Aus dem Zentralinstitut für Seelische Gesundheit
Abteilung Klinische Psychologie
Abteilungsleiter: Prof. Dr. phil. Peter Kirsch

Body matters in emotion: Interoceptive processing in patients with inflammatory bowel disease

Inauguraldissertation
zur Erlangung des Doctor scientiarum humanarum (Dr. sc. hum)
an der
Medizinischen Fakultät Mannheim
der Ruprecht-Karls-Universität
zu
Heidelberg

vorgelegt von
Konstantina Mihaylova Atanasova

aus
Varna, Bulgarien
2022

Dekan: Prof. Dr. med. Sergij Goerdt
Referentin: Prof. apl. Dr. biol. hom. Stefanie Lis

"We use our emotions. In their essence, they are simply part of the goodness of being alive, but instead of letting them be, we take them and use them to regain our ground. We use them to try to make everything secure and predictable and real again, to fool ourselves about what's really true. We could just sit with the emotional energy and let it pass. There's no particular need to spread blame and self-justification. Instead, we throw kerosene on the emotion so it will feel more real."

- *Pema Chödrön, When Things Fall Apart-*

TABLE OF CONTENT

LIST OF ABBREVATIONS

ACE	Adverse Childhood Experiences
ANS	Autonomic Nervous System
CBT	Cognitive Behavioral Therapy
CD	Crohn's Disease
CECA	Childhood Experiences of Care and Abuse
CNS	Central Nervous System
CTQ	Childhood Trauma Questionnaire
DV	Dependent Variable
ENS	Enteric Nervous System
FDR	False Detection Rate
GSA	Gastrointestinal-Specific Anxiety
HBT	Heartbeat Tracking Task
HC	Healthy Control
HPA	Hypothalamic-Pituitary-Adrenal
HR	Heart Rate
HRV	Heart Rate Variability
IAcc	Interoceptive Accuracy
IAw	Interoceptive Awareness
IBD	Inflammatory Bowel Disease
IBS	Irritable Bowel Syndrome
IL-12	Interleukin 12
IS	Interoceptive Sensibility
IV	Independent Variable
LEC	Life Events Checklist

MAIA	Multidimensional Assessment of Interoceptive Awareness
PCL	PTSD Checklist
PTSD	Posttraumatic Stress Disorder
TNF	Tumor Necrosis Factor
UC	Ulcerative Colitis
VSI	Visceral Sensitivity Index

1 INTRODUCTION

The term ‘interoception’ refers to one of the most basic human experiences – feeling and perceiving our own body (Ceunen et al., 2016; Craig, 2003). It comprises the brain-body communication and several models have emphasized the role of dysfunctional interoception in somatic and psychiatric disorders (Bonaz et al., 2021; Khalsa et al., 2018). Inflammatory bowel disease (IBD) is a chronic inflammatory condition characterized by considerable emotional and social burdens for the affected individuals (Neuendorf et al., 2016). As the course of the disease includes alternating periods of relapse and remission, patients with IBD tend to monitor their body signals in order to notice early signs of worsening disease symptoms (Phillips et al., 2014). In addition, IBD has been associated with altered processing of sensory information and disturbed brain-body signaling (Bonaz & Bernstein, 2013; Mawdsley & Rampton, 2006).

One factor potentially contributing to an impaired psychological well-being during the course of IBD is poor emotional functioning (Agostini et al., 2011; Banovic et al., 2020; Wilkinson et al., 2019). It is generally agreed upon the primary role of interoceptive signals for the conscious experience of emotions (Craig, 2002; Damasio, 2001; James, 1994), and a significant body of evidence demonstrated a link between interoception and emotion perception (Garfinkel et al., 2014; Wiens, 2005; Zamariola et al., 2019). Thus, disturbances in how individuals perceive and appraise their bodily sensations can result in emotional dysfunctions. Beyond its impact on emotion perception, interoception also plays a crucial role in how individuals perceive their bodies (Craig, 2003), how satisfied they are with their body appearance (Duschek et al., 2015; Todd et al., 2020), and to what extent individuals experience their bodies as belonging to themselves (Crucianelli et al., 2018; Tsakiris et al., 2011). While some previous studies have indicated disturbances in patients’ body ownership and body evaluation in immune-mediated diseases (Beese et al., 2019; Finotti & Costantini, 2016), evidence regarding the role of interoception in these facets of body perception in IBD is missing.

This dissertation is aimed at contributing to a better understanding of the complex interplay of interoception, emotional functioning, and body perception in IBD. In Chapter 1 of this thesis, I will provide the theoretical background, including a brief overview of the primary characteristics of IBD, followed by definitions and dimensions of interoception. Then, I will discuss how interoception is linked to emotion and body perception, especially with respect to IBD. At the end of Chapter 1, the four main research questions investigated in this thesis will

be introduced, followed by the empirical findings in Chapter 2. Finally, in Chapter 3, results will be discussed and integrated, examining their implications for future research on interoception in IBD.

1.1 Inflammatory bowel disease

Inflammatory bowel disease (IBD) is characterized by non-infectious chronic inflammation of the gastrointestinal tract which can affect any age group, leading to considerable societal and economic burden (Alatab et al., 2020). Primarily, IBD includes two types: Crohn's disease (CD) and Ulcerative colitis (UC). While CD can affect the entire gastrointestinal tract, UC affects the large intestine tract and is frequently associated with inflammation of the rectum but can also extend proximally to areas of the colon. Patients with IBD experience abdominal pain, diarrhea, unwanted weight loss, chronic fatigue, and sometimes extraintestinal manifestations such as joint or skin problems (Levine & Burakoff, 2011). IBD arises from the interaction between environmental and genetic factors, resulting in an immunological response of the body and inflammation in the intestine (Ananthakrishnan et al., 2018; Baumgart & Carding, 2007). Although the immune-mediated changes in IBD are already well investigated and described, the underlying triggers responsible for these changes are still unknown. Different incidence rates of IBD across the world might indicate different genetic backgrounds, however, more important factors which might trigger the development of IBD seem to be the environmental ones (Bernstein, 2017). The role of specific environmental factors is still poorly defined, one candidate being the exposure to adverse childhood experiences (ACE) (Dube et al., 2009; Fuller-Thomson et al., 2015; Wan et al., 2022).

1.1.1 Inflammatory bowel disease and adverse childhood experiences

Adverse childhood experiences encompass different types of childhood maltreatment, including physical abuse, sexual abuse, emotional abuse, physical neglect, and emotional neglect (Herzog & Schmahl, 2018; Klinitzke et al., 2012; McLaughlin et al., 2010). Emerging evidence suggests that experiences of childhood adversity is also associated with elevated levels of inflammation, a greater immune reactivity to stress and an increased risk of disease with inflammatory origin such as IBD in adulthood (Danese & Lewis, 2017; Danese et al., 2009; Dube et al., 2009; Osborn & Widom, 2020). One cohort study investigating the link between histories of childhood maltreatment and an IBD diagnosis in adulthood indicated that around

70 % of the examined CD patients reported a history of ACE (Ryan et al., 2013). Another population-based study showed that the prevalence of early life adversities was significantly higher in patients with UC compared to those with CD: around 26 % of the UC patients and 7 % of the CD experienced physical abuse during their childhood, compared to a 10 % prevalence among healthy control participants (Fuller-Thomson et al., 2015). Beyond physical abuse, histories of sexual abuse have also been frequently reported by IBD patients with a prevalence of 22 % (Drossman et al., 1990; Fuller-Thomson et al., 2015). Overall, the prevalence of at least one type of ACE in IBD patients is found to be above 60 % (Wan et al., 2022; Witges et al., 2019).

Although no causality should be inferred based on cross-sectional data, some possible mechanisms for this association have been discussed in the literature. Chronic exposure to early life stress has been repeatedly associated with a dysregulation of the hypothalamic-pituitary adrenal (HPA) axis, responsible for the cortisol release in response to stress (Dempster et al., 2020; Hertzman, 1999; Herzog & Schmahl, 2018; McLaughlin et al., 2015). Recent findings from animal studies support the assumption that a history of ACE increases the likelihood of experiencing a relapse from a quiescent IBD and has been identified as a risk factor for the development of IBD (Mawdsley & Rampton, 2005; Mawdsley & Rampton, 2006; Reber, 2012). However, with respect to the underlying neuroendocrine mechanisms, only little is known from human studies. Some evidence suggested hypercortisolism among patients with IBD, indicating that in this immune-mediated condition, the body fails to produce the adequate levels of cortisol (Mawdsley & Rampton, 2006; Mayer, 2000). As cortisol normally prevents the release of substances causing inflammation such as cytokines (e.g., IL-12, TNF- α), the prolonged lack of sufficient levels of anti-inflammatory glucocorticoids might favor the development of mucosal inflammation (Reber, 2012; Straub et al., 2002). Thus, alterations in the physiological stress response resulting from exposure to early life stress may represent one pathway through which a history of ACE contributes to an increased risk of developing IBD.

1.1.2 Inflammatory bowel disease and emotion processing

A significant body of literature has suggested a potential role of chronic inflammation in the pathophysiology of depression and anxiety disorders (Kohler et al., 2016; Leonard & Maes, 2012; Moylan et al., 2013; Vogelzangs et al., 2013). In case of IBD, the association between inflammation and mental disorders seems to be bidirectional: IBD patients reporting stronger

anxiety symptoms experience a relapse more often, while patients with more severe disease activity more often develop anxiety disorders (Gracie et al., 2018). One factor potentially contributing to the development and maintenance of psychopathological symptoms in IBD is poor emotional functioning (Wilkinson et al., 2019). Although more recent findings have strongly emphasized the important role of emotion processing for patients' mental well-being and quality of life (Banovic et al., 2020; Engel et al., 2021; Wilkinson et al., 2019), there is still little evidence about the mechanisms underlying altered emotion perception in IBD.

Most of the available studies on emotional experience in IBD have pointed towards the presence of emotional dysfunctions characterized by decreased sensitivity to positive emotional cues (Agostini et al., 2011; Wilkinson et al., 2019) and increased sensitivity to negative emotions (Vianna et al., 2006). Agostini et al. (2011) demonstrated a reduced activation within the limbic system in response to positive emotional stimuli in patients with UC, suggesting a decreased ability to perceive positive emotions such as happiness or joy. More recent findings found empirical support for an emotion recognition bias towards positive emotional stimuli among IBD patients, showing also its overreaching negative impact on patients' psychological well-being (Wilkinson et al., 2019). For a long time, IBD has been associated with alexithymia, that is, the inability to differentiate, recognize, and express emotions (Sifneos, 1996; Taylor & Bagby, 2000). A recent review revealed that while IBD patients show more alexithymic features than healthy individuals, these cannot be considered as clinically significant (Martino et al., 2020). Nevertheless, the failure to recognize emotional percepts is thought to promote vulnerability to stress and impaired psychological well-being in IBD (La Barbera et al., 2017; Viganò et al., 2018; Yanartaş et al., 2019).

Although contemporary findings point towards the high prevalence of ACE in IBD populations, no study has investigated whether childhood maltreatment may promote emotional dysfunctions in this patient group. Previous empirical evidence has indicated that early traumatized individuals show increased responsiveness to negative and threatening emotional cues (Dannlowski et al., 2012; Grant et al., 2011; Hein & Monk, 2017; Puetz et al., 2020). Moreover, individuals with a history of ACE exhibit persistent attention and perception biases characterized by higher sensitivity to threatening cues in emotionally ambiguous stimuli (Dannlowski et al., 2013; Pollak et al., 2000; Pollak & Sinha, 2002), a faster detection of negative emotional content (Iffland & Neuner, 2020) and an impaired recognition accuracy for positive affective stimuli (Young & Widom, 2014). Thus, it is conceivable that IBD patients

reporting histories of ACE may be more prone to poorer emotional functioning including increased emotional reactivity to negative emotions and difficulties with perceiving positive emotions.

1.2 Interoception: the sense of the physiological condition of the body

Interoception refers to the signaling and perception of internal bodily sensations (Garfinkel et al., 2015). Interoceptive signals arise from distinct biological system in the body including the cardiovascular (Oppenheimer & Cechetto, 2016), pulmonary (von Leupoldt et al., 2013), gastrointestinal (Mayer, 2011), genitourinary (Drake et al., 2010), nociceptive (Simons et al., 2014), thermoregulatory (Fealey, 2013), immune (Capuron & Miller, 2011), and the autonomic systems (Critchley & Harrison, 2013).

The neurophysiological term 'interoception' was first introduced by Sherrington in 1906 and aimed to describe the sensory input from receptors located inside the body (Sherrington, 1906). Neuroanatomic works from the same time period postulated the existence of two categories of neurons in the spinal cord and the brain stem: 'visceral' and 'somatic' neurons (Sherrington, 1952). However, empirical research failed to distinguish the determining features of these two categories in the brain and thus, for many years the term interoception referred simply to the visceral sensory input, i.e. the transmission of sensory afferent signals from the internal organs to the brain (Cameron & Minoshima, 2002; Strigo & Craig, 2016). Newer findings on the functional anatomy of the nervous system led to the suggestion that interoception has to be redefined as *"the physiological condition of the entire body, and not just the viscera"* (Craig, 2002). According to this newer and more inclusive definition, pain, thermal, and visceral sensations are all senses originating from the body tissue and are crucial to the maintenance of the body's homeostasis (Craig, 2003). Further definitions of interoception include also the perception of internal body states such as hunger or thirst (Khalsa et al., 2009), the influence of visceral sensations on brain functioning and behavior (Critchley & Harrison, 2013) and the integration of autonomic, hormonal, visceral, and immunological homeostatic signals (Barrett & Simmons, 2015; Ceunen et al., 2016). Although there is still no complete agreement on the exact definition, the focus has moved away from referring only to the transmission and processing of afferent signals in the body to a broader definition of the construct of interoception including the processes by which an individual interprets and regulates signals originating from the body (Garfinkel et al., 2015).

1.2.1 Dimensions of interoception and their assessment

Individuals differ in their ability to detect and be aware of their bodily sensations and thus, measuring these features is complex. The long-lasting debates regarding the accurate definition of interoception have resulted in significant inconsistencies in terms of the terminology to describe the different facets of interoception and their assessment. In the past, the terms *interoceptive sensitivity* and *interoceptive awareness* have often been used interchangeably to refer to the extent to which people are aware of their bodily signals, regardless of whether the accuracy of these judgments was measured with a behavioral task or a self-report questionnaire. As these measures are clearly very different, a consistent terminology was needed in the field of interoceptive research. To address this issue, a three-dimensional construct of interoception has been proposed by Garfinkel and colleagues, distinguishing between the objective, subjective, and metacognitive aspects of interoceptive perception (Garfinkel et al., 2015). In this thesis, I will adopt the terminology proposed in Garfinkel's framework and use the terms of interoceptive accuracy (**IAcc**), interoceptive sensibility (**IS**) and interoceptive awareness (**IAw**) to refer to the psychological dimensions of interoceptive processing described below.

Interoceptive accuracy (IAcc)

The first dimension of Garfinkel's model is called **Interoceptive Accuracy (IAcc)** and it refers to the objective measure of interoception. It is a multimodal construct and thus, it can be investigated in different interoceptive channels (e.g., cardiovascular, respiratory). The cardiac interoceptive channel is the easiest to measure and therefore, has been a classic way to assess one's objective interoceptive abilities for long time using experimental procedures such as the heartbeat tracking task (Schandry, 1981). In this task, participants are asked to count the number of heartbeats in intervals of varying duration while an ECG is recorded, allowing the quantification of participant's accuracy in detecting their heartbeats. As the field of interoception has grown rapidly and various interoceptive tasks have been developed, some authors have suggested that the ability to perceive body signals originating from one particular interoceptive system (e.g., cardiovascular) should be similar across the different interoceptive channels (Garfinkel et al., 2016), although some recent studies ague against this generalizability of IAcc (Ferentzi et al., 2018; Herbert et al., 2012a).

Interoceptive sensibility (IS)

The second dimension of interoception, **Interoceptive Sensibility (IS)**, refers to the self-perceived tendency to be aware of one's bodily sensations (e.g., muscle tension, pounding heart). IS represents individual's beliefs in their interoceptive abilities and the extent to which they feel engaged by their body signals (Garfinkel et al., 2015). Self-report questionnaires constitute one approach to quantify participant's IS. As the interest in interoception has grown in recent years and a measure assessing all different facets of IS was needed, Mehling and colleagues developed the Multidimensional Assessment of Interoceptive Awareness (MAIA; Mehling et al. (2012)). In contrast to previous self-report measures of IS (Mehling et al., 2009; Porges, 1993), MAIA aims to differentiate between functional and dysfunctional aspects of IS by assessing how bodily sensations are used and responded to. The 32-item questionnaire comprises eight facets of IS: *Noticing, Distraction, Worrying, Attention regulation, Emotional awareness, Self-regulation, Body listening*, and *Body trusting*. The dimension *Noticing* reflects individual's self-reported awareness of their body signals, such as their heartbeats. The remaining seven dimensions refer to regulatory aspects of IS, that is, how the bodily sensations are used to regulate psychological distress (*Self-regulation, Attention regulation*), to gain insight about perceived emotions (*Emotional awareness*) and how bodily sensations are responded to (*Distraction, Worrying*).

Interoceptive awareness (IAw)

Finally, **Interoceptive Awareness (IAw)** represents the third dimension of interoception and refers to the individual's metacognitive awareness of their interoceptive abilities (Garfinkel et al., 2015; Murphy et al., 2019). IAw captures the correspondence between IAcc, as measured with a behavioral task (e.g., heartbeat tracking task), and IS, as measured via self-reports (e.g., questionnaires). Higher levels of IAw indicate a greater meta-awareness of an individual to know whether they are accurately or inaccurately assessing their body signals.

Table 1. The three dimensions of interoception as described by Garfinkel et al. (2015)

	Interoceptive accuracy (IAcc)	**Interoceptive sensibility (IS)**	**Interoceptive awareness (Iaw)**
Definition	Individual's objective accuracy in detecting internal bodily sensations (e.g., heart beats)	Self-perceived tendency to be internally self-focused and aware of one's internal sensations	Metacognitive awareness of one's interoceptive abilities. Knowing whether one detects his/her sensations accurately or inaccurately
Assessment	via objective performance tests of interoceptive accuracy task,	via subjective self-report measures	Association between one's objective performance (Iacc) and one's beliefs regarding the accuracy of this performance (IS)
Example	e.g., heartbeat tracking task, heartbeat discrimination task	e.g., questionnaires (MAIA), confidence ratings during the heartbeat tracking task	e.g., correlations between accuracy and confidence/general beliefs about one's performance

IAcc, interoceptive accuracy; IS, interoceptive sensibility; IAw, interoceptive awareness; MAIA, Multidimensional Assessment of Interoceptive Awareness.

1.2.2 Interoception & emotion processing

The idea that bodily signals are a core component of emotional experience dates to the work of James and Lange who postulated that emotional states originate from the physiological responses in the body (James, 1994; Lange, 1885). According to their theory, emotional cues automatically evoke physiological reactions in the body without the individual necessarily being consciously aware of these bodily changes. Different emotional states are therefore associated with distinct physiological sensations and the intensity of one's emotional experience is strongly linked to the ability to detect these changes accurately (Ehlers et al., 1988; James, 1994). Over the course of the twentieth century, this theory has been criticized for reducing emotions only to the processing of afferent signals and ignoring other important factors such as individual's cognitions. As Cannon (1927) demonstrated that there is a general activation of the sympathetic nervous system across multiple emotional categories, no physiological system has been found to be complex enough to account for the experience of the different emotions. Since then, an ongoing debate took place in the field of psychological research regarding the exact relationship between bodily sensations and emotion perception (Two-factor theory of emotion, Schachter and Singer (1962); Appraisal theory of emotion, Lazarus (1991); The somatic marker hypothesis, Damasio et al. (1996); Theory of constructed emotion, Barrett (2017); A higher-order theory of emotional consciousness, LeDoux and Brown (2017)).

In recent years, a significant body of evidence has demonstrated a link between interoceptive and emotional processing (Barrett et al., 2004; Craig, 2009; Füstös et al., 2013; Garfinkel et al., 2014; Wiens, 2005; Zamariola et al., 2019). Several studies have investigated how the different interoceptive dimensions (IAcc, IS, IAw; see Section 1.2.1) influence the emotional experience suggesting that individuals with higher IAcc report a more intense emotional experience (Pollatos et al., 2007b), put greater emphasis on the arousal component of these experiences (Barrett et al., 2004; Herbert et al., 2007; Pollatos et al., 2005b), and exhibit a superior ability to recognize their own emotional states (Herbert et al., 2011; Schaan et al., 2019a). While less is known about the link between the remaining interoceptive dimensions and emotion processing, some evidence has indicated higher IS to be associated with a better emotion identification of one's own emotional state and more adaptive emotion regulation strategies (Schuette et al., 2020). Overall, these findings support the hypothesis that

interoception underlies emotional experience as proposed in the abovementioned theories of emotion (Craig, 2004, 2009; Damasio, 2001).

Numerous studies investigating the link between body signals and emotion perception have only focused on objective physiological markers such as heart rate. However, these have been shown to be only moderately associated with the actual emotional experience of an individual (Mauss et al., 2005). Thus, it has been suggested that it might be more reasonable to additionally examine the subjective experience of one's bodily sensations during emotional states (e.g., "I can feel my heart pounding when I'm afraid") (Mauss & Robinson, 2009). In accordance with this suggestion, Nummenmaa and colleagues introduced an innovative method to assess this by so-called "bodily maps of emotion" (Nummenmaa et al., 2014). In their original study, participants were shown two blank body silhouettes and were asked to paint the parts of the body where they perceived an increase or decrease of activation when experiencing an emotion (e.g., happiness). This was the first study to prove that there are, indeed, distinct patterns of subjectively perceived sensations in the body when individuals experience certain emotions. For example, the experience of anger, fear, happiness and surprise was associated with an increased bodily activation in the upper chest area and the upper limbs, while sadness was related to a decreased activation in the limbs (Nummenmaa et al., 2014). Based on these findings, it has been assumed that specific combinations of somatosensory and visceral afferent inputs may result in the conscious experience of emotion. This interpretation supports the idea that emotions originate from the integration of interoceptive cues and their representation in the somatosensory system (Critchley, 2005; Critchley et al., 2004).

1.2.3 Interoception, body ownership and body evaluation

While the number of studies investigating the role of emotional dysfunctions in physical and mental health is still increasing, less attention has been paid to body image disturbances, namely the perception, feelings, and cognitions towards the own body. Contemporary findings have suggested two facets of body perception to be of particular importance for individual's well-being, that is, the sense of body ownership and a positive body evaluation. Moreover, the current literature emphasizes that interoception affects a wide range of fundamental bodily experiences including body ownership and body evaluation (Badoud & Tsakiris, 2017).

The sense that this body is "my own" emerges from the multisensory integration of interoceptive and exteroceptive cues (Tsakiris et al., 2011). Several studies have demonstrated that interindividual differences in IAcc modulate the experience of one's body as own, with higher IAcc being associated with stronger sense of body ownership (Crucianelli et al., 2018; Suzuki et al., 2013; Tsakiris et al., 2011). Beyond the role of one's objective ability to detect their bodily sensations (IAcc), recent evidence suggests that greater IAw is also linked to the enhanced experience of the body as own (Bekrater-Bodmann et al., 2020). By contrast, less attention has been paid to the link between interoception and other aspects of the bodily experience such as body evaluation. Body evaluation is seen as one component of body image that comprises evaluative thoughts and feelings individuals have about their body (Gallagher, 2000). With respect to the role of interoceptive processing in how positive or negative individuals experience their bodies, evidence has revealed that individuals exhibiting higher cardiac IAcc tend to report significantly higher levels of body satisfaction (Emanuelsen et al., 2015). In line with these findings, further studies have indicated that not only superior cardiac interoception but also higher gastric IAcc is associated with more positive attitudes towards one's own body (Duschek et al., 2015; Todd et al., 2020; Zamariola et al., 2017). Recently, more attention has been directed to the remaining dimensions of interoception, demonstrating a similar relationship between IS and body evaluation: higher IS has been linked to stronger body appreciation and body pride in young healthy individuals (Todd et al., 2019a; Todd et al., 2019b). Taken together, the currently improving understanding of the interplay between interoception and bodily experiences can provide substantial clinical implications with respect to somatic and mental health disorders which have been associated with disturbances in body ownership and body evaluation (Badoud & Tsakiris, 2017).

Disturbances in bodily experiences, including a diminished sense of ownership and a more negative body evaluation, have been repeatedly observed in various mental disorders (Dyer et al., 2013a; Rosenström et al., 2013; Scheffers et al., 2018). One common factor, found to negatively affect individuals' body perception across different psychopathologies is a history of childhood maltreatment. Early traumatized individuals report diminished sense of ownership (Löffler et al., 2020; Rabellino et al., 2018), higher body dissatisfaction (Scheffers et al., 2017a), lower body-related esteem (Wenninger & Heiman, 1998), and more negative body attitudes (Borgmann et al., 2014; Dyer et al., 2013a). As childhood maltreatment takes place during critical developmental periods, experiences of abuse and neglect can lead to the disturbed perception of one's physical boundaries (Scheffers et al., 2017a; Straus, 1988),

threatened physical integrity (Sack et al., 2010), and rejection of the body (Van der Kolk, 2014). This impaired perception of one's own body can lead to feelings of detachment, contributing to the development of dissociative symptoms and difficulties to perceive body's inner sensations (Schaan et al., 2019b; Schmitz et al., 2021). Such disturbances may contribute to an altered sense of body ownership and lower body satisfaction in individuals reporting history of ACE. As contemporary findings indicated higher prevalence of childhood maltreatment in patients with immune-mediated diseases, and in particular in IBD (Wan et al., 2022), one should consider ACE as a risk factor for developing body perception disturbances in IBD populations.

1.2.4 Interoception & adverse childhood experiences

Childhood adversity has been repeatedly associated with an increased risk of mental and physical health problems in adulthood (Copeland et al., 2018; Wan et al., 2022). Although disturbances in interoception have been proposed as determinants of psychopathology and poorer psychological well-being in several clinical conditions (Khalsa et al., 2018; Khalsa & Lapidus, 2016), little is known about the role of interoception in the link between ACE and mental and somatic disorders.

So far, studies on the relationship between childhood maltreatment and interoception have demonstrated that individuals reporting a history of ACE tend to suppress and deny their bodily sensations during situations perceived as threatening (Schimmenti, 2018; Schulz et al., 2021; Terock et al., 2016). Moreover, contemporary evidence indicates that childhood maltreatment is associated with altered interoceptive processing during stress, as early traumatized individuals show decreased levels of IAcc after the exposure to an acute stressor (Schaan et al., 2019b). These findings can be interpreted based on the psychophysiological mechanisms underlying the effects of ACE on body perception (Dempster et al., 2020). As brain-body communication is mediated through the HPA axis and the autonomic nervous system (ANS), disturbances of these can affect the functioning of the sensory system (Bonaz & Bernstein, 2013; Mayer, 2011), promoting alterations in how body signals are perceived and responded to. Therefore, impairments in the physiological stress response, resulting from exposure to early life adversity, might contribute to the development of a disturbed brain-body communication, altered afferent signaling, and thus, to altered interoceptive processing as well (Dempster et al., 2020; Schaan et al., 2019b; Schulz & Vögele, 2015).

1.3 Inflammatory bowel disease and interoception

1.3.1 The multidimensional model of interoception in inflammatory bowel disease

To date, there is only little evidence with respect to interoception in patients with gastrointestinal disorders (Fournier et al., 2020; Gajdos et al., 2020; Longarzo et al., 2017). The only study examining interoceptive abilities in IBD, so far, demonstrated that compared to healthy individuals, patients with IBD report greater difficulties to understand their physical sensations, indicating inferior IS (Fournier et al., 2020). However, the self-report measure used to assess patients' interoceptive abilities comprised only two items from the Toronto Alexithymia Scale (Taylor et al., 2003) and thus, these findings have to be interpreted cautiously. In addition, evidence suggests that the continuous release of inflammatory mediators (e.g., cytokines) during periods of gastrointestinal inflammation can induce a sensitization of peripheral afferent nerves and promote the development of visceral hypersensitivity in IBD (Ceuleers et al., 2016). Visceral hypersensitivity refers to the increased perception of visceral signals from the gastrointestinal tract and thus, amplifies patients' sensitivity to those (Rubio et al., 2016). Furthermore, the observed alterations in the processing of sensory input in IBD has been accompanied by structural and functional changes in the brain regions involved in the processing of interoceptive signals (e.g., insular cortex, somatosensory cortex) (Agostini et al., 2017; Hong et al., 2014; Thomann et al., 2019). Hence, one may speculate that the prolonged exposure to abdominal pain symptoms and stronger visceral sensations in IBD, being associated with altered perception of body signals on neural level, might affect how patients perceive and evaluate their bodily sensations in general. However, experimental studies examining interoception as a multidimensional construct entailing IAcc, IS, and IAw are missing in IBD populations.

1.3.2 Interoception and emotion processing in inflammatory bowel disease

In IBD, biological and emotional factors interact trough the brain-gut axis, as brain regions from the limbic system (e.g., amygdala) communicate with the intrinsic neural network of the gastrointestinal tract (enteric nervous system, ENS) via the sympathetic and parasympathetic nerves (Mayer et al., 2006). There is a significant body of evidence supporting bidirectionality of interactions between the CNS and ENS, showing that emotional states influence the functioning of the gastrointestinal tract and vice versa (Bernstein, 2017; Mayer, 2011; Mayer et al., 2014; Tillisch et al., 2017). Therefore, it is conceivable that in IBD, interoceptive and

emotional processing interact with each other and alterations in the perception and appraisal of bodily sensations could promote emotional dysfunctions in this patient group (Agostini et al., 2011; Mayer et al., 2006). A study by Vianna and colleagues (2006) provided first insights into the interplay of visceral and emotion processing in IBD, demonstrating a strong association between patient's visceral response and the subjectively perceived arousal evoked by emotional stimuli.

Interoception and emotion share common neurobiological underpinnings (Critchley & Garfinkel, 2017) and several studies pointed towards the detrimental effects of childhood maltreatment on the emotional functioning (see Section 1.1.2) (Bérubé et al., 2021) and brain-body signaling in adulthood (see Section 1.2.4) (Coley et al., 2021; Schaan et al., 2019b). Thus, one may hypothesize that a history of ACE might promote the development of emotional dysfunctions through perturbations in the interoceptive processing. Here again, despite the high prevalence of ACE found in IBD samples (Fuller-Thomson et al., 2015; Ryan et al., 2013; Witges et al., 2019), no study has investigated early adversity as modulating factor of the interplay of interoception and emotion perception in IBD yet.

1.3.3 Interoception, body ownership and body evaluation in inflammatory bowel disease

Some recent findings have pointed towards the important role of the gastrointestinal interoceptive channel for the intact development of bodily self-consciousness (Azzalini et al., 2019; Monti et al., 2021), that is, the current experience of a body as one's own. As there is strong evidence that the brain-gut axis contributes to the homeostatic maintenance, altered interoceptive signals from the gastrointestinal system can affect the way how patients with IBD experience their bodies (Rebollo et al., 2018). In healthy individuals, altered stomach temperature and altered pH of the large intestine has been linked to an increased recognition of a virtual body as one's own with this association being moderated by individual's interoceptive abilities (Monti et al., 2021). Although only preliminary, these are the first results pointing towards the significant link between altered gastric sensations and the sense of body ownership. Changed gut signals and an amplified perception of these, as observed among patients with gastrointestinal disorders (Gajdos et al., 2020), may contribute to an enhanced sense that "this body belongs to me" and "it is my body experiencing these symptoms".

Another potentially overlooked issue in patients with IBD is their vulnerability to more negative body evaluations (Cushman et al., 2021; Saha et al., 2015). The severe disease symptoms, medication and surgical treatments in IBD can vastly affect patient's perception and evaluation of their bodies (McDermott et al., 2015; Saha et al., 2015). For example, patients with IBD may experience their bodies in a more negative way due to an unwanted weight loss, abdominal pain or extraintestinal manifestations of IBD. A lower body satisfaction and more negative attitudes about one's body can have detrimental effects on patient's mental well-being, as these have been previously associated with increased levels of depression and anxiety and lower self-esteem in IBD populations (Claytor et al., 2020; McDermott et al., 2015; Wertheim & Paxton, 2011). Beyond the crucial impact of disease-specific symptoms on how patients with IBD experience their bodies, one should consider interoception as another factor potentially associated with body evaluation in IBD (see Section 1.2.3). Recent findings suggest that the perception of visceral signals from the gastrointestinal system is not only linked to the sense of ownership but to body evaluation as well: Individuals who tend to detect changes in their gastrointestinal sensations more accurately report more positive attitudes towards the own body as well as greater body appreciation (Todd et al., 2020). Since gastrointestinal pathologies have been associated with changed perception and appraisal of visceral sensations (Gajdos et al., 2020; Icenhour et al., 2017; Rubio et al., 2014), it can be hypothesized that altered interoception may crucially affect body evaluation in IBD. However, empirical evidence of this relationship in patients with IBD is missing.

Finally, another risk factor which can potentially predispose IBD patients to more severe disturbances in their bodily experiences is a history of ACE. As described in section 1.2.3, childhood maltreatment can have detrimental effects on how individuals perceive their bodies, especially with respect to body ownership and body evaluation (Dyer et al., 2013b; Löffler et al., 2020). Since ACE can lead to dysregulations of the physiological stress response and thus, resulting in an impaired brain-body signaling, it can be speculated that alterations in how body signals are perceived and responded to may affect the different dimensions of bodily experiences which have been previously associated with interoceptive processing.

1.4 Research Questions

The research findings highlighted above speak to the strong involvement of interoception in multiple domains of emotion and body perception. Emotional dysfunctions in IBD can affect patients' coping with their disease and thus, their mental and physical well-being as well. In overall four research questions (RQ), we investigated the links between the multidimensional construct of interoception, emotion perception, body ownership and body evaluation in 41 IBD patients and 44 healthy participants. In three separate RQs, we examined whether altered emotion processing in IBD is associated with changes in the different dimensions of interoception. In **RQ I**, we investigated whether patients with IBD demonstrate changes in the three distinct components of interoception (IAcc, IS, IAw) and whether these are linked to altered emotion processing. **RQ II** and **III** focused on the perception of bodily sensations during emotional experience and its links to IS. **RQ IV** of this thesis examined whether patients with IBD differ in the way how they perceive their bodies with respect to body ownership and body evaluation and how IS is associated with changes in body perception. Finally, as a history of ACE is common in IBD populations, we additionally investigated whether an exposure to childhood maltreatment modulates the interplay of interoception, emotion, and body perception.

Interoception underlies emotional experience and an inferior accuracy to detect visceral signals promotes difficulties in perceiving emotional states, recognizing, and regulating these. Disturbed interoception has been recognized as an important feature of psychiatric disorders characterized by poor emotional functioning and history of childhood maltreatment. Empirical findings and clinical observations have indicated emotional dysfunctions in patients with IBD characterized by hyposensitivity to positive emotions and enhanced experience of negative emotions. However, no study has investigated whether and how the different dimensions of interoception (IAcc, IS, IAw) are associated with these alterations in emotion processing in IBD yet. Therefore, the questions addressed in **RQ I** (section 2.1) of this thesis aimed at investigating the relationship between the multidimensional construct of interoception and emotion perception in IBD and to examine whether history of ACE modulates the link between these two:

- Do IBD patients differ in their interoceptive accuracy, interoceptive sensibility, and interoceptive awareness from healthy individuals?
- Do IBD patients evaluate emotional stimuli differently compared to healthy individuals?

- Are alterations in emotional processing linked to changes in patients' interoceptive processing?
- Are disturbances in interoception and emotional processing as well as their link modulated by a history of ACE?

In the next RQs, we broadened our focus from emotion processing of external emotional cues to the experience of one's own emotions in the body. By implementing the 'bodily maps of emotions' (Nummenmaa et al., 2014) in **RQ II** and **III**, we examined whether IBD patients experience emotions in their bodies differently compared to healthy participants and whether IS is linked to the perception of emotion-related bodily sensations. As several findings have indicated that more interoceptively aware individuals put stronger emphasis on their subjectively perceived physiological arousal (Herbert et al., 2007; Pollatos et al., 2007a; Pollatos et al., 2005b), one can hypothesize that individuals who attend to their physical sensations more strongly may report a more intense emotional experience, reflected by stronger perception of emotion-related changes in one's bodily sensations. Since emotion research has been dominated by two models of emotion, that is the dimensional (Russell, 1980) and the categorical model (Ekman, 1992), in these two separate RQs we examined how patients with IBD experience emotions in their bodies according to each of these frameworks. While the dimensional model of emotion postulates that all emotions are characterized by the two dimensions of valence (pleasantness) and arousal (intensity), the categorical model assumes the existence of six basic emotions, that is, happiness, sadness, anger, fear, surprise and disgust. In **RQ II** (section 2.2), emotion experience in the body, interoception, and their interrelation according to the dimensional model of emotion were examined by investigating the following questions:

- Do IBD patients differ in the perceived intensity of emotion-related bodily sensations and the topography of these from healthy individuals?
- Is interoceptive sensibility associated with the experience of emotional valence and arousal in patients with IBD?

In **RQ III** (section 2.3), the following questions were investigated based on the categorical model of emotion:

- Do IBD patients show differences in the intensity and topography of perceived bodily sensations changes when experiencing the six basic emotions, happiness, sadness, anger, fear, surprise, and disgust, compared to healthy individuals?
- Is interoceptive sensibility linked to alterations in the emotion-related bodily sensations in IBD patients?
- Are alterations in the perceived emotion-related bodily sensations associated with individual's history of ACE?

Finally, **in RQ IV** (section 2.4), we investigated whether IBD is associated with alterations in body ownership and body evaluation. So far, most of the studies have focused on patient's body image evaluation, indicating lower levels of body satisfaction (Beese et al., 2019; Cushman et al., 2021). However, studies on body ownership are missing in IBD populations. While superior interoceptive abilities have been linked to stronger sense of ownership and more positive body-related attitudes, histories of childhood maltreatment have been shown to negatively affect these bodily experiences (see section 1.2.3). Given these findings, in **RQ IV**, we investigated the following questions:

- Do IBD patients exhibit altered sense of body ownership and a more negative body evaluation compared to healthy individuals?
- Do IBD patients experience certain parts of the body as less belonging to themselves?
- Do IBD patients report a more negative evaluation regarding certain body areas?
- Is interoceptive sensibility linked to alterations in body ownership and body evaluation in IBD?
- Is a history of ACE associated with alterations in body ownership and body evaluation in IBD and do ACE modulate the link between these bodily experiences and interoception in IBD?

Hypotheses, study design, procedures, and data analyses of **RQ I-IV** have been pre-registered and described in more detail in the sections 2.1-2.4.

2 EMPIRICAL FINDINGS

2.1 Research Question I | Multidimensional assessment of interoceptive abilities, emotion processing and the role of early life stress in inflammatory bowel diseases

An adapted version of this chapter has been published as: Atanasova, K., Lotter, T., Reindl, W., & Lis, S. (2021). Multidimensional Assessment of Interoceptive Abilities, Emotion Processing and the Role of Early Life Stress in Inflammatory Bowel Diseases. *Frontiers in Psychiatry, 12*(1020). doi:10.3389/fpsyt.2021.680878.

2.1.1 Abstract

Perception of internal bodily sensations includes three dissociable processes: interoceptive accuracy, interoceptive sensibility, and interoceptive awareness. Interoceptive abilities play a crucial role in emotion processing and impairments of these processes have been reported in several psychiatric disorders. Studies investigating interoceptive abilities and their role in emotional experience in individuals with somatic disorders such as inflammatory bowel diseases (IBD) are sparse. Recent findings suggested an association between adverse childhood experiences (ACE) and the development of gastrointestinal disorders. The aim of the current study was to investigate the associations between the different dimensions of interoception and emotional processing in IBD while taking ACE into account.

We recruited IBD patients in clinical remission (n=35) and 35 healthy control participants (HC) matched for age, education, and IQ. Interoception was measured as a three-dimensional construct. Interoceptive accuracy was assessed with the heartbeat tracking task and interoceptive sensibility with a self-report measure (Multidimensional Assessment of Interoceptive Awareness questionnaire). Emotional processing was measured using an experimental task, where participants were asked to rate the subjectively perceived valence and arousal when presented with positive, neutral and negative visual stimuli.

IBD patients significantly differed in two interoceptive sensibility domains, Emotional awareness and Not-distracting. Patients reported greater awareness of the connection between bodily sensations and emotional states, while showing a stronger tendency to use distraction from unpleasant sensations compared with HC. Higher emotional awareness was linked to higher perceived intensity and arousal of negative stimuli. The strength of this relation was

dependent on the severity of ACE, with severer traumatization being associated with a stronger association between emotional awareness and perceived valence and arousal.

Our findings suggest that it is the subjective component of interoception, especially the one assessing interoceptive abilities within the scope of emotional experience, which affects emotional processing in IBD. This is the first study providing evidence that IBD patients did not differ in their perception of visceral signals per se but only in the subjective ability to attribute certain physical sensations to physiological manifestations of emotions. Our findings support the hypothesis that ACE affect the association between interoception and emotional processing.

2.1.2 Introduction

Inflammatory bowel diseases (IBD) are immune mediated chronic diseases with a prevalence of 6.8 million cases globally. The incidence of IBD is continuously rising not only in industrialized countries of the northern hemisphere but also in developing countries (Alatab et al., 2020). IBD include primarily Crohn's disease and Ulcerative colitis, both characterized by various physical and psychological symptoms such as abdominal pain, diarrhea, unwanted weight loss, depression, and anxiety (Levine & Burakoff, 2011). The etiology of IBD is multifactorial including genetic, immune, and environmental factors. While the impact of the environment on the development of IBD is substantial, the role of specific factors is still poorly defined, one candidate being early life stress (Ananthakrishnan et al., 2018; Fuller-Thomson et al., 2015; Wintjens et al., 2019). Newer studies in IBD have suggested alterations in the brain-body communication, directly influencing the sensory and immune functions of the gastrointestinal tract (Farrell et al., 2020; Mawdsley & Rampton, 2006; Thomann et al., 2019). In line, gastrointestinal pathologies have been recently linked to altered interoceptive processes (Longarzo et al., 2017). Interoception is closely linked to emotional processing (Shah et al., 2016; Wiens, 2005) and might influence the severity of IBD symptoms and disease course by increasing the level of stress through an increased sensitivity towards negative emotional stimuli. So far, studies on changes in interoception and their relation to emotion processing in IBD are sparse (Vianna et al., 2006). The present study aims to contribute to the better understanding of these domains of functioning in IBD by investigating interoception as a multidimensional concept together with changes in emotion processing while taking the influence of early life stress into account.

Interoception refers to the sense through which bodily changes are signaled and perceived (Garfinkel et al., 2014). It is conceptualized as a three-dimensional construct,

comprising interoceptive accuracy (IACC), interoceptive sensibility (IS), and interoceptive awareness (IAw) (Garfinkel et al., 2015). Interoceptive accuracy refers to the correspondence between the actual and the perceived bodily signals. In contrast, IS is defined as the subjective belief to be internally focused and represents the extent to which individuals feel engaged by interoceptive signals (Garfinkel et al., 2015). IS includes not only individual's general awareness of bodily sensations but also beneficial and maladaptive forms of interoceptive engagement (Bornemann et al., 2015). Finally, interoceptive awareness represents the correspondence between interoceptive accuracy measured via behavioral tasks (e. g heartbeat tracking task) and subjectively reported general IS (Khalsa et al., 2018). It should be mentioned that the metacognitive component of interoceptive awareness should be measured only using interoceptive accuracy scores and respondent's ratings of the confidence in the accuracy of their performance in the applied task (for discussion see (Murphy et al., 2019)). In the present manuscript we retain the use of the term interoceptive awareness to refer to the correspondence between interoceptive accuracy scores and IS as measured via self-report measures. Interoceptive impairments have been linked to specific physical and mental health conditions, emphasizing the importance of precise body signals perception for the physical and mental well-being (Quadt et al., 2018). Although impairments in interoception may contribute to the pathophysiology of gastrointestinal disorders, there is, to our knowledge, no study that investigated interoceptive processing in IBD as a multidimensional concept. Enhanced visceral perception sensitivity ("visceral hypersensitivity") refers to the altered processing of visceral stimuli in gastrointestinal disorders (Farmer & Aziz, 2013). Current findings support the view that it results from disturbances along the brain-gut axis (Heymen et al., 2010) and is related to functional alterations in brain regions involved in visceral afferent processing, emotional arousal and pain perception (Icenhour et al., 2017; Tillisch et al., 2011). Visceral sensitivity in irritable bowel syndrome patients have been characterized by a biased appraisal of perceived bodily signals and enhanced selective attention to gastrointestinal sensations (Chapman & Martin, 2011; Icenhour et al., 2017; Larsson et al., 2012). Even though so far there is – to our best knowledge – no study investigating the link between visceral hypersensitivity and interoceptive processing, we suggest that IBD patients might exhibit stronger and more selective attention towards their bodily signals in order to recognize early signs of worsening disease activity and upcoming relapse, which might result in superior interoceptive abilities. To date, there are only few studies, which investigated interoceptive abilities in populations with gastrointestinal disorders. Findings suggest no alterations in the behavioral performance in interoceptive accuracy tasks, but only in self-reported IS in irritable bowel syndrome patients

(Gajdos et al., 2020). In contrast, a study by Fournier et al. (2020) found no differences in the interoceptive abilities of IBD patients measured with the Toronto Alexithymia Scale (Taylor et al., 2003). Although it can be assumed that chronic exposure to visceral pain in IBD might be associated with superior abilities to detect bodily signals, experimental studies examining this association using both behavioral and self-report measures are missing. In IBD patients, the perception of physiological stimuli is critical for the regulation of psychological mood, which in turn may affect the appraisal of gastrointestinal symptoms and also the disease course.

Besides their role in symptoms perception, interoceptive abilities are of particular importance for many higher order cognitive processes such as learning, decision making, and emotion processing (Murphy et al., 2017). The perception of physiological changes in the body is posited as a core component of emotional experience (Damasio, 1998; Garfinkel et al., 2014). Based on neurobiological findings, Craig (2002) postulated that interoception reflects the physiological condition of the entire body, including also the perception of the response of the body to different affective stimuli and its impact on emotional experience (Craig, 2002). Deficits in interoceptive abilities are associated with difficulties in identifying emotions, reduced emotional reactivity and inferior ability to downregulate negative emotions (Füstös et al., 2013). In contrast, superior interoceptive abilities are linked to stronger associations between individual's body response to emotional stimuli and subjective ratings of perceived arousal (Barrett et al., 2004; Füstös et al., 2013). Thus, altered processing of visceral signals, as observed in gastrointestinal disorders, may contribute to changes in patients' emotional functioning. A study by Vianna et al. (2006) suggested the relevance of this link in IBD: the association between stronger visceral responses and higher subjective arousal to emotional stimuli was significantly increased in acute Crohn's disease patients compared to healthy controls (HC), particularly for negative stimuli (Vianna et al., 2006). Additionally, findings from neuroimaging studies have indicated decreased sensitivity to positive emotional content in patients with Ulcerative colitis, suggesting the close connection between brain regions involved in the processing of interoceptive as well as emotional stimuli (Agostini et al., 2011). Impairments in emotional functioning may have crucial negative impact on patients' well-being (e.g. depression, anxiety). Although it is conceivable that alterations in interoceptive abilities may partially explain impairments in emotion processing in IBD, studies investigating this link are sparse (Fournier et al., 2020; Mayer, 2011).

One environmental factor that has been linked to an increased risk for mental and somatic disorders is a history of adverse childhood experiences (ACE). ACE, including

emotional and physical abuse as well as neglect, have permanent consequences for the mental and somatic health in adulthood (Copeland et al., 2018; Herzog & Schmahl, 2018). Individuals who report experiences of early life stress are more prone to developing chronic inflammation, cardiovascular disease and affective disorders compared to non-traumatized controls (Fagundes & Way, 2014). Some authors emphasized a potential role of ACE in gastrointestinal disorders (Fuller-Thomson et al., 2015; Witges et al., 2019). A cohort study revealed that the prevalence of at least one type of childhood adversity in IBD patients is above 70 % with most of the patients reporting death of a family member during childhood and 12-13% reporting sexual or physical abuse (Witges et al., 2019). One biological mechanism, which may explain the negative impact of ACE on physical health in later life is the dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis and alterations of the stress-response in individuals exposed to early life stress. Impaired physiological stress response affects the brain-body signaling, which in turn might lead to altered perception of bodily signals (Schaan et al., 2019b; Schulz & Vögele, 2015). Beyond its negative impact on body signals perception, ACE have been also linked to impaired emotion regulation and emotional processing (Marusak et al., 2015; Tottenham et al., 2010). Thus, early life stress might lead to dysregulation of the brain-body axis and altered interoception, leading to impairments of emotional processing (Löffler et al., 2018). However, the role of childhood adversity as vulnerability factor for altered perception of bodily signals and impaired emotional functioning in IBD is still unclear (Liu et al., 2017). Besides higher rates of ACE, newer findings suggest that one third of the IBD patients meet the criteria for clinically important symptoms of a post-traumatic stress disorder (PTSD), and patients attribute these to their disease (Taft et al., 2019). Thus, histories of childhood traumatization, as well as chronic stress associated with the disease experience itself constitute stressors, which may lead to changes in arousal, physiological reactivity and emotional experience.

The aim of the current study was to investigate alterations of interoceptive abilities and emotion processing in IBD compared to healthy participants. We proposed that the chronic exposure to gastrointestinal symptoms may lead to enhanced attention towards bodily signals, resulting in superior interoceptive abilities in IBD. The perception of physiological changes in the body is a core component of emotional experience and greater interoceptive accuracy is linked to more intense emotional experience and greater perceived arousal. Therefore, changes in visceral signals perception might explain altered emotional processing among IBD patients. To the best of our knowledge, this is the first study investigating interoception as a multidimensional construct and its effects on emotion processing in IBD by combining

behavioral and self-report measures. Measures of interoception included interoceptive accuracy using the heartbeat tracking task (HBT) (Schandry, 1981), IS assessed via self-reports (Mehling et al., 2012) and interoceptive awareness as the correspondence between interoceptive accuracy and IS. We focused on IBD patients in clinical remission to avoid a potentially confounding effect of active disease symptoms on the interoceptive measures. For the same reason we chose to assess interoceptive accuracy using the HBT. A high correlation between measures of cardiac and gastric interoception points to the presence of a general sensitivity for interoceptive cues across different sensory modalities (Herbert et al., 2012a; van Dyck et al., 2016). In line, we used the HBT as a substitute for measures of gastric interoceptive accuracy, since it is less susceptible to confounding effects of abdominal pain in this patients' group. HBT is a well-established method to measure interoceptive accuracy that is typically performed under conditions of physical rest (Schandry, 1981). However, when studying the relationship between interoception and emotional experience, an assessment of interoceptive accuracy under physical rest might fail to measure important characteristics of the cardiovascular system such as its dynamic responses to arousing stimuli (Khalsa & Lapidus, 2016). To overcome this shortcoming, we implemented a short physical exercise with the purpose of inducing a physiological reaction in our participants. According to previous findings by Schaan et al. (2019), increased heartrate resulting from a physical activation should lead to improvement in participants' interoceptive accuracy (Schaan et al., 2019a).

According to this rationale, we hypothesized that IBD patients will (I.) demonstrate superior interoceptive accuracy and IS, as well as greater congruency between these constructs and (II.) report higher arousal and emotional intensity when evaluating negative stimuli compared with a healthy control group. We hypothesized that (III.) greater interoceptive accuracy will be associated with higher arousal and emotional intensity ratings during emotional processing. Moreover, we expected that ACE will modulate alterations in interoception and emotional processing and strengthen the association between interoceptive accuracy and emotional processing. (IV.) We expected the performance of a short physical exercise to result in improved interoceptive accuracy. Therefore, we explored whether group differences in interoceptive accuracy increased after performing a physical challenge. Finally, we investigated whether heart rate and heart rate variability during the interoception and emotion processing tasks differed between IBD patients and healthy individuals and expected (V.) a decreased heart rate variability (HRV) in the IBD group compared with healthy participants as repeatedly shown in the literature before (Sadowski et al., 2020).

2.1.3 Methods

Participants

The study was approved by the Ethics Committee of the Medical Faculty Mannheim at Heidelberg University and all participants gave their written informed consent before participating in the study. The hypotheses, sample size, methods, exclusion criteria and planned analyses were preregistered before data collection and can be accessed at: https://aspredicted.org/blind.php?x=dj6fz9. All aspects of the study were carried out in accordance with the pre-registered protocol unless otherwise stated.

In total, 70 individuals in age 18-65 years participated in the study. Of these, 35 met the diagnostic criteria for IBD and 35 were HC. Both groups were matched for age, IQ (Multiple-Choice Word Test-B (MWT-B; (Lehrl et al., 1995)) and education. For age, we accepted a difference of ± 5 years in pairwise matches between patient's and HC's age. We aimed to achieve two samples comparable on a group level. Since equal education level was of particular importance for our matching procedure, we matched each healthy participant with the same education as the one reported by the IBD patient. Therefore, the final sample included more female participants in the HC group than in the IBD group. For further details, see Table 2.1. We excluded one participant of the IBD group from further analyses, since she/he reported no perceived heartbeats during the HBT. Thus, the final sample consisted of 34 IBD patients and 35 HC. According to our preregistered analyses a sample size of 120 participants was planned. However, due to the Covid-19 outbreak and the pandemic-related restrictions the number of participants was reduced.

IBD patients were recruited from the IBD outpatient unit at the University Medical Center Mannheim. Overall, 23 patients with Crohn's disease and 11 with ulcerative colitis in clinical remission were included in the IBD group. Crohn's disease patients exhibited mean Harvey-Bradshaw Index score of 1.43 ± 1.56 and UC patients mean Partial Mayo Score of 1.73 ± 1.49. The average age for disease onset was 25.65 ±10.83 years. The average disease duration was 15.67 ± 13.55 years. Overall, 10 IBD patients reported a history of Extraintestinal manifestations (Enteropathic arthritis n=6, Dermatitis n=4). Nineteen patients did not report histories of previous surgeries, while the remaining IBD patients underwent surgeries including ileal resection, ostomy, fistula removal and abscess drainage. Diagnostic procedures and gastroenterological examinations were carried out on all patients by fully trained physicians specialized in the care of patients with IBD. Exclusion criteria were biological signs of disease

activity (fecal calprotectin level in mg/L > 200), current use of corticosteroids, use of psychotropic medications other than SSRIs or SNRIs, and current or prior history of neurological or mental disorders. Thirty-three patients reported a current treatment with biologics and one using Mesalazine. Lastly, ten IBD patients reported having histories of further somatic diseases (pulmonary embolism n=2, pancreatitis n=2, diabetes n=1, chronic cystitis n=1, thrombocythemia n=1, asthma bronchiale n=1, and hypothyroidism n=2). Exclusion criteria for the HC group were chronic medical conditions, chronic medication intake, use of psychotropic medication, and current or prior history of neurological or psychiatric disease and general gastrointestinal complaints (e.g., abdominal pain, diarrhea) during the last 4 weeks prior to testing. For further details on sample characteristics, see Table 2.1.

