NourishED Research Foundation (NRFi)

Interoception & Interoceptive Awareness in Binge Eating Disorder

**Sept 25, 2024**

[nourished@nourishedRFi.org](mailto:nourished@nourishedrfi.org) | 206-819-9647

1207 Delaware Ave, Wilmington, DE, 19806

1821 Walnut Street, Boulder, CO 80302

[www.nourishedrfi.org](http://www.nourishedrfi.org)

A logo for a research foundation

Description automatically generated

Table of Contents

[I. Interoception in Eating Disorders & Mental Health 2](#_Toc178154740)

[II. Stress & Interoception Disruption 11](#_Toc178154741)

[III. Interoception in BED 12](#_Toc178154742)

[1. General 12](#_Toc178154743)

[2. Nadershahi, Bray 14](#_Toc178154744)

[3. Martin (not active clinical trial) 20](#_Toc178154745)

[4. No Control 20](#_Toc178154746)

[IV. Interoception in Other Eating Disorders 20](#_Toc178154747)

[1. “Mixed EDs” (which can include BED) 20](#_Toc178154748)

[2. “EDNOS” (“Eating Disorder Not Otherwise Specified,” which included BED before publication of the DSM-V in 2013). 20](#_Toc178154749)

[V. Autism in BED 21](#_Toc178154750)

# Interoception in Binge Eating Disorder: A Narrative Review

# Abstract

Interoception, the process by which the nervous system senses, interprets, and integrates signals originating from within the body, has gained significant attention in recent years due to its implications for mental health and eating disorders. This narrative review aims to explore the role of interoceptive awareness (IA) in binge eating disorder (BED), examining how stress modulates interoception, the relationship between interoception and other eating disorders, and the links between interoception and neurodivergent conditions such as autism and alexithymia. By synthesizing findings from 34 publications, this review highlights the importance of interoception in understanding and treating BED and other related conditions. Future research directions and potential therapeutic interventions targeting interoceptive deficits are also discussed.

# Introduction/Background

Interoception refers to 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). Interoceptive awareness (IA) is the conscious perception of these internal bodily signals and is typically measured using self-report questionnaires, behavioral tasks, and physiological assessments (e.g., heartbeat detection tasks). Recent research has shown that IA plays a crucial role in emotional regulation, cognitive processing, and overall well-being (Weng et al., 2020). In the context of eating disorders, deficits in IA have been linked to disordered eating behaviors, such as binge eating, anorexia nervosa, and bulimia nervosa (Martin et al., 2019). Understanding and improving IA may offer new therapeutic avenues for treating these conditions.

# Interoception in Binge Eating Disorder (BED)

## General Overview

Binge eating disorder (BED) is characterized by recurrent episodes of eating large quantities of food, often rapidly and to the point of discomfort, accompanied by a sense of loss of control. Interoceptive deficits have been associated with BED, suggesting that individuals with BED may have difficulty accurately perceiving and responding to internal bodily signals related to hunger and satiety (Martin et al., 2019).

## Specific Studies and Findings

* **Wiss & Avena (2020)**: This chapter discusses the biological basis of binge eating and the role of food addiction. It highlights the neurobiological vulnerabilities and controversies surrounding food addiction and its public health implications.
* **van Dyck et al. (2020)**: This study investigates gastric interoception and gastric motility in patients with bulimia nervosa and BED. It finds that patients with these disorders have a delayed response to satiation and abnormal gastric myoelectrical activity.
* **Romano et al. (2020)**: This research examines the association between somatic symptoms and binge eating in women’s daily lives. It suggests that somatic symptoms may serve as momentary correlates or proximal antecedents of binge eating behavior.
* **Vinai et al. (2015)**: This study evaluates psychopathology in obese patients with and without BED, finding that BED patients exhibit higher levels of psychopathology, including drive for thinness, bulimia, body dissatisfaction, and interoceptive awareness.
* **Martin et al. (2019)**: This systematic review explores the relationship between interoception and disordered eating. It finds that deficits in interoception are observed across various types of disordered eating and interoceptive modalities, suggesting that interoception may be a transdiagnostic feature of disordered eating.
* **Khalsa et al. (2018)**: This review highlights the role of interoception in mental health, including its contributions to the maintenance of homeostatic functioning, body regulation, and survival. It discusses the challenges and future directions for interoceptive research in mental health.

1. **Stress & Interoception Disruption**
2. **How Stress Modulates Interoceptive Awareness**

Stress can significantly modulate interoceptive awareness by disrupting the body’s ability to accurately perceive and interpret internal signals. Emerging theories emphasize the crucial role of allostasis (anticipatory and adaptive regulation of the body’s biological processes) and interoception in adjusting physiological responses to environmental and bodily demands (Santamaría-García et al., 2024). Disruptions in integrated allostatic interoceptive mechanisms have been observed in psychiatric and neurological disorders, including anxiety, depression, Alzheimer’s disease, and frontotemporal dementia. These disruptions can lead to altered brain structure and function, heart-brain interactions, respiratory-brain interactions, and gut-brain-microbiota axis, among other processes.

1. **Interoception in Other Eating Disorders**
2. **Mixed EDs and EDNOS**

Deficits in interoception have been observed across various types of disordered eating, suggesting that interoception may be a transdiagnostic feature of disordered eating (Martin et al., 2019). This includes mixed eating disorders (EDs) and Eating Disorder Not Otherwise Specified (EDNOS), which included BED before the publication of the DSM-V in 2013.

1. **Neurodivergence in Eating Disorders and Binge Eating Disorder**
2. **Connections to Conditions like Alexithymia and Autism**

Interoceptive deficits have also been linked to neurodivergent conditions such as autism and alexithymia. Alexithymia, characterized by difficulties in identifying and describing one’s own emotions, has been associated with poor interoceptive ability (Brewer et al., 2016). This suggests that interoceptive deficits may play a role in the emotional and cognitive challenges faced by individuals with these conditions.

* **Pruccoli et al. (2023)**: This case series reports on children and adolescents with comorbid feeding and eating disorders (FEDs) and neurodevelopmental disorders (NDDs), such as autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD). The study highlights the impact of NDDs on the diagnosis and treatment of FEDs.
* **Solmi et al. (2021)**: This study investigates the trajectories of autistic social traits in childhood and adolescence and their association with disordered eating behaviors. It suggests that greater autistic social traits in childhood could represent a risk factor for the development of disordered eating in adolescence.
* **Nickel et al. (2019)**: This systematic review explores the overlap between eating disorders, ASD, and ADHD. It highlights the frequent association between these conditions and the need for further research to understand the underlying mechanisms.
* **Dell’Osso et al. (2019)**: This study investigates the prevalence and features of sub-threshold autistic traits (ATs) among adults, suggesting that ATs may be associated with specific personality features and higher vulnerability towards psychopathology.
* **Nazar et al. (2016)**: This study examines the prevalence of ADHD in obese women with binge eating and bulimic behaviors, finding a higher rate of ADHD in this population and a significant correlation with more severe disordered eating patterns.

1. **Future Directions for Research**

Future research should focus on examining particular dimensions of interoception to provide insights into the specific interoceptive deficits associated with disordered eating. This could lead to the development of improved therapies targeting interoceptive awareness and its role in eating disorders (Martin et al., 2019). Additionally, longitudinal studies are needed to better understand the causal relationships between interoceptive deficits and disordered eating behaviors. Investigating the role of stress and its impact on interoception in different populations could also provide valuable insights for developing targeted interventions.

1. **Conclusions**

Interoception plays a crucial role in the understanding and treatment of binge eating disorder and other related conditions. Deficits in interoceptive awareness have been linked to disordered eating behaviors, stress, and neurodivergent conditions such as autism and alexithymia. By synthesizing findings from 34 publications, this narrative review highlights the importance of interoception in understanding and treating BED. Future research should focus on developing improved therapies targeting interoceptive deficits and exploring the underlying mechanisms of interoception in different populations.

1. **References**
2. Weng HY, Lewis-Peacock JA, Hecht FM, Uncapher MR, Ziegler DA, Farb NAS, et al. Focus on the Breath: Brain Decoding Reveals Internal States of Attention During Meditation. Frontiers in human neuroscience (2020) 14:336. Epub 2020/10/03. doi: 10.3389/fnhum.2020.00336.
3. van Dyck Z, Schulz A, Blechert J, Herbert BM, Lutz APC, Vögele C. Gastric Interoception and Gastric Myoelectrical Activity in Bulimia Nervosa and Binge-Eating Disorder. The International journal of eating disorders (2020). Epub 2020/05/14. doi: 10.1002/eat.23291.
4. Romano KA, Heron KE, Smith KE, Crosby RD, Engel SG, Wonderlich SA, et al. Somatic Symptoms and Binge Eating in Women’s Daily Lives. Journal of psychosomatic research (2020) 135:110161. Epub 2020/06/07. doi: 10.1016/j.jpsychores.2020.110161.
5. Martin E, Dourish CT, Rotshtein P, Spetter MS, Higgs S. Interoception and Disordered Eating: A Systematic Review. Neuroscience and biobehavioral reviews (2019) 107:166-91. Epub 2019/08/28. doi: 10.1016/j.neubiorev.2019.08.020

# Interoception in Mental Health

#### Santamaría-García, H., et al. (2024). "Allostatic Interoceptive Overload Across Psychiatric and Neurological Conditions." Biol Psychiatry.

###### Abstract

Emerging theories emphasize the crucial role of allostasis (anticipatory and adaptive regulation of the body's biological processes) and interoception (integration, anticipation, and regulation of internal bodily states) in adjusting physiological responses to environmental and bodily demands. In this review, we explore the disruptions in integrated allostatic interoceptive mechanisms in psychiatric and neurological disorders, including anxiety, depression, Alzheimer's disease, and frontotemporal dementia. We assess the biological mechanisms associated with allostatic interoception, including whole-body cascades, brain structure and function of the allostatic interoceptive network, heart-brain interactions, respiratory-brain interactions, the gut-brain-microbiota axis, peripheral biological processes (inflammatory, immune), and epigenetic pathways. These processes span psychiatric and neurological conditions and call for developing dimensional and transnosological frameworks. We synthesize new pathways to understand how allostatic interoceptive processes modulate interactions between environmental demands and biological functions in brain disorders. We discuss current limitations of the framework and future transdisciplinary developments. This review opens a new research agenda for understanding how allostatic interoception involves brain predictive coding in psychiatry and neurology, allowing for better clinical application and the development of new therapeutic interventions.

###### Intro

As a species, we regularly encounter a variety of environmental challenges, including infections, pollution, physical stress, so- cioeconomic disparities, and trauma. These factors influence our overall well-being (1). Our adaptive capacity is shaped by the intensity of these threats and our inherent biological pre- dispositions (2). Moreover, this adaptation relies on different regulatory physiological mechanisms that anticipate, mediate, and respond to the complexity of environmental and biological interactions (3,4). These regulatory physiological mechanisms can foster successful resilience or result in physical, neurolog- ical, and psychiatric disorders (5). Although previous evidence has focused on how our biological systems respond to external stressors, leading to either adaptability or the emergence of diseases (6), significant gaps in our knowledge persist.

Therefore, the mechanisms through which external chal- lenges (e.g., insufficient income) and internal alterations (e.g., dysregulation of the hypothalamic-pituitary-adrenal [HPA] axis) combine to induce psychiatric or neurological pathological outcomes remain unclear (7). Limited evidence details how stressors instigate disease by impacting various biological pathways (2,8). Predominant frameworks, such as diathesis- stress models, overlook the many biological processes that such threats may influence (9–12).

Emerging models could offer new perspectives. Recent studies have underscored the significance of anticipatory bio- logical reactions to upcoming external challenges, or allostasis (13,14), and the perception, regulation, and modulation of in- ternal states, or interoception (10,11,15,16) (Figure 1). Effectively coordinating anticipation of environmental demands and regu- lating internal bodily demands is crucial for adaptation. Conversely, dysregulation in this coordination is associated with psychiatric and neurological disorders. This dysregulation oc- curs when there is a mismatch between the anticipated energy expenditure and the actual energy required to cope with stressors, leading to physiological alterations due to overload (17–19). A deeper understanding of allostasis and interoceptive processes could elucidate the mechanisms that govern adapt- ability or vulnerability to psychiatric and neurological disorders (4,7,15,17,20), thereby offering an innovative framework for diagnosis, characterization, and intervention.

This review explores the allostatic interoceptive framework in psychiatric and neurological disorders, drawing on an extensive search of MEDLINE, Embase, and Web of Science databases for literature published from January 1, 1998, to June 30, 2023. The search utilized keywords related to external demands, biological processes, allostasis, interoception, and the disorders in question (see Supplemental Section S1). The review is divided into 4 main sections: 1) an overview of integrative models emphasizing allostatic interoception; 2) a detailed examination of allostatic interoceptive processes in disorders such as depression, anxiety, Alzheimer’s disease (AD), and behavioral- variant frontotemporal dementia (bvFTD); 3) an analysis of the

###### Figure 1 Legend

Figure 1. Allostatic interoception regulates environmental and biological interactions across the life span. The left panel outlines predictive allostatic interoceptive processes. The allostatic interoceptive system (A) is supported by the allostatic interoceptive network, which includes principal hubs such as the anterior midcingulate cortex (aMCC), pregenual anterior cingulate cortex (pACC), subgenual anterior cingulate cortex (sgACC), dorsal amygdala (dAmy), ventral-anterior insula (vaIns), dorsal midinsula (dmIns), and dorsal posterior insula (dpIns). The limbic cortices can be divided cytoarchitectonically into agranular regions that send prediction signals and (dys)granular regions that receive prediction error signals from the internal milieu, initiating psychological responses. Allostatic interoceptive processes, which are rooted in brain-body interactions including brain-heart, brain-respiratory, and brain-gut-microbiome systems, facilitate anticipation and guide responses to internal and external demands and threats, which may vary across the life span (B). Various biological predispositions can either dampen or amplify allostatic interoceptive processes, including the functioning of cardiovascular, metabolic, inflammatory, and stress-hormone systems (C). The degree of responses to external stimuli are influenced by genetic-epigenetic predispositions toward adaptive behaviors related to disease risks (D). Visuals in (A–C) are illustrative examples and do not represent actual data. GWAS, genome-wide association study.

Allostatic Interoception in Psychiatry and Neurology framework’s role in elucidating neurological and psychiatric diseases across the life span, including its interaction with the spatiotemporal dynamics of brain function; and 4) a discussion of the research and clinical implications of this framework.

We anticipated empirical support for the presence of allo- static and interoceptive alterations in psychiatric disorders (mainly depression and anxiety) and neurological disorders (mainly AD and FTD). We also expected that these alterations would be associated with the core clinical features of these disorders. Additionally, we hypothesized that pathophysio- logical mechanisms within the allostatic interoceptive frame- work could help explain the neurocognitive and behavioral alterations that we observed. Finally, we elaborate on how the allostatic interoceptive framework interacts with complemen- tary models to explain further normality and the emergence of psychiatric and neurological disorders.

###### ALLOSTASIS, ALLOSTASIS LOAD, AND INTEROCEPTION

Across the life span, humans face different environmental demands such as physical threats, air pollution, infections, and

stress, as well as social determinants of health, including social disparities and adversities, which together are known as the exposome (21–23). In adaptative situations, exposomes acti- vate physiological mechanisms to ensure survival and maintain internal equilibrium (14,24,25). Allostasis, which refers to the anticipatory and adaptive regulation of the body’s physiolog- ical processes, is central to adaptation (13). Allostasis is modulated by different biological processes, including genetic and epigenetics, that impact cardiovascular, inflammatory, and metabolic functioning (11,13,14) (Figure 1 and Box 1).

The cost of responding to external demands is known as allostatic load (15,16,20,26). When the exposome or internal bodily needs exceed an individual’s coping ability, allostatic overload ensues (26). Different triggers, including social dis- parities, adversities, lifestyles, and chronic stress, as well as dysregulated internal bodily processes, can result in a state of allostatic overload (24–30). Allostatic overload may trigger neurobiological changes, including oxidative stress; chronic inflammation (31); insulin resistance (32); reduced volume of the hippocampus, amygdala, and prefrontal cortex (19,24); and an imbalance in neurotransmission (33). As such, this state predisposes the organism to chronic diseases

###### Box 1. Glossary

Interoception: The process by which the nervous system senses, integrates, and anticipates bodily signals at both conscious and subconscious levels, providing a moment-to-moment mapping of the body’s internal landscape. Interoceptive skills encompass sensitivity (accurate detection of internal bodily signals), awareness (ability to be conscious of internal sensations), and metacognition (ability to reflect upon, infer, and evaluate one’s intero- ceptive skills), among other domains. Descending pathways play a crucial role in interoception by modulating these bodily signals through autonomic, endocrine, and immune systems, integrating higher brain functions with bodily regulation and maintaining homeostasis.

* Exteroception: The process of sensing stimuli originating outside the body. It encompasses the perception of environmental stimuli through sensory organs, enabling individuals to interact with their surroundings.
* Exposome: The totality of an individual’s environmental physical (i.e., pollution) and social (i.e., socioeconomic conditions) exposures across a lifetime that impact health, including pollutants, diet, lifestyles, social determinants of health, social adversities, and structural inequalities.
* Allostasis: The process of achieving stability through change, wherein the body anticipates and generates biological plans to face future needs. An illustrative example of allostatic interoception is how the brain anticipates the need for strenuous activity and prepares the muscles by increasing blood flow.
* Allostatic load: The cumulative strain on the body that results from repeated cycles of anticipatory biological changes designed to prepare the body for potential needs and stress. These changes involve necessary energy adjustments that maintain the body’s readiness for imminent biological responses.
* Allostatic overload: The amplified and dysregulated activation of anticipatory biological responses to potential needs, which lead to a state of wear and tear on the body. This increases the risk of amplified biological imbalances, which in turn trigger physical and psychological alterations.
* Predictive coding theory: A framework proposing that perception, cognition, and action are fundamentally influenced by the brain’s predictive mechanisms. The brain continually creates, infers, and updates a model of the body and environment to anticipate sensory input. Predictions about incoming sensory information are continuously compared with actual sensory input to identify and minimize prediction errors. Through active inference, the brain reduces prediction errors through actions that align the environment with its predictions. High-order areas guide anticipation and predictions, and low-order areas guide perceptual processes. High- and low-order areas feed into each other to minimize prediction errors.

The predictive allostatic interoceptive model: An active framework suggesting that the body anticipates and generates a model of the environment based on interoceptive inputs to face future needs and respond to external demands. Allostasis and interoception are crucial for maintaining physi- ological functioning and are believed to influence emotional, cognitive, and behavioral responses in humans. (14,24,26,28,33–35), such as cardiovascular and metabolic conditions (32,36), accelerated aging (34,37,38), and neuro- psychiatric disorders (27,28,39).

