayed a more compulsive pattern of reward responding.	30	
Jiang et al., 2019	AN-restrictive: 14; BN: 13; HC: 12	AN-restrictive: 24.94 (4.67); BN: 22.50 (2.88); HC 24.14 (3.06)	NR	NR	AN-restrictive/BN/ HC: 37/0, 100%	Task-based fMRI where participants were presented with food odors.	- Patients with BN had lower wanting scores for high EDF food odors.  - When hungry and comparing the rating the wanting for high versus low EDF food items, patients with BN had a lower activation of the anterior ventral pallidum	31.5	
Kim et al., 2012	AN-restrictive: 6; AN-binge/purge: 12; BN: 20; HC: 20	AN: 25.2 (4.2); BN: 22.9 (3.9); HC: 23.2 (1.8)	NR	Education (years): AN: 14.9 (1.5); BN: 15.5 (1.0); HC: 15.8 (4)	AN/BN/HC: 58/0, 100%	Task-based fMRI where participants were shown photographs of high caloric foods as well as non-food items and were asked to imagine eating the food items and to imagine using the non-food items	- Patients with BN had a higher activation right MFG, right insula, and cerebellum. They also had a stronger functional connectivity between the anterior insula and mOFC, and an effective connectivity between the left and right insula.	24.5	
Miranda-Olivos et al., 2021	BED: 10; HC-OB: 25; HC-NW: 31	BED: 39.70 (8.87); HC-OB: 37.56 (10.13); HC-NW: 29.65 (12.64)	NR	Education (years): BED: 12.60 (3.13); HC-OB: 12.96 (3.37); HC-NW: 15.35 (1.62)	BN/BED/HC-NW/ HC-OB: 66/0, 100%	Task-based fMRI where participants had to perform a monetary	- There were no differences in discounting rates	11.25	

(Continues)

TABLE 3 (Continued)

Article	Participants (n)	Age (mean, SD)	Race and ethnicity (n, %)	SES (mean, SD of n, %)	Sex ratio (F/M, %)	Modality/task	Main findings	Quality score
Monteleone et al., 2017	AN: 20; BN: 20; HC: 20 (8; HC: 27.1 (4.7)	AN: 25.5 (7.8); BN: 27.7 (8; HC: 27.1 (4.7)	AN/BN/HC: 18 + <sup>a</sup>	NR	NR	Task-based fMRI where Participants were presented with a pleasant (sucrose) and aversive taste (quinine) stimulus	- There were no differences between patients with BED and HC when investigating brain activity related to discounting when choosing immediate versus delayed rewards	31.5
Murao et al., 2017	AN-restrictive: 11; AN-binge/purge: 12; HC: 20	AN-restrictive: 30.9 (10.1); AN-binge/purge: 39.3 (7.0); HC: 33.2 (8.8)	AN-restrictive/AN-binge/purge/HC: 20–49 <sup>b</sup>	NR	Education (years): AN-restrictive: 14.9 (2.7); AN-binge/purge: 15.1 (1.8); HC: 14.9 (1.9)	AN-restrictive/AN-binge/purge/HC: 43.0, 100%	Task-based fMRI where participants had to perform a monetary incentive delay task	37.5

TABLE 3 (Continued)

Article	Participants (n)	Age (mean, SD)	Race and ethnicity (n, %)	SES (mean, SD of n, %)	Sex ratio (F/M, %)	Modality/task	Main findings	Quality score
Neveu et al., 2018	BN: 31; HC: 23	BN: 24 (3.87); HC: 23 (2.7)	BN/HC: 18–35 <sup>a</sup>	NR	BN/HC: 54/0, 100%	Task-based fMRI where participants had to rate the healthiness and tastiness of foods and then choose between foods	- Patients with BN rated the foods as less healthy, had a greater motivational index, and choice ratings were associated with tastiness and healthiness while they were only associated with tastiness in HC. - Patients with BN had a higher negative correlation between ventromedial PFC activity and healthiness ratings	36.5
Olsavsky et al., 2019	AN-ill: 19; AN-recovered: 20; BN: 20; HC: 43	AN-ill: 22.9 (5.0); AN-recovered: 19–45; BN: 20–37; HC: 19–43 <sup>b</sup>	AN-ill: 18–37; AN-recovered: 19–45; BN: 20–37; HC: 19–43 <sup>b</sup>	NR	AN-ill//AN-recovered/ BN/HC: 102/0, 100%	Task-based fMRI where participants had to perform a temporal difference model task	- There was no difference in value-related brain activity between patients with BN and HC	39.5
Reiter et al., 2017	BED: 22 HC: 22	BED: 29.0 (9.40); HC: 27.8 (4.54)	NR	School leaving qualification: BED: Intermediate school certificate (5.22.7%), university entrance qualification (17, 7.3%); HC: Intermediate school certificate (1.4.5%), university entrance qualification (21, 95.5%), and unemployment (years); BED: .7 (1.68); HC: .5 (1.05)	BED: 16/8, 62.3%; HC: 15/9, 53.3%	Task-based fMRI where participants had to perform a reward-guided decision-making task	- Patients with BED patients switched choices more frequently - When modeling PE's, patients with BED had a lower activation of the ventromedial PFC. - Ventromedial PFC brain activity was correlated with successful choices and negatively associated with switching behavior	15.5
Schiene et al., 2009	BN: 14; BED: 17; HC-NW: 19; HC-OW: 17	BN: 23.1 (3.8); BED: 24.4 (6.4); HC-NW 22.3 (2.6); HC-OW 25.0 (4.7)	NR	Education (years): BN: 12.7 (3); BED: 13.0 (1.5); HC-NW: 13.2 (9); HC-OW: 12.5 (1.9)	BN/BED/HC-NW/ HC-OW: 67/0, 100%	Task-based fMRI where participants had to passively view high-caloric food, disgusting items, and neutral items	- Patients with BED reported a greater sensitivity to rewards than all the other groups - There were no differences in valence or appetite ratings but patients with BN rated	30.5