To characterize the sample, we assessed psychological distress with the Brief Symptom Inventory (BSI-18) (Franke et al., 2011). BSI-18 is a is an 18 Items self-report instrument that measures somatization, depression, and anxiety in three subscales with 6 items each and a global symptom severity score (Global Severity Index (GSI)). BSI-18 is a reliable instrument for measuring psychological distress and comorbidities in patients with mental and somatic disorders (Carlson et al., 2004; Franke et al., 2017). The scores for the GSI range from 0 to 72 points and from 0 to 24 points for each subscale with higher scores indicating higher symptom severity. GSI total scores showed acceptable reliability in the present study, however the reliability of the subscale scores suggests that they have to be interpreted with care (IBD: Cronbach's α=.88, .61, .76, .83; HC: α=.85, .66, .87, .66).

Prior to testing, participants evaluated their current affective state with the state version of the State-Trait Anxiety Inventory (STAI; (Spielberger et al., 1983)). It is a 20 items scale, which measures subjective feelings of apprehension, tension, nervousness, worry, and activation/arousal of the autonomic nervous system on a 4-point Likert scale (1 "not at all" to 4 "very much so"). Items scores are added to obtain scale total score (range from 20 to 80) with higher scores indicating greater anxiety. Cronbach's α in the current study was α = .79 in the IBD sample and .91 in the HC group. Additionally, arousal, valence, and dominance levels were assessed via the Self-Assessment Manikin (SAM; (Bradley & Lang, 1994)). SAM is a non-verbal pictorial assessment technique that measures valence/pleasure, perceived arousal, and perceptions of dominance on a 9-point Likert scale. Higher scores indicate greater positive valence, higher arousal and higher perceived dominance.

Finally, visceral sensitivity was measured with the Visceral Sensitivity Index (VSI; (Labus et al., 2004)). The 15-item scale assesses gastrointestinal symptom-specific anxiety, comprising Worry, Fear, Vigilance, Sensitivity, and Avoidance as gastrointestinal-related cognitions and behaviors. Items are scored on a reversed 6-point scale ranging from 0 "strongly agree" to 5 "strongly disagree". VSI has been developed specifically for patients with functional gastrointestinal disorders. Since the VSI is not a suitable measure for healthy individuals', we utilized this self-report measure in the IBD group only. The overall VSI score ranges from 0 to 75 points with higher scores indicating more severe gastrointestinal-specific anxiety, as well as lower tolerance to visceral pain. Reliability in the current sample was Cronbach's α=.89.

Table 2.1 Sample characteristics

	HC (M±SD)		IBD (M±SD)		Test-statistics	p-value	
Demographics							
Age	37.06	±11.96	41.32	±14.36	1.34 [a]	.184	
Sex (female/male)	20/15		18/16		0.12 [b]	.726	
BMI	24.59	±4.52	25.09	±3.32	0.52 [a]	.607	
Years of education	12.97	±2.62	12.44	±3.11	-0.77 [a]	.445	
MWT-B	30.51	±3.71	29.79	±4.05	-0.77 [a]	.443	
Affective state							
STAI Anxiety (state)	32.23	±8.39	34.35	±5.82	0.99 [a]	.327	
SAM-Valence	3.81	±0.85	3.64	±0.99	-0.69 [a]	.492	
SAM-Arousal	2.03	±0.93	2.51	±0.98	2.06 [a]	.043	*
SAM-Dominance	3.70	±0.70	3.48	±0.62	-1.04 [a]	.302	
Psychological distress							
GSI	23.50	±5.94	28.90	±9.38	2.71 [a]	.009	**
Somatization	6.94	±1.56	9.63	±3.11	4.29 [a]	<.001	***
Depression	8.00	±3.24	9.47	±3.71	1.69 [a]	.096	
Anxiety	8.56	±2.60	9.80	±3.84	1.53 [a]	.131	
Visceral sensitivity							
VSI	-	-	28.87	±14.95	-	-	

IBD, inflammatory bowel diseases group; HC, healthy controls group; BMI, Body-Mass Index; MWT-B, Multiple Choice Word Test-B; STAI, State-Trait Anxiety Inventory; SAM, Self-Assessment Manikin; GSI, General symptom index; VSI, Visceral sensitivity index. * p<.05, ** p < .01, *** p < .001, [a] T-value, [b] Chi^2 statistic

Procedure

Participants evaluated their general interoceptive sensibility by a self-report questionnaire. Afterwards, the ECG assessment was started, and participants were asked to perform three experimental tasks, including an emotional processing task and the heartbeat tracking task followed by a time estimation task (see Figure 1).

Questionnaires

Interoceptive Sensibility: MAIA

We assessed IS using the Multidimensional Assessment of Interoceptive Awareness (MAIA; (Mehling, 2016; Mehling et al., 2012)). The 32 items self-report questionnaire measures eight different facets of interoceptive sensibility on a 6-point Likert-scale (0 = "never" - 5 = "always") with higher scores indicate greater sensitivity to signals from the body. MAIA provides a multidimensional profile of body awareness including the following eight subscales: *Noticing* (being aware of body sensations), *Not-Distracting* (being inclined to not distract or ignore painful or uncomfortable sensations), *Not-Worrying* (inclination to not be emotionally distressed by uncomfortable sensations), *Attention Regulation* (paying attention to and controlling attention on body sensations), *Emotional Awareness* (being aware of the connection between emotions and body sensations), *Self-Regulation* (regulating distress through paying attention to body sensations), *Body Listening* (purposefully listening for insight from the body) and *Trusting* (experiencing trust with and safety in the body) (Mehling et al., 2012). MAIA revealed good internal consistency in the current experiment with Cronbach's α=.91 in the IBD group and .94 in the HC group. A key advantage of MAIA is the possibility to assess various aspects of IS, including subscales distinguishing between beneficial and dysfunctional forms of IS. While "*Noticing"* assesses the awareness of bodily sensations in general, "*Attention Regulation"* and "*Not-Distracting"* measure individual differences in how engaged a person is regarding interoceptive cues (Mehling, 2016). Moreover, previous findings indicated that general IS ("*Noticing"* subscale) did not benefit from body-focused interventions, aiming at improving interoceptive abilities, while the ability to sustain and control attention to bodily sensations ("*Attention Regulation"* subscale) showed a significant improvement (Bornemann et al., 2015). The postulated association between bodily sensations and emotional experience is assessed by the subscale *"Emotional Awareness".* Since discrete emotions are linked to

physiological reactions, individuals might differ in terms of their ability to recognize these mind-body associations, which might lead to difficulties in recognizing their emotional state.

Childhood traumatization and PTSD symptoms severity

We assessed traumatization during childhood and adolescence as well as traumatic experiences during lifetime using a battery of psychometric measures. Severity of ACEs were measured with the German version of the Childhood Trauma Questionnaire (CTQ; (Klinitzke et al., 2012). This 28-item questionnaire (five-point Likert scale ranging = 1 “not at all” - 5 = “very often”) has been shown to have good psychometric properties in previous research (Klinitzke et al., 2012). The CTQ consists of five subscales including emotional abuse (Cronbach’s α in this study .79), physical abuse (α = .73), sexual abuse (α = .88), emotional neglect (α = .84), and physical neglect (α = .45) and a total score (Cronbach’s α in IBD: .86; HC: .73). Each subscale is represented by five questions with a score from 5 to 25. Scores fall into four severity categories: none to low, low to moderate, moderate to severe and severe to extreme traumata exposure for each subscale (see Table 2.2).

Furthermore, to assess additional types of early life stress such as parental loss, continuous separation from one or both parents and foster care experiences we used selected items (1a, 1b, 2a, 2b) of the Childhood Experience of Care and Abuse Questionnaire (CECA.Q, (Bifulco et al., 2005); German version: (Kaess et al., 2011)). Additionally, all participants were screened for potentially traumatic life events using the Life events Checklist for DSM-5 (LEC-5; (Weathers et al., 2013)). It is a self-report measure, which assesses exposure to 16 events known to potentially result in symptoms of posttraumatic stress disorder (PTSD) or distress. LEC-5 distinguishes not only between event types (e.g., physical or sexual assault, accident) but also between the ways a person was exposed to the stressor (e.g., direct exposure or witnessing the traumatic event). For each participant, the number of personally experienced traumatic events (direct exposure) were summed up, resulting in one sum score.

Severity of PTSD symptoms was evaluated with the PTSD Checklist for DSM-5 (PCL-5; (Weathers et al., 2013)). It is a 20-item self-report measure that assesses the presence and severity of symptoms after experiencing a traumatic event. Items correspond with DSM-5 criteria for PTSD including intrusion symptoms, avoidance, negative alterations in cognitions and mood and alterations in arousal and reactivity during the last 4 weeks. The rating scale ranges from 0 “not at all” to 4 “extremely” for each symptom. A total symptom severity score

is obtained, with higher scores indicating higher PTSD symptoms severity. PCL-5 revealed high reliability in the current study with Cronbach's α = .91 in IBD and .87 in HC. See Table 2.2.

Experimental tasks

Interoceptive Accuracy: HBT

Interoceptive accuracy was measured with a standard heartbeat tracking task (HBT, (Schandry, 1981)). Participants were seated upright in a quiet room with their eyes closed. They were asked to silently count the number of heartbeats occurring during five discrete time intervals of 25, 35, 45, 55, and 100 seconds. Participants were explicitly told not to estimate their heartbeats, but to count only those heartbeats they actually perceived. Intervals varied in their length and were presented in a randomized order counterbalanced across both groups. Before starting with the experimental task, a baseline measurement of cardiac activity was performed (Figure 1). Each HBT interval started after a resting period of 20 seconds. While counting their heartbeats, participants were not allowed to use a manual pulse. To explore the effects of dynamic alterations in the cardiovascular homeostasis on interoceptive accuracy, all participants were asked to perform a short physical exercise comprising ten squats (Figure 2). However, some of the IBD patients reported pain in the knees and refrained from performing this exercise. Therefore, data for the second run of the task was available only for a subsample of participants (24 IBD patients and 24 HC). To compute interoceptive accuracy scores, the ratio of the number of reported heart beats and number of R-waves in the ECG was calculated for each of the time intervals of the HBT and averaged across the five intervals ((1/5 $\sum$ (1-| actual heartbeats-counted heartbeats| /actual heartbeats)). In the present sample, interoceptive accuracy scores ranged from 0 to 1 (no over-reporters observed) with higher scores indicating greater interoceptive accuracy.

Time estimation task

Subject's performance on the HBT might be confounded by individuals' abilities to estimate time, and their knowledge about their own heart rate (Knapp-Kline & Kline, 2005; Ring et al., 2015). Therefore, we extended the experimental task by an additional time estimation task (Figure 2) (Shah et al., 2016). Participants were asked to estimate the elapsed time during five discrete time intervals of 25, 35, 45, 55 and 100 seconds. Time intervals were presented in

pseudorandomized order, counterbalanced across the experimental groups. The time estimation task was performed after the HBT prior and following the physical challenge. Similar to the computation of interoceptive accuracy scores, time estimation (TE) accuracy was calculated using the following formula (1/5 ∑ (1 – | actual elapsed time – estimated elapsed time| /actual elapsed time)) (Shah et al., 2016).

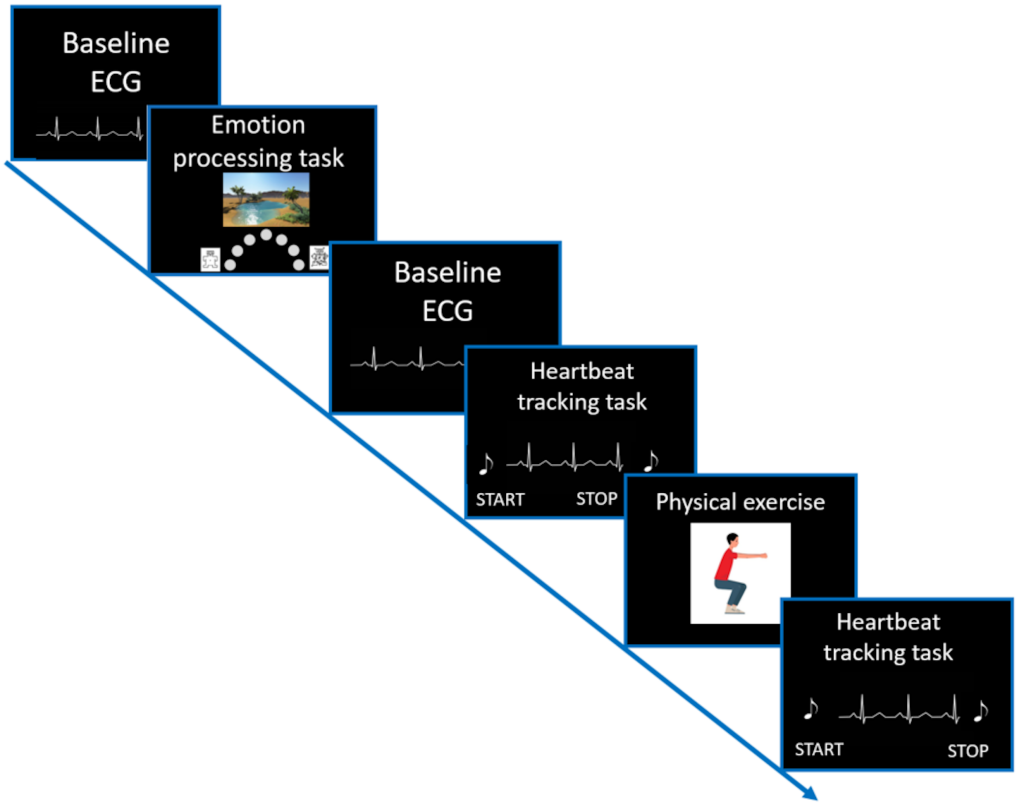

Figure 1. Visualization of the study setup. After completing all questionnaires, a resting ECG (duration of 2 minutes) was recorded. Afterwards, participants performed an emotion processing task. Again, before starting the Heartbeat tracking task, a resting ECG recording was conducted. For more details on the trial structure of the Heartbeat tracking task please see Fig. 2.

Table 2.2. Sample characteristics including childhood traumatization, traumatization in later life, and PTSD symptoms severity.

	HC (M±SD)		IBD (M±SD)		Test-statistics	p-value	
Trauma history							
Childhood trauma							
CTQ total	36.06	±7.00	35.73	±10.77	-0.15 [a]	.881	
None ACE	n = 21		n = 21		0.10 [b]	.758	
Low ACE	n = 13		n = 10		0.36 [b]	.551	
Moderate ACE	n = 1		n = 2		0.41 [b]	.520	
CTQ - EA	8.51	±2.96	8.18	±3.73	-0.41 [a]	.684	
CTQ - PA	5.80	±1.60	6.27	±2.53	0.92 [a]	.362	
CTQ - SA	5.14	±0.55	5.55	±2.00	1.12 [a]	.272	
CTQ - EN	9.63	±3.29	8.91	±3.79	-0.84 [a]	.405	
CTQ - PN	6.97	±1.71	6.81	±2.34	-0.31 [a]	.758	
Loss/death of a parent	n = 9		n = 10		0.26 [b]	.608	
Lifetime trauma							
LEC-5	1.11	±1.30	1.52	±1.56	1.15 [a]	.254	
PTSD symptoms							
PCL-5 total	5.54	±5.94	15.47	±12.37	4.13 [a]	<.001	***
Cluster B	1.43	±1.95	4.25	±3.69	3.86 [a]	<.001	***
Cluster C	0.74	±1.20	1.81	±2.13	2.50 [a]	<.013	*
Cluster D	1.86	±2.79	4.16	±3.55	2.96 [a]	.004	**
Cluster E	1.43	±1.70	4.84	±4.52	4.02 [a]	<.001	***

IBD, Inflammatory bowel diseases group; HC, healthy control group; CTQ, Childhood trauma questionnaire; EA: emotional abuse, PA: physical abuse, SA: sexual abuse, EN: emotional neglect, PN: physical neglect; ACE, Adverse childhood experiences; LEC-5, Life events checklist; PTSD, post-traumatic stress disorder; PCL-5, Post-traumatic stress disorder checklist for DSM-V; Cluster B = intrusion symptoms, Cluster C = avoidance, Cluster D = negative alterations in cognitions and mood, Cluster E = alterations in arousal and reactivity, * $p < .05$, ** $p < .01$, *** $p < .001$, [a] T-value, [b] Chi^2 statistic.

Emotional processing task

Emotional processing was measured by ratings of subjective intensity of arousal and valence when being presented with emotional stimuli. The task involved 90 pictures of three categories (30 positive, 30 negative, and 30 neutral pictures) from the OASIS data base ((Kurdi et al., 2017) www.benedekkurdi.com/#oasis), presented in a pseudorandomized order. Based on existing norms, 'negative' stimuli were selected based on high arousal (M = 4.12, SD = 0.45) and low valence ratings (2.58 ± 0.35), 'positive' pictures had high arousal (4.15 ± 0.48) and high valence ratings (6.04 ± 0.23), and 'neutral' stimuli had low arousal (2.36 ± 0.53) and moderate valence rating (4.08 ± 0.10). Emotional stimuli were presented on a computer screen and participants were asked to rate their subjectively experienced level of arousal and valence for each stimulus. Arousal and valence ratings were made in two separate blocks, each one consisting of 90 pictures, resulting in overall 180 trials. All ratings were performed on an 8-point scale (valence: 1 = "very unpleasant" - 8 = "very pleasant"; arousal: 1 = "not aroused at all" - 8 = "highly aroused") by moving a mouse cursor to one of the eight target buttons. Trials were self-paced, with participants signaling the start of the trial by moving the cursor to a start button that was placed in equal distance from the semicircular arranged target buttons.

ECG recording and preprocessing

Electrocardiogram (ECG; Einthoven II) was obtained by attaching two one-way hydrogel electrodes (Kendall ™ Covidien, Germany) under the right and the left clavicle, respectively, and a third electrode was placed on the left side under the lowest rib. Signals were recorded with a sample rate of 1024 Hz using a Varioport system (Becker, meditec). Participants were instructed to avoid body movements and to breathe in their natural manner. ECG was recorded during each experimental task as well as during two resting periods with a duration of two minutes each (Figure 1).

R-waves of the QRS-complex were determined by the Pan-Tompkins algorithm (Pan & Tompkins, 1985; Sedghamiz, 2014) using custom written scripts in Matlab 2020a (The Mathworks, Inc.). Accuracy of the automatic detection of R-waves was subsequently controlled by visual inspection to identify ectopic heart beats and time intervals confounded by artifacts. Following this preprocessing procedure, the number of heart beats for each of the time intervals of the HBT was determined and stored for further calculation of the interoceptive accuracy

scores. Additionally, heart rate (HR) and root mean square of the successive differences (RMSSD) were calculated separately for the HBT (averaged across all time intervals), the emotional processing task, as well as the resting ECGs recorded prior to the experimental tasks (Shaffer & Ginsberg, 2017). We calculated RMSSD of the normal-to-normal beat intervals (NN), while excluding each interval with an ectopic beat as well as the preceding and following RR interval, since these might be also distorted by the occurrence of ectopic beats (Choi & Shin, 2018). In general, RMSSD is considered to be a robust and statistically reliable HRV marker (Thomas et al., 2019). It represents short-term HRV (Electrophysiology, 1996) and is used as a marker for vagally mediated HRV.

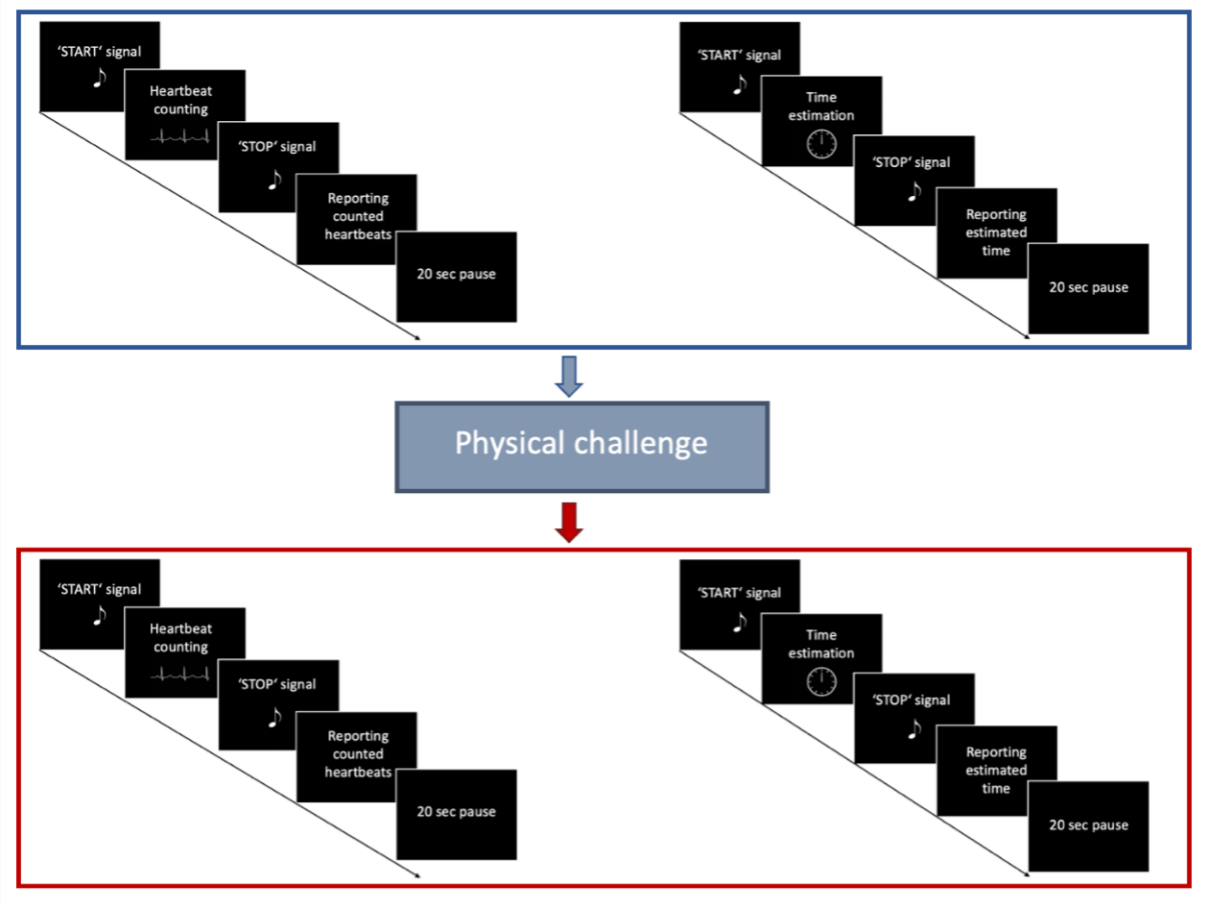

Figure 2. Trial structure of the Heartbeat tracking task. First, participants performed the HBT for five different time intervals in a pseudorandomized order. Afterwards, they performed a Time estimation task for the same time intervals. After a short physical challenge of ten squats was implemented, participants performed once again the HBT, followed by the Time estimation task.

Statistical analyses

Statistical analyses were carried out with SPSS v.25.0 (IBM Corp., USA). For all analyses statistical significance was set to $p < 0.05$.

Interoceptive accuracy and accuracy of time estimation

Interoceptive accuracy und TE accuracy scores were compared between experimental groups with independent samples t-tests. Additionally, we analyzed the effects of the physical challenge in a subsample of participants, for interoceptive accuracy and time estimation accuracy in two separate 2 × 2 mixed ANOVAs with the independent factor 'group' and the repeated measurement factor 'time' (pre/post physical challenge).

Interoceptive sensibility

To test group differences in IS, mean scores of all MAIA subscales were analyzed with multiple independent samples t-tests.

Interoceptive Awareness

Interoceptive awareness is defined as the correspondence between one's interoceptive accuracy, measured with an objective behavioral task, and IS that is the subjective evaluation of interoceptive abilities assessed via self-report measures. Previous studies investigating the link between behavioral measures of interoception (e.g., HBT) and MAIA subscales revealed associations only with the subscale "*Attention Regulation"* (Calì et al., 2015). Thus, it has been suggested that interoceptive accuracy measured by the HBT relates to more specific aspects of IS and not so much to general IS as assessed by the "*Noticing"* subscale. Since the HBT requires individual's ability to control and maintain attention towards bodily sensations, we assessed interoceptive awareness by computing Pearson's correlation coefficients between interoceptive accuracy scores and $IS_{\text{attention regulation}}$ scores across all participants in each experimental group (Garfinkel et al., 2015; Hina & Aspell, 2019). To investigate group differences in interoceptive awareness, correlation coefficients in the IBD and HC group were standardized and compared between groups (Eid et al., 2011).

Emotional processing

Differences in emotion processing between IBD and HC were analyzed with two separate 2 × 3 mixed-effects ANOVAs for the two dependent variables 'valence and 'arousal' with the between-subject factor 'group' and within factor 'stimulus valence' (positive/ neutral/negative). Degrees of freedom were corrected using Greenhouse-Geisser estimate of sphericity. Post-hoc comparisons were done by sub-designs of ANOVA design and/or pairwise comparisons.

The link between interoceptive accuracy and emotional processing

To investigate whether greater interoceptive accuracy was associated with higher levels of experienced valence and arousal during emotional experience, two linear regression analyses across all participants were computed. Valence and arousal ratings averaged separately for the three types of stimuli valence constituted the dependent variables (DV), while interoceptive accuracy scores were used as independent variable (IV). Beyond these preregistered analyses, we computed two additional linear regressions to test whether superior IS was associated with changes in perceived valence and arousal of emotional stimuli. Since we hypothesized that alterations in emotional processing linked to interoceptive processes will be more pronounced for negative stimuli, mean valence and mean arousal ratings only for negative stimuli were included in the analyses.

The role of ACE in interoception, emotional processing and their association in IBD

The effect of childhood traumatization on interoceptive accuracy and IS was investigated using two linear regression analyses with CTQ scores (IV) and interoceptive accuracy and IS scores (DV), respectively. Furthermore, to investigate whether severity of childhood traumatization does influence emotional processing, linear regression models for valence and arousal ratings were computed separately. Finally, the modulating effect of ACE on the relationship between interoceptive accuracy and emotional processing was investigated using separate moderation analyses with interoceptive accuracy scores (IV) and valence and arousal ratings (DV), respectively. Again, beyond the preregistered statistical analyses, we computed two additional moderation models with IS (IV) and valence and arousal ratings (DV).

Heart rate and heart rate variability

HR and RMSSD were compared between groups with independent t-tests. The effects of the physical activation on HR and HRV parameters were analyzed with a variance analytical design

including the independent factor ‘group’ and the repeated measurement factor ‘time’ (pre/post challenge) in the subgroup of participants who performed the short physical exercise. Finally, differences between baseline cardiac activity and physiological activation during the emotional processing were analyzed with a variance analytical design including the independent factor ‘group’ and the repeated measurement factor ‘time’ (baseline/task).

To control for multiple testing, we report the corresponding *p*-values adjusted according to Benjamini & Hochberg (1995) and indicated this by a subscript (p_{FDR}) (Benjamini & Hochberg, 1995).

2.1.4 Results

Interoceptive accuracy and time estimation accuracy:

Comparisons between IBD and HC revealed no differences between both groups either for the interoceptive accuracy scores or the TE scores (IACC: $t(67) = -0.432$, $p = .667$, TE: $t(67) = -0.047$, $p = .963$, see Table 2.3). An analysis of the effect of the physical challenge in a subgroup of participants showed also no group differences for interoceptive accuracy either in general or depending on the challenge (main effect ‘group’: $F(1,46) = 0.108$, $p = .744$; ‘group’ × ‘time’: $F(1,46) = 0.777$, $p = .383$). However, interoceptive accuracy after the physical challenge improved as non-significant trend (main effect ‘time’: interoceptive accuracy: $F(1,46) = 2.864$, $p = .097$). In contrast to interoceptive accuracy, HCs improved significantly in their TE performance after the physical challenge, whereas IBD patients did not show a significant difference (main effect ‘group’: $F(1,46) = 1.860$, $p = .179$; ‘group’ × ‘time’: $F(1,46) = 4.428$, $p = .041$).

Interoceptive Sensibility:

IBD patients reported a stronger tendency to distract themselves from unpleasant sensations ($IS_{\text{not-distracting}}$: $t(66) = -3.500$, $p_{FDR} = .004$) and superior awareness of physical sensations associated with emotional states ($IS_{\text{emotional awareness}}$: $t(66) = 3.504$, $p_{FDR} = .004$). For further details on MAIA subscales see Table 2.3.

Interoceptive Awareness:

Interoceptive accuracy and $IS_{\text{attention regulation}}$ scores showed a non-significant trend association in the IBD group but not in HC (all participants: $r(68) = -.151$, $p = .218$; IBD: $r(33) = -.317$, $p =$

.072; HCs group: $r(35) = .049$, $p = .779$). Interoceptive awareness differed between groups only as a non-significant trend ($Z = -1.49$, $p = .069$; Table 2.3).

Emotional processing task:

Valence ratings did not differ between both groups, either in general or dependent on the stimulus valence (main effect 'group': $F(1,64) = 2.08$, $p = .154$; 'group' × 'stimulus valence': $F(1,84) = 0.80$, $p = .407$) (Table 2.4). Arousal ratings differed between groups depending on the stimulus valence ('group' × 'stimulus valence': $F(1,96) = 3.64$, $p = .042$; main effect 'group': $F(1,64) = 0.43$, $p = .517$). Post-hoc analyses revealed a significant interaction effect 'group' × 'stimulus valence' ($F(1,64) = 5.329$, $p = .024$) with IBD patients exhibiting a greater difference in their perceived arousal between neutral and positive stimuli compared to HC (IBD: $M_{neutral} = 5.10 \pm 1.08$, $M_{positive} = 7.11 \pm 0.54$; HC: $M_{neutral} = 5.45 \pm 1.28$, $M_{positive} = 6.79 \pm 1.01$).

Interoception and emotional processing:

Regression analyses revealed no significant associations between interoceptive accuracy and subjective valence or arousal ratings (all $p > .05$). Since only $IS_{emotional\ awareness}$ and $IS_{not\text{-}distracting}$ scores revealed significant group differences, only these subscales were used to investigate the link between IS and emotional processing. $IS_{emotional\ awareness}$ was a significant predictor of perceived valence of negative stimuli in the whole sample ($b = -0.390$, $p_{FDR} = .012$) with participants reporting greater emotional awareness perceiving negative stimuli as more negative compared to those with lower emotional awareness. Further analyses revealed that this association was significant only in the IBD group ($b = -0.493$, $p_{FDR} = .024$) but not in the HC group ($b = -0.293$, $p_{FDR} = .371$) (Figure 3A). Similarly, $IS_{emotional\ awareness}$ showed a significant association with perceived arousal of negative stimuli for all participants ($b = 0.357$, $p_{FDR} = .034$), with greater emotional awareness being associated with higher arousal. A non-significant trend for this association was found in the IBD group ($b = 0.477$, $p_{FDR} = .069$) but not in HC ($b = 0.235$, $p_{FDR} = .371$) (Figure 3B). $IS_{not\text{-}distracting}$ was not significantly associated with emotional processing (all $p > .05$).

Table 2.3 Group differences in Interoceptive accuracy, Interoceptive sensibility and Interoceptive awareness.

	HC (M±SD)		IBD (M±SD)		Test-statistics	p-value	
Interoceptive accuracy (HBT)							
IACC	0.67	±0.21	0.65	±0.19	-0.432 [a]	.667	
TE accuracy	0.73	±0.15	0.73	±0.14	-0.047 [a]	.963	
Interoceptive sensibility (MAIA)							
Noticing	2.74	±1.03	2.61	±1.14	-0.492 [a]	.625	
Not distracting	3.10	±0.83	2.20	±1.09	-3.500 [a]	.004	**
Not worrying	2.88	±0.79	2.67	±1.10	-0.929 [a]	.356	
Attention regulation	2.41	±0.68	2.65	±0.89	1.243 [a]	.218	
Emotional awareness	2.72	±0.92	3.47	±0.83	3.504 [a]	.004	**
Self-regulation	1.95	±0.91	2.32	±1.03	1.561 [a]	.123	
Body listening	1.76	±1.10	1.95	±1.16	0.683 [a]	.497	
Trusting	3.04	±1.05	2.98	± 1.29	-0.205 [a]	.839	
Interoceptive awareness (IAcc*MAIA)							
IAw	.049 [b]		-.317[b]		-1.49 [c]	.069	(*)

IBD, Inflammatory bowel diseases group; HC, healthy control group; IACC, interoceptive accuracy; MAIA, Multidimensional Assessment of Interoceptive Awareness; IAw, interoceptive awareness. * $p < .05$, ** $p < .01$, *** $p < .001$, [a] t-value, [b] r, [c] Z-value

Table 2.4 Results of the analyses of variance for mean valence and arousal ratings with between-subject factor 'group' (IBD/HC) and within-subjects factor 'stimulus valence' (positive/neutral/negative).

Emotional processing task				
	F	*df1/df2*	*p-value*	
Valence ratings				
Group	2.08	1/64	.154	
Stimulus valence	301.63	1/84	<.001	***
Group × stimulus valence	0.80	1/84	.407	
Arousal ratings				
Group	0.43	1/64	.517	
Stimulus valence	312.54	1/96	<.001	***
Group × stimulus valence	3.64	1/96	.042	*

df, degrees of freedom; * $p < .05$, ** $p < .01$, *** $p < .001$

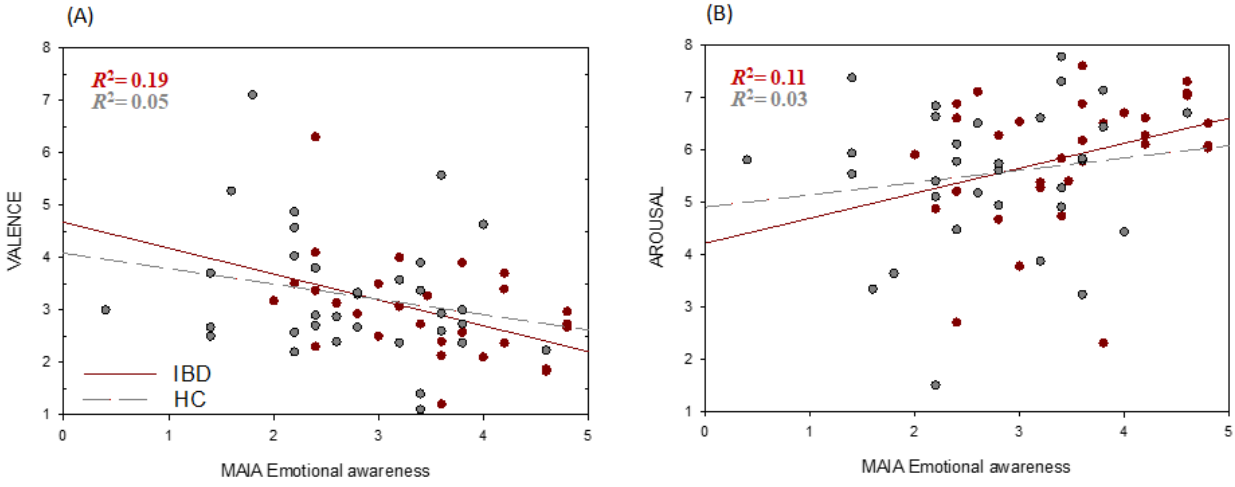

Figure 3. Associations between interoceptive sensibility and emotional processing. Higher $IS_{emotional\ awareness}$ (MAIA) scores were associated with higher negative valence (Fig. 3A) and arousal ratings (Fig. 3B) of negative stimuli.

Group differences in childhood traumatization, later traumatic experiences and PTSD symptom severity:

There were no significant differences between both groups regarding the severity of ACEs measured with the CTQ. An equal number of IBD patients and HCs reported separation or death of a parent during their childhood (IBD: 32.3 %, HC: 26,5 %, $\chi^2(1) = 0.263$, $p = .608$). Both groups did not differ in the number of traumatic events experienced in later life (IBD: M = 1.52, SD = 1.56; HC: M = 1.11, SD = 1.30), however, the IBD group exhibited a higher level of PTSD symptoms compared to HC $t(44) = 4.126$, $p < .001$. See Table 2.2 for further details.

Childhood traumatization and interoception:

Regression analyses revealed no significant associations between interoceptive accuracy and CTQ in the present sample (all $p > .05$). However, exploratory analysis showed that interoceptive accuracy after the physical challenge was lower in those participants with higher CTQ scores in the HC group ($r(24) = -.511$, $p_{FDR} = .022$), but not in the IBD group ($r(24) = .070$, $p_{FDR} = .752$, comparison between groups: $Z = -2.06$, $p = .020$) (Figure 4). CTQ scores did not show any significant links either to IS or interoceptive awareness (all $p > .05$).

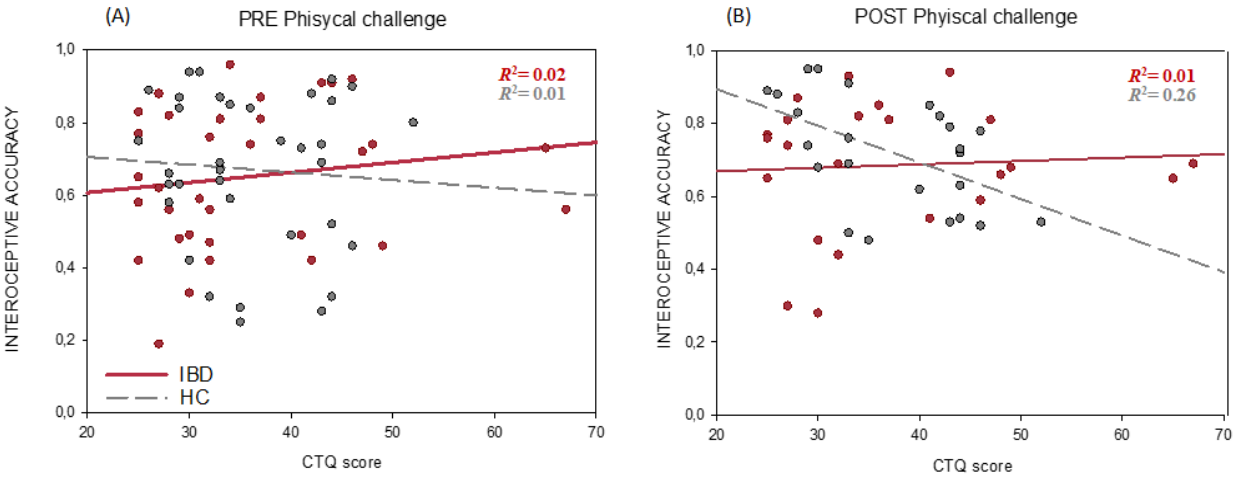

Figure 4. Associations between Interoceptive accuracy (HBT) and childhood traumatization (CTQ score) before (Fig. 4A) and after the physical challenge (Fig. 4B). In contrast to the IBD group (red line), HCs (grey dashed line) showed a significant negative correlation between interoceptive accuracy and CTQ scores after the physical challenge. Note: the physical challenge was implemented only in a subsample of 48 participants. CTQ, childhood trauma questionnaire; HC, healthy controls group; IBD, inflammatory bowel diseases group.

Childhood traumatization and emotional processing:

Linear regression analyses revealed no significant associations between CTQ scores and emotional processing (all $p > .05$).

The role of ACE in interoception, emotional processing and their association:

Moderation analyses showed no significant effects of CTQ scores on the link between interoceptive accuracy and emotional processing (all $p > .05$). However, CTQ severity significantly moderated the association between $IS_{emotional\ awareness}$ and valence ratings of negative stimuli ($R^2 = 0.22$, $F(3,61) = 5.588$, $p = .002$). A significant interaction was found between $IS_{emotional\ awareness}$ and CTQ scores ($b = -0.05$, $p = .009$), indicating that severer traumatization strengthens the negative relationship between $IS_{emotional\ awareness}$ and valence intensity. Individuals with severe histories of ACE and higher IS rated negative stimuli as more negative compared to individuals with higher IS but no histories of childhood traumatization (Figure 5A).

For arousal ratings, analyses revealed a non-significant trend effect of CTQ on the association between $IS_{emotional\ awareness}$ and perceived arousal of negative stimuli ($R^2 = 0.12$, $F(3,61) = 2.725$, $p = .052$). A significant interaction between $IS_{emotional\ awareness}$ and CTQ scores was found only for the highest CTQ severity ($b = 0.76$, $p = .007$) but not for the lower CTQ scores ($b = 0.28$, $p = .09$). These findings indicate that only severe ACE significantly amplified the positive relationship between $IS_{emotional\ awareness}$ and arousal, suggesting that individuals reporting higher levels of childhood traumatization and high IS, do experience negative stimuli as more arousing compared to individuals with high IS but no or low levels of childhood maltreatment (Figure 5B).

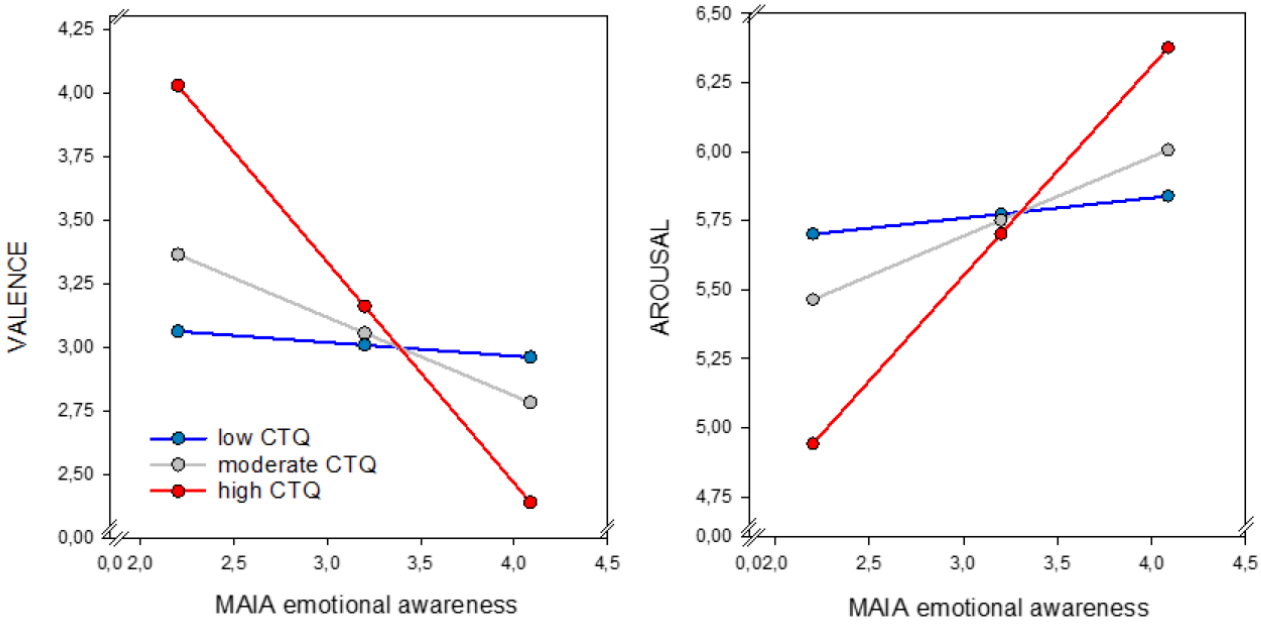

Figure 5. Moderation effect of childhood traumatization (CTQ) on the link between $IS_{emotional\ awareness}$ (MAIA) and perceived valence (Fig. 5A) and arousal (Fig. 5B) of negative stimuli. Participants reporting higher CTQ scores (red line) and high $IS_{emotional\ awareness}$ reported higher negative valence and arousal compared to individuals exhibiting high $IS_{emotional\ awareness}$ but moderate (grey line) or low (blue line) traumatization. IS, interoceptive sensibility; CTQ, childhood trauma questionnaire.

Heart rate and heart rate variability:

Heartbeat tracking task

Mean HR during the HBT did not differ significantly between IBD and HC before the physical challenge ($t(67) = 1.490$, $p = .141$). However, mean HR differed significantly before and after the physical challenge (main effect 'time': $F(1,46) = 5.372$, $p = .025$) and showed a non-significant trend for group differences (main effect 'group': $F(1,46) = 3.284$, $p = .076$; 'time × 'group': $F(1,46) = 0.059$, $p = .809$). Thus, HR increased after the physical challenge in both groups, indicating that the implemented manipulation was successful. Mean RMSSD during the HBT did not differ significantly between both groups ($t(67) = 0.367$, $p = .714$). However, mean RMSSD differed significantly before and after the physical challenge (main effect 'time:

$F(1,46) = 18.10$, $p < .001$) and differed between both groups only depending on the presence of physical challenge ('time × 'group': $F(1,46) = 9.66$, $p = .003$; main effect 'group': $F(1,46) = 0.24$, $p = .625$). Both groups exhibited increased HRV after the physical challenge. In the IBD group, however, this increase was less strong compared to HC.

Emotional processing task

Due to technical problems, baseline ECG data of three participants could not be analyzed. Mean HR and RMSSD at baseline and during the emotional processing task did not differ either in general or between both groups (all $p > .05$). For further details see Supplementary Material S1. Childhood traumatization was not associated with alterations in cardiac activity in the whole sample (all $p > .05$). In IBD, higher CTQ scores were associated with higher HR at baseline ($r(31) = .420$, $p = .019$). A non-significant trend association between mean RMSSD after the physical challenge and CTQ total score in the IBD group was found ($r(23) = -.376$, $p = .077$). No associations between cardiac activity and childhood traumatization could be found in HC. Because of the exploratory nature of these analyses, we did not correct for multiple comparisons (for more details see supplemental material S1, Table S1).

2.1.5 Discussion

The present study investigated alterations of interoception and its role in emotion processing in IBD. This is the first study to assess interoceptive abilities as multidimensional construct implementing both behavioral and self-report methods. Therefore, we were able to investigate changes in different facets of interoception in IBD and to link these to emotion processing. Furthermore, associations between interoceptive abilities and emotion processing were investigated while taking childhood traumatization into account.

Interoceptive accuracy

Our findings indicated no differences between IBD and HC in the objective ability to track and perceive internal bodily sensations. These results are in line with previous studies using the same experimental paradigm in somatoform disorders (Schaefer et al., 2012), fibromyalgia (Borg et al., 2018) and irritable bowel syndrome (Gajdos et al., 2020). Contrary to out hypothesis, IBD patients did not exhibit greater interoceptive accuracy of cardiac signals. One possible mechanism explaining this finding could be provided by current theories of somatization suggesting that the perception of bodily sensations is based on previously formed symptom-related memory structures (Brown, 2004; Witthöft et al., 2020). Potentially, IBD patients might be more focused on disease-specific visceral signals, which in turn captures cognitive resources and might impede an attentional shift to other internal signals such as their heartbeats. However, future studies need to assess interoceptive accuracy of other internal sensations (e.g., gastric signals) in IBD compared to healthy individuals, in order to provide empirical evidence whether disease-specific bodily sensations might be perceived more accurately. We implemented a short physical challenge to investigate whether activation of the cardiovascular system might influence individuals' abilities to track their heartbeats differentially in healthy individuals and patients with IBD. Our results showed that both groups improved as a non-significant trend in their interoceptive accuracy after the short physical exercise, indicating that induction of increased sympathetic activity elicits increased interoceptive accuracy. To our knowledge, this is the first study to investigate interoception by implementing a physical challenge in adults. Indeed, after the short physical activation participants improved in their interoceptive accuracy, showing that it might be useful to investigate interoceptive abilities after induced physiological arousal.

Interoceptive Sensibility

Although both groups did not differ in their objective abilities to perceive visceral signals (heartbeats), our findings indicate that IBD patients do differ in their subjective interoceptive abilities regarding two main facets of IS: the tendency how to cope with unpleasant bodily sensations ($IS_{not\text{-}distracting}$) and their ability to be focused on the body when experiencing various emotions ($IS_{emotional\ awareness}$). Our results show that IBD patients exhibit a stronger tendency to use distraction as a coping mechanism when experiencing discomfort and physical pain. Coping strategies modulate the effects of psychological distress on illness experience in IBD (Bitton et al., 2008b). In line with our findings, previous research demonstrated that IBD patients often use self-distracting and avoidance strategies to cope with IBD symptoms (Jones et al., 2006). In general, distraction is the most common coping style for managing pain in chronic pain patients (Mehling et al., 2013).

The current study expands existing findings on the association between emotional processing and interoception in IBD by showing a greater awareness of the connection between emotional states and bodily sensations in IBD patients. While the perception of visceral signals per se does not seem to be changed in remitted IBD patients, it is the appraisal of these sensations, which might be altered. When experiencing an emotion, IBD patients may appraise their bodily sensations differently from healthy individuals by putting greater emphasis on the perceived changes in the body, resulting in grater emotional awareness. Empirical findings from clinical and fundamental research have already demonstrated the physiological effects of gut microbiota on emotional processes, including emotion recognition. Tillisch et al. (2013) could show a reduced midbrain connectivity activity and therefore altered activity in brain areas associated with vigilance to emotional stimuli in individuals after a four-week therapy with probiotics (Tillisch et al., 2013). Alterations in gut microbiota, as frequently observed in IBD, might be linked to changes in emotion and sensory related brain regions (Mayer et al., 2014), leading to changes in emotional awareness. Individuals with superior interoceptive abilities perceive emotions as more intense (Herbert et al., 2007), which might be due to greater attention to emotion-related bodily changes and greater awareness of these mind-body associations. From a neurobiological perspective, the neural circuits involved in processing visceral information overlap with those involved in emotional processing (Critchley & Garfinkel, 2017; Singer et al., 2009).

Interoception & emotional processing

Our results indicated no group differences in the perceived valence of emotional stimuli. However, when evaluating their subjectively experienced arousal, IBD patients exhibited a greater arousal increase when being presented with neutral compared to positive stimuli. Interoceptive accuracy was not related to emotional processing in the present study. In contrast, $IS_{emotional\ awareness}$ was associated with perceived valence and arousal of negative stimuli. Individuals exhibiting superior $IS_{emotional\ awareness}$ experienced negative stimuli with a higher intensity, accompanied by higher levels of perceived arousal. However, these associations could be found only in the IBD group but not in HC (Figure 3). Our findings indicate that only emotional awareness as part of individual's interoceptive sensibility and not one's interoceptive accuracy influenced the perception of emotional stimuli. This pattern implies that altered processing of negative emotional content among IBD patients is not connected to changed perception of physiological stimuli but to their appraisal in the context of the emotional experience. These results could, therefore, indicate that the ability to identify and attribute physical sensations to certain emotional states (e.g., increased muscular tension and anger) might intensify patient's tendency to link bodily sensations to environmental triggers. In line with this interpretation, findings from fMRI studies also showed that individuals with high emotional awareness exhibit stronger emotion reactivity (Lichev et al., 2014; Terasawa et al., 2013). This might imply that IBD patients who are more aware of the physiological manifestations of emotions in the body may appraise these as more intense. Furthermore, neural correlates of emotional awareness include brain regions involved in the perception of both interoceptive signals and emotional cues (Critchley & Garfinkel, 2017; Zaki et al., 2012), suggesting that higher emotional awareness may be reflected by more efficient information exchange between these brain structures (Lutz et al., 2013). It is conceivable that, although the perception of internal signals (heartbeats) did not seem to be changed, IBD patients might experience more differentiated bodily feelings during emotional experience as result of a changed neural functional connectivity (Simmons et al., 2013). Since our results indicate that only the perception of negative stimuli was linked to emotional awareness, future studies need to investigate whether these effects can be explained by functional and structural changes in brain regions known to be relevant for the processing of negative emotions, visceral sensations, and interoceptive attention, such as the interior insula (Avery et al., 2014; Zaki et al., 2012).

The role of childhood traumatization

In contrast to previous findings, the IBD sample in the current study did not report higher levels of ACE compared to HC. A recent study found a significant percentage of IBD patients to have at least one ACE, stressing the possibility that childhood trauma might influence the course of IBD shown by a higher use of health care resources (Witges et al., 2019). However, in other population-based studies the link between maltreatment during childhood and IBD later in life was found only for Ulcerative colitis, but not for Crohn's disease (Fuller-Thomson et al., 2015). One possible explanation why the prevalence of ACE was not increased in our IBD sample might be that patients reporting current and/or lifetime psychiatric disorders were not included in the study. Early life stress has been repeatedly linked to higher risk for developing mental health problems. Previous studies investigating the prevalence ACE and IBD took primarily lifetime major depression and generalized anxiety disorders into account (Fuller-Thomson et al., 2015), but no further psychopathologies. However, none of these studies managed to disentangle the effects of ACE on IBD as well as on anxiety or depression symptoms by now. Further studies are required to investigate whether the interplay between interoception, emotion processing and ACE in IBD patients is influenced by psychiatric co-morbidities.

To the best of our knowledge, this is the first study to investigate the role of childhood maltreatment in interoception, emotional processing and their association. Our findings revealed no associations between ACE and interoceptive accuracy in IBD. Interestingly, we observed that in HC, ACE was negatively related to interoceptive accuracy only after the physical challenge. The implemented physical exercise was used to induce an increase in participants' heart rate and thereby enhanced cardiac signals perception (Herbert et al., 2012b). Our findings could, therefore, reflect the long-term negative impact of childhood maltreatment on individual's abilities to perceive visceral signals under conditions of physiological activation. Chronic early life stress leads to altered physiological response to arousal and dysregulation of the brain-body signaling (Schaan et al., 2019b; Schulz & Vögele, 2015). In line, various trauma-related disorders (e.g., PTSD) have been repeatedly linked to altered physiological reactions to external threat cues (Iffland et al., 2020; Lissek & van Meurs, 2015). In this case, threat perception might lead to maladaptive coping mechanism such as suppression and denial of bodily sensations due to overwhelming physiological reactions. In line with this interpretation, physical detachment is often observed in early-traumatized individuals as coping mechanism under high-stress conditions. Our results are also in line with Schaan et al. (2019) who found a negative relationship between early life stress and interoceptive abilities only after

an acute psychological stressor has been induced (Schaan et al., 2019b). Our findings suggest, however, that a physical stressor is also an eligible method to affect interoceptive accuracy and might be a useful approach to reveal possible associations between interoception and childhood traumatization.

Adverse childhood experiences have been repeatedly linked to impairments in affective processing (Dannlowski et al., 2012). However, studies investigating the role of childhood traumatization on the link between interoception and emotion processing are sparse. We observed that the association between $IS_{emotional\ awareness}$ and emotional processing of negative stimuli is moderated by severity of ACE independent of IBD diagnosis. This is a novel and interesting finding suggesting that among individuals with histories of childhood maltreatment, greater emotional awareness is associated with stronger intensity of negative affect and higher arousal to negative environmental stimuli. Previously, an attentional bias towards negative stimuli in individuals with ACE have been shown, indicating greater responsiveness to negative cues, heightened emotional response to possible threats and difficulties disengaging from negative emotional content (McLaughlin & Lambert, 2017). In the context of emotional experience, individuals with histories of childhood maltreatment might use their bodily signals in a more efficient way in order to track and recognize possible threats.

