The interplay of interoceptive processes and possible bias in pathological illness anxiety.

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Timo Slotta

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1 Introduction

1.1 Classification of pathological illness anxiety

Illness anxiety is characterized by excessive fear of or preoccupation with having or getting one or more serious illnesses (Axelsson & Hedman-Lagerlöf, 2023). The intensity of illness anxiety can vary on an intraindividual level over time (Noyes et al., 1994; Simon et al., 2001), as well as between individuals (Ferguson, 2009; Longley et al., 2010). Consequently, illness anxiety is understood as a continuum ranging from transient, possibly reasonable health concerns to persistent or recurrent, excessive, and rigid assumptions about one's health (Weck et al., 2014). The Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2013) provides two diagnostic categories accounting for pathological expressions of illness anxiety: Illness anxiety disorder and somatic symptom disorder. The former describes excessive preoccupation with having or getting a serious illness as its cardinal symptom. This preoccupation is accompanied by inappropriate health-related behaviors or avoidance.

While the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV; American Psychiatric Association, 2000) explicitly listed physical symptoms as a foundation of maladaptive misinterpretations in the diagnostic criteria of hypochondriasis, pronounced somatic symptoms are excluded within the diagnosis of a DSM-5 illness anxiety disorder. Instead, the DSM-5 states that illness fears may be based on physical sensations that are usually considered normal, or not a sign of illness. The suffering of affected persons thus primarily results not from somatic complaints, but from the associated anxiety (of having a serious illness; American Psychiatric Association, 2013).

1.2 Somatic symptoms in pathological illness anxiety

In fact, pathological illness anxiety is quite often accompanied by physical symptoms. In two samples of individuals with illness anxiety presenting for treatment, 52.5 - 73.4% reported distressing somatic symptoms (Fergus et al., 2019; Newby et al., 2017). It is estimated that 75% of all individuals who meet diagnostic criteria for hypochondriasis according to DSM-IV meet a diagnosis of DSM-5

somatic symptom disorder (American Psychiatric Association, 2013). The somatic symptom disorder is characterized by excessive thoughts, feelings, or behaviors in relation to bodily symptoms. That includes a wide variety of psychological processes, for example, preoccupation with having an illness, associated anxiety, and health-related or avoidance behaviors. Consequently, in the presence of illness anxiety, the severity of somatic symptoms is the distinguishing feature of these two diagnostic categories (somatic symptom disorder and illness anxiety disorder).

Similar to the minor role of symptom perception in the classification of illness anxiety disorder, etiological models also prioritize other processes (e.g., higher cognitive, emotional, and behavioral factors; Abramowitz et al., 2002; Warwick & Salkovskis, 1990). Illness anxiety disorder (or hypochondriasis, as its predecessor) has even been conceptualized as a "cognitive disorder" (Sørensen et al., 2011, p. 431). Against this backdrop, it does not seem too surprising that cognitive behavioral therapy achieves high effect sizes and response rates particularly when illness anxiety is associated with lower bodily distress (Olatunji et al., 2014).

The former DSM-IV classification of illness anxiety as a somatoform disorder has been criticized for slowing the development of explanatory models and therapeutic approaches in terms of an overemphasis on somatic factors (Olatunji et al., 2009). Since then, the focus on anxiety and cognitive processes was undoubtedly fruitful, but at the same time may have contributed to an underestimation of the etiological relevance of symptom perception. Existing models explaining altered symptom perception in somatic distress may also contribute to the etiology of pathological illness anxiety.

1.3 Etiological considerations on symptom perception in pathological illness anxiety

A whole series of models explaining bodily distress over the past 40 years postulates changes to varying degrees regarding physiological input, involved attentional processes, and the evaluation of bodily sensations (e.g., Barsky & Wyshak, 1990; Leventhal & Leventhal, 1993; Watson & Pennebaker, 1989). The somatosensory amplification model is widely received (Barsky & Wyshak, 1990). This model assumes an initial presence of mild physical stimuli, for example stemming from

heightened physiological arousal. Attention focused on these physical sensations then leads to more intense perceptions. This could ultimately result in perceptions entering consciousness that would otherwise not be consciously perceptible due to their low salience. This phenomenon is called somatosensory amplification. In other words, individuals high in somatosensory amplification exhibit higher somatic sensitivity. Secondly, this model postulates that the evaluation of bodily sensations as unpleasant, harmful, or threatening increases both physiological activation and the attentional focus on interoceptive processing. The empirical basis for the somatosensory amplification model, however, is insufficient. Individuals high in bodily distress do not necessarily show abnormal patterns of peripheral arousal or stress-related physiology: Studies investigating associations of medically unexplained symptoms and physiological deviations do not provide consistent evidence for a causal role of a specific physiological dysfunction (Van den Bergh et al., 2017). Moreover, evidence for a bias in actual attention to bodily stimuli, as measured using objective tasks (in contrast to elevated self-reported attention to bodily sensations) is scarce (Köteles & Witthöft, 2017; Van den Bergh et al., 2017).

The role of negative cognitive evaluations and assumptions, on the other hand, is well documented (Marcus et al., 2007). For example, catastrophic thinking predicts the extent of preoccupation with illness worries and associated anxiety (Woud et al., 2016). Remarkably, the same work showed no association between baseline cognitive preoccupation and later somatic symptom experience. Similarly, a somatic attribution style seems to be characteristic of bodily distress, but does not predict its course (Douzenis & Seretis, 2013). Nevertheless, symptom experience is a common accompanying feature of pathological illness anxiety (Fergus et al., 2019; Newby et al., 2017). Consequently, symptom perception should not be neglected as a possible etiological factor.

Taking into account different theoretical approaches, Richard J. Brown (2004) formulated an integrative cognitive model in an attempt to understand medically unexplained symptoms. This approach differs significantly from other recent models in one respect. Following the tradition of psychoanalytic considerations of bodily distress, this model does not consider physiological input necessary for the perception of somatic symptoms. Instead, chronically activated (unconscious)

symptom schemata are supposed to lead to conscious symptom experience, even in the absence of actual physiological stimulation. Attentional and attributional processes then further influence the resulting sensation. Building on Brown's work, a model has subsequently been proposed to explain discrepancies between actual physiological input and bodily symptom experience within the predictive coding framework (Van den Bergh et al., 2017).