Critically, allostasis processes are also determined by the prediction and integration of internal bodily states known together as interoception (10,11,15). Interoception refers to the process of sensing, integrating, and modeling internal body signals, providing a moment-to-moment mapping of the body’s internal landscape. Different domains constitute the interoceptive capacities, including sensitivity (the ability to detect internal bodily signals accurately), awareness (the ability to be aware of internal sensations in the body), and meta- cognition (the ability to reflect upon and infer one’s intero- ceptive skills) (11,15–17).

Interoception involves complex interactions between afferent (ascending) and efferent (descending) pathways that regulate the internal environment. Interoception allows us to anticipate and regulate sensory signals from innervated visceral organs, including cardiovascular, respiratory, and gastrointestinal systems (40). Interoception also involves che- mosensation, changes in the endocrine system (41), immune system (42), temperature, and affective touch (43). Interocep- tive pathways are mediated and regulated by autonomic pro- cesses; integration of ascending and descending neural information (8,16,44); and visuomotor and motor control pathways (17,45–48). On the functional level, interoception influences decision making, emotion regulation, memory, and social interaction (49).

Descendent pathways of interoception, which span the autonomic, endocrine, and immune systems, can originate centrally or reflexively in response to homeostatic disruptions. The central autonomic network, including regions like the anterior cingulate cortex, insular cortex, thalamus, hypothalamus, amygdala, periaqueductal gray, parabrachial nucleus, nucleus tractus solitarius, locus coeruleus, and ventrolateral medulla, broadly impacts sympathetic and para- sympathetic autonomic control of internal states, all responses essential for survival (50–53). These pathways influence organ function, modulate immune responses, and interact with higher brain functions, thereby integrating cognitive and affective processes with bodily regulation (11,50–56).

###### THE INTEGRATED ALLOSTATIC INTEROCEPTIVE FRAMEWORK

The allostatic interoception framework refers to the anticipa- tion and modeling of external demands based on perception, integration, and regulation of inner biological states. Allostatic interoceptive processes allow for the modulation of different biological processes that lead to adaptation or disease (15,16,20,26,57) (see Figure 1A). This framework is consistent with predictive coding, which states that the brain anticipates and models external demands based on internal cues and demands (16,20,58,59). A prediction error is generated when an anticipated modeled signal differs from the actual input. Prediction errors help refine future anticipations and adapt to new challenges (47,59). Discrepancies between predicted and actual signals can trigger dysfunctional responses (7,15,16,20,45,47,60). The Bayesian brain concept extends this idea, suggesting that the brain operates as a Bayesian infer- ence machine, wherein priors—preexisting information, con- straints, or knowledge biologically determined or learned (61)—are continuously updated with new sensory evidence to optimize perception and action (62). Thus, some biological priors, such as genetically encoded modulations or developmental patterns (4), play a crucial role in shaping these predictions.

The integrated allostatic interoceptive processes are asso- ciated with brain structure and function of a set of areas known together as the allostatic interoceptive network (AIN) (47), which include the anterior midcingulate cortex, pregenual anterior cingulate cortex, subgenual anterior cingulate cortex, dorsal amygdala, ventral-anterior insula, dorsal midinsula, and dorsal posterior insula (47). Allostatic interoceptive processes are also determined by interactions between the heart, breath, and the gut-brain axis as well as by epigenetic, metabolic, autonomic, inflammatory, immunological, and microbiota mechanisms (16,44,47,63) (Supplemental Section S2).

Under normal conditions, allostatic interoceptive processes synchronize internal sensing with anticipating external re- quirements (15,44,64), regulating biological cascades to respond appropriately. However, these processes can become overwhelmed and altered, leading to misreading real and imagined external demands, inaccurate anticipation, and amplified prediction errors (15,25,27,38,44,64). These alter- ations can trigger dysregulated inflammatory, immune, meta- bolic, and microbiome cascades, thereby contributing to neurological and psychiatric disorder symptoms (65). Vaso- vagal syncope exemplifies altered regulatory and anticipatory mechanisms in response to external demands (66) (see Supplemental Section S3).

###### THE INTEGRATED ALLOSTATIC INTEROCEPTIVE FRAMEWORK IN PSYCHIATRY AND NEUROLOGY

In psychiatry, a wide array of multigenic factors is recognized, but these are nonspecific due to pleiotropy (one gene linked to multiple traits) and cannot solely account for the onset of psychiatric disorders (67). Theoretical and empirical evidence instead points to complex interactions between environmental and biological factors as being fundamental to psychiatric diseases. Disruptions in anticipatory and regulatory mecha- nisms, particularly predictive allostatic interoceptive pro- cesses, are crucial in various psychiatric disorders, especially anxiety and depression. Evidence from interventions that target these processes further underscores their significance in the development of common psychiatric conditions (see Supplemental Section S4 and Figure 2) (68–73).

###### Anxiety

Anxiety is a complex emotional response encompassing fear, apprehension, and worry. It often arises in response to stress or perceived threats, whether real or imagined (74). Anxiety is an adaptative, natural human experience. When chronic or overwhelming, however, anxiety may interfere with daily functioning and lead to anxiety disorders (74). Anticipatory allostatic interoceptive processes are associated with anxiety symptoms and disorders (27,75).

Previous studies suggest heightened allostatic load in pa- tients with anxiety disorders like panic and generalized anxiety (26). This encompasses increases in proinflammatory cyto- kines, sympathetic dominance, altered HPA axis function, and elevated biogenic amines during fear reactions (24,33,36). Dysfunctions in the anterior insula and anterior cingulate cor- tex, key regions for allostatic processing, have been tied to

anxiety disorders (76). Allostatic overload manifests as symp- toms like autonomic discharges in panic disorders, appre- hensive anticipation, and somatic symptoms in generalized anxiety disorders (26,76,77).

Anxiety is also linked to heightened interoception and misinterpretation of bodily signals, causing symptoms like overmonitoring of physical responses, tension, tiredness, insomnia, heightened startle reflexes, and anxious affect (27,75,78). The discrepancy between expected and actual bodily signals can perpetuate anxiety and maintain a chronic stress response (60). Such alterations have been observed across panic disorders, phobias, and generalized anxiety dis- orders (27,75,78–81).

Although the evidence is not yet conclusive (77), some studies have indicated brain-heart desynchronization, altered heartbeat evoked potential (HEP) index (77,79,82), and heightened cardiac and respiratory interoceptive sensitivity in anxiety (83) and obsessive-compulsive disorder (77,80,84). This increased sensi- tivity may predispose individuals to anxiety disorders by leading them to interpret typical cardiac and respiratory symptoms as catastrophic and triggering different anxiety symptoms.

###### Depression

Depression is a mental health disorder characterized by persistent feelings of sadness, anhedonia, depressive thoughts, motor alterations, tiredness, fatigue, changes in appetite and sleep patterns, and alteration of daily functioning (85). Previous studies have studied depression as an allostatic load disorder (15,17,45,46,86) marked by irregularities in various biological processes (87), including metabolic imbal- ances (88) with abnormal HPA axis activity, proinflammatory states (10), and skewed autonomic processes (45,46,86). Chronic stress, a primary driver of allostatic load and depres- sion risk, induces changes in emotion- and memory-regulating brain structures like the hippocampus and amygdala (45,46).

Numerous studies have also indicated anomalies in intero- ceptive processing in depression, which often manifest as feelings of bodily disconnection or misjudgment of internal states (10,45,89). Evidence suggests altered interoceptive awareness in those patients (90–92). These interoceptive dis- turbances relate to emotion dysregulation and a negative attentional bias (93). Additionally, these deficits are correlated with structural and functional changes in the insula and other brain regions vital for interoceptive awareness (90,94).

Interoceptive changes can influence the allostatic system, contributing to depressive symptoms (45,46,95). Persistent ru- minations and abulia have been linked to disruptions in cardiac and gastric interoceptive feedback, impacting anticipatory allo- static processes (45,46,94,95). Depression’s hallmark symp- toms, such as anhedonia and fatigue, are related to heightened body awareness, reduced body trust, and attentional issues (92,93). Recent reviews indicate that moderate to severe depression is tied to interoceptive alterations affecting decision making and emotion regulation, regardless of comorbidities or treatments like selective serotonin reuptake inhibitors (89).

###### Explanatory Models

The connections between the allostatic interoceptive frame- work and psychiatric disorders are primarily based on correlational studies (96), which are valuable in cognitive neuroscience despite potential confounders and challenges in reproducing causal models (96). Association studies sup- port the framework’s relevance in depression and anxiety. In depression, the locked-in brain hypothesis suggests ineffi- cient energy regulation and insensitivity to prediction errors, leading to mood changes, reduced motivation, and difficulty engaging in activities (45). This is linked to changes in the subgenual anterior cingulate cortex, which regulates auto- nomic control and energy, contributing to depressive symptoms (45,97). Temporary changes in behaviors like eating, sleeping, or exercising can also lead to transient changes in energy regulation, thereby contributing to episodic depression (45).

Anxiety involves unadjusted allostatic interoceptive pro- cesses, altered predictions, and dysregulated energy expen- diture (20,60,77,98,99). This leads to overactivation of biological processes in response to perceived threats (99). Persistent stress can disrupt the HPA axis, elevate cortisol levels, and damage mood-regulating brain areas (18,99,100). Dysregulated interoceptive mechanisms exacerbate anxiety by leading to misinterpretation of bodily cues, which leads to emotional distress and defensive behaviors (18). This is mediated by the altered activity and dynamics of the AIN, salience, and executive control networks (14,45–47,101).

###### PREDICTIVE ALLOSTATIC INTEROCEPTION IN NEUROLOGICAL DISORDERS

Studies of allostatic interoception in neurological conditions have been mainly focused on neurodegenerative disorders (Table 1; Tables S1 and S2). Allostatic overload can heighten sensitivity to future stressors, resulting in a state of hypervig- ilance (24). Such a state can induce chronic stress, leading to inflammation, metabolic imbalances, and increased neurotox- icity, which in turn can cause neural damage. Over time, these detrimental effects may contribute to cognitive and behavioral decline and raise the risk of developing dementia (8,24,102) (Figure 2).

###### CONTRASTS BETWEEN THE ALLOSTATIC INTEROCEPTIVE PROCESSES AND OTHER MODELS OF DISEASE

The allostatic interoceptive framework offers a unique perspective compared with the diathesis-stress (128) and traditional homeostatic models (129). The diathesis-stress model links inherent biological vulnerabilities and external stressors to disorders, while the homeostatic model focuses on maintaining internal balance affected by predispositions and external factors. However, these models have limitations, such as in depression related to external stressors and spo- radic AD (105) and in failing to account for dynamic biological responses to various exposures (14,130).

In contrast, the allostatic interoceptive framework empha- sizes the dynamic interaction between biological factors and external threats based on internal sensing processes (17,47,64). This approach is consistent with enactive frame- works that view disease as changes in interactions between biological agents and the environment rather than merely as brain diseases (131). This enhances the understanding of multietiologic diseases from dimensional and transdiagnostic perspectives and helps to better explain altered cognitive and behavior patterns, consistent with frameworks such as the Research Domain Criteria and the Hierarchical Taxonomy of Psychopathology (Box 2).

###### NEW PERSPECTIVES OF THE ALLOSTATIC INTEROCEPTIVE FRAMEWORK IN PSYCHIATRY AND NEUROLOGY

The allostatic interoceptive framework opens new research avenues in psychiatry and neurology by examining how pre- dictive allostatic interoception processes are crucial during critical neurodevelopmental periods. Alterations in these pro- cesses have been linked to conditions like autism (132), attention disorders (132–135), depression, anxiety (8,11,15,102,136), and neurodegenerative diseases (8,44,47,63,109). Current research highlights gaps, such as the impact of neurodevelopmental changes and external threats, on these mechanisms (Box 3).

The proposed framework also interacts with brain spatio- temporal dynamics, where different time scales affect inter- oception and cognitive processes (137,138). For example, in depression, altered time scale processing affects anticipatory and interoceptive functions, leading to symptoms like reduced speed in processing prediction errors (139). Similarly, besides the allostatic interoceptive failure in bvFTD (63,102,109,111), patients with bvFTD exhibit impaired brain temporal dynamics with 2-fold transient altered temporal states leading to slow (apathy) or fast (disinhibition) neural states (44). Moreover, conditions like autism and schizophrenia (140,141) show de- viations in predictive oscillatory patterns that affect neural synchronization and responses to environmental challenges

(140,141) (Box 4). Despite the mentioned findings (140,141), current evidence on the role of an allostatic interoceptive framework on other disease models, including autism and schizophrenia, is still under debate (140,141). Future research should focus on generating contrastive and comparative studies on how the allostatic interoceptive framework and spatiotemporal approaches better explain the neurobiology and clinical manifestations observed in psychiatric disorders (for a further review of new perspectives of the allostatic interoceptive framework, see Supplemental Section S5).

###### DISCUSSION

The current scoping review highlighted the role of allostatic and interoceptive processes in integrating environmental and biological factors under normal and neuropsychiatric condi- tions. We gathered evidence showing how these processes are altered and directly impact clinical and neurocognitive profiles in depression, anxiety, AD, and FTD, as well as other

neuropsychiatric disorders (see Tables S1 and S2). Our review provides support for a more comprehensive understanding of multilevel biological alterations observed in psychiatric and neurological disorders in this model, compared with other approaches, such as the diathesis-stress model.

Our review identified proposed pathophysiological mecha- nisms altered in allostatic interoceptive processes that contribute to psychiatric and neurological disorders. These include disruptions in energy regulation, unadjusted prediction processes, impaired generation of internal and external models in response to environmental demands, and altered brain- biological systems underlying allostatic interoceptive pro- cesses in the context of neurodegeneration. These alterations stem from regulatory processes determined by the AIN and disrupted energy regulation and predictive processes at various biological levels, leading to cognitive and behavioral changes associated with clinical repertoires in psychiatry and neurology.

Current findings recognize that allostatic interoceptive dysregulations are intertwined with the cognitive, affective, and

emotional symptoms of psychiatric (45,46) and neurological conditions (102,109,111). Core evidence in depression and bvFTD support this view. Depression has been described as a systemic dysregulation of the body’s internal mechanisms in response to stress (90,93). Individuals with depression often display altered interoceptive processes. These alterations are associated with specific dysexecutive and emotional dysre- gulation in patients with depression (45,90). In bvFTD research, the alteration of allostatic interoceptive processes, as gauged by HEP modulation and altered connectivity in AIN, has been associated with executive dysfunction, behavioral distur- bances, and impaired emotion and social cognition (102,109,111).

Temporary changes in allostatic interoceptive processes and their impacts on biological cascades could explain the episodic symptomatic phases of psychiatric disorders, particularly in the presence of intense external demands (142).

In contrast, in neurodegenerative disorders, a more chronic, persistent, and accumulated dysregulation of the allostatic interoceptive mechanisms that affect the biology-environment interactions is expected (8,59). These dysfunctions could affect other mechanisms, including oxidative stress processes, mitochondrial breakdown, and altered protein recycling and aggregation (2,8,34,37,63,102,143). The precise mechanisms that lead to neurodegeneration or the temporary imbalances observed in psychiatric conditions remain unclear. New studies are required to explore the potential biological and environmental mechanisms that trigger temporary or chronic changes in psychiatric and neurological conditions.

###### NOVELTY OF THIS STUDY

Current evidence on an allostatic interoceptive framework for psychiatry and neurology faces essential caveats. Although some studies have analyzed combined alterations in allostatic interoceptive processes associated with behaviors (8,59,64) and psychiatric (45,46) and neurological (8,16,63,102,109,111,144) disorders, most research has focused on interoceptive impairments or allostatic overload in isolation. With some exceptions (102,109,111), studies have also focused on specific disorders, lacking dimensional alter- ations observed in psychiatric and neurological disorders. The current study bridges these gaps by analyzing the relationship between allostatic interoceptive mechanisms and biological, neurocognitive, and clinical changes in psychiatric and neurological conditions. It transcends traditional categorical approaches, integrating dimensional frameworks in neuro- psychiatry. It also shows how these processes evolve across the life span, impacting brain health, and interact with brain spatiotemporal dynamics.

New studies should implement specific metrics to capture allostatic and interoceptive processes in psychiatric and neurological disorders. These metrics should include allostatic load indices (27), which measure various biological levels affected by allostatic load processes, and assessments of interoception sensitivity and awareness (102,145,146). As- sessments of brain activity related to interoceptive processes, such as the HEP and the AIN dynamics, and their interaction with other networks could reveal the role of integrated allo- static interoceptive processes in these disorders (45,109). This

is consistent with recent calls for including interoception as a critical construct in neuropsychiatric disorders (54,134).

Evaluating multiple biological levels associated with allo- stasis and interoception will enhance the understanding of intervention impacts on reducing allostatic interoceptive overload (15). Nonpharmacological interventions focusing on respiration, body scanning, and relaxation techniques have shown promise in reducing allostatic interoceptive load, thus alleviating symptoms of anxiety, depression, and somatic is- sues (41,147,148).

Current studies have begun to explore the impact of spatiotemporal brain dynamics on regulating allostatic intero- ceptive processes (44). Different biological processes, including interoception, exteroception, and cognition, occur at varying spatiotemporal dynamics (44,139,149,150). New research could investigate spatiotemporal brain dynamics in altered allostatic interoceptive processes and associate these metrics with specific spatiotemporal brain patterns using whole-brain modeling and other relevant methods.

###### LIMITATIONS OF THE CURRENT FRAMEWORK

Our research underscores the significance of allostatic inter- oceptive processes in psychiatry and neurology, but significant challenges remain. Few studies have combined the effects of allostasis and interoception on these disorders, with most examining them separately. This has resulted in an under- standing based largely on correlations, highlighting the need for comprehensive studies that focus on longitudinal in- teractions between the environment and biology. There is also a notable lack of multilevel analyses, causal modeling, and complexity approaches in existing research.

###### CONCLUSIONS

This review emphasizes the crucial role of allostatic intero- ceptive processes in managing responses to environmental and biological interactions, leading to adaptive or dysregulated outcomes in psychiatric and neurological disorders. We pro- vide evidence of allostatic and interoceptive changes in con- ditions such as anxiety, depression, AD, and bvFTD. These changes can predict various physiological, neurocognitive, and clinical features across disorders. Advancing research in allostatic interoception is vital for developing more in-depth studies on its role in brain health and disease, leading to the implementation of new insights in clinical settings and personalized treatment strategies.

#### Khalsa, S. S., et al. (2018). "Interoception and Mental Health: A Roadmap." Biological Psychiatry: Cognitive Neuroscience and Neuroimaging 3(6): 501-513.