(Continues)

TABLE 3 (Continued)

Article	Participants (n)	Age (mean, SD)	Race and ethnicity (n, %)	SES (mean, SD of n, %)	Sex ratio (F/M, %)	Modality/task	Main findings	Quality score
Setsu et al., 2017	BN: 21; HC: 20	BN: 25 (5.63); HC: 27.09 (5.69)	BN: 18.6–36.3; HC: 20.7–36.4 <sup>b</sup>	Race: • BN/HC: Asian (41, 100%)	Education (years): BN: 13.89 (1.94); HC: 14.56 (1.04)	BN/HC: 41/0, 100%	Task-based fMRI where participants were administered a solution of monosodium glutamate or distilled water	the pictures as more arousing - When viewing pictures of food, Patients with BED had a higher activation of the medial and lateral OFC than patients with BN. Patients with BED had a higher activation of the medial OFC than HC-NW. Patients with BN had a higher activation of the ACC and insula than the other groups. Reward sensitivity correlated positively with activation in the ACC and medial OFC in patients in BED and with the ACC, medial OFC, and insula in patients with BN. Arousal scores correlated positively with activation in the ACC and medial OFC in patients with BED

TABLE 3 (Continued)

Article	Participants (n)	Age (mean, SD)	Age (range)	Race and ethnicity (n, %)	SES (mean, SD of n, %)	Sex ratio (F/M, %)	Modality/task	Main findings	Quality score
Simon et al., 2016	BED: 27; HC-BED: 28; BN: 29; HC-BN: 27	BED: 38.26 (13.75); HC-BED: 38 (10.85); BN: 27.45 (10.55); HC-BN: 25.74 (5.25)	BED: 19–61; HC-BED: NR; BN: 53; HC-BN: NR <sup>b</sup>	Education (years): BED: 12.06 (9.16); HC-BED: 12.18 (2.06); BN: 12.66 (1.40); HC-BN: 12.70 (8.7)	NR	NR	Task-based fMRI where participants had to perform a monetary incentive delay task and a food incentive delay task	- There was no difference in task performance between the participants - For reward anticipation, there was no difference between the groups during the MID. However, during the FID, patients with BED/BN displayed a lower activation of the PCC	33.75
Skandalis et al., 2021	BED: 7; PD: 15; HC: 17	BED: 49.43 (5.09); Problematic Gambling: 42.60 (11.81); HC: 43.29 (11.10)	NR	NR	PET with [11C] carfentanil, [11C] MADAM, and [18F] FDOPA. Separately, participants had to perform a risky decision-making task	PET with [11C] carfentanil, [11C] MADAM, and [18F] FDOPA. Separately, participants had to perform a risky decision-making task	- There were no differences between the groups in risk taking for rewards or losses - Risk-taking to rewards was positively correlated with mu-receptor availability in the striatum, dorsal cingulate, and insula	26.5	

(Continues)

TABLE 3 (Continued)

Article	Participants (n)	Age (mean, SD)	Age (range)	Race and ethnicity (n, %)	SES (mean, SD of n, %)	Sex ratio (F/M, %)	Modality/task	Main findings	Quality score
Voon et al., 2015	BED: 20; HC:OB: 20	BED: 43.95 (9.47); HC: OB: 44.70 (10.12)	NR	NR	BED: 12/8, 60%; HC-OB: 9/11, 45%	Structural MRI. Separately, participants had to perform a two-step task,	- Patients with BED displayed more model-free learning and more perseverance (step 1 stimulus regardless of the reward outcome) during the two-step task.	24.5	
Voon et al., 2020	BED: 7; PD: 15; HC: 17	BED: 49.43 (5.09); Problematic gambling: 42.60 (11.81); HC: 43.29 (11.10)	NR	NR	PET with [11C] carfentanil, [11C] MADAM, and [18F] FDOPA. Separately, participants had to perform a two-step task	- Patients with BED had higher perseveration scores than patients with problematic gambling	- There were no differences in the degree of model-based or model-free learning	30	
Wang et al., 2011	BED: 10; HC: 8	BED: 38.5 (13.3); HC: 41.8 (8.9)	BED: 21-54; HC: 28-56 <sup>b</sup>	NR	PET with [11C] raclopride where participants were presented with food or neutral tastants with or without the administration of methylphenidate	- There were no differences in hunger and desire for food ratings	- In HC, neutral stimuli with MPH, but not food stimuli with MPH, were related to an increase in dopamine release in the CN.	22.25	

TABLE 3 (Continued)

