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Interoception and disordered eating: a systematic review

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1. Introduction

A recent consensus statement defined interoception as "the process by which the nervous system senses, interprets, and integrates signals originating from within the body, providing a moment-by-moment mapping of the body's internal landscape across conscious and unconscious levels" (Khalsa et al. 2018). Traditionally, interoception was considered to relate to signals with internal origin (e.g. visceral signals, heartbeat, breathing rate) but more recent conceptualizations of interoception include representations of the skin and body temperature, pain, itch and sensual touch (Craig 2002; Ceunen et al., 2016). Interoception is important for the maintenance of stable internal states and for motivating behaviour and guiding decision making. For example, sensing of a depleted nutritional state of the body guides food seeking behaviours and consumption (for a recent review Maniscalco & Rinaman, 2018).

Dysfunctional interoceptive processing has been implicated in a number of mental health disorders including anxiety, panic disorder, depression and eating disorders (Ehlers & Breuer, 1996; Khalsa et al., 2018; Pollatos, Traut-Mattausch & Schandry, 2009; Simmons & Deville, 2017). Impaired interoception has long been considered to be a key feature of eating disorders (Silverstone & Russell, 1967). Bruch (1962) documented a disturbance in the perception of stimuli arising in the body of patients with anorexia that was subsequently labelled as a deficit in interoception (Garfinkel et al., 1978). Research into interoception and disordered eating has since employed a range of physiological, behavioural and imaging methods to assess the ability to detect and utilise cues from bodily systems to direct behaviour.

The widely-used Eating Disorders Inventory is a questionnaire designed to assess common traits of anorexia and bulimia (Garner, Olmstead & Polivy, 1983) and it includes 'interoceptive awareness' as a factor. Using this questionnaire, interoceptive impairments

have been noted in patients with anorexia and bulimia (Klabunde et al., 2013; Pollatos et al., 2008) and in subclinical populations with disordered eating behaviour (Brown et al., 2010; Koch & Pollatos 2014; Young et al., 2017). Another method to measure interoception that has been used to study participants with disordered eating is heartbeat counting (e.g. Eshkevari et al., 2014; Fischer et al., 2016). Sensitivity to painful stimuli has also been used to measure interoceptive sensitivity in eating disorders (e.g. Raymond et al., 1999a,b; Schmahl et al. 2010; Strigo et al., 2013). In addition, neuroimaging has been used to measure neural activity in interoception-related areas of the brain during performance of tasks that require monitoring the state of the body (e.g. Kerr et al., 2016; Strigo et al., 2013). The brain area most commonly associated with interoception is the insula (Critchley, Wiens, Rotshtein, Ohman & Dolan, 2004; Schulz, 2016; Stephan et al., 2003) and functional neuroimaging studies have identified differences in neural responses in the insula in healthy controls and individuals with eating disorders (Holsen et al., 2012; Wierenga et al., 2015,2017). Additional brain regions that have been associated with interoceptive dysfunction in disordered eating are the anterior cingulate cortex (Wierenga et al., 2015, 2017), and the somatosensory cortex (Lavagnino et al., 2014).

A search for existing reviews relevant to the role of interoception in eating disorders identified a recent narrative review (Simmons & DeVille, 2017) and two systematic reviews that assessed 1) the link between interoception and eating disorders using a questionnaire measure focused on the perception of hunger and satiety signals (Jenkinson, Taylor & Laws, 2018) and 2) the specific link between interoception and bulimia nervosa (Klabunde, Collado & Bohon, 2017). The results of these reviews provide evidence that interoceptive dysfunction is present in eating disorders but to date there has been no systematic review of the association between different types of eating disorders/disordered eating and interoception. This is significant because evidence that impairments in interoception occur across different

types of eating disorder and are observable in sub-clinical populations at risk for the development of eating disorders would suggest that interoception constitutes a transdiagnostic feature of eating disorders (Fairburn, Cooper, & Shafran, 2003). In addition, there has been no systematic examination of interoception in disordered eating according to the modality of the signal (type of sensory channel involved). Establishing whether interoceptive disturbances in people with disordered eating is specific to visceral signals relating to the processing of food or whether there are deficits in interoception regardless of the origin of the signals has implications for understanding the nature of the interoceptive deficits in disordered eating. Finally, there has been no evaluation of the evidence for a specific role of interoception in the development and/or maintenance of disordered eating. Poor interoception could be a factor that predisposes an individual to develop eating disorder symptoms but might also be related to conditions that are co-morbid with eating disorders, such as anxiety and depression. Interoceptive problems may also be a consequence of prolonged exposure to a starved or disordered eating state. Evidence that interoceptive deficits are present in individuals who go on to develop an eating disorder, and in individuals recovered from current eating disorder symptoms or their relatives would suggest that poor interoception constitutes a potential endophenotype.

Here, we present the results of the first systematic review of studies that have investigated interoceptive functioning across the spectrum of disordered eating behaviour, ranging from diagnosed anorexia and bulimia nervosa, to subclinical disordered eating behaviours such as emotional eating. We aim to synthesize evidence from studies that used a range of methods to assess interoception related to visceral signals and to signals related to pain, itch, temperature and sensual touch. To provide insight into the possible role of poor interoception as a predisposing factor in the development of eating disorders we also assess potential associations between interoception and disordered eating in longitudinal studies and in the

relatives of affected individuals. We also aim to assess the current evidence on potential moderators and mediators of the relationship between disordered eating and interoception. Hence, our aim is to answer four questions: 1) Is dysfunctional interoception present across the spectrum of disordered eating from subclinical to clinical and across eating disorder subtypes? 2) Is dysfunctional interoception associated with disordered eating present across interoceptive modalities? 3) What is the role of interoception in the onset versus maintenance of disordered eating? 4) Have moderators/mediators of the relationship between disordered eating and interoception been identified? Our evaluation of the current state of this research provides a guiding framework for future studies on the role of interoception in the development and maintenance of disordered eating.

2. Methods

2.1. Literature Search

A search for original research articles was performed in September 2018 by a single investigator. Databases used in the search were Web of Science (collection), PubMed Central (all databases) and Ovid databases. A full list of search terms used can be found in the supplementary material. The search included only papers written in English and using human participants. The Preferred Reporting items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart was used to guide the search for articles. Results were supplemented by searching reference lists of related articles and reviews.

2.2. Study selection

All original, peer reviewed research articles (e.g. no reviews/meta-analyses) assessing interoception/interoceptive processes in relation to disordered eating behaviour were included. The inclusive definition of interoception used here was based on the sensations

suggested by Craig (2002) and therefore, studies assessing sensations of hunger, fullness, heartbeat, pain, itch, temperature and sensual touch were included. Studies of taste processing were excluded because taste is classically considered an exteroceptive sense that relates to sensing of the environment rather than the internal milieu. In addition, many studies of taste processing in disordered eating have focussed on hedonic/reward related responses rather than taste sensation/perception. For fMRI studies, articles that reported neural activation as an outcome measure were included, provided the neural activation occurred during the performance of an interoception-related task or in relation to changes in interoceptive state. Studies assessing interoception in individuals recovered from eating disorders and their relatives were included. There was no exclusion based on the age of the study participants and the selected studies included children, adolescents and/or adults. Articles assessing the mediating effect of interoception on treatment outcome were also included. The Preferred Reporting items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart was used to guide the selection of articles.

2.3. Data Extraction

Data extraction was performed using standardized forms created for the review and each article was evaluated by two reviewers. The second reviewer (SH) confirmed the first reviewer's (EM) data extraction for completeness and accuracy The information extracted from each study was sample size; age and gender; eating disorder/disordered eating type; comorbidities; exclusion criteria; measure of interoception; measure of disordered eating; covariates/control measures; findings on differences in interoception between disordered eating groups. The quality of each study was assessed by two reviewers using a tailored quality assessment tool (Kmet, Cook & Lee, 2004). Items in the tool included assessment of the validity of the measurement methods, sample size and control for confounders. Reporting on the methodological aspects of the studies rather than relying on a numerical score for

quality is considered more appropriate for systematic reviews and meta-analyses (Jüni, Witschi, Bloch, & Egger, 1999). Therefore, we rated individual components of the checklist (criteria met, criteria not met, not reported) and provided an overall rating for the quality of the study (low, moderate or high). The second reviewer (EM) confirmed the first reviewer's (SH) quality assessment.

3. Results

3.1 Inclusion of Articles

Figure 1 shows the PRISMA flowchart used to guide selection of articles. Searches using the keywords (see Appendix A) generated 7316 results. 527 of these were from Web of Science, 1936 were from Ovid databases, and 4853 were from PubMed Central. After the removal of duplicates, initial screening based on relevance of the paper title and abstract to the research question was conducted. Following this step, and the removal of papers that were not original research articles or articles that were not written in English (4), 114 full-text articles remained to be assessed for eligibility for inclusion in the review. Further screening, based on full-text articles led to the exclusion of 19 articles that were not relevant to the research question. Three articles reported results from the same longitudinal cohort (Leon et al. 1993; Leon et al. 1995; Leon et al. 1999) and so only the article reporting on the full longitudinal data set was included in the qualitative synthesis (Leon et al. 199). Five further papers were found through a search of reference lists of related articles. This left 100 research articles for consideration. Two articles presented two studies relevant to the association between disordered eating and interoception (Maïano et al., 2016; Young et al., 2017) and one article presented three relevant studies (Lattimore et al., 2017). Therefore, the final number of studies included was 104.

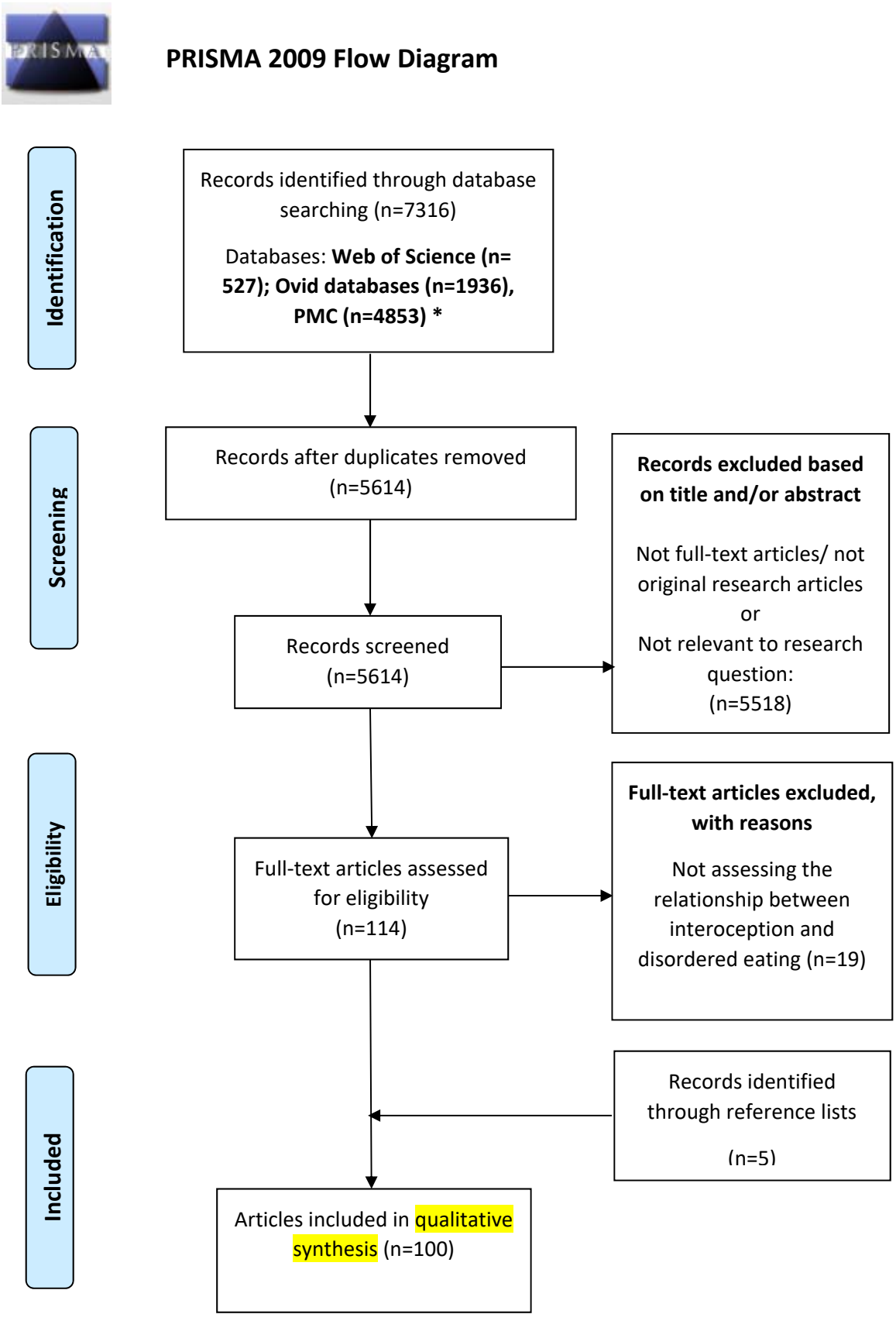


Figure 1. PRISMA flow diagram, showing process of article search and selection
*Number of records accurate for search conducted 26/09/2018

3.2 Characteristics of included articles

Across the 104 studies included, the total number of participants was 32883 with a minimum number of eight participants (Matsumo et al., 2006) and a maximum number of 5139 participants (Kim, Annunziato & Olatunji, 2018). The majority of studies (n =77, 74%) recruited women participants only. The remaining studies comprised 26 studies that included both men and women, and one study that recruited men only (Ussery & Prentice-Dunn, 1992). Of the 26 studies that recruited both men and women, the percentage of women participants ranged from 50-93%. The majority of studies (n = 93) recruited adult participants (mean age of participants = > 18). Ages of the participants across all samples ranged from 9 years (Koch & Pollatos, 2014) to 60 years (Fassino et al., 2004). Publication dates of the articles ranged from 1974 (Garfinkel et al., 1974) to 2018 (e.g. Berner et al., 2018; Romano et al., 2018). The majority of studies used a cross-sectional design (n=78), nine used longitudinal observational designs, seven used quasi-experimental pretest-posttest designs (one of which only ran a cross-sectional comparison of interoception), seven used an experimental design, and two used a cross-sectional family-based design.