1.4 The Predictive Coding Framework

The predictive coding framework has been highly influential in cognitive neuroscience over the past two decades (Millidge et al., 2022). It represents an attempt to unify the understanding of mechanisms in cortical processing. It defines the minimization of prediction errors as one of the core functions of the brain (i.e., the discrepancy between predicted and actual input is held minimal at all stages of neurocognitive processing; Friston et al., 2003). In this sense, the predictive coding approach postulates a fundamental processing style that may underlie numerous functions. The overriding goal of this processing style is nothing less than the construction of an adaptive model of the external and internal world. A model is considered adaptive if it allows to infer stimulus sources from the limited information available, to predict consequences, and to plan and execute economic responses (Van den Bergh et al., 2021). Different applications of the predictive coding framework locate these responses at physiological, emotional, cognitive, as well as behavioral levels.

To ensure this, bottom-up stimuli and top-down predictions (priors) are processed. Priors represent implicit predictions about future inputs. These can be shaped by past learning experiences as well as by dispositional factors. Priors and bottom-up information are processed at varying hierarchical levels of abstraction. The result of these comparisons are prediction errors, which the brain continuously strives to minimize. There are basically three mechanisms available for this purpose: Priors can be adjusted to the input (i.e., predictions are corrected), input can be adjusted to priors by active motor behavior (i.e., predicted sensations are generated), and the way sensory input is sampled can be changed (i.e., attention is modulated; Barrett & Simmons, 2015).

According to predictive coding theory, this process always results in the model that best minimizes the prediction error (i.e., the posterior belief). Both priors, prediction errors and posterior beliefs are understood as probability distributions with mean and variance. The inverse of the variance (i.e., precision) of priors and prediction errors characterizes their reliability (Friston, 2009). If the precision of the prediction error (or incoming stimuli) is low, it is given less weight in the construction of the posterior belief. Instead, processing is driven more heavily by the prior in such cases (Hohwy, 2012). The possibly conscious experience of the resulting sensation, however, does not feel less genuine than perceptions shaped by a precise, or strongly weighted input (Van den Bergh et al., 2021).

The described process may be subject to systematic bias. Indeed, the goal of this processing style is not necessarily the generation of maximally accurate models of the world, but those that are adaptive with respect to individual and evolutionary history (Lynn & Barrett, 2014): Deviations between accuracy and adaptivity in this regard might arise, if missing information is associated with significantly higher costs than repeated false alarms (e.g., in case of warning signs of a heart attack, a bias to threat might be vital). Further, in order to increase the accuracy of a model, sparsity must be sacrificed. However, the more saturated a model is, the less well suited it is to generalize experience across different contexts, or to learn from new experience. Consequently, bias can be understood as not only a mere dysfunctional source of error, but also a functional tool to guide adaptive responses. At the same time some authors argue, that a persistent bias to threat might evoke elevated levels of negative affective experience and represents a risk factor for psychopathology (Van den Bergh et al., 2021).

1.5 Dispositional negativity and "better safe than sorry" processing

There are numerous terms used in the literature to describe the tendency to experience frequent, intense, and persistent negative emotions (e.g., anger, sadness, anxiety). Some of these terms are negative affectivity, negative emotionality, or dispositional negativity. In this work, the term dispositional negativity is used. It is conceptualized as a fundamental personality dimension

that includes traits such as neuroticism, trait anxiety, or behavioral inhibition (Shackman et al., 2016). Dispositional negativity is a prospective predictor of the onset and course of several mental health problems (Shackman et al., 2016). Likewise, illness anxiety is associated with dispositional negativity (Cox et al., 2000; Ferguson, 2000). In a traditional diathesis-stress model, dispositional negativity acts as a vulnerability factor moderating the association between distress and psychopathology. Even though these associations have been repeatedly demonstrated, the exact nature of this vulnerability or underlying mechanisms remain largely unknown (Ormel et al., 2004).

Considerations within the predictive coding framework go further by conceptualizing dispositional negativity not as a distal risk factor, but as part of the active construction process described above (Van den Bergh et al., 2021). In this sense, past chronic experiences of threat or (anticipated) insufficiency of one's own resources might influence the processing of present information. More precisely, individuals might be prone to rapid threat-related processing and action, if their individual given history suggests that benefits of a “better safe than sorry” approach probably outweigh short-term costs (i.e., false alarms). To realize this approach, stimulus processing has to be driven by threat-related priors, neglecting detailed processing of concrete information in favour of abstract (over-)simplification. The by-product of this abstract stimulus processing style is the production of imprecise prediction errors. Precise prediction errors, however, play a crucial role in the correction of poorly adjusted threat-related priors. This might lead to a chronification of threat-related priors in long term and a continuous decoupling of posterior beliefs from actual input in the sense of a "better safe than sorry" strategy.

Van den Bergh and colleagues (2021) applied this approach to different cognitive processes and their bias (in the sense of a "better safe than sorry" strategy). In addition to biased attentional, memory, and formal thought processes, the authors also conceptualized biased perception of physical symptoms in the context of bodily distress.

1.6 Symptom perception as an active construction process

Interoception describes the perception of the physiological state of one's own body to ensure physical homeostasis (Craig, 2003). It can be understood as an active constructive process in terms of predictive coding theory (Van den Bergh et al., 2017). Following this approach, bodily sensations result from the bidirectional processing of both somatic bottom-up stimuli and somatosensory top-down predictions stemming from previous experiences and other dispositional factors. The neurocognitive processing of interoceptive signals is rather insensitive to prediction errors because of cytoarchitectural reasons (Barrett & Simmons, 2015). Therefore, priors may play a particularly crucial role in the perceptual construction of bodily sensations. At the same time, this may complicate the correction of biased interoceptive priors (Van den Bergh et al., 2021). Both circumstances might favor systematic interoceptive bias.