###### Abstract

Interoception refers to 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. Interoceptive signaling has been considered a component process of reflexes, urges, feelings, drives, adaptive responses, and cognitive and emotional experiences, highlighting its contributions to the maintenance of homeostatic functioning, body regulation, and survival. Dysfunction of interoception is increasingly recognized as an important component of different mental health conditions, including anxiety disorders, mood disorders, eating disorders, addictive disorders, and somatic symptom disorders. However, a number of conceptual and methodological challenges have made it difficult for interoceptive constructs to be broadly applied in mental health research and treatment settings. In November 2016, the Laureate Institute for Brain Research organized the first Interoception Summit, a gathering of interoception experts from around the world, with the goal of accelerating progress in understanding the role of interoception in mental health. The discussions at the meeting were organized around four themes: interoceptive assessment, interoceptive integration, interoceptive psychopathology, and the generation of a roadmap that could serve as a guide for future endeavors. This review article presents an overview of the emerging consensus generated by the meeting.

###### Intro

Interoception refers collectively to the processing of internal bodily stimuli by the nervous system. Parcellation of the nervous system’s processing of sensory signals into inter- oception, proprioception, and exteroception began more than 100 years ago (1), although it was predated by interest in linking body–brain interactions with conscious experience (2,3). Scientific interest in interoception has fluctuated (Figure 1A). During the 1980s, biological psychiatry was inundated with observations of interoceptive disturbances in panic disorder (4–7), although the trend receded after it became clear that the etiological mechanism was broader than a single molecular receptor target (8). Recent years have witnessed a surge of interest on the topic of inter- oception due in part to findings highlighting its integral role in emotional experience, self-regulation, decision making, and consciousness. Importantly, interoception is not limited to conscious perception or even unique to the human spe- cies. From this perspective, interdisciplinary efforts to un- derstand different features of interoception have been essential for advancing progress in cognitive and clinical neuroscience (Figure 1B).

###### ASSESSMENT

###### Body Systems of Interoception

Interoceptive processing occurs across all major biological systems involved in maintaining bodily homeostasis, including the cardiovascular (9,10), pulmonary (11), gastrointestinal (12,13), genitourinary (14), nociceptive (15), chemosensory (16), osmotic (17), thermoregulatory (18), visceral1 (19), immune (20,21), and autonomic systems (22,23) (Table 1). There has been relatively little focus overall on the integration across bodily systems; thus, it is not surprising that most in- vestigations of the topic have been siloed within distinct research areas or scientific disciplines [see (24,25) for note- worthy exceptions].

###### Features of Interoception

Interoception is not a simple process but rather has several facets (26). The act of sensing, interpreting, and integrating information about the state of inner body systems can be related to different elements such as interoceptive attention, detection, discrimination, accuracy, insight, sensibility, and self-report (Table 2). However, most interoceptive processes occur outside the realm of conscious awareness. Consciously experienced elements are measured clinically via subjective report, and there are few observable interoceptive signs (e.g., heart rate, respiration rate, pupillary dilation, flushing, perspi- ration, piloerection, nociceptive reflexes) (Table 3). Experi- mental approaches can quantify different body systems and features of interoceptive processing. Nevertheless, these measures are only partially overlapping and likely reflect somewhat distinct neural processes (27). Access to the full range of interoceptive signals often involves invasive ap- proaches, which tend to elicit physiological perturbations and index more objectively measurable features (28). However, many insights have been gained by the application of nonin- vasive approaches within neuroscience and psychological assessment contexts (29) (see “Eavesdropping on Brain–Body Communication” section below).

###### Importance of an Interoceptive Taxonomy

There is no generally agreed-on taxonomy for interoception science. Variable definitions have made it difficult to identify the features under investigation, let alone evaluate the quality of the findings. Based on the number of physiological systems involved, it could be questioned whether the terms “inter- oception” and “interoceptive awareness” are too broad. Interoceptive awareness is an umbrella term that was first used to describe a self-report subscale (30), but it has subsequently been used to encompass any (or all) of the different inter- oception features accessible to conscious self-report. Re- searchers from different fields developed definitions that only partially overlapped, reflecting the need for operationalization in neuroscience (31,32) and clinical practice (33,34). Here we develop a more coherent nomenclature for its various com- ponents (Table 2), mirroring developments in other fields, especially pain (35). One key aspect is the importance of dis- tinguishing sensation (i.e., the raw signals conveyed by bodily sensors) from perception (36,37). We return to this theme below.

###### Multilevel Investigations

While interoception research to date has typically focused on single organ systems, an expanded approach that assesses multiple interoceptive organ systems and/or elements is needed. Examples include targeting numerous interoceptive features simultaneously and employing different tasks that converge on the same feature (e.g., combining top-down assessments of interoceptive attention with bottom-up perturbation approaches in the same individual) (Figure 2A).

###### Sensing Perturbations

The inner and outer worlds of the body constantly fluctuate. The nervous system monitors these environmental changes and responds adaptively in order to maintain a homeostatic balance and promote survival. Because psychiatric disorders often promote or reflect the development of chronic ho- meostatic and allostatic disturbances (38), there is a need for methods capable of eliciting homeostatic perturbations in controlled settings, especially those assessing subjective and behavioral responses to valence and arousal deviations. However, interoception is not simply about afferent pro- cessing. The brain’s constant monitoring of the body occurs in service of optimizing homeostatic regulation. This efferent limb is understudied (39), and paradigms that can effectively measure visceromotor outputs will be critical to establish sensitive assays of dysfunctional interoception and homeo- static regulation (e.g., detection of visceromotor-efferent neural signals controlling baroreflex sensitivity during modu- lation of visceral-afferent input by sympathetic drugs). The reliability and validity of methods should be rigorously established.

###### INTEGRATION

###### Interoception and Domain Specificity Within the Brain

There are fundamentally differing ways to interpret the evolu- tion of brain and body signaling in humans. The processing of interoceptive input could be domain specific, with modular processing occurring in specialized, encapsulated neural cir- cuits [e.g., cardiac, respiratory, urinary, genital, chemical, hormonal; see (40) for a review of domain specificity] or func- tionally coupled (e.g., cardiorespiratory, genitourinary, che- mohormonal) and integrated within a single neural circuit. Understanding the adaptive origins and functions of intero- ceptive domain specificity (if present) could tell us how the implementation and deployment of interoceptive signals by the nervous system contributes to disordered mental health. Because interoceptive signaling involves afferent and efferent inputs across multiple hierarchies within the autonomic and central nervous systems, identifying where and how informa- tion processing dysfunctions negatively affect mental health represents a challenging problem.

###### Neural Pathways of Interoception

Several pathways have been implicated in the neural pro- cessing of interoceptive signals, beginning with a rich interface between autonomic afferents and the central nervous system. Relay pathways involve primarily spinal, vagal, and glossopharyngeal afferents, with multiple levels of processing and integration in autonomic ganglia and spinal cord (10,19,22,41). Several brainstem (nucleus of the solitary tract, parabrachial nucleus, and periaqueductal gray), subcortical (thalamus, hypothalamus, hippocampus, and amygdala), and cortical regions (insula and somato- sensory cortices) represent key afferent processing regions (22,42,43). A complementary set of regions involved in visceromotor actions represents key efferent processing regions, including the anterior insula, anterior cingulate, subgenual cingulate, orbitofrontal, ventromedial prefrontal, supplementary motor, and premotor areas (44–46). It is noteworthy that these neural regions coincide closely with other sensory processing systems, especially the nocicep- tive and affective systems. The degree to which these represent distinct or overlapping systems is currently unclear.

###### Linking Paradigms Across Units of Analysis

A particular challenge when examining interoception is the fact that afferent sensory signals are integrated on several levels (peripherally, within the spinal cord, and supraspinally) to form sets of interoceptive maps across different body systems. The brain appears to integrate information representing particular states of multiple systems simultaneously (cardiac, respiratory, chemical, hormonal, nociceptive, etc.) (41), and it is imperative to be able to model and comparatively evaluate such map- pings (Figure 2B). This poses many challenges. One approach might be to apply measures that assess multiple organ sys- tems or interoceptive features simultaneously [see (42,47,48)] or to record activity across the brain, spinal cord, and peripheral organs (49). However, it is also possible that multisystem as- sessments may reduce specificity for certain disorders and therefore may be unnecessary. For example, some patients with panic disorder may experience dyspnea but not palpita- tions. Localizing and then targeting the dysfunctional intero- ceptive domain would become more useful than broad multisystem interventions.

###### Timing and Rhythm in Interoceptive Circuits

The physiological timescales and amplitudes of interoceptive signaling vary dramatically (e.g., heart rate [0.5–3.3 Hz], res- piratory rate [0.08–1 Hz], gastric contractility [0.05–0.1 Hz], urinary frequency [0.000045–0.00012 Hz]), with even slower changes in humoral mediators (50) (Figure 2C, D). They also vary across individuals, and over the life span (e.g., increased heart rates in infants/children). Despite the variance, the brain tracks such changes in similar subregions, including the insula, somatosensory cortices, cingulate, amygdala, thal- amus, and brainstem (42,43,51–53). Temporal synchrony or dyssynchrony between these systems may affect interocep- tive experiences, affect, and behavior, although the exact mechanisms require further study (54). Repetitive events are

another important element for learning, and while there are numerous classic studies on visceral learning at the periph- eral organ system level (55,56), we know little about the central mapping of learned visceral memories, especially in psychiatric disorders (57).

###### PSYCHOPATHOLOGY Interoceptive Psychopathology

Several conceptual and heuristic models have linked dys- functions of interoception to mental health conditions. Spe- cifically, mood and anxiety disorders have been linked to failures to appropriately anticipate changes in interoceptive states (97). Eating disorders show behavioral and neural

abnormalities in interoceptive processing, particularly in the context of caloric anticipation (72,98–100), although it remains unclear whether this is due to altered afferent signaling, altered central sensory processing, abnormal temperament, and/or metacognition. Drug addiction, another condition marked by interoceptive disturbances, has an overlapping neural circuitry and abnormal responses to interoceptive cues (101–104). Interoceptive dysfunction also likely plays a role in conditions such as posttraumatic stress disorder and somatic symptom disorders (33). Other disorders also have interoceptive symp- tom overlap; however, the specific feature involved may differ according to the disorder or affected individual [e.g., chronic pain (105,106), Tourette’s syndrome and other tic disorders, borderline personality disorder, obsessive-compulsive disor- der, autism spectrum disorder (107), functional developmental disorders (108)]. Table 3 lists diagnostic symptoms and clinical signs indicative of interoceptive dysfunction in several psychi- atric disorders. Conditions that have a psychiatric component include fibromyalgia, chronic fatigue syndrome, irritable bowel syndrome, and functional disorders within medicine (e.g., noncardiac chest pain, functional dysphagia) as well as certain medical disorders (e.g., gastroesophageal reflux, asthma).

Alternatively, one can use a dimensional psychopathology approach to link processes underlying interoceptive dysfunc- tion to psychiatric disorders. Transdiagnostic perspectives such as those provided by the Research Domain Criteria (109) may be particularly helpful in identifying the potential role played by various interoceptive processes because several of these might not be readily identified at the symptom report

level relied on by clinicians and, accordingly, might not have entered into the diagnostic specifications for DSM. This would allow for identification of mechanistic dysfunctions across units of analyses and might bridge the biological gap in current diagnostic classification frameworks by directly probing the links between physiological and psychological dysfunctions. Interoceptive investigations in mental health populations might reveal evidence of 1) attentional bias (e.g., hypervigilance), 2) distorted physiological sensitivity (e.g., blunted or heightened magnitude estimation in response to a perturbation), 3) cognitive bias (e.g., catastrophizing in response to an antici- pated stimulus), 4) abnormal sensibility (e.g., tendency to label one’s experiences in a particular way), and 5) impaired insight (e.g., poor confidence–accuracy correspondence on a task).

Determining whether interoceptive processes are a cause or consequence of developmental psychopathology, and which factors might affect this development (such as early life stress or pain), will be an important area for future research. Such studies may benefit from the examination of younger (110,111) or older (112,113) samples and premorbid identification and longitudinal tracking of individuals (114). Investigating the role of social cognition/theory of mind in clinically relevant intero- ceptive inference generation represents another ripe opportu- nity (115).

Interoceptive Tests and/or Biomarkers

Because interoception is fundamentally a process linking body and brain, it is conceivable that objective measures of this process could serve as biological indicators of disease states. However, there is currently limited evidence for interoceptive predictors of diagnostic, prognostic, or treatment status (33,116,117). Biomarkers, such as those derived from neuro- imaging or blood measurements, should be sensitive, specific, and unaffected by cognitive and emotional influences. How- ever, it seems conceivable that the most clinically sensitive interoceptive measures might derive from probes that perturb physiological functions to engage specific metacognitive be- liefs and/or expectations about bodily states. Such measures could facilitate differential diagnosis testing by revealing the presence of interoceptive dysfunction of biological (within a physiological system or systems), psychological (e.g., overly precise expectations about bodily states), or metacognitive (e.g., discrepant self-efficacy beliefs with regard to homeo- static/allostatic regulation) origin (37). This approach could be seen as analogous to a cardiac stress test, such that adequate engagement of the system under ecologically valid conditions is required in order to measure its dysfunction.

The most common application of interoceptive evaluation in current clinical practice occurs during interoceptive exposure psychotherapy for panic disorder (118). During this procedure, patients self-induce varieties of interoceptive symptoms via low-arousal manipulations (e.g., hyperventilation, performing jumping jacks, spinning in a chair, breathing through a straw) while the clinician monitors their subjective distress level. Unfortunately these manipulations often fail to adequately reproduce the fear response, possibly because the patient retains full control over the stimulation (the patient can quit at any time) and the perturbation remains predictable with mini- mal uncertainty, raising the question of whether modulating

both physiological homeostasis and the perception of controllability might further improve the ecological validity and efficacy of interoceptive exposures (119). A test to verify suc- cessful interoceptive exposure therapy for panic disorder in- volves completion of a standardized behavioral avoidance paradigm (120). In this setting, the degree of tolerance to being enclosed in a small dark chamber for 10 minutes might provide behavioral evidence verifying tolerance to triggers of intero- ceptive dysregulation. There is also experimental evidence that pharmacological interoceptive exposure therapy can reduce anxiety disorder symptom severity either as monotherapy (7,121–123) or as an augmentative approach (124). However, there are few studies of these procedures to date, the impact of such interventions on longer term outcomes (e.g., 6 months or beyond) are unknown, and none of these approaches has translated into clinical practice.

###### Current Treatments Relevant to Interoception

Among the currently available therapies with an interoceptive basis are pharmacotherapies directly modulating interoceptive physiology. Examples include adrenergic blockade (e.g., pro- pranolol) or agonism (e.g., yohimbine), stimulants (e.g., methyl- phenidate), benzodiazepines, muscle relaxants, and opioids. A second example is cognitive behavioral therapy with exposure and response prevention to reverse or attenuate conditioned fears or form new learned associations. It is helpful in ameliorating cognitive biases in numerous disorders, including depression, obsessive-compulsive disorder, posttraumatic stress disorder (specifically prolonged exposure therapy), irritable bowel syn- drome, and chronic pain. Interoceptive exposure is a special example demonstrated to be effective in specific disorders (especially panic disorder). Behavioral activation therapy for depression sometimes includes exposure to experiences with positive interoceptive value. A third example is capnometry- assisted respiratory training. Based on the assumption that sustained hypocapnia resulting from hyperventilation is a key mechanism in the production and maintenance of panic, carbon dioxide capnography-assisted therapy aims to help patients voluntarily increase end-tidal partial pressure of carbon dioxide and tolerate physiological variability associated with panic at- tacks (125,126). As a fourth example, mindfulness-based stress reduction, yoga, and other meditation/movement-based treat- ments may be aimed at improving metacognitive awareness of mind–body connections by systematically attending to sensa- tions of breathing, cognitions, and/or other modulated body states (e.g., muscle stretching) (127).

###### Interoceptive Treatments on the Horizon

Several emerging technologies may have relevance for inter- oception and mental health, including Floatation-REST (reduced environmental stimulation therapy) and perturbation approaches.

###### Floatation-REST.

This intervention, which systematically attenuates exteroceptive sensory input to the nervous system, also appears to noninvasively enhance exposure to intero- ceptive sensations such as the breath and heartbeat (128). Preliminary data suggest that a single 1-hour session has a short-term anxiolytic and antidepressant effect in patients with

###### ROADMAP

###### The Road Ahead

Beyond the issues outlined previously, progress in determining the relevance of interoception for mental health relies on emphasizing the features that distinguish it from other sensory modalities. Interoception seemingly involves a high degree of connectivity within the brain (135). It appears to be tightly linked to the self and survival through homeostatic mainte- nance of the body, and by helping us to represent how things are going in the present with respect to the experienced past and the anticipated future. These computations may depend on what has occurred to shape the body’s internal landscape, and it is in this regard that learning, and malleability of repre- sentations over time, could play important roles.

The conceptual framework for investigating interoception may overlap with other processes, including emotion (136) and pain (137), because each is integral for maintaining bodily homeostasis. An important endeavor may involve the identification of which neural systems for interoception, emotion, cognition, and pain are overlapping, interdigitating, or even possibly identical. Additional effort is needed to define the neurophysiological nomenclature, core criteria, common features, developmental aspects, modulating fac- tors, functional consequences, and putative pathophysio- logic mechanisms of interoception in mental health disorders.

The current work offers some conceptual distinctions and some mutually agreed-on terminology, with many others still needed. Several low-hanging fruits, as well as promising emerging technologies and tools, have been mentioned. Further empirical work will be critical to delineate how inter- oception can be mapped to mental health measures, models, and approaches, and benchmarks for success/failure need to be established. Models of interoceptive processing that improve on the traditional stimulus, sensorimotor processing, and response function concepts have been described, but these models remain theoretical and await further testing. Therefore, the current document is best viewed as a work in progress.

#### Brewer, R., et al. (2016). "Alexithymia: a general deficit of interoception." R Soc Open Sci 3(10): 150664.

Alexithymia is a sub-clinical construct, traditionally characterized by difficulties identifying and describing one's own emotions. Despite the clear need for interoception (interpreting physical signals from the body) when identifying one's own emotions, little research has focused on the selectivity of this impairment. While it was originally assumed that the interoceptive deficit in alexithymia is specific to emotion, recent evidence suggests that alexithymia may also be associated with difficulties perceiving some non-affective interoceptive signals, such as one's heart rate. It is therefore possible that the impairment experienced by those with alexithymia is common to all aspects of interoception, such as interpreting signals of hunger, arousal, proprioception, tiredness and temperature. In order to determine whether alexithymia is associated with selectively impaired affective interoception, or general interoceptive impairment, we investigated the association between alexithymia and self-reported non-affective interoceptive ability, and the extent to which individuals perceive similarity between affective and non-affective states (both measured using questionnaires developed for the purpose of the current study), in both typical individuals (n = 105 (89 female), mean age = 27.5 years) and individuals reporting a diagnosis of a psychiatric condition (n = 103 (83 female), mean age = 31.3 years). Findings indicated that alexithymia was associated with poor non-affective interoception and increased perceived similarity between affective and non-affective states, in both the typical and clinical populations. We therefore suggest that rather than being specifically associated with affective impairment, alexithymia is better characterized by a general failure of interoception.