The majority of the studies assessed interoception using questionnaire measures (n = 66). Other methods employed were heartbeat perception tasks (n = 9), pain detection and threshold paradigms (n = 15), and neuroimaging, with tasks and conditions including comparisons of hungry/full, pain perception, and trials consisting of focussing on internal sensations (n = 11). One study used a drug to elicit interoceptive state changes, one compared the sensation of gastric fullness with gastric volume, and one compared pre- and post-meal aversion to glucose.

Thirty-one studies in this systematic review presented data relevant to the association between anorexia nervosa and interoception; 17 studies presented data relevant to the association between bulimia nervosa and interoception; 6 studies measured interoception in participants with clinical binge eating disorder; 26 studies collected data from participants with anorexia and participants with bulimia as part of a mixed 'eating disorder group' and 24 studies presented data relevant to the association between subclinical disordered eating behaviours and interoception.

To answer the questions posed by this review, in the following sections we first present data according to the type of eating disorder/disordered eating focusing on cross sectional studies that do not speak to the issue of whether dysfunctional interoception is a cause or consequence of disordered eating. Where relevant, these studies are organised according to whether the recruited participants had active or remitted illness. Neuroimaging studies are presented separately from studies using other methods. We then stratify the data according to the interoceptive modality studied (gastric, cardiac, pain, touch and other modalities) and finally we present the data from studies relevant to the potential role of interoception in onset versus maintenance of disordered eating. We found no studies that formally analysed potential moderators or mediators of the relationship between disordered eating and interoception. A summary of the studies included in this review are included in Table 1. A summary of the data from the cross sectional studies is presented in Figure 2.

3.3. Interoception in Anorexia Nervosa

3.3.1 Active Illness

Twelve cross sectional studies included in this systematic review presented data relevant to an association between active anorexia nervosa and interoception using measures other than neuroimaging. Of the 12 studies assessing interoception in active anorexia, 2 studied

participants with restricting-type only (Ambrosecchia et al., 2017; Goldzak-Kunik et al., 2011) 7 studied a combination of restricting and purging-type (e.g. Aguera et al., 2015; Amianto et al., 2017) and 3 did not specify the subtype (Brytek-Matera & Schiltz, 2009; Garfinkel et al., 1979; Maïano et al., 2016).

In 11 out of the 12 studies impairments were reported on at least one measure of interoception. The methods used to assess interoception in these studies included self-report (n = 5), heartbeat counting (n = 1), pain perception (n =1), aversion to glucose following satiety (n = 1), comparisons of gastric volume to self-reported fullness (n = 1), changes in gastric sensations over an eating period (n = 1) and drug-induced changes in interoceptive state (n = 1). One study (Ambrosecchia et al., 2017) found mixed results: participants with AN did not differ from controls in heartbeat perception but on self-reported measures they had poorer interoception. One study (Goldzak-Kunik, 2011) found no impairment in interoception in anorexia, and this study used a cold pain paradigm to assess interoception.

3.1.2. Recovered/remitted

Four cross sectional studies reported data relevant to the association between interoception and anorexia nervosa in a sample of participants recovered from anorexia (using measures other than neuroimaging). The methods employed in these studies were self-report (Casper et al., 1990; Srinivasagam et al., 1995), heartbeat counting (Pollatos et al., 2008) and pain perception (Krieg et al., 1993). Three of these studies found significant impairments in interoceptive processing in participants recovered/remitted from anorexia (Casper et al., 1990; Pollatos et al., 2008; Srinivasagam et al., 1995). The study that found no difference (Krieg et al., 1993) used a thermal pain paradigm to assess interoception, and showed that participants with intermediate outcome from anorexia, good outcome, restrained eaters and unrestrained eaters did not differ in pain threshold.

3.1.3 Neuroimaging of active illness

Three cross-sectional studies used brain imaging and heat pain thresholds to assess interoceptive processing in participants with active anorexia (Bär et al., 2013; 2014; Holsen et al. (2012). One of these studies (Holsen et al. 2012) included both a recovered and remitted group of patients with AN. Bär et al., (2013) found that in participants with anorexia, thermal pain evoked an increased activation in the left posterior insula compared with healthy controls. Bär et al. (2014) reported a positive correlation between pain threshold and dorsal posterior cingulate cortex (PCC) activation in participants with anorexia, but there was no correlation between pain threshold and PCC activation in healthy controls. Holsen et al. (2012) examined that effect of a meal on appetite ratings and found a negative correlation between right insula activation and hunger ratings in individuals with anorexia, whereas a positive correlation was observed in the control group.

3.1.4 Neuroimaging of recovered/remitted anorexia

Eight cross-sectional studies used brain imaging to assess interoceptive processing in participants recovered/remitted from anorexia. All measured various interoception processes, and reported differences in neural activation in relation to the task or manipulation in individuals remitted/recovered from anorexia. The most common measure of interoception was an indirect approach; the manipulation of internal state by food intake. Holsen et al (2012) found a greater activation in healthy controls when hungry versus full in the hypothalamus, amygdala and insula when viewing high caloric food pictures. Moreover while performing a delay discounting task, hunger increased neural activation in reward areas, whereas satiety evoked a greater response in cognitive control networks in healthy

women. In addition, cerebral blood flow (CBF) measures showed an effect of nutritional state in striatum, anterior cingulate cortex (ACC), and left posterior insula, which was reduced in remitted patients when hungry. The other studies showed an altered insula response in remitted anorexia patients in relation to visceral and cardio interception (Kerr et al 2016 & 2017), touch (Bischoff et al 2018), pain (Strigo et al 2013), and aversive breathing load (Berner et al 2018). However, activation in other limbic areas also appeared to be dysfunctional in anorexia (Kerr et al. 2017, Berner et al. 2018, Strigo et al 2013).

3.2 Interoception in Bulimia Nervosa

3.2.1. Active Illness

Ten cross sectional studies (e.g. Heilburn & Worobow, 1991; Pollatos & Georgiou, 2016) presented data relevant to interoceptive processing in participants with active bulimia nervosa. Seven studies found significant impairments in at least one measure of interoception. The methods used included measurement of pain detection and threshold (n = 4) and self-report (n = 3). One study (Faris et al., 1992) found mixed results: participants with BN had higher mechanical pain threshold than did healthy controls in pain perception, but there were no difference in tactile threshold perception. Three studies showed no impairment in interoception in participants with bulimia, of which two used self-report methods (Heilburn & Worobow, 1991; Schmahl et al., 2010) and one used heartbeat perception (Pollatos & Georgiou, 2016).

3.2.2. Recovered/Remitted

Three studies reported recruiting participants remitted/recovered from bulimia (Kaye et al., 1998; Klabunde et al., 2013; Stein et al., 2003) and all three of these studies reported significant impairments in interoception in participants recovered from bulimia. The methods

employed in these studies were heartbeat counting (n = 1), thermal and ischemic pain perception (n = 1) and self-report (n = 1).

3.2.3. Neuroimaging of active illness

One study (Lavagnino et al., 2014) used resting-state fMRI to assess interoceptive processing in participants with active bulimia nervosa and correlated BOLD activity with self-report measures of interoception. Significantly weaker functional connectivity in interoception-related areas was found in bulimia nervosa, and a significant negative correlation between interoceptive dysfunction and functional connectivity was reported.

3.2.4. Neuroimaging of recovered/remitted

No studies in this systematic review assessed neural correlates of interoceptive processing in participants recovered from bulimia nervosa.

3.3. Interoception in Binge Eating Disorder

The results of four cross sectional studies on patients with active illness are reported here. No studies in this systematic review measured interoception in participants recovered from binge eating disorder and there were no studies using neuroimaging.

3.3.1. Active Illness

All four cross sectional studies assessing interoception in binge eating disorder recruited participants with active binge eating disorder and found significant impairments in interoception. Three of these studies (Aloi et al., 2017; Ramaciotti et al., 2008; Vinai et al., 2015) used self-report measures and one measured mechanical pain threshold (Raymond et al., 1995).

3.4. Interoception in Mixed Diagnosis Groups

There were twenty-four cross sectional studies. The majority of these studies collected data from groups including participants with both anorexia and bulimia (e.g. Ciccolo et al., 2002; Halmi & Sunday, 1991), with the exception of Rossiter, Wilson & Goldstein (1989) and Laessle et al. (1989) who included participants with bulimia and 'restrained' participants. In studies with participants with bulimia and participants with anorexia, 8 studies also reported on additional eating disorder groups including binge eating disorder or eating disorder not otherwise specified (EDNOS) (Eshkevari et al., 2014; Fassino et al., 2004; Kim, Annunziato & Olatunji, 2018; Nevonen et al., 2006; Nyman-Carlsson et al., 2014; Preyde et al., 2016; Solmi et al., 2018; Van Dyck et al., 2016). There were no studies in participants recovered from eating disorders and no neuroimaging studies.

Overall, of the 24 cross sectional studies reporting data relevant to the association between a mixed eating disorder sample and interoception, 22 showed impairments in at least one measure of interoception. The methods employed in these studies included self-report (n = 18), pain perception (n = 3) and reporting of gastric sensations across eating episodes (n = 1). One study assessed differences in acceptance and clarity of interoceptive processing in eating disorders (Merwin et al., 2010) and found mixed results, with neither the acceptance nor clarity interoception subscales predicting bulimia and only 'lack of clarity' predicting restraint. One study (Eskevari et al., 2014) found no difference in interoceptive processing in an eating disorder sample using a heartbeat detection paradigm, however 83% of participants were 'poor' detectors of heartbeat, which may explain the null results.

3.5 Interoception in Subclinical Disordered Eating Behaviours/non-clinical samples

Twenty studies were cross sectional and none used neuroimaging techniques. The range of disordered eating behaviours in studies included in the current systematic review were emotional eating (e.g. Koch & Pollatos, 2014; Young et al., 2017), external eating (e.g. Koch & Pollatos, 2014), subclinical binge eating (e.g. Brown et al., 2010), restraint (e.g. Tylka & Wilcox, 2006) and mixed/composite measures from questionnaires (e.g. Anderson et al., 2016; Myers & Crowther, 2008).

All of the twenty cross sectional studies reporting data relevant to the association between disordered eating behaviour and interoception, found impairments in at least one measure of interoception. The majority of these studies (n = 18) used self-report methods and the two remaining studies used heartbeat counting and detection tasks. One study found results which were somewhat mixed: once anxiety and depression were controlled for, a significant relationship remained for only two measurements out of four: confidence in heartbeat counting, and the relationship between heartbeat perception and self-reported interoceptive impairments (Young et al. 2017, Study 1).

3.6 Interoceptive Modalities

A range of interoceptive modalities were investigated in the studies included in this systematic review including cardiac, respiratory, gastric, pain and touch interoception. The most commonly measured interoceptive modalities were gastric, cardiac and pain, with measurements of these modalities comprising 101 out of the 104 studies.