Dispositional negativity and anxiety both show significant associations with bodily distress (Van den Bergh et al., 2017). As described above, within the predictive coding framework, this can be understood as an indication of a "better safe than sorry" strategy (Van den Bergh et al., 2021). According to proponents of this notion, this processing strategy can be outlined as follows: Unexpected, ambiguous bodily signals (e.g., a light abdominal pain at rest) generate prediction errors. These turn out to be particularly high in individuals with pronounced intolerance of uncertainty or precise priors regarding a normal healthy bodily state (e.g., “Bodily complaints are always a sign of disease”; Rief et al., 1998). Both of these frequently co-occur with chronically high bodily distress (Boelen & Carleton, 2012; Rief et al., 1998). Resulting prediction errors can be reduced by adjusting the sampling strategy of bodily signals. To attain this, attention is shifted away from detailed stimulus processing, toward (over)simplistic categorization of possible physiological threat. If this categorization process is biased toward threat (i.e., a "better safe than sorry" strategy, possibly reflecting a history of threatened physical integrity or other predisposing factors), bodily sensations may be categorized as more intense, unpleasant, or threatening. Simultaneously, the differentiation of slightly different stimuli decreases (i.e., stimuli become overgeneralized; Petersen et al., 2014). For

example, an individual with an internistic history might experience a light abdominal pain at rest as more intense and identical to a threatening sensation that occurred during a workout a week ago.

The by-product of neglecting detailed sensory processing is the production of imprecise prediction errors, which in turn complicate the correction of threat-related interoceptive priors. At the same time, body perceptions biased toward threat (e.g., intensified sensations of abdominal pain) serve as the evidence base for future threat-related categorical priors. Therefore, the precision of these priors successively increases (e.g., each experience of abdominal pain might further shape expectancies of future intensive, frequent, or persistent episodes of pain). This processing style might lead to consecutive decoupling of symptom perception from underlying bodily signals, which, in extreme cases, may lead to illusory perceptions (e.g., experiences of abdominal pain without any physiological basis; Van den Bergh et al., 2017).

1.7 Empirical findings on anxiety and interoception

The model assumptions described above are contrasted with an ambiguous body of findings. Self-reported interoception (interoceptive sensibility; Garfinkel et al., 2015) is positively related to anxiety quite consistently across studies (e.g., Anderson & Hope, 2009; De Berardis et al., 2007; Gregor & Zvolensky, 2008; Olatunji et al., 2007; Palser et al., 2018). A different picture emerges with regard to the association between anxiety and interoceptive performance, which has been discussed as a central construct underlying other interoceptive measures in the past (Garfinkel et al., 2015). A systematic review was able to identify positive associations between cardioceptive performance and anxiety-related traits, as well as anxiety disorders (Domschke et al., 2010). However, findings are heterogeneous, with single studies reporting no effects (e.g., Dunn et al., 2010; Duschek et al., 2015) or a negative correlation (Werner et al., 2009). A recently published meta-analysis across 55 individual studies failed to identify a consistent association between cardioceptive performance and anxiety (Adams et al., 2022).

If interoceptive performance is investigated within signal detection paradigms that allow for a differentiation of sensitivity and response bias, evidence for altered interoception in anxiety

remains incosistent. A study on the perception of autonomic activation (spontaneous skin conductance fluctuations) reports an association of illness anxiety with a (“better safe than sorry”) bias, but not with sensitivity (Krautwurst et al., 2014). A study of respiratory interoception, on the other hand, was able to identify an association between anxiety and interoceptive sensitivity (Harrison et al., 2021).

The heterogeneity of findings can possibly be explained by differences in the operationalization of interoception, as well as the investigated samples: self-report measures frequently applied in an attempt to portray interoceptive sensibility actually assess different constructs (Desmedt, Heeren, et al., 2022). Abilities on different interoceptive modalities or channels (e.g., heartbeat perception, respiratory perception, perception of arousal) do not necessarily correspond to each other (Ferentzi et al., 2018; Garfinkel et al., 2016). Objective measures of interoceptive abilities might even differ from one another within the same modality (e.g., Corneille et al., 2020; Ring & Brener, 2018). While some paradigms assess mere performance, others are able to differentiate between sensitivity and response bias (Pohl et al., 2021). In addition, there are indications that characteristics of the respective sample also influence findings (Domschke et al., 2010). For example, differences between clinical and analogue samples or between different anxiety disorders are conceivable.

1.8 Aims of the present work

In line with the theoretical assumptions presented above, findings suggest that biased interoceptive processes in the sense of a "better safe than sorry" approach might represent a relevant etiological factor of symptom experience in pathological illness anxiety. Considering the rather heterogeneous body of evidence, the most important goal of this work is to portray interoceptive processes and their bias in sufficiently high resolution. This requires a differentiated investigation of interoceptive dimensions and processes. Specifically, this results in two subordinate aims:

First, the interplay between self-reported components of interoceptive processing, interoceptive performance, and trait anxiety will be investigated. This will generate information on

whether interoceptive performance represents a central construct underlying other interoceptive measures. Further, it will shed light on possible associations of a sub-facet of dispositional negativity (i.e., a possible substrate of a "better safe than sorry" processing style) with interoceptive measures. Second, we will investigate whether the postulated interoceptive bias can be identified in a clinical sample using a differential assessment of interoceptive performance in terms of signal detection parameters.

STUDY 1

2 Publications

2.1 Study 1: The interplay of interoceptive accuracy, facets of interoceptive sensibility, and trait anxiety: A network analysis.

Slotta, T., Witthöft, M., Gerlach, A. L., & Pohl, A. (2021). The interplay of interoceptive accuracy, facets of interoceptive sensibility, and trait anxiety: A network analysis. *Personality and Individual Differences*, *183*, 111133. https://doi.org/10.1016/j.paid.2021.111133

The aim of this study was to portray the differential interplay of self-reported and objective facets of interoception, as well as their associations with dispositional negativity. Interoceptive performance was assessed on the cardiac axis using an established heartbeat counting task. Even though previous research on interoceptive abilities has already frequently focused on the cardiac axis, most studies are limited to the examination of zero order correlations with either dispositional negativity or self-reported interoception.