Article	Participants (n)	Age (mean, SD)	Race and ethnicity (n, %)	SES (mean, SD of n, %)	Sex ratio (F/M, %)	Modality/task	Main findings	Quality score
Westwater et al., 2022	AN-bp: 22, BN: 33, HC: 30	AN-bp: 24.6 (4.7), BN: 23.6 (3.9), HC: 23.9 (3.5)	NR	Race: • AN-bp: White (19.8%), Asian (2.9%), Mixed (1.5%) • BN: White (27.83%), Asian (3.9%), Mixed (3.9%) • HC: White (21.70%), Asian (3.10%), Black (2.67%) Mixed (2.67%), Other (2.67)	AN-bp/BN/HC: 85/0, 100%	Single-photon magnetic resonance spectroscopy. Separately, participants had to perform an instrumental learning task.	- There were no behavioral differences on the instrumental learning task between patients and controls. - Patients with AN-bp with lower levels of NAA or higher levels of glutamate displayed more automaticity in the instrumental learning task.	37.5
Weygandt et al., 2012	BN: 14; BED: 17; HC-NW: 19; HC-OW: 17	BN: 23.1 (3.8); BED: 26.4 (6.4); HC-NW 22.3 (2.6); HC-OW 25.0 (4.7)	NR	Race: • BN/BED/HC-NW/ HC-OW: Caucasian (67, 100%)	BN/BED/HC-NW/ HC-OW: 67/0, 100%	Task-based fMRI where participants had to passively view high-caloric food, disgusting items, and neutral items	- Patients with BED and HC-NW were separated with classifiers in the right ACC, the left insula, medial OFC, and the right VS - Patients with BN and HC-OW were separated with classifiers in the left ACC, the right insula, and the left VS	30

(Continues)

TABLE 3 (Continued)

Article	Participants (n)	Age (mean, SD)	Race and ethnicity (n, %)	SES (mean, SD of n, %)	Sex ratio (F/M, %)	Modality/task	Main findings	Quality score
							<ul style="list-style-type: none"> <li>- Patients with BN and HC-OW were separated with classifiers in the right lateral OFC</li> <li>- Patients with BN and patients with BED were best separated with classifiers in the right ACC, the insula, and the left VS</li> </ul>	

Abbreviations: ACC, anterior cingulate cortex; AN, anorexia nervosa; BE, binge-eating disorder; BMI, body mass index; BN, bulimia nervosa; CN, caudate nucleus; DLPFC, dorsolateral prefrontal cortex; F, female; fMRI, functional magnetic resonance imaging; HC, healthy controls; IFG, inferior frontal gyrus; ITG, inferior temporal gyrus; M, male; MFG, middle frontal gyrus; MRI, magnetic resonance imaging; MTG, middle temporal gyrus; NAc, nucleus accumbens; NR, not reported; NW, normal weight; OB, obese; OFC, orbitofrontal cortex; PCC, posterior cingulate gyrus; PET, positron emission tomography; PFC, prefrontal cortex; PHG, parahippocampal gyrus; RQF, Regulated Qualifications Framework; SD, standard deviation; SES, socioeconomic status; STG, superior temporal gyrus.

<sup>a</sup>Age range stated the protocol.  
<sup>b</sup>Age range of the actual participants.