3.6.1. Gastric Interoception

Gastric interoception was the most common modality measured in studies assessing interoception in disordered eating. Seventy-four studies included in the systematic review measured gastric interoception, 19 of these studied gastric interoception in anorexia, 7 in

bulimia, 4 in binge eating disorder, 20 in mixed eating disorder groups and 24 in subclinical disordered eating. Of these studies, 72 found significant differences in gastric interoception associated with disordered eating. The most commonly used methods to measure gastric interoception (n=68) were self-report questionnaire measures. These included the Interoceptive Awareness subscale of the Eating Disorders Inventory (Garner, Olmstead & Polivy, 1983) and the Intuitive Eating Scale (Tylka 2006). One study compared gastric volume with self-reported hunger and fullness and found at each given stomach volume (Bluemel et al., 2017). Participants with anorexia reported higher fullness and lower hunger than control participants, however participants with anorexia had a slower gastric emptying rate, which may account for this difference. Five studies used neuroimaging methods and that dysfunctional gastric interoceptive processing was associated with disordered eating. Two studies (De Caro & Di Blasm 2016; Heilburn & Worobow, 1991) did not find that gastric interoception was associated with disordered eating.

3.6.2. Cardiac Interoception

Twelve studies measured detection of cardiac interoceptive signals. Six of these studies assessed cardiac interoception in participants with AN, 2 in participants with BN, 1 in a mixed eating disorder sample, and 3 in subclinical/ disordered eating behaviour. The most common method used to measure cardiac interoceptive signals was heartbeat detection which was used in 9 studies with significant impairments found in 7 studies. Of the two studies that did not show a significant association between cardiac interoception and disordered eating, one used a straightforward heartbeat counting paradigm (Ambrosecchia et al., 2017) and one used a heartbeat-detection paradigm, which required participants to discriminate their heartbeat from an auditory tone (Eshkevari et al., 2014). Eshkevari et al. (2014) reported that

83% of their participants were poor at detecting their heartbeat, which may explain this null result.

Two studies (Kerr et al., 2106; Kerr et al., 2017) used fMRI to assess interoceptive processing of cardiac signals and both found differences in neural processing of interoception in patients recovered from AN and healthy controls One study (Khalsa et al., 2015) used infusions of isoproterenol (a non-selective β adrenoceptor agonist) to elicit changes in cardiac activity and found that participants with anorexia reported increased cardiac sensations under low arousal states.

3.6.3. Pain Interoception

Seventeen studies measured pain-related responses. Seven of these studies measured pain interoception in participants with AN, five in BN, one in binge eating disorder, four in a mixed eating disorder sample and one in binge eating disorder. The majority of methods used to elicit pain were either temperature-based (utilising the application of either cold or hot stimuli to cause pain n = 11), or mechanical (utilising pressure to cause pain, n = 4). Two studies (Girdler et al., 1998; Stein et al., 2003) used submaximal effort tourniquet tests to measure ischemic pain. Fourteen out of the 17 studies found dysfunctional pain processing in participants with disordered eating.

Methods of quantifying pain included both the measurement of pain threshold (e.g. time taken for a stimulus to first cause a painful sensation) and the measurement of pain tolerance (e.g. time taken for a participant to withdraw from a painful stimulus). Three studies combined pain measurement with neuroimaging measures (Strigo et al., 2013; Bär et al., 2013; Bär et al., 2015) and all three of these studies found dysfunctional pain processing associated with disordered eating. Three studies that assessed pain threshold and tolerance

did not find a difference in pain in disordered eating (Goldzak-Kunik et al., 2011; Krieg et al., 1993; Schmahl et al., 2010). In the study by Goldzak-Kunik et al., 2011, neither threshold nor tolerance was assessed, instead participants completed Visual Analogue Scales of cold, unpleasantness and pain during application of an ice pack, which may explain the null effects since application of an ice pack is a non-standard test. Both the studies by Schmahl et al. 2010 and Krieg et al. 1993 used a thermal pain stimulus which suggests that the type of pain stimulus used may be important.

3.6.4. Other Interoceptive Modalities

Two studies measured other interoceptive modalities using fMRI, and both were in participants recovered from anorexia. One measured respiratory interoception (Berner et al., 2018) and the other measured touch (Bischoff-Grethe et al., 2018) and found significant differences in interoceptive processing between participants recovered from anorexia and healthy controls. The study Khalsa and colleagues (2015) that involved infusions of isoproterenol showed that participants with anorexia reported increased breathing sensations under states of low arousal.

3.7 Onset/maintenance

We found only nine studies that used prospective designs. Of these studies, all but one reported an association between interoceptive awareness and disordered eating risk/scores. De Caro & Di Blas (2016) found no significant relationship between interoception and bulimic tendencies over a seven month period but the sample size was a small group of self-selected teenagers. Most studies recruited non-clinical population-based samples of teenagers and assessed the factors predicting eating disorder risk at a later time point (e.g. Leon et al. 1999). Three studies recruited from clinical samples and examined predictors of changes in

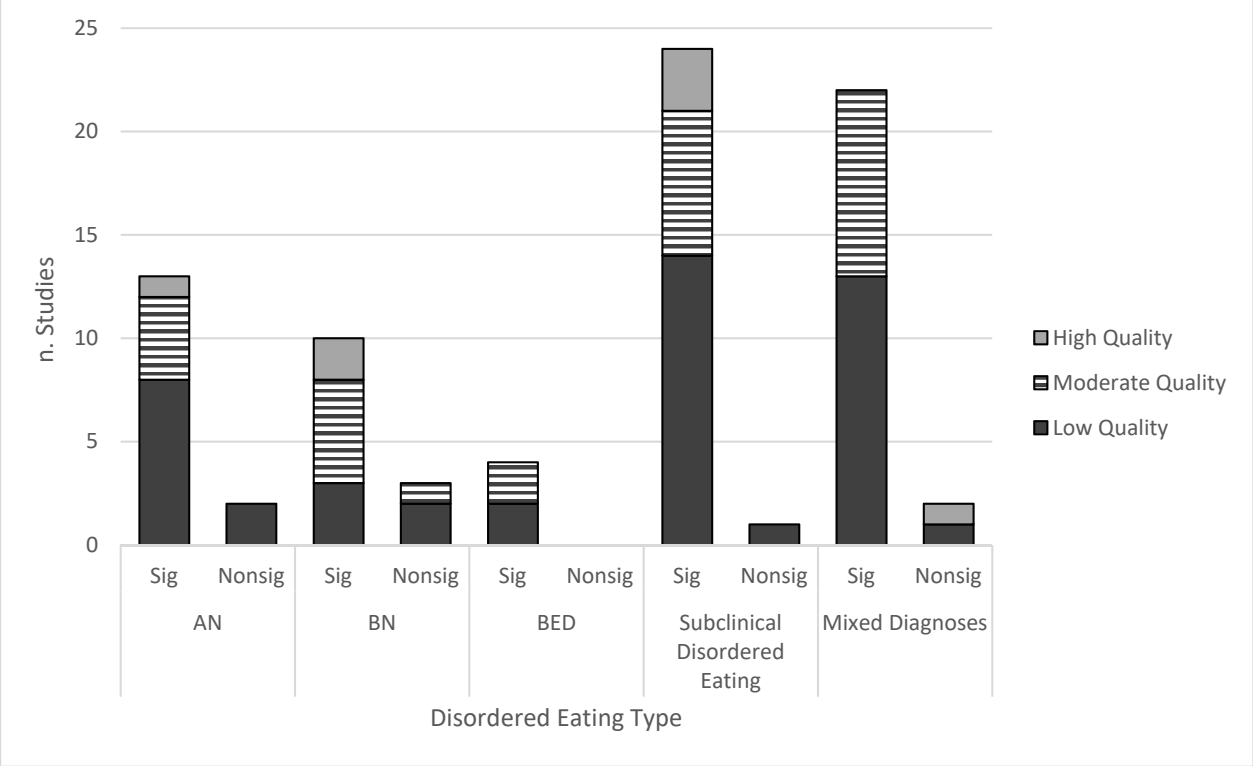
disordered eating over time (Amianto et al. 2017; Bär K-J et al. 2006; Bizuel et al. 2001). One study compared the baseline scores for girls asymptomatic at baseline who continued to be asymptomatic at follow-up with a group that developed partial syndrome (Kileen et al. 1996; average age at baseline 14.9 years). These authors reported that girls developing partial syndrome had higher scores on lack of interoceptive awareness at baseline. On the other hand, Koch and Pollatos (2014) reported that external and emotional eating in children with obesity, but not lean participants, predicted lack of interoceptive awareness at follow-up but not the other way round.

Two studies measured interoception in the relatives of individuals with disordered eating. These studies provide insight into whether disturbed interoception is a heritable feature that might predispose someone towards developing an eating disorder. One study assessed interoception in family members of women with bulimia (Lilenfield et al., 2000). This study found higher interoceptive impairments in first-degree relatives who had also experienced an eating disorder, but no significant difference between interoceptive impairments in never-ill relatives of bulimia patients and relatives of healthy controls. The second study that assessed interoception in family members recruited a sample of women recovered from anorexia and their relatives (Casper, 1990). There was no significant difference in interoceptive impairments between relatives of recovered patients and either recovered patients or healthy controls.

Seven studies in this systematic review used a quasi-experimental pretest-posttest design to assess changes in interoceptive processing over the course of therapy. Six studies reported improvements in interoceptive processing over the course of treatment. However, Fischer et al. (2016) found a cross-sectional influence of interoception on disordered eating (women

with AN scored higher than healthy controls at every time point on lack of interoceptive awareness), but there was no significant improvement in disordered eating over time in a small group of women with AN undergoing cognitive behaviour therapy.

Figure 2. Summary of evidence on the association between interoception and disordered eating behaviour. Bars represent the number of (non-imaging) studies presenting data relevant to disordered eating behaviour types showing significant differences (labelled Sig) or nonsignificant results (labelled Nonsig). Bars are split into number of low, moderate and high quality studies. AN Anorexia Nervosa, BN Bulimia Nervosa, BED Binge Eating Disorder.



3.8 Quality of included studies

Inter-rater agreement for quality assessment was good (kappa: 0.64, SE of kappa: 0.156, 95% CI: 0.34 to 0.947). Quality ratings varied significantly across studies. Most of the studies included were of either moderate (n = 44) or low (n = 48) quality. The remaining twelve studies were high quality (see Figure 2 for a summary). Small sample sizes and poor or no control for potential confounds were the main limitations. Most of the questionnaire studies

were not designed specifically to assess interoception but rather were validation studies of specific measures that happened to include a subscale relevant to interoception.

4. Discussion

To the best of our knowledge this is the first paper to systematically review the literature on interoception across the broad spectrum of disordered eating behaviours and interoceptive modalities. One hundred and four studies were included in the review and we find that all types of disordered eating behaviour are associated with impairments in interoceptive function across several modalities.

There was consistent evidence for a relationship between dysfunctional interoception and AN, with 92% of studies finding impaired interoceptive function in AN. Similarly, 93% of studies measuring interoception in a mixed group of eating disorders (e.g. AN, BN and BED/EDNOS) reported impairments in interoception relative to controls. Ninety-five percent of studies assessing a variety of disordered eating behaviours reported impaired interoception on at least one measure. The evidence to support the relationship between bulimia and interoceptive abilities was more mixed but still supportive of dysfunctional interoception associated with bulimia, with just over 80% of studies showing significant impairment in interoception. The strength of evidence is moderate because the majority of studies were limited by methodological issues, in particular the use of small sample sizes and poor control for confounds.

It is difficult to rule out that the association between interoceptive functioning and disordered eating is due to the confounding influence of comorbid psychiatric disorders such as anxiety and depression, which are known to influence interoceptive capabilities (Pollatos, Traut-Mattausch & Schandry, 2009) and are found in the majority of individuals with eating disorders (Kaye et al. 2004; Bulik, et al. (1997). Indeed, for many of the studies reviewed, the

eating disorder group had comorbid psychiatric disorders whereas the presence of psychiatric conditions was an exclusion criterion for the control groups. In studies that did control for potential confounds of comorbid disorders (Ambrosecchia et al., 2017; Lavagnino et al., 2014; Pollatos et al., 2008; Pollatos & Georgiou, 2016; Matsumo et al., 2006; Young et al., 2017), or that reported no significant differences in depression scores between participant groups (Strigo et al., 2013), the results were mixed. In some cases, where anxiety and depression were controlled for, no significant differences were found between disordered eating groups and controls (e.g. Ambrossechia et al., 2017; Young et al., 2017). However, in other studies (e.g. Pollatos et al., 2008) when controlling for anxiety and depression, the association between eating disorders and interoception remained significant, suggesting that the relationship between interoception and disordered eating is not fully accounted for by depression/anxiety. This conclusion is supported by the finding that depression was not a significant predictor of effect size in the meta-analysis conducted by Jenkinson and colleagues (2018). Future research might employ a propensity score matching approach by including additional control groups matched for levels of comorbidities. Alternatively, studying the relationship between interoception and disordered eating in non-clinical samples that have reduced prevalence of co-morbidities would also be informative.