#### Dunn, B. D., et al. (2010). "Listening to your heart. How interoception shapes emotion experience and intuitive decision making." Psychol Sci 21(12): 1835-1844.

Theories proposing that how one thinks and feels is influenced by feedback from the body remain controversial. A central but untested prediction of many of these proposals is that how well individuals can perceive subtle bodily changes (interoception) determines the strength of the relationship between bodily reactions and cognitive-affective processing. In Study 1, we demonstrated that the more accurately participants could track their heartbeat, the stronger the observed link between their heart rate reactions and their subjective arousal (but not valence) ratings of emotional images. In Study 2, we found that increasing interoception ability either helped or hindered adaptive intuitive decision making, depending on whether the anticipatory bodily signals generated favored advantageous or disadvantageous choices. These findings identify both the generation and the perception of bodily responses as pivotal sources of variability in emotion experience and intuition, and offer strong supporting evidence for bodily feedback theories, suggesting that cognitive-affective processing does in significant part relate to "following the heart."

# Contributions of Stress to Mental Health, Eating Disorders, & Interoceptive Deficits

## Stress in Interoceptive Awareness

#### Santamaría-García, H., et al. (2024). "Allostatic Interoceptive Overload Across Psychiatric and Neurological Conditions." Biol Psychiatry.

Emerging theories emphasize the crucial role of allostasis (anticipatory and adaptive regulation of the body's biological processes) and interoception (integration, anticipation, and regulation of internal bodily states) in adjusting physiological responses to environmental and bodily demands. In this review, we explore the disruptions in integrated allostatic interoceptive mechanisms in psychiatric and neurological disorders, including anxiety, depression, Alzheimer's disease, and frontotemporal dementia. We assess the biological mechanisms associated with allostatic interoception, including whole-body cascades, brain structure and function of the allostatic interoceptive network, heart-brain interactions, respiratory-brain interactions, the gut-brain-microbiota axis, peripheral biological processes (inflammatory, immune), and epigenetic pathways. These processes span psychiatric and neurological conditions and call for developing dimensional and transnosological frameworks. We synthesize new pathways to understand how allostatic interoceptive processes modulate interactions between environmental demands and biological functions in brain disorders. We discuss current limitations of the framework and future transdisciplinary developments. This review opens a new research agenda for understanding how allostatic interoception involves brain predictive coding in psychiatry and neurology, allowing for better clinical application and the development of new therapeutic interventions.

## Stress in Physical & Mental Health

Feletti ACES

# Neurobiology of Binge Eating Disorder

#### Frank, G. K. W., et al. (2019). "The Neurobiology of Eating Disorders." Child Adolesc Psychiatr Clin N Am 28(4): 629-640.

Eating disorders are severe psychiatric illnesses with a typical age of onset in adolescence. Brain research in youth and young adults may help us identify specific neurobiology that contributes to onset and maintenance of those disorders. This article provides a state-of-the-art review of our current understanding of the neurobiology of anorexia nervosa and bulimia nervosa. This includes brain structure and function studies to understand food restriction, binge-eating or purging behaviors, cognitive and emotional factors, as well as interoception. Binge-eating disorder and avoidant restrictive food intake disorder are also discussed, but the literature is still very small.

#### Martin, E., et al. (2019). "Interoception and disordered eating: A systematic review." Neurosci Biobehav Rev 107: 166-191.

Deficits in interoception have been associated with disordered eating but there has been no systematic review of whether the interoceptive deficits are observed across all types of disordered eating and across interoceptive modalities. There has also been no evaluation of whether deficits in interoception play a causal role in the development of disordered eating. Nor has there been a review of the moderating/mediating factors of the relationship between interoception and disordered eating. To address these gaps we conducted a systematic review using PRISMA guidelines. 104 studies with 32883 participants were included. Deficits in interoception were observed across disordered eating types and interoceptive modalities suggesting that interoception may constitute a transdiagnostic feature of disordered eating. There is currently limited evidence on the causal role of interoception in the development of disordered eating and no studies have formally analysed the moderators/mediators. Future mechanistic research examining particular dimensions of interoception will provide insights into the specific interoceptive deficits associated with disordered eating and could lead to the development of improved therapies.

#### Frank, G. K. (2015). "Advances from neuroimaging studies in eating disorders." CNS Spectr 20(4): 391-400.

Over the past decade, brain imaging has helped to better define eating disorder-related brain circuitry. Brain research on gray matter (GM) and white matter (WM) volumes had been inconsistent, possibly due to the effects of acute starvation, exercise, medication, and comorbidity, but newer studies have controlled for such effects. Those studies suggest larger left medial orbitofrontal gyrus rectus volume in ill adult and adolescent anorexia nervosa after recovery from anorexia nervosa, and in adult bulimia nervosa. The orbitofrontal cortex is important in terminating food intake, and altered function could contribute to self-starvation. The right insula, which processes taste but also interoception, was enlarged in ill adult and adolescent anorexia nervosa, as well as adults recovered from the illness. The fixed perception of being fat in anorexia nervosa could be related to altered insula function. A few studies investigated WM integrity, with the most consistent finding of reduced fornix integrity in anorexia and bulimia nervosa-a limbic pathway that is important in emotion but also food intake regulation. Functional brain imaging using basic sweet taste stimuli in eating disorders during the ill state or after recovery implicated repeatedly reward pathways, including insula and striatum. Brain imaging that targeted dopamine-related brain activity using taste-reward conditioning tasks suggested that this circuitry is hypersensitive in anorexia nervosa, but hyporesponsive in bulimia nervosa and obesity. Those results are in line with basic research and suggest adaptive reward system changes in the human brain in response to extremes of food intake-changes that could interfere with normalization of eating behavior.

# Interoception in Craving and Reward-Based Decision-Making

#### Kim, J. A., et al. (1999). "Drug-onset cues as signals: intraadministration associations and tolerance." J Exp Psychol Anim Behav Process 25(4): 491-504.

On the basis of a conditioning analysis of drug tolerance, drug-associated cues become associated with the drug effect. These cues elicit conditional compensatory responses and modulate the expression of tolerance. Although there are many findings consistent with the conditioning analysis of tolerance, there also are contrary findings. The results of these experiments suggest that some of the apparently contradictory findings result because interoceptive pharmacological cues, as well as exteroceptive environmental cues, are paired with a drug effect. That is, within each administration, early drug-onset cues may become associated with the later, larger drug effect, and these pharmacological cues may overshadow simultaneously present environmental cues. We demonstrate the contribution of such intraadministration associations to tolerance to the analgesic effect of morphine and to the expression of conditional compensatory hyperalgesia.

# Interoception in Eating Disorders

## General

#### Martin, E., et al. (2019). "Interoception and disordered eating: A systematic review." Neurosci Biobehav Rev 107: 166-191.

Deficits in interoception have been associated with disordered eating but there has been no systematic review of whether the interoceptive deficits are observed across all types of disordered eating and across interoceptive modalities. There has also been no evaluation of whether deficits in interoception play a causal role in the development of disordered eating. Nor has there been a review of the moderating/mediating factors of the relationship between interoception and disordered eating. To address these gaps we conducted a systematic review using PRISMA guidelines. 104 studies with 32883 participants were included. Deficits in interoception were observed across disordered eating types and interoceptive modalities suggesting that interoception may constitute a transdiagnostic feature of disordered eating. There is currently limited evidence on the causal role of interoception in the development of disordered eating and no studies have formally analysed the moderators/mediators. Future mechanistic research examining particular dimensions of interoception will provide insights into the specific interoceptive deficits associated with disordered eating and could lead to the development of improved therapies.

###### 3.2. Characteristics of included articles

Across the 104 studies included, the total number of participants was 32,883 with a minimum number of eight participants (Matsumoto et al., 2006) and a maximum number of 5139 participants (Kim et al., 2018). The majority of studies (n = 77, 74%) recruited women parti- cipants only. The remaining studies comprised 26 studies that included both men and women, and one study that recruited men only (Ussery and Prentice-Dunn, 1992). Of the 26 studies that recruited both men and women, the percentage of women participants ranged from 50 to 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 and Pollatos, 2014) to 60 years (Fassino et al., 2004). Publication dates of the articles ranged from 1974 (Garfinkel, 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-experi- mental 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 ques- tionnaire 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 AN and interoception; 17 studies presented data relevant to the association between BN and interoception; 6 stu- dies measured interoception in participants with clinical binge eating disorder; 26 studies collected data from participants with AN and par- ticipants with BN as part of a mixed ‘eating disorder group’ and 24 studies presented data relevant to the association between subclinical disordered eating behaviours and interoception.

###### 3.5. 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.

###### 3.5.1. 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; Ramacciotti et al., 2008; Vinai et al., 2015) used self-report measures and one measured mechanical pain threshold (Raymond et al., 1995).

###### 3.6. 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 AN and BN (e.g. Ciccolo and Johnsson, 2002 Halmi and Sunday, 1991), with the exception of Rossiter et al. (1989) and Laessle et al. (1989) who included participants with BN and ‘restrained’ participants. In studies including participants with BN and participants with AN, 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 et al., 2018; Nevonen et al., 2006; Nyman-Carlsson et al., 2015; 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 inter- oception, 22 showed impairments in at least one measure of inter- oception. 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 ac- ceptance and clarity of interoceptive processing in eating disorders (Merwin et al., 2010) and found mixed results, with neither the ac- ceptance 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.

###### 3.7. 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 in- cluded in the current systematic review were emotional eating (e.g. Koch and Pollatos, 2014; Young et al., 2017), external eating (e.g. Koch and Pollatos, 2014), subclinical binge eating (e.g. Brown et al., 2010), restraint (e.g. Tylka and Wilcox, 2006) and mixed/composite measures from questionnaires (e.g. Anderson et al., 2016; Myers and 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 ma- jority 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).

###### 3.8. Interoceptive modalities

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

###### 3.8.1. Gastric interoception

Gastric interoception was the most common modality measured in studies assessing interoception in disordered eating. Seventy-four stu- dies included in the systematic review measured gastric interoception, 19 of these studied gastric interoception in AN, 7 in bulimia, 4 in binge eating disorder, 20 in mixed eating disorder groups and 24 in sub- clinical disordered eating. Of these studies, 72 found significant dif- ferences 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 et al., 1983) and the Intuitive Eating Scale (Tylka, 2006). One study compared gastric volume with self-reported hunger and fullness found at each given stomach volume (Bluemel et al., 2017). Partici- pants with AN reported higher fullness and lower hunger than control participants, however participants with AN had a slower gastric emp- tying rate, which may account for this difference. Five studies used neuroimaging methods and found that dysfunctional gastric inter- oceptive processing was associated with disordered eating. Two studies (De Caro and Di Blas, 2016; Heilbrun and Worobow, 1991) did not find that gastric interoception was associated with disordered eating.

###### 3.8.2. 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 re- quired 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 AN reported in- creased cardiac sensations under low arousal states.

###### 3.8.3. 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 proces- sing 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 sensa- tion) and the measurement of pain tolerance (e.g. time taken for a participant to withdraw from a painful stimulus). Three studies com- bined pain measurement with neuroimaging measures (Strigo et al., 2013; Bär et al., 2013, 2015) and all three of these studies found dys- functional pain processing associated with disordered eating. Three studies that assessed pain threshold and tolerance did not find a dif- ference 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.

###### 3.8.4. Other interoceptive modalities

Two studies measured other interoceptive modalities using fMRI, and both were in participants recovered from AN. One measured re- spiratory 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 AN and healthy controls. The study by Khalsa and colleagues (2015) that in- volved infusions of isoproterenol showed that participants with AN reported increased breathing sensations under states of low arousal.

###### 3.9. 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 and 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-clin- ical 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 et al., 2006; Bizeul 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 syn- drome (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 (Lilenfeld 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 AN and their relatives (Casper, 1990). There was no significant difference in interoceptive impairments be- tween 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 in- teroceptive processing over the course of treatment. However, Fischer et al. (2016) found a cross-sectional influence of interoception on dis- ordered 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.

###### 3.10. 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 Fig. 2 for a summary). Small sample sizes and poor or no control for potential confounds were the main limita- tions. 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 hun- dred 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 dysfunc- tional interoception and AN, with 92% of studies finding impaired in- teroceptive function in AN. Similarly, 93% of studies measuring inter- oception 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 BN and interoceptive abilities was more mixed but still supportive of dysfunctional inter- oception associated with BN, 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 methodolo- gical 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 et al., 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 cri- terion 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 and Georgiou, 2016; Matsumoto et al., 2006 Young et al., 2017), or that reported no sig- nificant differences in depression scores between participant groups (Strigo et al., 2013), the results were mixed. In some cases, where an- xiety and depression were controlled for, no significant differences were found between disordered eating groups and controls (e.g. Ambrosecchia 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 inter- oception 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-clin- ical 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 et al., 2018), we find that inter- oceptive 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 AN and BN 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 et al., 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 inter- oceptive 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 as- sociated 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 re- searchers 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, sug- gesting 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 lim- itations 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 func- tionally 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 pro- blems 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 cur- rently only a small number of population based studies that have as- sessed 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 pro- blems 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 dis- order (e.g. Klabunde et al., 2013; Stein et al., 2003). Such an inter- pretation is supported by evidence, albeit currently limited, from family studies (Lilenfeld 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 inter- oceptive dysfunction does not constitute a heritable trait or en- dophenotype that is observable in non-affected first degree relatives of people with eating disorders.

One interpretation that could explain the existing data is that dys- functional interoception might predispose an individual towards the development of disordered eating but once disordered eating behaviour patterns become established, problems with interoception are accen- tuated. 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 inter- oception 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 dis- orders (Stice and Desjardins, 2018).

###### 4.4. 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 in- centive 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 BN (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 pro- cesses 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 de- pending 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, and Tsakiris, 2017).

There have also been fewer studies to date on the role of inter- oception in binge eating disorder than in AN and BN. BED was in- troduced as an eating disorder category in the Diagnostic and Statistical Manual of Disorders, Fifth Edition (DSM-5) in 2013 (American Psychiatric Association, 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 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 in- sight and conscious awareness of these responses. Three psychological dimensions of interoception that relate to the perception of inter- oceptive responses have been distinguished: interoceptive accuracy, sensibility, and awareness (Garfinkel et al., 2015). Interoceptive accu- racy 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 in- formation or to adaptively switch between interoceptive and ex- teroceptive representations (Quadt et al., 2018).

At present it is unknown whether dysfunctional interoception as- sociated with disordered eating is due to dysfunctional afferent sig- nalling, central sensory processing of interoceptive stimuli or percep- tion 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 mea- sured more than one dimension of interoception (e.g. Ambrosecchia et al., 2017; Young et al., 2017), and some of these assessed the asso- ciation 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 Ambrosecchia et al. (2017) found that participants self- reported poorer interoceptive sensibility, but had interoceptive accu- racy 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 in- teroceptive 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 in- dividuals with eating disorders and healthy controls, it is not a measure that was designed specifically to assess visceral interoceptive sensi- bility. 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 re- quired 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 acti- vation to infer the engagement of specific mental processes e.g. in- ferring that activation of the insula is related to interoceptive proces- sing 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 et al., 2012) altered the fullness of the stomach and inferred that the differences in brain re- sponses between a AN group and the control group was due to differ- ences 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 and 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 re- lationship 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 i nteroceptive events but decreased activation during an aversive in- teroceptive event (e.g. Berner et al., 2018; Strigo et al., 2013). For ex- ample, 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 re- ported 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 an- xiety disorders (Paulus and Stein, 2010) and are a core feature of pre- dictive coding accounts of interoception (Barrett and Simmons, 2015; Seth and Critchley, 2013).

Predictive processing Merwin et al. (2010) is a theoretical model of neural functioning (Friston, 2010) that has recently been applied to the study of interoception. Rather than assuming that interoceptive per- ceptions are linked directly to internal bodily sensations, predictive processing accounts suggest that perceptions arise from a comparison between representations of anticipated sensations and current inter- oceptive 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 predictions (Barrett and Simmons, 2015; Seth and 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 per- ceptions, or trigger changes in the body that fulfil those predictions. This account is similar to that proposed by Higgs (2005) who has ar- gued that feelings of satiety are cognitively constructed in the brain; a process that involves integrating current internal state cues with in- formation in memory about recent eating to predict the effects of fur- ther consumption.

Within a predictive/constructive interoceptive framework, dys- functional 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 influ- enced 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 in- coming sensory signals with anticipated states. Further research guided by the predictive/constructive framework is needed to test these hypotheses.

###### 4.5. Strengths and limitations of the current systematic review

We conceptualized 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 in- teroceptive sensibility were designed as questionnaire validation stu- dies, which resulted in suboptimal study designs and the potential for biased results. Finally, due to the heterogeneity of the studies, parti- cularly with respect to the methodologies and outcomes used, a meta- analysis was not considered feasible.

###### 4.6. Clinical implications

If further research confirms that interoceptive dysfunction predis- poses individuals to the development of eating disorders then assess- ment of interoception may be useful in identifying those at risk of de- veloping 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 et al., 2017, 2018) and de- pression (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 in- teroceptive signals (Feinstein et al., 2018). Future work could also ex- amine 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.

###### 4.7. 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.

#### Jenkinson, P. M., et al. (2018). "Self-reported interoceptive deficits in eating disorders: A meta-analysis of studies using the eating disorder inventory." J Psychosom Res 110: 38-45.

###### Abstract

OBJECTIVE: An impairment of the ability to sense the physiological condition of the body - interoception - has long been proposed as central to the onset and maintenance of eating disorders. More recent attention to this topic has generally indicated the presence of interoceptive deficits in individuals with an eating disorder diagnosis; however, possible links with specific diagnosis, BMI, age, illness duration, depression, and alexithymia remain unclear from individual studies. This meta-analysis aimed to provide a necessary quantitative overview of self-reported interoceptive deficits in eating disorder populations, and the relationship between these deficits and the previously mentioned factors. METHODS: Using a random effects model, our meta-analysis assessed the magnitude of differences in interoceptive abilities as measured using the Eating Disorder Inventory in 41 samples comparing people with eating disorders (n = 4308) and healthy controls (n = 3459). Follow-up and moderator analysis was conducted, using group comparisons and meta-regressions. RESULTS: We report a large pooled effect size of 1.62 for eating disorders with some variation between diagnostic groups. Further moderator analysis showed that BMI, age and alexithymia were significant predictors of overall effect size. CONCLUSION: This meta-analysis is the first to confirm that large interoceptive deficits occur in a variety of eating disorders and crucially, in those who have recovered. These deficits may be useful in identifying and distinguishing eating disorders. Future research needs to consider both objective and subjective measures of interoception across different types of eating disorders and may fruitfully examine interoception as a possible endophenotype and target for treatment.