In contrast, we employed a network analysis to identify the differential interplay of interoceptive facets with dispositional negativity. Eight sub-facets of interoceptive sensibility were included as separate nodes in the network analysis, therefore bypassing challenges associated with generally inconsistent operationalizations of interoceptive sensibility. In concordance with the network approach of mental disorders, we did not consider either interoceptive skills or beliefs as manifestations of latent factors. Rather, emerging associations between nodes themselves (e.g., of specific interoceptive beliefs and more general patterns of dispositional negativity) might mark possibly relevant etiological factors.

2.2 Study 2: Respiratory Interoception and Pathological Illness Anxiety: Disentangling Bias.

Slotta, T., Wolters, C., Marx, Z., Witthöft, M., Gerlach, A. L., & Pohl, A. (2023). Respiratory interoception and pathological illness anxiety: disentangling bias. *Psychosomatic medicine*. https://doi.org/10.1097/PSY.0000000000001244

Study 1 did not identify any links between interoceptive performance on the cardiac axis and sub-facets of interoceptive sensibility or dispositional negativity. This might contradict previous findings and theoretical assumptions considering interoceptive abilities an etiological factor of psychopathology. There are, however, two major limitations to study 1 that do not necessarily allow a conclusive judgement. These limitations stem from the applied heartbeat perception task, as well as the non-clinical nature of the sample examined. Though widely used, the heartbeat perception task employed in study 1 has previously been subject to sound criticism. Indeed, a significant weakness of the task relates to its inability to separate cardioceptive sensitivity from bias. In consequence, the influence of potentially valid perceptual processes (e.g., prior somatosensory expectations) has usually been viewed as error variance. We consider the detection of said processes crucial in order to test model assumptions of the predictive coding framework.

Consequently, we decided to apply an interoceptive signal detection task in study 2. We planned to assess interoceptive sensitivity and bias on the respiratory axis, as respiratory stimuli may resemble relevant symptom experience. Another reason study 1 may have failed to identify potential differences in interoceptive abilities lies in the non-clinical nature of the sample. To allow for more robust etiological conclusions in study 2, we planned to recruit individuals with pathological illness anxiety.

3 Discussion and outlook

3.1 Summary of the main findings

The aim of the present work was to identify interoceptive processes and their bias in pathological illness anxiety at a sufficiently high level of resolution. Two research questions were derived from this. The first focused on the interplay between self-reported components of interoceptive processing, interoceptive performance, and trait anxiety. The present work was supposed to determine whether interoceptive performance underlies other interoceptive measures and identify the extent to which trait anxiety as a sub-facet of dispositional negativity is related to interoceptive measures. In study 1, no relation was found between cardioceptive performance and self-reported sub-facets of interoception in a nonclinical sample. Furthermore, facets of interoceptive sensibility were related to trait anxiety via the evaluation of one's own body as safe and trustworthy. This correlation illustrates that specific negative somatosensory expectations go hand in hand with general dispositional patterns of worry and negative affective states.

The second research question aimed to identify a "better safe than sorry" strategy as a feature of fundamental interoceptive processing in pathological illness anxiety. This was not achieved in study 2. While there was a group difference in categorization bias, it manifested itself in unexpected direction: individuals with pathological illness anxiety systematically *under*estimated more intense stimuli. Due to the nature of the applied paradigm, this finding can unfortunately not be interpreted unambiguously. The observed bias in respiratory stimulus processing could arise from multiple sources. On the one hand, individuals with pathological illness anxiety might actually underestimate respiratory stimuli and thus not resort to the postulated "better safe than sorry" but, on the contrary, to a "wait and see" strategy. Paradoxically, the results can also be interpreted in terms of a "better safe than sorry" strategy at other stages of processing. For example, the retrieval of somatosensory memory content might be biased or external (resp. cross-modal) cues might shape perception to a greater extent in individuals with illness anxiety.

In terms of their sensitivity in the categorization of respiratory stimuli, individuals with pathological illness anxiety did not differ from the control group.

3.2 Theoretical and empirical integration

The association of self-reported facets of interoception with trait anxiety is congruent with the predictive coding approach. Low expressions of individual trust in one's own body might resemble precise priors regarding the occurrence of harmful physical symptoms at hierarchically higher levels of interoceptive processing. These precise priors might be the result of past prediction errors associated with negative affect through repeated experience of unexpected bodily symptoms. The association between interoceptive sensibility and anxiety is compatible with other findings, although the direction of the association usually depends on the particular interoceptive measure applied. Questionnaires assessing an individual's experience of aversive physical states show positive associations with trait anxiety (Grossi et al., 2017; Palser et al., 2018). Negative correlations, as in the present work, typically emerge whenever questionnaires target more functional approaches to bodily sensations (Mallorquí-Bagué et al., 2014; Mehling et al., 2018).

Cardioceptive performance and interoceptive sensibility were not related in Study 1. This finding contradicts original assumptions of interoceptive abilities building the basis of other interoceptive dimensions (Garfinkel et al., 2015). While several studies report at least weak associations of interoceptive questionnaires with objective measures of interoception (Calì et al., 2015; Murphy et al., 2020; Zamariola et al., 2018), the present finding lines up with other works that failed to find a relation (Critchley et al., 2004; Gabriele et al., 2022; Körmendi et al., 2023).

In study 2, no difference in respiratory sensitivity was found between individuals with and without pathological illness anxiety. This finding is consistent with theoretical approaches stressing the importance of interoceptive bias in detachments of symptom experience and physiological input. In contrast to previous theories, they assume no necessary change in sensitivity (Van den Bergh et al., 2017). At the same time, the present findings challenge theoretical assumptions that attribute a protective effect (against chronic bias) to high interoceptive sensitivity (Ainley et al., 2016). Previous work has demonstrated reduced (Tiller et al., 1987) or increased (Vanden Bogaerde et al., 2011) respiratory sensitivity in anxiety disorders. Associations between anxiety and increased interoceptive sensitivity was also found on other modalities. In a review, Domschke and colleagues (2010)

identified a relation between cardioceptive performance and trait anxiety. Recent meta-analyses, however, did not replicate this finding (Adams et al., 2022; Desmedt, Van Den Houte, et al., 2022). Illness anxiety in particular does not appear to be associated with altered interoceptive sensitivity across modalities (Barsky et al., 1995; Krautwurst et al., 2014).