4.1. Disordered eating/eating disorder types

In line with the findings from a recent meta-analysis of the data on self-reported interoceptive impairments in eating disorders using the Eating Disorder Inventory (Jenkinson, Taylor & Laws, 2018), we find that interoceptive impairments exist across the spectrum of disordered eating from subclinical populations with emotional eating and binge eating to individuals with clinically diagnosed eating disorders including anorexia (AN) and bulimia (AN) and

binge eating disorder (BED). The finding that interoceptive impairments occur in different types of eating disorders/disordered eating suggests interoception may constitute a transdiagnostic feature of eating disorders (Fairburn, Cooper, & Shafran, 2003).

The role of interoception in disordered eating could be investigated further by adopting a dimensional research framework, such as that advocated by the National Institute of Mental Health Research Domain Criteria (RDoC) initiative which argues for the study of fundamental components of behaviour (domains) using different units of analysis that link brain and behaviour (Insel et al. 2010). Studies of interoceptive processes in both clinical and subclinical populations using validated instruments that assess self-report, behaviour, physiology, neural circuits and genetics could provide novel insights into the nature of the relationship between interoception and disordered eating and identify potential biomarkers relevant to the diagnosis and treatment of eating disorders.

4.2. Interoceptive Modalities

To assess the specificity of interoceptive impairments in disordered eating, we stratified our findings by the interoceptive modality that was measured. The modality in which impairments were most consistently associated with disordered eating was gastric interoception, with 96% of studies measuring gastric interoception reporting impairments associated with disordered eating. This finding may be a result of the characteristics of disordered eating itself, as gastric interoception is strongly associated with eating. However, it is also important to note that gastric interoception was measured using self-report methods more often than any other modality. Hence, it is possible that the association between gastric interoception and disordered eating reflects a specific problem in conscious processing of interoceptive signals measured using self-report tools. In addition, it should also be noted that studies of gastric interoception may predominate due to a perception by researchers that interoception is most easily studied by assessing gastric function.

A number of studies assessed pain and cardiac interoception in disordered eating. In both of these modalities, just over 80% of studies reported aberrant processing associated with disordered eating, suggesting that these modalities are also affected. Although heartbeat counting tasks are commonly used to assess interoception due the ease of measurement it should be noted that there are methodological limitations to this approach (Brener and Ring, 2016). For example, knowledge of one's resting heart rate influences the accuracy on heat beat counting tasks (Murphy et al. 2018). In addition, only around a third of participants can accurately count their own heat beat at rest, which opens up the possibility that floor effects may explain some null findings (Khalsa & Lapidus 2016). In relation to pain processing, variability of the results might be explained by a lack of consistency of measures across studies e.g. the use of heat vs. cold stimuli.

The finding that impaired interoception is seen across different modalities could be explained by aberrant signalling within an afferent neural system that represents all aspects of interoception (Craig 2009). Indeed, for cardiac and gastric signalling there are partially overlapping cortical representations within the mid insula and so it is possible that aberrant insula activity and functional connectivity may contribute to interoceptive dysfunction across modalities in eating disorders. The extent to which interoception is served by a unitary system remains unclear at present, although most models emphasize the role of functionally coupled circuits rather than modular processing in specialised domain specific systems (e.g. Craig, 2009; Quattrocki and Friston, 2014). Further investigation of the neurobiological mechanisms that underpin interoceptive dysfunction in disordered eating could shed further light on this issue.

4.3. Onset/maintenance

Our review found evidence that impairments in interoception are present in individuals who have recovered from an eating disorder (e.g. Khalsa et al., 2015; Klabunde et al., 2013), which suggests that problems with interoception are not solely explained by features associated with an active illness, such as severe calorie restriction or binge-purge behaviours. These data imply that dysfunctional interoception might be a predisposing factor for the onset of disordered eating. This proposal is supported by data from prospective longitudinal studies indicating that problems with interoception predict changes in eating disorder risk (e.g. Leon et al. 1999). Although it should be noted that there is currently only a small number of population based studies that have assessed the role of interoception in illness onset.

The suggestion that problems with interoception might predispose an individual to develop an eating disorder is supported by data from studies that have linked dysfunctional interoception to specific genetic variants (Frieling et al., 2006). However, there are also reports that impaired interoception is reversed as a result of successful therapy (e.g. Matsumoto et al., 2006), which implies that at least some of the problems with interoception might be a complication of the eating disorder that resolves with treatment rather than constituting a predisposing factor. In fact, it is possible the problems with interoception that are observed in recovered patients might reflect an enduring change in interoception or a scarring effect of having experienced an eating disorder (e.g. Klabunde et al., 2013; Stein et al., 2003). Such an interpretation is supported by evidence, albeit currently limited, from family studies (Lilenfield et al., 2000; Casper 1990), which have found that family members of patients, without a history of eating disorders, do not show impairments in interoception. These data suggest that interoceptive dysfunction does not constitute a heritable trait or endophenotype that is observable in non-affected first degree relatives of people with eating disorders.

One interpretation that could explain the existing data is that dysfunctional interoception might predispose an individual towards the development of disordered eating but once disordered eating behaviour patterns become established, problems with interoception are accentuated. However, there is currently limited evidence on the causal role of interoception in the development of disordered eating. Prospective longitudinal studies that include a pre-morbid baseline assessment provide the most rigorous test of whether or not dysfunction in interoception plays a causal role in the development of disordered eating but these are costly and difficult to implement since very large sample sizes are required due to the relatively small number of individuals who go on to develop an eating disorder. An alternative is to use a high-risk design in which the incidence of a diagnosis at follow-up is increased by following individuals already deemed high-risk for future eating disorders (Stice & Desjardins, 2018).

4.5 Gaps in knowledge and directions for future research

This review has highlighted a lack of research on the moderators and mediators of the relationship between interoception and disordered eating. Not all individuals with dysfunction in interoceptive processing will develop disordered eating and so identifying potential moderators will be an important avenue for future research. For example, there may be personality factors such as impulsivity or obsessive–compulsive traits that interact with interoceptive dysfunction, and the presence or absence of these traits may determine the likelihood of interoceptive dysfunction leading to disordered eating.

Future research should also address the mechanisms mediating the relationship between interoception and disordered eating behaviours/eating disorders. Interoceptive states may influence eating behaviours via changes in the reward value of food. Information about the

state of the body is passed to areas of the brain involved in computing the incentive salience of a food so that its motivational value is increased when in a state of food deprivation and decreased in a replete state (Cabanac 1971). Dysfunction in interoceptive signalling might reduce the motivating effect of food deprivation on behaviour as has been observed in women who are in remission from AN (Wierenga et al. 2015). Furthermore, a failure to downregulate food reward with food consumption might promote overeating once eating has begun, which could facilitate binge like eating as has been observed in bulimia (Ely et al. 2017). Thus, future studies could examine the potential mediating role of reward responsiveness in the relationship between interoception and disordered eating. In addition, problems with interoceptive processes could result in bodily signals related to nutrient ingestion or nutrient deficits not being factored into more complex decision making processes that mediate food consumption and food choices (Higgs 2008). In this case, decisions are more likely to be influenced by other inputs e.g. external cues. Thus, overeating or undereating might occur depending on the predominant influences on the food-related decision making at any one time for an individual, which might be weight concerns, emotional concerns or hedonic goals. Such links between interoceptive capabilities and responses to different types of external cues have yet to be fully explored. Finally, problems with interoception might also promote disordered patterns of eating via dysfunctional body perception/evaluation which could lead to disordered eating through body dissatisfaction (Badoud, & Tsakiris, 2017).

There have also been fewer studies to date on the role of interoception in binge eating disorder than in AN and AN. BED was introduced as an eating disorder category in the Diagnostic and Statistical Manual of Disorders, Fifth Edition (DSM-5) in 2013 (APA, 2013). It is the most prevalent form of eating disorder and one of the primary chronic illnesses among adolescents (Nicholls and Barrett 2015). Hence further investigation of the role of interoception in in binge eating disorder is advised.

The current systematic review considered 'interoception' in general due to the broad focus of research to date, but a number of separate facets of interoceptive insight have been described (Khalsa et al. 2018). In order to further understand of the role of interoception in disordered eating it will be necessary delineate different aspects of interoception (Khalsa et al. 2018). Interoception encompasses functioning at many different levels including physical responses in the body, the neural representations of these responses and their perception, as well as insight and conscious awareness of these responses. Three psychological dimensions of interoception that relate to the perception of interoceptive responses have been distinguished: interoceptive accuracy, sensibility, and awareness (Garfinkel et al. 2015). Interoceptive accuracy refers to the process of detecting and counting internal bodily sensations and is measured using methods such as heartbeat counting. Interoceptive sensibility refers to self-evaluated interoceptive capability and is usually assessed by questionnaire measures. Interoceptive awareness refers to the correspondence between interoceptive accuracy and insight into one's own interoceptive performance and so represents a metacognitive aspect of interoception. An additional dimension of interoceptive awareness has been suggested recently which describes a person's ability to flexibly attend to, and utilize, interoceptive information or to adaptively switch between interoceptive and exteroceptive representations (Quadt et al. 2018).

At present it is unknown whether dysfunctional interoception associated with disordered eating is due to dysfunctional afferent signalling, central sensory processing of interoceptive stimuli or perception or insight into interoceptive performance. It is possible that there is no dysfunction in afferent interoceptive signalling (e.g. the presence and magnitude of signals is detected), but there may be dysfunction in signal monitoring (accuracy) and/or the tendency to focus on signals (sensibility). A small number of studies in this systematic review measured more than one dimension of interoception (e.g. Ambrosecchia et al., 2017; Young

et al., 2017), and some of these assessed the association between dimensions (e.g. Pollatos et al., 2008). Interestingly, some studies found impairment in one dimension of interoception (e.g. sensibility), but no impairment in another dimension (e.g. accuracy). For example Ambrossechia et al. (2017) found that participants self-reported poorer interoceptive sensibility, but had interoceptive accuracy that was comparable to healthy controls. Similarly, Pollatos et al. (2008) found no association between interoceptive awareness and sensitivity. However, it should be noted that these studies assessed interoceptive accuracy in the cardiac domain and sensibility using the Interoceptive subscale of the Eating Disorders Inventory (EDI) rather than assessing accuracy and sensibility within the same modality. In addition, while the EDI has been shown to discriminate between individuals with eating disorders and healthy controls, it is not a measure that was designed specifically to assess visceral interoceptive sensibility. Future systematic studies that assess interoception across a range of modalities and include measures of neural signalling, behavioural performance, and self-evaluated interoceptive capability, alongside metacognitive measures both within and between modalities, are required to uncover the specific nature of the interoceptive dysfunction associated with disordered eating.

The evidence reviewed here from studies that assessed neuronal activation using fMRI suggests that disordered eating is associated with dysfunction in the neural processing of interoception compared with individuals without disordered eating. The majority of the studies linked differences in neural responses in the insula to dysfunctional interoception. However, it should be noted that an issue with the fMRI methods used in a number of studies in this systematic review is the reliance on reverse inference, which is using specific patterns of activation to infer the engagement of specific mental processes e.g. inferring that activation of the insula is related to interoceptive processing because the insula has been previously implicated in such processes. The reliance of a study's conclusion on reverse

inference depends on the paradigm used (Poldrack, 2011). For example several studies (Wierenga et al 2015, 2017 and Holsen 2012) altered the fullness of the stomach and inferred that the differences in brain responses between a AN group and the control group was due to differences in interoception. However, interoception defined as accuracy in sensing the internal state of the body was not measured directly and so these studies rely on reverse inference. To address the issue of reverse inference, predictive modelling techniques (Varoquaux & Poldrack 2019) may be valuable to identify a neural signature for interoception that predicts interoceptive capability and hence could be used as a biomarker in future studies. In addition, the interpretation of the relationship of the reported neural activity to interoceptive abilities is not straightforward since reduced activity in the insula for example could represent more efficient processing of interoceptive signals or reduced inputs. Nevertheless, the fMRI data reviewed here suggest that neural signalling in the insula depends upon the specific context in which that activity is assessed (e.g. Berner et al., 2018; Bischoff-Grethe et al., 2018). In particular, there is evidence that patients recovered from AN show increased neural activation in insula in anticipation of interoceptive events but decreased activation during an aversive interoceptive event (e.g. Berner et al., 2018; Strigo et al., 2013). For example, during anticipation of pain, patients recovered from AN showed greater activation in right anterior insula than did healthy controls but showed significantly decreased posterior insula activation during pain processing (Strigo et al., 2013). This pattern of responses may indicate heightened interoceptive responses in anticipation of pain but poorer processing of interoceptive stimuli. However, other studies have reported an opposite pattern of results, whereby recovered AN patients had a reduced activation in right mid-insula in the anticipatory period but increased bilateral, anterior, mid-, posterior insula activation during and after an aversive breathing load task (Berner et al. 2018). One possibility is that some interoceptive problems in AN arise from a mismatch between predictions about how

the body should feel and the information coming from the body, which has been referred to as an interoceptive prediction error. Such prediction errors have also been hypothesized to account for aberrant interoceptive functioning in anxiety disorders (Paulus & Stein 2010) and are a core feature of predictive coding accounts of interoception (Barrett & Simmons 2013; Seth & Critchley 2013).