Finally, exploratory analyses of the data revealed higher PTSD symptoms severity including negative alterations in cognitions and mood, hyperarousal, and reactivity in the IBD group. Some evidence indicates a higher risk for developing PTSD symptoms in IBD due to the challenges of the disease course most of the patients' experience (Taft et al., 2019). In summary, these findings emphasize the influence of early life adversity and higher frequency of posttraumatic stress symptoms in IBD. Since posttraumatic stress has been linked to worse IBD course through behavioral and physiological pathway, this might indicate a new possible target for intervention improvement (Weaver & Szigethy, 2020).

Limitations

Finally, some limitations of the present study have to be addressed. First, although we aimed to investigate a bigger sample (N=120), the final sample consisted of 69 participants. Thus, given the smaller sample size larger effect size was needed to detect significant effects. Post-hoc sensitivity analyses showed that our study was sensitive to detect effect sized of d = 0.68 with 80% power in contrast to d = 0.52 for the planned sample size of N=120). Moreover, it should

be mentioned that although all IBD patients were in clinical remission, some of them reported minor health problems (e.g., knee pain), whereas all healthy control participants did not declare any health-related complaints. In line with other studies using this task, we found relatively poor mean interoceptive accuracy scores between 0.50 and 0.70 (Reinhardt et al., 2020; Schaefer et al., 2012). Thus, the observed variance in both groups was quite low. It should be emphasized that there is a considerable body of evidence from physiological studies supporting the construct and criterion validity of the HBT (Fukushima et al., 2011; Herbert et al., 2012b; Pollatos et al., 2005a). Thus, the reported poor validity of interoceptive accuracy measures in some studies result to a large extent from insufficiently controlled experimental environments or non-standardized changes in participant's physiological reactions (e.g. changing body posture during the task) (Ainley et al., 2020). Previous studies found a strong association between cardiac and gastric sensitivity suggesting the presence of a general sensitivity for interoceptive cues across the cardiac and gastric modalities (Herbert et al., 2012a; van Dyck et al., 2016). Following these considerations, we decided to use the HBT as a measure of the general interoceptive abilities in IBD. However, a recent study by Ferentzi and colleagues (2018) has suggested that different interoceptive accuracy tasks reveal significant associations only when belonging to the same sensory modality, indicating HBT as a not specific measure of gastrointestinal interoceptive accuracy (Ferentzi et al., 2018). In contrast, Whitehead and Drescher (1980) could show a moderate correlation between heartbeat perception and perception of gastric contractions, when using the Heartbeat discrimination task, indicating a generalized tendency to be aware of visceral signals (Whitehead & Drescher, 1980). Since both cardiac and gastric signals are transmitted to the brain partially through the vagus nerve, it is conceivable that their perception is closely related. Furthermore, one may critically discuss whether the correspondence between the observed interoceptive accuracy during the heartbeat tracking task and the self-reported interoceptive sensibility indeed reflect the construct of interoceptive awareness (Garfinkel et al., 2015). A recent model proposed by Murphy et al. (2019) stressed the need for a careful differentiation between individual's interoceptive accuracy and interoceptive attention (Murphy et al., 2020; Murphy et al., 2019). Accordingly, interoceptive awareness of one's interoceptive accuracy as a metacognitive construct should be assessed as the relationship between one's behavioral performance and the corresponding awareness of particularly this performance, e.g., measured by ratings of the participants' confidence in the accuracy of their performance. Thus, in the current study the approach to estimate interoceptive awareness corresponds more closely to the concept of interoceptive attention as to interoceptive awareness when conceptualized as a metacognitive construct (see

(Murphy et al., 2019)). In consequence, further studies are required to investigate whether IBD patients' interoceptive awareness assessed as confidence ratings on their HBT performance might be affected. Finally, it should be mentioned that the severity of ACE in the present sample was only low to moderate (Klinitzke et al., 2012), which might be due to the exclusion of individuals reporting current or lifetime psychiatric diagnoses. IBD patients reporting moderate traumatization, but no histories of mental disorders might represent a subgroup of patients with a less severe IBD course or resilient individuals who exhibited an adaptive coping with the experiences of traumatization. This restricts the generalizability of our findings to IBD patients with comorbid mental disorders. Since the significance of childhood traumatization in IBD might be underestimated in the current sample, our findings on the influence of ACE in IBD need to be interpreted with caution.

2.1.6 Conclusions

In conclusion, IBD patients did not exhibit changes in the accuracy to perceive bodily signals such as their heartbeats. Our results demonstrate that the ability to attribute certain physiological sensations to emotional states intensifies the experience of negative emotions among IBD patients. As this population is quite prone to emotional distress and emotion dysregulation, future psychotherapeutic treatments should target patients' appraisals of physiological feedback during negative emotional states. Finally, the present findings point towards the important effect of early life stress on the interaction between mind and body, suggesting that individuals with histories of childhood traumatization might use their bodily sensations more efficiently in order to recognize negative emotional content and possible threats.

2.1.7 Supplemental material S1

Heart rate and heart rate variability

Repeated measures ANOVA with a between-subjects factor 'group' (IBD/HC) and repeated measures factor 'time' (baseline/time) revealed no differences in HR and HRV (RMSSD).

HR:
main effect 'time': $F(1,64) = 1.195$, $p = .278$

main effect 'group': $F(1,64) = 0.416$, $p = .521$

interaction effect 'time' × 'group': $F(1,64) = 0.079$, $p = .780$

RMSSD:
main effect 'time': $F(1,64) = 0.191$, $p = .663$

main effect 'group': $F(1,64) = 0.355$, $p = .554$

interaction effect 'time' × 'group': $F(1,64) = 2.215$, $p = .142$

Table S1. Correlations between HR, RMSSD, and CTQ (Pearson's correlation coefficients), p-values not corrected for multiple comparisons

	Whole sample		**IBD**		**HC**	
	r	*p*	*r*	*p*	*r*	*p*
HR baseline	.199	.110	.420	.019 *	-.058	.742
HR Pre challenge	.038	.761	.151	.401	-.082	.639
HR Post challenge	.000	.999	.057	.797	-.073	.734
HR Emotion processing	.014	.913	.178	.320	-.158	.366
RMSSD baseline	-.071	.574	-.240	.194	.216	.212
RMSSD Pre challenge	-.070	.573	-.161	.370	.115	.511
RMSSD Post challenge	-.153	.304	-.376	.077 (*)	.104	.630
RMSSD Emotion processing	-.021	.863	-.249	.162	.230	.184

(*) $p < .10$ * $p < .05$

2.2 Research Question II | Is it a gut feeling? Bodily sensations associated with the experience of valence and arousal in patients with inflammatory bowel disease

An adapted version of this chapter has been submitted as: Atanasova, K., Lotter, T., Bekrater-Bodmann, R., Kleindienst, N., Reindl, W., & Lis, S. Is it a gut feeling? Bodily sensations associated with the experience of valence and arousal in patients with inflammatory bowel disease (in review). *Submitted to Frontiers in Psychiatry*

2.2.1 Abstract

Background: Previous studies have shown dysfunctional emotion processing in patients with inflammatory bowel diseases (IBD), characterized by a hypersensitivity to negative emotions and a hyposensitivity to positive emotions. Models of emotion processing emphasize the importance of bodily sensations to the experience of emotions. Since there have been no studies on whether emotion-associated bodily sensations are changed in IBD, we investigated the experience of bodily sensations related to valence and arousal, together with their links to emotional awareness, as one domain of interoceptive sensibility relevant to emotion processing.

Methods: Using a topographical self-report measure, 41 IBD patients in clinical remission and 44 healthy control (HC) participants were asked to indicate where and how intensely in their body they perceive changes when experiencing emotions of positive and negative valence, as well as relaxation and tension. Additionally, we used self-report questionnaires to assess emotional awareness as one domain of an individual's interoceptive sensibility, gastrointestinal-specific anxiety, and psychological distress.

Results: Patients with IBD reported higher emotional awareness but lower intensities of perceived changes in their bodily sensations related to valence and arousal of emotional processing. IBD patients reported less intense bodily activation during positive emotions and less intense bodily deactivation during negative emotional states in comparison to HC participants. Higher emotional awareness and psychological distress were linked to stronger experiences of emotion-related bodily sensations in IBD patients.

Conclusions: IBD patients exhibited alterations in how they link bodily sensations to their emotional experience. Such persistent changes can affect a patient's well-being and are related to higher levels of anxiety and depression among IBD patients, even in remission.

2.2.2 Introduction

Patients with inflammatory bowel disease (IBD) report poorer quality of life, including impairments in their physical and mental well-being, than healthy individuals (Knowles et al., 2018). IBD is often accompanied by increased attention to and anxiety about gastrointestinal sensations, resulting in greater psychological distress (Bannaga & Selinger, 2015). Psychological distress and biased emotion experience have been shown to be subjectively and objectively related to disease activity (Araki et al., 2020; Mawdsley & Rampton, 2005). These relationships are consistent with the biopsychosocial model of illness, according to which the disease course affects and is affected by biological, social, and psychological factors, such as emotions and cognitions (Bevers et al., 2016). The perception of bodily sensations significantly influences the experience of stress and emotion and has an impact on an individual's well-being (Chen et al., 2021; Craig, 2002). Thus, chronic conditions associated with altered visceral and interoceptive processing, such as gastrointestinal inflammation, might result in impaired emotional functioning affecting patients' quality of life (Kano et al., 2020).

Studies on emotional experience in IBD have pointed toward a decreased sensitivity to positive emotional content (Agostini et al., 2011; Wilkinson et al., 2019) and increased arousal during negative emotional states (Vianna et al., 2006). According to dimensional models of emotion, emotions are arranged in a two-dimensional space defined by the dimensions of valence and arousal (Russell, 1980). Valence refers to the hedonic value of an emotion, that is, the subjective feeling of pleasantness or unpleasantness. Arousal refers to the subjective state of feeling relaxation or tension (Barrett, 1998) and represents the level of autonomic activation that an emotions elicits. Both dimensions influence peoples' approach–avoidance behavior: high positive arousal states trigger the appetitive motivational system, while low negative arousal states are experienced as not rewarding and are therefore avoided (Lang & Bradley, 2013). An individual's level of emotional arousal is modulated by interoceptive processes (Pollatos et al., 2007a). Part of an individual's interoceptive abilities is the ability to link the conscious experience of emotions to the physiological sensations perceived in different regions of the body (Wiens, 2005). A study by Nummenmaa et al. (2014) showed that the experience of emotions is linked to topographical patterns of activation and deactivation perceived in the body, suggesting their representation in the somatosensory system (Nummenmaa et al., 2014; Ruben et al., 2001). Emotional awareness constitutes a distinct feature of one's interoceptive sensibility and describes the ability to attribute specific bodily sensations to physiological manifestations of emotions (Mehling et al., 2012). Although it has

been shown that IBD patients exhibit certain alterations in both emotion and interoceptive processing (Atanasova et al., 2021), no study has investigated the role of interoceptive sensibility in the embodiment of valence and arousal among patients with IBD.

The present study aims to contribute to the understanding of how emotional valence and arousal are subjectively experienced in the body among patients with IBD and whether emotion-related sensations, possibly altered by increased anxiety about gastrointestinal sensations (Garland et al., 2012), are linked to patients' emotional awareness. Using a topographical self-report measure adapted from Nummenmaa et al. (2014), we assessed perceived changes in bodily sensations associated with experiences of positive and negative valence, as well as tension and relaxation, among patients with IBD and healthy control participants. We hypothesized that (I.) IBD patients would report stronger bodily sensations for negative emotions and more attenuated sensations for positive emotions than healthy control participants. We also expected that (II.) interoceptive sensibility and gastrointestinal-specific anxiety would be related to the severity of alterations in emotion-related bodily sensations in IBD, particularly for negative emotions. To investigate whether these changes show distinct topographical patterns, especially in body areas strongly related to IBD symptoms, we explored whether IBD patients exhibit altered bodily sensations in the abdomen related to the experience of valence and arousal.

2.2.3 Methods

Participants

A total of 86 individuals between 18 and 65 years of age participated in the study. Of these, 42 met the diagnostic criteria for IBD, and 44 were healthy control (HC) participants. We excluded one participant from the IBD group because of a lack of understanding of the instructions. Thus, the final sample consisted of 41 IBD patients (20 female, 21 male) and 44 HC participants (30 female, 14 male; Table 3.1). We recruited adults with diagnosed IBD attending the IBD outpatient unit at the University Medical Center Mannheim. Overall, 29 patients with Crohn's disease (CD) and 12 patients with ulcerative colitis (UC) in clinical remission were included. We focused on examining IBD patients in clinical remission to avoid potentially confounding effects of active disease symptoms on the measures of emotional experience. Furthermore, we were interested in examining whether alterations in emotion experience could also be observed during clinical remission, potentially affecting a patient's well-being even when acute disease

symptoms have subsided. CD patients exhibited a mean Harvey–Bradshaw Index score (Harvey & Bradshaw, 1980) of 1.76 ± 1.83 (range: 0–16), and UC patients exhibited a mean Partial Mayo Score (Schroeder et al., 1987) of 1.58 ± 1.51 (range: 0–7). The average age for disease onset reported by the patients was 25.54 ±10.24 years. The mean disease duration reported by the patients was 14.65 ± 12.64 years. Diagnostic procedures and gastroenterological examinations were carried out on all patients by fully trained physicians specialized in the care of patients with IBD. Exclusion criteria were biological signs of disease activity (fecal calprotectin level > 200 mg/L), current use of corticosteroids, use of psychotropic medications, and current or past neurological or psychiatric diseases. For further details on sample characteristics, see Table 3.1. Details on treatment medication, comorbidities, previous surgeries, and extraintestinal manifestations were collected from medical reports and are provided in Table S2 in supplemental material S2.

Exclusion criteria for the HC group were chronic medical conditions, chronic medication intake, use of psychotropic medication, and current or past neurological or psychiatric diseases, as well as general gastrointestinal complaints during the 4 weeks prior the experiment. The study was approved by the Ethics Committee of the Medical Faculty Mannheim at Heidelberg University, and all participants gave their written informed consent before participating in the study. Please note that a subsample of participants from the IBD and the healthy control group in this study was also included in another manuscript on interoception and emotion perception published by our group (see Atanasova et al. (2021)).

All of the participants completed a battery of psychometric questionnaires assessing psychological distress, interoceptive sensibility, and gastrointestinal-specific anxiety. The participants then performed a computer-based task, and changes in the participants' bodily sensations when experiencing valence and arousal were assessed.

Questionnaires

Brief Symptom Inventory (BSI-18)

To characterize the participants, we assessed psychological distress using the Brief Symptom Inventory (BSI-18) (Franke et al., 2011). BSI-18 is a self-report measure of somatization, depression, and anxiety. Scores on three subscales with six items each are combined into a global symptom severity index (GSI). GSI scores range from 0 to 72 points, and scores on each

of the three subscales range from 0 to 24 points, with higher scores indicating higher symptom severity. Cronbach's alphas for the 18 items were 0.86 for the IBD group and 0.81 for the HC group.

Affective state

Prior to testing, the current affective states of the participants were evaluated using the state version of the State–Trait Anxiety Inventory (STAI; Spielberger et al. (1983)). The STAI is a 20-item scale that measures subjective feelings of apprehension, tension, nervousness, worry, and activation of the autonomic nervous system on a four-point Likert scale. Item scores are added to obtain the scale total score (which ranges from 20 to 80), with higher scores indicating higher anxiety. Internal consistency was good, with Cronbach's $\alpha = 0.76$ for the IBD group and 0.90 for the HC group. Arousal, valence, and dominance levels were assessed using the Self-Assessment Manikin (SAM; Bradley and Lang (1994)). The SAM is a non-verbal pictorial assessment technique that measures valence/pleasure, perceived arousal, and perceptions of dominance on a nine-point Likert scale. Higher scores indicate more positive valence, higher arousal, and higher perceived dominance.

Visceral Sensitivity Index (VSI)

Gastrointestinal-specific anxiety (GSA) was measured using the Visceral sensitivity index (VSI; Labus et al. (2004)). The 15-item scale assesses worry, fear, vigilance, sensitivity, and avoidance, as well as gastrointestinal-related cognitions and behaviors. Items are scored on a reversed six-point scale. The overall VSI score ranges from 0 to 75, with higher scores indicating more severe GSA. VSI was developed specifically for patients with functional gastrointestinal disorders and is not suitable for assessment of healthy individuals. For that reason, we utilized this self-report measure for the IBD group only. The internal consistency of this scale for the current IBD sample was good, with Cronbach's $\alpha = 0.89$.

Multidimensional Assessment of Interoceptive Awareness (MAIA)

We assessed *Emotional Awareness* as the feature of interoceptive sensibility that is most strongly related to the experience of emotions in the body, as it comprises an individual's awareness that certain physical sensations are the sensory aspects of emotional states. For this purpose, we used the Multidimensional Assessment of Interoceptive Awareness (MAIA;

Mehling et al. (2012)) and its *Emotional Awareness* subscale, which comprises five items assessed on a six-point Likert scale. The subscale score is calculated as the mean item score, with higher scores indicating higher emotional awareness. *Emotional Awareness* exhibited acceptable internal consistency, with Cronbach's $\alpha = 0.76$ for the IBD group and 0.86 for the HC group. For further details on the MAIA and its subscales, see the Supplemental Material.

Experimental procedure

Participants were asked to indicate changes in their bodily sensations when they experienced emotional states of different valence (positive/negative) and arousal (relaxation/tension) during everyday life, using a topographical self-report method adapted from Nummenmaa et al. (2014). Initially, participants were familiarized with the task and instructed to evaluate which bodily regions they typically felt as being activated or deactivated when experiencing a particular emotional state. Thus, the task did not involve inducing actual emotions by experimental manipulation. To indicate these changes, participants were asked to color the body areas where they perceived sensations of activation and deactivation by selecting a color from a nine-point color bar ranging from blue (-4 = "very strong deactivation") to red (+4 = "very strong activation") (see Figure S1, supplemental material S2). Participants indicated their responses by painting the bodily regions using successive strokes on the presented body templates. If they did not perceive any changes in some parts of the body, participants were instructed to leave these uncolored. The four instructions (positive emotions, negative emotions, relaxation, tension) were presented in a pseudorandomized order. The task was presented on a 14" computer screen. The front and back body templates comprised 366 × 195 pixels, and the diameter of the painting tool was 13 pixels. The task was programmed using the Presentation® software (Version 20.1, Neurobehavioral Systems, Inc., Berkeley, CA, www.neurobs.com).

Dependent variables

For each participant and trial, color code values (ranging from -4 to +4) were stored in a numeric array for each pixel of the body templates and spatially smoothed by averaging the color code value of each pixel and its surrounding pixels (± 3 pixels).

To assess changes in bodily sensations, we calculated a) a change score representing the average of the absolute values of the pixels and b) a change score across those pixels that indicated either a deactivation or an activation. This procedure was conducted for all pixels of the body

templates to derive a global whole-body score, as well as for different regions of interest (ROIs). The ROIs were predefined based on the findings of Nummenmaa et al. (2014) and included the head, chest, arms, abdomen, legs, and back as separate body regions (see supplemental material S2, Figure S2). Whole-body and ROI analyses were performed using custom pipelines run with MATLAB 2020a (The MathWorks, Inc.).

Table 3.1. Sample characteristics

	HC (M±SD)		IBD (M±SD)		Test-statistics	*p*-value	
Demographics							
Age	36.11	±12.29	40.20	±13.87	1.44 [a]	0.154	
Sex (female/male)	30/14		20/21		3.30 [b]	0.069	
BMI	24.16	± 4.72	26.65	± 6.46	1.99 [a]	0.050	(*)
Years of education	12.84	± 2.40	12.32	± 3.01	-0.89 [a]	0.376	
MWT-B	30.09	± 3.60	29.84	± 3.57	-0.77 [a]	0.443	
Affective state							
STAI Anxiety (state)	32.66	± 8.20	33.13	± 5.28	0.31 [a]	0.754	
SAM-Valence	3.77	± 0.85	3.75	± 0.98	-0.11 [a]	0.911	
SAM-Arousal	1.98	± 0.86	2.34	± 1.00	1.78 [a]	0.079	
SAM-Dominance	3.68	± 0.66	3.63	± 0.98	-3.41 [a]	0.734	
Psychological distress							
GSI	22.42	± 4.91	28.97	± 9.26	3.66 [a]	0.001	**
Somatization	6.74	± 1.27	9.97	± 3.51	5.31 [a]	<0.001	***
Depression	7.58	± 2.81	9.22	± 3.97	1.85 [a]	0.068	(*)
Anxiety	8.09	± 2.22	9.78	± 3.65	2.45 [a]	0.017	*
Interoceptive sensibility							
Emotional Awareness	2.77	± 0.88	3.32	± 0.92	0.56 [a]	0.006	**
Gastrointestinal-specific anxiety							
VSI	-	-	27.42	±15.28	-	-	

IBD, inflammatory bowel diseases group; HC, healthy control group; BMI, Body-Mass Index; MWT-B, Multiple Choice Word Test-B; STAI, State–Trait Anxiety Inventory; SAM, Self-Assessment Manikin; GSI, General symptom index; Emotional Awareness: subscale of the Multidimensional Assessment of Interoceptive Awareness; VSI, Visceral sensitivity index.
(*) $p < 0.10$, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, [a] t-value, [b] Chi^2.

Data analysis

The dependent variables were analyzed separately for the experience of valence and arousal using mixed-effects analysis-of-variance designs (mixed-effects ANOVAs). Testing for normality of residuals (Kolmogorov–Smirnov test, visual inspection of Q–Q plots) revealed that the normality assumptions underlying parametric analyses were violated. Therefore, a non-parametric approach was employed, using a rank-aligned ANOVA (Kay & Wobbrock, 2019; Wobbrock et al., 2011). Global change scores were analyzed in 2 × 2 designs with the between-subjects factor "group" (IBD/HC) and an additional experimental factor, i.e., "valence" (positive/negative) in one case and "arousal" (relaxation/tension) in another. To analyze more specifically the changes in activation and deactivation, we extended these designs by an additional within-subject "type of change" (activation/deactivation) factor, resulting in two 2 × 2 × 2-mixed ANOVA designs. To further characterize the effects in the ANOVA designs, post hoc comparisons were conducted using ANOVA sub-designs and pairwise comparisons. To investigate the links between participants' emotion-related bodily sensations, gastrointestinal-specific anxiety, and emotional awareness, Spearman's rank correlation coefficients were calculated. In addition to our preregistered analyses (see below), ROI scores for the experience of valence and arousal in distinct parts of the body were analyzed using exploratory 2 × 2 × 2 rank-aligned ANOVA designs with the same factors as those used in the whole-body analyses. The statistical analyses were carried out using SPSS v.27.0 (IBM Corp., USA) and the ARTool package implemented in RStudio v.1.2.1335 (RStudio, PBC, Boston, MA, **http://www.rstudio.com/**). The significance level was set to $p < 0.05$. To control for multiple testing in the correlation analyses, we applied a false-discovery rate (FDR) correction, as recommended by Benjamini and Hochberg (1995), and we reported the corresponding p-values, denoted as p_{FDR}. For all analyses of an exploratory nature, uncorrected p-values are reported.

Preregistration

The hypotheses, sample size, methods, exclusion criteria, and planned analyses were preregistered before data collection and can be accessed at https://aspredicted.org/blind.php?x=hu4n7k. According to our preregistration, a sample size of 120 participants was planned. However, because of the Covid-19 outbreak and pandemic-related restrictions, the number of participants was reduced. All remaining aspects of the study were carried out in accordance with the pre-registered protocol unless stated otherwise. Note that because of length restrictions, only data on emotional experience of valence and arousal

are reported in this manuscript. Data on body image perception and the experience of specific emotions, as described in the same preregistration, are reported in separate articles.

2.2.4 Results

Positive and negative valence

Whole-body sensations

IBD patients reported significantly less perceived change in their bodily sensations compared to HC (main effect "group": $F_{1,83} = 6.90$, $p = 0.010$), without a difference between positive and negative emotions (main effect "valence": $F_{1,83} = 0.23$, $p = 0.635$; group*valence: $F_{1,83} < 0.01$, $p = 0.988$; Figure 6).

Separating the changes in bodily activation and deactivation revealed that differences between the groups depended on whether the participants judged activation or deactivation for positive or negative emotions (group*valence*type of change: $F_{1,249} = 6.47$, $p = 0.012$). Decomposing the design into 2 × 2 ANOVA sub-designs revealed a significant group difference for bodily deactivation, influenced by the emotional valence (group*valence: $F_{1,83} = 9.56$, $p = 0.003$): Compared with HC, IBD patients reported a smaller difference in the perceived deactivation between positive and negative emotions ($p = 0.005$), caused by a lower deactivation associated with negative emotions ($p = 0.015$, positive emotions: $p = 0.746$; see Figure 1). For bodily activation, the groups differed depending on the emotional valence at a trend-level significance level (2 × 2 ANOVA sub-design for activation: main effect "group": $F_{1,83} = 4.84$, $p = 0.031$; group*valence: $F_{1,83} = 3.81$, $p = 0.054$). Compared with HC, the IBD group reported a smaller difference between positive and negative emotions ($p = 0.018$). This effect was caused by a significantly lower bodily activation during positive emotions ($p = 0.015$) but not during negative emotions in the IBD group ($p = 0.587$; see Figure 1). All main and interaction effects are reported in Table 3.2 but are not further described because of their restricted interpretability caused by higher-order interaction effects.

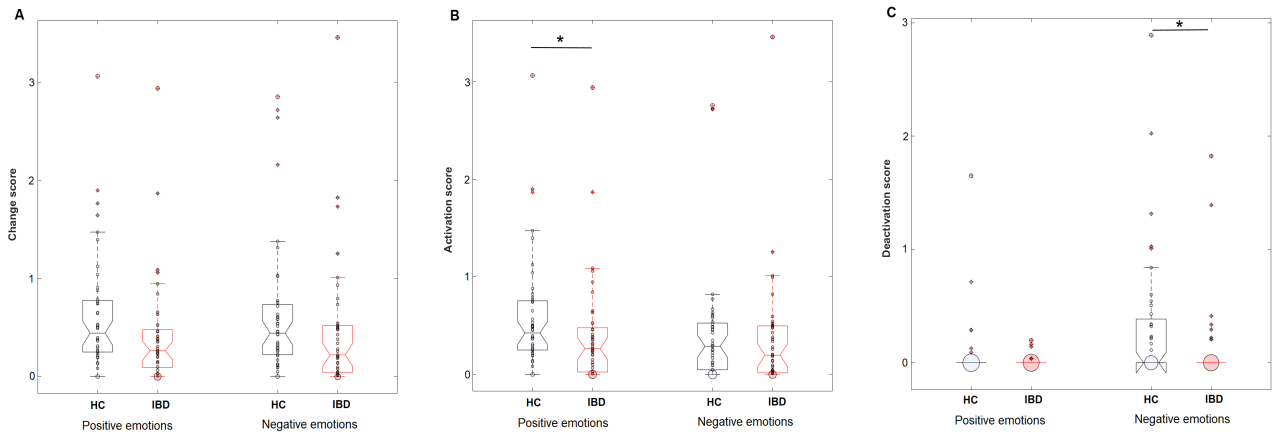

Figure 6. Perceived levels of overall changes in the body (A), sensations of activation (B), and sensations of deactivation (C) in the body during the experience of positive and negative emotions in HC (n = 44) and IBD (n = 41). * $p < 0.05$

Exploratory ROI analyses

Statistical analyses of the ROI scores revealed that the groups differed only in the overall change in their bodily sensations experienced in the back (main effect "group": $F_{1,83} = 7.75$, $p = 0.007$), with IBD patients reporting less change of sensation in this area compared to HC (see Table S3, supplemental material S2).

IBD and HC participants differed in their differentiation between bodily activation and deactivation depending on whether they evaluated positive or negative emotions. This pattern was observed for the chest, legs, and back, as well as at trend-level significance levels for the head, arms, and abdomen (group*valence*type of change; see Table 3.3). 2 × 2 ANOVA sub-designs revealed that compared to HC, IBD patients reported smaller differences in their bodily deactivation between positive and negative emotions for the head, chest, arms, back, and abdomen (all $ps < 0.03$), resulting from a lower perceived deactivation during negative emotions (all $ps \leq 0.044$) but not during positive emotions (all $ps \geq 0.890$; see Figure 7). For body activation, the two groups differed significantly, with IBD patients reporting less perceived activation in the back and legs, independent of the emotional valence (2 × 2 ANOVA sub-design for activation: main effects "group": all $ps \leq 0.014$; group*valence: $ps = 0.081$). For further details, see Figure S3, supplemental material S2.

Arousal: relaxation and tension

Whole-body emotion-associated sensations

IBD patients reported less perceived change in their bodily sensations related to the experience of arousal (main effect "group": $F_{1,83}$ = 10.20, p = 0.002) without a difference between the experiences of relaxation and tension (group*arousal: $F_{1,83}$ = 0.52, p = 0.474; main effect "arousal": $F_{1,83}$ = 0.52, p = 0.474). The medians and data ranges for these conditions are shown in Figure 8.

When separating the effects of bodily activation and deactivation, analyses showed a significant effect of the type of change on the group difference for relaxation and tension (group*arousal*type of change: $F_{1,249}$ = 7.06, p = 0.008). 2 × 2 ANOVA sub-designs revealed a significant group difference for the perceived bodily deactivation, depending on whether participants evaluated relaxation or tension (group*arousal: $F_{1,83}$ = 6.05, p = 0.016). Compared to HC, IBD patients reported a smaller difference in the experienced bodily deactivation during relaxation and tension (p = 0.001). For bodily activation, the two groups differed significantly depending on whether relaxation or tension was evaluated (2 × 2 ANOVA sub-design for activation: group*arousal: $F_{1,83}$ = 9.39, p = 0.003): Compared to HC, the IBD group exhibited a smaller difference in their experienced bodily activation for relaxation and tension, resulting from a significantly lower perceived activation during tension (p = 0.002; Figure 9) but not during relaxation (p = 0.152). For further details, see Table 3.2.

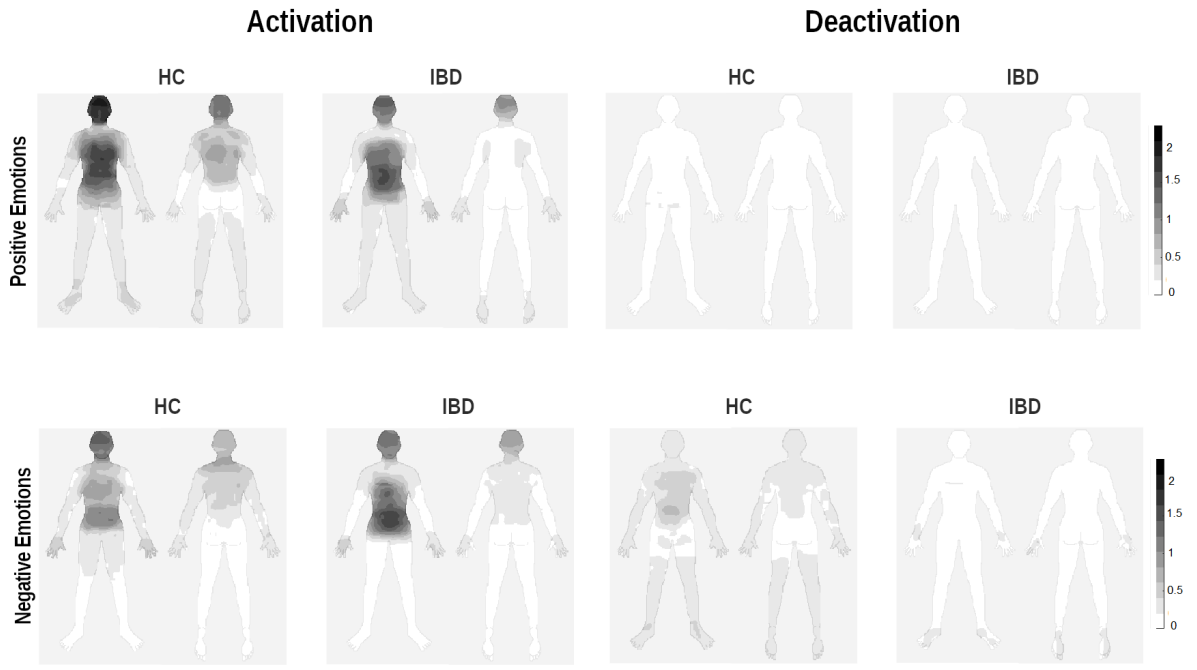

Figure 7. Whole-body topographies visualizing the perceived activation and deactivation for the experience of positive and negative emotions in IBD patients and HC (0 = "no activation/deactivation"; 4 = "very strong activation/deactivation").

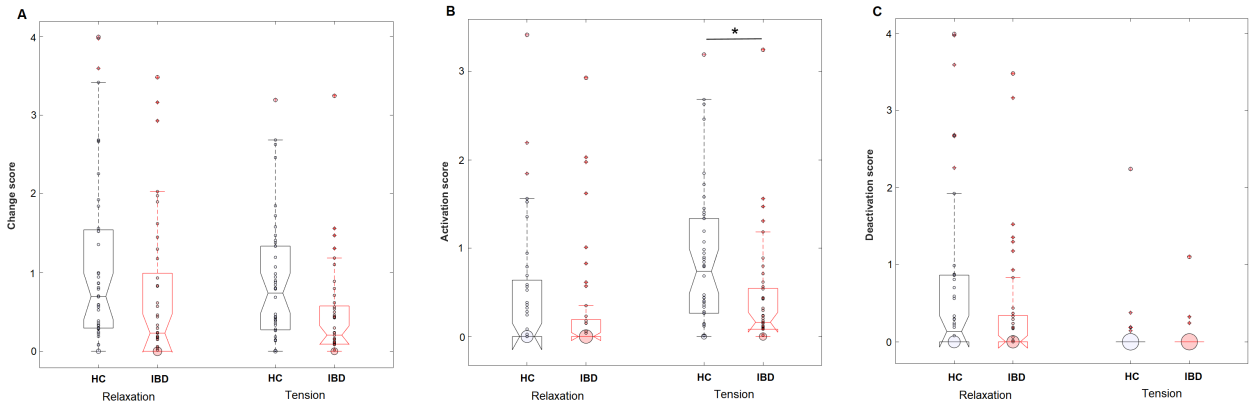

Figure 8. Perceived levels of overall changes in the body (A), sensations of activation (B), and sensations of deactivation (C) in the body during the experiences of relaxation and tension in HC (n = 44) and IBD (n = 41).

Table 3.2 Results of the 2 × 2 × 2 rank-aligned ANOVA for whole-body valence and arousal scores

	F	*df*	*p*-value		η_p^2
Valence					
Group	7.95	1/83	0.006	**	0.082
Emotional valence	3.69	1/249	0.056	(*)	0.002
Type of change	107.91	1/249	< 0.001	***	0.043
Group*Emotional valence	0.14	1/249	0.707		0.011
Group*Type of change	1.08	1/249	0.300		< 0.001
Emotional valence*Type of change	18.53	1/249	< 0.001	***	0.073
Group*Emotional valence*Type of change	6.47	1/249	0.012	*	0.025
Arousal					
Group	12.94	1/83	< 0.001	***	0.133
Arousal	4.03	1/249	0.046	*	0.029
Type of change	7.01	1/249	0.009	**	0.203
Group*Arousal	0.00	1/249	0.956		< 0.010
Group*Type of change	2.82	1/249	0.094	(*)	0.007
Arousal*Type of change	56.16	1/249	< 0.001	***	0.252
Group*Arousal*Type of change	7.06	1/249	0.008	**	0.006

(*) non-significant trend, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Exploratory ROI analyses

IBD patients reported less perceived change in their bodily sensations across all ROIs (all main effects "group": *ps* < 0.044), except for the abdomen ($p = 0.987$; see Table S3, supplemental material S2).

For the head and the arms, the statistical analysis results showed that the differences between the two groups were influenced by whether the participants judged changes to be linked to relaxation or tension and activation or deactivation (group*arousal*type of change, see Table 3.3). 2 × 2 ANOVA sub-designs showed that the group difference in bodily deactivation and activation was influenced by whether relaxation or tension was evaluated (group*arousal for deactivation: *ps* ≤ 0.003; activation: *ps* ≤ 0.011). Compared to HC, IBD patients exhibited a significantly smaller difference in their perceived bodily deactivation

during relaxation and tension (all *ps* ≤ 0.005), caused by less perceived deactivation for relaxation in the head and arms in IBD (*ps* ≤ 0.097; see Figure 9). For bodily activation, the difference between relaxation and tension was significantly smaller in the IBD group than in the HC group (*p*s ≤ 0.001): IBD patients reported significantly lower levels of activation during tension than those in the HC group (*ps* ≤ 0.009). For further details, see Figure S4 in supplemental material S2.

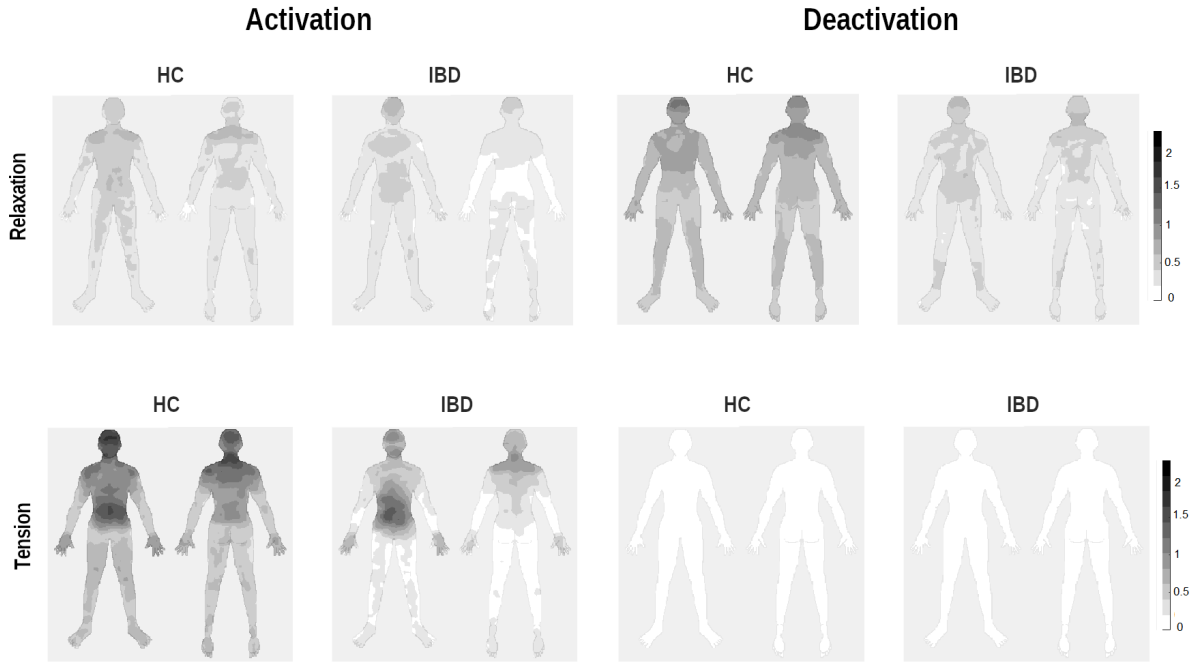

Figure 9. Whole-body topographies visualizing perceived activation and deactivation for the experiences of relaxation and tension in IBD patients and HC participants (0 = "no activation/deactivation"; 4 = "very strong activation/deactivation").

Table 3.3 Interaction effects between the factors "Group" (IBD/HC), "Valence" (positive/negative), "Arousal" (relaxed/tensed), and "Type of change" (activation/deactivation) for all predefined ROI.

	Valence			*Arousal*		
	Group*Valence*Type of change			Group*Arousal*Type of change		
	$F_{1, 249}$	p		$F_{1, 249}$	p	
Abdomen	3.46	0.064	(*)	0.67	.414	
Head	2.76	0.098	(*)	11.56	< 0.001	***
Chest	6.37	0.012	*	2.46	0.118	
Arms	3.04	0.082	(*)	7.09	0.008	**
Legs	6.31	0.013	*	1.88	0.171	
Back	3.92	0.049	*	2.18	0.141	

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$; for details on the other experimental factors, see the supplemental material S2, Table S4.

Correlations between emotion-associated bodily sensations and interoceptive sensibility or gastrointestinal-specific anxiety

Emotional awareness

While changes in bodily sensations for valence and arousal were stronger in participants reporting higher levels of emotional awareness, there were no differences between the groups in these relationships. For further details, see Table S5, supplementary material S2.

Valence: In the differentiation between bodily activation and deactivation, higher emotional awareness was linked to greater bodily activation for the experience of positive emotions only for the IBD group (IBD: $r_s = 0.462$, $p = 0.002$, $p_{FDR} = 0.004$; HC: $r_s = 0.116$, $p = 0.454$, $p_{FDR} = 0.454$, comparison between groups: $Z = 1.702$, $p = 0.044$). In contrast, higher emotional awareness was linked to stronger bodily activations to a comparable extent for both groups (IBD: $r_s = 0.381$, $p = 0.014$, $p_{FDR} = 0.028$; HC: $r_s = 0.304$, $p = 0.045$, $p_{FDR} = 0.090$, comparison between groups $Z = 0.388$, $p = 0.349$).

Arousal: Higher emotional awareness was associated with higher levels of bodily activation during tension in the IBD group at trend-level significance. The two groups did not differ in the strength of this association (IBD: $r_s = 0.339$, $p = 0.030$, $p_{FDR} = 0.060$; HC: $r_s = 0.284$, $p = 0.062$, $p_{FDR} = 0.124$; $Z = 0.271$, $p = 0.393$). No significant associations were found for relaxation (IBD: $r_s = 0.188$, $p = 0.238$, $p_{FDR} = 0.238$; HC: $r_s = 0.271$, $p = 0.076$, $p_{FDR} = 0.152$; comparison between groups: $Z = -0.389$, $p = 0.348$).

There were no significant associations between emotional awareness and perceived bodily deactivation for either valence or arousal for either group (all $p_{FDR} \geq 0.426$).

Gastrointestinal-specific anxiety (GSA)

For the IBD group, the correlation analysis results revealed no significant associations between GSA and patients' perceived bodily sensations related to the experience of valence and arousal (all $p_{FDR} \geq 0.252$).

Anxiety and depression symptoms

Although all IBD patients met the criteria for clinical remission, they reported higher levels of anxiety and — at least on a descriptive level — depression than the HC participants (see Table 3.1). Therefore, we performed additional correlation analyses to explore whether symptoms of anxiety and depression are related to the experience of valence and arousal in the body. In the IBD group, greater anxiety and depression were associated with higher bodily activation during negative emotions (all $ps < 0.001$) and tension (all $ps \leq 0.011$) and higher levels of deactivation when feeling relaxed (all $ps \leq 0.019$). For further details, see supplementary material S2, Table S5.

2.2.5 Discussion

How bodily sensations are perceived and evaluated in the context of emotional experiences is essential to the way people perceive emotions in everyday life and — in the case of IBD — ultimately how these influence a patient's quality of life. Therefore, the main objective of this study was to investigate the potential alterations in emotion-related bodily sensations and their links to interoceptive sensibility and gastrointestinal-specific anxiety (GSA) in remitted IBD patients in comparison to healthy individuals. Based on the dimensional model of emotion (Russell, 1980), we investigated how the two dimensions of valence and arousal are

experienced in an embodied way by examining perceived bodily activation and deactivation during positive and negative emotions, relaxation, and tension.

Compared to healthy individuals, patients with IBD reported less intense bodily changes associated with the experience of valence and arousal. Moreover, IBD patients varied differently in their perceived sensations of the opposite poles of these dimensions, that is, positive and negative emotions for valence and relaxation and tension for arousal, respectively. Our findings support the need for fine-grained analysis to capture the complex changes in emotion-related bodily sensations, since group differences depend on whether participants evaluate perceived activation or deactivation in different areas of the body. For IBD patients, the patterns of bodily activation and deactivation reported for positive and negative emotions, as well as for relaxation and tension, were more similar than these observed among healthy individuals. The reduced bodily activation during negative and highly arousing emotional states reported for the IBD group might suggest less intense and thereby less distressing emotional experience. However, lower levels of activation linked to positive emotions and decreased deactivation during relaxation might point to detrimental alterations in these domains of emotional experience, which might be of particular importance for patients' well-being. Finally, we found that anxiety and depression modulate the experience of valence and arousal in the body. Our results highlight the connection between psychological distress and the experience of emotions in IBD patients.

Experience of valence in the body

Overall, IBD patients exhibited significantly less change in their bodily sensations associated with the embodiment of valence and arousal. Despite the higher levels of subjectively perceived emotional awareness observed in the IBD group, when asked to identify emotion-related changes in their bodies, patients reported less intense experiences of bodily activation and deactivation compared to healthy individuals. This finding may indicate that patients with IBD are less able to differentiate between the bodily sensations linked to specific emotion experiences.

Compared to HC, IBD patients reported significantly less deactivation perceived during negative emotions and less bodily activation for positive emotions. We observed decreased body deactivation during negative emotional states in IBD for several body areas, including the one most affected by IBD symptoms, that is, the abdomen, as well as other less directly disease-related body regions. Thus, altered experience of negative emotions in the body is not limited

only to body regions associated with aberrant physiological feedback in IBD, such as gastric sensations, for example, as initially expected. In contrast to Vianna et al. (2006), who suggested that emotional dysfunctions occur only for acute IBD patients, we found differences in how emotions are experienced among remitted IBD patients. More precisely, our findings of less activation during positive emotional states suggest decreased sensitivity to positive emotional content among patients with IBD. Previous studies have suggested functional alterations in brain regions associated with the processing of affective information (Agostini et al., 2011) and visceral signals in IBD patients (Fan et al., 2020; Mayer et al., 2005). Therefore, impaired integration of affective and visceral signals in IBD patients could result in less intense experience of positive emotions, leading to more depressive symptoms (Leppänen, 2006), which can in turn affect the course of the disease (Wilkinson et al., 2019). As these findings indicate persistent alterations in the experience of positive emotions, even in the remitted stage of the disorder, it might be useful to coach patients to notice sensations of activation in the body specifically related to positive emotions. Psychotherapeutic approaches, such as mindfulness-based stress reduction (Kabat-Zinn, 2003), emphasize the focus on bodily sensations and the appraisal of those sensations as crucial to an individual's coping with stress and emotions (de Jong et al., 2016; Garland et al., 2012; Lutz et al., 2013). Such interventions are believed to enhance an individual's sensitivity to body-related emotional information and to encourage the implementation of skillful strategies for coping with difficult emotions. Short interoceptively focused interventions can be applied to train patients to localize changes in their visceral sensations and learn to perceive emotion-specific changes in their bodily sensations, focusing on particular body areas (e.g., gut or heart) (Davey et al., 2020; Fischer et al., 2017). Mind–body interventions can improve patients' ability to evaluate visceral sensations associated with emotional events and detect the potential need to implement regulatory strategies to cope with these emotions. By modifying how patients attend to their interoceptive signals, elicited by emotional triggers, and providing them with adaptive emotion regulation skills, mind–body interventions can improve patients' flexibility in perceiving emotions, even during stressful situations (Ardi et al., 2021; Wynne et al., 2019).

Experience of arousal in the body

Our results show that, with respect to arousal, IBD patients perceive less bodily activation during tension than HC, while noticing smaller differences in deactivation experienced during relaxation and tension. In contrast to valence, this pattern was reported only for body areas not directly related to IBD symptomatology. Despite patients' lower levels of bodily activation

when feeling tense, our results indicate that patients with IBD perceive less bodily deactivation during relaxation and therefore less successfully reduce perceived stress and tension (Jacobson, 1938; Pawlow & Jones, 2002). This result indicates that IBD patients may benefit from practicing relaxation techniques, such as autogenic training or progressive muscle relaxation, in order to better differentiate between bodily sensations caused by tension and relaxation (Jacobson, 1938; Schultz & Luthe, 1959). Previous studies have shown the positive effects of such interventions on stress reduction in psychosomatic disorders, suggesting potential benefits for IBD patients' mental and physical well-being (Shah et al., 2020). Few clinical trials on the effects of mind–body approaches to IBD management have demonstrated positive effects of interoceptively focused exercises, such as body scanning, mindful breathing, and yoga, on patients' anxiety and depression symptoms (Ewais et al., 2020; Hood & Jedel, 2017; Neilson et al., 2015; Wilke et al., 2021). Taken together, these findings could indicate that psychological interventions targeting the link between body and emotion perceptions could be used to treat or even prevent mental health problems in high-risk individuals, such as those with active IBD symptoms.

Our findings of significantly less intense perceived bodily sensations associated with valence and arousal may indicate the use of emotional avoidance as an emotion regulation strategy among IBD patients. A more detached bodily experience of emotions may allow patients to avoid confronting overly intense physiological sensations and thereby reduce psychological distress. Consistent with this interpretation, a recent study by Banovic et al. (2020) found stronger emotional avoidance and emotional suppression among Crohn's disease patients than among healthy controls (Banovic et al., 2020). However, another explanation for our results could be the use of distraction as a regulatory strategy. Contemporary findings point to the benefits of different emotion regulation mechanisms depending on the intensity of the emotional state (Sheppes et al., 2014). While cognitive reappraisal is thought to be more adaptive in the case of low negative emotional intensities, distraction is preferable when individuals face emotions of high intensity (Sheppes, 2020). As high emotional intensity usually results in greater activation of the autonomic nervous system, it is conceivable that individuals who are more sensitive to these physiological changes may prefer to use distraction to cope with highly arousing emotions (Ardi et al., 2021). Future studies should investigate whether altered processing of bodily sensations is linked to different emotion regulation strategies and whether these are differentially advantageous for coping with disease-related psychological distress and IBD symptoms. Such research might improve our understanding of the mechanisms underlying the interplay between emotion regulation and the experience of

emotions in the body and thereby facilitate the development of personalized psychotherapeutic interventions for IBD.

Correlations with interoceptive sensibility, gastrointestinal-specific anxiety, and psychological distress

IBD patients reporting higher levels of emotional awareness, that is, a feature of one's interoceptive sensibility, exhibit increased bodily sensations during positive and negative emotions, as well as tension (Schuette et al., 2020). The effects of interoception on emotional experience have been discussed repeatedly in the literature, suggesting that interoceptively aware individuals report higher emotional intensity and arousal (Barrett et al., 2004; Herbert et al., 2007). IBD patients exhibiting higher emotional awareness also report higher levels of bodily activation during positive emotions. Thus, our findings support the hypothesis that the ability to notice bodily changes related to affective states can also have beneficial effects in clinical samples. Although positive valence is associated with less perceived bodily activation in IBD patients, greater awareness of the connection between physiological sensations and emotions can positively affect the experience of positive emotions. One possible explanation for this effect might be that body- and emotion-related processes share common neural underpinnings (Zaki et al., 2012), playing crucial roles in the integration of interoceptive and emotional cues (Berntson & Khalsa, 2021; Critchley & Harrison, 2013). Critchley et al. (2004) demonstrated that representations of internal bodily sensations in the insula are crucial for the conscious experience of emotions. This suggests that somato-visceral information influences emotion perception in a bottom-up way, indicating that individuals who are more aware of their bodily signals exhibit higher emotional awareness and thus perceive more intense emotions.

Our results did not reveal any associations between gastrointestinal-specific anxiety (GSA) and emotion experience in the body. In contrast to GSA, which solely reflects patients' disease-related cognitions, more pronounced general anxiety and depression symptoms were linked to greater bodily activation during positive and negative emotions. This finding is in line with previous evidence that suggests that highly anxious individuals experience emotions in a more intense and threatening way (Paulus & Stein, 2010). As acute disease activity is normally linked to higher levels of anxiety and depression, this result might indicate that among acute IBD patients, increased emotion-related bodily sensations linked to psychological distress might result in exaggerated emotion perception having detrimental effects on patients' stress levels, at least for those patients with psychiatric co-morbidities (Hu et al., 2021).

Given these new findings regarding the role of bodily sensations related to the experience of valence and arousal in IBD, the implementation of interoceptively focused techniques to improve patients' emotion experience through greater bodily awareness as a supplementary part of patients' treatment might be of particular importance. Our results raise the possibility that psychological interventions aimed at the improvement of emotion perception in IBD could provide patients with useful skills for engaging with their emotions. As impairments in emotion perception have been shown to be part of the link between disease severity and depression, such supplementary interventions could improve the quality of life for IBD patients.

Limitations

Some limitations of the present study have to be addressed. First, as we did not include a clinical control group (e.g., irritable bowel syndrome), we cannot conclude that our findings are limited only to IBD or that they may represent a transdiagnostic feature across several gastrointestinal disorders or even across somatic and mental disorders. Second, we did not directly induce any emotional states but rather asked participants to indicate changes in their bodily sensations based on what they typically perceive when experiencing the presented emotional state. Thus, the participants' judgments resulted from their recollections of bodily sensations during emotional states in the past. This recall process might be biased by one's current mood or by recalling only recent situations. Therefore, future studies need to control for these effects by asking participants to indicate their bodily sensations during direct emotion induction. Furthermore, interoception-related features were assessed only via self-report measures, which often do not correspond to participant's actual interoceptive abilities (Murphy et al., 2020; Murphy et al., 2019). Finally, we cannot draw conclusions regarding the direction of causality of any of the observed associations because of the cross-sectional design of the study.

2.2.6 Conclusions

Our results indicate that IBD is associated with lower intensities of perceived changes in the body related to emotional valence and arousal. The diminished perception of bodily activation and deactivation might be the result of emotion avoidance or distraction as coping strategies among patients with IBD. Our findings suggest that IBD patients might benefit from interventions focusing on the link between physical sensations and emotional feelings and specifically targeting the perception of bodily activation during positive emotions and bodily deactivation during relaxation.

2.2.7 Supplemental material S2

Table S2. Disease-related characteristics of the recruited IBD patients (N = 41)

IBD medication (N)	
Biologics	40
Mesalazine	1
Mean age at disease onset	25.54 ±10.24
Mean disease duration (yrs)	14.65 ± 12.64
Other somatic condition (N)	
Pulmonary embolism	2
Pancreatitis	2
Diabetes	1
Chronic cystitis	1
Thrombocythemia	1
Asthma bronchiale	1
Hypothyoroidism	2
BD-related surgeries (N)	
No surgeries	19
Ileal resection	9
Fistula removal	8
Abscess	5
Extraintestinal manifestations (N)	
Entheropathic arthritis	6
Dermatitis	4

Interoceptive sensibility: Multidimensional Assessment of Interoceptive Awareness (MAIA)

The 32 items self-report questionnaire measures subjective interoceptive abilities as a complex construct involving attentional and emotional processes. MAIA provides a multidimensional profile of body awareness including following eight subscales: *Noticing*, *Not-Distracting*, *Not-Worrying*, *Attention Regulation*, *Emotional Awareness*, *Self-Regulation*, *Body Listening* and *Trusting*. With respect to interoceptive sensibility, the Emotional awareness subscale assesses individual's awareness of the connection between bodily sensations and emotional states (item example: "I notice how my body changes when I am angry") (Mehling et al., 2012). The scores of all subscales range between 0 and 5 with higher scores indicating greater interoceptive sensibility.