Instead, study 2 identified a systematic bias at a fundamental level of respiratory stimulus processing. Unfortunately, an unambiguous interpretation regarding the origin and exact nature of the observed bias is not possible, since not only perceptual but also learning processes and attentional effects potentially influence results of the applied paradigm.

Individuals with pathological illness anxiety de facto underestimated respiratory stimuli during the employed classification task. One possible interpretation refers to the occurrence of an avoidant attentional bias. Generally, higher levels of illness anxiety are characterized by increased attention to threat-relevant (e.g., health-related) stimuli (Jasper & Witthöft, 2011). Subgroups exhibiting an avoidant coping style, however, tend to quickly redirect their attention away from potentially threatening stimuli (Kim & Lee, 2016; Lee et al., 2013). This phenomenon can be conceptualized according to the vigilance avoidance model (Mogg & Bradley, 2002). In this sense, individuals in the present work might have turned their attention away from particularly threatening (i.e., intense) respiratory stimuli quickly after a preceding shift of attention to those stimuli.

Another origin of underestimation of respiratory stimuli may lie in biased memory-related processes. A bias in retrospective symptom reports has been widely demonstrated (Van den Bergh & Walentynowicz, 2016). For example, assessment of dyspnea symptoms is higher in retrospective than during symptom presentation (Walentynowicz et al., 2018). Similarly, there are consistent reports of biased recall of health-related words in pathological illness anxiety (Brown et al., 1999; Gropalis et al., 2013; Pauli & Alpers, 2002). In terms of predictive coding theory, this can be interpreted as evidence for a "better safe than sorry" strategy. If memory content is processed in little detail, imprecise prediction errors result. Consequently, retrieval is strongly driven by priors that are potentially characterized by overgeneralization and threat relevance (analogous to postulations of reduced autobiographical memory specificity in depression or past traumatic experience; Van den

Bergh et al., 2021). Within the paradigm applied in study 2, retrieved memories of respiratory stimuli (that have been presented during learning trials) might thus represent overestimations of actual intensities. During recognition, the matching of current stimuli with upward biased memory content might ultimately lead to an underestimation of these respiratory stimuli.

Another way of explaining the observed bias might lie in the cross-modal integration of physical and external stimuli. In general, the integration of information, for example from different sensory channels, is thought to be an important capability of interoceptive networks (Quigley et al., 2021). Multimodal signals modulate attentional processes and may be associated with higher sensitivity (Tang et al., 2016). Even information originating from outside interoceptive systems appears to influence basic interoceptive processing (Zacharioudakis et al., 2020, 2023), for example, via the modification of expectations (Lang et al., 2011). In view of these findings, the presentation of stimulus labels (A1-B4) during learning trials of the present paradigm might have biased perception. This phenomenon might also be understood in terms of a "better safe than sorry" strategy within the predictive coding framework. The information that a stimulus belongs to the "B" category might have increased the precision of threat-related interoceptive priors in individuals with illness anxiety (whereas threat-irrelevant information regarding "A" stimuli might have had little influence on interoceptive priors). During recognition, the matching of current stimuli with upward biased perceptions of the learning trials might also lead to an underestimation of these stimuli.

3.3 Clinical implications

Even though the present study could not deliver clear evidence for a "better safe than sorry" bias of symptom perception in pathological illness anxiety, the findings provide relevant indications for clinical practice. Possible clinical implications can be derived with regard to psychoeducational interventions as well as with regard to interventions directly targeting changes in symptom processing.

Psychoeducation is an effective component in the treatment of pathological illness anxiety (Bouman, 2014). Assumed mechanisms of change include increasing motivation to change and

correcting dysfunctional appraisals (Mühlig & Jacobi, 2011). Individuals with pathological illness anxiety tend to consider their own interoceptive sensitivity particularly high (Barsky et al., 1995). Thus, it might be useful to question the validity of one's symptom perception in order to promote a more functional attributional style with regard to bodily sensations. Established psychoeducational modules are often based on the somatosensory amplification model (e.g., Weigel et al., 2023). Alternatively, psychoeducational interventions could convey that individuals with pathologically illness anxiety do not differ from others with regard to their interoceptive sensitivity. Rather, the relation between anxiety and a "better safe than sorry" strategy in processing bodily signals could be elaborated (analogous to approaches used in the treatment of other anxiety disorders). Clarifying the benefits (i.e., rapid, economical response to potential danger) and costs (i.e., failure to correct bias due to inaccurate sensory processing) of this processing style provide a possible maintaining factor that could strengthen treatment motivation.

Another approach might be the modification of biased symptom perception. It should be noted here that the present work was able to demonstrate biased categorization of interoceptive stimuli, but not necessarily a "better safe than sorry" processing strategy. However, general considerations about specific treatment optimizations can be derived from assumptions of the predictive coding approach. In order to correct distorted interoceptive priors, the way somatic information is sampled has to be altered in the sense of a more detailed sensory processing, even if stimulus material is aversive (Van den Bergh et al., 2017). At the same time, defensive behaviors (originally linked to threat-related priors) should be refrained from in terms of a "wait and see" strategy (Van den Bergh et al., 2021).