Predictive processing is a theoretical model of neural functioning (Friston, 2010) that has recently been applied to the study of interoception. Rather than assuming that interoceptive perceptions are linked directly to internal bodily sensations, predictive processing accounts suggest that perceptions arise from a comparison between representations of anticipated sensations and current interoceptive signals. Interoceptive perceptions are thought to mainly reflect the anticipated state of the body based on what is predicted given past experience, but, incoming sensory information about the actual state of the body provides a check on the accuracy of these prediction (Barrett & Simmons 2013; Seth & Critchley 2013). If a mismatch between actual and predicted states, or a prediction error, is detected then this error may be used to update the predictions, and possibly change perceptions, or trigger changes in the body that fulfil those predictions. This account is similar to that proposed by Higgs (2005) who has argued that feelings of satiety are cognitively constructed in the brain; a process that involves integrating current internal state cues with information in memory about recent eating to predict the effects of further consumption.

Within a predictive/constructive interoceptive framework, dysfunctional interoception could arise if the incoming sensory signals are noisy or unreliable (see Paulus, et al. 2019 for a recent review). In such circumstances, predictions (and perceptions) might be strongly influenced by external sources of information or beliefs that are not updated by prediction

error. For example, the perception of the body as it relates to food deprivation or repletion in patients with eating disorders might be influenced by beliefs that are not updated by incoming interoceptive signals. A similar situation might arise from a failure to integrate incoming sensory signals with anticipated states. Further research guided by the predictive/constructive framework is needed to test these hypotheses.

4.6 Strengths and limitations of the current systematic review

We conceptualised disordered eating as a continuum ranging from normal eating to eating disorders and considered studies using a range of interoceptive modalities which enabled a large number of studies to be systematically reviewed. However, there may be a language and a publication bias, as the search was limited to studies written and published in the English language. However, the number of non-English language studies identified was only four. The majority (77%) of studies in the current systematic review recruited women only. Therefore, the results should be applied to males with caution, particularly as one longitudinal study suggested that sex may moderate the relationship between interoception and disordered eating. This finding highlights the need for more research into interoception and disordered eating behaviour in males. In addition, many studies published in this area were not designed to explore an association between interoception and disordered eating. For example, most studies comparing self-rated interoceptive sensibility were designed as questionnaire validation studies, which resulted in suboptimal study designs and the potential for biased results. Finally, due to the heterogeneity of the studies, particularly with respect to the methodologies and outcomes used a meta-analysis was not considered feasible.

4.7. Clinical implications

If further research confirms that interoceptive dysfunction predisposes individuals to the development of eating disorders then assessment of interoception may be useful in identifying those at risk of developing eating disorders and hence could be valuable for prevention programmes. There is evidence that interoceptive function can change over time and be modified by treatment (see results from this review and that of Khalsa et al. 2018) and so interoceptive dysfunction could also be a useful focus for the treatment of eating disorders and other conditions with comorbid eating disturbances such as Attention Deficit Hyperactivity Disorder (ADHD) (Kaisari, Dourish and Higgs 2017, Kaisari, Dourish, Rotshtein and Higgs 2018) and depression (Simmons and Deville 2017). There are opportunities for treatments based on stimulating afferent interoceptive signalling e.g. vagus nerve stimulation (De Couck et al. 2017) or flotation therapies that reduce exteroceptive signals allowing enhanced exposure to interoceptive signals (Feinstein et al. 2018). Future work could also examine the potential for using drug therapies to target interoceptive dysfunction in patients with eating disorders. There is growing interest in the role of the hormone oxytocin in interoception (Betka et al. 2018; Quattrocki and Friston, 2014) and given that oxytocin has already been found to improve some of the symptoms of AN (e.g. Kim et al. 2014), future studies could examine whether intranasal administration of oxytocin improves interoception in disordered eating.

4.8. Conclusions

The majority of studies included in the current systematic review reported significant impairments in interoceptive processes associated with disordered eating behaviour and eating disorders. Impairments were observed across eating disorder types and interoceptive modalities suggesting that interoception may constitute a transdiagnostic feature of eating

disorders that is related to dysfunction in a common neural system which underpins the processing of different types of interoceptive signals. There is currently limited evidence on the potential causal role of interoception in the development of disordered eating and on the moderating and mediating mechanisms. Future research that examines specific dimensions of interoception in both clinical and subclinical populations at different levels of analysis may provide novel insights into the underlying dysfunction in interoception associated with disordered eating and which could potentially lead to the development of improved therapies for eating disorders.

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Competing Interests Statement

Author Colin T Dourish is an employee, Director and shareholder of P1vital Limited and a Director and shareholder of P1vital Products Limited. All other authors declare no competing interests.

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Appendix A

Supplementary figure 1. Search terms used in the current systematic review. Within each search term category (interoception or disordered eating: presented here in separate columns), separate search terms were separated with the Boolean operator 'OR'. The two search term categories were separated with the Boolean operator 'AND'.

Interoception search terms		Disordered Eating search terms
		eating disorder
		feeding disorder*
		EDNOS
		OSFED
		disordered eat*
		body dysmorph* disorder*
		eating behav*
interocept*		eating patholog*
interocept* awareness		eating psychopatholog*
interocept* detection		abnormal eating
interocept* sensitivity		binge*
interocep* process*		binging
interocep* deficit		binge-eating disorder
heartbeat detection		grazing
heartbeat counting		graze
detection of pain*		purging
perception of pain*		purge*
sensitivity to pain*		vomiting
pain threshold		chaotic eating
pain tolerance		bulimia

painful stimuli		bulimia nervosa
detection of temperature		bulimi* behav*
perception of temperature	**AND**	anorexia
sensitivity to temperature		anorexia nervosa
detection of sati*		restrictive eating
sensitivity to sati*		restrictive food intake
detection of hunger		selective eating
sensitivity to hunger		avoidant restrictive food intake disorder
detection of internal cues		ARFID
sensitivity to internal cues		Pica
reliance on internal cues		night eating
detection of internal state		NES
sensitivity to internal state		eating habit*
internal cues of satiation		eating pattern*
somatosensory awareness		eating attitude*
perception of bodily signals		eating problem*
bodily perception		loss of control
intuitive eating		lack of control
		overeat*
		over eat*
		excessive eat*
		hyperphagia
		compulsive eat*
		compulsive food intake
		excessive appetite

Table 1. Characteristics of included studies

Authors & Year	Sample Size	Gender / Average age (years)	Disordered eating type	Comorbidities	Exclusion criteria	Measure of interoception	Measure of disordered eating	Covariates	Results
Abbate-Daga et al. (2014)	AN:94 HC:59	Female AN:25y HC:25y	AN	BDI recorded	Male, IQ<85, active medical problems, history of head injury abuse HC: no psychotropic medication, Current/lifetime ED/any other Axis I	EDI-IA	Diagnosed with AN	None reported	AN scored higher than HC on lack of IA
Aguera et al. (2015)	AN: 118 HC: 143	Female AN 25y HC 25y	AN	None reported	Endocrine disorders, males, <18yrs controls: lifetime diagnosis of ED and BMI <18.5 >25.	EDI-IA	Diagnosed by psychiatrist	None reported	At baseline, both AN-R and AN-BP had higher lack of IA scores than HC.
Aloi et al. (2017) 58	Obese (no BED): 20 Subthreshold BED: 16 BED:22	62% female Obese: 51y Subthreshold BED:43y	BED Subthreshold BED	SubBED and BED scored higher on BDI than OB	Drug dependence history medical illness/ neurological	EDI-IA	Binge eating scale and clinical interview	None reported	BED scored higher than OB on lack of IA

		BED:44y			comorbidities, pharmacological treatment inducing cognitive impairment.				
Ambrosecchia et al. (2017)	24 AN-restrictive 25 HC	Female AN:23y HC:23y	AN-restrictive	None reported	Past/present cognitive disorders, psychiatric disorders, neurological and cardio-respiratory disorders, substance dependence medications altering cardio-respiratory activity.	EDI-IA Heartbeat perception counting (HBP)	Diagnosis made by psychiatrist EDI-3 EDEQ	ANCOVA correcting for Age, BMI, anxiety and depression	AN scored significantly higher in lack of IA, no significant differences between the two groups in HBP.
Amianto et al. (2016)	ED:158 HC:80	Female AN:25y BN:28y HC:23y	Mixed: AN:53 BN:71	No MDD or OCD	Severe mental retardation, psychosis, bipolar disorder, EDNOS.	EDI-IA	SCID diagnosis made by psychiatrist	ANCOVA correcting for age and BMI	BN scored higher than AN, AN scored higher than HC on lack of IA
Amianto et al. (2017)	AN: 59	Female Time 0: 30y Time 1: 37y	AN	None	Previous or current comorbidities Lifetime psychosis or other major	EDI-IA	Diagnosis made by psychiatrist EDI-2 BES	Age, age of onset and years of study	Lack of interoceptive awareness significantly reduced at follow up.

					psychiatric disease				
Anderson et al. (2015)	Non clinical: 125	64.6% women 19y	Non-clinical sample	N/A	None reported	IES	Eating disorder diagnostic scale (EDDS) Three-factor eating questionnaire (TFEQ) restraint subscale	Gender, Baseline hunger ratings	Negative correlation between IES total and TFEQ restraint. Negative correlation between all subscales of IES and EDDS. Unconditional permission to eat and Eating for physical reasons (IES) were significant, predictors of EDDS
Bär K-J et al. (2006)	AN: 15	Female 16-17y	AN	None reported	History of peripheral neuropathies, cardiac arrhythmia, substance abuse psychiatric disease	Heat pain - threshold	Psychiatric diagnosis	Resting skin temperature	AN had significantly elevated pain thresholds in acute state of disease, and after regaining weight, but not 6 months after regaining weight
Bär K-J et al.	AN: 19,	6 male, 32	AN	None of the	medical or	Warmth	Psychiatric	Regressions	Pain thresholds

(2013)	HC: 19	female (number of men matched across groups) AN: 23y HC: 24y		patients had a history of major depression or any further psychiatric disease.	neurological conditions	perception and thermal pain thresholds fMRI	diagnosis AN quantified by EDI-2, EAT	were performed with both BDI scores and BMI as variables of interest	were higher for AN than control Increased L insula activity in controls during pain. Increased activity in cerebellum and brainstem in AN.
Bär et al. (2014)	AN-Res:26 HC:26	AN: 3 male, 23 female (number of men matched across groups) AN-Res: 23y HC: 24y	AN-res	None reported	History of MDD or other psychiatric disease	Thermal pain and fMRI	Met DSM criteria for diagnosis	None reported	Higher pain threshold in AN-Res. Pain threshold positively correlated with dorsal PCC activity
Berner et al. (2018)	AN-Rec:20 HC:26	Female AN-Rec:27y HC:28y	AN-Rec	None reported	Alcohol or substance dependence in past 3m, lifetime bipolar or psychotic disorder, ADHD, use of psychotropic medication in past 3 months	Breathing load paradigm and fMRI	SCID-I		Reduced activation in right post mid-insula in anticipatory period but increased activation during and after aversive stimulus
Berntova & Svetlak (2017)	ED:73 HC:207	Female	Mixed	None reported	None reported	Body perception	Diagnosis according to ICD-10		ED groups had lower BPQ

		Average age of sample 22y				questionnaire	General Food Craving Questionnaire (G-FCQ-Trait) Revised Restraint Scale (RS)		autonomic nervous system reactivity scores than controls. No correlation between GFCQ and BPQ. Correlation between RS and both BPQ subscales
Bischoff-Grethe et al. (2018)	AN-rec: 18	Female 26y	AN-Rec	None reported	Current DSM-IV Axis I diagnosis, psychotropic medication 3 months before study, history of alcohol or drug abuse, 3 months before study, left-handed, MRI exclusions,	Soft touch with brush, cued with an arrow to record anticipatory responses as well as stimulation	Current/past psychiatric history assessed with MINI international neuropsychiatric interview.	None reported	Decreased activation in ventral mid insula during anticipation, but increased during soft touch in AN-rec versus HC
Bizuel et al. (2001)	AN-Rec: 13 AN-poor outcome:13	AN-Rec: 30y AN-poor outcome:32y	AN-Rec AN-poor outcome	None reported	Long term antidepressant medication	EDI-IA	AN diagnosis	Disease duration, BN subtype, Sex, age, BMI	Higher initial lack of IA scores associated with poor outcome at follow-up
Bluemel et al.	24 AN	AN: All	AN	None reported	<18y or >60y;	Comparison of	DSM-IV criteria	None	At each given

(2017)	20 HC	Female, 23y HC: 85% female, 24y OB: 69% female, 32y			medical conditions drug/alcohol abuse, abdominal surgery, medication altering gut function, MRI exclusions, pregnancy, lactation	gastric volume and self-reported hunger/ fullness	Inpatients	reported	gastric volume, AN reported higher fullness and lower hunger than controls
Brown et al. (2010)	Non-clinical: 90	Female 18-30y	Non-clinical sample	None reported	Pregnant/ planning to become pregnant	Interoceptive Awareness Questionnaire (IAQ-E)	Binge Eating Scale (BES) Weight efficacy lifestyle questionnaire Mizes anorectic cognitions scale	Baseline IAQ-E entered as covariate	Appetite awareness mediated the relationship between group assignment (intervention control) and post-treatment binge-eating symptoms and the relationship between group and weight-control self-efficacy.
Brytek-Matera (2009)	AN: 95	Female AN:18y/22y HC: 20y /21y	AN	None reported	None reported	EDI-IA	Diagnosed AN patients	None reported	AN groups scored higher on lack of IA than HC groups.