###### Intro

Eating disorders (EDs) are characterised by an ongoing disturbance of eating or eating-related behaviour, which leads to changes in the consumption or absorption of food, and significantly impaired physical health or psychosocial functioning [3]. EDs are a pervasive psychiatric disturbance, associated with severe negative consequences, including significant distress, depression, suicide, substance abuse and even death [5,74,75]. As such, EDs represent a major clinical challenge, and priority for research to identify their aetiology, and develop effective treatments. Unfortunately, the cause of EDs remains poorly understood, with several biological, social and psychological factors identified as important in the onset and maintenance of different EDs [22].

The task of identifying the causal mechanisms underlying EDs is complicated by the fact that a different combination of factors may contribute to various subtypes of ED. The current Diagnostic and

Statistical Manual (DSM-5; APA 2013) identifies three primary ED di- agnoses: Anorexia Nervosa (AN; characterised by restrictive eating, severe weight loss, and an intense fear of gaining weight), Bulimia Nervosa (BN; characterised by a preoccupation with body weight and shape, normal body weight, and episodes of binge eating with com- pensatory behaviours such as purging), and Binge Eating Disorder (BED; characterised by frequent binge eating with feelings of loss of control, but no use of compensatory behaviours). Two further cate- gories (Other Specified Feeding or Eating Disorder (OSFED), and Unspecified Feeding or Eating Disorder (UFED)1), also exist to classify EDs that do not more accurately fit into AN, BN, or BED, such as aty- pical presentations of the above or other feeding and eating disorders.

Notably, early clinical descriptions of EDs highlighted “disturbances in accuracy of perception or cognitive interpretation of stimuli arising from the body” ([12], p. 189). These dual aspects have been examined under the modern-day concepts of interoception (i.e. the ability to sense t he physiological condition of the body [19], and alexithymia (i.e. difficulty identifying and describing feelings/emotions; see [80]). Such difficulties in perceiving signals arising from the body and/or identi- fying and interpreting emotional states have since been established as a core psychopathological element of several ED [32,80].

Difficulties with somatic perception/awareness may contribute to EDs because individuals incorrectly interpret bodily signals referring to hunger and satiety cues [12]. A difficulty perceiving hunger cues may result in skipped meals, or the restriction of food intake until intense feelings of hunger occur. By contrast, difficulty in detecting normal levels of fullness could cause binging or overeating [32,50]. In addition, deficits in identifying emotional states may contribute to difficulties with emotional regulation; a multidimensional construct characterised by flexible modulation strategies, behavioral control, emotional awareness and distress tolerance [43,52]. ED patients may confuse their internal bodily signals with emotions, and have difficulties experien- cing and differentiating different emotions, or modulating or attenu- ating their intensity [15,52]. Such maladaptive emotion regulation or

emotional dysregulation is a key psychological problem in EDs, related to mood instability, impulsivity, recklessness, anger and self-destructive- ness [52].

The majority of data concerning interoceptive deficits in EDs is based on self-reports obtained from the Eating Disorder Inventory (EDI; [42]), which primarily assesses the interpretative component of inter- oceptive deficits rather than somatic awareness. The EDI includes an “Interoceptive Awareness” subscale, comprising 10 questions reflecting “a lack of confidence in recognising and accurately identifying emo- tions and sensations of hunger or satiety” ([42], p. 18). Using the EDI and subsequent revisions (EDI-2, [40], EDI-2, [41]; EDI-VS, [58]), self- reported interoceptive deficits of this interpretative kind have been found consistently across patients with various EDs [32,52].

Importantly, although interoceptive deficits are widely reported as being a core psychopathological component of several EDs, it is not known whether the effect size is the same across the spectrum of EDs, or whether a particular diagnosis is associated with greater interoceptive deficits. In addition, several variables are known to interact and overlap with interoceptive processing and EDs, such as age, disease duration, Body Mass Index (BMI), depression and alexithymia [4,44,45,57,64,67,76]. However, these factors have not consistently been taken into account when examining interoceptive processes in patients with ED. Taking these factors into consideration, and identi- fying to what extent and how deficits in the interpretation of signals arising from the body contribute to different EDs, might allow for more targeted and effective interventions to be administered. Therefore, the current study first aimed to compare the magnitude of interoceptive deficits (as measured using the EDI) across different types of ED. Sec- ondly, we aimed to examine whether age, illness duration, BMI, de- pression, and alexithymia serve as moderators for any interoceptive deficits observed in ED overall, and whether these were further specific to different subtypes of ED. We did not have any a-priori predictions regarding the directionality of interoceptive deficits across different ED subtypes, or how these deficits might be moderated by the factors mentioned above, since individual studies have often not specifically examined or had statistical power to address such questions in an ED population, have used different measures to assess interception, or have produced contradictory results in healthy and ED populations (e.g. see [57] for interesting work on the relationship between interoception and alexitymia); as such, our meta-analyses represent a novel, quantitative exploration into these questions.

###### 3. Results

The analysis included 29 studies and 41 samples, providing a total sample of 4308 eating disorder participants and 3459 controls (7746 when controls are repeated in separate comparisons, see Table 1). The first, main analysis revealed significantly greater interoceptive deficits in the ED patients (SMD = 1.62: 95% CI = 1.46 to 1.77, p < 0.001)2 compared with healthy controls, indicating an 87% chance that a person picked at random from the ED group will have a greater inter- oceptive deficit than a person picked at random from the control group (probability of superiority). The studies were heterogeneous, (Q (40) = 386.10, p < 0.001) with an I2 value of 89.64. The high level of heterogeneity validated the suitability of a random-effects model and suggested the possible existence of moderating variables contributing to heterogeneity that required further investigation. Examination for publication bias Using Duval and Tweedie's [26] Trim and Fill method highlighted two potentially missing studies, though it made no sub- stantive difference to the effect size (SMD = 1.57: 95% CI = 1.41 to 1.73, p < 0.001).

###### 3.1. Interceptive deficits in different types of ED

Moderator analysis was undertaken to examine the impact of ED type on interoceptive deficit effect size (see Fig. 2). The initial analysis included all 29 studies and 41 samples. The samples comprised: AN (k=12), BN (k=10), BED (k=5), EDNOS (k=3), Mixed ED (k=9) and participants recovered from AN or BN (k = 2). A significant difference in pooled effect size was found amongst the various diagnostic groups (Q(5) = 50.30, p < 0.001).

We subsequently compared the size of interoceptive deficits across different ED diagnoses (see Fig. 2 for individual forest plots). In ac- cordance with the minimum study criteria for moderator analysis spe- cified above (k≥4), patients with EDNOS (k=3) and participants recovered from AN or BN (k = 2) were not analysed as part of sub- sequent comparisons. In addition, as the mixed group combined several types of ED (including AN, BN and BED) it could not be meaningfully compared with the separate ED subtypes, and was not included in follow-up comparisons. The remaining comparisons between AN, BN and BED indicated that patients with BN report the greatest deficit overall, with interoceptive awareness being significantly lower in BN than BED (Q(1) = 41.72, p < 0.001), but not compared with AN (Q (1)=2.57, p=0.11. In addition, patients with AN showed a sig- nificantly greater interoceptive deficit compared with BED (Q (1) = 25.27, p = 0.001). The level of heterogeneity (I2) was lower in each of these separate ED subsamples (AN = 77.91%, BN = 71.17%, BED=38.31%) compared to when all ED types were grouped and analysed together (89.64%), as might be expected; however, the rela- tively high level of heterogeneity remaining in these sub-samples sug- gests that there may still be other unidentified sources of heterogeneity. We explored these factors in further moderator analyses below.

###### 3.2. Further moderator analysis

The influence of age, illness duration, BMI, depression, and alex- ithymia on interoceptive awareness were analysed using meta-regres- sion. As indicated above, meta-regressions were not run with sub- samples fewer than six or in mixed samples. In addition, analyses were not run where the target measure was not reported or sufficiently variable for analyses to be run on the sample. Table 1 provides a summary of the meta-regressions conducted.

###### 3.2.1. Age

Meta-regression revealed greater interoceptive deficits in younger samples when samples of all ED subtypes were included in the analyses (k = 28). However, sub-analysis of patients with BN (k = 6) and AN (k = 9) separately indicated that interoceptive deficits were, contrast- ingly, significantly larger in older groups.

###### 3.2.2. Illness duration

There were too few samples to run regression analysis on illness duration.

###### 3.2.3. BMI

Across 17 samples that included all types of ED diagnoses, sig- nificantly greater interoception deficits occurred in samples with lower mean BMI.

###### 3.2.4. Depression

Depression was recorded in 8 ED samples which included the di- agnoses AN, BN, EDNOS and BED. Meta-regression of these samples revealed that average depression score was not a significant predictor of effect size.

###### 3.2.5. Alexithymia

A meta-regression of 6 samples which included the diagnoses AN, BN and BED found significantly greater interoception deficits in sam- ples with lower mean alexithymia scores (i.e. less alexithymia/better at identifying and labelling emotions).

###### 4. Discussion

The aim of the current meta-analysis was to investigate the extent of self-reported interoceptive deficits in EDs, and examine how various factors (i.e. ED diagnosis, age, illness duration, BMI, depression and alexithymia) may influence interoceptive deficits in ED. We identified 41 ED samples comprising 4308 people with various types of ED (in- cluding AN, BN, BED, and EDNOS), and compared these with 3459 healthy controls. A significant interoceptive deficit was found across this ED sample, with a very large effect size (SMD) of 1.62. This equates to there being approximately 87% chance that a person picked at random from the ED group will have a greater interoceptive deficit compared with a person picked at random from the control group. Furthermore, comparison across different ED subtypes revealed the novel finding that interoceptive deficits appear to exist on a continuum in EDs, with BN and AN patients experiencing significantly more pro- nounced interoceptive deficits compared to patients with BED. Our analyses also revealed that interoceptive deficits are greater in ED pa- tients with a lower BMI and younger age. Separate moderator analyses of BN and AN patients, however, revealed a contrasting pattern in which interoceptive deficits are greater in older patients. Finally, we found that interoceptive deficits across several EDs were not related to levels of depression; however, individuals with lower levels of alex- ithymia report greater interoceptive deficits. We discuss these findings in greater detail below.

Our first, overall finding of an interoceptive deficit in patients with ED is consistent across samples and studies, and accords with the long proposed disturbance of interoception in EDs [12]. More importantly, we document for the first time that a large and significant interoception deficit occurs across a wide range of eating disorders. Analysis of spe- cific EDs revealed large effect sizes in each group: AN (SMD = 1.71), BN (SMD = 1.96), BED (SMD = 0.76); EDNOS (SMD = 1.72), mixed diagnoses (SMD = 1.71) and those who had recovered from eating disorders (SMD = 0.76). We also present the hitherto unreported finding that BN and AN samples experience the greatest impairment of interoceptive abilities, whereas BED samples were found to report the smallest. Interestingly, even recovered AN and BN samples displayed a large effect size (Fig. 2F). The observation that substantial interoceptive deficits remain after recovery suggests a relative trait stability of such deficits and may have clinical implications for defining recovery from an eating disorder. For example, recovery of interoceptive abilities may not be a useful indicator for assessing ED recovery; however, the modest number of recovered samples (K = 2) means this finding should be interpreted cautiously.

Our finding that significant interoception deficits occur in all ED diagnoses lends support to a continuum or transdiagnostic approach to ED, which supposes that ED lie on a spectrum of dieting and weight concerns rather than being qualitatively distinct [23,71]. The core symptomology of EDs is the same, but can be expressed differently through the varying severity and kinds of eating behaviours displayed throughout the course of the disorder [30]. In line with this approach, we found that although interoceptive deficits are consistent across all EDs, significant inter-diagnostic differences emerge in the degree of impairment. Previous research has explored a variety of en- dophenotypes3 in EDs (for a discussion see [14,77]) and the accumu- lated evidence presented here points to interoception deficits as a candidate endophenotype for EDs. However, it remains unclear whe- ther these deficits play a role in the onset and maintenance of the disorders, or are caused in some way by the disorder and its symptoms. In this context, Lilenfeld et al. [55] posit an interesting distinction

3 “Endophenotypes are considered to be measureable biological markers for a disease which are associated with the illness in the general population, are observable regardless of whether the illness is active, are observed in unaffected family members of probands at a higher rate than in the general population, and are heritable” ([77], p. 4).

regarding traits that persist after recovery from an eating disorder and in particular to whether such traits reflect either “...a potential vul- nerability factor contributing to the development of the ED or a ‘ scar’ (i.e. consequence) of the illness.” (p. 1400). Lilenfeld et al. found di- minished interoceptive awareness amongst previously eating-dis- ordered relatives of bulimic probands when compared to their never-ill relatives. They interpret this as consistent with their “scar” model, i.e. that having had an eating disorder leaves a “scar”; however, as they later note “...it is impossible to definitively determine which may be ‘scar effects’ and which may be predisposing factors at the present time” ([56], p. 313). Nonetheless, a large prospective study of junior high and high school students found that poor interoceptive awareness (from the EDI) predicted risk of eating disorders one year later [54]. Thus, a next step to further explore this line of thinking would be for future studies to assess interoception in the unaffected first degree relatives of those with EDs.

We found that mean age was a significant predictor of interoception deficit, being greater in younger samples; however separate analyses of AN and BN samples revealed contrastingly greater interoceptive deficits in older samples. The separate analysis of age and interoceptive deficit in BN patients included only a small number of samples, and this limits the conclusions that can be drawn regarding this finding. It is possible that the overall analysis may have been influenced by diagnosis, as BED samples typically had a higher average sample age and were found to have significantly smaller effect sizes, which may explain the difference in direction of the relationship found in the overall and sub-analyses. Unfortunately, there were too few samples to also analyse the effect of illness duration on interoceptive deficits, and so it is not possible to determine whether the link between age and interoceptive deficit is simply a result of the illness length, or if interoceptive deficits are a stable trait that do not change over time. In order to draw such con- clusions, future studies are needed that record illness duration.

We also found that individuals with lower BMIs have significantly greater interoceptive deficits; however, the finding of a negative re- lationship between effect size and BMI may have again been influenced by ED subtype. Unfortunately, it was not possible to carry out further analysis of individual ED subtypes because of limitations in the re- corded range of BMI and/or too few studies reporting BMI for meta- regression to be performed. Nevertheless, we note that the samples with larger BMIs were those with a BED diagnoses, which were also found in the current analyses to have significantly smaller interoceptive deficits than samples with BN or AN. Our attempts to analyse BMI and inter- oceptive deficits in EDs highlights potential difficulties in examining the influence of BMI across ED samples more generally. The link be- tween interoceptive deficits, BMI and EDs may be more complex than is currently understood based on the limited evidence available, and ad- ditional research, which includes a range of BMIs and weight-recovered AN patients, is needed to examine these relationships.

Our meta-regression of alexithymia indicated that individuals with poor emotional awareness do not necessarily have poor interoception. Surprisingly, we found that greater levels of alexithymia (i.e. poorer ability to identify/label emotions/feelings) predicted fewer self-re- ported interoception deficits (i.e. better interoception). This finding is based on the results of only six studies and samples with relatively high levels of alexithymia overall (the mean across our samples ranged be- tween 54.1 and 67.05, and a TAS-20 score of 61 or above indicates high levels of alexithymia; [7]), and so should be interpreted with care and/ or limited to individuals with relatively high alexithymia. Nevertheless, the analysis included several types of ED, and confirms the high oc- currence of alexithymia in EDs [80]. Moreover, this finding is parti- cularly notable given similarities between the interpretative aspect of interoception (as measured by the EDI) and alexithymia (see [28]). Our result provides further insight into current debates and contrasting findings regarding the relationship between alexithymia and inter- oception (see [57,81]). The findings are consistent with previous re- search suggesting that greater levels of alexithymia are related to better interoception (i.e. individuals with poor emotional awareness report greater somatic awareness; [27,57]). This seemingly counterintuitive relationship can be explained by the suggestion that paying attention to interoceptive sensations (i.e. high interoception) may hamper the in- terpretation of one's emotional feelings (i.e. high alexithymia), and contribute to somatoform disorders via the misinterpretation of phy- sical sensations [57].

Finally, we found that depression, as measured by the BDI [8], was not a significant predictor of interoception deficit effect size. Indeed, the association between depressive symptoms and interoceptive abil- ities has not always been consistent in previous research. For example, Dunn et al. [25] found a significant difference in interoception (as measured using a heartbeat perception task; see [72]) between in- dividuals with moderate depression and controls, but no significant difference between severely depressed individuals and controls. Pol- latos et al. [69] found evidence of a significant negative relationship between depression and scores on a heartbeat perception measure of interoception in healthy participants, however also found a significant interaction with anxiety, where this relationship only remained sig- nificant at high levels of anxiety. Therefore, both the severity of de- pressive symptoms and levels of anxiety in the samples used in this analysis may have had an influence over the relationship between de- pression symptoms and effect size, and may explain why no significant relationship was found. The average BDI scores of the samples analysed were also within the minimal-to-moderate range according to estab- lished BDI cut-offs. This limited variability in depression scores ne- cessarily limits the generalisability of our findings to individuals with mild to moderate depression.

###### 4.1. Limitations and recommendations

An important caveat of our findings is that the conclusions drawn relate only to self-reported interoceptive deficits measured by the Interoceptive Awareness subscale of the Eating Disorder Inventory (EDI). This leads to two potential limitations. Firstly, the EDI has been criticised as an assessment of interoception, as it primarily considers the interpretative, emotional aspect of interoception [28], and fails to dif- ferentiate between a confusion or lack of clarity regarding internal experiences and non-acceptance of affective arousal [60]. Moreover, it is possible that, despite self-reporting more interoceptive deficits, in- dividuals with certain types of ED lack insight and consequently un- derreport the true extent of their interoceptive deficits. This would, for example, be consistent with the differing symptomology of AN and BN, where patients with AN often lack insight into or deny their illness and symptoms, whereas patients with BN are typically more motivated to recover [51]. This difference in awareness may, therefore, account to some extent for the differences found in interoceptive deficits between AN and BN patients.

Second, recent research distinguishes between different types or levels of interoceptive ability [38], with interoceptive sensibility referring to the subjective, self-evaluation of interoceptive ability; interoceptive accuracy referring to an individual's objective accuracy in detecting and tracking internal bodily sensations; and interoceptive awareness referring to the a meta-cognitive measure of the correspondence between the objective and subjective measures (see also [16] for discussion of the origin and development of interoception as a concept). As mentioned above, Bruch [12] also distinguished between two kinds of inter- oceptive ability in ED (perception vs. interpretation of body signals). Importantly, the different dimensions of interoception may be distinct and dissociable [37,39]. Unfortunately, our systematic search identified only three studies that examined interoceptive ability objectively in an ED sample [33,50,68], using a heartbeat detection task [72], and so it was not possible to include these in our meta-analysis and/or conduct any meaningful comparisons. Therefore, an important aim for future ED research should be to include both objective and subjective measures of interoceptive ability, to look at awareness across different modalities

(e.g. cardiovascular, gastrointensinal, pain and pleasant touch; see [20,21,46] for examples), and to see how deficits relate to body image and ownership (see [6,20,21]). Although no “gold standard” measure of interoception exists, new methods have been developed to capture the multidimensional nature of interoception (see [38,57,61,62]), and va- lidated in a clinical eating disorder sample (e.g. [11]).