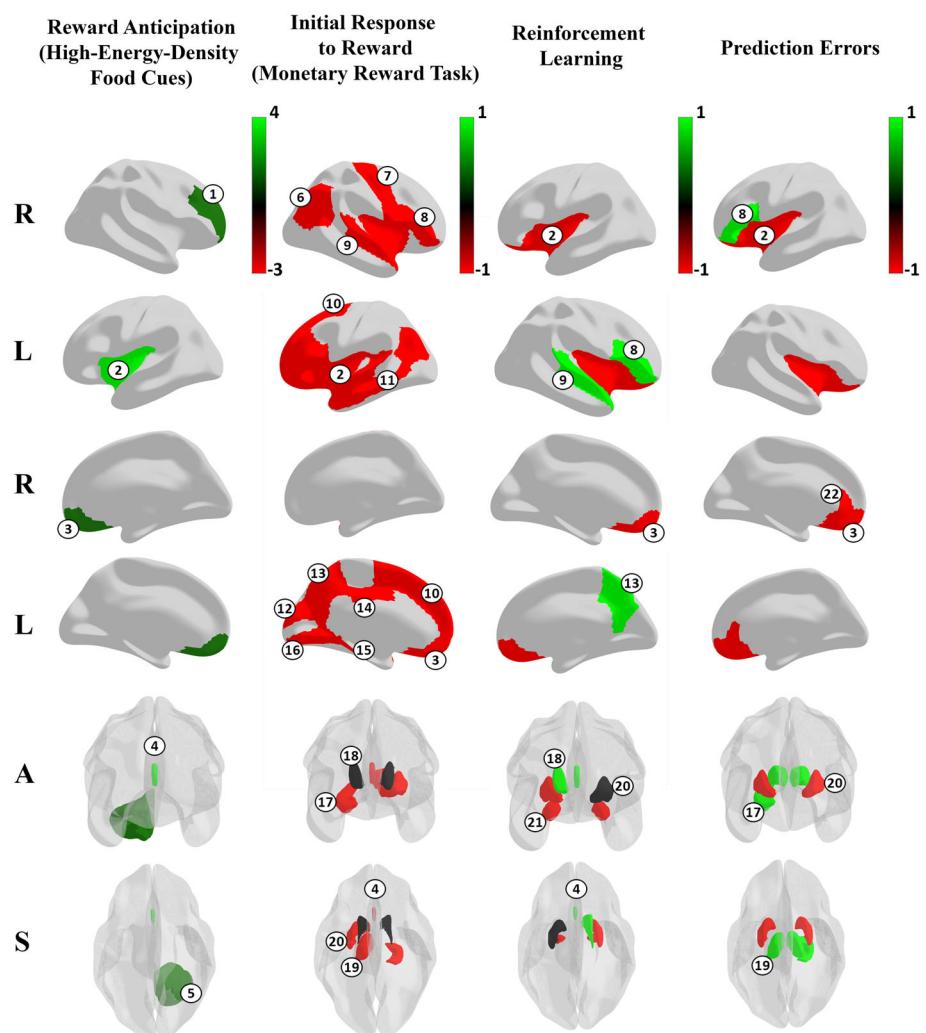
higher volume of the medial/total OFC ( $n = 4$ , 29%), right ventral striatum/NAc ( $n = 2$ , 14%), left insula ( $n = 2$ , 14%), left postcentral gyrus ( $n = 2$ , 14%), and ACC ( $n = 2$ , 14%) (Amianto et al., 2013; Coutinho et al., 2014; Frank et al., 2013; Murray, Duval, et al., 2022; Schäfer et al., 2010; Turan et al., 2021; Voon et al., 2015). There were two (14%) studies that followed participants longitudinally (Cyr et al., 2017; Zhang et al., 2021). One of these reported that a higher volume of the right putamen and globus pallidus at age 14 was predictive of developing BE in the next 2 to 5 years (Zhang et al., 2021). Only two (14%) studies investigated the relationship between volume and reward processing (Frank et al., 2013; Murray, Duval, et al., 2022). Although both studies found a higher OFC volume, one study did so in adult patients with a higher reward sensitivity while another study in adolescents found an association with lower behavioral approach scores (i.e., the drive to approach rewards) (Murray, Duval, et al., 2022). This could indicate that the relationship between volume and reward processing differs depending on the age or illness duration of the patient. In summary, the studies find that individuals who binge eat have a higher volume of the ACC, insula, and OFC as well as a lower volume of the CN. The relation between these findings and reward processing varied and could be dependent on the age and illness duration of the patient.

### Connectivity

Several types of connectivity can be distinguished, namely structural, functional, and effective connectivity (Fingelkurts et al., 2005). Structural connectivity investigates WM tracts connecting different areas of the brain, functional connectivity is based on statistical dependencies among remote neurophysiological events, and effective connectivity looks at the causal influence that one neural system exerts over another.

Structural connectivity: There were six studies that looked at structural connectivity of which five (83%) studies had a sample of patients with BN and one (17%) had a sample of patients with BED. There were four (67%) studies that used diffusion tensor imaging (DTI) to investigate the axonal integrity of fiber tracts. The results of these studies pointed to a lower integrity of the fiber bundles between the frontal cortex and other cortical (parietal, temporal, and occipital) and subcortical (thalamus) areas in both patients with BN and BED (Estella et al., 2020; He et al., 2016; Mettler et al., 2013). This lower integrity was also associated with a higher BE frequency in patients with BN (He et al., 2016). Another two (33%) studies investigated the structural connectivity (i.e., the number of fibers) between brain regions through fiber tracking and found a higher connectivity between the OFC, insula, and striatum in patients with BN (Frank, Shott, Riederer, & Pryor, 2016; Wang et al., 2019). Taken together, these results suggest that individuals who BE have more fibers connecting the OFC, insula, and striatum, but that the integrity of these fibers is lower. Frank, Shott, Riederer, and Pryor (2016) state that this is also seen in other populations and pose that the higher number of fibers could be a compensation for the lower fiber bundle integrity.

**FIGURE 4** Representation of the results concerning reward anticipation (high-energy-density food cues), initial response to reward (monetary reward task), reinforcement learning, and prediction errors. Only RDoC subconstructs with more than one study describing changes in brain activity have been included in this figure. The results are shown on a scale representing the number of studies that found a lower or higher task-based neural activity in individuals who binge eat. Numbers: 1, middle frontal gyrus; 2, insula; 3 orbitofrontal gyrus; 4, anterior cingulate cortex; 5, cerebellum; 6, precuneus; 7, precentral gyrus; 8, inferior frontal gyrus; 9, superior temporal gyrus; 10, middle frontal gyrus; 11, middle temporal gyrus; 12, cuneus; 13, precuneus; 14, posterior cingulate cortex; 15, parahippocampal gyrus; 16, lingual gyrus; 17, hippocampus; 18, caudate nucleus; 19, thalamus; 20, putamen; 21, amygdala; 22, ventromedial prefrontal cortex. Abbreviations: A, anterior; L, left; R, right; S, superior