Camilleri et al. (2015)	Non clinical: 632 completed IES 521 completed TFEQ	Male:297 Female:335 53% women 49y	Non-clinical sample	None reported	Current dieting for medical reasons, pregnancy	IES	TFEQ-R21: Restraint, emotional eating, uncontrolled eating.	None reported	IES-2 total score was negatively related to restraint, emotional eating and uncontrolled eating
Carbonneau et al. (2016)	Non clinical 260	Women 30y	Non-clinical sample	None reported	Pregnancy	IES	EDI	None reported	IES score negatively correlated with EDI scores, including 'bulimia' score
Casper (1990)	AN-Rec:25 HC:23 Sisters of recovered: 15 Paired AN-Rec:15	AN-Rec: 25y HC:26y Sisters of recovered: 26y Paired AN-Rec:25y	AN-Rec	AN scored higher on BDI compared with controls	None reported	EDI-IA	Group allocation based on assessment of physical and psychological symptoms	None reported	Lack of IA significantly higher in AN-Rec than in healthy controls.
Ciccolo et al. (2002)	Mixed: 107	Female ED:55 HC:53	Mixed	None reported	None reported	EDI-IA	Met diagnostic criteria for ED	None reported	The lowest lack of IA was in HC, then lack of IA increased with EDI scores
Cuzzocrea et al. (2015)	28 moderate binging (MB) 53 without	MB: 15 male, 13 female NB: 32 male,	Non-clinical sample	None reported	Severe binging	EDI-IA	Binge Eating Scale (BES)	None reported	MB had higher lack of IA scores than NB

	binge (NB)	21 female Mean age 17y							
Dancyger & Garfinkel (1995)	Full symptom (FS): 30, Partial symptom (PS): 51, HC: 57	Female Average age 17y	Mixed AN BN	None reported	None reported	EDI-IA	Fulfilling DSMI-IV criteria. EAT	None reported	FS scored higher than PS and HC on lack of IA
De Caro & Di Blas (2016)	Non clinical: 142	Female:76 Male:66 Average age 16y	Non-clinical sample	None reported	16 < BMI > 30	EDI-IA	EDI		Bulimia score at T2 was not predicted by lack of IA at T1.
De Vries & Muele (2016)	BN:115, HC:341	Female BN:26y HC:26y	BN	None reported	BMI < 18.5 Males	EDI-IA	Diagnosis made based on Eating Disorder Diagnostic Scale (EDDS)	None reported	BN scored higher on lack of IA than HC
Denny et al. (2013)	Non clinical: 2287	45.2% male 54.9% female Average age 25y	Non-clinical sample	None reported	None reported	2 items taken from IES: ‘‘I trust my body to tell me how much to eat’’ and ‘‘I stop eating when I am full’’	Weight control behavior and Binge eating	Age, ethnicity, SES, BMI	Interoception associated with lower odds of disordered eating behaviours
Eshkevari et	HC:60	Female	Mixed	None	Male, left	Heartbeat	SCID-I and EDI-3	None	The difference

al. (2014)	ED:74	Age range 18-55y			handed. No history of head-brain injury drug/alcohol abuse, no learning disability, no medical illness, only fluent english speakers for HCs no history of having BMI < 17.5, no history of disordered eating, no current or prior diagnosis of a psychiatric disorder	detection.		reported	between the HC and ED groups on Heartbeat detection scores was non-significant.
Faris et al. (1992)	BN: 27 HC: 31	Female BN: 19-45y HC age matched	BN	None reported	Psychoactive medications or drug abuse during the preceding 6 months	Mechanical pain (pressure to finger tip) Tactile perception (nylon fibre touching)	DSM criteria.	None reported	Tactile thresholds did not differ between BN and HC Pain detection and tolerance were increased in BN
Fassino et al. (2004)	AN-Restricting 61 AN-BP 61	Female Age range 20-60y	AN-Restricting AN-BP BN	None reported	Diagnosis of mood, anxiety, EDNOS, psychotic	EDI-IA	SCID criteria	EDI-2 subscales TCI scores, BMI, age, illness	All 5 ED groups scored higher on lack of IA scale than 'normal

	BN 104 BED-OB 48 BED 47		BED-OB BED		disorder, other disorder			duration	range' BN > AN-BP, BED-OB
Fernandez-Aranda et al. (2009)	BN: 150 female BN: 19 male	Male 22y Female 26y	BN	None reported	<18 y, AN or BED, (c) missing values for any diagnostic items, current alcohol/drug abuse, or (e) current psychotic disorder	EDI-IA	Patients met DSM-V-TR criteria for BN and EDNOS-BN	Adjusted for age, starting BMI, duration of illness, and diagnosis subtype	Lower scores on lack of IA after treatment.
Fischer et al. (2016)	AN: 15 HC: 15	Female AN:27y HC:28y	AN-Restricting	Depression treated with SSRIs(n=4), borderline PD (n=1)	Any medication past/current ED, other psychiatric disorders. Within AN: any current purging behaviours.	Heartbeat Detection EDI-IA	ICD-10 criteria	None reported	Heartbeat Detection lower in AN than HC at all 3 timepoints Higher lack of IA in AN No effect of treatment
Fitzgibbon et al. (2002)	Obese nonbingers: 24 subthreshold BED: 9 BED: 64 subthreshold BN:105 BN:123	Female 27-41y	Mixed: BN BED subBN subBED	None reported	BMI < 18	EDI-IA	Questionnaire on Eating and Weight	MANCOVA controlling for age and BMI	BED and BN groups reported greater interoception deficits than obese non-binge group

Fujimori et al. (2011)	ED:80 HC:120	Female ED:27y HC:19y	Mixed AN-R AN-BP BN-P BN-NP EDNOS	Study was assessing self-injury in ED	None reported	EDI-IA	Diagnosis based on DSM-IV criteria	None reported	ED groups scored higher than HC on lack of IA
Garfinkel (1974)	HC:11 AN:11	Female 16-23y	AN	None reported	HC: no history of 'weight' problems, previous treatment for 'emotional illness' or current use of medication.	Modified Hunger-Satiety Questionnaire	AN group defined by criteria: weight loss greater than 25% of body weight, morbid aversion to food, conscious dietary restriction; amenorrhoea; absence of primary organic illness	None reported	No difference in hunger sensations in AN and HC. AN less likely to report feeling full stomach/ stopping eating because of feeling hungry AN more likely to report having no stomach sensations, feeling bloated, stopping eating because of diet-limit.
Garfinkel et al. (1979)	AN:16 HC:13	Female AN: 22y HC: 22y	AN	None reported	Controls: no history of eating problems or psychiatric treatment	Satiety-aversion to sucrose test	Met diagnostic criteria for AN	None reported	AN did not show satiety-related aversion to sucrose
Garner et al. (1982)	AN: 133 AN-Rec: 17 HC:743	AN: female	AN, BN	None reported	None reported	EDI-IA	Met diagnostic criteria for AN	None reported	AN scored higher on lack of IA than recovered AN and

		HC: Male and female Average age range: 20-37y							HC.
Girdler et al. (1998)	HC: 14 BN: 14	Female	BN	MDD (53% history, 7% current). Anxiety (20% history, 47% current). Panic disorder (13% past history, 13% current) AN (13% past history, 0% current)	Current drug abuse, current chronic pain condition	Submaximal effort tourniquet procedure for pain threshold and tolerance.	Diagnostic interview with psychiatrist	None reported	BN had higher threshold and tolerance compared with controls
Goldzak-Kunik et al. (2011)	15 AN 15 HC	28 female 2 male An 15y HC 15y	AN	None reported	None reported	Cold pain, VAS for cold, unpleasantnes s and pain.	Diagnosed patients	None reported	No significant effects in MANOVA but Post-hoc comparison found AN had higher ratings of 'cold' at 45s
Gross et al. (1986)	20 BN 20 HC	Female BN:22y HC:24y	BN	None reported	HC: history of ED, currently weight-loss diet, had to have 'average' weight	EDI	Met DSM criteria	None reported, but no group differences in age,	BN scored significantly higher on lack of IA subscale than control

								education, marital or occupational status	
Gustafsson et al. (2010)	Non clinical: 429	Female T1:14y T2:18y	Nonclinical: split into group (disordered eating (DE); intermediate eating concern (IE); healthy eating (HE)	Non-clinical	None reported	EDI-IA		None reported	HE group reported significantly lower scores on Lack of interoceptive awareness than IE or DE
Halmi & Sunday (1991)	ED:84 HC:19	Female AN-R: 19y AN-BP: 22y BN: 22y	Mixed	None reported	None reported	Before- and after-meal hunger and fullness ratings	Met DSM criteria Inpatients	None reported	Both ED groups showed abnormal patterns of hunger and fullness across the premeal and postmeal conditions.
Heilburn & Worobow (1991)	Non clinical: 80	Female 18y	Non-clinical sample with BN-like symptoms	None reported	None reported	Self-report: 2 questions on 1-5 likert scale for 1) awareness and 2) 'action' – for both eating and drinking	EDI (Body dissatisfaction and Bulimia scale)	None reported	No effect of group on 'awareness'or 'action'

Herraiz-Serrano (2015)	ED:196 HC:127	No sex reported 23y	Mixed: AN:43 BN:74 EDNOS:79	State and trait anxiety higher in ED than control	Control students with at-risk scores	EDI-IA	EAT-40, BITE, Body-shape questionnaire Participants had diagnoses of ED	Age differed between groups but showed no relationship to outcomes, so was not controlled in the analysis	AN, BN and EDNOS all scored higher than HC on lack of IA
Holsen et al. (2012)	AN-Active: 12 AN-weight restored: 10 HC: 11	Female Age range 19-28y	AN-Active illness AN- weight restored (WR)	In AN group: GAD (n=3), ADHD (n=1), MDD (n=2), depressive disorder NOS (n=1) 1 with GAD, history of bipolar disorder, ADHD and history of PTSD Weight restored: MDD+GAD (n=1) MDD+social phobia(n=1)	Use of hormones, history of psychosis, objective binging/purging behaviours more than once a month in last 3 months, type 2 diabetes, active substance abuse, unsuitable for MRI, past GI surgery. For HC: history of binge/purge, amenorrhea, excessive exercise in last 3 months, any psychiatric disorder	Differences in brain activation pre- and post satiation	DSM-IV criteria	Groups matched for handedness and sex. Analysis controlled for % ideal body weight	Premeal, HC showed higher left and right insula activation than AN, but not WR-AN. Postmeal, HC showed higher left insula activation, and AN-WR showed higher left insula activation than HC