The current review also highlighted how most existing ED studies have assessed samples of AN and BN, with only three samples of EDNOS, despite this being the most common eating disorder seen in outpatient settings [29]. Our review also identified only a limited number of studies involving recovered and BED samples, again high- lighting a clear gap in the current literature. Understandably, fewer studies have focused on BED in comparison to other diagnoses, since it was only recently introduced as a diagnostic category in DSM-5 [3]. A particular focus is required on future studies with recovered eating disorder samples, EDNOS and BED in order to more accurately de- termine the pathogenesis of these EDs, and to assess the validity of introception as an endophenotype.

Finally, in additional to the limited number of studies looking at certain ED subtypes, our review of the literature identified that im- portant clinical variables, such as illness duration and BMI, were not always reported by existing studies. Our meta-analysis was unable to examine the potentially important relationships between illness dura- tion, overall disorder severity and interoceptive abilities, as the ma- jority of studies did not report on the illness duration or severity of their samples. Overall, these issues highlight the need for future research to consistently report on key clinical variables, as well as the need for more research to examine the relationship between the variables and interoception directly using multiple measures.

###### 5. Conclusion

We confirm the existence of a substantial, self-reported inter- oceptive deficit in all types of EDs examined. Impaired interoception may, therefore, be considered a transdiagnostic characteristic of EDs and a possible endophenotype. The degree of interoceptive deficit varies across ED subtypes and may provide a useful distinguishing feature of different EDs. They may also play a maintenance role in eating disorders, and consequently be an appropriate target for treat- ment or prevention. The extent of interoceptive deficit may be influ- enced by several factors, such as age, BMI, and alexithymia; however, further evidence is needed to substantiate these conclusions, with fu- ture studies reporting these factors as well as illness duration, and employing both objective and subjective measures in direct examina- tions of interoceptive process across all types of EDs.

#### Lattimore, P., et al. (2017). "‘I can’t accept that feeling’: Relationships between interoceptive awareness, mindfulness and eating disorder symptoms in females with, and at-risk of an eating disorder." Psychiatry Res 247: 163-171.

Mindfulness based therapies (MBTs) for eating disorders show potential benefit for outcomes, yet evidence is scarce regarding the mechanisms by which they influence remission from symptoms. One way that mindfulness approaches create positive outcomes is through enhancement of emotion regulation skills. Maladaptive emotion regulation is a key psychological feature of all eating disorders. The aim of the current study was to identify facets of emotion regulation involved in the relationship between mindfulness and maladaptive eating behaviors. In three cross-sectional studies, clinical (n=39) and non-clinical (n=137 & 119) female participants completed: 1) the Eating Disorder Inventory (EDI) eating specific scales (drive-for-thinness and bulimia) and the EDI psychological symptom scales (emotion dysregulation and interoceptive deficits); and 2) mindfulness, impulsivity, and emotion regulation questionnaires. In all samples mindfulness was significantly and inversely associated with EDI eating and psychological symptom scales, and impulsivity. In non-clinical samples interoceptive deficits mediated the relationship between mindfulness and EDI eating specific scales. Non-acceptance of emotional experience, a facet of interoceptive awareness, mediated the relationship between mindfulness and eating specific EDI scores. Further investigations could verify relationships identified so that mindfulness-based approaches can be optimized to enhance emotion regulation skills in sufferers, and those at-risk, of eating disorders.

#### Fitzgibbon, M. L., et al. (2003). "A test of the continuity perspective across bulimic and binge eating pathology." International Journal of Eating Disorders 34(1): 83-97.

Abstract: Objective: This article examines the continuity/discontinuity perspective of eating pathology among 375 women seeking treatment. Methods: Participants were categorized into five separate groups: obese nonbingers, subthreshold binge eating disorder (BED), BED, subthreshold bulimics, and bulimics. We tested whether differences in core eating pathology (drive for thinness, body dissatisfaction, current body image, body image ideal) and psychiatric symptoms (depression, interoceptive awareness) differentiated the groups quantitatively (supporting the continuity perspective) or qualitatively (supporting the dis- continuity perspective). Results: Our results, overall, supported the continuity perspective of eating pathology. A discriminant function analysis using the eating pathology and psychiatric symptom variables as predictor variables found that one primary factor differentiated the five groups on both core eating pathology and psychiatric variables. Discussion: The impli- cations of testing this model within a treatment-seeking sample are discussed. # 2003 by Wiley Periodicals, Inc. Int J Eat Disord 34: 83–97, 2003.

## Interoception in Binge Eating Disorder

#### Romano, K. A., et al. (2020). "Somatic symptoms and binge eating in women's daily lives." J Psychosom Res 135: 110161.

###### Abstract

OBJECTIVE: The present study aimed to determine whether the momentary severity of women's somatic symptoms was concurrently and prospectively associated with their engagement in binge eating in naturalistic settings. METHOD: Thirty women (M(age) = 34.13, SD = 13.92) who had engaged in binge eating at least once over the month prior to study entry completed a 14-day ecological momentary assessment (EMA) protocol. During each of the 14 days, participants received five semi-random surveys via text message that assessed momentary somatic symptom severity (i.e., headaches, stomachaches/pain, chest/heart pain, faintness/dizziness, shortness of breath, fatigue) and disordered eating behaviors. Generalized estimating equations were used to determine whether momentary somatic symptoms were concurrently and prospectively (i.e., by participants' next assessment) associated with the occurrence of binge eating behavior, while controlling for age and body mass index. RESULTS: At the within-person level, more severe stomachaches/pain, faintness/dizziness, shortness of breath, and fatigue were concurrently associated with an increased likelihood of engaging in binge eating. Further, at the between-person level, more severe stomachaches/pain, chest/heart pain, shortness of breath, and fatigue in general were associated with binge eating across the EMA protocol. Momentary stomachache/pain severity also prospectively predicted women's engagement in binge eating behavior at the next assessment. CONCLUSIONS: The present results provide initial evidence that multiple somatic symptoms may serve as momentary correlates or proximal antecedents of binge eating behavior in women's daily lives. Somatic symptoms may consequently prove useful to target in eating disorder treatments, perhaps via interoceptive exposure interventions.

###### Introduction

Binge eating is prevalent among adult women and is a well-estab- lished correlate of multiple physical and mental health concerns, in- cluding somatic and psychosomatic symptoms (i.e., physical health concerns that are incited or exacerbated by psychosocial factors) [1,2]. Indeed, individuals who frequently engage in binge eating commonly exhibit symptoms that have both psychogenic and physiological ori- gins, such as gastrointestinal concerns (e.g., stomachaches or pains), chest and heart pain, headaches, faintness, shortness of breath, and fatigue [1,3–6]. Given that individuals may be more likely to report somatically-based versus disordered eating symptoms to healthcare

providers [7], enhancing the current understanding of the interplay between binge eating and somatic comorbidities may help improve current screening efforts for binge eating pathology and facilitate in- dividuals' connection with treatment.

###### 1.1. Somatic symptoms and binge eating

Existing research examining somatic symptoms and binge eating has largely focused on identifying how between-person differences in par- ticular somatic symptoms are associated with binge eating pathology [1,3–6]. For example, in a large sample of Swedish individuals with lifetime binge eating disorder and healthy controls, those with binge eating disorder were more likely to report various neurologic (e.g., headaches, migraines), gastrointestinal, respiratory, and circularity system concerns [6]. Although informative, little is known about so- matic symptom-binge eating comorbidities beyond bivariate between- person associations of this nature. However, more generally, in- dividuals with binge eating symptoms commonly exhibit interoceptive deficits [8–11], or dysfunction in the ability to sense and process visceral bodily experiences and states such as pain, hunger, satiety, and heartbeat sensations [12]. Such difficulties in effectively connecting with internal experiences can translate to individuals' engagement in adverse health behaviors like binge eating as a means of experiential avoidance. This can serve as an impediment to adequate body regula- tion that is integral to maintaining health and well-being [9].

Of note, although between-person research consistently suggests that interoceptive processes are skewed among individuals with eating disorders characterized by binge eating [8–11], the nature of this dys- function is equivocal. For example, some research suggests that in- dividuals with binge eating pathology exhibit hypersensitivity and others hyposensitivity to certain interoceptive signals [9]. This equi- vocality poses different implications for individuals' responses to their internal bodily signals. Hypersensitive or exaggerated responses to in- ternal sensations can lead to subsequent binge eating wherein, for ex- ample, internal signals of depleted energy that are sensed by the body (e.g., fatigue, faintness, hunger) promote behaviors such as binge eating that are designed to address these cues and are maintained over time via reinforcement-based processes [11,13]. In contrast, hyposensitive or blunted responses to interoceptive signals, such as stomachaches/ pain or satiety, can propagate subsequent binge eating via the body's inability to signal the significance of these somatic cues and, in turn, prevent individuals' engagement in this adverse health behavior [13].

###### 1.2. Ecological Momentary Assessment (EMA)

Existing between-person findings on interoceptive processes can be extended and the evidence-base's equivocality potentially clarified by examining whether various somatic symptoms serve as momentary correlates or proximal triggers of binge eating behavior. EMA is a particularly well-suited methodology that can aid in determining how somatic symptom-binge eating patterns manifest in individuals' daily lives. To date, however, between-person cross-sectional and, to a lesser degree, traditional longitudinal methods have strictly been used to examine somatic symptom and binge eating associations [1,3–6]. These two methods provide limited information about the functionality of these associations and are subjected to retrospective recall bias that can decrease the validity of ensuing results [15]. In contrast, EMA permits the examination of psycho-behavioral factors in individuals' daily lives via brief repeated assessments. Given this, EMA minimizes the influence of recall bias inherent within cross-sectional survey research, increases ecological validity, and enables the examination of novel research questions that address the temporal sequencing of psycho-behavioral factors in naturalistic settings [15].

Although no existing research has examined naturalistic associa- tions between somatic symptoms and binge eating behavior, a growing body of research has used EMA to examine how internal bodily signals such as affect and hunger are associated with binge eating [16–18]. Regarding the latter, meta-analytic evidence suggests that individuals' hunger levels are generally lower prior to binge eating episodes when compared to normative eating episodes [18]. This finding aligns with between-person cross-sectional research that suggests that individuals who engage in binge eating exhibit hyposensitive interoceptive re- sponses to somatic cues [13,14]. However, it remains unknown whe- ther this result generalizes from internal hunger sensations to somatic symptoms and whether there are variations in these associations as a function of somatic symptom type.

###### 4. Results

There were 1558 EMA recordings across the 14-day assessment period. On average, participants responded to 51.93 prompts (SD = 13.49; range = 16–70) and compliance, defined as individuals' average number of completed prompts divided by the total number of possible prompts, was good (78.3%). At baseline, the average number of objective binge eating episodes reported in the past 28 days via the EDE interview was 12.27 (SD=13.78; Range=1–76). Participants endorsed binge eating during 13.7% (213 episodes) of the survey prompts. The number of EMA recordings completed was unrelated to demographic variables. Further, across ratings, participants' somatic symptom severity was generally low, with the average headache pain severity rating being 1.69 (SD = 1.08), as well as 1.60 (SD = 1.01) for stomachaches/pains, 1.08 (SD = 0.35) for chest/heart pains, 1.31 (SD = 0.71) for faintness/dizziness, 1.16 (SD = 0.55) for shortness of breath, and 2.48 (SD = 1.41) for fatigue.

Tables 2 and 3 present the concurrent and prospective (i.e., time- lagged) models for somatic symptom and binge eating associations, respectively. Regarding the concurrent results, significant within- and between-person effects were found for associations between experien- cing stomachaches/pain, shortness of breath, and fatigue relative to binge eating. That is, at times over the hours following participants' previous assessments when they reported more severe stomachaches/ pains, shortness of breath, and fatigue than their averages, they were more likely to concurrently report binge eating episodes. Further, par- ticipants who generally experienced more extreme stomachaches/

pains, shortness of breath, and fatigue than others engaged in more binge eating behavior throughout the EMA protocol. In addition, a significant within- but not between-person effect was found for faint- ness/dizziness and a between- but not within-person effect was found for chest/heart pain severity as correlates of concurrent binge eating behavior. More specifically, at times when participants indicated that they experienced higher levels of faintness/dizziness than they nor- mally did, they were more likely to report having engaged in binge eating and, further, participants who generally experienced more se- vere chest/heart pain than others were more likely to engage in binge eating across assessments.

Regarding the time-lagged analyses, which examined associations between individuals' somatic symptoms at a given assessment and their reports of binge eating at their next assessment, significant within- and between-person effects were found for stomachache/pain severity. In particular, at times when participants experienced more severe sto- machaches/pain than they normally did, they were more likely to en- gage in binge eating by their next survey prompt. Further, participants who generally experienced more severe stomachaches/pains than others were more likely to engage in binge eating by their next as- sessments across the EMA protocol. Significant time-lagged, between- person effects were also found for chest/heart pain severity and shortness of breath, such that participants who typically experienced more severe chest/heart pain and shortness of breath than others were more likely to binge eat by their next assessments across the EMA protocol. All concurrent and prospective associations between head- ache severity and binge eating were not significant.

###### 5. Discussion

Although existing between-person research has consistently found that various somatic symptoms are associated with elevated binge eating severity [1,3–6], no prior studies have examined whether these symptoms serve as concurrent correlates or proximal antecedents of binge eating behavior when assessed in ecologically valid settings. To address this research gap, the present study was the first to use EMA to examine whether women's somatic symptom severity (headaches, sto- machaches/pain, chest/heart pain, faintness/dizziness, shortness of breath, fatigue) at a given moment was independently associated with their engagement in binge  
and prospectively (i.e., by  
indicated that, at the within-person level, more severe gastrointestinal and pulmonary somatic symptoms, alongside signs of depleted energy (faintness/dizziness, fatigue), were concurrently associated with a greater likelihood of engaging in binge eating and that, at the between- person level, an increased severity of most of these symptoms plus chest/heart pain were concurrently associated with a higher probability of binge eating across assessments. Further, intraindividual differences in stomachache/pain severity were also prospectively associated with women's increased likelihood of engaging in binge eating. Considered together, these results provide initial evidence that visceral sensations that span across various domains of bodily functioning may serve as concurrent correlates or proximal antecedents of binge eating and prove useful to target in existing eating disorder treatments.

###### 5.1. Hypersensitive responses to somatic symptoms

That experiencing more severe somatic symptoms was generally associated with an increased likelihood of concurrent binge eating in the present study aligns with existing between-person research de- monstrating that individuals who engage in binge eating may exhibit hypersensitive responses to interoceptive signals [9,13]. The present within-person findings extend this literature by suggesting that at times when women with elevated binge eating severity experience more se- vere gastrointestinal and pulmonary symptoms, as well as internal cues related to depleted energy (faintness/dizziness, fatigue), than they ty- pically do, they are more vulnerable to engaging in binge eating be- havior at that time. Notably, given that the parameters for these con- current within-person somatic symptom-binge eating associations were generally comparable in size, there appears to be little differentiation in the strength of these associations as a function of somatic symptom type. Consequently, the assessed symptoms appear to be similarly im- pactful.

That within-person differences in concurrent associations between most somatic symptoms and binge eating did not generally differ as a function of somatic symptom type may reflect a negative attribution style that women with elevated binge eating severity have in response to interoceptive signals in general or serve as a marker of emotion dysregulation that commonly manifests in this population [25]. Binge eating may consequently serve as a form of experiential avoidance, wherein women engage in this behavior in an attempt to distance themselves from and quell these adversely perceived internal cues and, instead, experience rewarding and reinforcing effects that are asso- ciated with binge eating in the short-term [9,13]. Previous between- person neuropsychological research has supported this perspective by demonstrating how internal signs of depleted energy (e.g., faintness/ dizziness, fatigue) relate to elevated binge eating pathology, and the present findings extend this work by showing that similar processes occur across somatic symptoms not strictly related to diminished energy reserves at the momentary level of analysis. This prior research centers on the concept of positive alliesthesia [26], which suggests that hy- persensitive responses to indications of low energy incite visceral-be- havioral responses that help the body achieve a state of homeostasis and maintain health. Individuals' motivation to consume food increases during times when their energy is low due, in part, to the rewarding properties associated with such consumption. In those vulnerable to binge eating, the motivational salience of food heightens via re- inforcement-based processes and, in turn, increases individuals' sus- ceptibility to eating beyond their energy needs at a given moment [11]. As an important extension of the present study, it will prove useful for future research to merge this prior evidence with the current findings via multi-modal assessment. Specifically, such work should examine whether objective differences in neural activity in cortical areas asso- ciated with reward, motivation, interoception, and impulsivity mod- erate momentary associations between self-reported somatic symptoms and binge eating behavior that are assessed in daily life.

###### 5.2. Gastrointestinal and cardiovascular somatic symptoms

Elevated stomachache/pain severity was the only within-person effect that was prospectively associated with an increased risk of binge eating at a subsequent timepoint. This suggests that, when compared to other somatic symptoms, experiencing adverse gastrointestinal sensa- tions at a given time may uphold a particularly harmful and enduring role in promoting subsequent binge eating. It is unclear why this so- matic symptom, in particular, appears to subsist. Given that the sto- mach may be more centrally implicated in body image than somatic sensations in other body areas (e.g., headaches, fatigue), it is possible that experiencing elevated gastrointestinal pain may simultaneously heighten women's awareness of their stomachs at large and, in turn, propagate an increase in negative body image and negative affect. Considering that negative body image and negative affect serve as disordered eating behavior triggers [16,27], these psychologically- based concerns may consequently account for or otherwise influence the present prospective associations between elevated stomachache/ pain severity and binge eating behavior. Thus, these constructs warrant assessment as mediators and/or moderators of these associations in future research.