Mehling, W. E., Price, C., Daubenmier, J. J., Acree, M., Bartmess, E., & Stewart, A. (2012). The Multidimensional Assessment of Interoceptive Awareness (MAIA). *PLoS One, 7*(11), e48230. https://doi.org/10.1371/journal.pone.0048230

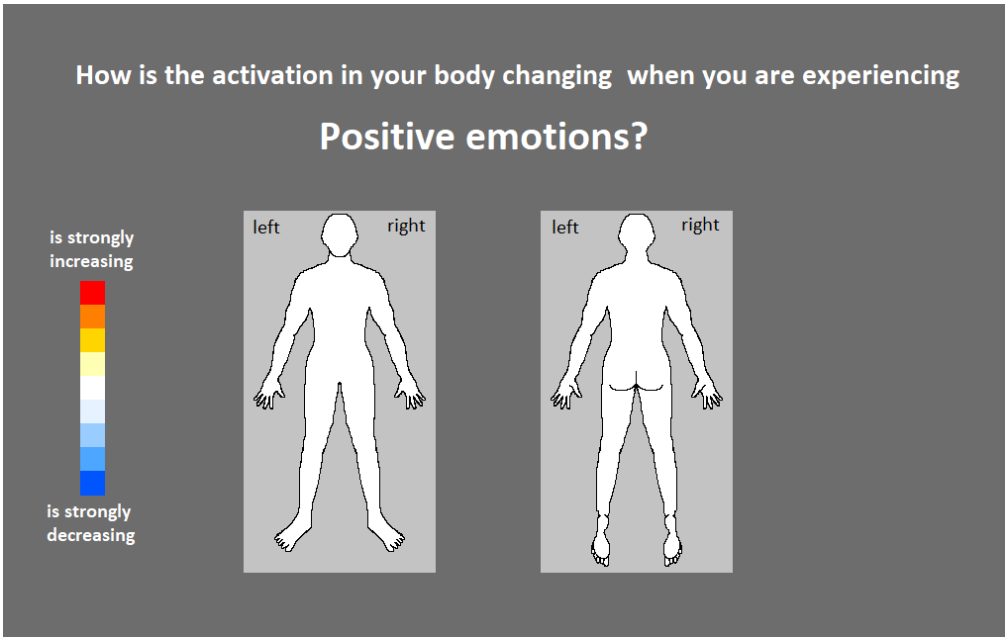

Figure S1. Experimental task overview. Participants were asked to color the body areas they feel becoming more activated or deactivated by selecting a color from a 9-point color bar ranging from blue (- 4 = "very strong deactivation") to red (4 = "very strong activation").

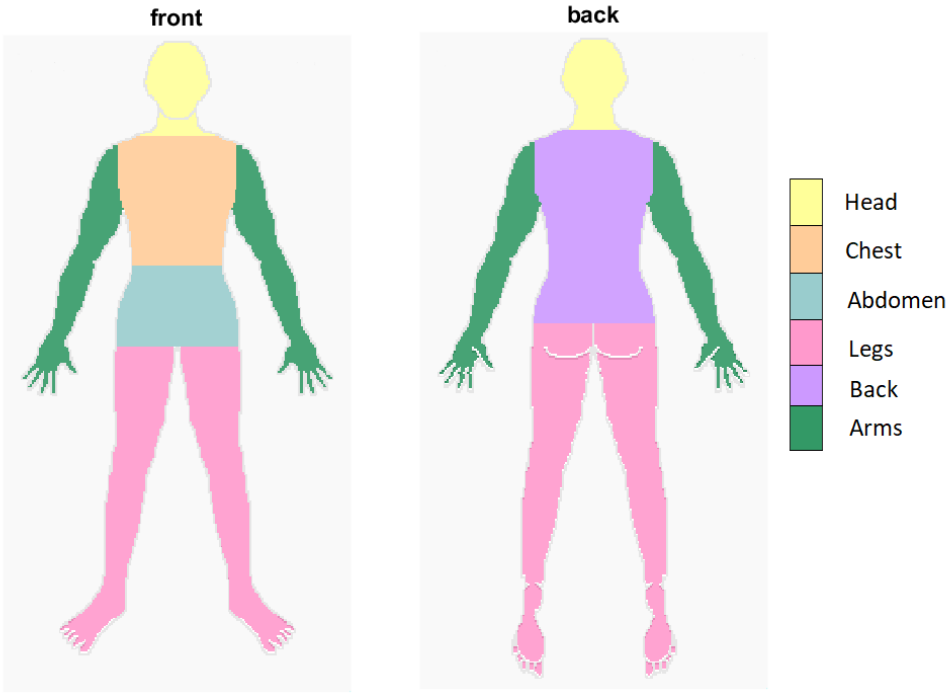

Figure S2. Pre-defined regions of interest (ROI). ROI included the head, chest, arms, abdomen, legs, and the back of the presented body template.

Table S3. Results of 2 × 2 mixed-effects ANOVA designs with factors "group" (IBD/HC) and the additional factor "valence" (positive/negative emotions) or "arousal" (relaxation/tension) on the overall perceived changes in the body for ROIs.

	Dimension: Valence			*Dimension: Arousal*		
	$F_{1,83}$	*p*-value		$F_{1,83}$	*p*-value	
Abdomen						
Group	0.29	.595		0.00	.987	
dimension	0.54	.464		0.55	.458	
Group*dimension	0.15	.697		0.57	.451	
Head						
Group	**2.97**	**.089**	**(*)**	**4.17**	**.044**	*
dimension	3.53	.064	(*)	0.05	.821	
Group*dimension	2.27	.135		0.03	.872	
Chest						
Group	**3.36**	**.069**	**(*)**	**5.99**	**.016**	*
dimension	2.55	.114		**7.06**	**.009**	**
Group*dimension	1.08	.301		2.35	.129	
Arms						
Group	**3.61**	**.061**	**(*)**	**8.69**	**.004**	**
dimension	1.46	.230		**8.83**	**.004**	**
Group*dimension	0.53	.470		3.43	.068	
Legs						
Group	**3.34**	**.071**	**(*)**	**4.70**	**.033**	*
dimension	0.04	.847		2.89	.093	(*)
Group*dimension	0.48	.492		1.36	.248	
Back						
Group	**7.75**	**.007**	**	**8.53**	**.005**	**
dimension	0.35	.554		**6.23**	**.015**	*
Group*dimension	0.65	.424		1.40	.241	

Notes: statistically significant effects including the factor 'group' are marked in bold.
(*) $p < .10$, * $p < .05$, ** $p < .01$

Table S4. Results of the 2 × 2 × 2 mixed-effects ANOVA designs on the ROIs scores.

	Dimension: Valence				*Dimension: Arousal*			
	F	*df*	*p*-value		*F*	*df*	*p*-value	
Abdomen								
Group	**3.07**	**1/83**	**.084**	**(*)**	0.30	1/83	.582	
Dimension	1.12	1/249	.292		9.62	1/249	.002	**
Type of change	76.79	1/249	< .001	***	28.16	1/249	< .001	***
Group*Dimension	**5.88**	**1/249**	**.016**	*	0.16	1/249	.691	
Group* Type of change	**5.94**	**1/249**	**.016**	*	1.18	1/249	.279	
Dimension* Type of change	2.28	1/249	.132		36.69	1/249	< .001	***
Group*Dimension* Type of change	**3.46**	**1/249**	**.064**	**(*)**	.67	1/249	.414	
Head								
Group	2.10	1/83	.151		**8.69**	**1/83**	**.004**	**
Dimension	13.98	1/249	< .001	***	8.39	1/249	.004	**
Type of change	254.50	1/249	< .001	***	2.82	1/249	.094	(*)
Group*Dimension	0.04	1/249	.839		3.24	**1/249**	**.073**	**(*)**
Group* Type of change	**13.69**	**1/249**	**< .001**	***	**3.56**	**1/249**	**.061**	**(*)**
Dimension* Type of change	5.10	1/249	.025	*	52.04	1/249	< .001	***
Group*Dimension* Type of change	**2.76**	**1/249**	**.098**	**(*)**	**11.56**	**1/249**	**< .001**	***
Chest								
Group	**3.26**	**1/83**	**.075**	**(*)**	**4.72**	**1/83**	**.033**	*
Dimension	16.71	1/249	< .001	***	5.17	1/249	.024	*
Type of change	129.67	1/249	< .001	***	32.25	1/249	< .001	***
Group*Dimension	2.68	1/249	.103		0.08	1/249	.779	
Group* Type of change	1.57	1/249	.211		**3.27**	**1/249**	**.071**	**(*)**
Dimension* Type of change	9.10	1/249	.003	**	39.02	1/249	< .001	***
Group*Dimension* Type of change	**6.37**	**1/249**	**.012**	*	2.46	1/249	.118	
Arms								
Group	**2.87**	**1/83**	**.094**	**(*)**	**8.61**	**1/83**	**.004**	**
Dimension	0.50	1/249	.479		4.72	1/249	.031	*
Type of change	10.34	1/249	.001	**	0.043	1/249	.836	
Group*Dimension	0.86	1/249	.354		.432	1/249	.511	
Group* Type of change	0.52	1/249	.472		2.05	1/249	.154	
Dimension*	1.52	1/249	.218		38.34	1/249	< .001	***

Type of change								
Group*Dimension* Type of change	**3.04**	**1/249**	**.082**	**(*)**	**7.09**	**1/249**	**.008**	****
Legs								
Group	**9.72**	**1/83**	**.002**	**	1.52	1/83	.221	
Dimension	0.14	1/249	.710		7.36	1/249	.007	**
Type of change	1.05	1/249	.308		2.17	1/249	.142	
Group*Dimension	0.08	1/249	.777		0.77	1/249	.380	
Group* Type of change	0.70	1/249	.403		2.39	1/249	.123	
Dimension* Type of change	9.41	1/249	.002	**	6.47	1/249	.012	*
Group*Dimension* Type of change	**6.31**	**1/249**	**.013**	*	1.88	1/249	.171	
Back								
Group	**16.57**	**1/83**	**< .001**	***	**6.11**	**1/83**	**.015**	*
Dimension	1.92	1/249	.167		3.88	1/249	.050	*
Type of change	63.01	1/249	< .001	***	13.15	1/249	< .001	***
Group*Dimension	1.52	1/249	.219		0.75	1/249	.386	
Group* Type of change	**19.69**	**1/249**	**< .001**	***	**3.85**	**1/249**	**.051**	**(*)**
Dimension* Type of change	1.56	1/249	.212		48.85	1/249	< .001	***
Group*Dimension* Type of change	**3.92**	**1/249**	**.049**	*	2.17	1/249	.141	

Notes: Main and interaction effects including the factor ‘group’ are marked in bold.

(*) $p < .10$, * $p < .05$, ** $p < .01$, *** $p < .001$

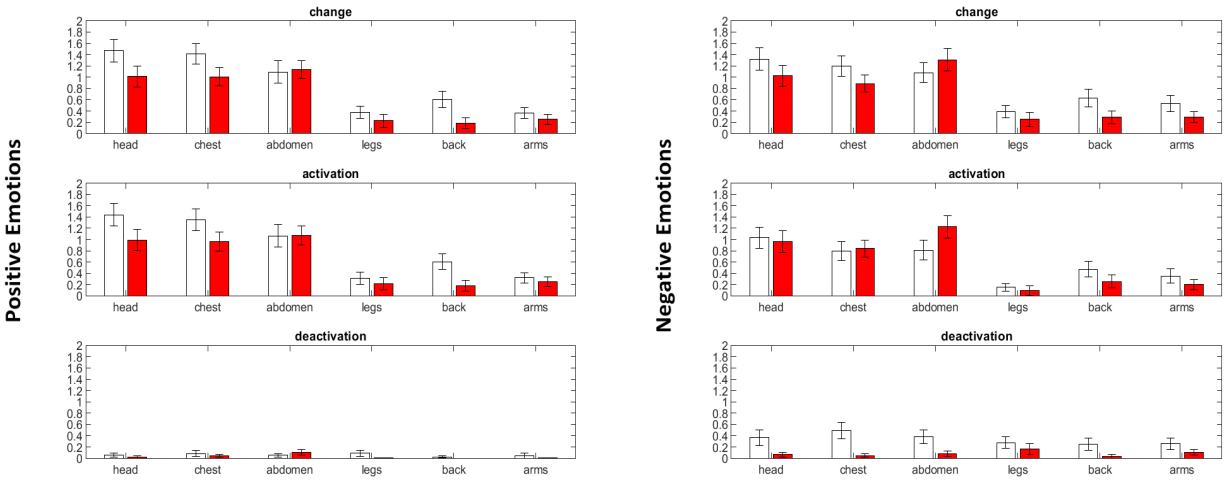

Figure S3. Means and standard deviations of the reported overall perceived bodily changes, activation, and deactivation in all pre-defined regions of interest for positive emotions (left plot) and negative emotions (right plot). Red bars indicate IBD group, white bars indicate HC group.

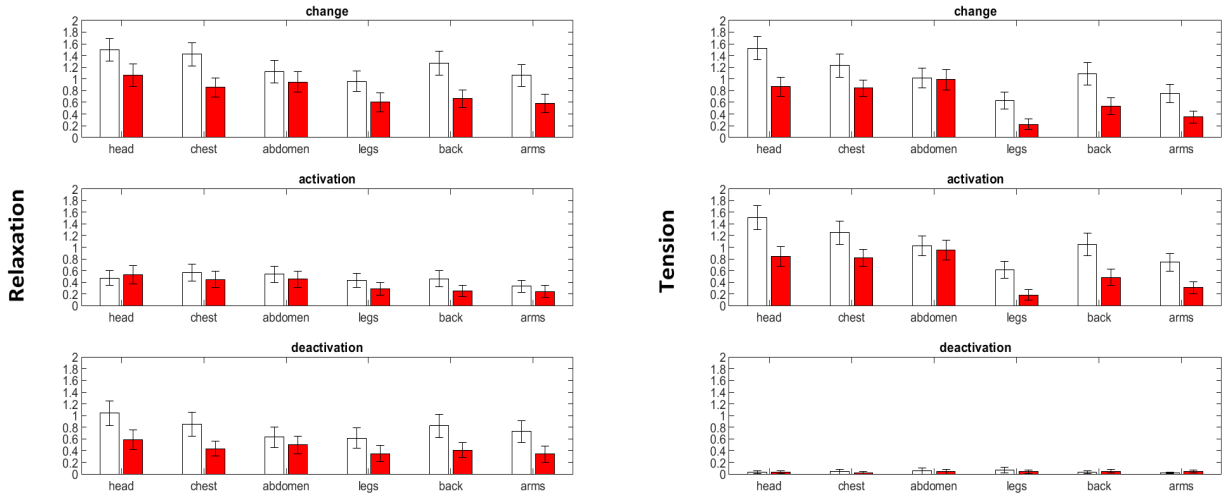

Figure S4. Means and standard deviations of the reported overall perceived bodily changes, activation, and deactivation in all pre-defined regions of interest for relaxation (left plot) and tension (right plot). Red bars indicate IBD group, white bars indicate HC group.

Table S5. Correlations between emotional awareness and general bodily changes.

	IBD		HC		IBD vs. HC	
	r_s	p FDR	r_s	p FDR	Z	p
Emotional awareness						
Valence						
Positive emotions	.461	.004 *	.154	.317	1.53	.064 (*)
Negative emotions	.393	.011 *	.322	.066 (*)	0.36	.359
Arousal						
Relaxation	.310	.049 *	.424	.008 *	-0.59	.279
Tension	.356	.044 *	.282	.064 (*)	0.37	.357

FDR, false discovery rate, (*) $p < .10$, * $p < .05$

2.3 Research Question III | The experience of basic emotions in patients with inflammatory bowel disease

2.3.1 Abstract

Background: Previous studies have linked inflammatory bowel diseases (IBD) to higher psychological stress and poorer emotional functioning. The perception and appraisal of bodily sensations has been postulated to represent a core component of emotion experience. By now, no study has investigated whether patients with IBD differ in their emotion-associated bodily sensations and whether specific factors such as emotional awareness and history of adverse childhood experiences modulate altered emotional body experiences in IBD.

Methods: Forty-one IBD patients in clinical remission and 44 healthy control (HC) participants indicated where and how intensely they perceived changes in their bodily sensations, using an emotional body map task, when experiencing the six basic emotions: happiness, sadness, anger, fear, disgust, and surprise. Emotional awareness, a history of childhood adversities, and psychopathology were assessed via self-report questionnaires.

Results: Compared to HC participants, IBD patients reported higher emotional awareness but lower intensities of perceived changes in their bodily sensations associated with the experience of happiness, anger, fear, and surprise. Higher emotional awareness was associated with stronger changes in patients' bodily sensations during happiness. A history of abuse during childhood positively correlated with bodily sensations for the experience of anger. In IBD, higher anxiety symptoms were linked to stronger experience of negative emotions in the whole body.

Conclusions: Our results indicate decreased bodily experiences associated with certain emotions in IBD, characterized by decreased perception of bodily sensations' changes. An altered emotional functioning might affect a patient's well-being through its links to anxiety and depression symptoms.

2.3.2 Introduction

Inflammatory bowel disease (IBD) is a chronic inflammatory condition characterized by considerable emotional and social burdens for the affected individuals (Neuendorf et al., 2016). Depression and anxiety symptoms affect up to 35 % of the patients with IBD, a prevalence twice higher than in people without IBD (Bromet et al., 2011). In this clinical population, the failure to recognize emotional stimuli correctly plays a crucial role in stress perception and stress management, resulting in worsened disease symptoms and increased levels of depression (Kano et al., 2020; La Barbera et al., 2017). One mechanism potentially underlying altered emotion processing in IBD might be a changed perception and appraisal of visceral sensations, also known as interoception (Critchley & Garfinkel, 2017). There are three dimensions of interoception: sensitivity (i.e., the objective detection of bodily signals), sensibility (i.e., the subjective experience of bodily activity), and awareness (i.e., the extent of correspondence between one's sensitivity and sensibility) (Garfinkel et al., 2015). While IBD patients do not exhibit altered ability to detect bodily signals, findings suggest that they appraise these differently, resulting in altered subjective experience of bodily sensations (Atanasova et al., 2021; Fournier et al., 2020).

As emotion experience is strongly linked to the bodily sensations and an individual's appraisal of those (Damasio, 2001; Damasio et al., 1996), altered interoceptive processes might contribute to impairments in patient's emotional functioning. The importance of emotion perception for individual's well-being has been previously emphasized, suggesting that avoidance of emotions is linked to greater risk of developing psychopathology and emotion dysregulation (Aldao et al., 2010; Hayes et al., 1996). Moreover, Wilkinson et al. (2019) demonstrated that current IBD activity negatively affects patient's depressive symptoms, partially through altered emotion perception, emphasizing the crucial impact of emotional functioning on patient's quality of life (Wilkinson et al., 2019). As a significant percentage of the IBD patients still report higher levels of psychological distress, even when the severe IBD symptoms have subsided, an altered emotion experience may contribute to the maintenance of depression and anxiety symptoms during remission.

Studies on emotional experience in IBD demonstrated hyposensitivity to positive emotions (Agostini et al., 2011; Wilkinson et al., 2019) and hypersensitivity to negative emotional states (Vianna et al., 2006). In a recent study, we reported that patients with IBD exhibit decreased bodily sensations related to emotions of positive valence (Atanasova et al., in

review). However, no study so far has investigated whether patients with IBD differ in their bodily sensations associated with the experience of specific emotions.

The categorical theory of emotion posits the existence of six primary, distinct, and universal emotions (Ekman, 1992; Ekman & Friesen, 1971): happiness, sadness, anger, fear, disgust, and surprise. How individuals perceive emotions is strongly modulated by their interoceptive abilities. Emotional awareness constitutes a distinct feature of one's interoceptive sensibility and describes the ability to attribute specific bodily sensations to physiological manifestations of emotions (Mehling et al., 2012). Although the experience of distinct emotions is linked to specific topographical patterns of bodily sensations (Nummenmaa et al., 2014; Ruben et al., 2001), no study has investigated the association between emotional awareness and emotion-related bodily sensations yet.

Altered emotion experience is a common feature of many mental disorders, especially Those that are related to psychological traumatization (Dannlowski et al., 2012). Individuals with a history of adverse childhood experiences (ACE) tend to detect faster and allocate greater attention resources to negative emotional cues (Iffland & Neuner, 2020), while exhibiting difficulties in recognizing positive emotional stimuli (for a review see: Bérubé et al. (2021)). According to previous findings, a substantial percentage of about 60 % of IBD patients has experienced at least one type of ACE (Fuller-Thomson et al., 2015; Ryan et al., 2013; Witges et al., 2019). Although it is conceivable that history of ACE might modulate impairments in emotion perception in IBD, there is no research focusing on this link so far.

The present study aims to contribute to the understanding how distinct emotions are subjectively experienced in the body among patients with IBD and whether emotion-related sensations, possibly altered by history of ACE (Van der Kolk, 2014), are linked to one's interoceptive sensibility. Using a topographical self-report measure adapted from Nummenmaa et al. (2014), we assessed the subjectively perceived changes in bodily sensations associated with the experience of the basic emotions (happiness, sadness, anger, fear, disgust, and surprise) among patients with IBD and healthy control (HC) participants. We hypothesized that (I.) IBD patients will differ in the reported intensity of bodily sensations, reporting stronger sensations for negative emotions and attenuated sensations when experiencing positive emotions. (II.) We expected that emotional awareness, will modulate the severity of alterations in emotion-related bodily sensations in IBD and (III.) history of ACE will exaggerate disturbances in emotion experience in IBD.

2.3.3 Methods

Participants

Eighty-six individuals between 18 and 65 years participated in the study. Of these, 42 met the diagnostic criteria for IBD and 44 were HC participants. One participant of the IBD group was excluded due to lack of understanding the instructions, resulting in a final sample of 41 IBD patients (20 female, 21 male) and 44 HC participants (30 female, 14 male; see Table 4.1 for further demographic characteristics). All IBD patients attended the IBD outpatient unit at the University Medical Center Mannheim and were personally contacted for participation in the study. Twenty-nine patients were diagnosed with Crohn's disease (CD) and 12 patients with ulcerative colitis (UC), with all patients being currently in remission. Fully trained physicians specialized in the care of patients with IBD carried out all diagnostic procedures and gastroenterological examinations. Exclusion criteria included biological signs of disease activity (fecal calprotectin level in mg/L > 200), use of corticosteroids, use of psychotropic medication, and current or past neurological or psychiatric disorders. Details on treatment medication, disease duration, age for disease onset, history of further somatic diseases, previous surgeries, and history of extraintestinal manifestations were collected from previous medical reports and are provided in Table S2, supplementary material S2. In the HC group, exclusion criteria included chronic medical conditions, chronic medication intake, use of psychotropic medication, current or past neurological or psychiatric disorders, and any gastrointestinal complaints during the last 4 weeks prior the experiment. The study was approved by the Ethics Committee of the Medical Faculty Mannheim at Heidelberg University and all participants gave their written informed consent before participating in the study. Please note that a subsample of participants from both groups was included in a study on interoception and emotion experience (Atanasova et al., 2021).

Table 4.1 Sample characteristics including demographic data, affective state and psychopathological symptoms.

	HC (N=44) (M±SD)		IBD (N=41) (M±SD)		Test-statistics	*p*-value	
Demographics							
Age	36.11	±12.29	40.20	±13.87	1.44 [a]	.154	
Sex (female/male)	30/14		20/21		3.30 [b]	.069	
Disease activity							
Crohn's disease (HBI)	-	-	1.76	±1.83	-	-	
Ulcerative colitis (Partial Mayo Score)	-	-	1.58	±1.51	-	-	
Affective state							
STAI: Anxiety	32.66	±8.20	33.13	±5.28	0.31 [a]	.754	
SAM: Valence	3.77	±0.85	3.75	±0.98	-0.11 [a]	.911	
SAM: Arousal	1.98	±0.86	2.34	±1.00	1.78 [a]	.079	
SAM: Dominance	3.68	±0.66	3.63	±0.98	-3.41 [a]	.734	
Psychopathological symptoms							
BSI: Global severity index	22.42	±4.91	28.97	±9.26	3.66 [a]	.001	***
BSI: Somatization	6.74	±1.27	9.97	±3.51	5.31 [a]	<.001	***
BSI: Depression	7.58	±2.81	9.22	±3.97	1.85 [a]	.068	
BSI: Anxiety	8.09	±2.22	9.78	±3.65	2.45 [a]	.017	*
Interoceptive sensibility							
MAIA: Emotional Awareness	2.77	±0.88	3.32	±0.92	0.56 [a]	.006	**
History of ACE							
CTQ: Total score	36.06	±7.00	34.71	±10.15	801.00 [c]	.373	
CTQ: Emotional abuse	8.51	±3.47	7.90	±2.96	832.50 [c]	.533	
CTQ: Physical abuse	5.80	±1.60	6.15	±2.32	831.50 [c]	.420	
CTQ: Sexual abuse	5.14	±0.55	5.37	±1.76	867.00 [c]	.543	

CTQ: Emotional neglect	9.63	±3.29	8.63	±3.64	808.50 [c]	.406
CTQ: Physical neglect	6.97	±1.71	6.66	±2.21	817.50 [c]	.440

HC, healthy controls group; IBD, inflammatory bowel disease group; HBI, Harvey-Bradshaw Index; STAI, State-Trait Anxiety Inventory – State; SAM, Self-Assessment Manikin; BSI, Brief Symptom Inventory; GSI, Global Severity Index; MAIA, Multidimensional Assessment of Interoceptive Awareness; ACE, Adverse Childhood Experiences; CTQ, Childhood Trauma Questionnaire. * $p < .05$, ** $p < .01$, *** $p < .001$, [a] t-value, [b] Chi^2, [c] Mann-Whitney U

All participants completed a battery of psychometric questionnaires assessing psychopathological symptoms, affective state at time of investigation, interoceptive sensibility, and history of adverse childhood experiences. Afterwards, participants performed a computer-based task, where they were asked to recall their bodily sensations during the experience of the six basic emotions: happiness, sadness, anger, fear, disgust, and surprise.

Questionnaires

Brief Symptom Inventory (BSI-18)

Psychopathological symptoms and psychological distress were measured using the Brief Symptom Inventory (BSI-18) (Franke et al., 2011). BSI-18 is a self-report instrument to assess symptoms of somatization, depression, and anxiety (subscale range: 0-24). By adding up all subscale scores, a global severity index (GSI) is computed, with higher GSI indicating higher general symptom severity (GSI range: 0-72). Cronbach's α for the 18 items was .86 in the IBD group and .81 in the HC group.

Affective state

To control for participant's levels of anxiety at the time of investigation, all participants were asked to complete the state version of the State-Trait Anxiety Inventory (STAI; Spielberger et al. (1983)). STAI is 20-item scale measuring individual's feelings of apprehension, tension, nervousness, worry, and activation of the autonomic nervous system on a 4-point Likert scale. A total score is calculated by adding up all items' scores (range: 20 to 80), with higher scores

indicating higher anxiety. Internal consistency was good with Cronbach's $\alpha = 0.76$ in the IBD sample and .90 in the HC group. In addition, participants were asked to rate their levels of subjective arousal, valence/pleasure, and dominance on a 9-point Likert scale using the Self-Assessment Manikin (SAM; Bradley and Lang (1994)). Higher scores indicate higher arousal, greater positive valence, and higher perceived dominance.

Multidimensional Assessment of Interoceptive Awareness (MAIA)

As we were particularly interested in the experience of emotions in the body, we focused on the one feature of interoceptive sensibility, that is individual's subjective belief to be interoceptively cognizant (Garfinkel et al., 2015). One key feature of individual's interoceptive sensibility refers to one's ability to be aware that certain bodily sensations are linked to the experience of emotions, a construct known as emotional awareness. To assess it, we used the subscale *Emotional Awareness* of the Multidimensional Assessment of Interoceptive Awareness (MAIA; Mehling et al. (2012)), which comprises 5 items assessed on a 6-point Likert scale. Individual's level of emotional awareness is computed as the mean item score (range: 0-5) with higher scores indicating higher emotional awareness. *Emotional Awareness* exhibited acceptable internal consistency with Cronbach's $\alpha = .76$ in the IBD group and .86 in the HC group. For further details on the MAIA and its subscales see supplementary material S2.

History of adverse childhood experiences

History of ACE was assessed via self-reports using the German version of the Childhood Trauma Questionnaire (CTQ; Klinitzke et al. (2012)). The 28-item questionnaire consists of five subscales including *emotional abuse, physical abuse, sexual abuse, emotional neglect*, and *physical neglect,* and a total score. Each subscale includes five questions (subscale range: 5-25) and adding up all items results in a total score (range: 25-125). Higher CTQ scores indicate a severer history of childhood adversity. CTQ revealed acceptable to good internal consistency with Cronbach's $\alpha = .86$ in the IBD group and .76 in the HC group. For details on trauma history see Table 4.1.

Experimental procedure

Using an adapted version of the topographical self-report method established by Nummenmaa et al. (Nummenmaa et al., 2014), all participants were asked to indicate the perceived changes in their bodily sensations when experiencing the six basic emotions: happiness, sadness, anger, fear, disgust, and surprise. Respondents were instructed to evaluate which body regions they typically felt as being activated or deactivated when experiencing each specific emotion (for further details see supplemental material S3). To control for potential baseline differences, we asked participants to indicate whether they experience changes in their bodily sensations also during a neutral emotional state. To indicate their responses, participants were asked to color the body templates by selecting a color from a 9-point color bar ranging from blue (- 4 = "very strong deactivation") to red (+ 4 = "very strong activation"). In case that participants could not perceive any changes in a particular body area, they were instructed to leave it uncolored. All seven blank body maps were presented in a randomized order on a 14'' computer screen. The front and back body templates comprised 366 x 195 pixels, and the diameter of the painting tool was 13 pixels. The task was programmed with Presentation® software (Version 18.0, Neurobehavioral Systems, Inc., Berkeley, CA, **www.neurobs.com**).

Dependent variables

The analysis pipeline used in this manuscript was already implemented in another study of our group and is described in more detail in Atanasova et al. (in review). After applying a spatial smoothing (see supplemental material S3), an overall change score was calculated across all pixels within the body template summarizing the extent of change for both perceived activation and deactivation: $sum(\sqrt{change^2})$. To further explore whether these changes are associated rather with sensations of bodily activation or deactivation, separate scores for the type of change were computed. Overall change, activation, and deactivation scores were computed for the whole-body template and for several pre-defined regions of interest (ROI). The ROI corresponded to the findings of Nummenmaa et al. (2014) and included: the head, chest, abdomen, upper limbs, lower limbs, and the back (see supplemental material S2, Figure S2). All analyses were performed using custom pipelines run with MATLAB 2020a (The MathWorks, Inc.).

Data analysis

Group differences in the overall change scores were analyzed with Wilcoxon rank-sum test. In addition to our preregistered analyses (see below), we analyzed the activation and deactivation scores using mixed-effects analysis-of-variance designs (mixed-design ANOVA) to differentiate between the type of change perceived during the emotion experience. Since the data violated the normality assumptions (Kolmogorov-Smirnov test, visual inspection of Q-Q plots), a non-parametric approach was applied by implementing a rank-aligned ANOVA (Kay & Wobbrock, 2019; Wobbrock et al., 2011). The 2 × 2 rank-aligned ANOVA designs for the six emotions included the between-subject factor "group" (IBD/HC) and the within-subject factor "type of change" (activation/deactivation). To explore significant interaction effects, post-hoc comparisons were done by pairwise comparisons (Wilcoxon rank-sum test). Group differences for the reported overall change in the different ROIs were analyzed with Wilcoxon rank-sum tests. Again, to differentiate between the type of change perceived in the ROI, exploratory 2 × 2 rank-aligned ANOVA designs with the factors "group" (IBD/HC) and "type of change" (activation/deactivation) were computed. Finally, Spearman's rank correlation coefficients were used to examine the associations between participants' emotion-related bodily sensations, emotional awareness, and history of childhood adversity.

Statistical analyses were carried out with SPSS v.27.0 (IBM Corp., USA) and the ARTool package of RStudio v.4.0.0 (RStudio, PBC, Boston, MA, **http://www.rstudio.com/**). Significance level was set to $p < 0.05$.

Preregistration

This study was preregistered before data collection. The hypotheses, sample size, methods, exclusion criteria, and planned analyses can be accessed at https://aspredicted.org/blind.php?x=hu4n7k. According to this preregistration, a sample size of 120 participants was planned. However, due to the Covid-19 pandemic-related restrictions, the number of participants recruited was reduced. All remaining aspects of the study were carried out in accordance with the pre-registered protocol unless stated otherwise. Note that only data on the experience of specific emotions are reported in the present manuscript. Data on body image perception and the experience of valence and arousal, as recorded in the same preregistration protocol, are reported in separate articles.

2.3.4 Results

Whole-body sensations: overall change

Compared to HC participants, IBD patients reported significantly less perceived changes in their bodily sensations when experiencing *happiness, anger, fear*, and *surprise* (all *ps* < .049; Table 4.2, Figure 10), but not *sadness* and *disgust* (Figure S5, supplemental material S3). In the control condition, where participants evaluated the changes in their bodily sensations during a neutral emotional state, no group differences were observed ($p = .160$).

Table. 4.2 Pairwise comparisons for perceived changes in the bodily sensations

	Mann-Whitney U	***p*-value**	
Happiness	667.00	.048	*
Sadness	728.00	.126	
Anger	552.00	.002	**
Fear	583.00	.005	**
Disgust	728.00	.125	
Surprise	571.50	.004	**
Neutral	759.50	.160	

*$p < .05$, **$p < .01$

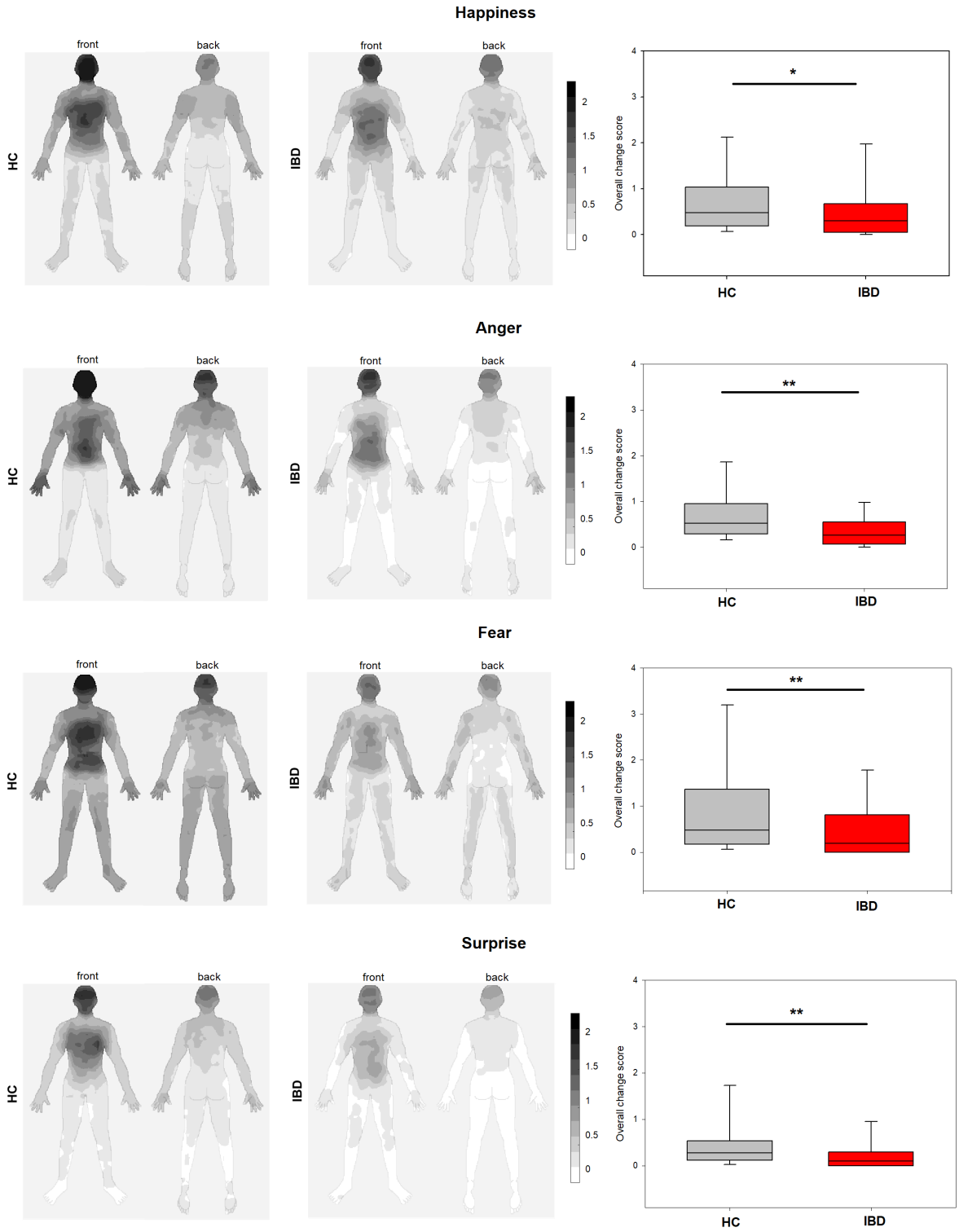

Figure 10. Left panel: Whole-body templates visualizing the distribution of the experienced changes in the body. Right panel: Overall change scores for the bodily experiences of happiness, anger, fear, and surprise. * $p < .05$, ** $p < .01$

Whole-body sensations: activation and deactivation

When differentiating between the type of perceived changes in the body, analyses revealed that group differences in the emotional experience were dependent on whether participants judged perceived activation or deactivation in the body (see Table S6, supplementary material S3). Pairwise comparisons showed that for *happiness, anger, fear*, and *surprise* these effects were driven by lower levels of perceived bodily activation, but not deactivation, in the IBD group (IBD vs. HC: activation: all $ps \leq .031$; deactivation, all $ps \geq .060$). For the experience of *disgust*, however, IBD patients exhibited a smaller difference between the levels of perceived activation and deactivation ($Z = -3.32$, $p = .001$): While the IBD group reported descriptively lower bodily activation than the HC group ($p = .149$), they also experienced higher levels of bodily deactivation ($p = .161$). Consistently with the findings for the overall change score, there were no group differences for the experience of sadness and a neutral emotional state (all $ps > .075$). For further details see Table S6 and Figure S6, supplemental material S3.

ROI analyses: overall change

In IBD, the experience of basic emotions was associated with decreased changes in the bodily sensations perceived in different areas of the body depending on the specific emotion. Results for all ROI scores across the six basic emotions are visualized in Figure 11. Summary of the group comparisons and the 2 × 2 rank-aligned ANOVAs are reported in Table S7 and S8 in supplemental material S3.

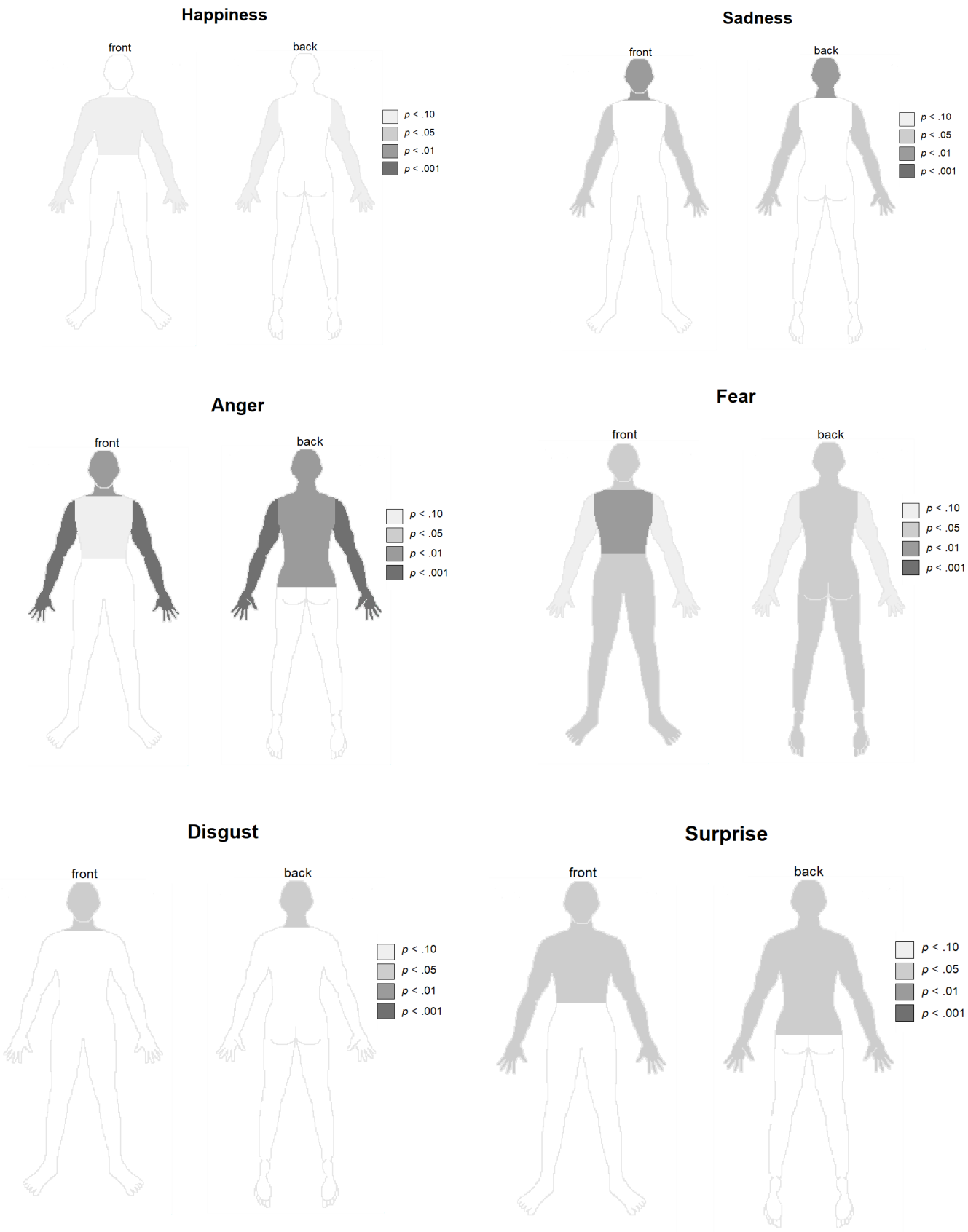

Figure 11. Group differences in the perceived overall changes in the bodily sensations across all ROI.

Correlations between emotion-associated bodily sensations and emotional awareness

Correlation analyses revealed that across all participants, higher emotional awareness was associated with stronger perceived changes in the bodily sensations for the experience of happiness (r_s = .265, p = .014). This significant link was found in both IBD (r_s = .357, p = .022) and HC group (r_s = .391, p = .009). However, both groups did not differ in the strength of this association (Z = -0.18, p = .430). For further details on the correlations between emotional awareness and the experience of all basic emotions, see Table S9, supplemental material S3.

Correlations between emotion-associated bodily sensations and history of ACE

Across all participants, a more severe history of ACE was associated with higher levels of changes in one's bodily sensations when experiencing *anger* (r_s = .240, p = .027). However, this association was significant only in the IBD group (r_s = .318, p = .043), but not in the HC group (r_s = .090, p = .559; IBD vs. HC: Z = 1.06, p = .144). No significant relationships were found with the remaining basic emotions (all $ps \geq .277$). Exploratory analyses with the different types of ACE in the IBD group revealed that greater changes in the bodily sensations associated with *anger* were linked to a more severe history of abuse (r_s = .395, p = .011) but not of neglect (r_s = .199, p = .213).

Correlations between emotion-associated sensations and psychopathological symptoms

Although all patients met the criteria for clinical remission, the IBD group reported higher levels of anxiety and – at least on a descriptive level – depression compared to HC participants (see Table 4.1). Therefore, we performed additional correlation analyses to explore whether anxiety and depression symptoms are related to the experience of emotions in the body. In IBD, greater anxiety symptoms were linked to stronger changes in the bodily sensations during sadness (r_s = .341, p = .039), anger (r_s = .461, p = .004), and fear (r_s = .440, p = .006). Higher levels of depression symptoms were associated with greater changes in the body only for the experience of anger (r_s = .562, p < .001). No further significant relationships were found for the other emotions (all $ps \geq .063$).

2.3.5 Discussion

The perception and appraisal of bodily sensations elicited by emotional events is essential to how intense people experience emotions in everyday life. In the case of IBD, emotion perception is crucial to patients' coping mechanisms with their disease symptoms and therefore, their quality of life (Gracie et al., 2017). Patients in remission might still experience higher psychological distress due to emotional dysfunctions even if the severe disease symptoms have already subsided (Iglesias et al., 2009). Thus, the main objective of this study was to investigate whether IBD patients in remission differ in their emotion-associated bodily sensations compared to healthy individuals. We aimed to understand whether individual's awareness of their bodily sensations and a history of childhood maltreatment are linked to altered emotional body experience in IBD.

In line with previous studies indicating a hyposensitivity to positive emotional stimuli in IBD, we found diminished body experiences for *happiness* in this clinical sample (Agostini et al., 2011; Wilkinson et al., 2019). This finding is also in line with unpublished data of our research group showing decreased bodily activation for emotions of positive valence, but not for those of negative valence (Atanasova et al., in review). These results support the hypothesis of biased perception of positive emotions in IBD, independently of whether general emotional categories (e.g., positive emotions) or specific emotions (e.g., happiness) are used (see Atanasova et al., in review). Furthermore, this is the first study demonstrating that the diminished perception of *happiness* in IBD is associated with altered experience of bodily sensations in particular parts of the body. Patients exhibited less perceived changes in the chest and the upper limbs, two regions strongly associated with stronger changes in the bodily sensations during positive emotions as demonstrated in Nummenmaa et al. (2014). In IBD, decreased sensations in the chest might indicate hyposensitivity to changes in one's heart rate (e.g., heart pounding) during positive emotional events. However, while Nummenmaa et al. (2014) suggested that stronger sensations in the upper limbs may be characteristic for approach-oriented emotions such as happiness, lower activation in this body area among patients with IBD may indicate that these can less accurately differentiate between emotions triggering approach- and avoidance behavior. This interpretation is in line with our unpublished data showing that patients differentiated less between the perceived bodily sensations during positive and negative emotions, as well as during relaxation and tension compared to healthy individuals (Atanasova et al., in review). However, since in both studies the identical sample

of participants have been included, replication of our results in an independent sample is required.

In contrast to Vianna et al. (2006), who did not find alterations in the emotion processing among IBD patients with inactive disease compared to those with active disease, our results showed decreased bodily perceptions related to the experience of *anger*, *fear,* and *surprise*. These emotional states were also linked to decreased bodily sensations in the upper body, including the head, chest, and the upper limbs. Especially these parts of the body have been previously linked to higher bodily activation during anger and fear in the general population (Nummenmaa et al., 2014). Thus, although patients with IBD did not differ in their topographies of experienced changes in the bodily sensations, they consistently demonstrated lower intensities of these changes compared to healthy participants. These findings suggest the potential use of emotional avoidance as emotion regulation strategy among patients with IBD. Avoidance or distraction from highly intense emotions and the concomitant physiological changes in the body can prevent the confrontation with overwhelming and undesirable emotional states, which could overstep individual's coping resources (Sheppes et al., 2011). In line with this interpretation, a recent study by Banovic et al. (2020) found stronger emotional avoidance and emotional suppression among Crohn's disease patients (Banovic et al., 2020). Since emotional avoidance has been associated with higher levels of anxiety and affective distress (Bardeen et al., 2014; Feldner et al., 2003; Kelly & Forsyth, 2009), it is conceivable that this emotion regulation strategy could potentially explain why depression and anxiety symptoms remain severe in IBD patients even during the periods of disease remission.

Moreover, previous studies on attachment and mentalizing in IBD revealed stronger avoidance strategies in this clinical population (Agostini et al., 2019). An avoidant attachment style has been associated with cognitive distancing from emotions and our findings indicate that this might be accompanied by stronger detachment from emotion-related bodily sensations as well. Based on previous findings, avoidance tendencies in IBD might further impede patients' mentalization abilities and their capacity to accurately identify and differentiate between emotional states (Agostini et al., 2019). Through the more detached emotional body experience, patients may try to avoid strong changes in their visceral sensations by suppressing the physiological feedback associated with emotional triggers. In IBD, this could be a coping strategy to minimize the potential risk of triggering the disease symptoms. Since we investigated only patients in clinical remission, future studies are required to examine the links

between bodily emotion experience and avoidance strategies in active and inactive disease patients.

Our results showed that higher emotional awareness was associated with greater changes in bodily sensations perceived during happiness in both IBD and HC participants. This result is partially in line with previous findings, suggesting a link between interoception and emotional experience, suggesting that interoceptively aware individuals perceive emotions more intensely (Herbert et al., 2007). It has been repeatedly demonstrated that representations of internal bodily sensations in the insula are crucial for the conscious experience of emotions (Critchley et al., 2004). The enhanced insular reactivity previously observed in patients with IBD (Agostini et al., 2017; Rubio et al., 2016) might constitute the neural correlate of an increased perception of visceral sensations in IBD and a stronger experience of emotion-related sensations, particularly in those patients who report to be more aware of their body signals.

As histories of early adversity have been repeatedly linked to altered experience of emotions (for a review see: (Bérubé et al., 2021)), our study aimed to investigate the link between a history of ACE and altered bodily experience of emotion in IBD. Our findings suggest that there are differential patterns of associations between ACE and emotion perception in IBD and healthy individuals. Among IBD patients, higher trauma severity and particularly more severe experiences of abuse were linked to greater changes in bodily sensations during the experience of *anger*. This finding is in line with clinical and empirical observations indicating that patients with trauma-related disorders tend to experience stronger feelings of anger and rage and report greater difficulties to downregulate these emotions compared to individuals without a history of maltreatment (Eshel et al., 2021; Olatunji et al., 2010). In IBD, the increased experience of anger in the body might result in stronger activation of the 'fight or flight' system, associated with an amplified physiological stress response of the HPA axis and worsening gastrointestinal inflammation (Mawdsley & Rampton, 2005). Hence, it could be speculated that IBD patients with history of ACE represent an especially vulnerable population, in which these mechanisms might promote greater inflammatory activation associated with the experience of emotional stress (Moulton et al., 2019; Wan et al., 2022).

Finally, the present study shed light on the observation that a significant percentage of the IBD patients in remission experience greater levels of psychological distress compared to healthy individuals. We found a positive correlation between the reported psychopathological symptoms and the experience of negative emotions in the body: Higher levels of anxiety and

depression symptoms were linked to stronger changes in the bodily sensations during *sadness*, *anger*, and *fear* in the IBD group. As these findings are only of correlational nature, no direction of these relationships can be implied. Nevertheless, these preliminary results emphasize the important role of emotional functioning for the patients' well-being: Patients reporting higher psychological distress might experience stronger physiological activation during negative emotional states or strengthened experience of negative emotions might predispose IBD patients to greater anxiety and depression symptoms. In line with this interpretation, Wilkinson et al. (2019) demonstrated that depression might occur as result of dysfunctional processing of emotions in patients with acute IBD symptoms, emphasizing the importance of psychological interventions targeting emotion perception biases to potentially treat or prevent depression in IBD.

Given our findings of altered experience of positive and negative emotions in the body among patients with IBD, some clinical implications can be considered. While the decreased levels of bodily activation during anger and fear might prevent patients from states of hyperarousal in the short term, avoidance of emotions and the associated bodily sensations might constitute a risk factor for developing psychopathological symptoms in the long term (Feldner et al., 2003; Hayes et al., 1996). Thus, one could speculate that mind-body interventions might be useful in the segment of IBD patients reporting greater emotional burden and difficulties in recognizing or coping with negative feelings (for a review of mind-body interventions in IBD see: (Ewais et al., 2019)). By modifying how patients attend to their body signals, elicited by emotional triggers, and providing them with adaptive emotion regulation skills, such interventions can improve patients' flexibility in emotional experience (Wynne et al., 2019) and prevent an overgeneralization of avoidance strategies of disease related bodily sensations to those associated with emotions. As impairments in emotion perception have been shown to modulate the link between disease severity and psychological well-being in IBD (Wilkinson et al., 2019), such supplemental interventions could improve patients' abilities to differentiate between emotions, potentially having positive effects on the patient's mental health and quality of life. Given the potentially bidirectional relationship between emotion perception and psychopathological symptoms, it should be noted that as our results are only of correlational nature, so that clinical implications are only speculative and need further investigation.

Limitations

The present study has several limitations. First, since no clinical control group has been included in the study, we cannot conclude whether our findings and the observed alterations are limited to IBD or might be markers of several gastrointestinal disorders. Future studies need to examine the generalizability of our findings in larger clinical samples with gastrointestinal pathologies, taking the potential effects of psychopathology into account. Moreover, no direct emotion induction was performed, and participants were asked to recall how a particular emotion felt in their bodies when they experienced it. This recall process might have been biased through recalling only recent and immediately available examples or might be based on stereotypes of bodily sensations associated with a particular emotional category (Nummenmaa et al., 2014). Thus, future studies need to control for these effects by implementing emotion induction during the experimental task. Furthermore, interoception-related features were assessed only via self-report measures, which often do not correspond to participant's actual interoceptive abilities (Murphy et al., 2019). Again, future research is required to examine how the objective ability to detect one's body signals might be linked to the experience of less intense changes in the bodily sensations among patients with IBD.

2.3.6 Conclusions

Taken together, our results indicate that IBD is associated with lower intensities of perceived changes in body related to several emotional states of positive and negative valence, including happiness, anger, fear, and surprise. The decreased emotional reactivity experienced in the body might indicate the avoidance of intense emotions as coping mechanism in IBD. While patients reporting greater emotional awareness experienced positive emotions more strongly in their bodies, a history of childhood maltreatment was linked to a stronger experience of anger in IBD. These findings provide first insights into the complex interplay of interoception, emotion, and a history of childhood adversity in this clinical population.

2.3.7 Supplemental material S3

Experimental task and data analysis:

Participants were asked to indicate changes in their bodily sensations when they experienced specific emotions during everyday life. These included: happiness, sadness, anger, fear, disgust, and surprise. Initially, participants were familiarized with the task and instructed to evaluate which bodily regions they typically felt as being activated or deactivated when experiencing a particular emotion. Thus, the task did not involve inducing actual emotions by experimental manipulation. To indicate these changes, participants were asked to color the body areas where they perceived sensations of activation and deactivation by selecting a color from a nine-point color bar ranging from blue (-4 = "very strong deactivation") to red (+4 = "very strong activation"). Participants indicated their responses by painting the bodily regions using successive strokes on the presented body templates. If they did not perceive any changes in some parts of the body, participants were instructed to leave these uncolored. The seven instructions (happiness, sadness, anger, fear, disgust, surprise, neutral) were presented in a pseudorandomized order. The task was presented on a 14" computer screen. The front and back body templates comprised 366 × 195 pixels, and the diameter of the painting tool was 13 pixels. The task was programmed using the Presentation® software (Version 20.1, Neurobehavioral Systems, Inc., Berkeley, CA, www.neurobs.com). For each participant and trial, color code values (ranging from -4 to +4) were stored in a numeric array for each pixel of the body templates and spatially smoothed by averaging the color code value of each pixel and its surrounding pixels (± 3 pixels).