Kaye et al. (1998)	BN-Rec:30 HC:31	Female BN:26y HC:22y	BN-Rec	MDD (68%) OCD (25%) GAD (11%) Alcohol Dep (32%) Substance Dep (21%)	Not meeting 'recovered' criteria for past year	EDI-IA	Group allocation based on past diagnosis of BN	None reported	BN-Rec scored higher than on HC on lack of IA
Kerr et al. (2016)	AN-Rec:15 HC:15	Female AN: 17y HC: 18y	AN-Rec (weight restored)	MDD (n = 5), OCD (n = 2), social phobia (n = 1), PTSD (n = 1), GAD (n = 1), mood disorder due to a general medical condition, with depressive features (n = 1), and adjustment disorder with depressed mood (n = 1).	History of any major medical or neurological disorders, head injuries, current pregnancy, MRI exclusion. Excessive fMRI motion or poor data quality	fMRI during task involving attending to internal sensations from heart, stomach and bladder.	Semi-structured interview with psychiatrist and SIAB	STAI trait anxiety, SIGH-A, TAS Difficulty Identifying Feelings (TAS-F1), and TCI Harm Avoidance (TCI-HA).	Decreased activity during stomach-based IA in AN compared to HC in left dorsal mid-insula.
Kerr et al. (2017)	AN-Rec:20 HC:20	Female AN-Rec:17y CON:18y	AN-Rec	MDD (n=7), GAD (n=3), Social Phobia(n=3), OCD (n=1), PTSD (n=1), Phobia(n=1)	HC: no history of psychiatric disorder	fMRI during task involving attending to internal sensations from heart,	Diagnosed using Structured Interview for Anorexic and Bulimic Disorders	Organ intensity rating entered as covariate. BMI and	STOMACH: Food pictures-AN: positive relationship between stomach intensity ratings

						stomach and bladder.		anxiety in response to food>non-food.	and food-image related activation in the posterior insula negative relationship in the amygdala High palatable food pictures- AN: negative association between stomach ratings and activation in ventral pallidum and VTA, positive relationship between stomach and activation in ACC and amygdala. HEART: AN: negative relationship between heart ratings and vmpfc act to food pictures HC showed opposite relationship in ALL

									conditions
Khalsa et al. (2015)	AN: HC:15	Female AN: 23y HC:22y	AN	GAD (n=27), MDD (n=13), OCD(n=13) >2 comorbities (n=13)	ALL: lifetime neurological, cardiac, respiratory disease BMI<17 HC: no current major psychiatric illness.	Infusions of isoproterenol (to increase heart rate) and continuous rating of intensity of heartbeat and breathing: before and after 1000kcal meal	Current/lifetime DSM5 diagnosis of AN	None reported	AN more likely to report interoceptive changes across all conditions, more likely to incorrectly report changes (e.g. in saline conditions
Killen et al. (1996)	825 At baseline: 789 no symptom 36 partial syndrome	Female Baseline:15y	BN – partial syndrome	None reported	Data excluded from longitudinal analysis if participants were symptomatic at baseline.	EDI-IA	Structured interview used to assess ED symptoms – DSM III criteria Questionnaire on weight concern	None reported	Girls who developed partial syndrome eating disorder scored significantly higher on lack of IA at baseline than those who did not
Kim, Annunziato & Olatunji (2018)	Mixed: 5193	Female	AN BN EDNOS	None reported	BMI below 14/over 40	EDI-IA	DSM criteria EDI at intake and discharge	None reported	Scores on lack of IA were significantly lower post-treatment than pre-treatment
Klabunde et al.	BN-Rec:9	Female	BN-Rec	None reported	History of	Heartbeat	SCID criteria & Yale	Age	Higher mean

(2013)	HC:10	Age range 18-45y			alcohol or substance abuse. Neurological/ medical conditions Use of psychotropic medication 3mo prior.	Counting	Brown Cornell Eating Disorder Scale		proportion correct counts higher in the control group than BN group
Koch & Pollatos (2014)	Non-clinical: Baseline: 1657 T2: 1610	T1: 52% female, average age 8y T2: 51.9% female, average age 9y	Non-clinical sample	None reported	None reported	Heartbeat counting	Emotional eating subscale 'emotional overeating' External eating subscale of the DEBQ	Age	External eating behavior at T1 was a negative predictor and emotional overeating at T1 was a positive predictor for the HBP-Score at T2 in the overweight group only
Krieg et al. (1993)	AN-intermediate outcome: 9 AN-good outcome: 14 Restrained-eaters:21 Unrestrained eaters:20	Female Intermediate :21y Good:24y Restrained: 23y Unrestrained :24y	AN	None reported	None reported	Heat pain threshold – thermode with increasing temperature	Lifetime diagnosis of AN according to DSM.	None reported	4 groups did not differ significantly in pain thresholds
Laessle et al. (1989)	BN:20 Restrained-	Female	BN	None reported	None reported	EDI-IA	Diagnosis made using DSM	None reported	BN scored higher than unrestrained

	eaters :20 HC:20		Restrained Unrestrained (HC)					(groups did not differ on age, height weight or BMI)	lack of IA, unrestrained scored higher than restrained
Lammers et al. (2015)	BED: 431 began, 341 completed treatment 304 completed post-treatment, 190 completed 6mo follow up	Women:399 Men:32 36y	BED	None reported	Concurrent treatment for BED or weight problem, acute comorbid psychiatric conditions pregnancy and age below 18 or above 65 years.	EDI-IA	Participants met DSM-IV for BED. EDI Bulimia scale	Receipt of any additional intervention after treatment	Interoceptive awareness at post-treatment predicted EDI-bulimia at follow-up
Lattimore et al. (2017) Study 1	AN:7 BED:4 BN:16 EDNOS:12	Female 18-50 29y	AN BED BN EDNOS	None reported	None reported	EDI-IA	ED participants had diagnosis of eating disorder	None reported	Lack of IA did not significantly correlate with EDI subscales drive for thinness or bulimia.
Study 2	Non-clinical: 137	Female 21y	Non-clinical sample	None reported	Past or present treatment of eating disorder	EDI-IA	EDI-3	None reported	Lack of IA significantly positively correlated with drive for thinness

									and bulimia.
Study 3	Non-clinical: 119	Female 18-27 20y	Non-clinical sample	None reported	Past or present treatment of eating disorder	EDI-IA	EDI-3	None reported	Lack of IA correlated with drive for thinness and bulimia subscales
Lautenbacher (1991)	AN: 19 BN:20 HC: 21	Female AN: 22y BN:22y HC:22y	BN AN	None reported	Other psychiatric /somatic disorders, substance abuse, long-term medication use	Pain thresholds, measured by heat stimulus	DSM criteria	Menstrual variations in pain perception: participants only tested in first 14 days of cycle	Higher pain threshold in AN than BN, higher in BN than HC
Lavagnino et al. (2014)	BN:16 HC:18	Female BN:23y HC:23y	BN	Mild depressive symptoms (n=8)	Major medical illness, neurological disorders, head trauma, use of psychotropic medications, or treatments in the last 6 months, presence of other psychiatric diagnoses except mild depressive symptoms, MRI exclusion	Seed-based resting functional connectivity using EDI-2 interoceptive awareness subscale	DSM criteria EDI bulimia and body dissatisfaction	Age, education, depressive symptoms	Lack of IA higher in BN than HC Weaker functional connectivity in interoception-related areas in BN, and found a significant negative correlation between interoceptive deficits and functional connectivity.
Leon et al.	Sub-clinical:	51% female	Subclinical	None reported	None reported	EDI-IA	Eating disorder risk	Various risk	Interoceptive

(1999) (same cohort reported on in Leon et al. 1993 and Leon et al 1995)	1424	Age range 12-18y	endorsement of disordered eating symptoms				variable based on Eating Disorder Risk Factor Index	factors included in SEM model	awareness contributed to negative affect latent construct which was a significant contributor to eating disorder risk.
Lilenfield et al. (2000)	BN:47 (16 recovered) BNrelatives:89 HC:44 HCrelatives:100	Female BN:24y BN-Rec:27y HC:26y	BN	Participants were not screened for lifetime history of any other EDs.	Control: no history of ED ED(recovered): no binge/purge/restrictive eating patterns in last year.	EDI-IA	Lifetime DSM-IV diagnosis of BN	None reported	BN>BN-R>HC on lack of IA Relatives: ED>pastED>no history
Linardon & Mitchell (2017)	Non-clinical: 372	74 men 301 women Average age 25y	Non-clinical sample	None reported	None	IES	EDEQ TFEQ	IES was added in the third regression model, so variance associated with dietary control (rigid and flexible) were both controlled for	IES scores significantly predicted binge eating frequency and disinhibited eating.
Maganto et al. (2016)	Non-clinical: 1075	536 male (49.9%) 539 female (50.1%)	Non-clinical sample	None reported	None	EDI-IA	EDI-2 used to allocated high risk group	None reported	Those in the at-risk group scored significantly higher on lack of

									IA than without-risk group.
Maïano et al. (2016) Studies 1 and 5.	Study 1: 291 Study 5: HC: 19 AN: 19	Study 1: 14y, 54% male. Study 5: 16y, 50% female	Study 1: Non-clinical sample Study 5: AN	None reported	None reported	EDI-IA And EDI VS - IA	EDI/EDI-VS Study 5: AN participants were allocated to group based on diagnosis	None reported	Study 1: Lack of IA positively correlated with bulimia and drive for thinness Study 5: AN sample scored significantly higher than HC on lack of IA
Matsumoto et al. (2006)	AN-R = 3 AN-BP = 5	Female Average age 19y	AN-R AN-BP	None reported	None reported	EDI-IA	DSM-IV criteria	EDI, Eating Attitude Test (EAT), Self-Rating Depression Scale (SDS), State-Trait Anxiety Inventory (STAI) treated as covariates of interest	Lack of IA showed significant improvement pre and post treatment.
Merwin et al. (2009)	Mixed: 50	94% female Average age 23y	AN BN EDNOS	None reported	None reported	Difficulties in emotion regulation scale	Dietary restraint and binge eating subscale of EDE	Age, BMI and illness duration.	Neither lack of clarity nor non-acceptance subscales predicted bulimia Non-acceptance

									only predicted restraint
Myers & Crowther (2008)	Non-clinical: 195	Female	Non-clinical sample	None Reported	None reported	EDI-IA.	EAT	None reported	Higher lack of IA associated with more disordered eating
Nevonen et al. (2006)	ED: 978 Psychiatric Out Patients (POP): 106 HC: 602	Female 18-50y	ED included: AN: 179 (18%); BN: 432 (44%); EDNOS: 367 (38%).	None reported	HC who reported currently or previously having an eating disorder	EDI-IA	Patients met DSM-IV criteria	None reported	ED>POP>HC on lack of IA
Nyman-Carlsson et al. (2014)	Mixed: 1080	Female ED:21y Psychiatric Out Patients (POP):37y HC:20y	Mixed	None reported	Reported for POP only: Men/patients with incomplete data	EDI-IA	DSM-IV diagnoses.	None reported	ED> POP> HC on lack of IA
Papezova Yamamotova & Uher (2005)	HC:17 AN-Res:16 ANBP:5 BN:18	Female	AN-Res AN-BP BN	Affective disorder (n=4), anxiety (n=2), history of substance abuse (n=4), history of suicide attempt (n=2)	Current analgesic medication, pregnancy, diabetes or neurological illness	Thermal pain threshold	DSM criteria	Medication, comorbidity	ED group had higher(longer) pain threshold than control group. Comparisons showed BN and AN-BP had higher pain thresholds than HC, but not

									AN-Res.
Pollatos & Georgiou (2016)	BN:23 HC:23	Female BN:24y HC:25y	BN	MDD(n=3), Anxiety disorder (n=5), MDD+anxiety (n=2)	Intake of psychotropic medication	Heartbeat counting EDI-IA	SCID-I criteria	BMI, alexithymia, depression and anxiety.	No difference in heartbeat counting. Significant negative correlation between heartbeat counting and EDI subscale in BN only
Pollatos et al. (2008)	AN:28 HC:28	Female Average age 21y	AN	MDD (32%) MMD+anxiety disorder (7%) Anxiety disorder (7%)	Past/ present psychotic disorders	Heartbeat counting EDI-IA	Structured Interview for Anorexic and Bulimic Syndromes for DSM-IV and ICD-10	Anxiety & depression	Heartbeat counting poorer in AN versus HC
Preyde et al. (2016)	BN: 29 AN-BP: 22 AN-R:19 EDNOS:6	92.4% female	Mixed: BN AN-BP AN-R EDNOS	Not reported	Psychiatric hospitalization in past six weeks, hospitalization for feeding within the past month, actively suicidal, active alcohol and/or drug dependence, history of stomach	EDI-IA combined with emotional dysregulation subscale to create 'affective problems composite'	Inpatients, all diagnosed with one of the EDs Eating disorder risk composite (EDRC, subscale of EDI-3)	None reported	Positive change in 'affective problems composite' during the treatment was predictive of lower EDRC scores at discharge.