A strength of EMA includes the method's ability to permit the se- paration of within- and between-person effects [15,24]. This helps de- termine whether associations among psycho-behavioral factors exist at times when individuals experience higher levels of various symptoms than they typically do and/or reflect differences in aggregate levels of symptoms that vary between participants. In this regard, it is note- worthy that the between-, but not within-, person association between elevated chest/heart pain severity and an increased likelihood of binge eating was significant and larger than all other assessed concurrent and prospective somatic symptom-binge eating associations. These findings align with prior between-person research that found that various cir- culatory system diseases associated with chest/heart pain exhibit some of the strongest associations with binge eating symptoms [1,5,6]. It is plausible that the present findings similarly reflect individual differ- ences in cardiac-based somatic morbidities that are associated with elevated binge eating behavior. Indeed, as within-person differences in

chest/heart pain severity were not also associated with concurrent binge eating in the present study, this symptom does not appear to serve as a concurrent correlate or a prospective antecedent of binge eating and, instead, appears to reflect trait-level interindividual differences. Future research that controls for cardiac-based somatic morbidities is needed to determine whether this factor accounts for the observed chest/heart pain-binge eating associations.

###### 6. Clinical implications

The present findings can help inform existing eating disorder treatments focused on decreasing individuals' binge eating symptoms. Specifically, the present findings suggest that women's experiences of various somatic symptoms are associated with hypersensitive inter- oceptive responses that are concurrently and, for stomachache/pain severity, prospectively linked to binge eating behavior. Incorporating interoceptive exposure interventions and interventions that more broadly target emotion dysregulation into existing treatment protocols can help encourage individuals to identify and sit with adversely per- ceived internal cues of this nature, rather than attempt to temporarily quell them by engaging in binge eating [28]. Given that stomachache/ pain severity was shown to exhibit a precipitating role in inciting this behavior, addressing adversely perceived internal signals in the sto- mach area may serve as a particularly important somatic symptom to target. In session, this may include directing individuals' attention to stomach pains and tight clothing, associated thoughts, feelings, and sensations that arise, and urges to engage in avoidance strategies (e.g., binge eating) as an (ineffective) means of lessening the sensations in the short-term [28]. Psychoeducation on the role of neural plasticity fol- lowing the normalization of individuals' eating patterns in creating new brain pathways that promote effective, rather than over-active, re- sponses to somatic symptoms can also serve as a viable adjunctive treatment component.

###### 7. Limitations

Although strengths of the current study include the use of EMA with women with elevated binge eating pathology, certain limitations war- rant mention. First, the present sample was all female and most parti- cipants identified as White. Future research with a more gender and racially diverse sample is needed to increase the generalizability of our findings. Second, although EMA studies commonly use single-item questions to examine disordered eating behaviors and correlates of such [16] as a means of decreasing participant burden owing to the heigh- tened frequency of EMA reports, the use of a single-item variable to assess individuals' binge eating behavior in the present study may not have fully captured this construct when compared to multi-item mea- sures. Further, the concurrent models attest to participants' reported somatic symptoms and binge eating behavior over the hours since their last assessment. Consequently, the temporal ordering of these symptom experiences is unclear (i.e., somatic➔binge eating, binge eating➔so- matic). Future research using event-contingent reports and that which examines whether binge eating prospectively predicts somatic symptom severity could help clarify the directionality of these associations. In addition, the present study included 30 participants. Although the use of repeated sampling increased our power to test the present study aims, this is a relatively small between-persons sample size and these findings should be replicated with a larger sample. In addition, al- though all participants needed to report recent objective binge eating to be included in the present study, there was some variation in partici- pants' ED symptom patterning. Consequently, future research with a larger sample is needed to examine whether ED diagnostic differences influences the assessed somatic symptom-binge eating associations. Finally, although the six assessed somatic symptoms have been con- sistently shown to adversely impact individuals with binge eating pa- thology [1,4–6], it would be informative for future studies to examine the momentary impact of additional gastrointestinal symptoms beyond stomachaches/pain alone (e.g., bloating, diarrhea) on women's binge eating.

###### 8. Conclusions

The present study was the first to use EMA to examine whether women's somatic symptoms (headaches, stomachaches/pain, chest/ heart pain, faintness/dizziness, shortness of breath, fatigue) at a given moment were independently associated with their engagement in binge eating behavior both concurrently and prospectively (i.e., by their next assessment). The present results indicated that more severe experiences of all assessed somatic symptoms apart from headache severity were concurrently associated with an increased likelihood of engaging in binge eating behavior at the within- and/or between-person levels. Intraindividual differences in stomachache/pain severity were also prospectively associated with women's increased likelihood of engaging in binge eating. The present results provide initial evidence that mul- tiple visceral sensations may serve as momentary correlates or proximal antecedents of binge eating and prove useful to target in existing eating disorder treatments.

#### van Dyck, Z., et al. (2020). "Gastric interoception and gastric myoelectrical activity in bulimia nervosa and binge-eating disorder." Int J Eat Disord.

OBJECTIVE: Identifying factors that control food intake is crucial to the understanding and treatment of eating disorders characterized by binge eating. In healthy individuals, stomach distension plays an important role in the development of satiation, but gastric sensations might be overridden in binge eating. The present study investigated the perception of gastric signals (i.e., gastric interoception) and gastric motility in patients experiencing binge-eating episodes, that is, bulimia nervosa (BN) and binge-eating disorder (BED). METHOD: Twenty-nine patients with BN or BED (ED group) and 32 age-, sex-, and BMI-matched healthy controls (HC group) participated in the study. The onset of satiation and stomach fullness were assessed using a novel 2-step water load test (WLT-II). Gastric myoelectrical activity (GMA) was measured by electrogastrography (EGG) before and after ingestion of noncaloric water. RESULTS: Individuals in the ED group drank significantly more water until reporting satiation during the WLT-II. The percentage of normal gastric myoelectrical power was significantly smaller in the ED group compared to HC, and negatively related to the number of objective binge-eating episodes per week in patients with BN or BED. Power in the bradygastria range was greater in ED than in HC participants. DISCUSSION: Patients with EDs have a delayed response to satiation compared to HC participants, together with abnormal GMA. Repeated binge-eating episodes may induce disturbances to gastric motor function.

#### Aloi, M., et al. (2017). "Social Cognition and Emotional Functioning in Patients with Binge Eating Disorder." Eur Eat Disord Rev 25(3): 172-178.

OBJECTIVE: This study aims to evaluate the theory of mind ability in a sample of obese patients with and without binge eating disorder (BED) and to explore the correlations between emotional and clinical assessments. METHODS: Overall, 20 non-BED, 16 under-threshold BED and 22 BED obese patients completed a battery of tests assessing social cognition and eating disorder psychopathology. RESULTS: Binge eating disorder, non-BED and under-threshold-BED obese patients showed similar ability to recognise others' emotions, but BED obese patients exhibited a deficit in recognising their own emotions as demonstrated by more impaired levels of alexithymia and interoceptive awareness and were more depressed. High positive correlations were evident between binging, depression, interoceptive awareness and alexithymia. CONCLUSIONS: Binge eating disorder patients have a comparable ability to understand others' emotions but a more impaired capacity to understand and code their own emotions compared with non-BED obese patients. This impairment is highly correlated with depression. Copyright © 2017 John Wiley & Sons, Ltd and Eating Disorders Association.

#### Vinai, P., et al. (2015). "Psychopathological characteristics of patients seeking for bariatric surgery, either affected or not by binge eating disorder following the criteria of the DSM IV TR and of the DSM 5." Eat Behav 16: 1-4.

We evaluate whether there are any significant differences in psychopathology between severe obese patients affected by Binge Eating Disorder diagnosed following both the DSM IV TR and the DSM5 criteria, and severe obese patients not having an eating disorder. METHOD: 118 severe obese patients seeking treatment at a center for bariatric surgery in northern Italy were asked to take part in the current study for a period of six months. Average participant age was 44.27 years, SD 12.42. Age ranged from 18 to 67 years. Average patient BMI was 45.03, SD 7.11, ranging from 32.14 to 66.16 kg/m(2). Seventy seven of the patients (65.3%) were females and 41 (34.7%) were males. BED diagnosis was determined following the diagnostic criteria of both the DSM IV TR and the DSM 5. The presence of other eating disorders was excluded through a clinical screening using the Eating Disorder Inventory (EDI). Patient eating habits and the presence of emotional eating were appraised using the Three-Factor Eating Questionnaire. Levels of depression and anxiety were evaluated using the Beck Depression Inventory and the State Trait Anxiety Inventory. RESULTS: 57 out of 118 patients were found to be affected by BED following the DSM 5 criteria; among them 24 followed those of the DSM IV TR. BED patients scored higher on four subscales of the Eating Disorders Inventory: Drive for thinness (DT), Bulimia (B), Body dissatisfaction (BD) and Interoceptive awareness (IA) on the STAI and on the Disinhibition and Hunger subscales of the TFEQ. DISCUSSION: The results confirm the presence of high levels of psychopathology among patients diagnosed with BED, even if they have been diagnosed following the criteria of the DSM 5. There is a great overlap in psychopathology between BED patients diagnosed following the DSM IV TR and the DSM 5 criteria.

#### Ramacciotti, C. E., et al. (2008). "Shared psychopathology in obese subjects with and without binge-eating disorder." Int J Eat Disord 41(7): 643-649.

OBJECTIVE: To investigate obese people with/without binge-eating Disorder (BED) in terms of shared psychopathological features pertaining to spectrum of eating disorders. METHOD: One-hundred obese adult patients with a BMI > 30 kg/m(2) referred to an Eating Disorder Unit and/or hospital weight-loss programs were administered the BED Clinical Interview, the Eating Disorder Inventory, and the Structured Clinical Interview for Anorexic-Bulimic Spectrum, Self-Report. RESULTS: Twenty-seven subjects satisfied DSM-IV research criteria for current BED; compared to nonbingeing obese subjects, BED ones were characterized by greater weight-shape concerns influencing self-esteem (p = .05), overall impairment due to the overweight condition (p < .005), psychological distress leading to professional help (p < .001), dichotomous reasoning (p = .01) and secondary social phobia due to the overweight condition (p < .005). Compared to the other group, BED obese subjects scored higher at the following EDI subscales: bulimia (p < .0001), ineffectiveness (p < .01), interoceptive awareness and social insecurity (p < .05). CONCLUSION: The results of this study highlight the role of cognitive mechanisms such as dichotomous reasoning and weight-shape concerns unduly influencing self-esteem as a hallmark of BED in obese patients, and the importance of investigating eating disorder psychopathology by adopting a dimensional perspective, rather than strictly focusing on categories when dealing with obese patients.

#### Raymond, N. C., et al. (1995). "Pain thresholds in obese binge-eating disorder subjects." Biol Psychiatry 37(3): 202-204.

#### de Zwaan, M., et al. (1994). "Eating related and general psychopathology in obese females with binge eating disorder." Int J Eat Disord 15(1): 43-52.

One hundred obese women with a mean age of 39.2 years, and a mean body mass index (BMI) of 35.9 kg/m2 were evaluated before entering a treatment study for weight reduction. According to the results of a structured interview, subjects were divided into four groups: (1) no overeating episodes, (2) episodic overeating episodes without the feeling of loss of control, (3) overeating plus the sense of loss of control (binge eating), and (4) full diagnostic criteria for binge eating disorder (BED). One-way analyses of variance (ANOVAs) revealed significant positive associations between binge eating and eating/weight-related characteristics such as a history of frequent weight fluctuations, the amount of time spent dieting, drive for thinness, and a tendency for disinhibition of eating. Furthermore, subjects exhibited more feelings of ineffectiveness, stronger perfectionistic attitudes, more impulsivity, less self-esteem, and less interoceptive awareness the more problems with binge eating they reported. The results support the idea that binge eaters might be a distinct subgroup among the obese population, and corroborate the utility of a diagnosis of BED in identifying the most disturbed obese subjects with regard to the variables tested.

#### Khalsa, S. S., et al. (2018). "Interoception and Mental Health: A Roadmap." Biological Psychiatry: Cognitive Neuroscience and Neuroimaging 3(6): 501-513.

Interoception refers to 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. Interoceptive signaling has been considered a component process of reflexes, urges, feelings, drives, adaptive responses, and cognitive and emotional experiences, highlighting its contributions to the maintenance of homeostatic functioning, body regulation, and survival. Dysfunction of interoception is increasingly recognized as an important component of different mental health conditions, including anxiety disorders, mood disorders, eating disorders, addictive disorders, and somatic symptom disorders. However, a number of conceptual and methodological challenges have made it difficult for interoceptive constructs to be broadly applied in mental health research and treatment settings. In November 2016, the Laureate Institute for Brain Research organized the first Interoception Summit, a gathering of interoception experts from around the world, with the goal of accelerating progress in understanding the role of interoception in mental health. The discussions at the meeting were organized around four themes: interoceptive assessment, interoceptive integration, interoceptive psychopathology, and the generation of a roadmap that could serve as a guide for future endeavors. This review article presents an overview of the emerging consensus generated by the meeting.

#### Aloi, M., et al. (2017). "Social Cognition and Emotional Functioning in Patients with Binge Eating Disorder." Eur Eat Disord Rev 25(3): 172-178.

OBJECTIVE: This study aims to evaluate the theory of mind ability in a sample of obese patients with and without binge eating disorder (BED) and to explore the correlations between emotional and clinical assessments. METHODS: Overall, 20 non-BED, 16 under-threshold BED and 22 BED obese patients completed a battery of tests assessing social cognition and eating disorder psychopathology. RESULTS: Binge eating disorder, non-BED and under-threshold-BED obese patients showed similar ability to recognise others' emotions, but BED obese patients exhibited a deficit in recognising their own emotions as demonstrated by more impaired levels of alexithymia and interoceptive awareness and were more depressed. High positive correlations were evident between binging, depression, interoceptive awareness and alexithymia. CONCLUSIONS: Binge eating disorder patients have a comparable ability to understand others' emotions but a more impaired capacity to understand and code their own emotions compared with non-BED obese patients. This impairment is highly correlated with depression. Copyright © 2017 John Wiley & Sons, Ltd and Eating Disorders Association.

#### Lattimore, P., et al. (2017). "‘I can’t accept that feeling’: Relationships between interoceptive awareness, mindfulness and eating disorder symptoms in females with, and at-risk of an eating disorder." Psychiatry Res 247: 163-171.

Mindfulness based therapies (MBTs) for eating disorders show potential benefit for outcomes yet evidence is scarce regarding the mechanisms by which they influence remission from symptoms. One way that mindfulness approaches create positive outcomesis through enhancement of emotion regulation skills. Maladaptive emotion regulation is akey psychological feature of all eating disorders. The aim of the current study was to identify facets of emotion regulation involved in the relationship between mindfulness and maladaptive eating behaviours. In three cross-sectional studies, clinical (n=39) and non-clinical (n=137 & 119) female participants completed: 1) the Eating Disorder Inventory (EDI) eating specific scales (drive-for-thinness and bulimia) and the EDI psychological symptom scales (emotion dysregulation and interoceptive deficits); and 2) mindfulness, impulsivity, and emotion regulation questionnaires. In all samples mindfulness was significantly and inversely associated with EDI eating and psychological symptom scales, and impulsivity. In non-clinical samples interoceptive deficits mediated the relationship between mindfulness and EDI eating specific scales. Non-acceptance of emotional experience, a facet of interoceptive awareness, mediated the relationship between mindfulness and eating specific EDI scores. Further investigations could verify relationships identified so that mindfulness based approaches can be optimised to enhance emotion regulation skills in sufferers, and those at-risk, of eating disorders.

#### Lammers, M. W., et al. (2015). "Predictors of outcome for cognitive behavior therapy in binge eating disorder." European Eating Disorders Review 23(3): 219-228.

The aim of this naturalistic study was to identify pretreatment predictors of response to cognitive behavior therapy in treatment-seeking patients with binge eating disorder (BED; N = 304). Furthermore, we examined end-of-treatment factors that predict treatment outcome 6 months later (N = 190). We assessed eating disorder psychopathology, general psychopathology, personality characteristics and demo- graphic variables using self-report questionnaires. Treatment outcome was measured using the bulimia subscale of the Eating Disorder Inventory 1. Predictors were determined using hierarchical linear regression analyses. Several variables significantly predicted outcome, four of which were found to be both baseline predictors of treatment outcome and end-of-treatment predictors of follow-up: Higher levels of drive for thinness, higher levels of interoceptive awareness, lower levels of binge eating pathology and, in women, lower levels of body dissatisfaction predicted better outcome in the short and longer term. Based on these results, several suggestions are made to improve treatment outcome for BED patients. Copyright © 2015 John Wiley & Sons, Ltd and Eating Disorders Association.

#### Fassino, S., et al. (2004). "Clinical, psychopathological and personality correlates of interoceptive awareness in anorexia nervosa, bulimia nervosa and obesity." Psychopathology 37(4): 168-174.

Objective: To determine the levels of interceptive awareness (IA), which measures the ability of an individual to discriminate between sensations and feelings, and between the sensations of hunger and satiety, in eating disorder patients and to identify the clinical, psycho- pathological and personal variables correlated with IA. Sampling and Methods: Sixty-one restrictor anorectics, 61 binge-purging anorectics, 104 purging bulimics, 49 obese subjects with binge eating disorder (BED) and 47 obese subjects without BED were compared. They were assessed with the Eating Disorder Inventory-2, the Temperament and Character Inventory, and the Beck Depression Inventory, and their clinical and sociodemographic features were recorded. Results: In all patients, the levels of lA were higher than the 'normal' ones; in bulimia nervosa, they were higher than in anorexia nervosa and obesity. Similar personal features and eating attitudes are shared by patients with bulimia nervosa and BED. In the total sample, the following variables independently correlate with IA: the Beck Depression Inventory, self-directedness and persistence. Conclusions: The importance of an altered Al ni eating disorders is supported. Both depression and a perfectionist and poorly self- directive personality can lead to greater difficulties in discriminating hunger and satiety.

#### Fitzgibbon, M. L., et al. (2003). "A test of the continuity perspective across bulimic and binge eating pathology." International Journal of Eating Disorders 34(1): 83-97.

Abstract: Objective: This article examines the continuity/discontinuity perspective of eating pathology among 375 women seeking treatment. Methods: Participants were categorized into five separate groups: obese non-binge-eaters, subthreshold binge eating disorder (BED), BED, subthreshold bulimics, and bulimics. We tested whether differences in core eating pathology (drive for thinness, body dissatisfaction, current body image, body image ideal) and psychiatric symptoms (depression, interoceptive awareness) differentiated the groups quantitatively (supporting the continuity perspective) or qualitatively (supporting the dis- continuity perspective). Results: Our results, overall, supported the continuity perspective of eating pathology. A discriminant function analysis using the eating pathology and psychiatric symptom variables as predictor variables found that one primary factor differentiated the five groups on both core eating pathology and psychiatric variables. Discussion: The impli- cations of testing this model within a treatment-seeking sample are discussed. # 2003 by Wiley Periodicals, Inc. Int J Eat Disord 34: 83–97, 2003.

# Interoception in Other Eating Disorders

## “Mixed EDs” (which can include BED)

(1)

#### Dancyger, I. F. and P. Garfinkel (1995). "The relationship of partial syndrome eating disorders to anorexia nervosa and bulimia nervosa1." Psychol Med 25(5): 1019-1025.