**Functional connectivity:** A total of six studies investigated resting-state functional connectivity. There were four (75%) studies with a sample of patients with BN and three (50%) with a sample of patients with BED. Of these studies, there were five (83%) that used a seed-based approach and one (17%) that used a graph theory-based approach. Their results showed a higher connectivity between the different regions of the striatum in patients with BN, a lower connectivity between the frontal cortex and striatum in patients with BN and BED, as well as a lower connectivity between the different regions of the frontal cortex in patients with BN and BED (Canna et al., 2017; Haynos et al., 2021; Murray, Alba, et al., 2022; Wang et al., 2017; Wang et al., 2019). A lower frontostriatal connectivity was also related to a higher BE frequency (Haynos et al., 2021). One (20%) of the studies also used an independent component analysis (ICA) in patients with BN and BED. It found a lower connectivity of the ACC within the salience network in both patients with BN and BED but this was more pronounced in patients with BN (Stoprya et al., 2019). The results also showed a lower connectivity of the mPFC within the default-mode network in patients with BED but a higher connectivity in patients with BN (Stoprya et al., 2019). To summarize, studies find that individuals who binge eat display a common lower functional

connectivity between the different frontal cortex regions as well as between the frontal cortex and striatum, but that there are also differences in the functional connectivity of specific networks between the different disorders.

#### Perfusion

There was one study that investigated perfusion with arterial spin labeling (ASL). Here, patients with BN or BED had a higher cerebral blood flow (CBF) in the medial PFC, OFC, inferior/middle temporal gyrus, insula, and ACC (Martins et al., 2020). The relation of these results with reward processing was not investigated but a higher CBF in these regions was associated with a higher disease severity (Martins et al., 2020).

#### Metabolites

Only one study investigated metabolite concentrations in the brain with magnetic resonance spectroscopy (MRS). In this study, patients with AN-BP had lower levels of myo-inositol and N-acetylaspartate (NAA) in the inferior left PFC, but this was not the case in patients with BN (Westwater et al., 2022). These lower levels of myo-inositol and NAA were associated with eating disorder and depressive symptoms in the BN group, but not in patients with AN-BP.

### 3.3.2 | Task

The following findings concern differences in the neurobiological reward system reported by studies using a task. Of the 32 studies, there were 29 (91%) that used MRI and 3 (9%) that used PET. A univariate voxel-based or ROI-based analysis was performed in 27 (84%) studies, a multivariate machine learning approach was used in 2 (6%), and functional or effective connectivity was investigated in 7 (22%).

#### Reward responsiveness

**Reward anticipation:** Of the 13 studies looking at reward anticipation, there were 8 (62%) that showed images of food, 1 (8%) that presented food odors, and 4 (31%) that used a monetary or food reward task. There were 6 (46%) studies with a sample of patients with BN, 3 (23%) with a sample of patients with BED, 1 (8%) with a mixed sample of patients with BN or BED, 3 (23%) with a sample of individuals who binge eat, and 1 (8%) with a sample of patients with AN-BP. When showing images of high-energy-density food, a higher activity of the ACC ( $n = 2$  studies, 25%), anterior insula ( $n = 2$ , 25%), and mOFC ( $n = 1$ , 13%) was found across the different samples, as well as a higher functional connectivity between the insula and mOFC (Geliebter et al., 2016; Kim et al., 2012; Schienle et al., 2009). Patients with BN displayed more activation of the ACC while patients with BED displayed more activation of the mOFC (Schienle et al., 2009). There was no difference in liking and wanting scores between patients and controls and the scores were not correlated with the findings. However, activation in the ACC and mOFC in patients with BN or BED was positively associated with behavioral approach system scores, suggesting that these results are related to the drive to acquire rewards (Schienle et al., 2009). Contrastingly, a lower activity of the anterior insula was found when patients with BN viewed images of food in general (Brooks et al., 2011). This suggests that different types of food are associated with different brain activity changes in individuals who binge eat. This was also found in the study presenting food odors. Here, patients with BN had lower wanting scores and a lower activation of the anterior ventral pallidum and anterior insula when rating high-energy-density food odors, but a lower activation in the CN when they were rating food odors in general (Jiang et al., 2019). Of the four studies using a monetary or food reward task, three (75%) used a monetary incentive delay task (MID) or a food incentive delay task (FID) and one (25%) used a reward-guessing task. In the MID and FID, participants were shown a possible reward or loss and needed to press a button as quickly as possible in order to win the reward or prevent the loss. In the reward-guessing task, participants were asked to guess the value of a card before being shown a potential win or loss and then the outcome. Most studies ( $n = 3$ , 75%) found no difference in brain activity during the anticipation of money (Bodell et al., 2018; Murao et al., 2017; Simon et al., 2016). The study looking at the anticipation of food found that patients with BED or BN had a lower activation of the PCC during the FID, but this was not related to food craving (Bodell et al., 2018; Murao et al., 2017; Simon et al., 2016). To summarize, individuals who binge eat show a higher activity of the ACC,

insula, and OFC when anticipating food rewards, but not monetary rewards, and this could be related to a higher drive to acquire food.