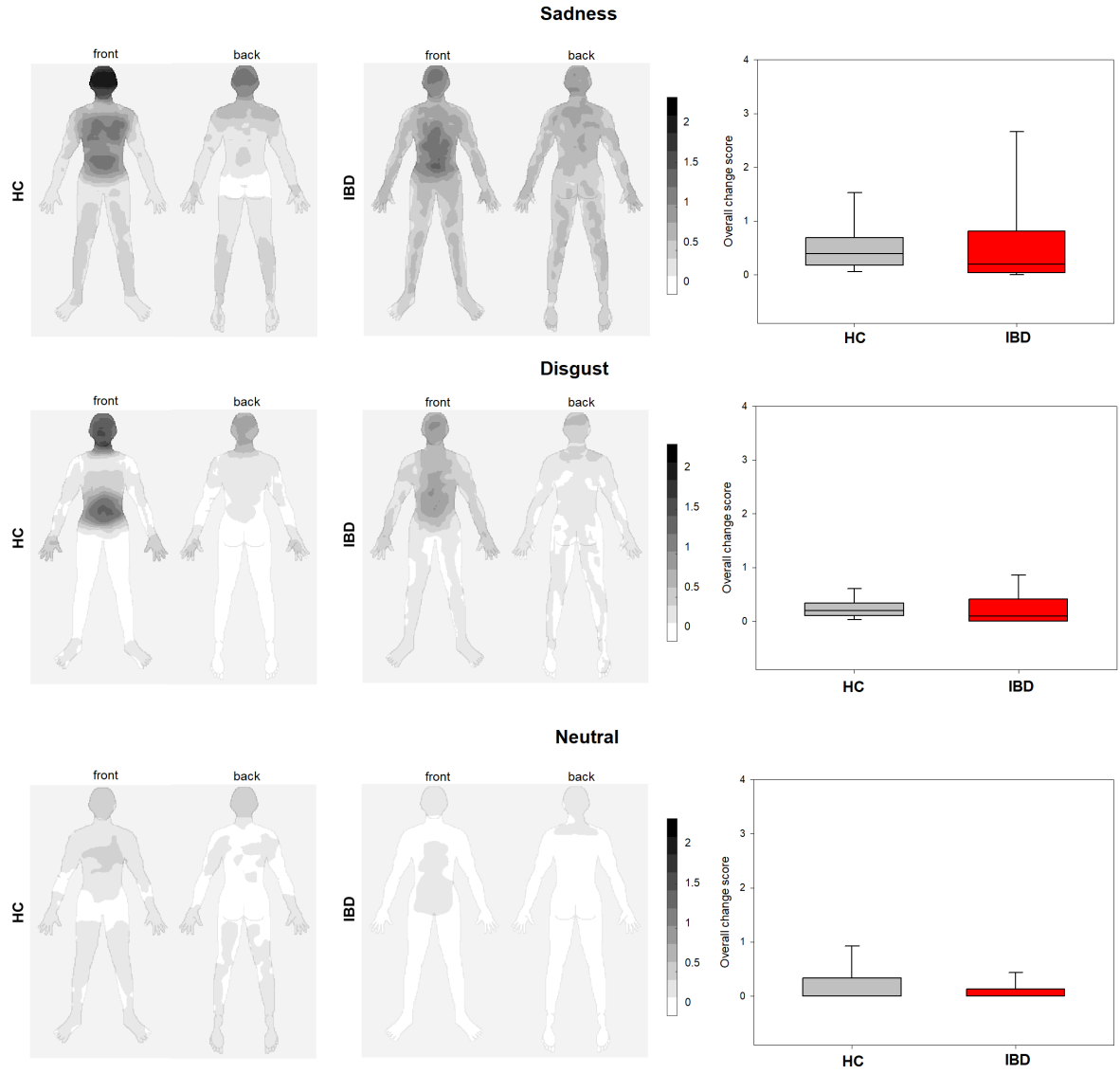

Figure S5. Perceived changes in the bodily sensations for the experience of sadness, disgust, and a neutral emotional state.

Table S6. Group effects according to the 2 × 2 rank-aligned ANOVA with whole-body scores

	F	*p*-value		η_p^2
Happiness				
Group	15.02	<.001	***	.153
Type of change	192.40	<.001	***	.699
Group*Type of change	14.35	<.001	***	.147
Sadness				
Group	0.97	.328		.012
Type of change	4.77	.032	*	.054
Group*Type of change	2.28	.135		.027
Anger				
Group	18.58	<.001	***	.158
Type of change	105.85	<.001	***	.561
Group*Type of change	10.53	.002	**	.113
Fear				
Group	14.72	<.001	***	.151
Type of change	61.57	<.001	***	.426
Group*Type of change	10.06	.002	**	.108
Disgust				
Group	9.30	.003	**	.101
Type of change	112.80	<.001	***	.576
Group*Type of change	7.59	.007	**	.084
Surprise				
Group	16.36	<.001	***	.165
Type of change	126.28	<.001	***	.603
Group*Type of change	19.11	<.001	***	.187

df = 1, 83; * $p < .05$, ** $p < .01$, *** $p < .001$

Table S7. Group comparisons for the reported changes in the bodily sensations across all pre-defined ROI

	HC (n = 44) (Mdn)	IBD (n = 41) (Mdn)	*Z*	*p*-value	
Happiness					
Head	1.28	1.26	-1.05	.293	
Chest	0.97	0.73	-1.70	.089	(*)
Upper limbs	0.28	0.03	-1.75	.080	(*)
Abdomen	0.11	0.55	-0.13	.899	
Lower limbs	0.00	0.00	-0.54	.591	
Back	0.01	0.00	-1.17	.243	
Sadness					
Head	1.51	0.37	-2.60	.009	**
Chest	0.77	0.53	-0.63	.530	
Upper limbs	0.09	0.00	-2.08	.038	*
Abdomen	0.27	0.59	-0.94	.346	
Lower limbs	0.00	0.00	-0.13	.896	
Back	0.00	0.00	-0.13	.900	
Anger					
Head	1.75	0.97	-2.63	.009	**
Chest	1.10	0.55	-1.73	.084	(*)
Upper limbs	0.53	0.00	-3.86	< .001	***
Abdomen	0.53	0.01	-0.39	.696	
Lower limbs	0.00	0.00	-0.64	.526	
Back	0.02	0.00	-2.83	.005	**
Fear					
Head	1.68	0.50	-2.41	.016	*
Chest	1.09	0.13	-2.88	.004	**
Upper limbs	0.12	0.00	-1.86	.063	(*)
Abdomen	0.40	0.00	-2.29	.022	*
Lower limbs	0.03	0.00	-2.08	.037	*
Back	0.05	0.00	-2.36	.019	*
Disgust					
Head	0.67	0.36	-2.15	.031	*
Chest	0.38	0.02	-0.97	.330	
Upper limbs	0.00	0.00	-0.34	.736	
Abdomen	0.30	0.00	-1.45	.146	

Lower limbs	0.00	0.00	-0.74	.462	
Back	0.00	0.00	-1.40	.162	
Surprise					
Head	1.16	0.39	-2.01	.045	*
Chest	0.78	0.16	-2.59	.010	*
Upper limbs	0.03	0.00	-2.41	.016	*
Abdomen	0.04	0.00	-0.40	.687	
Lower limbs	0.00	0.00	-0.24	.812	
Back	0.00	0.00	-2.03	.042	*
Neutral					
Head	0.00	0.00	-1.23	.220	
Chest	0.00	0.00	-1.06	.291	
Upper limbs	0.00	0.00	-1.68	.093	(*)
Abdomen	0.00	0.00	-0.30	.766	
Lower limbs	0.00	0.00	-0.92	.359	
Back	0.00	0.00	-0.80	.421	

(*) $p < .10$, * $p < .05$, ** $p < .01$, *** $p < .001$

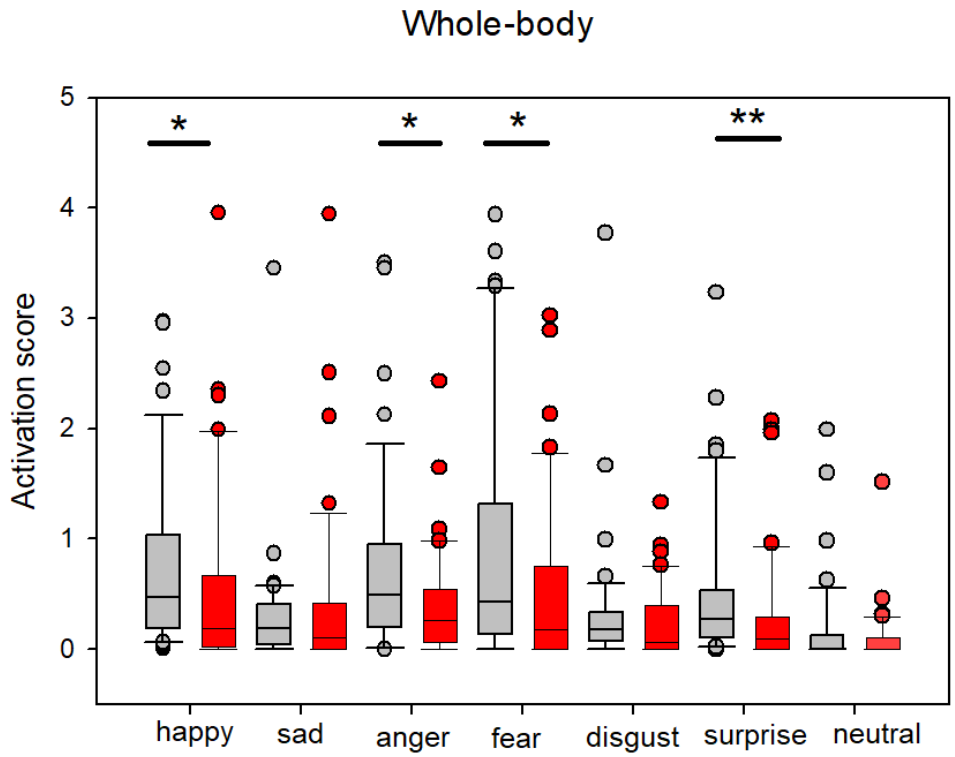

Figure S6. Bodily activation associated with the experience of the six basic emotions in IBD (red) and HC (grey). * $p < .05$, ** $p < .01$

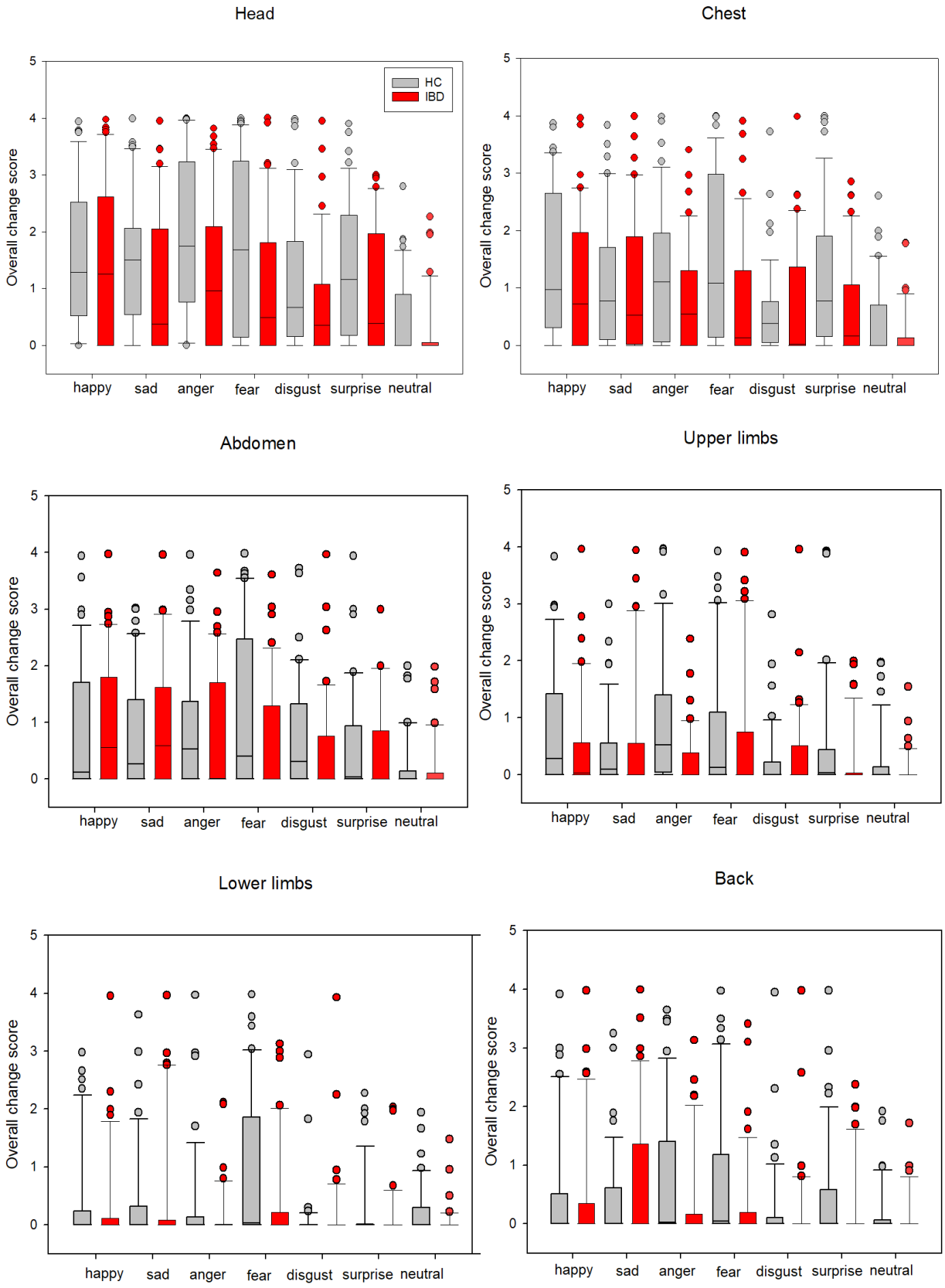

Figure S7. Box plots visualizing the medians and data ranges of the reported overall bodily changes across all ROI.

Table S8. Results of the 2 × 2 ANOVA with ROI scores

	Group			Type of change			Group*Type of change		
	F	p		F	p		F	p	
Head									
Happiness	9.99	.002	**	225.01	<.001	***	8.35	.005	**
Sadness	9.51	.003	**	26.54	<.001	***	5.24	.025	*
Anger	22.44	<.001	***	96.13	<.001	***	9.75	.002	**
Fear	19.28	<.001	***	79.12	<.001	***	10.65	.002	**
Disgust	11.13	.001	**	78.19	<.001	***	8.95	.004	**
Surprise	15.13	<.001	***	127.36	<.001	***	20.80	<.001	***
Neutral	6.22	.015	*	12.35	.001	**	3.93	.051	(*)
Chest									
Happiness	14.39	<.001	***	152.40	<.001	***	15.08	<.001	***
Sadness	1.21	.274		11.56	.001	**	0.17	.680	
Anger	16.65	<.001	***	67.49	<.001	***	8.43	.005	***
Fear	18.74	<.001	***	61.50	<.001	***	12.43	.001	***
Disgust	6.50	.013	*	55.09	<.001	***	2.12	.150	
Surprise	15.66	<.001	***	110.33	<.001	***	18.80	<.001	***
Neutral	5.02	.028	*	9.15	.003	**	4.05	.047	*
Abdomen									
Happiness	5.02	.028	*	71.78	<.001	***	4.87	.030	*
Sadness	1.20	.276		2.32	.131		0.90	.345	
Anger	5.67	.020	*	41.59	<.001	***	7.57	.007	**
Fear	10.50	.002	**	34.57	<.001	***	4.24	.043	*
Disgust	9.39	.003	**	38.61	<.001	***	11.79	<.001	***
Surprise	3.24	.075	(*)	35.68	<.001	***	4.45	.038	*
Neutral	0.92	.341		6.11	.015	*	1.57	.214	
Arms									
Happiness	15.00	< .001	***	55.95	< .001	***	16.87	<.001	***
Sadness	1.45	.231		1.82	.181		0.02	.887	
Anger	16.05	< .001	***	29.69	< .001	***	8.96	.004	**
Fear	7.13	.009	**	30.99	< .001	***	6.36	.014	*
Disgust	3.00	.087	(*)	14.14	< .001	***	0.75	.389	
Surprise	9.25	.003	**	25.86	< .001	***	8.26	.005	**
Neutral	5.11	.026	*	5.52	.021	*	2.41	.124	
Back									
Happiness	6.44	.013	*	31.15	< .001	***	3.82	.054	(*)
Sadness	0.37	.544		0.68	.412		0.01	.926	
Anger	8.72	.004	**	22.08	< .001	***	6.53	.012	*
Fear	9.23	.003	**	18.43	< .001	***	3.55	.063	(*)
Disgust	1.23	.270		9.18	.003	**	0.61	.436	
Surprise	7.26	.009	**	22.84	< .001	***	7.87	.006	**
Neutral	1.72	.193		2.70	.104		0.93	.337	
Legs									
Happiness	4.63	.034	*	31.06	< .001	***	5.58	.020	*
Sadness	3.13	.080	(*)	7.90	.006	**	0.00	.967	
Anger	1.78	.186		1.55	.216		0.37	.542	
Fear	9.23	.003	**	18.43	< .001	***	3.55	.063	(*)
Disgust	0.57	.454		1.98	.163		0.94	.336	
Surprise	1.54	.218		16.71	< .001	***	2.70	.104	
Neutral	0.52	.474		0.17	.681		0.01	.931	

Note: df's=1,83; (*) $p < .10$, * $p < .05$, ** $p < .01$, *** $p < .001$

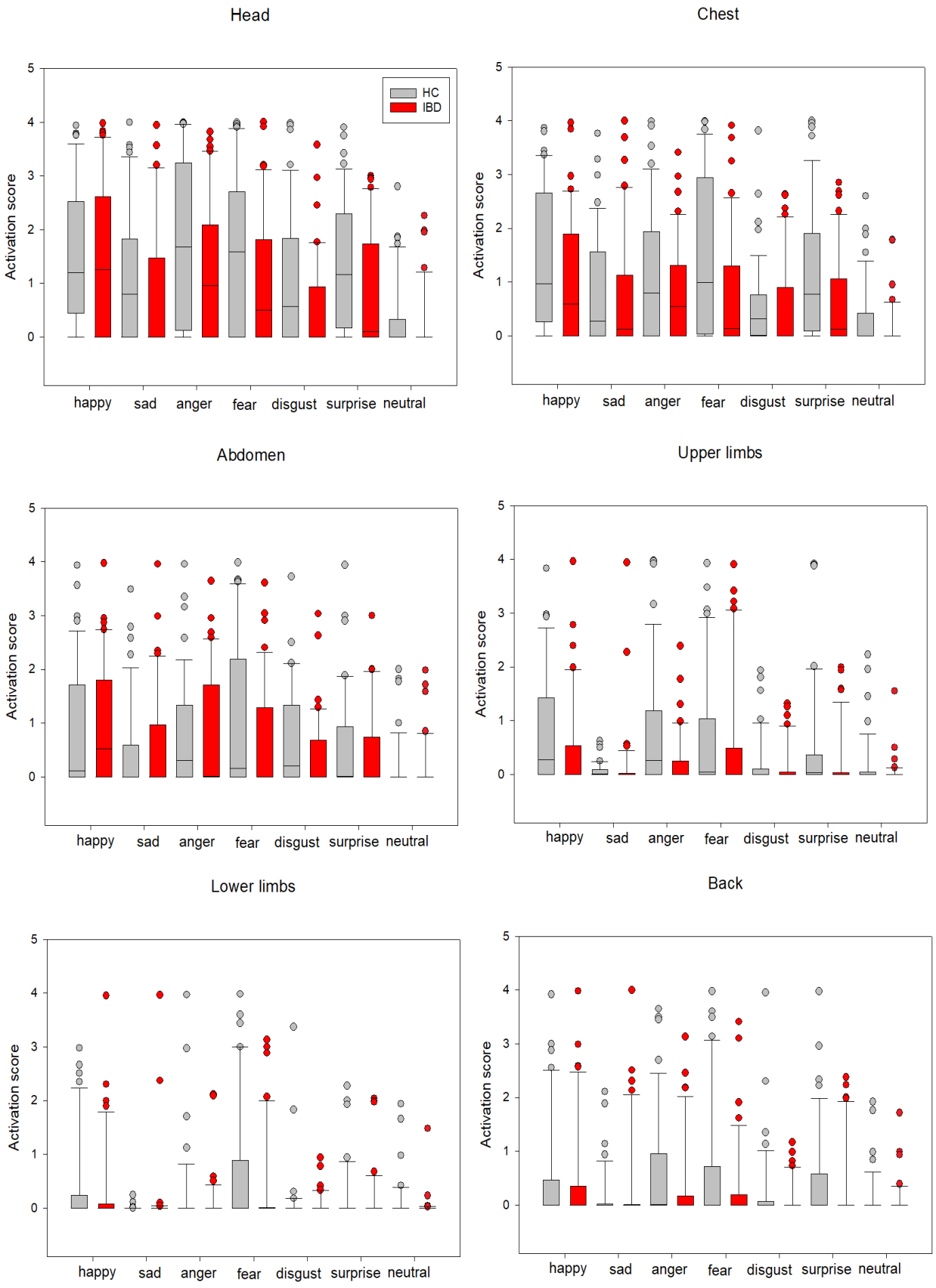

Figure S8. Box plots visualizing the medians and data ranges of the reported bodily activation across all ROI.

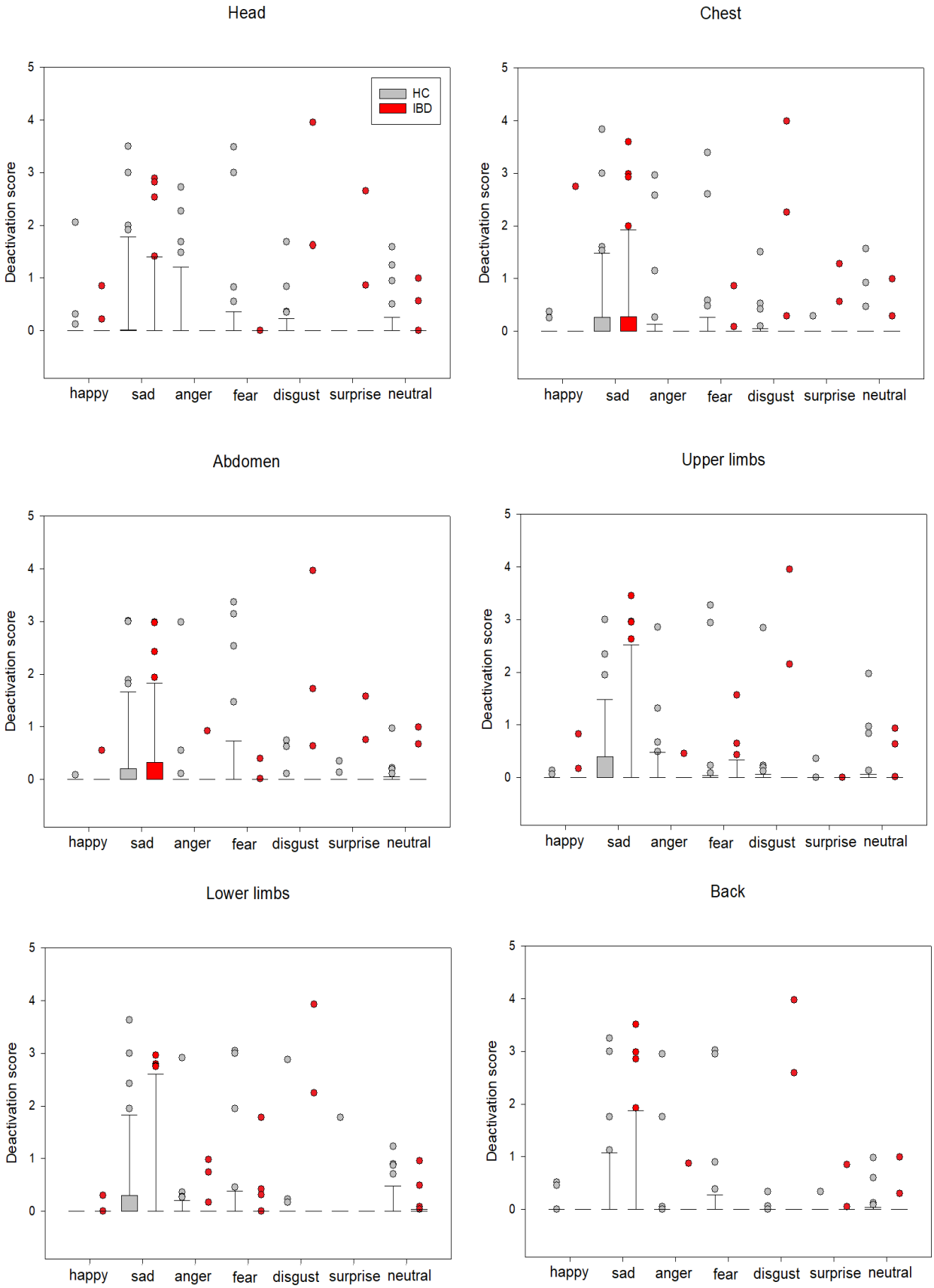

Figure S9. Box plots visualizing the medians and data ranges of the reported bodily deactivation across all ROI.

Table S9. Correlations between Emotional Awareness and the reported whole-body overall change scores

	Whole sample		**HC**		**IBD**		**HC vs. IBD**	
	r_s	p	r_s	p	r_s	p	Z	p
Emotional Awareness								
Happiness	**.265**	**.014**	**.391**	**.009 ****	**.357**	**.022 ***	0.18	.430
Sadness	.189	.083 (*)	**.365**	**.015 ***	.213	.180	0.37	.230
Anger	.175	.109	**.332**	**.028 ***	.284	.071 (*)	0.24	.407
Fear	.157	.152	**.407**	**.006 ****	.201	.207	1.01	.155
Disgust	.064	.560	-.005	.974	.252	.112	-1.17	.122
Surprise	.033	.762	.169	.274	.106	.511	0.29	.388

IBD, inflammatory bowel disease; HC, healthy control participants

(*) $p < .10$, * $p < .05$, ** $p < .01$

2.4 Research Question IV| Body evaluation and body ownership in patients with inflammatory bowel disease: the role of interoceptive sensibility and adverse childhood experiences

2.4.1 Abstract

Background: Inflammatory bowel diseases (IBD) are often accompanied by symptoms which might affect the patients' body representation such as their body evaluation and body ownership. The aim of this study was to investigate alterations in these body representations in IBD and their link to interoceptive sensibility, gastrointestinal-specific anxiety, self-esteem, and history of childhood maltreatment.

Methods: Body evaluation and body ownership was assessed in 41 clinically remitted IBD patients and 44 healthy controls (HC) using a topographical self-report method. Rating scores were computed for the whole-body as well as for the abdomen, the back, and the head as regions of interest related to the experience of pain. Interoceptive sensibility, gastrointestinal-specific anxiety and a history of childhood maltreatment were assessed via self-report questionnaires.

Results: A more negative body evaluation of the abdomen was linked to higher gastrointestinal-specific anxiety, while patients reporting higher levels of interoceptive sensibility perceived their bodies in a more positive manner. While no differences were found for body evaluation, IBD patients reported lower sense of ownership for their abdomen. Moderation analyses indicated that among IBD patients, the strength of the association between interoceptive sensibility and ownership for the abdomen was dependent on the reported severity of childhood trauma.

Conclusions: Altered body representations of areas associated with the experience of disease-related pain are linked to higher symptom-specific anxiety and lower levels of interoceptive sensibility in IBD. Particularly in patients with a history of childhood maltreatment, higher levels of interoceptive sensibility might have a beneficial effect on the patients' ownership for the disease affected body region.

2.4.2 Introduction

Inflammatory bowel diseases (IBD) are chronic immune-mediated inflammatory conditions of the gastrointestinal tract, hallmarked by severe symptoms known to negatively affect how patients perceive their bodies (Cushman et al., 2021). From a clinical point of view, two facets of body representations are of particular interest in IBD: body evaluation, that is, individual's attitude towards the own body, and body ownership, the sense that the body is belonging to oneself. Several studies have demonstrated dysfunctional body-related attitudes in patients with IBD, characterized by lower levels of body satisfaction (Claytor et al., 2020; Cushman et al., 2021; McDermott et al., 2015; Saha et al., 2015). Moreover, IBD symptoms can be experienced as an attack originating from within the body, affecting patient's experience of the body as own (Finotti & Costantini, 2016). To date, little is known about the role of specific psychological factors in those facets of body representations in IBD.

Contemporary findings have emphasized the important role of body signals perception and their appraisal for how individuals perceive their bodies, suggesting poorer interoceptive abilities to be associated with decreased levels of body satisfaction (Badoud & Tsakiris, 2017; Emanuelsen et al., 2015; Todd et al., 2019a). While patients with IBD do not differ in their objective ability to perceive visceral sensations (interoceptive accuracy), they appraise these differently (interoceptive sensibility) compared to unaffected individuals (Atanasova et al., 2021). Furthermore, IBD patients reporting greater levels of gastrointestinal-specific anxiety (GSA) experience disease-related bodily sensations as more distressing (Labus et al., 2007), which can aggravate disturbances in patients' body representations. Although no study has investigated the role of interoceptive processes in how patients with IBD evaluate their bodies, it is conceivable that alterations in their interoceptive sensibility and GSA might contribute to the development and maintenance of body perception disturbances during the disease course.

The sense of body ownership arises from the multisensory integration of interoceptive and exteroceptive cues. For that reason, the extent to which one perceives their body as belonging to themselves depends on individual's sensitivity to their bodily signals (Crucianelli et al., 2018; Suzuki et al., 2013; Tsakiris et al., 2011). While some previous evidence has indicated impairments in the multisensory integration in patients with immune-mediated diseases, resulting in disturbed sense of body ownership (Finotti & Costantini, 2016), no study has investigated this topic in IBD populations yet. As IBD patients tend to pay greater attention

to their disease-related visceral signals (Srinath et al., 2014), this might be linked to a stronger perception of the body as "their own" as it is the "own" body that experiences these symptoms. However, as body ownership depends on the constant flow of sensory input, the occurrence of pain symptoms over a prolonged period of time may promote alterations in the integration of interoceptive signals, resulting in a disturbed sense of ownership for the affected part of the body (Cordier et al., 2020; Lewis et al., 2007; Solcà et al., 2020).

Body representation disturbances have been repeatedly observed not only in medical conditions (Finotti & Costantini, 2016; Hassani et al., 2020; Markey et al., 2020) but also in several mental disorders (Dyer et al., 2013b; Löffler et al., 2020; Scheffers et al., 2017b). Especially experiences of adversity during childhood and adolescence seem to negatively affect how individuals perceive their bodies in adulthood. Adverse childhood experiences (ACE) are often characterized by physical traumata, resulting in stronger feelings of detachment from one's own body, a diminished sense of body ownership (Löffler et al., 2020) and more negative body-related attitudes (Dyer et al., 2013b). Although newer findings have indicated higher rates of histories of ACE among patients with IBD (Wan et al., 2022; Witges et al., 2019), no study has investigated its links to body evaluation and body ownership in this clinical population yet.

Thus, the aim of the present study was to examine the complex interplay of body representations, interoception, GSA, and history of childhood maltreatment in IBD. We hypothesized that compared to healthy individuals, IBD patients will (I.) report a more negative body evaluation and (II.) this more negative body evaluation will be associated with higher GSA, lower interoceptive sensibility, lower self-esteem, and a history of ACE. Furthermore, we expected the IBD group to (III.) report greater levels of whole-body ownership due to patients' increased attention towards their disease-related bodily sensations and that (IV.) higher interoceptive sensibility in IBD will be linked to stronger whole-body ownership. Finally, we expected that (V.) a history of ACE will be negatively associated with body ownership and will (VI.) moderate the association between body ownership and interoceptive sensibility in IBD.

2.4.3 Methods

Participants

The study was approved by the Ethics Committee of the Medical Faculty Mannheim at Heidelberg University and all participants gave their written informed consent before participating in the study. The hypotheses, sample size, methods, exclusion criteria, and planned analyses were preregistered before data collection and can be accessed at https://aspredicted.org/blind.php?x=hu4n7k. All aspects of the study were carried out in accordance with the pre-registered protocol unless stated otherwise. Note that due to length restrictions only data on body evaluation and ownership are reported in the present manuscript. Data on emotion-specific bodily sensations, as described in the same preregistration, will be reported in a separate article.

In total, 86 individuals (age 18 - 65 years) participated in the study. Of these, 42 met the diagnostic criteria for IBD and 44 were healthy control participants (HC). We excluded one participant of the IBD group, since she/he did not understand the instructions of the experimental task correctly. Thus, the final sample consisted of 41 IBD patients (20 female, 21 male) and 44 HC (30 female, 14 male). Exclusion criteria for the HC group were chronic medical conditions, chronic medication intake, use of psychotropic medication, and current or past neurological or psychiatric diseases as well as general gastrointestinal complaints (e.g., abdominal pain, diarrhoea, constipation) during the last 4 weeks prior to the experiment. IBD outpatients were recruited from the IBD outpatient unit at the University Medical Centre Mannheim during the routinely control visits and invited to participate in the study. Patients, who met the inclusion and exclusion criteria and provided written informed consent, took part in the study after the physical examination. Overall, 29 patients with Crohn's disease (CD) and 12 patients with ulcerative colitis (UC) in clinical remission (Harvey-Bradshaw Index < 5; Partial Mayo Score ≤ 3; fecal calprotectin < 200 mg/kg; C-reactive protein < 5 mg/L) were included in the IBD group. We focused on IBD patients in clinical remission to avoid potentially confounding effects of active disease symptoms (e.g., strong abdominal pain) on the body evaluation and body ownership measures. Diagnostic procedures and gastroenterological examinations were carried out on all patients by fully trained physicians specialized in the care of patients with IBD. Exclusion criteria were biological signs of disease activity (faecal calprotectin level in mg/kg > 200; C-reactive protein > 5 mg/L), current use of corticosteroids,

use of psychotropic medications and current or past neurological or psychiatric diseases. For further details on sample characteristics see Table 5.1. Details on treatment medication, disease duration, symptoms severity, extraintestinal manifestations, history of further somatic diseases, and disease-related surgeries is provided in Table S2, supplemental material S2.

All participants answered a battery of psychometric questionnaires assessing psychological distress, GSA, interoceptive sensibility, self-esteem, and histories of childhood maltreatment. After completing these, participants performed a computer-based task, assessing their body evaluation, body ownership and the experience of pain in the body.

Questionnaires

Brief Symptom Inventory (BSI-18)

Psychological distress was assessed with the Brief Symptom Inventory (BSI-18) (Franke et al., 2011). BSI-18 is a self-report measure of somatization, depression, and anxiety (subscale range: 0-24). The three subscales with 6 items each are combined into a Global Severity Index (GSI) (GSI range: 0-72). Higher scores indicate higher symptom severity. Cronbach's α for the 18 items was .86 in the IBD group and .81 in the HC group.

Affective state

To control for participant's levels of anxiety at the time of investigation, all participants were asked to complete the state version of the State-Trait Anxiety Inventory (STAI; Spielberger et al. (1983)). STAI is a 20-item scale, which measures subjective feelings of apprehension, tension, nervousness, worry, and activation of the autonomic nervous system on a 4-point Likert scale. Item scores are added to obtain the scale total score (range: 20 to 80), with higher scores indicating higher anxiety. Internal consistency was good with Cronbach's $\alpha = 0.76$ in the IBD sample and .90 in the HC group.

Additionally, arousal, valence, and dominance levels were assessed via the Self-Assessment Manikin (SAM) (Bradley & Lang, 1994). SAM is a non-verbal pictorial assessment technique that measures valence/pleasure, perceived arousal, and perceptions of dominance on a 9-point Likert scale. Higher scores indicate greater positive valence, higher arousal, and higher perceived dominance.

Visceral Sensitivity Index (VSI)

Gastrointestinal-specific anxiety (GSA) was measured with the Visceral Sensitivity Index (VSI) (Labus et al., 2004). The 15-item scale assesses worry, fear, vigilance, sensitivity, and avoidance as well as gastrointestinal-related cognitions and behaviours. Items are scored on a reversed 6-point scale with an overall VSI score (range: 0-75), with higher scores indicating more severe GSA. VSI has been developed specifically for patients with functional gastrointestinal disorders. For that reason, we utilized this self-report measure in the IBD group only. The internal consistency of this scale for the current IBD sample was good, with Cronbach's $\alpha = 0.89$.

Multidimensional Assessment of Interoceptive Awareness (MAIA)

Interoceptive sensibility was assessed using the Multidimensional Assessment of Interoceptive Awareness (MAIA) (Mehling et al., 2012). The 32-item self-report questionnaire provides a multidimensional profile of interoceptive sensibility, including the following eight subscales: *Noticing*, *Not-Distracting*, *Not-Worrying*, *Attention Regulation*, *Emotional Awareness*, *Self-Regulation*, *Body Listening*, and *Trusting* (subscale range: 0-5). Higher scores indicate higher interoceptive sensibility. As we did not have specific hypotheses regarding the link between these different aspects of interoceptive sensibility and body representations, only the mean MAIA total score (range: 0-40) was used for statistical analyses. MAIA revealed good internal consistency with Cronbach's $\alpha = 0.91$ in the IBD group and $\alpha = .94$ in the HC group.

Rosenberg Self-Esteem Scale (RSES)

Self-esteem was assessed using the Rosenberg Self-Esteem Scale (Rosenberg, 1965). The 10-item self-report questionnaire measures general self-esteem on a 4-point Likert scale, with higher scores indicating greater self-esteem. Cronbach's α in the current sample was .86 in the IBD group and .85 in the HC group.

Adverse childhood experiences

The German version of the Childhood Trauma Questionnaire (CTQ) (Klinitzke et al., 2012) was used to assess the history of childhood maltreatment. The 28-item questionnaire consists of five subscales including *Emotional abuse*, *Physical abuse*, *Sexual abuse*, *Emotional neglect*,

and *Physical neglect* (subscale range: 0-25) as well as a total score (range: 0-125). Higher CTQ scores indicate a severer history of childhood adversities.

Lifetime traumatic experiences and post-traumatic stress symptoms

All participants were screened for potentially traumatic life events using the Life Events Checklist for DSM-5 (LEC-5) (Weathers et al., 2013), a self-report measure assessing the exposure to 16 events known to potentially result in PTSD or distress. LEC-5 distinguishes not only between event types but also between the ways a person was exposed to the stressor. For each participant, the number of personally experienced traumatic events (direct exposure) was summed up, resulting in a single sum score (range: 0-16). Severity of PTSD symptoms was evaluated with the PTSD Checklist for DSM-5 (PCL-5) (Weathers et al., 2013), that is, a 20-item self-report measure assessing the presence and severity of posttraumatic stress. Items correspond with DSM-5 criteria for PTSD including intrusion symptoms, avoidance, negative alterations in cognitions and mood, and alterations in arousal and reactivity during the last 4 weeks (range: 0-80). Higher scores indicate higher PTSD symptoms severity.

Experimental procedure and dependent variables

Participants were asked to appraise their body evaluation and body ownership using a topographical self-report method adapted from Nummenmaa et al. (Nummenmaa et al., 2014) and customized for the purposes of this study. At the beginning of the task, participants were familiarized with the concepts of body evaluation and body ownership. In two separate trials, respondents were shown two blank silhouettes of the front and the back of a human body and were asked to colour the areas of the bodies according to a) their subjective evaluation of each body area or b) the extent to which they feel a body area as belonging to themselves. To indicate their response, participants could choose different colours from a pre-defined colour bar to paint the corresponding body areas by successive strokes or continuous painting with a computer mouse. Participants evaluated to what extent they like their bodies and to what extent they perceive their bodies as belong to themselves on a 9-point colour bar ranging from blue (-4= “very much dislike”; “does not belong to myself”) to red (4 = “very much like”; “belongs to myself”). In two additional trials, participants’ pain experience at the time of the experiment and during the preceding four weeks was assessed using a 5-point colour bar corresponding to the different intensities of the perceived pain (0 = “no pain at all” to 4 = “very strong pain”).

All four instructions were presented in a pseudorandomized order. The task was presented on a 14'' computer screen. Front and back body templates comprised 366 x 195 pixels and the diameter of the painting tool was 12 pixels. The task was programmed using Presentation® software (Version 18.0, Neurobehavioral Systems, Inc., Berkeley, CA, www.neurobs.com). For each participant, we calculated a whole-body score and scores for the regions of interest (ROI) defined by the reported experience of pain. Computations were done after applying a spatial smoothing of 3
pixels at a single-subject level by averaging the colour code value of each coloured pixel and its surrounding pixels.

Whole-body scores:

First, whole-body scores were averaged separately for each participant and experimental condition across the colour codes of all pixels of the presented body template, which were coloured by the participant.

Pain-related ROI:

Based on the reported mean pain ratings across all participants, pain-related ROI were defined as pixels with a mean pain intensity ≥ 1.60 during the preceding four weeks (Figure 12A). Three distinct body areas were identified: head (ROI size: 757 pixels), abdomen (2227 pixels) and back (877 pixels) (see Figure S10, S11 in supplemental material S4). Since we aimed to investigate IBD-specific alterations in body representations, we decided to differentiate between disease-specific (DS: abdomen) and disease-unspecific (DU: head, back) ROI. For these two ROI, intensity scores were averaged separately for each participant and experimental condition. Whole-body and ROI analyses were performed using custom pipelines run with MATLAB 2020a (The MathWorks, Inc.).

Table 5.1 Sample characteristics

	HC (M±SD)		IBD (M±SD)		Test-statistics	p-value	
Demographics							
Age	36.11	±12.29	40.20	±13.87	1.44 [a]	.154	
Sex (female/male)	30/14		20/21		3.30 [b]	.069	
BMI	24.16	±4.72	26.65	±6.46	1.99 [a]	.050	*
Years of education	12.84	±2.40	12.32	±3.01	-0.89 [a]	.376	
MWT-B	30.09	±3.60	29.84	±3.57	-0.77 [a]	.443	
Affective state							
STAI Anxiety (state)	32.66	±8.20	33.13	±5.28	0.31 [a]	.754	
SAM-Valence	3.77	±0.85	3.75	±0.98	-0.11 [a]	.911	
SAM-Arousal	1.98	±0.86	2.34	±1.00	1.78 [a]	.079	
SAM-Dominance	3.68	±0.66	3.63	±0.98	-3.41 [a]	.734	
Psychological distress							
GSI	4.42	± 4.91	10.42	± 8.74	3.66 [a]	<.001	***
Somatization	0.74	± 1.27	3.97	± 3.51	5.31 [a]	<.001	***
Depression	1.58	± 2.81	3.00	± 3.80	1.85 [a]	.040	*
Anxiety	2.09	± 2.22	3.78	± 3.65	2.45 [a]	.020	*
Interoceptive sensibility							
MAIA	2.57	±0.54	2.58	±0.57	0.70 [a]	.944	
Visceral sensitivity							
VSI	-	-	27.42	±15.28	-	-	
Self-esteem							
RSES	34.86	±4.33	33.54	±5.26	-1.23 [a]	.222	

IBD, inflammatory bowel diseases group; HC, healthy controls group; BMI, Body-Mass Index; MWT-B, Multiple Choice Word Test-B; STAI, State-Trait Anxiety Inventory; SAM, Self-Assessment Manikin; GSI, General symptom index; MAIA, Multidimensional Assessment of Interoceptive Awareness; VSI, Visceral sensitivity index; RSES, Rosenberg Self-Esteem Scale. * $p < .05$, *** $p < .001$, [a] t-value, [b] Chi^2.

Data analysis

Whole-body and ROI scores were compared between both groups using Mann-Whitney U tests separately for body evaluation, body ownership and pain ratings. To analyse covariation between body representation scores and participants' interoceptive sensibility, history of ACE, and self-esteem, Spearman's rank correlation coefficients were computed. Additionally, we analyzed the association between body representations and GSA in the IBD group using Spearman's rank correlation coefficients. To test ACE severity as potential moderator of the association between body ownership and interoceptive sensibility, a moderation analysis with bootstrapping (5,000 samples with replacement) was applied (PROCESS SPSS macro version 3.5.2) (Hayes, 2017). Since the observed variance within the different types of ACE was rather low, contrary to our preregistered hypotheses, we used the CTQ total scores instead of the subscale scores for physical and sexual abuse to perform these moderation analyses.

Statistical analyses were carried out with SPSS v.25.0 (IBM Corp., USA). For all analyses, statistical significance was set to $p < .05$. The level of confidence for all reported confidence intervals was set to 95%. To control for multiple testing, we applied a false-discovery rate (FDR) correction according to Benjamini & Hochberg (1995) (Benjamini & Hochberg, 1995) and reported the corresponding *p*-values indicated this by the subscript p_{FDR}. For whole-body scores, FDR correction was applied for the number of instructions being compared, while for group comparisons of the ROI scores within each instruction, *p*-values were adjusted according to the number of ROI.

Table 5.2 Sample characteristics including a history of childhood trauma, traumatization in later life, and PTSD symptoms severity.

	HC (M±SD)		IBD (M±SD)		Test-statistics	p-value	
Trauma history							
Childhood trauma							
CTQ total	36.06	±7.00	35.73	±10.77	-0.15 [a]	.881	
CTQ - EA	8.51	±2.96	8.18	±3.73	-0.41 [a]	.684	
CTQ - PA	5.80	±1.60	6.27	±2.53	0.92 [a]	.362	
CTQ - SA	5.14	±0.55	5.55	±2.00	1.12 [a]	.272	
CTQ - EN	9.63	±3.29	8.91	±3.79	-0.84 [a]	.405	
CTQ - PN	6.97	±1.71	6.81	±2.34	-0.31 [a]	.758	
Lifetime trauma							
LEC-5	1.11	±1.30	1.52	±1.56	1.15 [a]	.254	
PTSD symptoms							
PCL-5 total	5.54	±5.94	15.47	±12.37	4.13 [a]	<.001	***
Cluster B	1.43	±1.95	4.25	±3.69	3.86 [a]	<.001	***
Cluster C	0.74	±1.20	1.81	±2.13	2.50 [a]	<.013	*
Cluster D	1.86	±2.79	4.16	±3.55	2.96 [a]	.004	**
Cluster E	1.43	±1.70	4.84	±4.52	4.02 [a]	<.001	***

IBD, Inflammatory bowel diseases group; HC, healthy control group; CTQ, Childhood trauma questionnaire; EA: emotional abuse, PA: physical abuse, SA: sexual abuse, EN: emotional neglect, PN: physical neglect; LEC-5, Life events checklist; PTSD, post-traumatic stress disorder; PCL-5, Post-traumatic stress disorder checklist for DSM-V; Cluster B = intrusion symptoms, Cluster C = avoidance, Cluster D = negative alterations in cognitions and mood, Cluster E = alterations in arousal and reactivity, * $p < .05$, *** $p < .001$, [a] Mann-Whitney U, [b] Chi^2.

2.4.4 Results

Whole-body and ROI analyses

For illustrative purposes, grand averages of the body topographies are displayed for each group and experimental condition with body silhouettes as overlays (Figure 12). Whole-body analyses revealed no differences between IBD patients and HC either for their pain experience during the experiment (U (n_{IBD} = 41, n_{HC} = 44) = 787.00, p = .299, p_{FDR} = .598) or the preceding four weeks (U = 855.50, p = .826, p_{FDR} = .826), their body evaluation (U = 807.50, p = .913, p_{FDR} = .913) or body ownership (U = 560.50, p = .094, p_{FDR} = .188).

ROI analyses revealed stronger pain experience in the abdomen in the IBD group compared to HC during task solving (U = 622.00, p = .001, p_{FDR} = .002) as well as during the last four weeks (U = 550.00, p = .001, p_{FDR} = .002). While both groups did not differ in their evaluation of this body area (U = 666.50, p = .862, p_{FDR} = .862), IBD patients experienced the abdomen as significantly less belonging to themselves compared with HC (U = 453.00, p = .012, p_{FDR} = .024; IBD: Median (*Mdn*) = 2.99; HC: *Mdn* = 3.83). There were no group differences for DU-ROI (all $p_{FDR} \geq .526$; see Table 5.3). Both groups did not differ in the number of coloured pixels either for body evaluation or body ownership trials (for more information see supplemental material S4, Table S10).

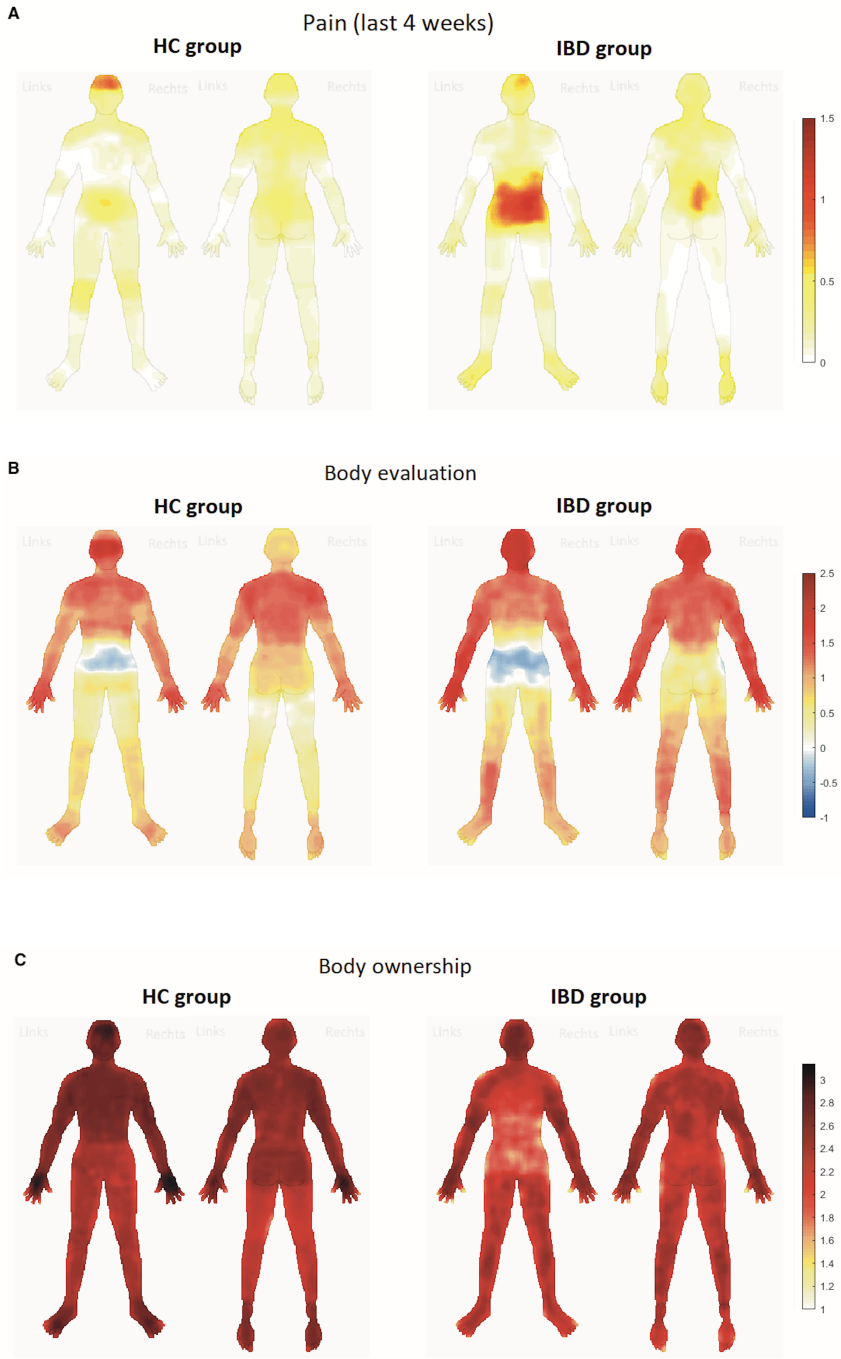

Figure 12. Grand averages of the body topographies for (A) reported pain experience during the last four weeks preceding the experiment (0/white = "no pain at all"; 4/red= "very strong pain"), (B) body evaluation (-4/blue = "very much dislike"; 4/red= "very much like"), and (C) body ownership (-4/blue= "does not belong to myself"; 4/red= "belongs to myself"). Note: for illustration purposes the colour bars have been adjusted differentially to the range of values for the different instructions.

Correlation analyses

Associations of body evaluation and body ownership with gastrointestinal-specific anxiety

A more negative evaluation of the abdomen, but not of the whole body or of the DU-ROI (all $p_{FDR} \geq .130$), was related to higher GSA in the IBD group (r_s =-.373, p = .033, Figure 13). However, this association did not survive the correction for multiple comparisons (p_{FDR} = .066). Body ownership was not associated with GSA (all $p_{FDR} \geq .425$).

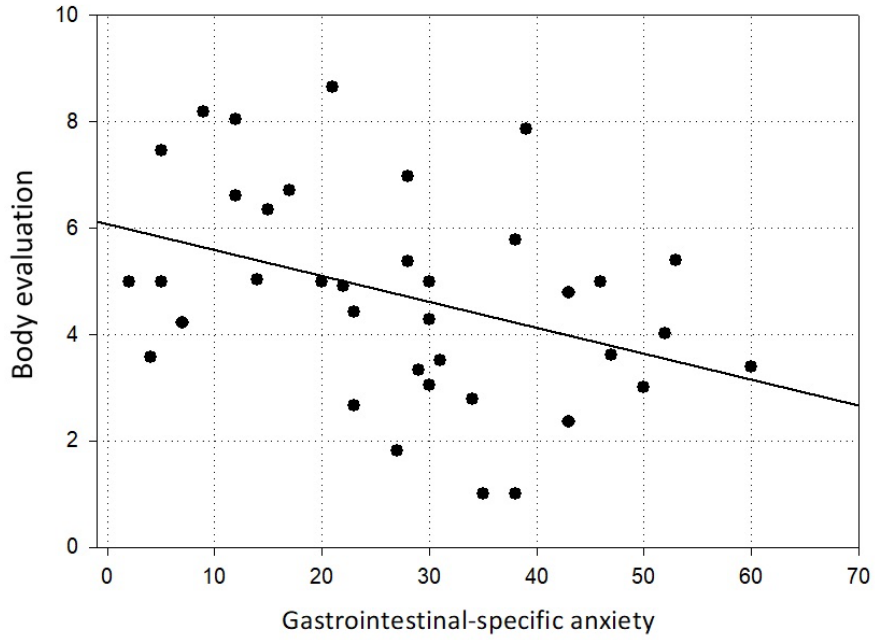

Figure 13. Association between gastrointestinal-specific anxiety (VSI total score) and body evaluation of the abdomen (0 = "very negative"; 9 = "very positive") among IBD patients. Participants reporting higher gastrointestinal-specific anxiety rated their abdomen as less positive, indicating higher body dissatisfaction with this pain-associated body area.