					reduction surgery, a goal of weight loss rather than weight gain, , unstable diabetic condition, binge-eating disorder, or a psychotic illness				
Ramaciotti et al. (2008)	BED:27 HC:63	BED:87.5% Female 37y HC:91.6% Female 42y	BED	None reported	None reported	EDI-IA	Binge eating disorder clinical interview Structured clinical interview for anorexic-bulimic spectrum	None reported, but no differences between two groups in demographic measurements	BED scored higher than HC on lack of IA
Raymond et al. (1995)	BED:27 OB:33 HC:44	Female Age range 19-50 y	Binge eating	None reported	Psychoactive or analgesic medications, history of psychiatric disorder major medical illness.	Mechanical pain thresholds	DSM criteria	age	Pain detection: BED>HC
Raymond et al. (1999a)	AN:43 HC:65	Female Age range 16-43y	AN	None reported	History of substance abuse, psychotic symptoms, current suicidality,	Mechanical pressure pain detection thresholds	Met DSM-IV criteria for AN.	None	Pain detection threshold was significantly higher in AN than HC

					comorbid medical condition that would interfere with pain testing				Pain tolerance thresholds were not significantly different.
Raymond et al. (1999b)	BN: 9	Female 24y	BN	MDD (n=2) Social phobia (n=2)	Active suicidal ideation, diagnosis of schizophrenia or bipolar disorder, substance use disorder in the prior 6 months, or the use of psychoactive medication /pain medication	Mechanical pressure pain thresholds during bulimic episode	DSM-III-R criteria for BN	Depression and anxiety	On the binge/vomit episode day, there was a significant decrease in pain threshold immediately after vomiting and for 1 hour after.
Romano et al. (2018)	Non-clinical: 902	68.2% female 24y	Nonclinical sample	5% reported lifetime ED, 4% reported clinically severe current ED	None reported	IES-2	EDE-Q	Age, gender and BMI	IES-2 negatively predicted EDE-Q global scores. Addition of EDE-Q scores into model already including age, gender and bmi caused significant change in model fit.
Rossiter, Wilson & Goldstein	BN:10 'Restrained'	Female 22y	BN	None reported	No use of self-induced vomiting,	EDI-IA	TFEQ: restraint, hunger, disinhibition	None reported	BN>Restrained>Unrestrained on lack of IA

(1988)	and 'not restrained' eating: 20				laxative, or diuretic abuse				
Schmahl et al. (2010)	BN: 20 HC:24	Female	BN	In BN group: AN, drug dependence, alcohol abuse, antidepressant use.	Pregnancy, psychiatric disorders substance dependence or abuse during the last 6 months, organic brain disease, medical illnesses, and medication with analgesic properties	Thermal pain thresholds using contact thermode	SCID	Age, BMI, BDI scores	No difference in heat or cold pain thresholds in BN compared to HC
Schoemaker et al. (1997)	BN:78 POP:67	Female (reports for BN only) BN:30y POP:32y	BN	None reported	POP: diagnosis of AN/BN or reporting frequent binge eating	EDI-IA	Meeting DSM criteria for BN	None reported (but no difference in age or BMI)	BN scored significantly higher than POP on lack of IA
Sehm & Warschburger (2018)	BED: 1039	49.7% boys 14y	BED	None reported	None reported	EDI-IA at T1 and T2	EDI- IA subscale		Lack of IA correlated with binge eating at both timepoints. Lack of IA predicted binge

									eating longitudinally.
Sim & Zeman (2004)	BN:19 Depression: 19 HC:19	Female 16y	BN EDNOS	In BD group: Panic disorder (n=1) MDD (n=3) Depressive disorder NOS (n=1).	HC participants with past mental health history or current depression/ED were excluded	EDI-IA	Group classifications based on diagnosis performed by psychiatrist, psychologist and nutritionist.	None statistically, but separate analyses run to assess effects of medication status	Lack of IA was highest in BN, and higher in depression than HC.
Solmi et al. (2018)	AN:955 BN:813 BED:300	96.6% Female AN:23Y BN:26Y BED: 35y	Mixed	None reported	Severe comorbidity: schizophrenia, acute manic episode, or alcohol addiction.	EDI-IA	Had current diagnosis of AN, BN or BED according to DSM-5. EDI body dissatisfaction, drive for thinness and bulimia were considered ED-core symptom measured	BMI, duration of illness, depression and anxiety	In network analysis: interoceptive deficits had high network centrality.
Srinivasagam et al. (1995)	AN-Rec: 20 HC: 16	Female AN:24y HC:22y	AN-Rec	None reported	None reported	EDI-IA	Group allocation based on previous diagnosis of anorexia.	None reported	AN scored significant higher than HC on lack of IA.
Stein et al. (2002)	BN-rec: 11 HC:15	BN:29y HC:25y	BN-Rec	None: screened by exclusion criteria	Any axis I disorder in the past year. Ever having a bipolar disorder, a schizophrenic spectrum	Pain perception: Thermal pain latency. Submaximal	Previous DSM-IV diagnosis. (past year maintenance of stable weight, no bingeing or	Tested in follicular phase to control for menstrual variations on pain	Greater % of BN-R had thermal pain thresholds longer than set 'end' of experiment

					disorder, organic brain syndrome, and dementia. Present or past medical illness, or chronic pain condition; not used psychoactive medications in the past year; no current or regular use of analgesics or of any other medications	effort tourniquet test (ischemic pain)	restrictive eating, normal menstruation)	perception.	Longer ischemic pain threshold in BN-R.
Strigo et al. (2013)	AN-Rec: 12 HC: 12	Female AN-Rec:25y HC:30y	AN-Rec	Lifetime diagnoses, AN only: MDD (n = 7), anxiety (n = 6), OCD (n = 3), alcohol dependence (n = 1)	Substance dependence, psychotropic medication in past 4 weeks, clinically significant comorbid medical conditions, MRI exclusion, current or past chronic pain	Thermal pain fMRI during anticipatory and reception phases.	SCID by doctoral level clinicians, final diagnosis in meeting with psychiatrist	None reported but groups were not different on depression, anxiety or alexithymia	During anticipation of pain: AN-Rec showed significantly greater activation in right anterior insula than HC in low and unknown pain conditions, and significantly lower insula activation during pain processing in both high and low pain

Taylor et al. (1996)	AN-Res:30 AN-BP:18 30 matched controls NB only these participants were used in analysis of EDI between groups 234 unmatched controls	Matched control: All female 27y Unmatched HC: 50% female	AN-Res AN-BP	None reported	HCs excluded if they had a history of any ED	EDI-IA	ED participants met DSM-III criteria for AN.	None reported	Patients scored significantly higher on lack of IA than HC.
Thompson et al. (1987)	Non-clinical: 95	Female 21y	Non-clinical sample	None reported	None reported	EDI-IA	Eating patterns questionnaire - EPQ EDI - Bulimia, drive for thinness	None reported	Bulimic group scored higher than symptom-free and bulimic-like on lack of IA
Tylka & Subich (2004)	Non-clinical: 463	Women 23y	Non-clinical sample	Nonclinical:	None reported	EDI-IA	Questionnaire for eating disorder diagnoses (Q-EDD) EAT-26	Pressure for thinness Friend social support Family social support Internalisatio	EAT-26: Positive path coefficient between poor interoception and ED symptoms =

								n of thin ideal Negative affect Body image disturbance	Q-EDD: Positive path coefficient between poor interoception and Q-EDD group rank
Tylka & Wilcox (2006)	Non-clinical: 340	Female 18y	Non-clinical sample	None	None reported	IES subscales: unconditional permission to eat; eating for physical reasons and reliance on hunger/satiety cues	EAT-26 subscales dieting and bulimia/food preoccupation.	None reported	All 3 IES subscales correlated with EAT-26 measures
Ussery & Practice-Dunn (1992)	Non-clinical: 96	Male No age reported	Non-clinical sample	None reported	None reported	EDI-IA	The Binge Scale Bulimia test (BULIT)	None reported	Lack of IA correlated positively with binge scale and BULIT. Lack of IA was a sig predictor for BULIT but not for the binge scale.
Van Dyck et al. (2016)	ED:87 HC:835	Female ED: 26y HC: 25y	Mixed	None reported	History of eating disorder for HC	IES	Participants who indicated that they had received an official diagnosis by	Gender	ED scored higher than HC on IES

							a mental health professional		
Van Strien et al. (2005)	HC: 436 ED:332	16y	Mixed	None reported	None reported	EDI-IA	ED sample defined using DSM-IV EDI-SC DEBQ	None reported	ED scored significantly higher than HC on lack of IA
Villarroel et al. (2009)	Non-clinical: 751	Female 22y	Non-clinical sample	None reported	None reported	EDI-IA	EDEQ	None reported	Lack of IA correlated with restraint and with eating concern
Vinai et al. (2015)	BED:57 HC:61	BED: 75% Female 44y HC: 56% Female 45y	Binge Eating	BED scored higher on depression and anxiety	Other eating disorders excluded through clinical interview	EDI-IA	Diagnosis made by an eating disorder professional	None reported – no difference between groups in age or BMI	BED scored higher on lack of IA than HC
Wierenga et al. (2015)	AN-Rec:23 HC:17	Female HC=25y AN-Rec = 28y	AN-Rec	MDD (n=17), anxiety (n=8), OCD (n=4), past drug/alcohol abuse (n=3)	No current diagnosis or history within 3-months of drug/alcohol abuse, no medical or neurological concerns, MRI exclusion, no psychotropic medication 3	Differences in BOLD activation in reward-related areas when satiated vs hungry	Diagnosis of AN	None reported: no group difference in age, BMI etc.	In HC: hunger increased brain responses in reward circuit areas, and satiety increased response in cognitive control areas. In AN-Rec: no influence of hunger state

					months prior				
Wierenga et al. (2017)	AN-Rec:21 HC:16	Female AN = 27y HC = 24y	AN	Lifetime diagnoses: HC= none. AN= MDD (n=14), OCD (n=4), anxiety (n=7), alcohol abuse (n=3).	Binging/purging /restrictive eating for min 1y prior Current DSM-IV axis 1 diagnosis, taking	Differences in Cerebral Blood Flow (CBF) (Hunger vs fed)	SCID	None reported	HC showed increased CBF when hungry, AN-Rec showed decreased CBF when hungry
Yamamotova et al. (2017)	AN:31 BN:30 HC:30	Female AN:24y BN:25y HC:23y	Mixed	Affective disorder (n=3), anxiety(n=3), history of substance abuse (n=5), history of self-injury (n=21)	EDNOS, current use of psychoactive substances, analgesic medication, pregnancy, diabetes or neurologic illness.	Thermal pain threshold	DSM-IV criteria for AN or BN	None reported	Patients with AN and BN had higher pain thresholds than controls
Yamatova et al. (2009)	BN:21 HC:21	BC: 23y HC: 23y	BN	Depression (n=2) Anxiety (n=2) Substance abuse (n=2)	Use of analgesic medication in the past week, not pregnant, no history of neurological illness or diabetes, no psychotic illness or substance	Heat pain threshold using Analgesia Meter – radiant heat applied to 1cm	Participants met DSM-IV criteria for BN	Additional analysis was run on the 14 BN who were medication free and without comorbidity	BN had higher pain threshold than HC. BN had shorter tolerance latency of cold pressor than HC

					dependence on structured psychiatric interview				
Young et al. (2016) Study 1	Non-clinical: 36	Female 24y	Non-clinical sample	None reported	Metabolic or cardiovascular disorder, gastrointestinal problems, pregnancy, current mood/eating disorder, medications or supplements to manage weight/appetite	Interoceptive Accuracy (counting) Awareness (confidence in counting), Sensibility (MAIA) Trait prediction error (difference between Accuracy and sensibility)	Dutch Eating Behaviour Questionnaire subscales: Emotional Eating External eating Restrained eating	Anxiety, depression and self-confidence	Positive association between Accuracy & Emotional Eating (EE) Negative relationship between awareness and EE Positive association between prediction error and EE Once anxiety and depression controlled for only awareness and prediction error were significant
Study 2	Non-clinical: 37	Female 21y	Non-clinical sample	None reported	Metabolic or cardiovascular disorder, gastrointestinal	Interoceptive accuracy (heartbeat discrimination	Dutch Eating Behaviour Questionnaire subscales:	Anxiety, depression and confidence	Those who were able to discriminate heartbeat

					problems, pregnancy, current mood/eating disorder, medications or supplements to manage weight/appetite	task)	Emotional Eating External eating Restrained eating		reported greater propensity towards emotional eating

Key: ADHD = Attention Deficit Hyperactivity Disorder, **AN** = Anorexia Nervosa, **AN-Res** = Anorexia Restricting Subtype, **AN-BP** = Anorexia Nervosa Binge–Purging Type, **AN-Rec** = Recovered/Remitted Anorexia, **BITE** = Bulimic Investigatory Test, Edinburgh, **BN-Rec** = Recovered/Remitted Bulimia, **BN** = Bulimia Nervosa, **BED =** Binge Eating Disorder, **BES**= Binge Eating Scale, **BDI=** Beck's Depression Inventory, **HC** = Healthy Control, **EAT**= Eating Attitudes Test, **EDEQ** = Eating Disorder Examination Questionnaire, **EDNOS** = Eating Disorder Not Otherwise Specified, **EDI** = Eating Disorder Inventory, **EDI-IA** = interoceptive awareness subscale of Eating Disorder Inventory, **GAD** = Generalized Anxiety Disorder, **ICD-10** = International Statistical Classification of Diseases and Related Health Problems, **MDD =** Major Depressive Disorder, **EDEQ** =Eating Disorder Examination Questionnaire, **BMI =** body mass index. **OCD** = Obsessive-Compulsive Disorder, **POP** Psychiatric Out Patients **PTSD** = Post-