**Initial response to reward:** There were nine studies that investigated the initial response to reward. Of these studies, five (55%) presented a taste stimulus and four (45%) used a monetary or food reward task. A sample of patients with BN in five (56%) studies, a sample of patients with BED in two (22%), a mixed sample of patients with BN or BED in one (11%), and a sample of individuals who binge eat in one (11%) were included. The studies giving a taste stimulus found that patients with BED, but not HC, had a significant dopamine release in the CN and putamen and that this was related to BE frequency (Wang et al., 2011). Their results also provide evidence for different taste stimuli being related to different changes in brain activity in patients with BN. Opposite to HC, they had a larger response to sucrose than to a bitter stimulus in the left dlPFC, brainstem, OFC, and right post-central gyrus (Monteleone et al., 2017). But after giving an umami stimulus, patients with BN reported lower liking scores and displayed more activity of the right middle insula and ACC (Setsu et al., 2017). Of the four studies that used a reward task, there were two (50%) that used a MID or FID, one (25%) that used a reward-guessing task, and one (25%) that used a spatial learning task where participants needed to navigate a maze in order to find rewards. They found a lower responsivity to monetary rewards and a higher responsivity to food rewards in individuals who binge eat. During the spatial learning task, where visuospatial memory was important, patients with BN had a lower activation in the right anterior hippocampus and left SFG (Cyr et al., 2016). In the MID, where the delivery of the reward depended on the performance of the participant, a lower activation of the insula, CN, NAc, ACC, STG, IFG, and MFG was found in patients with BED (Balodis et al., 2013). In contrast, during the reward-guessing task, where the delivery of the reward was randomized, a higher activity of the CN was found in individuals who BE (Bodell et al., 2018). When it comes to the FID, patients with BN or BED had a higher activation of the mOFC, PCC, anterior medial PFC, and angular gyrus (Simon et al., 2016). Taken together, the results point to a lower responsivity to monetary rewards and a higher responsivity to food rewards in individuals who binge eat. However, there is considerable variability in the brain regions involved which could be due to differences between the tasks and the populations of the studies.

**Reward satiation:** As part of a sensitivity analysis, one study that presented a sucrose and bitter stimulus also looked at the effect of the repetition of the stimuli in patients with BN and HC and found no differences between the groups (Monteleone et al., 2017).

#### Reward learning

**Reinforcement learning:** In total, five studies investigated reinforcement learning. Of these, one (20%) used a spatial learning task, one (20%) used a temporal difference model task where participants learned to associate a taste stimulus with a visual stimulus, one (20%) used a weather prediction task (WPT) where participants needed to find out which cards predict a certain weather condition, and two

(40%) used a two-step task where participants needed to learn which symbols were associated with the greatest reward. There were two (40%) studies that included a sample of patients with BN, two (40%) that included a sample of patients with BED, and one (20%) that included a sample of individuals who binge eat. Patients with BED displayed more model-free learning during the two-step task in one (20%) study, but no behavioral differences were found in the other studies (Voon et al., 2015). There were differences in brain activity, but they varied greatly. During the temporal difference model task, patients with BN had a lower activity in the putamen, amygdala, insula, and OFC (Frank et al., 2011). However, in the WPT, individuals who binge eat had a greater activity of the CN, ACC, and DLPFC (Celone et al., 2011). During the spatial learning task, patients with BN had a higher activity of the right IFG (Cyr et al., 2016). Summarized, these studies find that individuals who binge eat display more model-free learning and that reward learning is encoded differently in the brain of individuals who binge eat. However, the brain areas involved differed between the studies, which could be due to differences between the tasks and the populations of the studies.

**Prediction errors:** In total, five studies looked at prediction errors. There were three (60%) studies that used a temporal difference model task where sometimes a sucrose solution was given when none was expected and vice versa, one (20%) study used a spatial learning task, and one (20%) study used a “reward-guided decision-making task.” In the “reward-guided decision-making task,” participants needed to choose between two cards where one card had a high probability of a reward and the other a high probability of a loss. After a certain number of trials, these probabilities switched. A sample of patients with BN was included in four (80%) studies, a sample of patients with BED in two (40%), and a sample of individuals who binge eat in one (20%). During the temporal difference model task, one (33%) study found that patients with BN had lower responses to prediction errors in the putamen, insula, and OFC but no differences were found in two (67%) other studies with larger sample sizes (Frank et al., 2011; Frank et al., 2021; Olsavsky et al., 2019). In the spatial learning task, patients with BN had a higher activation of the right anterior hippocampus when receiving unexpected rewards and a higher activation of the bilateral thalamus, left SFG, and IFG when not receiving expected rewards (Cyr et al., 2016). In the study using the “reward-guided decision-making task,” patients with BED showed more switching behavior and a lower activity in the vmPFC (Reiter et al., 2017). In summary, the results of these studies are inconclusive with studies reporting a higher PE response, a lower PE response, or no difference at all. This could be due to the studies using different rewards (i.e., food or money) in different contexts (i.e., a passive or active task).

**Habits:** There were four studies that investigated habits. Of these, two (50%) used an instrumental learning task where participants needed to learn which stimulus led to a reward. Afterwards, the reward was devalued (e.g., participants were required to eat when the reward was a food item) and the task was performed again.