Associations of body evaluation and body ownership with interoceptive sensibility

Whole-body evaluation was not related to interoceptive sensibility across all participants (r_s = .187, p = .112, p_{FDR} = .149). Separate analyses for both groups revealed that this link was significant in the IBD group (r_s = .344, p = .038, p_{FDR} = .038), but not in the HC group (r_s = -

.060, $p = .707$, $p_{FDR} = .924$). A similar significant association was also found for the DS-ROI ($r_s = .366$, $p = .031$, $p_{FDR} = .038$) and DU-ROI scores ($r_s = .450$, $p = .007$, $p_{FDR} = .021$) among the IBD patients, indicating that a more positive evaluation of both disease-related and disease-unrelated body areas was associated with higher interoceptive sensibility. Interoceptive sensibility was not significantly linked to body ownership either across all participants (all $p_{FDR} \geq .185$), or in separate correlation analyses for the IBD and the HC group (all $p_{FDR} \geq .552$).

Table 5.3 Group differences in pain experience, body evaluation and body ownership. DS-ROI included the abdomen area, while DU-ROI included the head and the back.

	IBD (M±SD)		**HC (M±SD)**		**Mann-Whitney U**	**p-value**		
						p	p_{FDR}	
Pain experience								
Pain – last 4 weeks	1.61	± 0.64	1.62	± 0.84	855.50	.826	.826	
Pain – state	0.84	± 0.81	0.65	± 0.69	787.00	.299	.598	
DS-ROI – 4 weeks	1.18	± 1.10	0.49	± 0.92	550.00	.001	.002	**
DU-ROI – 4 weeks	0.72	± 0.80	0.49	± 0.92	884.50	.875	.875	
DS-ROI – state	0.56	± 0.87	0.08	± 0.32	622.00	.001	.002	**
DU-ROI – state	0.19	± 0.42	0.14	± 0.30	878.00	.772	.875	
Body evaluation								
Whole-body score	1.08	± 1.74	1.16	± 1.61	807.50	.913	.913	
DS-ROI	-0.14	± 2.36	0.01	± 2.43	666.00	.862	.862	
DU-ROI	1.59	± 1.69	1.49	± 1.55	641.00	.791	.791	
Body ownership								
Whole-body score	2.90	± 0.95	3.13	± 1.07	560.50	.094	.188	
DS-ROI	2.25	± 1.98	3.08	± 1.58	453.00	.012	.024	*
DU-ROI	2.97	± 0.92	3.07	± 1.23	577.50	.186	.372	

IBD, inflammatory bowel disease group; HC, healthy control group; DS, disease-specific; DU, disease-unspecific; ROI, region of interest; FDR, False Discovery Rate; *$p < .05$, **$p < .01$

Associations of body evaluation and body ownership with history of ACE

Whole-body evaluation and ownership scores were not associated with a history of ACE either in IBD ($p_{FDR} \geq .316$) or HC ($p_{FDR} \geq .936$). After applying correction for multiple comparisons, no significant associations were found for ROI body evaluation scores in IBD (all $p_{FDR} \geq .094$) or HC ($p_{FDR} \geq .788$). In line with our hypothesis, higher childhood trauma severity was associated with lower ownership scores for the abdomen among IBD patients (r_s = -.383, p = .194, p_{FDR} = .038), but not in HC (r_s = .077, p = .651, p_{FDR} = .651).

Moderation of the associations of body ownership with interoceptive sensibility by ACE

Moderation analyses across all participants revealed a significant moderation effect of ACE severity on the association between interoceptive sensibility and DS-ROI ownership scores (B = 0.12, CI [0.009, 0.241], p = .035). The model explained 9% of the variance (R^2) (R^2 = .09; F (3,81) = 2.25, p = .09). To further explore the nature of this effect, two separate moderation analyses for the IBD and the HC group were computed. A significant interaction effect between interoceptive sensibility and ACE severity was found in the IBD group (B = 0.18, CI [0.012, 0.338], p = .036), but not in the HC group (B = - 0.04, CI [- 0.226, 0.144], p = .652) (Figure 14). Further analyses within the IBD group revealed that the moderating effect of ACE was significant only for those IBD patients with moderate CTQ scores (B = 2.58, CI [0.074, 5.094], p = .044) but not for those without ACE or low ACE severity (all $p \geq .216$). Thus, ACE severity strengthened the positive association between interoceptive sensibility and body ownership scores only in those patients reporting higher trauma load (Figure 14A). ACE severity did not moderate the link between interoceptive sensibility and whole-body or DU-ROI ownership scores (all $p \geq .212$).

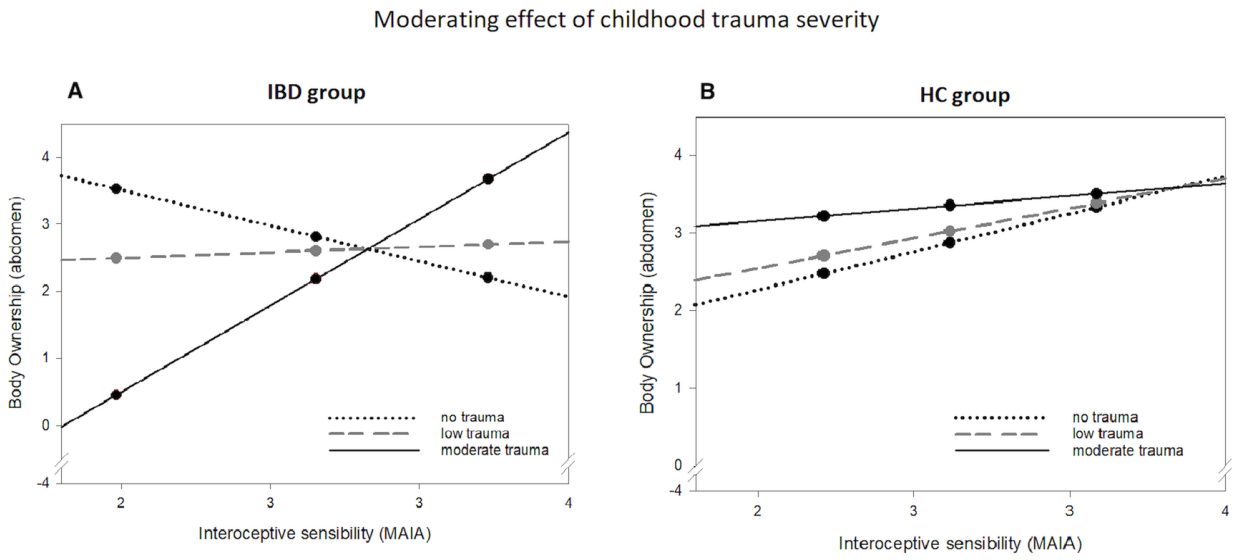

Figure 14. Moderation effect of adverse childhood experiences (CTQ total score) on the link between interoceptive sensibility (MAIA total score) and body ownership of the abdomen (- 4= "low ownership"; 4= "high ownership") in IBD (Fig. 14A) and HC participants (Fig. 14B). The interaction between ACE and interoceptive sensibility was significant only in the IBD group and only for patients with moderate CTQ scores (solid black line in Fig. 14A).

Associations between body evaluation, self-esteem and BMI

Contrary to our hypothesis, general self-esteem was not associated with whole-body, DS-ROI or DU-ROI evaluation ratings across all participants ($p_{FDR} \geq .090$). However, separate analyses for both groups revealed that in IBD, higher self-esteem was linked to a more positive evaluation of the DS-ROI ($r_s = .531$, $p = .002$, $p_{FDR} = .004$). This association could not be found in HC ($r_s = .006$, $p = .974$, $p_{FDR} = .974$). BMI was not associated with body evaluation either among the IBD patients (all $p_{FDR} \geq .326$) or the HC participants (all $p_{FDR} \geq .309$). Exploratory analyses revealed no sex differences regarding body evaluation either in the IBD group ($p \geq .195$), in the HC group ($p \geq .219$) or between both groups (women: $p \geq .579$; men: $p \geq .774$). Among the IBD patients, number of previous disease-related surgeries was not associated with body evaluation ($p \geq .459$) (see supplemental material S4, Table S11).

2.4.5 Discussion

In IBD, the severe disease symptoms, medication, and surgical treatments can vastly affect patient's perception and satisfaction with their bodies (McDermott et al., 2015; Saha et al., 2015). On the other hand, body representation disturbances have been associated with severer disease activity, lower quality of life, and lower self-esteem in this clinical population (for a review: Beese et al. (2019)). Furthermore, lower satisfaction with one's own body has been linked to increased levels of depression, anxiety, and lower self-esteem in IBD samples, indicating the complex interplay of body perception disturbances, psychological well-being and disease severity in IBD (Claytor et al., 2020; McDermott et al., 2015; Wertheim & Paxton, 2011). The aim of the present study was to investigate whether patients with IBD show alterations in the way they perceive their bodies, especially with respect to how positive or negative they tend to evaluate their bodies and to what extent they perceive their bodies as belonging to themselves. We aimed at contributing to the better understanding of the links between body perception disturbances, gastrointestinal-specific anxiety, interoceptive sensibility, and a history of adverse childhood experiences (ACE).

Our findings revealed no differences in body evaluation between IBD patients and unaffected individuals. In IBD, a more negative body evaluation of the abdomen was associated with higher levels of gastrointestinal-specific anxiety and lower self-esteem, while a more positive evaluation of the whole body was related to higher levels of interoceptive sensibility. With respect to body ownership, IBD patients perceived their abdomen as significantly less belonging to themselves compared to the healthy individuals, indicating that disturbances in the sense of ownership might affect especially body areas associated with the experience of disease-specific pain symptoms. In contrast to body evaluation, body ownership did not show significant associations with gastrointestinal-specific anxiety, interoceptive sensibility or self-esteem. Finally, moderation analyses indicated that in IBD, the link between body ownership and interoceptive sensibility was dependent on the reported severity of childhood maltreatment. However, this moderating effect was found only for the abdomen.

Whole-body and ROI scores

Contrary to our hypothesis, we did not find differences in body evaluation between remitted IBD patients and healthy participants. Previous findings have suggested lower body satisfaction in patients with active disease compared to those in clinical remission, showing a

significant link between a more negative body evaluation and disease severity (McDermott et al., 2015). Our findings indicate no alterations in the whole-body evaluation of IBD patients in clinical remission, suggesting that disease activity might crucially affect patients' level of satisfaction with their bodies. As we could not observe persistent negative effects of IBD on body evaluation in the present sample, decreased body satisfaction observed in previous studies might reflect state-like effects, primarily associated with the acute disease symptoms. However, it should be noted that previous studies, reporting more negative body evaluations and decreased body satisfaction in IBD, did not include healthy control groups and thus, had no reference to values from a healthy population (Cushman et al., 2021; McDermott et al., 2015; Saha et al., 2015). Thus, future studies are asked to examine the interplay of symptoms severity and body evaluation in IBD by investigating their relationship in larger IBD samples including patients in remission as well as those with active disease and compare them to unaffected individuals.

In addition to body evaluation, we investigated one further facet of body representations in IBD – the sense of body ownership. Contrary to our hypothesis, we did not find differences in whole-body ownership between the IBD and HC group. In contrast to other studies reporting alterations in body ownership in patients with medical conditions (Finotti & Costantini, 2016; Matamala-Gomez et al., 2020) or mental disorders (Löffler et al., 2020), IBD patients did not exhibit alterations regarding the extent to which they perceive their bodies as belonging to themselves. It is known that especially severe injuries of the nervous system can result in disturbed body representations and altered sense of body ownership (Matamala-Gomez et al., 2020). However, our findings suggest that IBD might not affect patients' whole-body ownership to such a significant extent. One possible explanation might be that in contrast to more severe disorders, such as schizophrenia, personality disorders or stroke, IBD symptoms do not include changes of the self-consciousness or disturbed presentation of the self. However, IBD patients exhibited significantly lower sense of ownership for the abdomen, that is, the body area most affected by gastrointestinal pain (Ceuleers et al., 2016) and for which significantly higher pain symptoms were reported by the IBD group. This finding is in line with previous studies showing that patients with regional pain syndrome report a feeling of "foreignness" towards the affected body parts (Bultitude & Rafal, 2010). Multiple neuroimaging studies have found that both body ownership and pain perception share common neural underpinnings, including the somatosensory cortex and the insular cortex (Brooks & Tracey, 2007; Tsakiris et al., 2006). In IBD, a changed cortical thickness in these regions has been demonstrated which

may be related to the chronically increased afferent input from the gut due to relapsing mucosal inflammation (Hong et al., 2014). Thus, cortical changes associated with the processing of visceral pain, might potentially contribute to a disturbed sensory integration (Finotti & Costantini, 2016; Suzuki et al., 2013), promoting alterations in patients' sense of ownership for body parts affected by these pain symptoms. Future studies need to further investigate how altered functional activity and connectivity in brain regions involved in the processing of afferent input in IBD (Thomann et al., 2019) might be linked to disturbances in the sense of body ownership.

Associations with gastrointestinal-specific anxiety, interoceptive sensibility and self-esteem

Our results indicate that higher gastrointestinal-specific anxiety in IBD is associated with a more negative evaluation of the abdomen but not with a diminished sense of ownership for this part of the body. A recent study with young adolescents diagnosed with IBD has demonstrated lower satisfaction with the abdomen in these. This result suggests the crucial role of disease symptoms such as abdominal pain for patients' body evaluation (Cushman et al., 2021). In line with these findings, our results suggest that even in the absence of acute gastrointestinal symptoms, greater anxiety and worries about those are essential for how patients perceive their bodies. However, it should be mentioned that this association was only marginally significant after the applied correction for multiple comparisons and thus, it needs to be interpreted cautiously.

Further, we found that higher interoceptive sensibility was linked to a more positive body evaluation specifically for the IBD group. This link was not specific for body areas associated with pain symptoms, suggesting a more general relationship between body evaluation and interoceptive abilities in IBD. This finding is in line with previous research showing that individuals who are more aware of their bodily sensations, report higher body satisfaction (Todd et al., 2019a). However, since this association was significant only for the IBD group, this might imply that interoceptive sensibility may have potentially beneficial effects for patient's body evaluation. In line with this interpretation, previous studies investigating mind-body interventions in gastrointestinal pathologies demonstrated that practicing systematic attention to one's body signals can have positive effects on the reported disease-specific anxiety and quality of life (Ewais et al., 2019; Hood & Jedel, 2017; Shah et al., 2020). As a more negative body evaluation has been linked to poor quality of life and greater

psychological distress (Kearney et al., 2011), such interventions might be of particular importance in IBD populations.

Finally, our findings revealed a positive association between self-esteem and body evaluation of the abdomen in the IBD group. This result suggests that a more negative attitude toward body areas associated with disease-specific pain might be an essential factor for developing general impairments of the self-esteem (Cruz-Sáez et al., 2020). Furthermore, lower self-esteem has been repeatedly associated with chronic conditions and somatic disorders, suggesting that disturbances could also have a negative impact patient's psychological well-being (Kleindienst et al., 2014; Pinquart, 2013). As our results only indicate an association between individuals' self-esteem and body evaluation, further studies are needed to examine the nature and causality of this relationship. Depending on its direction, future therapeutic interventions could either focus on improving patients' self-esteem in order to prevent body evaluation disturbances or on targeting patients' perception and appraisal of body areas associated with their gastrointestinal complaints, potentially resulting in improved self-esteem.

Body evaluation, body ownership and adverse childhood experiences (ACE)

A history of ACE was not associated with whole-body evaluation or body ownership. However, we found that IBD patients reporting severer history of maltreatment perceived their abdomen as less belonging to themselves. Furthermore, the severity of ACE moderated the relationship between interoceptive sensibility and body ownership in the IBD group. Patients with severer history of maltreatment showed a diminished sense of body ownership compared to those with no or only mild severity. This finding is in line with previous studies showing body ownership disturbances in patients with trauma-related disorders (Löffler et al., 2020). However, our results revealed that in the group of patients reporting severer history of maltreatment, increasing levels of interoceptive sensibility led to increase in the perceived body ownership. This might indicate that the increased attention to interoceptive sensations may contribute to an improved integration of sensory input, resulting in stronger sense of ownership. One could speculate that especially in patients with a history of ACE, lower levels of body ownership could be potentially balanced out through an improvement in patients' awareness of their body signals. Future studies need to further examine the effects of childhood maltreatment severity on body awareness and their link to body representations. Although preliminary, our findings

point towards the importance of taking the history of childhood trauma into account in case of psychotherapeutic treatments in IBD.

Limitations

Some limitations of the present study have to be addressed. First, while the IBD group consisted of equal number of male and female participants, more female than male healthy participants were included in the HC group. As females are more prone to a more negative body evaluation, (Grogan, 2016), this might partially explain the lower body satisfaction among the healthy individuals. Moreover, this unequal sex distribution between both groups may have masked existing stronger differences between IBD and healthy populations. Second, based on our results, one cannot draw conclusions whether the observed body perception disturbances are also present in patients with severer disease symptoms. Thus, future research is asked to examine body representations and their link to IBD symptoms severity during the course of the disease in a longitudinal manner. While our findings indicate the importance of ACE as moderating factor in the interplay of interoception and body ownership, our sample reported only low to moderate severity of ACE according to the cut-off scores established in the previous literature (Klinitzke et al., 2012). Contemporary studies suggest a strong association between inflammation and history of maltreatment in immune-mediated diseases (Wan et al., 2022), it is conceivable that history of ACE might promote stronger inflammatory activity and the development of a psychiatric comorbidities. Therefore, the exclusion of patients with active disease and mental disorders might explain the lower prevalence of childhood maltreatment in the present sample. Finally, in contrast to previous studies investigating the link between interoception and the sense of ownership, we implemented only self-report measures to assess these constructs. However, as the objective performance on experimental tasks measuring body perception (e.g., rubber hand illusion, heartbeat perception tasks) often do not correspond with individual's self-reports, one should interpret our findings cautiously.

2.4.6 Conclusions

In conclusion, our results demonstrate that even in clinical remission, patients with IBD still experience body parts associated with disease symptoms differently than unaffected individuals. As higher anxiety about gastrointestinal symptoms was found to be related to a more negative body evaluation in IBD, this implies that even in the absence of acute disease,

patients' exaggerated appraisal of their body signals might negatively affect their body perception. This is the first study showing that patients with IBD experience pain-related body parts also as less belonging to themselves and this association was stronger in individuals reporting history of childhood maltreatment. As patients with history of adversity might constitute an especially vulnerable population, it might be useful to screen those for potential body perception disturbances in order to potentially provide them with proper psychological support and supplemental psychotherapeutic interventions.

2.4.7 Supplemental material S4

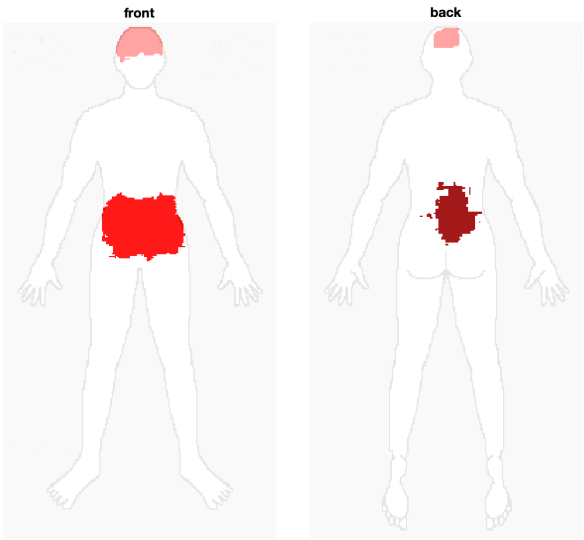

Figure S10. Pain-related ROI with mean pain intensity ≥ 1.60 computed across all participants (N=85). Colored body areas (head, abdomen, back) were used as pre-defined ROI for further analyses. Disease-specific ROI includes the abdomen (red area), disease-unspecific ROI included the head (pink area) and the back (dark red area).

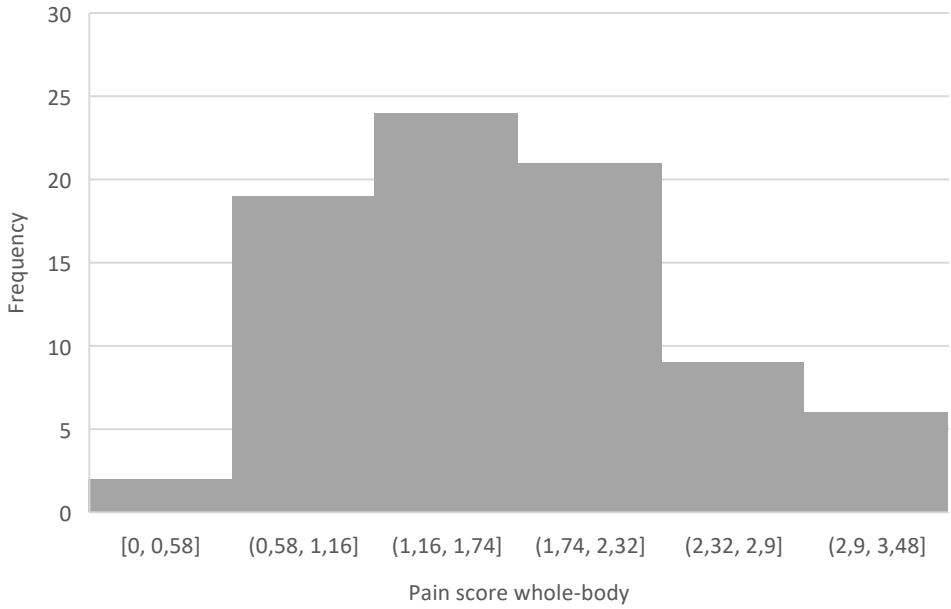

Figure S11. Distribution of whole-body scores for pain experience during the last four weeks prior the experiment. Scores were computed across n=85 participants (M = 1.61; SD = 0.74).

Table S10. Number of coloured pixels within the whole-body template and the pre-defined ROI.

	IBD	HC	p-value
	N pixels	N pixels	*p*
Body evaluation			
Whole-body	26382.3	28022.3	.717
Head	289.3	223.4	.066
Abdomen	1678.6	1687.0	.922
Back	514.4	541.8	.767
Body ownership			
Whole-body	33608.3	34172.6	. 201
Head	320.6	315.0	.880
Abdomen	1807.8	1742.3	.789
Back	678.8	687.3	.689

Note: group comparisons were computed using Mann-Whitney U tests

Table S11. Spearman rank correlations (r_s) between Body image scores, BMI, number of IBD-related surgeries in the past and IBD symptoms severity.

	BMI		Number of surgeries		IBD severity	
	r_s	*p*	r_s	*p*	r_s	*p*
Body evaluation						
Whole-body	-.202	.217	-.021	.897	-.072	.709
DS-ROI	-.260	.131	-.010	.953	-.154	.443
DU-ROI	-.034	.848	-.129	.459	-.138	.501
Body ownership						
Whole-body	-.220	.190	-.028	.870	-.119	.554
DS-ROI	-.182	.282	.123	.469	-.041	.837
DU-ROI	-.226	.184	.082	.636	-.001	.996

Note: correlations were computed only in the IBD group (n=41). IBD, inflammatory bowel disease group; HC, healthy control group; BMI, body mass index; ROI, region of interest; DS, disease-specific (abdomen); DU, disease-unspecific (head, back).

3 GENERAL DISCUSSION

The main aim of this thesis is to contribute to a better understanding of the interplay between interoception, emotion processing and body perception in IBD. Given previous findings demonstrating poor emotional functioning in IBD, we investigated whether changes in patients' ability to perceive and appraise their bodily sensations are linked to altered emotion perception. Furthermore, as IBD has been associated with more negative body-related attitudes, disturbances in patients' sense of body ownership and body evaluation were investigated by linking those to interoceptive processing. Finally, since contemporary findings have indicated a significantly higher prevalence of adverse childhood experiences (ACE) in IBD populations, the modulating role of ACE on the link between interoception, emotion and body perception was examined. In the following section, the empirical findings presented in Chapter 2 will be discussed and integrated into previous research. While taking some limitations of the present work into account, the current results will be concluded with an emphasis on their clinical relevance and implications for future research.

3.1 Summary of empirical findings and integration into previous research

Given previous findings indicating poor emotional functioning and increased levels of psychological distress in IBD populations, the first goal of this thesis is to gain a deeper understanding of the role of body signals in how patients with IBD perceive emotions (**RQ I**) and whether changes in the interoceptive processing are related to emotional dysfunctions in IBD, e.g., through changes in the perceived emotion-related bodily sensations (**RQ II** and **III**).

In **RQ I**, interoception was investigated as a multidimensional construct assessing its three components: interoceptive accuracy (IAcc), interoceptive sensibility (IS) and interoceptive awareness (IAw). Contrary to our hypothesis, patients with IBD did not show superior IAcc or IAw compared to healthy individuals and thus, did not differ in their objective ability to perceive signals originating from the body or in their meta-awareness of this ability. With respect to IS, patients reported a stronger tendency to use distraction to cope with unpleasant sensations and exhibited higher emotional awareness, that is, the awareness that certain physical sensations are the sensory aspects of emotions. Distraction is considered as a maladaptive and a non-mindful form of IS (Mehling, 2016; Mehling et al., 2013; Williams, 2010) associated with poorer quality of life, increased levels of psychological distress and

symptoms of anxiety and depression in IBD populations (Bitton et al., 2008a; Jones et al., 2006; Levy et al., 2016). Since only patients in clinical remission were investigated in this thesis, this finding suggests that even when the severe disease symptoms have already subsided, patients with IBD still apply dysfunctional strategies to manage bodily sensations perceived as unpleasant or painful. Further, as no differences between IBD and HC participants were found in their ability to regulate psychological distress by attention to their interoceptive signals, one could speculate that that in the absence of proper regulatory strategies, maladaptive coping with bodily sensations can have detrimental impact on how patients manage their disease symptoms (Goubert et al., 2004).

With respect to emotional awareness, evidence suggests that this form of IS can have ambiguous effects, both advantageous and disadvantageous for an individual, as it can be negatively and positively associated with anxiety symptoms (Mehling et al., 2012). Results of **RQ I** revealed that IBD patients reporting higher levels of emotional awareness perceived negative emotional stimuli as more unpleasant and more arousing. Furthermore, in **RQ II** and **III** a significant link between emotional awareness and patients' emotional reactivity in the body was found: patients reporting higher levels of emotional awareness experienced stronger bodily activation during positive and negative emotions. In line with previous studies, these findings suggest that a higher sensitivity to emotion-related bodily sensations might result in a more intense emotional experience of both positive and negative emotions (Lichev et al., 2014; Mehling, 2016; Terasawa et al., 2013). However, in the absence of adaptive regulatory strategies in IBD, the latter can result in a greater psychological distress and anxiety symptoms (Mehling, 2016). Since no significant associations between IAcc and emotion processing were observed, the presented results indicate only emotional awareness, as one feature of IS, to be a significant predictor of how patients with IBD perceive emotions. Thus, altered emotion processing in IBD is not necessarily linked to a stronger perception of bodily sensations per se but rather to the appraisal of those in the context of emotional experience (Zamariola et al., 2019). The stronger tendency to link specific bodily sensations to emotional triggers seems to intensify patients' experience of both positive and negative emotions. As IBD patients showed a decreased experience of positive emotions in **RQ II**, and in particular of happiness in **RQ III**, this finding might imply that an improvement in patients' ability to connect bodily sensations with certain emotional states could promote the stronger experience of positive emotions. However, as higher emotional awareness can also result in an increased experience of aversive emotions in this patient group, it might be useful not only to target an improvement of individual's emotional awareness but also to improve patients' abilities to regulate emotional

distress through attention to their bodily sensations. Furthermore, in IBD, patients reporting higher levels of emotional awareness experienced tension more strongly in their bodies (**RQ II**). This fining is in line with previous studies indicating that individuals who are more aware of their interoceptive signals put stronger emphasis on the arousal component of emotions (Barrett et al., 2004; Pollatos et al., 2005b). However, as emotional awareness was not linked to a stronger experience of relaxation in the body, one could argue that without the proper skills to use bodily sensations to regulate tension in the body (Mehling, 2016), even highly emotionally aware patients might fail to successfully cope with stress.

The empirical findings presented in this thesis revealed a decreased emotional reactivity in IBD related to the experience of emotional valence and arousal in the body (**RQ II & III**). Our results indicate that approach-oriented emotions of positive valence, including happiness as one basic positive emotion, are perceived less intensely by IBD patients, characterized by decreased emotion-related sensations in the upper parts of the body (e.g., chest, upper limbs). While diminished sensations in the chest might suggest a hyposensitivity to changes in one's heart rate (e.g., heart pounding), we did not find alterations in how patients perceived their heartbeats at rest (**RQ I**). Taken together, these findings indicate that altered perception of body signals in IBD is specific for the experience of emotions and suggest a stronger detachment from one's emotion-related bodily sensations. In line with this assumption, we observed less intense changes in patients' bodily sensations when experiencing negative emotions (**RQ II & III**), characterized by a decreased emotional reactivity to anger and fear. In contrast to Nummenmaa and colleagues (2014) who found that in healthy individuals these emotional states are associated with a stronger activation in the upper parts of the body (e.g., head, chest, upper limbs, abdomen), in IBD, the experience of anger and fear was characterized by less intense changes in these body areas. While Vianna and colleagues (2006) suggested that altered emotion perception in IBD is linked to aberrant bodily sensations from the gastrointestinal tract, our findings indicate that it is not the visceral sensations per se which are crucial for the observed emotional dysfunctions in IBD but rather the general avoidance of one's bodily sensations during the experience of emotions.

As patients with IBD tend to use distraction from their bodily sensations in order to cope with their disease symptoms (Jones et al., 2006), the stronger detachment from one's body during emotional experience may indicate the use of avoidance as an emotion regulatory strategy in IBD. Contemporary findings point to the benefits of different emotion regulation

mechanisms depending on the intensity of the experienced emotion (Sheppes et al., 2014). According to these, distraction is preferable when individuals face emotions of high intensity (Sheppes, 2020). As high emotional intensity usually results in greater activation of the ANS, it is conceivable that individuals who are more sensitive to these physiological changes may prefer to apply distraction strategies to cope with highly arousing emotions (Ardi et al., 2021). Thus, IBD patients might perceive emotional avoidance or distraction as helpful to avoid a confrontation with overwhelming emotions, which could overstep their coping resources (Sheppes et al., 2011). In line with this interpretation, a recent study by Banovic et al. (2020) found stronger emotional avoidance and emotional suppression among Crohn's disease patients. While these strategies might be helpful in the short term, emotional avoidance has been associated with higher levels of anxiety and affective distress in the long term (Bardeen et al., 2014; Hayes et al., 1996; Kelly & Forsyth, 2009). Thus, one could speculate that the prolonged use of this emotion regulation strategy may potentially explain why depression and anxiety symptoms remain severe for some patients even during the periods of remission. Further, several studies have linked IBD to a more insecure attachment style, characterized by attachment avoidance (Agostini et al., 2010; Agostini et al., 2016). Avoidant patients tend to use cognitive distancing and suppression from their emotions as a defensive strategy in order to cope with psychological distress (Agostini et al., 2019; Agostini et al., 2016). Hence, an avoidant attachment style can promote interpersonal difficulties in patients with IBD, which in turn can exacerbate their stress levels because of lack of social support and thus, exaggerating patient's emotional dysfunctions.

IBD has not only been associated with poor emotional functioning but also with severe changes in how patients perceive their bodies due to the chronicity of their disease. In **RQ IV,** we investigated whether patients with IBD experience their bodies differently compared to unaffected individuals, especially with respect to their sense of body ownership and body evaluation. With respect to body ownership, our results revealed that patients with IBD perceive their abdomen as less belonging to themselves compared to healthy individuals. This observation is not surprising as this part of the body is the one most strongly associated with the experience of abdominal pain and other IBD-related symptoms (Cushman et al., 2021). In line with our findings, other pain-related conditions have been also associated with a feeling of "foreignness" toward the body parts affected by the pain symptoms (Bultitude & Rafal, 2010), indicating that chronic pain symptoms can, indeed, modulate the extent to which the body is perceived as belonging to oneself (Cordier et al., 2020; Kammers et al., 2011). As body

ownership is found to result from the multisensory integration of interoceptive and exteroceptive input in the brain, it is conceivable that pain perception can influence it, given that, nociceptive signals are processed in the same brain regions involved in the processing of interoceptive signals (Matamala-Gomez et al., 2021; Solcà et al., 2020). Evidence from neuroimaging studies indicated that both structural and functional changes in these brain areas can be found in IBD and these alterations are possibly due to the chronically increased afferent input from the gut and the prolonged exposure to pain in this clinical population (Hong et al., 2014; Rubio et al., 2016). Hence, changes associated with the processing of visceral pain, might potentially contribute to a disturbed sensory integration (Finotti & Costantini, 2016; Suzuki et al., 2013), promoting alterations in patients' sense of body ownership toward body parts affected by pain symptoms. While body ownership seems to be affected by IBD even when the severe symptoms have already subsided, no such alterations in patient's body evaluation could be found in the present IBD sample. While previous studies pointed towards patients' vulnerability to more negative body attitudes and lower body satisfaction (Cushman et al., 2021), IBD patients did not show persistent alterations with respect to their body evaluation once a remission has been reached. Since higher body dissatisfaction in IBD has been repeatedly associated with severer disease activity (McDermott et al., 2015), negative body-related attitudes, as reported in previous studies, might reflect state-like conditions, primarily associated with the experience of acute disease symptoms and pain.

With respect to interoception, our results did not reveal significant associations between IS and the perceived sense of body ownership. This finding contradicts previous studies suggesting a stronger body ownership in more interoceptively aware individuals (Crucianelli et al., 2018; Monti et al., 2021; Tsakiris et al., 2011). Thus, in IBD, patient's subjective beliefs to be interoceptively cognizant did not promote an enhanced experience of the body as own. In contrast, greater IS was linked to a more positive body evaluation in IBD. As individuals reporting higher levels of IS tend to pay greater attention to their body signals, this might result in a stronger perceived connectedness with the own body and a more positive attitude toward it. In line with this interpretation, the experience of body pride and body appreciation was found to be significantly stronger in healthy individuals who report to be more aware of their bodily sensations (Todd et al., 2019a). Taken together, these results indicate that the way in which interoceptive signals are appraised is crucial to how individuals perceive their bodies and might have important clinical implications for IBD populations. While we did not find patients in clinical remission to evaluate their bodies more negatively, one could argue that

the potentially advantageous impact of IS on individual's body evaluation, found in **RQ IV,** might be of particular importance for patients with active disease symptoms.

Finally, this thesis aimed at gaining further insight into the role of ACE in the interplay of interoception, emotion and body perception in IBD. For this purpose, we investigated whether a history of ACE is associated with a changed perception and appraisal of body signals and whether it modulates the link between interoception and emotional experience. Furthermore, we examined whether the potentially modulating role of childhood maltreatment can be extended to the association between interoception and body ownership and body evaluation in IBD. In **RQ I**, we found a history of ACE to influence the association between interoception and emotion perception: Individuals with high levels of emotional awareness who reported a history of severe childhood maltreatment perceived negative emotions as more unpleasant and more arousing. Moreover, in line with numerous studies on emotion perception and ACE (fore review see: Bérubé et al. (2021)), patients reporting early life adversities exhibited a stronger emotional reactivity in the body when experiencing anger (**RQ III**), a negative emotion commonly observed in early traumatized individuals (Glück et al., 2017; Orth & Wieland, 2006). Taken together, these findings suggest that a history of ACE exaggerates the perception of negative emotions, being linked to greater subjectively perceived arousal in the body, especially in those individuals who tend to attribute physiological sensations to emotional states more strongly. Therefore, individuals who have been exposed to maltreatment may learn to use their bodily sensations in a more efficient way in order to recognize possible threats and adjust their approach-avoidance behavior accordingly. In IBD, this coping mechanism might result in a stronger activation of the 'fight or flight' system (Jansen et al., 1995), leading to an amplified physiological stress response of the HPA axis and worsening gastrointestinal inflammation (Mawdsley & Rampton, 2005). Hence, it could be speculated that IBD patients reporting a history of ACE represent an especially vulnerable population, in which these biological and psychological mechanisms might contribute to the greater risk of developing a psychopathology (Moulton et al., 2019; Wan et al., 2022). Beyond its influence on emotion perception, childhood maltreatment was also found to modulate the association between interoception and body ownership in patients with IBD (**RQ IV**). In line with findings from trauma-related mental disorders (Löffler et al., 2020; Rabellino et al., 2018), patients reporting a severe history of ACE exhibited diminished levels of body ownership, particularly for the parts of the body affected by their disease symptoms. However, with increasing IS, the sense of ownership improved, suggesting an advantageous influence of interoception on this

facet of body representations in patients reporting early life adversity. One possible explanation for this link might be that individuals with a history of ACE tend to use physical detachment as a coping strategy under high-stress conditions (Terock et al., 2016). When not treated timely, the denial of bodily signals can result in dissociative behavior which is, however, not limited only to threatening situations. Thus, it is conceivable that individuals who tend to use these coping strategies on a regular basis, may exhibit persistent alterations in their body perception, especially with respect to their sense of body ownership. Given our results of stronger body ownership with higher IS, findings suggest that disturbances in this facet of body representations in IBD might be balanced out through an improved ability to perceive and evaluate interoceptive cues.

In recent years, the biopsychosocial model of disease has been repeatedly used to explain the potential impact of various psychological factors on the development and maintenance of IBD symptoms (Bitton et al., 2008a; Engel, 1981). In this section, I will integrate the empirical findings presented in this doctoral thesis into this model, discussing their role in the IBD symptomatology (Figure 16). As patients with IBD tend to experience disease-related symptoms as distressing, this might result in an increased fear of unpleasant bodily sensations and pain. To avoid confrontation with these, patients apply distraction as a maladaptive coping mechanism, which in turn may reinforce patients' visceral hypersensitivity and gastrointestinal-specific anxiety. However, as intense emotions can be characterized by strong visceral signals, which can be misinterpreted as disease-related sensations, patients with IBD tend to extend their avoidance strategy also to the experience of emotions. This results in a decreased perception of emotion-related bodily sensations and a more attenuated emotional experience. Furthermore, the distraction from pain-related symptoms can result in a stronger detachment from the body parts affected by these symptoms, leading to the experience of the body as less belonging to oneself. As patients with IBD did not exhibit changes in the ability to perceive their body signals accurately (IAcc) and also no alterations in their visceral sensations (HRV) were found, the findings presented in this thesis imply that altered emotion processing and body perception disturbances in IBD are rather associated with alterations in the appraisal of these sensations.

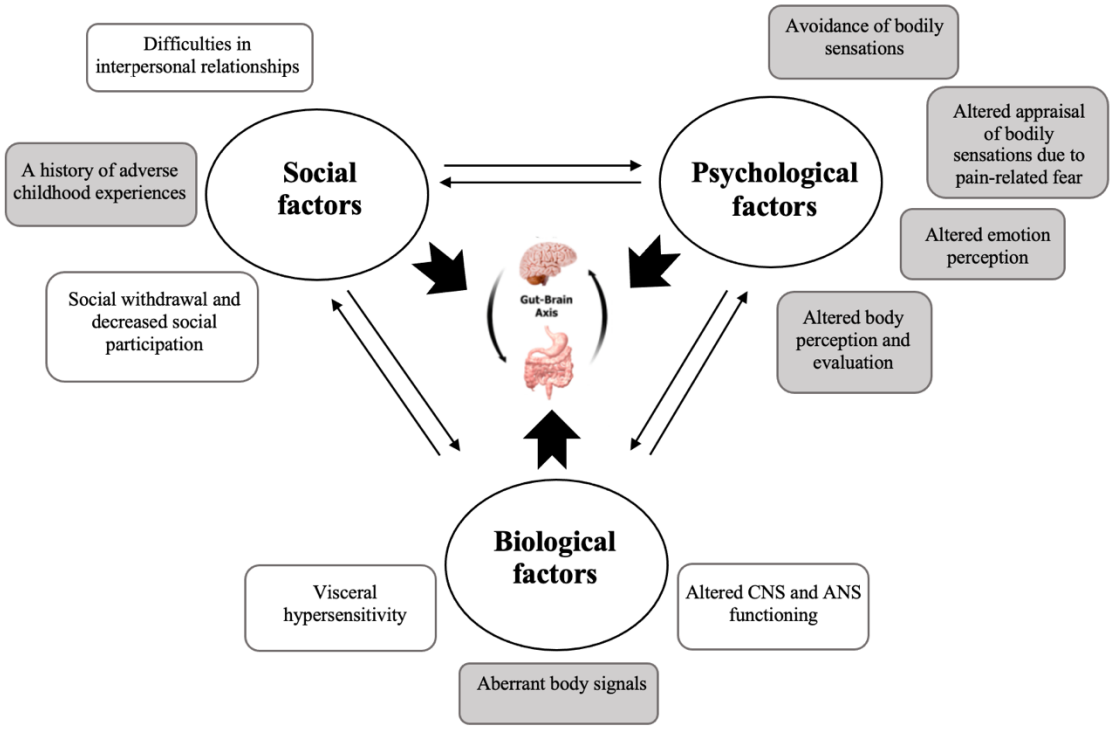

Figure 15. The biopsychosocial model of disease integrating biological, psychological, and social factors of particular importance for the maintenance of the IBD symptomatology. Constructs investigated in the present thesis are colored in grey.

3.2 Clinical implications

As several studies have indicated a significantly higher prevalence of ACE and psychiatric comorbidities in IBD populations (Bernstein et al., 2018; Fuller-Thomson et al., 2015; Lewis et al., 2019; Wan et al., 2022), some clinical implications for the implementation of psychotherapeutic treatments in IBD should be discussed based on the results presented in this dissertation.

Given our findings of altered emotion perception in IBD, the implementation of interoceptively focused techniques as a supplementary part of patients' treatment might be of particular importance. Mind-body interventions, such as mindfulness-based stress reduction (Kabat-Zinn, 2003), emphasize the role of bodily sensations and their appraisal as crucial for how individuals cope with stress and emotions (de Jong et al., 2016; Garland et al., 2012; Lutz et al., 2013). Applying such interventions in IBD can enhance patients' sensitivity to their emotion-related bodily signals (Bornemann et al., 2015; Davey et al., 2020; Fischer et al., 2017)

while simultaneously promoting the implementation of skillful strategies for coping with intense emotional states. In addition, cognitive behavioral therapy (CBT) can improve patients' ability to implement more adaptive regulatory strategies to cope with emotional stress, including relaxation techniques (Jacobson, 1938), cognitive reappraisal and acceptance (Wolgast et al., 2011). Through acceptance of their emotions and the corresponding physiological reactions of the body, patients can learn to observe these sensations without immediately feeling overwhelmed and trying to avoid these by using distraction. Therefore, by modifying how patients evaluate the bodily sensations elicited by emotional triggers, such interventions can improve patients' flexibility in their emotional experience in everyday life (Ardi et al., 2021; Wynne et al., 2019). Beyond their impact on emotional functioning, interoceptively focused interventions can improve patients' interoceptive sensibility and thus, promoting more positive body-related attitudes in those patients who report difficulties in perceiving their bodies as belonging to themselves or exhibit body image disturbances.

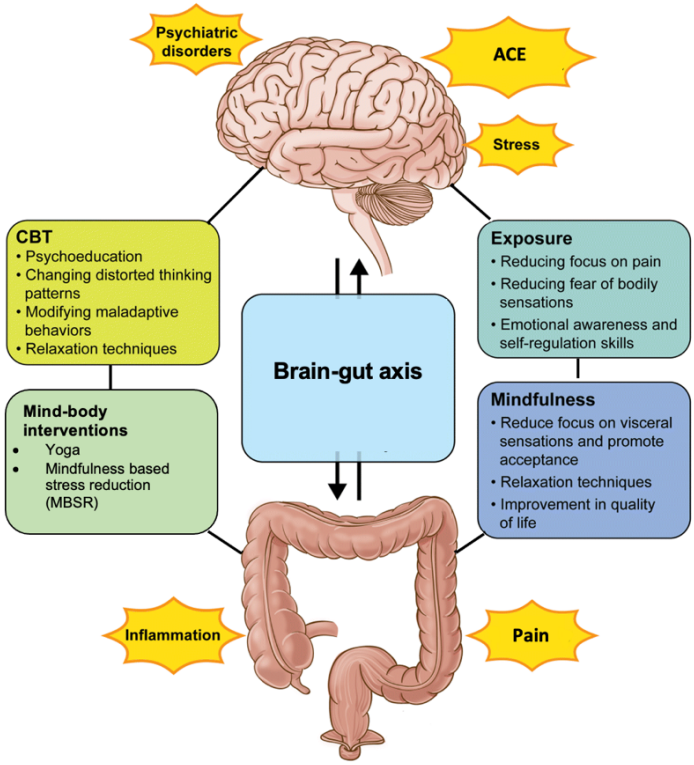

Figure 16. IBD characterized by dysregulations of the brain-gut axis. Interventions such as cognitive behavioral therapy, mindfulness and interceptive exposure are believed to address these dysregulations in IBD through their effects on the central nervous system and the gut. Figure adapted from "Brain-Gut Therapies for Pediatric Functional Gastrointestinal Disorders and Inflammatory Bowel Disease" by H. Person & L. Keefer, 2019, *Current Gastroenterology Reports, 21(4),*12. With permission from Springer (License number: 5235421441263, Jan 24, 2022).

3.3 Limitations

Some limitations of the present work have to be considered. Firstly, as no clinical control group was included, we cannot conclude whether our findings are limited only to IBD populations. Since several previous studies demonstrated similar emotional dysfunctions in patients with other gastrointestinal pathologies (e.g., irritable bowel syndrome), it is conceivable that the observed alterations might constitute a transdiagnostic features of disorders characterized by disturbances of the brain-gut axis (Berens et al., 2021; Elsenbruch et al., 2010).

Secondly, as the heartbeat tracking task has been heavily criticized for assessing IAcc at rest, we tried to overcome this limitation by implementing a short physical exercise and examining whether an increased activation of the ANS will affect participants' interoceptive abilities. However, as some patients reported joint pain, restraining them from performing this physical challenge, the second run of the heartbeat tracking task included less participants than the first one. Thus, future studies on interoception in IBD should consider implementing other procedures to non-invasively increase the strength of participants' heartbeats, such as a breath-holding condition during the heartbeat tracking procedure (see Smith et al. (2021)). While the lack of confidence ratings in this task can be considered as one further limitation (Murphy et al., 2019), one should note that given the overall twenty trials performed by each participant, asking these about their confidence after each trial would have extended the experimental procedure significantly. Thus, in order to avoid higher psychological distress in the IBD group due to an extremely long duration of the experiment, no data on participants' confidence judgments were collected.

Furthermore, in no one of the tasks, used to examine emotion processing, an emotion induction was implemented. Instead, we asked participants to recall how their bodily sensations change when they experience a particular emotion. Hence, we could not control whether participants recalled comparably strong emotional situations and to what extent this recall might have been biased. Moreover, because of the cross-sectional design of these data, we cannot draw conclusions in regard to the direction of causality of the link between emotional experience and interoception. Therefore, it remains unclear whether higher awareness of one's interoceptive signals intensifies the experience and the recall of emotion-related bodily sensations or whether a stronger emotional experience promotes the improvement of one's interoceptive sensibility.

With respect to the investigated sample, one should note that while our aim was to recruit two groups equal in their number of female and male participants, the final HC group consisted of slightly more females. Although our results did not reveal any significant effects of this unequal gender distribution on emotion and body perception, future studies are asked to replicate our findings in bigger samples by controlling for potential gender effects.

Finally, it should be mentioned that the severity of ACE reported in the IBD sample was only moderate (Klinitzke et al., 2012). As contemporary findings emphasize the common pathophysiological mechanisms between immune-mediated diseases, early life stress, and psychopathology (Wan et al., 2022), one explanation for the lower prevalence of ACE could be the exclusion of patients with comorbid psychiatric disorders. Thus, the present sample may represent a rather resilient population with more adaptive coping with their experiences of maltreatment. This restricts the generalizability of our findings to IBD patients with more severe histories of ACE and comorbid mental disorders. Since the significance of childhood traumatization in IBD might be underestimated in the current sample, our findings on the effects of ACE need to be interpreted with caution.

3.4 Implications for future studies

With respect to interoception as multidimensional construct, our results point towards group differences only in one of its dimensions: interoceptive sensibility (IS). As body signals perception might be influenced by previously formed symptom-related memory structures, in IBD, interoceptive signals from the gastrointestinal system might be perceived differently than cardiac sensations. Hence, future studies investigating interoceptive abilities in this clinical population are asked to implement measures of gastric interoception, such as the water load test (WLT). In this non-invasive task, participants are asked to drink water until they feel sated and again, until they can perceive their maximum stomach fullness (Herbert et al., 2012a; van Dyck et al., 2016). By combining measures of cardiac and gastrointestinal IAcc, future studies can shed light on the generalizability of interoceptive abilities in IBD.

Yet, patients with IBD were found to perceive less intense changes in their body signals when experiencing positive and negative emotions. It remains, however, unclear whether decreased emotion-related sensations are necessarily because of avoidance or distraction strategies. For that reason, future studies are asked to examine the links between emotion regulation and the perception of emotion-associated sensations in IBD. Since high emotional awareness can result in an exaggerated perception of negative emotional states when

adaptive regulatory mechanisms are missing, future research should further examine whether higher emotional awareness is necessarily of advantage in IBD populations.

Contrary to our expectations, patients with IBD reported similar rates of ACE as healthy participants. However, most of the studies suggesting a higher prevalence of childhood maltreatment in IBD populations investigated mixed samples including patients with active disease and comorbid psychiatric disorders (Ryan et al., 2013; Wan et al., 2022). Since ACE can lead to dysfunctions of the HPA axis and the glucocorticoid signaling, both being crucial to stress perception and inflammation, it can be speculated that patients reporting early life stress might experience more often a relapse than non-affected patients. Moreover, contemporary findings suggest high co-occurrence of history of ACE and psychiatric disorders in patients with IBD (Wan et al., 2022). While this might explain why we did not observe higher rates of ACE in the present IBD sample, future studies are needed to examine in more detail how disease activity is linked to psychiatric comorbidity and a history of childhood maltreatment. Especially the biological and neuroendocrine mechanisms underlying elevated inflammation in individuals with ACE should be further investigated to gain more insight into the pathophysiology of IBD and comorbid depression and anxiety.

While various studies demonstrated that interoception shares common neural underpinnings with emotion and body perception (Craig, 2004; Terasawa et al., 2013; Zaki et al., 2012), this thesis did not focus on the neural correlates of interoception. While our results suggest a diminished perceived emotional reactivity in IBD, we cannot conclude whether these alterations are associated with an aberrant representation of the emotion-related visceral sensations in the somatosensory or the insular cortex (Berntson & Khalsa, 2021; Critchley & Harrison, 2013; Singer et al., 2009; Wang et al., 2019). Here again, future research is needed to examine whether the observed decreased emotional reactivity in IBD indicates an emotion regulatory mechanism or an impaired integration of visceral and emotional percepts in the brain (Azzalini et al., 2019). Moreover, as the sense of body ownership arises from the multisensory integration of interoceptive and exteroceptive cues (Tsakiris et al., 2011), further insights into the functional activity of interoception-related brain regions can contribute to a better understanding of the observed diminished levels of body ownership in IBD (Craig, 2010; Mayer et al., 2006).

3.5 Conclusions

Despite the increasing interest in psychological factors affecting IBD, studies on emotion processing are sparse and many questions remain unanswered. Not only emotional dysfunctions but also disturbances in patients' body perception have been shown to negatively influence patients' well-being (Banovic et al., 2020; Saha et al., 2015; Wilkinson et al., 2019). Beyond its role in homeostatic regulation, interoception has been shown to shape individual's emotion, cognition, and behavior. Thus, this doctoral thesis was aimed at contributing to a better understanding of the interplay between interoceptive processing, emotion and body perception in IBD and how a history of adverse childhood experiences modulates their interrelations.

The empirical findings presented in this thesis indicate that while patients with IBD do not differ in the ability to perceive their body signals, patients tend to appraise their visceral sensations differently from healthy individuals. While IBD patients reported higher emotional awareness, that is, the awareness that certain changes in one's bodily sensations are triggered by the experience of emotions, they also demonstrated a significantly lower emotional reactivity, characterized by diminished bodily sensations related to the experience of positive and negative emotions. However, higher levels of emotional awareness were found to intensify the perception of these emotion-related sensations, indicating a significant link between emotional awareness, as one key feature of interoceptive sensibility, and emotion processing in IBD. In addition to the observed stronger detachment from one's bodily sensations during emotional experience, patients demonstrated diminished sense of body ownership toward body parts affected by their pain-related symptoms. While interoceptive sensibility was not linked to the extent to which patients experience their bodies as belonging to themselves, patients who reported to be more aware of their interoceptive signals evaluated their bodies more positively. Finally, a history of adverse childhood experiences was found to modulate the links between interoception, emotion processing and body perception, being associated with stronger experience of negative emotions and a significantly diminished sense of body ownership.

Overall, the data presented and discussed in the scope of this doctoral thesis indicate persistent alterations in emotion and body perception in IBD. Our findings contribute to a better understanding of emotional dysfunctions in IBD by demonstrating a diminished experience of emotional states in the body, potentially resulting from the overgeneralized tendency to avoid visceral sensations. The observed stronger detachment from one's bodily sensations may reflect a regulatory mechanism emerging from patients' attempt to avoid distressing bodily sensations,

associated with disease-related pain symptoms, which results not only in an altered experience of emotions but also in a stronger detachment from the body parts affected by these symptoms. As IBD patients reporting a history of ACE constitute an especially vulnerable population and ACE was found to exaggerate disturbances in emotion processing, future psychological interventions are asked to focus on these alterations and their links to childhood maltreatment.

4 SUMMARY

Inflammatory bowel disease (IBD) is an immune-mediated condition, characterized by chronic inflammation of the gastrointestinal tract. Since the course of the disease consists of alternating periods of relapse and remission, patients with IBD experience higher levels of psychological distress, poor quality of life, emotional and social burdens. In IBD, poor emotional functioning as well as disturbances in patients' body perception have been shown to negatively influence patients' well-being. Beyond its role in body's homeostasis, interoception shapes individual's emotions and cognitions. The aim of this dissertation was to contribute to a better understanding of the interplay between interoceptive processing, emotion and body perception in IBD and how a history of adverse childhood experiences modulates their interrelations.