Exposure-based cognitive behavioral therapy has been shown to be an effective treatment for pathological illness anxiety (Visser & Bouman, 2001; Weck et al., 2014). The goal of exposure is to create contexts that enable patients to adaptively adjust dysfunctional expectations to new information (Paul et al., 2019). One potentially involved mechanism of change is expectancy violation in terms of inhibitory learning (Craske et al., 2008). This approach postulates that discrepancies between prior expectation and actual experience (i.e., prediction error) must be maximized to

promote optimal learning. Consequently, this approach is very much compatible with assumptions of predictive coding theory (Gropalis et al., 2018). It may be possible to further optimize exposure-based therapies in line with the theoretical assumptions discussed above. The proposed focus on detailed sensory processing while foregoing defensive responses in the sense of a "wait and see" approach (Van den Bergh et al., 2021) largely corresponds to techniques introduced by third wave cognitive behavioral therapies (e.g., detached mindfulness or non-reactivity; Wells, 2005; Zou et al., 2020). They aim for the conscious awareness of internal events without their conceptual analysis, goal-directed reactions, or attempts of manipulation. In fact, this may represent a mechanism of change in exposure therapy of pathological illness anxiety (Hedman et al., 2017).

Another promising approach targets the direct modification of interoceptive processes, for example in the form of biofeedback. To date, findings mainly provide evidence for a possible efficacy in bodily distress (but not specifically in pathological illness anxiety): Heartbeat perception training was associated with reductions in somatic symptoms and trait anxiety in a nonclinical sample (Sugawara et al., 2020). Bodily distress also decreased in individuals with somatic symptom disorder after cardioceptive training (Schaefer et al., 2014). Similarly, there is evidence for efficacy of biofeedback on other channels. Feedback of heart rate variability resulted in reductions of clinically pronounced bodily distress in a recent pilot study (Krempel & Martin, 2023). Biofeedback of signs of physiological arousal contributed to a reduction in catastrophizing somatic attributions in another study of individuals with marked bodily distress (Nanke & Rief, 2003). Exact mechanisms of change of biofeedback procedures are unclear (Weerdmeester et al., 2020). Conceivably, certain subgroups benefit to varying degrees from perceptual training. For example, the aforementioned study by Schaefer and colleagues (2014) demonstrated that at baseline, individuals high in illness anxiety showed higher interoceptive performance than individuals with low illness anxiety and did not further improve during training. This matches the suggestion of other colleagues concerning differential indications according to patients' interoceptive sensitivity (Ainley et al., 2016). The relevance of biofeedback specifically in the context of pathological illness anxiety should be subject of future research.

3.4 Outlook

The body of interoceptive research has witnessed significant growth over the past 20 years (Khalsa et al., 2018). Results of this work have led to the assumption that altered interoception is a risk factor of psychopathology (Brewer et al., 2021). However, heterogeneous findings within the research field, as well as the present results indicate that a differential consideration of individual interoceptive processes is crucial in order to improve the etiological understanding of mental disorders and their therapy.

In the recent past, various classifications of interoceptive processes have been proposed (Desmedt et al., 2023; Garfinkel et al., 2015; Murphy et al., 2019). In addition, objective measures of interoceptive performance should be able to differentiate between individual differences in sensitivity and potential bias. Possible influences of perceptual, attentional, and memory processes on performance should not be overlooked. Likewise, construct validity of instruments assessing self-reported components of interoception should be optimized. This includes the differentiation of, for example, cognitive and metacognitive facets, attribution styles, or evaluations of own capabilities. This requires the use of valid measurement tools (Garfinkel et al., 2022). The present work identified shortcomings in the applied procedures. The results of Study 1 suggest that the instrument used to assess interoceptive sensibility covers separate constructs (Mehling et al., 2022). Study 2 demonstrated that the applied respiratory categorization paradigm does not allow for the identification of the exact source of biased response behavior.

The development of valid measurement procedures thus remains an immense but potentially rewarding challenge for the field of interoceptive research (Garfinkel et al., 2022). A long-term goal of interoceptive research in sufficiently high resolution should be the understanding of the differential interplay of interoceptive processes, specific for distinct psychopathological phenomena. In this context, predictive coding theory provides a suitable framework enabling a theory-guided approach (Van den Bergh et al., 2017). Future research on a "better safe than sorry" strategy at different hierarchical levels of interoceptive processing could expand our understanding of

interactions between symptom perception and illness anxiety. Derived findings could support the optimization of diagnostics and treatment of pathological illness anxiety.

4 Literature

Abramowitz, J. S., Schwartz, S. A., & Whiteside, S. P. (2002). A Contemporary Conceptual Model of Hypochondriasis. *Mayo Clinic Proceedings*, *77*(12), 1323–1330. https://doi.org/10.4065/77.12.1323

Adams, K. L., Edwards, A., Peart, C., Ellett, L., Mendes, I., Bird, G., & Murphy, J. (2022). The association between anxiety and cardiac interoceptive accuracy: A systematic review and meta-analysis. *Neuroscience & Biobehavioral Reviews*, *140*, 104754. https://doi.org/10.1016/j.neubiorev.2022.104754

Ainley, V., Apps, M. A. J., Fotopoulou, A., & Tsakiris, M. (2016). 'Bodily precision': A predictive coding account of individual differences in interoceptive accuracy. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *371*(1708), 20160003. https://doi.org/10.1098/rstb.2016.0003

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders (4th ed.)*. https://doi.org/10.1176/appi.books.9780890425596

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

Anderson, E. R., & Hope, D. A. (2009). The relationship among social phobia, objective and perceived physiological reactivity, and anxiety sensitivity in an adolescent population. *Journal of Anxiety Disorders*, *23*(1), 18–26. https://doi.org/10.1016/j.janxdis.2008.03.011

Axelsson, E., & Hedman-Lagerlöf, E. (2023). Validity and clinical utility of distinguishing between DSM-5 somatic symptom disorder and illness anxiety disorder in pathological health anxiety: Should we close the chapter? *Journal of Psychosomatic Research*, *165*, 111133. https://doi.org/10.1016/j.jpsychores.2022.111133

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

Barsky, A. J., Brener, J., Coeytaux, R. R., & Cleary, P. D. (1995). Accurate awareness of heartbeat in hypochondriacal and non-hypochondriacal patients. *Journal of Psychosomatic Research*, *39*(4), 489–497. https://doi.org/10.1016/0022-3999(94)00166-3

Barsky, A. J., & Wyshak, G. (1990). Hypochondriasis and Somatosensory Amplification. *The British Journal of Psychiatry*, *157*(3), 404–409. https://doi.org/10.1192/bjp.157.3.404

Boelen, P. A., & Carleton, R. N. (2012). Intolerance of Uncertainty, Hypochondriacal Concerns, Obsessive-Compulsive Symptoms, and Worry. *The Journal of Nervous and Mental Disease*, *200*(3), 208. https://doi.org/10.1097/NMD.0b013e318247cb17

Bouman, T. K. (2014). Psychological treatments for hypochondriasis: A narrative review. *Current Psychiatry Reviews*, *10*(1), 58–69.