Another study (25%) used a reversal learning task where participants were presented with two patterns and needed to learn which pattern led to a reward. After every 10 correct choices, the strategy switched and participants needed to change their reactions and choose the formerly wrong stimulus. Another study (25%) used a two-step task where the probability of a stimulus leading to a certain reward varied over time. A sample of patients with BED were included in three (75%) studies, a sample with AN-BP in one (25%) study, and a sample with BN in one (25%) study. When it comes to behavior, patients with BED displayed more compulsive decision-making during the two-step task and patients with AN-BP and BN reported higher scores on the Creature of Habit Scale (COHS) (Voon et al., 2015; Westwater et al., 2022). Furthermore, there were behavioral differences that were linked to changes in brain connectivity and metabolites. The lower resting-state connectivity between the NAc and SFG in patients with BED was correlated with more habit-directed behavior in the reversal learning task (Haynos et al., 2021). The lower levels of NAA in the left inferior PFC in patients with AN-BP were associated with higher automaticity scores on the COHS (Westwater et al., 2022). Summarized, these studies suggest that individuals who binge eat display more habitual behavior and that this could be linked to a lower frontostriatal functional connectivity and lower levels of NAA in the frontal cortex.

#### Reward valuation

Two studies looked at reward valuation in patients with BN. One study looked at the expected value of trials during a temporal difference model task with food and found no difference in brain activity between patients and HC (Olsavsky et al., 2019). Another study let participants rate the healthiness and tastiness of food items and made them decide between them. Patients rated the food items as unhealthier and were more decisive about their choices (Neveu et al., 2018). Also, healthiness and tastiness both played a role in decision-making in patients but only tastiness played a role in HC (Neveu et al., 2018). Overall, choice ratings were correlated with activity in the vmPFC, but the correlation with healthiness was more negative in patients (Neveu et al., 2018). Together, these results suggest that both healthiness and tastiness are important for the valuation of food items in patients with BN and that the vmPFC plays a key role in this process.

**Risk/ambiguity:** One study investigated risk with a risky decision-making task. Here, participants could choose to get a certain reward/loss or choose to gamble. Across all participant groups, risk taking for rewards was positively correlated with  $\mu$ -opioid receptor availability in the striatum, dorsal cingulate, and insula (Skandali et al., 2021). No differences in risk-taking for rewards were seen between patients with BED or HC. However, patients with BED had a lower striatal  $\mu$ -opioid receptor availability and tended to display less risk-taking for rewards.

**Effort:** No studies were identified that investigated effort.

**Delay:** There were two studies that looked at the effect of delay during reward valuation. They did so in patients with BED and used a delay

discounting task (DDT). During this task, participants were required to choose between a certain immediate amount of money versus another delayed amount of money. This made it possible to investigate delay discounting (i.e., the preference for more immediate rewards). However, no differences in delay discounting or brain response during the DDT were found (Haynos et al., 2021; Miranda-Olivos et al., 2021).

## 4 | DISCUSSION

This systematic review has the following two objectives: to interpret results from neuroimaging studies that investigate the reward system in BE and to formulate directions for future research.

Across samples, imaging studies at rest report three main findings in BE: First, a higher volume and CBF of cortical areas such as the ACC, insula, and OFC and a lower functional connectivity between these regions. Second, a higher volume of the NAc, a lower volume of the CN, a lower striatal dopamine transmission, and a higher functional connectivity between the striatal subregions. Third, a lower functional connectivity, a lower fiber tract integrity, and a higher structural connectivity between the frontal cortex and striatum.

The overlap between the cortical regions with a higher volume and a higher CBF is not surprising as previous studies report that these measures covary and that increases in CBF are mediated by increases in volume (Vaidya et al., 2007). However, the implication of these results for reward processing is unclear. The studies in this review find a relation between a higher OFC volume and a lower reward sensitivity in adolescence, but the opposite in adults (Frank et al., 2013; Murray, Duval, et al., 2022). Furthermore, a higher volume of the putamen and globus pallidus is predictive of developing BE, but no difference in the volume of these regions is found in individuals who have BE episodes (Zhang et al., 2021). This could imply that changes in the volume of certain brain areas are associated with developing BE, but that BE itself can lead to changes in the volume of other brain areas. Indeed, studies in rodents have found that repeated ingestion of high-energy-density food can lead to morphological changes in the neurons in the OFC (Seabrook & Borgland, 2020). However, whether this is the reason behind the conflicting results remains uncertain. This is because most structural studies in BE have been cross-sectional or only followed participants over a short period of time. Future structural studies should therefore aim to follow individuals who binge eat for a longer time period, across different ages and illness stages.

The findings in this review suggest that individuals who binge eat show a structural and functional disconnect between the frontal cortex and striatum, that they display more habitual behavior, and that there is a relationship between the two. This is similar to findings in patients with an obsessive-compulsive disorder where a lower frontostriatal connectivity is also seen and where this is related to more habitual behavior (Vaghi et al., 2017). It also illustrates that reward processing is the result of a network of interactions and not always a simple hyper- or hypoactivity of a single brain region (Zald &

Treadway, 2017). Future studies should keep this in mind and consider exploring connectivity in their analyses.

Across imaging studies investigating BE with a task, two main findings are reported: First, a higher activity of the OFC, ACC, and striatum during the anticipation and receipt of high-energy-density food, but a lower activity during the anticipation and receipt of money. Second, more model-free reinforcement learning and habitual behavior are seen together with an altered encoding of reward learning and reward valuation in the ACC, PFC, and striatum.