Interoception was examined as a multidimensional construct with its three dissociable components: interoceptive accuracy, interoceptive sensibility, and interoceptive awareness. Patients with IBD did not differ in their ability to perceive signals originating from the body (interoceptive accuracy) or in their meta-awareness of this ability (interoceptive awareness). With respect to their subjective experience of bodily sensations (interoceptive sensibility), patients reported a stronger tendency to use distraction from interoceptive signals and to be more aware that certain changes in one's bodily sensations are associated with the experience of emotions. Despite their higher emotional awareness, patients with IBD exhibited decreased emotional reactivity, characterized by stronger detachment from their emotion-related bodily sensations. As emotions can be associated with the perception of intense visceral signals, which can be misinterpreted as disease-related sensations, patients with IBD seem to extend their distraction strategy to the experience of emotions in the body. Furthermore, as patients reported to experience body areas affected by their pain-related symptoms as less belonging to themselves, this might imply that the distraction from unpleasant bodily sensations can result in a stronger detachment from the body, contributing to body perception disturbances. With respect to interoceptive sensibility, higher levels of emotional awareness were found to intensify the perception of emotion-related bodily sensations in IBD. While interoceptive sensibility was not linked to the extent to which patients experience their bodies as belonging to themselves, patients who reported to be more aware of their visceral sensations evaluated their bodies more positively. Finally, a history of adverse childhood experiences was found to modulate the links between interoception, emotion processing and body perception, being associated with stronger experience of negative emotions and a significantly diminished sense of body ownership.

Overall, the findings presented in this doctoral thesis point towards alterations in emotion processing and body perception in IBD, which are still persistent during the periods of disease remission. As the segment of IBD patients reporting adverse childhood experiences constitutes an especially vulnerable group, future psychological interventions are asked to focus on these specific alterations and their links to childhood maltreatment.

5 LIST OF FIGURES

6 LIST OF TABLES

7 CURRICULUM VITAE

PERSONALIEN

Name:	Konstantina Mihaylova Atanasova
Geburtsdatum:	01. März 1994
Geburtsort:	Varna, Bulgarien

SCHULISCHER WERDEGANG

2001 – 2008	Grundschule „Sachari Stojanow“ Varna, Bulgarien
2008 – 2013	Erstes Fremdsprachengymnasium Varna, Bulgarien
07/2013	Abitur (Note 1,0)

UNIVERSITÄRER WERDEGANG

10/2013 – 09/2016	Studium der Psychologie an der Ruprecht-Karls-Universität Heidelberg
27.09.2016	Bachelor of Science im Fach Psychologie (Abschlussnote: 1,5) Titel der Bachelorarbeit: Neuromagnetic Representation of Pitch and Consonance in the Human Auditory Cortex: an MEG study
09/2016 – 07/2018	Studium der Psychologie an der Universität Mannheim Schwerpunkt Kognitive und klinische Psychologie
24.07.2018	Master of Science im Fach Psychologie (Abschlussnote: 1,7) Titel der Masterarbeit: The influence of Justice Sensitivity on Costly Punishment in Second- and Third-Party Punishment: an fMRI study
08/2018 – 01/2022	Wissenschaftliche Mitarbeiterin und Doktorandin am Zentralinstitut für Seelische Gesundheit Mannheim

	Arbeitsgruppe Experimentelle Psychologie (Prof. Dr. Stefanie Lis) Promotionsprojekt im Rahmen des Graduiertenkollegs (GRK) 2350 am Zentralinstitut für Seelische Gesundheit Mannheim

WEITERE TÄTIGKEITEN

10/2021 – heute	postgraduale Weiterbildung zur psychologischen Psychotherapeutin (Verhaltenstherapie) am Zentrum für Psychologische Psychotherapie Mannheim
WS 2021/2022	Lehrtätigkeit an der Medizinischen Fakultät Mannheim der Universität Heidelberg (Fach: Medizinische Psychologie und Soziologie)

8 PUBLICATIONS

Atanasova, K., Lotter, T., Reindl, W., & Lis, S. (2021). Multidimensional Assessment of Interoceptive Abilities, Emotion Processing and the Role of Early Life Stress in Inflammatory Bowel Diseases. *Frontiers in Psychiatry, 12*(1020). doi:10.3389/fpsyt.2021.680878.

Atanasova, K., Lotter, T., Bekrater-Bodmann, R., Kleindienst, N., Reindl, W., & Lis, S. Is it a gut feeling? Bodily sensations associated with the experience of valence and arousal in patients with inflammatory bowel disease (in review). *Submitted to Frontiers in Psychiatry*

Biermann, M., Schulze, A., Unterseher, F., **Atanasova, K.**, Watermann, P., Krause-Utz, A., . . . Lis, S. (2021). Trustworthiness appraisals of faces wearing a surgical mask during the Covid-19 pandemic in Germany: An experimental study. *PLoS One, 16*(5), e0251393.

Feng, C., Yang, Q., Azem, L., **Atanasova, K. M.**, Gu, R., Luo, W., . . . Krueger, F. (2021). An fMRI investigation of the intention-outcome interactions in second- and third-party punishment. *Brain Imaging Behav*. doi:10.1007/s11682-021-00555-z.

Galinsky, D. F., Erol, E., **Atanasova, K.**, Bohus, M., Krause-Utz, A., & Lis, S. (2020). Do I trust you when you smile? Effects of sex and emotional expression on facial trustworthiness appraisal. *PLoS One, 15*(12), e0243230.

Work in preparation:

Atanasova, K., Lotter, T., Bekrater-Bodmann, R., Kleindienst, N., Thomann, A., Lis, S., & Reindl, W. The experience of basic emotions in the body in patients with inflammatory bowel disease (in preparation)

Atanasova, K., Lotter, T., Bekrater-Bodmann, R., Kleindienst, N., Thomann, A., Lis, S., & Reindl, W. Body representations in patients with inflammatory bowel disease: the role of interoceptive sensibility and adverse childhood experiences (in preparation)

9 REFERENCES

Agostini, A., Ballotta, D., Righi, S., Moretti, M., Bertani, A., Scarcelli, A., Sartini, A., Ercolani, M., Nichelli, P., Campieri, M., & Benuzzi, F. (2017, Oct). Stress and brain functional changes in patients with Crohn's disease: A functional magnetic resonance imaging study. *Neurogastroenterol Motil, 29*(10), 1-10. https://doi.org/10.1111/nmo.13108

Agostini, A., Filippini, N., Cevolani, D., Agati, R., Leoni, C., Tambasco, R., Calabrese, C., Rizzello, F., Gionchetti, P., Ercolani, M., Leonardi, M., & Campieri, M. (2011, Aug). Brain functional changes in patients with ulcerative colitis: a functional magnetic resonance imaging study on emotional processing. *Inflamm Bowel Dis, 17*(8), 1769-1777. https://doi.org/10.1002/ibd.21549

Agostini, A., Rizzello, F., Ravegnani, G., Gionchetti, P., Tambasco, R., Straforini, G., Ercolani, M., & Campieri, M. (2010). Adult attachment and early parental experiences in patients with Crohn's disease. *Psychosomatics, 51*(3), 208-215.

Agostini, A., Scaioli, E., Belluzzi, A., & Campieri, M. (2019). Attachment and Mentalizing Abilities in Patients with Inflammatory Bowel Disease. *Gastroenterol Res Pract, 2019*, 7847123. https://doi.org/10.1155/2019/7847123

Agostini, A., Spuri Fornarini, G., Ercolani, M., & Campieri, M. (2016, Nov). Attachment and perceived stress in patients with ulcerative colitis, a case-control study. *J Psychiatr Ment Health Nurs, 23*(9-10), 561-567. https://doi.org/10.1111/jpm.12331

Ainley, V., Tsakiris, M., Pollatos, O., Schulz, A., & Herbert, B. M. (2020, 2020/04/01/). Comment on "Zamariola et al. (2018), Interoceptive Accuracy Scores are Problematic: Evidence from Simple Bivariate Correlations"—The empirical data base, the conceptual reasoning and the analysis behind this statement are misconceived and do not support the authors' conclusions. *Biological Psychology, 152*, 107870. https://doi.org/https://doi.org/10.1016/j.biopsycho.2020.107870

Alatab, S., Sepanlou, S. G., Ikuta, K., Vahedi, H., Bisignano, C., Safiri, S., Sadeghi, A., Nixon, M. R., Abdoli, A., Abolhassani, H., Alipour, V., Almadi, M. A. H., Almasi-Hashiani, A., Anushiravani, A., Arabloo, J., Atique, S., Awasthi, A., Badawi, A., Baig, A. A. A., Bhala, N., Bijani, A., Biondi, A., Borzì, A. M., Burke, K. E., Carvalho, F., Daryani, A., Dubey, M., Eftekhari, A., Fernandes, E., Fernandes, J. C., Fischer, F., Haj-Mirzaian, A., Haj-Mirzaian, A., Hasanzadeh, A., Hashemian, M., Hay, S. I., Hoang, C. L., Househ, M., Ilesanmi, O. S., Jafari Balalami, N., James, S. L., Kengne, A. P., Malekzadeh, M. M., Merat, S., Meretoja, T. J., Mestrovic, T., Mirrakhimov, E. M., Mirzaei, H., Mohammad, K. A., Mokdad, A. H., Monasta, L., Negoi, I., Nguyen, T. H., Nguyen, C. T., Pourshams, A., Poustchi, H., Rabiee, M., Rabiee, N., Ramezanzadeh, K., Rawaf, D. L., Rawaf, S., Rezaei, N., Robinson, S. R., Ronfani, L., Saxena, S., Sepehrimanesh, M., Shaikh, M. A., Sharafi, Z., Sharif, M., Siabani, S., Sima, A. R., Singh, J. A., Soheili, A., Sotoudehmanesh, R., Suleria, H. A. R., Tesfay, B. E., Tran, B., Tsoi, D., Vacante, M., Wondmieneh, A. B., Zarghi, A., Zhang, Z.-J., Dirac, M., Malekzadeh, R., & Naghavi, M. (2020). The global, regional, and national burden of inflammatory bowel disease in 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *The Lancet Gastroenterology & Hepatology, 5*(1), 17-30. https://doi.org/10.1016/s2468-1253(19)30333-4

Aldao, A., Nolen-Hoeksema, S., & Schweizer, S. (2010, 2010/03/01/). Emotion-regulation strategies across psychopathology: A meta-analytic review. *Clinical Psychology Review, 30*(2), 217-237. https://doi.org/https://doi.org/10.1016/j.cpr.2009.11.004

Ananthakrishnan, A. N., Bernstein, C. N., Iliopoulos, D., Macpherson, A., Neurath, M. F., Ali, R. A. R., Vavricka, S. R., & Fiocchi, C. (2018, 2018/01/01). Environmental triggers in IBD: a review of progress and evidence. *Nature Reviews Gastroenterology & Hepatology, 15*(1), 39-49. https://doi.org/10.1038/nrgastro.2017.136

Araki, M., Shinzaki, S., Yamada, T., Arimitsu, S., Komori, M., Shibukawa, N., Mukai, A., Nakajima, S., Kinoshita, K., & Kitamura, S. (2020). Psychologic stress and disease activity in patients with inflammatory bowel disease: A multicenter cross-sectional study. *PLoS One, 15*(5), e0233365.

Ardi, Z., Golland, Y., Shafir, R., Sheppes, G., & Levit-Binnun, N. (2021). The Effects of Mindfulness-Based Stress Reduction on the Association Between Autonomic Interoceptive Signals and Emotion Regulation Selection. *Psychosomatic medicine, 83*(8), 852-862.

Atanasova, K., Lotter, T., Reindl, W., & Lis, S. (2021, 2021-June-24). Multidimensional Assessment of Interoceptive Abilities, Emotion Processing and the Role of Early Life Stress in Inflammatory Bowel Diseases [Original Research]. *Frontiers in Psychiatry, 12*(1020). https://doi.org/10.3389/fpsyt.2021.680878

Avery, J. A., Drevets, W. C., Moseman, S. E., Bodurka, J., Barcalow, J. C., & Simmons, W. K. (2014, 2014/08/01/). Major Depressive Disorder Is Associated With Abnormal Interoceptive Activity and Functional Connectivity in the Insula. *Biological Psychiatry, 76*(3), 258-266. https://doi.org/https://doi.org/10.1016/j.biopsych.2013.11.027

Azzalini, D., Rebollo, I., & Tallon-Baudry, C. (2019, 2019/06/01/). Visceral Signals Shape Brain Dynamics and Cognition. *Trends in Cognitive Sciences, 23*(6), 488-509. https://doi.org/https://doi.org/10.1016/j.tics.2019.03.007

Badoud, D., & Tsakiris, M. (2017, 2017/06/01/). From the body's viscera to the body's image: Is there a link between interoception and body image concerns? *Neuroscience & Biobehavioral Reviews, 77*, 237-246. https://doi.org/https://doi.org/10.1016/j.neubiorev.2017.03.017

Bannaga, A. S., & Selinger, C. P. (2015). Inflammatory bowel disease and anxiety: links, risks, and challenges faced. *Clinical and experimental gastroenterology, 8*, 111-117. https://doi.org/10.2147/CEG.S57982

Banovic, I., Montreuil, L., Derrey-Bunel, M., Scrima, F., Savoye, G., Beaugerie, L., & Gay, M.-C. (2020, 2020-April-30). Toward Further Understanding of Crohn's Disease-Related Fatigue: The Role of Depression and Emotional Processing [Brief Research Report]. *Frontiers in Psychology, 11*(703). https://doi.org/10.3389/fpsyg.2020.00703

Bardeen, J. R., Tull, M. T., Stevens, E. N., & Gratz, K. L. (2014, 2014/09/01/). Exploring the relationship between positive and negative emotional avoidance and anxiety symptom severity: The moderating role of attentional control. *Journal of Behavior Therapy and Experimental Psychiatry, 45*(3), 415-420. https://doi.org/https://doi.org/10.1016/j.jbtep.2014.04.006

Barrett, L. (1998, 07/01). Discrete Emotions or Dimensions? Th e Role of Valence Focus and Arousal Focus. *Cognition and Emotion, 12*, 579-599. https://doi.org/10.1080/026999398379574

Barrett, L. F. (2017). The theory of constructed emotion: an active inference account of interoception and categorization. *Social Cognitive and Affective Neuroscience, 12*(1), 1-23. https://doi.org/10.1093/scan/nsw154

Barrett, L. F., Quigley, K. S., Bliss-Moreau, E., & Aronson, K. R. (2004, Nov). Interoceptive sensitivity and self-reports of emotional experience. *J Pers Soc Psychol, 87*(5), 684-697. https://doi.org/10.1037/0022-3514.87.5.684

Barrett, L. F., & Simmons, W. K. (2015, 2015/07/01). Interoceptive predictions in the brain. *Nature Reviews Neuroscience, 16*(7), 419-429. https://doi.org/10.1038/nrn3950

Baumgart, D. C., & Carding, S. R. (2007). Inflammatory bowel disease: cause and immunobiology. *The Lancet, 369*(9573), 1627-1640.

Beese, S. E., Harris, I. M., Dretzke, J., & Moore, D. (2019). Body image dissatisfaction in patients with inflammatory bowel disease: a systematic review. *BMJ Open Gastroenterology, 6*(1), e000255. https://doi.org/10.1136/bmjgast-2018-000255

Bekrater-Bodmann, R., Azevedo, R. T., Ainley, V., & Tsakiris, M. (2020). Interoceptive Awareness Is Negatively Related to the Exteroceptive Manipulation of Bodily Self-Location. *Frontiers in Psychology, 11*, 562016-562016. https://doi.org/10.3389/fpsyg.2020.562016

Benjamini, Y., & Hochberg, Y. (1995). Controlling the False Discovery Rate: A Practical and Powerful Approach to Multiple Testing. *Journal of the Royal Statistical Society: Series B (Methodological), 57*(1), 289-300. https://doi.org/https://doi.org/10.1111/j.2517-6161.1995.tb02031.x

Berens, S., Schaefert, R., Ehrenthal, J. C., Baumeister, D., Eich, W., & Tesarz, J. (2021, 2021-March-29). Different Dimensions of Affective Processing in Patients With Irritable Bowel Syndrome: A Multi-Center Cross-Sectional Study [Original Research]. *Frontiers in Psychology, 12*(926). https://doi.org/10.3389/fpsyg.2021.625381

Bernstein, C. N. (2017, Dec). The Brain-Gut Axis and Stress in Inflammatory Bowel Disease. *Gastroenterol Clin North Am, 46*(4), 839-846. https://doi.org/10.1016/j.gtc.2017.08.006

Bernstein, C. N., Hitchon, C. A., Walld, R., Bolton, J. M., Sareen, J., Walker, J. R., Graff, L. A., Patten, S. B., Singer, A., Lix, L. M., El-Gabalawy, R., Katz, A., Fisk, J. D., & Marrie, R. A. (2018). Increased Burden of Psychiatric Disorders in Inflammatory Bowel Disease. *Inflammatory Bowel Diseases, 25*(2), 360-368. https://doi.org/10.1093/ibd/izy235

Berntson, G. G., & Khalsa, S. S. (2021, 2021/01/01/). Neural Circuits of Interoception. *Trends in Neurosciences, 44*(1), 17-28. https://doi.org/https://doi.org/10.1016/j.tins.2020.09.011

Bérubé, A., Turgeon, J., Blais, C., & Fiset, D. (2021). Emotion recognition in adults with a history of childhood maltreatment: a systematic review. *Trauma, Violence, & Abuse*, 15248380211029403.

Bevers, K., Watts, L., Kishino, N. D., & Gatchel, R. J. (2016). The biopsychosocial model of the assessment, prevention, and treatment of chronic pain. *US Neurol, 12*(2), 98-104.

Bifulco, A., Bernazzani, O., Moran, P. M., & Jacobs, C. (2005, Nov). The childhood experience of care and abuse questionnaire (CECA.Q): validation in a community series. *Br J Clin Psychol, 44*(Pt 4), 563-581. https://doi.org/10.1348/014466505x35344

Bitton, A., Dobkin, P., Edwardes, M. D., Sewitch, M., Meddings, J., Rawal, S., Cohen, A., Vermeire, S., Dufresne, L., & Franchimont, D. (2008a). Predicting relapse in Crohn's disease: a biopsychosocial model. *Gut, 57*(10), 1386-1392.

Bitton, A., Dobkin, P. L., Edwardes, M. D., Sewitch, M. J., Meddings, J. B., Rawal, S., Cohen, A., Vermeire, S., Dufresne, L., Franchimont, D., & Wild, G. E. (2008b, Oct). Predicting relapse in Crohn's disease: a biopsychosocial model. *Gut, 57*(10), 1386-1392. https://doi.org/10.1136/gut.2007.134817

Bonaz, B., Lane, R. D., Oshinsky, M. L., Kenny, P. J., Sinha, R., Mayer, E. A., & Critchley, H. D. (2021, 2021/01/01/). Diseases, Disorders, and Comorbidities of Interoception. *Trends in Neurosciences, 44*(1), 39-51. https://doi.org/https://doi.org/10.1016/j.tins.2020.09.009

Bonaz, B. L., & Bernstein, C. N. (2013). Brain-gut interactions in inflammatory bowel disease. *Gastroenterology, 144*(1), 36-49.

Borg, C., Chouchou, F., Dayot-Gorlero, J., Zimmerman, P., Maudoux, D., Laurent, B., & Michael, G. A. (2018). Pain and emotion as predictive factors of interoception in fibromyalgia. *J Pain Res, 11*, 823-835. https://doi.org/10.2147/jpr.S152012

Borgmann, E., Kleindienst, N., Vocks, S., & Dyer, A. S. (2014, 2014/07/25). Standardized mirror confrontation: Body-related emotions, cognitions and level of dissociation in patients with Posttraumatic Stress Disorder after childhood sexual abuse. *Borderline Personality Disorder and Emotion Dysregulation, 1*(1), 10. https://doi.org/10.1186/2051-6673-1-10

Bornemann, B., Herbert, B. M., Mehling, W. E., & Singer, T. (2015, 2015-January-06). Differential changes in self-reported aspects of interoceptive awareness through 3 months of contemplative training [Original Research]. *Frontiers in Psychology, 5*(1504). https://doi.org/10.3389/fpsyg.2014.01504

Bradley, M. M., & Lang, P. J. (1994, Mar). Measuring emotion: the Self-Assessment Manikin and the Semantic Differential. *J Behav Ther Exp Psychiatry, 25*(1), 49-59. https://doi.org/10.1016/0005-7916(94)90063-9

Bromet, E., Andrade, L. H., Hwang, I., Sampson, N. A., Alonso, J., De Girolamo, G., De Graaf, R., Demyttenaere, K., Hu, C., & Iwata, N. (2011). Cross-national epidemiology of DSM-IV major depressive episode. *BMC medicine, 9*(1), 1-16.

Brown, R. J. (2004, Sep). Psychological mechanisms of medically unexplained symptoms: an integrative conceptual model. *Psychol Bull, 130*(5), 793-812. https://doi.org/10.1037/0033-2909.130.5.793

Bultitude, J. H., & Rafal, R. D. (2010, Jul). Derangement of body representation in complex regional pain syndrome: report of a case treated with mirror and prisms. *Exp Brain Res, 204*(3), 409-418. https://doi.org/10.1007/s00221-009-2107-8

Calì, G., Ambrosini, E., Picconi, L., Mehling, W. E., & Committeri, G. (2015). Investigating the relationship between interoceptive accuracy, interoceptive awareness, and emotional susceptibility. *Front Psychol, 6*, 1202. https://doi.org/10.3389/fpsyg.2015.01202

Cameron, O. G., & Minoshima, S. (2002). Regional brain activation due to pharmacologically induced adrenergic interoceptive stimulation in humans. *Psychosomatic medicine, 64*(6), 851-861.

Cannon, W. B. (1927). The James-Lange theory of emotions: A critical examination and an alternative theory. *The American journal of psychology, 39*(1/4), 106-124.

Capuron, L., & Miller, A. H. (2011, 2011/05/01/). Immune system to brain signaling: Neuropsychopharmacological implications. *Pharmacology & Therapeutics, 130*(2), 226-238. https://doi.org/https://doi.org/10.1016/j.pharmthera.2011.01.014

Carlson, L. E., Angen, M., Cullum, J., Goodey, E., Koopmans, J., Lamont, L., MacRae, J. H., Martin, M., Pelletier, G., Robinson, J., Simpson, J. S., Speca, M., Tillotson, L., & Bultz, B. D. (2004, Jun 14). High levels of untreated distress and fatigue in cancer patients. *Br J Cancer, 90*(12), 2297-2304. https://doi.org/10.1038/sj.bjc.6601887

Ceuleers, H., Van Spaendonk, H., Hanning, N., Heirbaut, J., Lambeir, A.-M., Joossens, J., Augustyns, K., De Man, J. G., De Meester, I., & De Winter, B. Y. (2016). Visceral hypersensitivity in inflammatory bowel diseases and irritable bowel syndrome: The role of proteases. *World journal of gastroenterology, 22*(47), 10275-10286. https://doi.org/10.3748/wjg.v22.i47.10275

Ceunen, E., Vlaeyen, J. W. S., & Van Diest, I. (2016, 2016-May-23). On the Origin of Interoception [Review]. *Frontiers in Psychology, 7*(743). https://doi.org/10.3389/fpsyg.2016.00743

Chapman, S., & Martin, M. (2011). Attention to pain words in irritable bowel syndrome: Increased orienting and speeded engagement. *British Journal of Health Psychology, 16*(1), 47-60. https://doi.org/https://doi.org/10.1348/135910710X505887

Chen, W. G., Schloesser, D., Arensdorf, A. M., Simmons, J. M., Cui, C., Valentino, R., Gnadt, J. W., Nielsen, L., Hillaire-Clarke, C. S., Spruance, V., Horowitz, T. S., Vallejo, Y. F., & Langevin, H. M. (2021). The Emerging Science of Interoception: Sensing, Integrating, Interpreting, and Regulating Signals within the Self. *Trends in Neurosciences, 44*(1), 3-16. https://doi.org/10.1016/j.tins.2020.10.007

Choi, A., & Shin, H. (2018). Quantitative Analysis of the Effect of an Ectopic Beat on the Heart Rate Variability in the Resting Condition. *Frontiers in physiology, 9*, 922-922. https://doi.org/10.3389/fphys.2018.00922

Claytor, J. D., Kochar, B., Kappelman, M. D., & Long, M. D. (2020, 2020/08/01/). Body Image Dissatisfaction among Pediatric Patients with Inflammatory Bowel Disease. *The Journal of Pediatrics, 223*, 68-72.e61. https://doi.org/https://doi.org/10.1016/j.jpeds.2020.04.045

Coley, E. J., Mayer, E. A., Osadchiy, V., Chen, Z., Subramanyam, V., Zhang, Y., Hsiao, E. Y., Gao, K., Bhatt, R., & Dong, T. (2021). Early life adversity predicts brain-gut alterations associated with increased stress and mood. *Neurobiology of stress*, 100348.

Copeland, W. E., Shanahan, L., Hinesley, J., Chan, R. F., Aberg, K. A., Fairbank, J. A., van den Oord, E., & Costello, E. J. (2018, Nov 2). Association of Childhood Trauma Exposure With Adult Psychiatric Disorders and Functional Outcomes. *JAMA Netw Open, 1*(7), e184493. https://doi.org/10.1001/jamanetworkopen.2018.4493

Cordier, L., Fuchs, X., Herpertz, S., Trojan, J., & Diers, M. (2020, 2020/05/01/). Synchronous Stimulation With Light and Heat Induces Body Ownership and Reduces Pain Perception. *The Journal of Pain, 21*(5), 700-707. https://doi.org/https://doi.org/10.1016/j.jpain.2019.10.009

Craig, A. D. (2002, Aug). How do you feel? Interoception: the sense of the physiological condition of the body. *Nat Rev Neurosci, 3*(8), 655-666. https://doi.org/10.1038/nrn894

Craig, A. D. (2003, Aug). Interoception: the sense of the physiological condition of the body. *Curr Opin Neurobiol, 13*(4), 500-505. https://doi.org/10.1016/s0959-4388(03)00090-4

Craig, A. D. (2004, Jun). Human feelings: why are some more aware than others? *Trends Cogn Sci, 8*(6), 239-241. https://doi.org/10.1016/j.tics.2004.04.004

Craig, A. D. (2009, 2009/01/01). How do you feel — now? The anterior insula and human awareness. *Nature Reviews Neuroscience, 10*(1), 59-70. https://doi.org/10.1038/nrn2555

Craig, A. D. (2010, Jun). The sentient self. *Brain Struct Funct, 214*(5-6), 563-577. https://doi.org/10.1007/s00429-010-0248-y

Critchley, H. D. (2005). Neural mechanisms of autonomic, affective, and cognitive integration. *Journal of Comparative Neurology, 493*(1), 154-166. https://doi.org/https://doi.org/10.1002/cne.20749

Critchley, H. D., & Garfinkel, S. N. (2017, 2017/10/01/). Interoception and emotion. *Current Opinion in Psychology, 17*, 7-14. https://doi.org/https://doi.org/10.1016/j.copsyc.2017.04.020

Critchley, H. D., & Harrison, N. A. (2013, Feb 20). Visceral influences on brain and behavior. *Neuron, 77*(4), 624-638. https://doi.org/10.1016/j.neuron.2013.02.008

Critchley, H. D., Wiens, S., Rotshtein, P., Ohman, A., & Dolan, R. J. (2004, Feb). Neural systems supporting interoceptive awareness. *Nat Neurosci, 7*(2), 189-195. https://doi.org/10.1038/nn1176

Crucianelli, L., Krahé, C., Jenkinson, P. M., & Fotopoulou, A. (2018, 2018/07/01/). Interoceptive ingredients of body ownership: Affective touch and cardiac awareness in

the rubber hand illusion. *Cortex, 104*, 180-192. https://doi.org/https://doi.org/10.1016/j.cortex.2017.04.018

Cruz-Sáez, S., Pascual, A., Wlodarczyk, A., & Echeburúa, E. (2020). The effect of body dissatisfaction on disordered eating: The mediating role of self-esteem and negative affect in male and female adolescents. *Journal of Health Psychology, 25*(8), 1098-1108. https://doi.org/10.1177/1359105317748734

Cushman, G., Stolz, M. G., Shih, S., Listernick, Z., Talmadge, C., Gold, B. D., & Reed, B. (2021). Age, Disease Symptoms, and Depression are Associated With Body Image Dissatisfaction in Newly Diagnosed Pediatric Inflammatory Bowel Disease. *Journal of pediatric gastroenterology and nutrition, 72*(3), e57-e62. https://doi.org/10.1097/MPG.0000000000002943

Damasio, A. (2001, 2001/10/01). Fundamental feelings. *Nature, 413*(6858), 781-781. https://doi.org/10.1038/35101669

Damasio, A. R. (1998). Emotion in the perspective of an integrated nervous system. *Brain research reviews, 26*(2-3), 83-86.

Damasio, A. R., Everitt, B. J., Bishop, D., Roberts, A. C., Robbins, T. W., & Weiskrantz, L. (1996). The somatic marker hypothesis and the possible functions of the prefrontal cortex. *Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences, 351*(1346), 1413-1420. https://doi.org/doi:10.1098/rstb.1996.0125

Danese, A., & Lewis, S. J. (2017). Psychoneuroimmunology of early-life stress: the hidden wounds of childhood trauma? *Neuropsychopharmacology, 42*(1), 99-114.

Danese, A., Moffitt, T. E., Harrington, H., Milne, B. J., Polanczyk, G., Pariante, C. M., Poulton, R., & Caspi, A. (2009). Adverse childhood experiences and adult risk factors for age-related disease: depression, inflammation, and clustering of metabolic risk markers. *Archives of pediatrics & adolescent medicine, 163*(12), 1135-1143.

Dannlowski, U., Kugel, H., Huber, F., Stuhrmann, A., Redlich, R., Grotegerd, D., Dohm, K., Sehlmeyer, C., Konrad, C., & Baune, B. T. (2013). Childhood maltreatment is associated with an automatic negative emotion processing bias in the amygdala. *Human Brain Mapping, 34*(11), 2899-2909.

Dannlowski, U., Stuhrmann, A., Beutelmann, V., Zwanzger, P., Lenzen, T., Grotegerd, D., Domschke, K., Hohoff, C., Ohrmann, P., Bauer, J., Lindner, C., Postert, C., Konrad, C., Arolt, V., Heindel, W., Suslow, T., & Kugel, H. (2012, Feb 15). Limbic scars: long-term consequences of childhood maltreatment revealed by functional and structural magnetic resonance imaging. *Biol Psychiatry, 71*(4), 286-293. https://doi.org/10.1016/j.biopsych.2011.10.021

Davey, S., Bell, E., Halberstadt, J., & Collings, S. (2020, 2020/07/14). Where is an emotion? Using targeted visceroception as a method of improving emotion regulation in healthy participants to inform suicide prevention initiatives: a randomised controlled trial. *Trials, 21*(1), 642. https://doi.org/10.1186/s13063-020-04479-9

de Jong, M., Lazar, S. W., Hug, K., Mehling, W. E., Hölzel, B. K., Sack, A. T., Peeters, F., Ashih, H., Mischoulon, D., & Gard, T. (2016). Effects of Mindfulness-Based Cognitive Therapy on Body Awareness in Patients with Chronic Pain and Comorbid Depression. *Front Psychol, 7*, 967. https://doi.org/10.3389/fpsyg.2016.00967

Dempster, K. S., O'Leary, D. D., MacNeil, A. J., Hodges, G. J., & Wade, T. J. (2020, Dec 21). Linking the hemodynamic consequences of adverse childhood experiences to an altered HPA axis and acute stress response. *Brain Behav Immun*. https://doi.org/10.1016/j.bbi.2020.12.018

Drake, M. J., Fowler, C. J., Griffiths, D., Mayer, E., Paton, J. F. R., & Birder, L. (2010). Neural control of the lower urinary and gastrointestinal tracts: Supraspinal CNS mechanisms. *Neurourology and Urodynamics, 29*(1), 119-127. https://doi.org/https://doi.org/10.1002/nau.20841

Drossman, D. A., Leserman, J., Nachman, G., Li, Z., Gluck, H., Toomey, T. C., & Mitchell, C. M. (1990). Sexual and physical abuse in women with functional or organic gastrointestinal disorders. *Annals of internal medicine, 113*(11), 828-833.

Dube, S. R., Fairweather, D., Pearson, W. S., Felitti, V. J., Anda, R. F., & Croft, J. B. (2009). Cumulative childhood stress and autoimmune diseases in adults. *Psychosomatic medicine, 71*(2), 243.

Duschek, S., Werner, N. S., del Paso, G. A. R., & Schandry, R. (2015). The contributions of interoceptive awareness to cognitive and affective facets of body experience. *Journal of Individual Differences*.

Dyer, A., Borgmann, E., Feldmann, R. E., Kleindienst, N., Priebe, K., Bohus, M., & Vocks, S. (2013a, 2013/03/01/). Body image disturbance in patients with borderline personality disorder: Impact of eating disorders and perceived childhood sexual abuse. *Body Image, 10*(2), 220-225. https://doi.org/https://doi.org/10.1016/j.bodyim.2012.12.007

Dyer, A., Borgmann, E., Kleindienst, N., Feldmann Jr, R. E., Vocks, S., & Bohus, M. (2013b). Body Image in Patients with Posttraumatic Stress Disorder after Childhood Sexual Abuse and Co-Occurring Eating Disorder. *Psychopathology, 46*(3), 186-191. https://doi.org/10.1159/000341590

Ehlers, A., Margraf, J., Roth, W. T., Taylor, C. B., & Birbaumer, N. (1988, 1988/01/01/). Anxiety induced by false heart rate feedback in patients with panic disorder. *Behaviour Research and Therapy, 26*(1), 1-11. https://doi.org/https://doi.org/10.1016/0005-7967(88)90028-9

Eid, M., Gollwitzer, M., & Schmitt, M. (2011). *Statistik und Forschungsmethoden* (Vol. 2. Auflage).

Ekman, P. (1992). An argument for basic emotions. *Cognition & Emotion, 6*(3-4), 169-200.

Ekman, P., & Friesen, W. V. (1971, Feb). Constants across cultures in the face and emotion. *J Pers Soc Psychol, 17*(2), 124-129. https://doi.org/10.1037/h0030377

Electrophysiology, T. F. o. t. E. S. o. C. t. N. A. S. o. P. (1996). Heart rate variability: standards of measurement, physiological interpretation, and clinical use. *Circulation, 93*(5), 1043-1065.

Elsenbruch, S., Rosenberger, C., Enck, P., Forsting, M., Schedlowski, M., & Gizewski, E. R. (2010). Affective disturbances modulate the neural processing of visceral pain stimuli in irritable bowel syndrome: an fMRI study. *Gut, 59*(4), 489. https://doi.org/10.1136/gut.2008.175000

Emanuelsen, L., Drew, R., & Köteles, F. (2015). Interoceptive sensitivity, body image dissatisfaction, and body awareness in healthy individuals. *Scandinavian Journal of Psychology, 56*(2), 167-174. https://doi.org/https://doi.org/10.1111/sjop.12183

Engel, F., Berens, S., Gauss, A., Schaefert, R., Eich, W., & Tesarz, J. (2021, 2021-June-24). Higher Levels of Psychological Burden and Alterations in Personality Functioning in Crohn's Disease and Ulcerative Colitis [Original Research]. *Frontiers in Psychology, 12*(2550). https://doi.org/10.3389/fpsyg.2021.671493

Engel, G. L. (1981). The clinical application of the biopsychosocial model. The Journal of Medicine and Philosophy: A Forum for Bioethics and Philosophy of Medicine,

Eshel, N., Maron-Katz, A., Wu, W., Abu-Amara, D., Marmar, C. R., & Etkin, A. (2021). Neural correlates of anger expression in patients with PTSD. *Neuropsychopharmacology*, 1-8.

Ewais, T., Begun, J., Kenny, M., Headey, A., Tefay, M., & Kisely, S. (2020). Mindfulness-based cognitive therapy experiences in youth with inflammatory bowel disease and depression: findings from a mixed methods qualitative study. *BMJ open, 10*(11), e041140-e041140. https://doi.org/10.1136/bmjopen-2020-041140

Ewais, T., Begun, J., Kenny, M., Rickett, K., Hay, K., Ajilchi, B., & Kisely, S. (2019, 2019/01/01/). A systematic review and meta-analysis of mindfulness based interventions and yoga in inflammatory bowel disease. *Journal of Psychosomatic Research, 116*, 44-53. https://doi.org/https://doi.org/10.1016/j.jpsychores.2018.11.010

Fagundes, C. P., & Way, B. (2014, 2014/08/01). Early-Life Stress and Adult Inflammation. *Current Directions in Psychological Science, 23*(4), 277-283. https://doi.org/10.1177/0963721414535603

Fan, Y., Bao, C., Wei, Y., Wu, J., Zhao, Y., Zeng, X., Qin, W., Wu, H., & Liu, P. (2020, 2020/12/01). Altered functional connectivity of the amygdala in Crohn's disease. *Brain Imaging and Behavior, 14*(6), 2097-2106. https://doi.org/10.1007/s11682-019-00159-8

Farmer, A. D., & Aziz, Q. (2013, Feb). Gut pain & visceral hypersensitivity. *Br J Pain, 7*(1), 39-47. https://doi.org/10.1177/2049463713479229

Farrell, D., Artom, M., Czuber-Dochan, W., Jelsness-Jørgensen, L. P., Norton, C., & Savage, E. (2020, Apr 16). Interventions for fatigue in inflammatory bowel disease. *Cochrane Database Syst Rev, 4*(4), Cd012005. https://doi.org/10.1002/14651858.CD012005.pub2

Fealey, R. D. (2013). Chapter 7 - Interoception and autonomic nervous system reflexes thermoregulation. In R. M. Buijs & D. F. Swaab (Eds.), *Handbook of Clinical Neurology* (Vol. 117, pp. 79-88). Elsevier. https://doi.org/https://doi.org/10.1016/B978-0-444-53491-0.00007-9

Feldner, M. T., Zvolensky, M. J., Eifert, G. H., & Spira, A. P. (2003, 2003/04/01/). Emotional avoidance: an experimental test of individual differences and response suppression using biological challenge. *Behaviour Research and Therapy, 41*(4), 403-411. https://doi.org/https://doi.org/10.1016/S0005-7967(02)00020-7

Ferentzi, E., Bogdány, T., Szabolcs, Z., Csala, B., Horváth, Á., & Köteles, F. (2018). Multichannel Investigation of Interoception: Sensitivity Is Not a Generalizable Feature. *Front Hum Neurosci, 12*, 223. https://doi.org/10.3389/fnhum.2018.00223

Finotti, G., & Costantini, M. (2016, 2016/02/12). Multisensory body representation in autoimmune diseases. *Scientific Reports, 6*(1), 21074. https://doi.org/10.1038/srep21074

Fischer, D., Messner, M., & Pollatos, O. (2017, 2017-September-12). Improvement of Interoceptive Processes after an 8-Week Body Scan Intervention [Original Research]. *Frontiers in Human Neuroscience, 11*(452). https://doi.org/10.3389/fnhum.2017.00452

Fournier, A., Mondillon, L., Luminet, O., Canini, F., Mathieu, N., Gauchez, A. S., Dantzer, C., Bonaz, B., & Pellissier, S. (2020). Interoceptive Abilities in Inflammatory Bowel Diseases and Irritable Bowel Syndrome. *Front Psychiatry, 11*, 229. https://doi.org/10.3389/fpsyt.2020.00229

Franke, G. H., Ankerhold, A., Haase, M., Jäger, S., Tögel, C., Ulrich, C., & Frommer, J. (2011, Feb). [The usefulness of the Brief Symptom Inventory 18 (BSI-18) in psychotherapeutic patients]. *Psychother Psychosom Med Psychol, 61*(2), 82-86. https://doi.org/10.1055/s-0030-1270518 (Der Einsatz des Brief Symptom Inventory 18 (BSI-18) bei Psychotherapiepatienten.)

Franke, G. H., Jaeger, S., Glaesmer, H., Barkmann, C., Petrowski, K., & Braehler, E. (2017, Jan 26). Psychometric analysis of the brief symptom inventory 18 (BSI-18) in a representative German sample. *BMC Med Res Methodol, 17*(1), 14. https://doi.org/10.1186/s12874-016-0283-3

Fukushima, H., Terasawa, Y., & Umeda, S. (2011, 2011/02/01/). Association between interoception and empathy: Evidence from heartbeat-evoked brain potential. *International Journal of Psychophysiology, 79*(2), 259-265. https://doi.org/https://doi.org/10.1016/j.ijpsycho.2010.10.015

Fuller-Thomson, E., West, K. J., Sulman, J., & Baird, S. L. (2015, Nov). Childhood Maltreatment Is Associated with Ulcerative Colitis but Not Crohn's Disease: Findings from a Population-based Study. *Inflamm Bowel Dis, 21*(11), 2640-2648. https://doi.org/10.1097/MIB.0000000000000551

Füstös, J., Gramann, K., Herbert, B. M., & Pollatos, O. (2013, Dec). On the embodiment of emotion regulation: interoceptive awareness facilitates reappraisal. *Soc Cogn Affect Neurosci, 8*(8), 911-917. https://doi.org/10.1093/scan/nss089

Gajdos, P., Chrisztó, Z., & Rigó, A. (2020, Jun 15). The association of different interoceptive dimensions with functional gastrointestinal symptoms. *J Health Psychol*, 1359105320929426. https://doi.org/10.1177/1359105320929426

Gallagher, S. (2000, 2000/01/01/). Philosophical conceptions of the self: implications for cognitive science. *Trends in Cognitive Sciences, 4*(1), 14-21. https://doi.org/https://doi.org/10.1016/S1364-6613(99)01417-5

Garfinkel, S. N., Manassei, M. F., Hamilton-Fletcher, G., In den Bosch, Y., Critchley, H. D., & Engels, M. (2016). Interoceptive dimensions across cardiac and respiratory axes. *Philosophical Transactions of the Royal Society B: Biological Sciences, 371*(1708), 20160014. https://doi.org/doi:10.1098/rstb.2016.0014

Garfinkel, S. N., Minati, L., Gray, M. A., Seth, A. K., Dolan, R. J., & Critchley, H. D. (2014, May 7). Fear from the heart: sensitivity to fear stimuli depends on individual heartbeats. *J Neurosci, 34*(19), 6573-6582. https://doi.org/10.1523/JNEUROSCI.3507-13.2014

Garfinkel, S. N., Seth, A. K., Barrett, A. B., Suzuki, K., & Critchley, H. D. (2015, Jan). Knowing your own heart: distinguishing interoceptive accuracy from interoceptive awareness. *Biol Psychol, 104*, 65-74. https://doi.org/10.1016/j.biopsycho.2014.11.004

Garland, E. L., Gaylord, S. A., Palsson, O., Faurot, K., Douglas Mann, J., & Whitehead, W. E. (2012). Therapeutic mechanisms of a mindfulness-based treatment for IBS: effects on visceral sensitivity, catastrophizing, and affective processing of pain sensations. *Journal of behavioral medicine, 35*(6), 591-602. https://doi.org/10.1007/s10865-011-9391-z

Glück, T. M., Knefel, M., & Lueger-Schuster, B. (2017, 2017/11/30). A network analysis of anger, shame, proposed ICD-11 post-traumatic stress disorder, and different types of childhood trauma in foster care settings in a sample of adult survivors. *European Journal of Psychotraumatology, 8*(sup3), 1372543. https://doi.org/10.1080/20008198.2017.1372543

Goubert, L., Crombez, G., Eccleston, C., & Devulder, J. (2004, 08/01). Distraction from chronic pain during a pain-inducing activity is associated with greater post-activity pain. *Pain, 110*, 220-227. https://doi.org/10.1016/j.pain.2004.03.034

Gracie, D. J., Guthrie, E. A., Hamlin, P. J., & Ford, A. C. (2018, 2018/05/01/). Bi-directionality of Brain–Gut Interactions in Patients With Inflammatory Bowel Disease. *Gastroenterology, 154*(6), 1635-1646.e1633. https://doi.org/https://doi.org/10.1053/j.gastro.2018.01.027

Gracie, D. J., Irvine, A. J., Sood, R., Mikocka-Walus, A., Hamlin, P. J., & Ford, A. C. (2017, 2017/03/01/). Effect of psychological therapy on disease activity, psychological comorbidity, and quality of life in inflammatory bowel disease: a systematic review and meta-analysis. *The Lancet Gastroenterology & Hepatology, 2*(3), 189-199. https://doi.org/https://doi.org/10.1016/S2468-1253(16)30206-0

Grant, M. M., Cannistraci, C., Hollon, S. D., Gore, J., & Shelton, R. (2011). Childhood trauma history differentiates amygdala response to sad faces within MDD. *Journal of psychiatric research, 45*(7), 886-895.

Grogan, S. (2016). Women and body image. In *Body Image* (pp. 52-88). Routledge.

Harvey, R. F., & Bradshaw, M. J. (1980, May 24). Measuring Crohn's disease activity. *Lancet, 1*(8178), 1134-1135. https://doi.org/10.1016/s0140-6736(80)91577-9

Hassani, F., Koraei, A., Yaghoobi, R., & Zarea, K. (2020). An evaluating of the relationship between body image, body satisfaction, depression, marital quality, and self-esteem in patients with psoriasis. *Psychology, Health & Medicine*, 1-11. https://doi.org/10.1080/13548506.2020.1766093

Hayes, A. F. (2017). *Introduction to mediation, moderation, and conditional process analysis: A regression-based approach*. Guilford publications.

Hayes, S. C., Wilson, K. G., Gifford, E. V., Follette, V. M., & Strosahl, K. (1996). Experiential avoidance and behavioral disorders: A functional dimensional approach to diagnosis and treatment. *Journal of Consulting and Clinical Psychology, 64*(6), 1152.

Hein, T. C., & Monk, C. S. (2017). Research Review: Neural response to threat in children, adolescents, and adults after child maltreatment – a quantitative meta-analysis. *Journal of Child Psychology and Psychiatry, 58*(3), 222-230. https://doi.org/https://doi.org/10.1111/jcpp.12651

Herbert, Muth, E. R., Pollatos, O., & Herbert, C. (2012a). Interoception across modalities: on the relationship between cardiac awareness and the sensitivity for gastric functions. *PLoS One, 7*(5), e36646. https://doi.org/10.1371/journal.pone.0036646

Herbert, B. M., Herbert, C., & Pollatos, O. (2011). On the relationship between interoceptive awareness and alexithymia: is interoceptive awareness related to emotional awareness? *Journal of personality, 79*(5), 1149-1175.

Herbert, B. M., Herbert, C., Pollatos, O., Weimer, K., Enck, P., Sauer, H., & Zipfel, S. (2012b, 2012/01/01/). Effects of short-term food deprivation on interoceptive awareness, feelings and autonomic cardiac activity. *Biological Psychology, 89*(1), 71-79. https://doi.org/https://doi.org/10.1016/j.biopsycho.2011.09.004

Herbert, B. M., Pollatos, O., & Schandry, R. (2007, Sep). Interoceptive sensitivity and emotion processing: an EEG study. *Int J Psychophysiol, 65*(3), 214-227. https://doi.org/10.1016/j.ijpsycho.2007.04.007

Hertzman, C. (1999). The biological embedding of early experience and its effects on health in adulthood. *Annals of the New York Academy of Sciences, 896*(1), 85-95.

Herzog, J. I., & Schmahl, C. (2018). Adverse Childhood Experiences and the Consequences on Neurobiological, Psychosocial, and Somatic Conditions Across the Lifespan. *Front Psychiatry, 9*, 420. https://doi.org/10.3389/fpsyt.2018.00420

Heymen, S., Maixner, W., Whitehead, W. E., Klatzkin, R. R., Mechlin, B., & Light, K. C. (2010, Feb). Central processing of noxious somatic stimuli in patients with irritable bowel syndrome compared with healthy controls. *Clin J Pain, 26*(2), 104-109. https://doi.org/10.1097/AJP.0b013e3181bff800

Hina, F., & Aspell, J. E. (2019, 2019/08/01/). Altered interoceptive processing in smokers: Evidence from the heartbeat tracking task. *International Journal of Psychophysiology, 142*, 10-16. https://doi.org/https://doi.org/10.1016/j.ijpsycho.2019.05.012

Hong, J.-Y., Labus, J. S., Jiang, Z., Ashe-Mcnalley, C., Dinov, I., Gupta, A., Shi, Y., Stains, J., Heendeniya, N., Smith, S. R., Tillisch, K., & Mayer, E. A. (2014). Regional Neuroplastic Brain Changes in Patients with Chronic Inflammatory and Non-Inflammatory Visceral Pain. *PLoS One, 9*(1), e84564. https://doi.org/10.1371/journal.pone.0084564

Hood, M. M., & Jedel, S. (2017, Dec). Mindfulness-Based Interventions in Inflammatory Bowel Disease. *Gastroenterol Clin North Am, 46*(4), 859-874. https://doi.org/10.1016/j.gtc.2017.08.008

Hu, S., Chen, Y., Chen, Y., & Wang, C. (2021, 2021-October-08). Depression and Anxiety Disorders in Patients With Inflammatory Bowel Disease [Review]. *Frontiers in Psychiatry, 12*(1643). https://doi.org/10.3389/fpsyt.2021.714057

Icenhour, A., Witt, S. T., Elsenbruch, S., Lowen, M., Engstrom, M., Tillisch, K., Mayer, E. A., & Walter, S. (2017). Brain functional connectivity is associated with visceral sensitivity in women with Irritable Bowel Syndrome. *Neuroimage Clin, 15*, 449-457. https://doi.org/10.1016/j.nicl.2017.06.001

Iffland, B., Klein, F., Rosner, R., Renneberg, B., Steil, R., & Neuner, F. (2020). Cardiac reactions to emotional words in adolescents and young adults with PTSD after child abuse. *Psychophysiology, 57*(1), e13470. https://doi.org/https://doi.org/10.1111/psyp.13470

Iffland, B., & Neuner, F. (2020, 2020-April-16). Varying Cognitive Scars – Differential Associations Between Types of Childhood Maltreatment and Facial Emotion Processing [Original Research]. *Frontiers in Psychology, 11*(732). https://doi.org/10.3389/fpsyg.2020.00732

Iglesias, M., Barreiro de Acosta, M., Vázquez, I., Figueiras, A., Nieto, L., Lorenzo, A., & Domínguez-Muñoz, J. E. (2009, 2009/04//). Psychological impact of Crohn's disease on patients in remission: anxiety and depression risks. *Revista espanola de enfermedades digestivas : organo oficial de la Sociedad Espanola de Patologia Digestiva, 101*(4), 249-257. http://europepmc.org/abstract/MED/19492900

Jacobson, E. (1938). *Progressive Relaxation: A Physiological and Clinical Investigation of Muscular States and Their Significance in Psychology and Medical Practice*. University of Chicago Press. https://books.google.de/books?id=d5MKAAAAMAAJ

James, W. (1994). The physical basis of emotion.

Jansen, A. S., Nguyen, X. V., Karpitskiy, V., Mettenleiter, T. C., & Loewy, A. D. (1995, Oct 27). Central command neurons of the sympathetic nervous system: basis of the fight-or-flight response. *Science, 270*(5236), 644-646. https://doi.org/10.1126/science.270.5236.644

Jones, M. P., Wessinger, S., & Crowell, M. D. (2006, Apr). Coping strategies and interpersonal support in patients with irritable bowel syndrome and inflammatory bowel disease. *Clin Gastroenterol Hepatol, 4*(4), 474-481. https://doi.org/10.1016/j.cgh.2005.12.012

Kabat-Zinn, J. (2003). Mindfulness-based stress reduction (MBSR). *Constructivism in the Human Sciences, 8*(2), 73.

Kaess, M., Parzer, P., Mattern, M., Resch, F., Bifulco, A., & Brunner, R. (2011, Jul). [Childhood Experiences of Care and Abuse (CECA) - validation of the German version of the questionnaire and interview, and results of an investigation of correlations between adverse childhood experiences and suicidal behaviour]. *Z Kinder Jugendpsychiatr Psychother, 39*(4), 243-252. https://doi.org/10.1024/1422-4917/a000115 (Validierung der deutschen Version von Fragebogen und korrespondierendem Interview sowie Ergebnisse einer Untersuchung von Zusammenhangen belastender Kindheitserlebnisse mit suizidalen Verhaltensweisen.)

Kammers, M. P. M., Rose, K., & Haggard, P. (2011, 2011/04/01/). Feeling numb: Temperature, but not thermal pain, modulates feeling of body ownership. *Neuropsychologia, 49*(5), 1316-1321. https://doi.org/https://doi.org/10.1016/j.neuropsychologia.2011.02.039

Kano, M., Muratsubaki, T., Yagihashi, M., Morishita, J., Mugikura, S., Dupont, P., Takase, K., Kanazawa, M., Van Oudenhove, L., & Fukudo, S. (2020). Insula activity to visceral stimulation and endocrine stress responses as associated with alexithymia in patients with irritable bowel syndrome. *Psychosomatic medicine, 82*(1), 29-38.

Kearney, D. J., McDermott, K., Martinez, M., & Simpson, T. L. (2011). Association of participation in a mindfulness programme with bowel symptoms, gastrointestinal symptom-specific anxiety and quality of life. *Alimentary Pharmacology & Therapeutics, 34*(3), 363-373. https://doi.org/https://doi.org/10.1111/j.1365-2036.2011.04731.x

Kelly, M. M., & Forsyth, J. P. (2009, 2009/04/01/). Associations between emotional avoidance, anxiety sensitivity, and reactions to an observational fear challenge procedure. *Behaviour Research and Therapy, 47*(4), 331-338. https://doi.org/https://doi.org/10.1016/j.brat.2009.01.008

Khalsa, S. S., Adolphs, R., Cameron, O. G., Critchley, H. D., Davenport, P. W., Feinstein, J. S., Feusner, J. D., Garfinkel, S. N., Lane, R. D., Mehling, W. E., Meuret, A. E., Nemeroff, C. B., Oppenheimer, S., Petzschner, F. H., Pollatos, O., Rhudy, J. L., Schramm, L. P., Simmons, W. K., Stein, M. B., Stephan, K. E., Van den Bergh, O., Van Diest, I., von Leupoldt, A., & Paulus, M. P. (2018, Jun). Interoception and Mental Health: A Roadmap. *Biol Psychiatry Cogn Neurosci Neuroimaging, 3*(6), 501-513. https://doi.org/10.1016/j.bpsc.2017.12.004

Khalsa, S. S., & Lapidus, R. C. (2016). Can Interoception Improve the Pragmatic Search for Biomarkers in Psychiatry? *Front Psychiatry, 7*, 121. https://doi.org/10.3389/fpsyt.2016.00121

Khalsa, S. S., Rudrauf, D., Feinstein, J. S., & Tranel, D. (2009, 2009/12/01). The pathways of interoceptive awareness. *Nature Neuroscience, 12*(12), 1494-1496. https://doi.org/10.1038/nn.2411

Kleindienst, N., Priebe, K., Borgmann, E., Cornelisse, S., Krüger, A., Ebner-Priemer, U., & Dyer, A. (2014, 2014/04/10). Body self-evaluation and physical scars in patients with borderline personality disorder: an observational study. *Borderline Personality Disorder and Emotion Dysregulation, 1*(1), 2. https://doi.org/10.1186/2051-6673-1-2

Klinitzke, G., Romppel, M., Häuser, W., Brähler, E., & Glaesmer, H. (2012, Feb). [The German Version of the Childhood Trauma Questionnaire (CTQ): psychometric characteristics in a representative sample of the general population]. *Psychother Psychosom Med Psychol, 62*(2), 47-51. https://doi.org/10.1055/s-0031-1295495 (Die deutsche Version des Childhood Trauma Questionnaire (CTQ) - psychometrische Eigenschaften in einer bevölkerungsrepräsentativen Stichprobe.)