Brewer, R., Murphy, J., & Bird, G. (2021). Atypical interoception as a common risk factor for psychopathology: A review. *Neuroscience & Biobehavioral Reviews*, *130*, 470–508. https://doi.org/10.1016/j.neubiorev.2021.07.036

Brown, H. D., Kosslyn, S. M., Delamater, B., Fama, J., & Barsky, A. J. (1999). Perceptual and memory biases for health-related information in hypochondriacal individuals. *Journal of Psychosomatic Research*, *47*(1), 67–78. https://doi.org/10.1016/S0022-3999(99)00011-2

Calì, G., Ambrosini, E., Picconi, L., Mehling, W., & Committeri, G. (2015). Investigating the relationship between interoceptive accuracy, interoceptive awareness, and emotional susceptibility. *Frontiers in Psychology*, *6*. https://www.frontiersin.org/articles/10.3389/fpsyg.2015.01202

Corneille, O., Desmedt, O., Zamariola, G., Luminet, O., & Maurage, P. (2020). A heartfelt response to Zimprich et al. (2020), and Ainley et al. (2020)'s commentaries: Acknowledging issues with the HCT would benefit interoception research. *Biological Psychology*, *152*, 107869. https://doi.org/10.1016/j.biopsycho.2020.107869

Cox, B. J., Borger, S. C., Asmundson, G. J. G., & Taylor, S. (2000). Dimensions of hypochondriasis and the five-factor model of personality. *Personality and Individual Differences*, *29*(1), 99.

Craig, A. (2003). Interoception: The sense of the physiological condition of the body. *Current Opinion in Neurobiology*, *13*(4), 500–505. https://doi.org/10.1016/S0959-4388(03)00090-4

Craske, M. G., Kircanski, K., Zelikowsky, M., Mystkowski, J., Chowdhury, N., & Baker, A. (2008). Optimizing inhibitory learning during exposure therapy. *Behaviour Research and Therapy*, *46*(1), 5–27. https://doi.org/10.1016/j.brat.2007.10.003

Critchley, H. D., Wiens, S., Rotshtein, P., Öhman, A., & Dolan, R. J. (2004). Neural systems supporting interoceptive awareness. *Nature Neuroscience*, *7*(2), Article 2. https://doi.org/10.1038/nn1176

De Berardis, D., Campanella, D., Gambi, F., La Rovere, R., Sepede, G., Core, L., Canfora, G., Santilli, E., Valchera, A., Mancini, E., Salerno, R. M., Moschetta, F. S., & Ferro, F. M. (2007). Alexithymia, Fear of Bodily Sensations, and Somatosensory Amplification in Young Outpatients With Panic Disorder. *Psychosomatics*, *48*(3), 239–246. https://doi.org/10.1176/appi.psy.48.3.239

Desmedt, O., Heeren, A., Corneille, O., & Luminet, O. (2022). What do measures of self-report interoception measure? Insights from a systematic review, latent factor analysis, and network approach. *Biological Psychology*, *169*, 108289. https://doi.org/10.1016/j.biopsycho.2022.108289

Desmedt, O., Luminet, O., Maurage, P., & Corneille, O. (2023). Discrepancies in the Definition and Measurement of Human Interoception: A Comprehensive Discussion and Suggested Ways Forward. *Perspectives on Psychological Science*, 17456916231191537. https://doi.org/10.1177/17456916231191537

Desmedt, O., Van Den Houte, M., Walentynowicz, M., Dekeyser, S., Luminet, O., & Corneille, O. (2022). How Does Heartbeat Counting Task Performance Relate to Theoretically-Relevant Mental Health Outcomes? A Meta-Analysis. *Collabra: Psychology*, *8*(1), 33271. https://doi.org/10.1525/collabra.33271

Domschke, K., Stevens, S., Pfleiderer, B., & Gerlach, A. L. (2010). Interoceptive sensitivity in anxiety and anxiety disorders: An overview and integration of neurobiological findings. *Clinical Psychology Review*, *30*(1), 1–11. https://doi.org/10.1016/j.cpr.2009.08.008

Douzenis, A., & Seretis, D. (2013). Descriptive and predictive validity of somatic attributions in patients with somatoform disorders: A systematic review of quantitative research. *Journal of Psychosomatic Research*, *75*(3), 199–210. https://doi.org/10.1016/j.jpsychores.2013.05.005

Dunn, B. D., Stefanovitch, I., Evans, D., Oliver, C., Hawkins, A., & Dalgleish, T. (2010). Can you feel the beat? Interoceptive awareness is an interactive function of anxiety- and depression-specific symptom dimensions. *Behaviour Research and Therapy*, *48*(11), 1133–1138. https://doi.org/10.1016/j.brat.2010.07.006

Duschek, S., Werner, N. S., Reyes del Paso, G. A., & Schandry, R. (2015). The contributions of interoceptive awareness to cognitive and affective facets of body experience. *Journal of Individual Differences*, *36*(2), 110–118. https://doi.org/10.1027/1614-0001/a000165

Ferentzi, E., Bogdány, T., Szabolcs, Z., Csala, B., Horváth, Á., & Köteles, F. (2018). Multichannel Investigation of Interoception: Sensitivity Is Not a Generalizable Feature. *Frontiers in Human Neuroscience*, *12*. https://www.frontiersin.org/articles/10.3389/fnhum.2018.00223