The findings concerning the anticipation and receipt of high-energy-density food are in line with the incentive-sensitization theory of BE. This theory hypothesizes that repeated BE episodes sensitize the brain to food and that this leads to a higher incentive salience (i.e., wanting) for food (Robinson & Berridge, 1993). This sensitization of the brain could be the reason why a higher activity of the ACC, insula, and mOFC is seen during the anticipation of high-energy-density food, but not money. These differences could also be related to a higher incentive salience as the studies find that a higher ACC and mOFC activity is associated with a higher drive to acquire rewards (Schienle et al., 2009). This is strengthened by findings in other populations where a higher activation of the ACC is linked to focusing on the edibility of food and where a higher activation of the insula is related to planning to eat until full (Roefs et al., 2018). Further evidence for the incentive sensitization theory can be seen in the striatal dopamine response to food in patients with BN, but not in controls, which is similar to animal research (Robinson & Berridge, 1993; Wang et al., 2011). This is combined with lower pre-synaptic dopamine levels and a lower dopamine release at rest, which has been found in substance use disorders as well and could be a downregulation in response to repeated dopamine release (Trifilieff et al., 2017).

Of the studies investigating reinforcement learning, only one finds a difference in behavior. In this study, individuals who binge eat display more model-free learning, meaning that they rely more on previous prediction errors (i.e., previous rewards) to make decisions (Voon et al., 2015). This is in line with the acquired preparedness model which hypothesizes that individuals develop BE because they show a stronger response to learning events during which BE is rewarding (Combs et al., 2010). However, the other studies report no behavioral differences, but find changes in brain activity in the ACC, dlPFC, and striatum. This contrast could imply that there are behavioral differences but that the tasks in the studies could not detect them. This could be the result of a lack of specificity for BE as the tasks focus on more general reinforcement learning processes with money as the reward. Future studies should therefore consider using tasks that are more adapted to BE. This could be done by using food as a reward and by investigating reward learning in more specific contexts such as during moments of stress. However, as the studies in this review suggest that different types of food are processed differently, special attention should be given to the food that is offered as a reward.

Only a small number of studies included more than one eating disorder subtype with BE and an even smaller number actually

compared these different subtypes. These show that there are similarities such as a higher OFC volume, a lower functional connectivity of the ACC in the salience network, and a higher activity of the ACC during the anticipation of high-energy-density food. They also show that there are differences, such as patients with BN having an even greater OFC volume and activation of the ACC during the anticipation of high-energy-density food compared to patients with BED. Future studies should consider comparing subgroups more to further unravel the extent of their similarities and dissimilarities.

#### 4.1 | Limitations

This systematic review has several limitations. First, the studies in this review have used widely different designs which have made it unfeasible to perform a meta-analysis. Some designs have only been used by a small number of studies, making it difficult to make conclusions about certain aspects of reward processing (e.g., reward valuation or reward satiation). Researchers should consider focusing on these aspects in future studies. Second, only a minority of studies have reported and evaluated the impact of factors such as comorbidities, race, ethnicity, socioeconomic status, and sex on their results. Furthermore, most of the studies reporting race or ethnicity show a lack of diversity. As studies have shown these factors are important in disordered eating behaviors, future research should evaluate their impact on results (Rodgers et al., 2018). Third, only half of the studies that included patients with BED had a control group with overweight or obesity. Including no overweight control group makes it difficult to know whether differences in patients with BED are due to the presence of BE behavior or differences in weight. Future studies looking at patients with BED should therefore aim to include a weight-matched control group. Fourth, as this systematic review wants to discuss the role of the reward system in BE, only studies specifically investigating the reward system are included. However, during our search, we have found that 13 studies have used similar designs to the ones included in this review but without the reward system in mind. Of these, three (23%) have investigated inhibitory or self-control, three (23%) have focused on attention, three (23%) have studied self-referential processing, and three (23%) have not reported any behavioral constructs of interest. When it comes to PET, there are three studies that investigate serotonin transporter availability with one of them also looking at dopamine transporter availability (Galusca et al., 2014; Kuikka et al., 2001; Tauscher et al., 2001). There are three studies that look at GMV or the cerebral surface of patients with BN (Berner et al., 2018; Marsh et al., 2015; Oliva et al., 2021). There are another four studies looking at resting-state functional connectivity (Domakonda et al., 2019; Lavagnino et al., 2014; Lee et al., 2014; Spalatro et al., 2019). Another three studies that showed images of food (Joos et al., 2011; Uher et al., 2004; Van den Eynde et al., 2013). The fact that these studies use the same design to study different mental processes is problematic for the interpretation of their

results and shows that studies need to use a design that is specific for reward processing in BE.

## 5 | CONCLUSION

The studies in this review show that there are structural and functional differences in the neurobiological reward system in BE. In some cases, this could be linked to differences in reward processing such as a higher sensitivity to food rewards, more model-free learning, and more habitual behavior. However, the implication of a number of results for reward processing needs to be explored further. Future studies should use reward-related measures that are specific to BE, include more than one participant group with BE, and investigate the impact of factors such as illness duration, race, and sex.

## AUTHOR CONTRIBUTIONS

**Nicolas Leenaerts:** Conceptualization; investigation; methodology; visualization. **Daniëlle Jongen:** Conceptualization; investigation; methodology. **Jenny Ceccarini:** Conceptualization. **Lukas van Oudenhove:** Conceptualization. **Elske Vrieze:** Conceptualization; supervision.

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## CONFLICT OF INTEREST

The authors have no conflict to declare.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author.

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#### SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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