Knapp-Kline, K., & Kline, J. P. (2005, Jul). Heart rate, heart rate variability, and heartbeat detection with the method of constant stimuli: slow and steady wins the race. *Biol Psychol, 69*(3), 387-396. https://doi.org/10.1016/j.biopsycho.2004.09.002

Knowles, S. R., Graff, L. A., Wilding, H., Hewitt, C., Keefer, L., & Mikocka-Walus, A. (2018). Quality of Life in Inflammatory Bowel Disease: A Systematic Review and Meta-analyses—Part I. *Inflammatory Bowel Diseases, 24*(4), 742-751. https://doi.org/10.1093/ibd/izx100

Kohler, O., Krogh, J., Mors, O., & Benros, M. E. (2016). Inflammation in Depression and the Potential for Anti-Inflammatory Treatment. *Curr Neuropharmacol, 14*(7), 732-742. https://doi.org/10.2174/1570159x14666151208113700

Kurdi, B., Lozano, S., & Banaji, M. R. (2017, 2017/04/01). Introducing the Open Affective Standardized Image Set (OASIS). *Behavior Research Methods, 49*(2), 457-470. https://doi.org/10.3758/s13428-016-0715-3

La Barbera, D., Bonanno, B., Rumeo, M. V., Alabastro, V., Frenda, M., Massihnia, E., Morgante, M. C., Sideli, L., Craxì, A., Cappello, M., Tumminello, M., Micciché, S., & Nastri, L. (2017, 2017/02/02). Alexithymia and personality traits of patients with inflammatory bowel disease. *Scientific Reports, 7*(1), 41786. https://doi.org/10.1038/srep41786

Labus, J. S., Bolus, R., Chang, L., Wiklund, I., Naesdal, J., Mayer, E. A., & Naliboff, B. D. (2004, Jul 1). The Visceral Sensitivity Index: development and validation of a gastrointestinal symptom-specific anxiety scale. *Aliment Pharmacol Ther, 20*(1), 89-97. https://doi.org/10.1111/j.1365-2036.2004.02007.x

Labus, J. S., Mayer, E. A., Chang, L., Bolus, R., & Naliboff, B. D. (2007). The central role of gastrointestinal-specific anxiety in irritable bowel syndrome: further validation of the visceral sensitivity index. *Psychosomatic medicine, 69*(1), 89-98.

Lang, P. J., & Bradley, M. M. (2013). Appetitive and Defensive Motivation: Goal-Directed or Goal-Determined? *Emotion Review, 5*(3), 230-234. https://doi.org/10.1177/1754073913477511

Lange, C. G. (1885). The mechanism of the emotions. *The classical psychologists*, 672-684.

Larsson, M. B., Tillisch, K., Craig, A., Engström, M., Labus, J., Naliboff, B., Lundberg, P., Ström, M., Mayer, E. A., & Walter, S. A. (2012). Brain responses to visceral stimuli reflect visceral sensitivity thresholds in patients with irritable bowel syndrome. *Gastroenterology, 142*(3), 463-472. e463.

Lazarus, R. S. (1991). Progress on a cognitive-motivational-relational theory of emotion. *American psychologist, 46*(8), 819.

LeDoux, J. E., & Brown, R. (2017). A higher-order theory of emotional consciousness. *Proceedings of the National Academy of Sciences, 114*(10), E2016-E2025. https://doi.org/10.1073/pnas.1619316114

Lehrl, S., Triebig, G., & Fischer, B. (1995, May). Multiple choice vocabulary test MWT as a valid and short test to estimate premorbid intelligence. *Acta Neurol Scand, 91*(5), 335-345. https://doi.org/10.1111/j.1600-0404.1995.tb07018.x

Leonard, B., & Maes, M. (2012, Feb). Mechanistic explanations how cell-mediated immune activation, inflammation and oxidative and nitrosative stress pathways and their sequels and concomitants play a role in the pathophysiology of unipolar depression. *Neurosci Biobehav Rev, 36*(2), 764-785. https://doi.org/10.1016/j.neubiorev.2011.12.005

Leppänen, J. M. (2006). Emotional information processing in mood disorders: a review of behavioral and neuroimaging findings. *Current Opinion in Psychiatry, 19*(1), 34-39. https://doi.org/10.1097/01.yco.0000191500.46411.00

Levine, J. S., & Burakoff, R. (2011). Extraintestinal manifestations of inflammatory bowel disease. *Gastroenterology & hepatology, 7*(4), 235-241. https://pubmed.ncbi.nlm.nih.gov/21857821
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3127025/

Levy, R. L., van Tilburg, M. A. L., Langer, S. L., Romano, J. M., Walker, L. S., Mancl, L. A., Murphy, T. B., Claar, R. L., Feld, S. I., Christie, D. L., Abdullah, B., DuPen, M. M., Swanson, K. S., Baker, M. D., Stoner, S. A., & Whitehead, W. E. (2016). Effects of a Cognitive Behavioral Therapy Intervention Trial to Improve Disease Outcomes in Children with Inflammatory Bowel Disease. *Inflammatory Bowel Diseases, 22*(9), 2134-2148. https://doi.org/10.1097/mib.0000000000000881

Lewis, J. S., Kersten, P., McCabe, C. S., McPherson, K. M., & Blake, D. R. (2007). Body perception disturbance: a contribution to pain in complex regional pain syndrome (CRPS). *PAIN®, 133*(1-3), 111-119.

Lewis, K., Marrie, R. A., Bernstein, C. N., Graff, L. A., Patten, S. B., Sareen, J., Fisk, J. D., Bolton, J. M., Burden, C. T. i. D. t., & Disease, M. t. E. o. I.-M. I. (2019). The Prevalence and Risk Factors of Undiagnosed Depression and Anxiety Disorders Among Patients With Inflammatory Bowel Disease. *Inflammatory Bowel Diseases, 25*(10), 1674-1680. https://doi.org/10.1093/ibd/izz045

Lichev, V., Sacher, J., Ihme, K., Rosenberg, N., Quirin, M., Lepsien, J., Pampel, A., Rufer, M., Grabe, H.-J., Kugel, H., Kersting, A., Villringer, A., Lane, R. D., & Suslow, T. (2014). Automatic emotion processing as a function of trait emotional awareness: an fMRI study. *Social Cognitive and Affective Neuroscience, 10*(5), 680-689. https://doi.org/10.1093/scan/nsu104

Lissek, S., & van Meurs, B. (2015, 2015/12/01/). Learning models of PTSD: Theoretical accounts and psychobiological evidence. *International Journal of Psychophysiology, 98*(3, Part 2), 594-605. https://doi.org/https://doi.org/10.1016/j.ijpsycho.2014.11.006

Liu, S., Hagiwara, S. I., & Bhargava, A. (2017, Sep). Early-life adversity, epigenetics, and visceral hypersensitivity. *Neurogastroenterol Motil, 29*(9). https://doi.org/10.1111/nmo.13170

Löffler, A., Foell, J., & Bekrater-Bodmann, R. (2018, Mar 28). Interoception and Its Interaction with Self, Other, and Emotion Processing: Implications for the Understanding of Psychosocial Deficits in Borderline Personality Disorder. *Curr Psychiatry Rep, 20*(4), 28. https://doi.org/10.1007/s11920-018-0890-2

Löffler, A., Kleindienst, N., Cackowski, S., Schmidinger, I., & Bekrater-Bodmann, R. (2020, Mar-Apr). Reductions in Whole-body Ownership in Borderline Personality Disorder - A Phenomenological Manifestation of Dissociation. *J Trauma Dissociation, 21*(2), 264-277. https://doi.org/10.1080/15299732.2019.1678213

Longarzo, M., Quarantelli, M., Aiello, M., Romano, M., Del Prete, A., Cimminiello, C., Cocozza, S., Olivo, G., Loguercio, C., Trojano, L., & Grossi, D. (2017, Aug). The influence of interoceptive awareness on functional connectivity in patients with irritable bowel syndrome. *Brain Imaging Behav, 11*(4), 1117-1128. https://doi.org/10.1007/s11682-016-9595-5

Lutz, J., Herwig, U., Opialla, S., Hittmeyer, A., Jäncke, L., Rufer, M., Grosse Holtforth, M., & Brühl, A. B. (2013). Mindfulness and emotion regulation—an fMRI study. *Social Cognitive and Affective Neuroscience, 9*(6), 776-785. https://doi.org/10.1093/scan/nst043

Markey, C. H., Dunaev, J. L., & August, K. J. (2020, 2020/03/01/). Body image experiences in the context of chronic pain: An examination of associations among perceptions of pain, body dissatisfaction, and positive body image. *Body Image, 32*, 103-110. https://doi.org/https://doi.org/10.1016/j.bodyim.2019.11.005

Martino, G., Caputo, A., Schwarz, P., Bellone, F., Fries, W., Quattropani, M. C., & Vicario, C. M. (2020, 2020-August-19). Alexithymia and Inflammatory Bowel Disease: A Systematic Review [Systematic Review]. *Frontiers in Psychology, 11*(1763). https://doi.org/10.3389/fpsyg.2020.01763

Marusak, H. A., Martin, K. R., Etkin, A., & Thomason, M. E. (2015, Mar 13). Childhood trauma exposure disrupts the automatic regulation of emotional processing. *Neuropsychopharmacology, 40*(5), 1250-1258. https://doi.org/10.1038/npp.2014.311

Matamala-Gomez, M., Malighetti, C., Cipresso, P., Pedroli, E., Realdon, O., Mantovani, F., & Riva, G. (2020, 2020-August-21). Changing Body Representation Through Full Body Ownership Illusions Might Foster Motor Rehabilitation Outcome in Patients With Stroke [Perspective]. *Frontiers in Psychology, 11*(1962). https://doi.org/10.3389/fpsyg.2020.01962

Matamala-Gomez, M., Maselli, A., Malighetti, C., Realdon, O., Mantovani, F., & Riva, G. (2021). Virtual Body Ownership Illusions for Mental Health: A Narrative Review. *Journal of Clinical Medicine, 10*(1), 139. https://www.mdpi.com/2077-0383/10/1/139

Mauss, I. B., Levenson, R. W., McCarter, L., Wilhelm, F. H., & Gross, J. J. (2005). The tie that binds? Coherence among emotion experience, behavior, and physiology. *Emotion, 5*(2), 175.

Mauss, I. B., & Robinson, M. D. (2009). Measures of emotion: A review. *Cognition and Emotion, 23*(2), 209-237.

Mawdsley, J. E., & Rampton, D. S. (2005). Psychological stress in IBD: new insights into pathogenic and therapeutic implications. *Gut, 54*(10), 1481-1491. https://doi.org/10.1136/gut.2005.064261

Mawdsley, J. E., & Rampton, D. S. (2006). The role of psychological stress in inflammatory bowel disease. *Neuroimmunomodulation, 13*(5-6), 327-336. https://doi.org/10.1159/000104861

Mayer, E. A. (2000). The neurobiology of stress and gastrointestinal disease. *Gut, 47*(6), 861-869.

Mayer, E. A. (2011, 2011/08/01). Gut feelings: the emerging biology of gut–brain communication. *Nature Reviews Neuroscience, 12*(8), 453-466. https://doi.org/10.1038/nrn3071

Mayer, E. A., Berman, S., Suyenobu, B., Labus, J., Mandelkern, M. A., Naliboff, B. D., & Chang, L. (2005). Differences in brain responses to visceral pain between patients with irritable bowel syndrome and ulcerative colitis. *Pain, 115*(3), 398-409.

Mayer, E. A., Naliboff, B. D., & Craig, A. B. (2006). Neuroimaging of the brain-gut axis: from basic understanding to treatment of functional GI disorders. *Gastroenterology, 131*(6), 1925-1942.

Mayer, E. A., Savidge, T., & Shulman, R. J. (2014). Brain-gut microbiome interactions and functional bowel disorders. *Gastroenterology, 146*(6), 1500-1512. https://doi.org/10.1053/j.gastro.2014.02.037

McDermott, E., Mullen, G., Moloney, J., Keegan, D., Byrne, K., Doherty, G. A., Cullen, G., Malone, K., & Mulcahy, H. E. (2015). Body Image Dissatisfaction: Clinical Features, and Psychosocial Disability in Inflammatory Bowel Disease. *Inflammatory Bowel Diseases, 21*(2), 353-360. https://doi.org/10.1097/mib.0000000000000287

McLaughlin, K. A., Conron, K. J., Koenen, K. C., & Gilman, S. E. (2010). Childhood adversity, adult stressful life events, and risk of past-year psychiatric disorder: a test of the stress sensitization hypothesis in a population-based sample of adults. *Psychological medicine, 40*(10), 1647-1658. https://doi.org/10.1017/S0033291709992121

McLaughlin, K. A., & Lambert, H. K. (2017, Apr). Child Trauma Exposure and Psychopathology: Mechanisms of Risk and Resilience. *Curr Opin Psychol, 14*, 29-34. https://doi.org/10.1016/j.copsyc.2016.10.004

McLaughlin, K. A., Sheridan, M. A., Tibu, F., Fox, N. A., Zeanah, C. H., & Nelson, C. A. (2015). Causal effects of the early caregiving environment on development of stress response systems in children. *Proceedings of the National Academy of Sciences, 112*(18), 5637-5642. https://doi.org/10.1073/pnas.1423363112

Mehling, W. (2016, Nov 19). Differentiating attention styles and regulatory aspects of self-reported interoceptive sensibility. *Philos Trans R Soc Lond B Biol Sci, 371*(1708). https://doi.org/10.1098/rstb.2016.0013

Mehling, W. E., Daubenmier, J., Price, C. J., Acree, M., Bartmess, E., & Stewart, A. L. (2013). Self-reported interoceptive awareness in primary care patients with past or current low back pain. *J Pain Res, 6*, 403-418. https://doi.org/10.2147/jpr.S42418

Mehling, W. E., Gopisetty, V., Daubenmier, J., Price, C. J., Hecht, F. M., & Stewart, A. (2009). Body awareness: construct and self-report measures. *PLoS One, 4*(5), e5614.

Mehling, W. E., Price, C., Daubenmier, J. J., Acree, M., Bartmess, E., & Stewart, A. (2012). The Multidimensional Assessment of Interoceptive Awareness (MAIA). *PLoS One, 7*(11), e48230. https://doi.org/10.1371/journal.pone.0048230

Monti, A., Porciello, G., Panasiti, M. S., & Aglioti, S. M. (2021). Gut markers of bodily self-consciousness. *bioRxiv*, 2021.2003.2005.434072. https://doi.org/10.1101/2021.03.05.434072

Moulton, C. D., Pavlidis, P., Norton, C., Norton, S., Pariante, C., Hayee, B., & Powell, N. (2019). Depressive symptoms in inflammatory bowel disease: an extraintestinal manifestation of inflammation? *Clinical & Experimental Immunology, 197*(3), 308-318.

Moylan, S., Maes, M., Wray, N. R., & Berk, M. (2013, May). The neuroprogressive nature of major depressive disorder: pathways to disease evolution and resistance, and therapeutic implications. *Mol Psychiatry, 18*(5), 595-606. https://doi.org/10.1038/mp.2012.33

Murphy, J., Brewer, R., Catmur, C., & Bird, G. (2017, Feb). Interoception and psychopathology: A developmental neuroscience perspective. *Dev Cogn Neurosci, 23*, 45-56. https://doi.org/10.1016/j.dcn.2016.12.006

Murphy, J., Brewer, R., Plans, D., Khalsa, S. S., Catmur, C., & Bird, G. (2020). Testing the independence of self-reported interoceptive accuracy and attention. *Quarterly Journal of Experimental Psychology, 73*(1), 115-133. https://doi.org/10.1177/1747021819879826

Murphy, J., Catmur, C., & Bird, G. (2019, 2019/10/01). Classifying individual differences in interoception: Implications for the measurement of interoceptive awareness. *Psychonomic Bulletin & Review, 26*(5), 1467-1471. https://doi.org/10.3758/s13423-019-01632-7

Neilson, K., Ftanou, M., Monshat, K., Salzberg, M., Bell, S., Kamm, M. A., Connell, W., Knowles, S. R., Sevar, K., Mancuso, S. G., & Castle, D. (2015). A Controlled Study of a Group Mindfulness Intervention for Individuals Living With Inflammatory Bowel Disease. *Inflammatory Bowel Diseases, 22*(3), 694-701. https://doi.org/10.1097/mib.0000000000000629

Neuendorf, R., Harding, A., Stello, N., Hanes, D., & Wahbeh, H. (2016). Depression and anxiety in patients with inflammatory bowel disease: a systematic review. *Journal of Psychosomatic Research, 87*, 70-80.

Nummenmaa, L., Glerean, E., Hari, R., & Hietanen, J. K. (2014, Jan 14). Bodily maps of emotions. *Proc Natl Acad Sci U S A, 111*(2), 646-651. https://doi.org/10.1073/pnas.1321664111

Olatunji, B. O., Ciesielski, B. G., & Tolin, D. F. (2010, 2010/03/01/). Fear and Loathing: A Meta-Analytic Review of the Specificity of Anger in PTSD. *Behavior Therapy, 41*(1), 93-105. https://doi.org/https://doi.org/10.1016/j.beth.2009.01.004

Oppenheimer, S., & Cechetto, D. (2016, Mar 15). The Insular Cortex and the Regulation of Cardiac Function. *Compr Physiol, 6*(2), 1081-1133. https://doi.org/10.1002/cphy.c140076

Orth, U., & Wieland, E. (2006). Anger, hostility, and posttraumatic stress disorder in trauma-exposed adults: a meta-analysis. *Journal of Consulting and Clinical Psychology, 74*(4), 698.

Osborn, M., & Widom, C. S. (2020). Do documented records and retrospective reports of childhood maltreatment similarly predict chronic inflammation? *Psychological medicine, 50*(14), 2406-2415. https://doi.org/10.1017/S0033291719002575

Pan, J., & Tompkins, W. J. (1985). A real-time QRS detection algorithm. *IEEE transactions on biomedical engineering*(3), 230-236.

Paulus, M. P., & Stein, M. B. (2010). Interoception in anxiety and depression. *Brain Structure and Function, 214*(5), 451-463.

Pawlow, L. A., & Jones, G. E. (2002, 2002/07/01/). The impact of abbreviated progressive muscle relaxation on salivary cortisol. *Biological Psychology, 60*(1), 1-16. https://doi.org/https://doi.org/10.1016/S0301-0511(02)00010-8

Phillips, K., Wright, B. J., & Kent, S. (2014, 2014/07/01/). Irritable bowel syndrome and symptom severity: Evidence of negative attention bias, diminished vigour, and autonomic dysregulation. *Journal of Psychosomatic Research, 77*(1), 13-19. https://doi.org/https://doi.org/10.1016/j.jpsychores.2014.04.009

Pinquart, M. (2013). Self-esteem of children and adolescents with chronic illness: a meta-analysis. *Child: Care, Health and Development, 39*(2), 153-161. https://doi.org/https://doi.org/10.1111/j.1365-2214.2012.01397.x

Pollak, S. D., Cicchetti, D., Hornung, K., & Reed, A. (2000). Recognizing emotion in faces: developmental effects of child abuse and neglect. *Developmental psychology, 36*(5), 679.

Pollak, S. D., & Sinha, P. (2002). Effects of early experience on children's recognition of facial displays of emotion. *Developmental psychology, 38*(5), 784.

Pollatos, O., Gramann, K., & Schandry, R. (2007a, Jan). Neural systems connecting interoceptive awareness and feelings. *Hum Brain Mapp, 28*(1), 9-18. https://doi.org/10.1002/hbm.20258

Pollatos, O., Herbert, B., Matthias, E., & Schandry, R. (2007b, 02/01). Heart rate response after emotional presentation is modulated by interoceptive awareness. *International journal of psychophysiology : official journal of the International Organization of Psychophysiology, 63*, 117-124. https://doi.org/10.1016/j.ijpsycho.2006.09.003

Pollatos, O., Kirsch, W., & Schandry, R. (2005a). Brain structures involved in interoceptive awareness and cardioafferent signal processing: A dipole source localization study. *Human Brain Mapping, 26*(1), 54-64. https://doi.org/https://doi.org/10.1002/hbm.20121

Pollatos, O., Kirsch, W., & Schandry, R. (2005b, 2005/12/01/). On the relationship between interoceptive awareness, emotional experience, and brain processes. *Cognitive Brain Research, 25*(3), 948-962. https://doi.org/https://doi.org/10.1016/j.cogbrainres.2005.09.019

Porges, S. (1993). Body perception questionnaire. *Laboratory of Developmental Assessment, University of Maryland*.

Puetz, V. B., Viding, E., Gerin, M. I., Pingault, J. B., Sethi, A., Knodt, A. R., Radtke, S. R., Brigidi, B. D., Hariri, A. R., & McCrory, E. (2020, Jun). Investigating patterns of neural response associated with childhood abuse v. childhood neglect. *Psychological medicine, 50*(8), 1398-1407. https://doi.org/10.1017/s003329171900134x

Quadt, L., Critchley, H. D., & Garfinkel, S. N. (2018, Sep). The neurobiology of interoception in health and disease. *Ann N Y Acad Sci, 1428*(1), 112-128. https://doi.org/10.1111/nyas.13915

Rabellino, D., Burin, D., Harricharan, S., Lloyd, C., Frewen, P. A., McKinnon, M. C., & Lanius, R. A. (2018). Altered Sense of Body Ownership and Agency in Posttraumatic Stress Disorder and Its Dissociative Subtype: A Rubber Hand Illusion Study. *Front Hum Neurosci, 12*, 163. https://doi.org/10.3389/fnhum.2018.00163

Reber, S. (2012). Stress and animal models of inflammatory bowel disease—an update on the role of the hypothalamo–pituitary–adrenal axis. *Psychoneuroendocrinology, 37*(1), 1-19.

Rebollo, I., Devauchelle, A.-D., Béranger, B., & Tallon-Baudry, C. (2018). Stomach-brain synchrony reveals a novel, delayed-connectivity resting-state network in humans. *Elife, 7*, e33321.

Reinhardt, K. M., Zerubavel, N., Young, A. S., Gallo, M., Ramakrishnan, N., Henry, A., & Zucker, N. L. (2020, Nov 1). A multi-method assessment of interoception among sexual trauma survivors. *Physiol Behav, 226*, 113108. https://doi.org/10.1016/j.physbeh.2020.113108

Ring, C., Brener, J., Knapp, K., & Mailloux, J. (2015, Jan). Effects of heartbeat feedback on beliefs about heart rate and heartbeat counting: a cautionary tale about interoceptive awareness. *Biol Psychol, 104*, 193-198. https://doi.org/10.1016/j.biopsycho.2014.12.010

Rosenberg, M. (1965). Rosenberg self-esteem scale (RSE). *Acceptance and commitment therapy. Measures package, 61*(52), 18.

Rosenström, T., Jokela, M., Hintsanen, M., Josefsson, K., Juonala, M., Kivimäki, M., Pulkki-Råback, L., Viikari, J. S. A., Hutri-Kähönen, N., Heinonen, E., Raitakari, O. T., & Keltikangas-Järvinen, L. (2013, 2013/09/05/). Body-image dissatisfaction is strongly associated with chronic dysphoria. *Journal of Affective Disorders, 150*(2), 253-260. https://doi.org/https://doi.org/10.1016/j.jad.2013.04.003

Ruben, J., Schwiemann, J., Deuchert, M., Meyer, R., Krause, T., Curio, G., Villringer, K., Kurth, R., & Villringer, A. (2001, May). Somatotopic organization of human secondary somatosensory cortex. *Cereb Cortex, 11*(5), 463-473. https://doi.org/10.1093/cercor/11.5.463

Rubio, A., Pellissier, S., Picot, A., Dantzer, C., & Bonaz, B. (2014, Aug). The link between negative affect, vagal tone, and visceral sensitivity in quiescent Crohn's disease. *Neurogastroenterol Motil, 26*(8), 1200-1203. https://doi.org/10.1111/nmo.12373

Rubio, A., Pellissier, S., Van Oudenhove, L., Ly, H. G., Dupont, P., Tack, J., Dantzer, C., Delon-Martin, C., & Bonaz, B. (2016). Brain responses to uncertainty about upcoming rectal discomfort in quiescent Crohn's disease–a fMRI study. *Neurogastroenterology & Motility, 28*(9), 1419-1432.

Russell, J. A. (1980). A circumplex model of affect. *Journal of personality and social psychology, 39*(6), 1161.

Ryan, J. D., Silverberg, M. S., Xu, W., Graff, L. A., Targownik, L. E., Walker, J. R., Carr, R., Clara, I., Miller, N., Rogala, L., & Bernstein, C. N. (2013). Predicting complicated Crohn's disease and surgery: phenotypes, genetics, serology and psychological characteristics of a population-based cohort. *Alimentary Pharmacology & Therapeutics, 38*(3), 274-283. https://doi.org/https://doi.org/10.1111/apt.12368

Sack, M., Boroske-Leiner, K., & Lahmann, C. (2010, 2010/05/01/). Association of nonsexual and sexual traumatizations with body image and psychosomatic symptoms in psychosomatic outpatients. *General Hospital Psychiatry, 32*(3), 315-320. https://doi.org/https://doi.org/10.1016/j.genhosppsych.2010.01.002

Sadowski, A., Dunlap, C., Lacombe, A., & Hanes, D. (2020, Dec 18). Alterations in Heart Rate Variability Associated With Irritable Bowel Syndrome or Inflammatory Bowel Disease: A Systematic Review and Meta-Analysis. *Clin Transl Gastroenterol, 12*(1), e00275. https://doi.org/10.14309/ctg.0000000000000275

Saha, S., Zhao, Y.-Q., Shah, S. A., Esposti, S. D., Lidofsky, S., Bright, R., Law, M., Moniz, H., Samad, Z., Merrick, M., & Sands, B. E. (2015). Body Image Dissatisfaction in Patients with Inflammatory Bowel Disease. *Inflammatory Bowel Diseases, 21*(2), 345-352. https://doi.org/10.1097/mib.0000000000000270

Schaan, L., Schulz, A., Nuraydin, S., Bergert, C., Hilger, A., Rach, H., & Hechler, T. (2019a, Apr). Interoceptive accuracy, emotion recognition, and emotion regulation in preschool children. *Int J Psychophysiol, 138*, 47-56. https://doi.org/10.1016/j.ijpsycho.2019.02.001

Schaan, V. K., Schulz, A., Rubel, J. A., Bernstein, M., Domes, G., Schächinger, H., & Vögele, C. (2019b). Childhood Trauma Affects Stress-Related Interoceptive Accuracy. *Front Psychiatry, 10*, 750. https://doi.org/10.3389/fpsyt.2019.00750

Schachter, S., & Singer, J. (1962). Cognitive, social, and physiological determinants of emotional state. *Psychological review, 69*(5), 379.

Schaefer, M., Egloff, B., & Witthöft, M. (2012, Aug). Is interoceptive awareness really altered in somatoform disorders? Testing competing theories with two paradigms of heartbeat perception. *J Abnorm Psychol, 121*(3), 719-724. https://doi.org/10.1037/a0028509

Schandry, R. (1981, Jul). Heart beat perception and emotional experience. *Psychophysiology, 18*(4), 483-488. https://doi.org/10.1111/j.1469-8986.1981.tb02486.x

Scheffers, M., Hoek, M., Bosscher, R. J., van Duijn, M. A. J., Schoevers, R. A., & van Busschbach, J. T. (2017a, 2017/01/01). Negative body experience in women with early childhood trauma: associations with trauma severity and dissociation. *European Journal of Psychotraumatology, 8*(1), 1322892. https://doi.org/10.1080/20008198.2017.1322892

Scheffers, M., Kalisvaart, H., van Busschbach, J. T., Bosscher, R. J., van Duijn, M. A. J., van Broeckhuysen-Kloth, S. A. M., Schoevers, R. A., & Geenen, R. (2018, 2018/10/22). Body image in patients with somatoform disorder. *BMC Psychiatry, 18*(1), 346. https://doi.org/10.1186/s12888-018-1928-z

Scheffers, M., Van Busschbach, J. T., Bosscher, R. J., Aerts, L. C., Wiersma, D., & Schoevers, R. A. (2017b). Body image in patients with mental disorders: Characteristics, associations with diagnosis and treatment outcome. *Comprehensive psychiatry, 74*, 53-60.

Schimmenti, A. (2018). The trauma factor: Examining the relationships among different types of trauma, dissociation, and psychopathology. *Journal of Trauma & Dissociation, 19*(5), 552-571.

Schmitz, M., Bertsch, K., Löffler, A., Steinmann, S., Herpertz, S. C., & Bekrater-Bodmann, R. (2021, 2021/05/17). Body connection mediates the relationship between traumatic childhood experiences and impaired emotion regulation in borderline personality disorder. *Borderline Personality Disorder and Emotion Dysregulation, 8*(1), 17. https://doi.org/10.1186/s40479-021-00157-7

Schroeder, K. W., Tremaine, W. J., & Ilstrup, D. M. (1987). Coated oral 5-aminosalicylic acid therapy for mildly to moderately active ulcerative colitis. *New England Journal of Medicine, 317*(26), 1625-1629.

Schuette, S. A., Zucker, N. L., & Smoski, M. J. (2020, 2020/06/16). Do interoceptive accuracy and interoceptive sensibility predict emotion regulation? *Psychological Research*. https://doi.org/10.1007/s00426-020-01369-2

Schultz, J. H., & Luthe, W. (1959). Autogenic training: A psychophysiologic approach to psychotherapy.

Schulz, A., Deuter, C. E., Breden, I.-H., Vögele, C., Wingenfeld, K., Otte, C., & Kuehl, L. K. (2021). Noradrenergic activation induced by yohimbine decreases interoceptive accuracy in healthy individuals with childhood adversity. *Development and Psychopathology*, 1-12.

Schulz, A., & Vögele, C. (2015). Interoception and stress. *Front Psychol, 6*, 993. https://doi.org/10.3389/fpsyg.2015.00993

Sedghamiz, H. (2014). Matlab implementation of Pan Tompkins ECG QRS detector. *Code Available at the File Exchange Site of MathWorks*.

Shaffer, F., & Ginsberg, J. (2017). An overview of heart rate variability metrics and norms. *Frontiers in public health, 5*, 258.

Shah, K., Ramos-Garcia, M., Bhavsar, J., & Lehrer, P. (2020, 2020/05/01/). Mind-body treatments of irritable bowel syndrome symptoms: An updated meta-analysis. *Behaviour Research and Therapy, 128*, 103462. https://doi.org/https://doi.org/10.1016/j.brat.2019.103462

Shah, P., Hall, R., Catmur, C., & Bird, G. (2016, 2016/08/01/). Alexithymia, not autism, is associated with impaired interoception. *Cortex, 81*, 215-220. https://doi.org/https://doi.org/10.1016/j.cortex.2016.03.021

Sheppes, G. (2020). Chapter Four - Transcending the "good & bad" and "here & now" in emotion regulation: Costs and benefits of strategies across regulatory stages. In B. Gawronski (Ed.), *Advances in Experimental Social Psychology* (Vol. 61, pp. 185-236). Academic Press. https://doi.org/https://doi.org/10.1016/bs.aesp.2019.09.003

Sheppes, G., Scheibe, S., Suri, G., & Gross, J. J. (2011). Emotion-Regulation Choice. *Psychological science, 22*(11), 1391-1396. https://doi.org/10.1177/0956797611418350

Sheppes, G., Scheibe, S., Suri, G., Radu, P., Blechert, J., & Gross, J. J. (2014). Emotion regulation choice: a conceptual framework and supporting evidence. *Journal of Experimental Psychology: General, 143*(1), 163.

Sherrington, C. (1952). *The integrative action of the nervous system*. CUP Archive.

Sherrington, C. S. (1906). Observations on the scratch-reflex in the spinal dog. *The Journal of Physiology, 34*(1-2), 1-50. https://doi.org/https://doi.org/10.1113/jphysiol.1906.sp001139

Sifneos, P. E. (1996). Alexithymia: past and present. *The American journal of psychiatry*.

Simmons, W. K., Avery, J. A., Barcalow, J. C., Bodurka, J., Drevets, W. C., & Bellgowan, P. (2013). Keeping the body in mind: Insula functional organization and functional connectivity integrate interoceptive, exteroceptive, and emotional awareness. *Human Brain Mapping, 34*(11), 2944-2958. https://doi.org/https://doi.org/10.1002/hbm.22113

Simons, L. E., Elman, I., & Borsook, D. (2014, 2014/02/01/). Psychological processing in chronic pain: A neural systems approach. *Neuroscience & Biobehavioral Reviews, 39*, 61-78. https://doi.org/https://doi.org/10.1016/j.neubiorev.2013.12.006

Singer, T., Critchley, H. D., & Preuschoff, K. (2009, 2009/08/01/). A common role of insula in feelings, empathy and uncertainty. *Trends in Cognitive Sciences, 13*(8), 334-340. https://doi.org/https://doi.org/10.1016/j.tics.2009.05.001

Smith, R., Feinstein, J. S., Kuplicki, R., Forthman, K. L., Stewart, J. L., Paulus, M. P., Aupperle, R. L., Bodurka, J., Savitz, J. B., Victor, T. A., Khalsa, S. S., & Tulsa, I. (2021, 2021/01/22). Perceptual insensitivity to the modulation of interoceptive signals in depression, anxiety, and substance use disorders. *Scientific Reports, 11*(1), 2108. https://doi.org/10.1038/s41598-021-81307-3

Solcà, M., Park, H.-D., Bernasconi, F., & Blanke, O. (2020, 2020/08/15/). Behavioral and neurophysiological evidence for altered interoceptive bodily processing in chronic pain. *NeuroImage, 217*, 116902. https://doi.org/https://doi.org/10.1016/j.neuroimage.2020.116902

Spielberger, C., Goruch, R., Lushene, R., Vagg, P., & Jacobs, G. (1983). Manual for the state-trait inventory STAI (form Y). *Mind Garden, Palo Alto, CA, USA*.

Srinath, A., Young, E., & Szigethy, E. (2014). Pain Management in Patients with Inflammatory Bowel Disease: Translational Approaches from Bench to Bedside. *Inflammatory Bowel Diseases, 20*(12), 2433-2449. https://doi.org/10.1097/mib.0000000000000170

Straub, R. H., Herfarth, H., Falk, W., Andus, T., & Schölmerich, J. (2002, May). Uncoupling of the sympathetic nervous system and the hypothalamic-pituitary-adrenal axis in inflammatory bowel disease? *J Neuroimmunol, 126*(1-2), 116-125. https://doi.org/10.1016/s0165-5728(02)00047-4

Straus, M. B. (1988). *Abuse and victimization across the life span*. Johns Hopkins University Press Baltimore, MD.

Strigo, I. A., & Craig, A. D. (2016). Interoception, homeostatic emotions and sympathovagal balance. *Philosophical Transactions of the Royal Society B: Biological Sciences, 371*(1708), 20160010. https://doi.org/doi:10.1098/rstb.2016.0010

Suzuki, K., Garfinkel, S. N., Critchley, H. D., & Seth, A. K. (2013, 2013/11/01/). Multisensory integration across exteroceptive and interoceptive domains modulates self-experience in the rubber-hand illusion. *Neuropsychologia, 51*(13), 2909-2917. https://doi.org/https://doi.org/10.1016/j.neuropsychologia.2013.08.014

Taft, T. H., Bedell, A., Craven, M. R., Guadagnoli, L., Quinton, S., & Hanauer, S. B. (2019, Aug 20). Initial Assessment of Post-traumatic Stress in a US Cohort of Inflammatory Bowel Disease Patients. *Inflamm Bowel Dis, 25*(9), 1577-1585. https://doi.org/10.1093/ibd/izz032

Taylor, G. J., & Bagby, R. M. (2000). An overview of the alexithymia construct.

Taylor, G. J., Bagby, R. M., & Parker, J. D. (2003, Sep). The 20-Item Toronto Alexithymia Scale. IV. Reliability and factorial validity in different languages and cultures. *J Psychosom Res, 55*(3), 277-283. https://doi.org/10.1016/s0022-3999(02)00601-3

Terasawa, Y., Fukushima, H., & Umeda, S. (2013). How does interoceptive awareness interact with the subjective experience of emotion? An fMRI Study. *Human Brain Mapping, 34*(3), 598-612. https://doi.org/https://doi.org/10.1002/hbm.21458

Terock, J., Van der Auwera, S., Janowitz, D., Spitzer, C., Barnow, S., Miertsch, M., Freyberger, H. J., & Grabe, H.-J. (2016). From childhood trauma to adult dissociation: the role of PTSD and alexithymia. *Psychopathology, 49*(5), 374-382.

Thomann, A. K., Reindl, W., Wüstenberg, T., Kmuche, D., Ebert, M. P., Szabo, K., Wolf, R. C., Hirjak, D., Niesler, B., Griebe, M., & Thomann, P. A. (2019, Jun). Aberrant brain structural large-scale connectome in Crohn's disease. *Neurogastroenterol Motil, 31*(6), e13593. https://doi.org/10.1111/nmo.13593

Thomas, B. L., Claassen, N., Becker, P., & Viljoen, M. (2019). Validity of commonly used heart rate variability markers of autonomic nervous system function. *Neuropsychobiology, 78*(1), 14-26.

Tillisch, K., Labus, J., Kilpatrick, L., Jiang, Z., Stains, J., Ebrat, B., Guyonnet, D., Legrain-Raspaud, S., Trotin, B., Naliboff, B., & Mayer, E. A. (2013, Jun). Consumption of fermented milk product with probiotic modulates brain activity. *Gastroenterology, 144*(7), 1394-1401, 1401.e1391-1394. https://doi.org/10.1053/j.gastro.2013.02.043

Tillisch, K., Mayer, E. A., Gupta, A., Gill, Z., Brazeilles, R., Le Nevé, B., van Hylckama Vlieg, J. E. T., Guyonnet, D., Derrien, M., & Labus, J. S. (2017). Brain Structure and Response to Emotional Stimuli as Related to Gut Microbial Profiles in Healthy Women. *Psychosomatic medicine, 79*(8), 905-913. https://doi.org/10.1097/PSY.0000000000000493

Tillisch, K., Mayer, E. A., & Labus, J. S. (2011, 2011/01/01/). Quantitative Meta-analysis Identifies Brain Regions Activated During Rectal Distension in Irritable Bowel Syndrome. *Gastroenterology, 140*(1), 91-100. https://doi.org/https://doi.org/10.1053/j.gastro.2010.07.053

Todd, J., Aspell, J., Barron, D., & Swami, V. (2019a, 06/01). Multiple Dimensions of Interoceptive Awareness are Associated with Facets of Body Image in British Adults. *Body Image, 29*, 6-16. https://doi.org/10.1016/j.bodyim.2019.02.003

Todd, J., Aspell, J. E., Barron, D., & Swami, V. (2019b, 2019/12/01/). An exploration of the associations between facets of interoceptive awareness and body image in adolescents. *Body Image, 31*, 171-180. https://doi.org/https://doi.org/10.1016/j.bodyim.2019.10.004

Todd, J., Aspell, J. E., Barron, D., Toh, E. K. L., Zahari, H. S., Mohd. Khatib, N. A., Laughton, R., & Swami, V. (2020, 2020/09/01/). Greater gastric interoception is associated with more positive body image: Evidence from adults in Malaysia and the United Kingdom. *Body Image, 34*, 101-111. https://doi.org/https://doi.org/10.1016/j.bodyim.2020.05.011

Tottenham, N., Hare, T. A., Quinn, B. T., McCarry, T. W., Nurse, M., Gilhooly, T., Millner, A., Galvan, A., Davidson, M. C., Eigsti, I. M., Thomas, K. M., Freed, P. J., Booma, E. S., Gunnar, M. R., Altemus, M., Aronson, J., & Casey, B. J. (2010, Jan 1). Prolonged institutional rearing is associated with atypically large amygdala volume and difficulties in emotion regulation. *Dev Sci, 13*(1), 46-61. https://doi.org/10.1111/j.1467-7687.2009.00852.x

Tsakiris, M., Hesse, M. D., Boy, C., Haggard, P., & Fink, G. R. (2006). Neural Signatures of Body Ownership: A Sensory Network for Bodily Self-Consciousness. *Cerebral Cortex, 17*(10), 2235-2244. https://doi.org/10.1093/cercor/bhl131

Tsakiris, M., Jiménez, A. T.-., & Costantini, M. (2011). Just a heartbeat away from one's body: interoceptive sensitivity predicts malleability of body-representations. *Proceedings of the Royal Society B: Biological Sciences, 278*(1717), 2470-2476. https://doi.org/doi:10.1098/rspb.2010.2547

Van der Kolk, B. (2014). *The body keeps the score: Mind, brain and body in the transformation of trauma*. Penguin UK.

van Dyck, Z., Vögele, C., Blechert, J., Lutz, A. P., Schulz, A., & Herbert, B. M. (2016). The Water Load Test As a Measure of Gastric Interoception: Development of a Two-Stage Protocol and Application to a Healthy Female Population. *PLoS One, 11*(9), e0163574. https://doi.org/10.1371/journal.pone.0163574

Vianna, E. P., Weinstock, J., Elliott, D., Summers, R., & Tranel, D. (2006, Jun). Increased feelings with increased body signals. *Soc Cogn Affect Neurosci, 1*(1), 37-48. https://doi.org/10.1093/scan/nsl005

Viganò, C. A., Beltrami, M. M., Bosi, M. F., Zanello, R., Valtorta, M., & Maconi, G. (2018, 2018-August-03). Alexithymia and Psychopathology in Patients Suffering From Inflammatory Bowel Disease: Arising Differences and Correlations to Tailoring Therapeutic Strategies [Original Research]. *Frontiers in Psychiatry, 9*(324). https://doi.org/10.3389/fpsyt.2018.00324

Vogelzangs, N., Beekman, A. T. F., de Jonge, P., & Penninx, B. W. J. H. (2013, 2013/04/01). Anxiety disorders and inflammation in a large adult cohort. *Translational Psychiatry, 3*(4), e249-e249. https://doi.org/10.1038/tp.2013.27

von Leupoldt, A., Chan, P. Y., Esser, R. W., & Davenport, P. W. (2013, Apr). Emotions and neural processing of respiratory sensations investigated with respiratory-related evoked potentials. *Psychosomatic medicine, 75*(3), 244-252. https://doi.org/10.1097/PSY.0b013e31828251cf

Wan, A., Bernstein, C. N., Graff, L. A., Patten, S. B., Sareen, J., Fisk, J. D., Bolton, J. M., Hitchon, C., Marriott, J. J., Marrie, R. A., Burden, f. t. C. T. i. D. t., & Disease, M. t. E. o. I.-m. I. (2022). Childhood Maltreatment and Psychiatric Comorbidity in Immune-Mediated Inflammatory Disorders. *Psychosomatic medicine, 84*(1), 10-19. https://doi.org/10.1097/psy.0000000000001025

Wang, X., Wu, Q., Egan, L., Gu, X., Liu, P., Gu, H., Yang, Y., Luo, J., Wu, Y., & Gao, Z. (2019). Anterior insular cortex plays a critical role in interoceptive attention. *Elife, 8*, e42265.

Weathers, F. W., Litz, B. T., Keane, T. M., Palmieri, P. A., Marx, B. P., & Schnurr, P. P. (2013). The ptsd checklist for dsm-5 (pcl-5). *Scale available from the National Center for PTSD at www. ptsd. va. gov, 10*.

Weaver, E., & Szigethy, E. (2020, Mar 17). Managing Pain and Psychosocial Care in IBD: a Primer for the Practicing Gastroenterologist. *Curr Gastroenterol Rep, 22*(4), 20. https://doi.org/10.1007/s11894-020-0757-7

Wenninger, K., & Heiman, J. R. (1998). Relating body image to psychological and sexual functioning in child sexual abuse survivors. *Journal of Traumatic Stress, 11*(3), 543-562. https://doi.org/https://doi.org/10.1023/A:1024408830159

Wertheim, E. H., & Paxton, S. J. (2011). Body image development in adolescent girls.

Whitehead, W. E., & Drescher, V. M. (1980). Perception of Gastric Contractions and Self-Control of Gastric Motility. *Psychophysiology, 17*(6), 552-558. https://doi.org/https://doi.org/10.1111/j.1469-8986.1980.tb02296.x

Wiens, S. (2005). Interoception in emotional experience. *Current Opinion in Neurology, 18*(4), 442-447. https://doi.org/10.1097/01.wco.0000168079.92106.99

Wilke, E., Reindl, W., Thomann, P. A., Ebert, M. P., Wuestenberg, T., & Thomann, A. K. (2021, Jul 29). Effects of yoga in inflammatory bowel diseases and on frequent IBD-

associated extraintestinal symptoms like fatigue and depression. *Complement Ther Clin Pract, 45*, 101465. https://doi.org/10.1016/j.ctcp.2021.101465

Wilkinson, B., Trick, L., Knight, A., Valton, V., Goodhand, J., Kennedy, N. A., Heerasing, N., Ahmad, T., Bland, A., Elliott, R., Roiser, J. P., & Dickens, C. (2019). Factors associated with depression in people with inflammatory bowel disease: The relationship between active disease and biases in neurocognitive processing. *Neurogastroenterology & Motility, 31*(8), e13647. https://doi.org/https://doi.org/10.1111/nmo.13647

Williams, J. M. G. (2010). Mindfulness and psychological process. *Emotion, 10*(1), 1.

Wintjens, D. S. J., de Jong, M. J., van der Meulen-de Jong, A. E., Romberg-Camps, M. J., Becx, M. C., Maljaars, J. P., van Bodegraven, A. A., Mahmmod, N., Markus, T., Haans, J., Masclee, A. A. M., Winkens, B., Jonkers, D., & Pierik, M. J. (2019, Mar 30). Novel Perceived Stress and Life Events Precede Flares of Inflammatory Bowel Disease: A Prospective 12-Month Follow-Up Study. *J Crohns Colitis, 13*(4), 410-416. https://doi.org/10.1093/ecco-jcc/jjy177

Witges, K. M., Bernstein, C. N., Sexton, K. A., Afifi, T., Walker, J. R., Nugent, Z., & Lix, L. M. (2019, Sep 18). The Relationship Between Adverse Childhood Experiences and Health Care Use in the Manitoba IBD Cohort Study. *Inflamm Bowel Dis, 25*(10), 1700-1710. https://doi.org/10.1093/ibd/izz054

Witthöft, M., Bräscher, A.-K., Jungmann, S. M., & Köteles, F. (2020). Somatic Symptom Perception and Interoception. *Zeitschrift für Psychologie, 228*(2), 100-109. https://doi.org/10.1027/2151-2604/a000403

Wobbrock, J. O., Findlater, L., Gergle, D., & Higgins, J. J. (2011). The aligned rank transform for nonparametric factorial analyses using only anova procedures. In *Proceedings of the SIGCHI Conference on Human Factors in Computing Systems* (pp. 143–146). Association for Computing Machinery. https://doi.org/10.1145/1978942.1978963

Wolgast, M., Lundh, L.-G., & Viborg, G. (2011). Cognitive reappraisal and acceptance: An experimental comparison of two emotion regulation strategies. *Behaviour Research and Therapy, 49*(12), 858-866.

Wynne, B., McHugh, L., Gao, W., Keegan, D., Byrne, K., Rowan, C., Hartery, K., Kirschbaum, C., Doherty, G., Cullen, G., Dooley, B., & Mulcahy, H. E. (2019, 2019/03/01/). Acceptance and Commitment Therapy Reduces Psychological Stress in Patients With Inflammatory Bowel Diseases. *Gastroenterology, 156*(4), 935-945.e931. https://doi.org/https://doi.org/10.1053/j.gastro.2018.11.030

Yanartaş, Ö., Kani, H. T., Kani, A. S., Akça, Z. N. D., Akça, E., Ergün, S., Tezcan, N., Atug, Ö., İmeryüz, N., & Sayar, K. (2019, 2019/10/02). Depression and anxiety have unique contributions to somatic complaints in depression, irritable bowel syndrome and inflammatory bowel diseases. *Psychiatry and Clinical Psychopharmacology, 29*(4), 418-426. https://doi.org/10.1080/24750573.2019.1589177

Young, J. C., & Widom, C. S. (2014, 2014/08/01/). Long-term effects of child abuse and neglect on emotion processing in adulthood. *Child Abuse & Neglect, 38*(8), 1369-1381. https://doi.org/https://doi.org/10.1016/j.chiabu.2014.03.008

Zaki, J., Davis, J. I., & Ochsner, K. N. (2012, 2012/08/01/). Overlapping activity in anterior insula during interoception and emotional experience. *NeuroImage, 62*(1), 493-499. https://doi.org/https://doi.org/10.1016/j.neuroimage.2012.05.012

Zamariola, G., Cardini, F., Mian, E., Serino, A., & Tsakiris, M. (2017, 2017/03/01/). Can you feel the body that you see? On the relationship between interoceptive accuracy and body image. *Body Image, 20*, 130-136. https://doi.org/https://doi.org/10.1016/j.bodyim.2017.01.005

Zamariola, G., Frost, N., Van Oost, A., Corneille, O., & Luminet, O. (2019, 2019/03/01/). Relationship between interoception and emotion regulation: New evidence from mixed

methods. *Journal of Affective Disorders, 246*, 480-485. https://doi.org/https://doi.org/10.1016/j.jad.2018.12.101

10 DANKSAGUNG

Mein Dank gilt an erster Stelle meiner Doktormutter Prof. Dr. Stefanie Lis für ihre stetige Unterstützung, die durchgehende Begleitung meines Promotionsvorhabens, ihre wertvollen fachlichen Anregungen und ihr Vertrauen in mich und meine Arbeit. Ihre Begeisterung für die Forschung hat mich immer wieder inspiriert. Besonders dankbar bin ich dafür, dass sie immer dafür gesorgt hat, dass ich im Laufe dieser Arbeit mein Ziel im Auge behalte und nicht aufgebe. Ohne ihre Expertise und Unterstützung wäre diese Arbeit nicht möglich gewesen. Danke für die Überlassung dieses Promotionsthemas und die Möglichkeit diese Arbeit zu schreiben!

Ich danke ebenso PD Dr. Wolfgang Reindl für seine wissenschaftlichen Anregungen und fachliche Unterstützung. Sein konstruktives Feedback zu meiner Arbeit war mir immer eine große Hilfe und hat maßgeblich dazu beigetragen, mein wissenschaftliches Arbeiten zu verbessern. Er und seine Kollegen am Universitätsklinikum Mannheim haben mich stets bei der Rekrutierung der Patienten unterstützt und haben dadurch das Projekt am Laufen gehalten.

Auch meinen Kollegen vom GRK 2350 möchte ich ganz herzlich für die großartige Zusammenarbeit danken. Es war eine riesige Hilfe dieses feste soziale Netzwerk im Laufe der Promotion zu haben und zu wissen, dass man nie im Stich gelassen wird. Die letzten 3 Jahre waren aufregend, stressig, bereichernd, manchmal auch anstrengend und schwierig. Es war aber eine der schönsten Erfahrungen, dass ich diese Zeit zusammen mit meinen Kollegen und Freunden vom GRK verbringen durfte. Ich habe in dieser Gruppe Menschen kennengelernt, die mir ans Herz gewachsen sind. Vor allem möchte ich mich bei Ezgi Erol bedanken für die wunderbare, lustige und aufregende Zeit, die wir zusammen verbracht haben. Danke, dass du trotz allem an meiner Seite geblieben bist und immer an mich geglaubt hast! Außerdem bedanke ich mich herzlich bei Anna Schulze dafür, dass sie den Endspurt dieser Arbeit erleichtert hat, immer ein offenes Ohr für mich hatte und für ordentlich Weingummis-Nachschub gesorgt hat.

Mein besonderer Dank gilt meinen Freunden, die diese harte Zeit mit mir durchgemacht haben. Vor allem Radina Petkova, die fast alle Phasen dieser Arbeit hautnah erleben durfte. Danke, dass du mich nie aufgegeben hast und dass du mich immer ermutigt hast. Ich habe in dir eine Freundin fürs Leben gefunden und ohne deine stetige emotionale Unterstützung in den letzten Jahren hätte ich wahrscheinlich schon längst meine wissenschaftliche Karriere aufgegeben. Danke, dass du zu jeder Tages- und Nachtzeit für mich da warst, unabhängig davon, was ich

gerade gebraucht habe. Ein herzliches Dankeschön gilt meinen Freundinnen Kalina Vasileva, Gabriela Stoyanova und Sophie Speth. Danke, dass ihr mich immer ermutigt habt und mich immer zum Lachen gebracht habt, selbst wenn es mir zum Weinen zumute war. Es tut mir aufrichtig leid, dass ich euch häufig wegen dieser Arbeit vernachlässigt habe. Ich weiß eure Unterstützung zu schätzen!

Ich möchte mich außerdem bei allen meinen ZIPP Kollegen für die inspirierenden Gespräche, Kaffeepausen und fachlichen Diskussionen bedanken. Es war mir eine Freude mit euch zu arbeiten. Ihr habt die Pandemie für mich weniger einsam und deutlich erträglicher gemacht.

Besonders dankbar bin ich Dr. Andreas Böhringer. Dich zu Beginn dieser Reise zu treffen war das Schönste, was mir passieren konnte. Danke, dass du meine Hand gehalten hast, mir immer Mut gemacht hast und die Klangschale angeschlagen hast, wenn das alles mir doch viel zu viel geworden ist (buchstäblich und metaphorisch). Du hast alle Phasen dieser Arbeit miterlebt und bist dennoch bis zum Schluss da geblieben, dafür danke ich dir aus tiefstem Herzen!

Voller Dankbarkeit bin ich meiner Familie, die nie daran gezweifelt hat, dass ich diese Arbeit erfolgreich abschließen werde. Ihr wart mit eurer bedingungslosen Liebe immer für mich da. Vor allem bin ich meiner Mutter dankbar, dass sie an mich geglaubt hat und mir geholfen hat, meine Träume zu verwirklichen. Ohne deine Unterstützung hätte ich das alles nicht erreichen können, Mama! Nicht zuletzt möchte ich mich bei meinen Großeltern bedanken. Meiner Oma, die mich immer aufgemuntert hat und meinem Opa, der mir alle Fertigkeiten beigebracht hat, die diese Arbeit überhaupt möglich gemacht haben.

Diese Arbeit widme ich meinem Opa Vilya.

На семейството ми:

Благодаря ви, че през цялото това време изпълнено с трудности, радост, успехи и емоции не ме оставихте нито за миг да се съмнявам в успеха на тази работа. На първо място благодаря на родителите си, че никога не загубиха вяра в мен. Мамо, тате, вие винаги бяхте на разположение и споделихте с мен както хубавите така и трудните страни на тази работа, за това ще съм ви вечно благодарна! Мамо, благодаря, че вярваш в мен и позволи на мечтите ми да станат реалност. Без твоята подкрепа нямаше да бъда тук, където съм

сега. От все сърце благодаря на моите баба и дядо, Калина и Виля Томашевски, които ме дариха със своята безусловна обич. Дядо, благодаря ти, че ме научи да преследвам целите си с дисциплина и отдаденост.
Тази работа посвещавам на теб.