A variety of sociocultural, familial and individual features associated with the eating disorders were examined in subjects with full syndrome (FS) and partial syndrome (PS) eating disorders and in normal high school students. The EAT-26 was administered to 995 high school students. This was followed by individual interviews with those who scored in the symptomatic range. Fifty-one students with PS eating disorders, 57 students without eating disorders (normal controls) and 30 hospital patients with FS, anorexia nervosa or bulimia nervosa were compared on subscales of the Eating Disorder Inventory, the Diagnostic Survey for Eating Disorders and the Beck Depression Inventory. The three groups displayed statistically significant differences on dimensions of EDI subscales Ineffectiveness and Interoceptive Awareness and also with respect to depression, history of being overweight and past history of emotional problems, as well as having mothers with medical illnesses. On these characteristics, the FS subjects displayed higher levels than the PS subjects, who in turn were higher than the NC subjects. The PS subjects displayed elevations on Body Dissatisfaction (EDI subscale), past medical illnesses, and mother's over-concern with eating and weight. These data support a continuum model of the eating disorders, but a continuum of multiple associated features rather than of dieting.

## “EDNOS” (“Eating Disorder Not Otherwise Specified,” which included BED before publication of the DSM-V in 2013).

(2-4)

#### Nyman-Carlsson, E., et al. (2015). "Eating Disorder Inventory-3, validation in Swedish patients with eating disorders, psychiatric outpatients and a normal control sample." Nordic Journal of Psychiatry 69(2): 142-151.

*Background:* The Eating Disorder Inventory-3 (EDI-3) is designed to assess eating disorder psychopathology and the associated psychological symptoms. The instrument has been revised and has not yet been validated for Swedish conditions in its current form. *Aims:* The aim of  
this study was to investigate the validity and reliability of this inventory and present national norms for Swedish females. *Methods:* Data from patients with eating disorders (*n*292), psychiatric outpatients (*n*140) and normal controls (*n*648), all females, were used to study the internal consistency, the discriminative ability, and the sensitivity and specificity of the inventory using preliminary cut-offs for each subscale and diagnosis separately. Swedish norms were compared with those from Denmark, USA, Canada, Europe and Australian samples. *Results:* The reliability was acceptable for all subscales except Asceticism among normal controls. Analysis of variance showed that the EDI-3 discriminates significantly between eating disorders and normal controls. Anorexia nervosa was significantly discriminated from bulimia nervosa and eating disorder not otherwise specified on the Eating Disorder Risk Scales. Swedish patients scored significantly lower than patients from other countries on the majority of the subscales. Drive for Thinness is the second best predictor for an eating disorder. The best predictor for anorexia nervosa was Interoceptive Deficits and Bulimia for the other diagnoses. *Conclusions/clinical implications:* The EDI-3 is valid for use with Swedish patients as a clinical assessment tool for the treatment planning and evaluation of patients with eating-related problems. However, it still exist some uncertainty regarding its use as a screening tool.

#### Herraiz-Serrrano, C., et al. (2015). "Parental rearing and eating psychopathology." Actas Esp Psiquiatr 43(3): 91-98.

**Introduction.** The aim of the study was to identify the relationship between perceived rearing styles and the clini- cal expression of Eating Disorders (ED).

**Methods.** One hundred and ninety-six patients diag- nosed of an ED and 127 healthy student as controls selected from the Nursing College were evaluated for general psy- chopathology (STAI, BDI II, RSE), and for abnormal eating attitudes (EAT, EDI-II, BITE). The EMBU (‘my memories of up- bringing’) was administered for the assessment of perceived parental rearing styles and was used a questionnaire to as- sess familial variables.

**Results.** In relation to the control group, patients with ED perceived greater rejection, overprotection and less warmth than the controls. Patients who perceived greater paternal favoritism, maternal overprotection and low pater- nal emotional warmth, showed higher levels of anxiety. Pa- ternal affection and maternal attitudes of rejection, over- protection and favoritism were related to lower self-esteem. Regarding abnormal eating attitudes, body dissatisfaction inversely correlated with paternal emotional care and ma- ternal favoritism. The EDI subscales: ineffectiveness, perfec- tionism and ascetism were associated to parental rejection. Maternal rejection also related with drive for thinness, in- teroceptive awareness and impulse regulation. Perceived emotional warmth was related with perfectionism. Bulimia subscale and BITE scores were inversely associated to pater- nal overprotection and affection, and scored significantly higher in paternal favoritism and rejection from both par- ents.

**Conclusions.** Perceived parental bonding is different in the various subtypes of EDs. Patients diagnosed of Bulimia Nervosa or Eating Disorders Not Otherwise Specified perceived greater rejection, less affection and a greater overprotection than Anorexia Nervosa patients and controls.

#### Nevonen, L., et al. (2006). "Validating the EDI-2 in three Swedish female samples: eating disorders patients, psychiatric outpatients and normal controls." Nordic Journal of Psychiatry 60(1): 44-50.

The aim of the current study was to validate the Eating Disorders Inventory 2 (EDI-2) in a Swedish population by investigating how it discriminates between three female samples aged 18 to 50 years: patients with eating disorders (n /978), psychiatric outpatients (n /106) and normal controls (n/602), as well as between different eating disorder diagnoses. The internal consistency of the EDI-2 was above 0.70 for most subscales. The EDI-2 discriminated well between patients with eating disorders and normal controls on all subscales. On the symptom- related subscales, eating disorder patients scored highest followed by psychiatric controls and normals. All subscales except Perfectionism, Interoceptive awareness and Asceticism discrimi- nated eating disorder patients and psychiatric controls. Bulimia patients scored higher than anorexics on the symptom subscales. It is concluded that the EDI-2 discriminates well between eating disorder patients and both psychiatric and normal controls.

# Autism in BED

(5-11)

#### Pruccoli, J., et al. (2023). "Food and Development: Children and Adolescents with Neurodevelopmental and Comorbid Eating Disorders-A Case Series." Behav Sci (Basel) 13(6).

The impact of psychiatric comorbidities in the diagnosis and treatment of feeding and eating disorders (FEDs) represents an emerging research topic. The current literature, nonetheless, lacks studies investigating the developmental paths of individuals with FEDs and comorbid neurodevelopmental disorders (NDDs). Here, we report 11 cases of children and adolescents with comorbid FEDs and NDDs, as assessed along the neuropsychological, psychopathological, and nutritional developmental pathways. The onset of FED-related psychopathology was preceded, sometimes undiagnosed, by altered neurodevelopmental features leading to specific NDD diagnoses (autism spectrum disorder-ASD; attention-deficit/hyperactivity disorder-ADHD; specific learning disorder-SLD). NDDs appeared to influence the diagnoses and treatments of FEDs, frequently with an impact on socio-relational and emotional premorbid features, and on the possibility to receive and attend FED-targeted treatments. Further studies should longitudinally contribute to assessing the experiences of care and neurodevelopmental pathways of children with FEDs and specific NDD comorbidities.

#### Price, D. (2022). Unmasking Autism: Discovering the New Faces of Neurodiversity. NY, Harmony Books.

For every visibly Autistic person you meet, there are countless “masked” Autistic people who pass as neurotypical. Masking is a common coping mechanism in which Autistic people hide their identifiably Autistic traits in order to fit in with societal norms, adopting a superficial personality at the expense of their mental health. This can include suppressing harmless stims, papering over communication challenges by presenting as unassuming and mild-mannered, and forcing themselves into situations that cause severe anxiety, all so they aren’t seen as needy or “odd.”

In Unmasking Autism, Dr. Devon Price shares his personal experience with masking and blends history, social science research, prescriptions, and personal profiles to tell a story of neurodivergence that has thus far been dominated by those on the outside looking in. For Dr. Price and many others, Autism is a deep source of uniqueness and beauty. Unfortunately, living in a neurotypical world means it can also be a source of incredible alienation and pain. Most masked Autistic individuals struggle for decades before discovering who they truly are. They are also more likely to be marginalized in terms of race, gender, sexual orientation, class, and other factors, which contributes to their suffering and invisibility. Dr. Price lays the groundwork for unmasking and offers exercises that encourage self-expression, including:

• Celebrating special interests

• Cultivating Autistic relationships

• Reframing Autistic stereotypes

• And rediscovering your values

It’s time to honor the needs, diversity, and unique strengths of Autistic people so that they no longer have to mask—and it’s time for greater public acceptance and accommodation of difference. In embracing neurodiversity, we can all reap the rewards of nonconformity and learn to live authentically, Autistic and neurotypical people alike.

#### Solmi, F., et al. (2021). "Trajectories of autistic social traits in childhood and adolescence and disordered eating behaviours at age 14 years: A UK general population cohort study." J Child Psychol Psychiatry 62(1): 75-85.

BACKGROUND: Some people with eating disorders have difficulties with social communication. However, no longitudinal evidence regarding the direction of this association exists. We investigated trajectories of autistic social traits across childhood and adolescence in adolescents with and without disordered eating behaviours in early adolescence. METHODS: We used data from the Avon Longitudinal Study of Parents and Children. Our disordered eating measure indicated presence of any, monthly and weekly disordered eating (fasting, purging, dieting, binge eating) at age 14 years. Autistic social traits were reported by mothers using the Social and Communication Disorders Checklist (SCDC) at age seven, 11, 14 and 16 years. We modelled SCDC score trajectories using multilevel negative binomial models adjusting for a number of child- and maternal-level confounders. RESULTS: Of the 5,381 adolescents included in our sample, 421 (7.8%) experienced one or more disordered eating behaviours, and 148 (2.8%) weekly episodes. Adolescents with disordered eating had a 20% increase in SCDC scores (relative risk (RR) 1.23, 95% confidence interval (CI):1.14, 1.32) compared to those without disordered eating. This association was particularly apparent for those reporting weekly (RR 1.43, 95%CI: 1.27, 1.61) as opposed to monthly disordered eating (RR 1.12, 95%CI: 1.01, 1.22). CONCLUSIONS: Greater autistic social traits in childhood could represent a risk factor for the development of disordered eating in adolescence. Although mechanisms of this association need to be elucidated, clinicians should be aware that autistic social traits could have predated the eating disorder when managing people with these conditions.

#### Björk, A., et al. (2021). "High prevalence of neurodevelopmental problems in adolescents eligible for bariatric surgery for severe obesity." Acta Paediatr 110(5): 1534-1540.

AIM: To assess the prevalence of neurodevelopmental problems in adolescents with severe obesity and their associations with binge eating and depression. METHODS: Data were collected at inclusion in a randomised study of bariatric surgery in 48 adolescents (73% girls; mean age 15.7 ± 1.0 years; mean body mass index 42.6 ± 5.2 kg/m(2) ). Parents completed questionnaires assessing their adolescents' symptoms of attention-deficit/hyperactivity disorder and autism spectrum disorder and reported earlier diagnoses. Patients answered self-report questionnaires on binge eating and depressive symptoms. RESULTS: The parents of 26/48 adolescents (54%) reported scores above cut-off for symptoms of the targeted disorders in their adolescents, but only 15% reported a diagnosis, 32% of adolescents reported binge eating, and 20% reported symptoms of clinical depression. No significant associations were found between neurodevelopmental problems and binge eating or depressive symptoms. Only a third of the adolescents reported no problems in either area. CONCLUSION: Two thirds of adolescents seeking surgical weight loss presented with substantial mental health problems (reported by themselves or their parents). This illustrates the importance of a multi-professional approach and the need to screen for and treat mental health disorders in adolescents with obesity.

#### Nickel, K., et al. (2019). "Systematic Review: Overlap Between Eating, Autism Spectrum, and Attention-Deficit/Hyperactivity Disorder." Front Psychiatry 10: 708.

Background: Links between eating disorders (EDs) [e.g., anorexia nervosa (AN), bulimia nervosa (BN), and binge eating disorder (BED)] and the major neurodevelopmental disorders of autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD) have been repeatedly highlighted. In both ASD and ADHD, these links range from an elevated risk for EDs to common symptomatic overlaps and etiological commonalities with EDs. Methods: We performed a systematic literature search (through July 2019) with Medline via Ovid for epidemiological data on EDs (AN, BN, and BED) in combination with both ASD and ADHD. Results: The reviewed studies showed that, on average, 4.7% of patients with certain ED diagnoses (AN, BN, or BED) received an ASD diagnosis. Reliable data on the prevalence of EDs in ASD samples are still scarce. Comorbid ASD is most commonly diagnosed in patients with AN. The prevalence of ADHD in EDs ranged between 1.6% and 18%. Comorbid ADHD was more often reported in the AN-binge eating/purging subtype and BN than in the AN restrictive subtype. The prevalence of EDs in ADHD ranged between no association and a lifetime prevalence of 21.8% of developing an ED in women with ADHD. Conclusions: Studies on the prevalence rates of EDs in ADHD and ASD and vice versa are heterogeneous, but they indicate frequent association. While there is growing evidence of clinical overlaps between the three disorders, it remains difficult to determine whether overlapping characteristics (e.g., social withdrawal) are due to common comorbidities (e.g., depression) or are instead primarily associated with EDs and neurodevelopmental disorders. Furthermore, prospective studies are required to better understand how these disorders are related and whether ADHD and ASD could be either specific or nonspecific predisposing factors for the development of EDs.

#### Dell'Osso, L., et al. (2019). "Autistic Traits and Illness Trajectories." Clin Pract Epidemiol Ment Health 15: 94-98.

In the framework of increasing attention towards autism-related conditions, a growing number of studies have recently investigated the prevalence and features of sub-threshold Autistic Traits (ATs) among adults. ATs span across the general population, being more pronounced in several clinical groups of patients affected by psychiatric disorders. Moreover, ATs seem to be associated with specific personality features in non-clinical population, implying both a higher vulnerability towards psychopathology and extraordinary talents in specific fields. In this framework, the DSM-5's Autism Spectrum Disorder (ASD) presentations may be considered as the tip of an iceberg that features several possible clinical and non-clinical phenotypes. Globally, the autism spectrum may be considered as a trans-nosographic dimension, which may not only represent the starting point for the development of different psychopathological trajectories but also underlie non-psychopathological personality traits. These different trajectories might be shaped by the specific localization and severity of the neurodevelopmental alteration and by its interaction with the environment and lifetime events. In this wider framework, autistic-like neurodevelopmental alterations may be considered as a general vulnerability factor for different kinds of psychiatric disorders, but also the neurobiological basis for the development of extraordinary abilities, eventually underlying the concept of geniality. Moreover, according to recent literature, we hypothesize that ATs may also be involved in the functioning of human mind, featuring the peculiar sense of "otherness" which can be found, with different grades of intensity, in every human being.

#### Nazar, B. P., et al. (2016). "ADHD Rate in Obese Women With Binge Eating and Bulimic Behaviors From a Weight-Loss Clinic." Journal of Attention Disorders 20(7): 610-616.

Objective: Few studies have demonstrated a possible association between ADHD and obesity in adults. The aim of this study was to investigate the prevalence of ADHD in a sample of obese women seeking treatment, and its relations with binge eating and bulimic behaviors. Method: We performed a cross-sectional study in a clinical sample of one hundred fifty-five women, with a mean age of 38.9 (+10.7) years and a mean body mass index (BMI) of 39.2 (+5.29). Participants were evaluated with semistructured interviews and completed self-report psychiatric rating scales. Results: The rate of ADHD in the sample was of 28.3%. The presence of ADHD was significantly correlated with more severe binge eating, bulimic behaviors, and depressive symptomatology. Conclusion: Similar to previous studies, a higher than expected rate of ADHD was observed among obese women. ADHD in obese individuals may be a risk factor for greater severity of disordered eating patterns.

# References

1. Dancyger IF, Garfinkel P. The Relationship of Partial Syndrome Eating Disorders to Anorexia Nervosa and Bulimia Nervosa1. *Psychological medicine* (1995) 25(5):1019-25.

2. Nyman-Carlsson E, Engström I, Norring C, Nevonen L. Eating Disorder Inventory-3, Validation in Swedish Patients with Eating Disorders, Psychiatric Outpatients and a Normal Control Sample. *Nordic Journal of Psychiatry* (2015) 69(2):142-51.

3. Herraiz-Serrrano C, Rodríguez-Cano T, Beato-Fernández L, Latorre-Postigo JM, Rojo-Moreno L, Vaz-Leal FJ. Parental Rearing and Eating Psychopathology. *Actas espanolas de psiquiatria* (2015) 43(3):91-8.

4. Nevonen L, Clinton D, Norring C. Validating the Edi-2 in Three Swedish Female Samples: Eating Disorders Patients, Psychiatric Outpatients and Normal Controls. *Nordic Journal of Psychiatry* (2006) 60(1):44-50.

5. Nazar BP, de Sousa Pinna CM, Suwwan R, Duchesne M, Freitas SR, Sergeant J, et al. Adhd Rate in Obese Women with Binge Eating and Bulimic Behaviors from a Weight-Loss Clinic. *Journal of Attention Disorders* (2016) 20(7):610-6. doi: 10.1177/1087054712455503.

6. Dell'Osso L, Lorenzi P, Carpita B. Autistic Traits and Illness Trajectories. *Clin Pract Epidemiol Ment Health* (2019) 15:94-8. Epub 2019/12/11. doi: 10.2174/1745017901915010094.

7. Pruccoli J, Guardi G, La Tempa A, Valeriani B, Chiavarino F, Parmeggiani A. Food and Development: Children and Adolescents with Neurodevelopmental and Comorbid Eating Disorders-a Case Series. *Behav Sci (Basel)* (2023) 13(6). Epub 2023/06/27. doi: 10.3390/bs13060499.

8. Björk A, Dahlgren J, Gronowitz E, Henriksson Wessely F, Janson A, Engström M, et al. High Prevalence of Neurodevelopmental Problems in Adolescents Eligible for Bariatric Surgery for Severe Obesity. *Acta Paediatr* (2021) 110(5):1534-40. Epub 2020/12/17. doi: 10.1111/apa.15702.

9. Nickel K, Maier S, Endres D, Joos A, Maier V, Tebartz van Elst L, et al. Systematic Review: Overlap between Eating, Autism Spectrum, and Attention-Deficit/Hyperactivity Disorder. *Frontiers in psychiatry* (2019) 10:708. Epub 2019/10/28. doi: 10.3389/fpsyt.2019.00708.

10. Solmi F, Bentivegna F, Bould H, Mandy W, Kothari R, Rai D, et al. Trajectories of Autistic Social Traits in Childhood and Adolescence and Disordered Eating Behaviours at Age 14 Years: A Uk General Population Cohort Study. *Journal of child psychology and psychiatry, and allied disciplines* (2021) 62(1):75-85. Epub 2020/05/04. doi: 10.1111/jcpp.13255.

11. Price D. *Unmasking Autism: Discovering the New Faces of Neurodiversity*. 1 ed. NY: Harmony Books (2022).