Fergus, T. A., Kelley, L. P., & Griggs, J. O. (2019). Examining the Whiteley Index-6 as a screener for DSM-5 presentations of severe health anxiety in primary care. *Journal of Psychosomatic Research*, *127*, 109839. https://doi.org/10.1016/j.jpsychores.2019.109839

Ferguson, E. (2000). Hypochondriacal concerns and the five factor model of personality. *Journal of Personality*, *68*(4), 705–724. https://doi.org/10.1111/1467-6494.00113

Ferguson, E. (2009). A taxometric analysis of health anxiety. *Psychological Medicine*, *39*(2), 277–285. https://doi.org/10.1017/S0033291708003322

Friston, K. J. (2009). The free-energy principle: A rough guide to the brain? *Trends in Cognitive Sciences*, *13*(7), 293–301. https://doi.org/10.1016/j.tics.2009.04.005

Friston, K. J., Harrison, L., & Penny, W. (2003). Dynamic causal modelling. *NeuroImage*, *19*(4), 1273–1302. https://doi.org/10.1016/S1053-8119(03)00202-7

Gabriele, E., Spooner, R., Brewer, R., & Murphy, J. (2022). Dissociations between self-reported interoceptive accuracy and attention: Evidence from the Interoceptive Attention Scale. *Biological Psychology*, *168*, 108243. https://doi.org/10.1016/j.biopsycho.2021.108243

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/10.1098/rstb.2016.0014

Garfinkel, S. N., Schulz, A., & Tsakiris, M. (2022). Addressing the need for new interoceptive methods. *Biological Psychology*, *170*, 108322. https://doi.org/10.1016/j.biopsycho.2022.108322

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

Gregor, K. L., & Zvolensky, M. J. (2008). Anxiety sensitivity and perceived control over anxiety-related events: Evaluating the singular and interactive effects in the prediction of anxious and fearful responding to bodily sensations. *Behaviour Research and Therapy*, *46*(9), 1017–1025. https://doi.org/10.1016/j.brat.2008.06.003

Gropalis, M., Bailer, J., Weck, F., & Witthöft, M. (2018). Optimierung von Expositionstherapie bei pathologischen Krankheitsängsten: Theoretische Grundlagen und praktische Implikationen. *Psychotherapeut*, *63*. https://doi.org/10.1007/s00278-018-0285-1

Gropalis, M., Bleichhardt, G., Hiller, W., & Witthöft, M. (2013). Specificity and modifiability of cognitive biases in hypochondriasis. *Journal of Consulting and Clinical Psychology*, *81*(3), 558–565. https://doi.org/10.1037/a0028493

Grossi, D., Longarzo, M., Quarantelli, M., Salvatore, E., Cavaliere, C., De Luca, P., Trojano, L., & Aiello, M. (2017). Altered functional connectivity of interoception in illness anxiety disorder. *Cortex*, *86*, 22–32. https://doi.org/10.1016/j.cortex.2016.10.018

Harrison, O. K., Köchli, L., Marino, S., Luechinger, R., Hennel, F., Brand, K., Hess, A. J., Frässle, S., Iglesias, S., Vinckier, F., Petzschner, F. H., Harrison, S. J., & Stephan, K. E. (2021). Interoception of breathing and its relationship with anxiety. *Neuron*, *109*(24), 4080-4093.e8. https://doi.org/10.1016/j.neuron.2021.09.045

Hedman, E., Hesser, H., Andersson, E., Axelsson, E., & Ljótsson, B. (2017). The mediating effect of mindful non-reactivity in exposure-based cognitive behavior therapy for severe health anxiety. *Journal of Anxiety Disorders*, *50*, 15–22. https://doi.org/10.1016/j.janxdis.2017.04.007

Hohwy, J. (2012). Attention and Conscious Perception in the Hypothesis Testing Brain. *Frontiers in Psychology*, *3*. https://www.frontiersin.org/articles/10.3389/fpsyg.2012.00096

Jasper, F., & Witthöft, M. (2011). Health anxiety and attentional bias: The time course of vigilance and avoidance in light of pictorial illness information. *Journal of Anxiety Disorders*, *25*(8), 1131–1138. https://doi.org/10.1016/j.janxdis.2011.08.004

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., … Zucker, N. (2018). Interoception and Mental Health: A Roadmap. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *3*(6), 501–513. https://doi.org/10.1016/j.bpsc.2017.12.004

Kim, S., & Lee, J.-H. (2016). Time course of attentional bias for health-related information in individuals with health anxiety. *Journal of Health Psychology*, *21*(8), 1527–1535. https://doi.org/10.1177/1359105314557976

Körmendi, J., Ferentzi, E., Petzke, T., Gál, V., & Köteles, F. (2023). Do we need to accurately perceive our heartbeats? Cardioceptive accuracy and sensibility are independent from indicators of negative affectivity, body awareness, body image dissatisfaction, and alexithymia. *PLOS ONE*, *18*(7), e0287898. https://doi.org/10.1371/journal.pone.0287898

Köteles, F., & Witthöft, M. (2017). Somatosensory amplification – An old construct from a new perspective. *Journal of Psychosomatic Research*, *101*, 1–9. https://doi.org/10.1016/j.jpsychores.2017.07.011

Krautwurst, S., Gerlach, A. L., Gomille, L., Hiller, W., & Witthöft, M. (2014). Health anxiety – An indicator of higher interoceptive sensitivity? *Journal of Behavior Therapy and Experimental Psychiatry*, *45*(2), 303–309. https://doi.org/10.1016/j.jbtep.2014.02.001

Krempel, L., & Martin, A. (2023). Efficacy of Heart Rate Variability Biofeedback for Somatic Symptom Disorder: A Pilot Randomized Controlled Trial. *Psychosomatic Medicine*, *85*(1), 61. https://doi.org/10.1097/PSY.0000000000001143

Lang, P. J., Wangelin, B. C., Bradley, M. M., Versace, F., Davenport, P. W., & Costa, V. D. (2011). Threat of suffocation and defensive reflex activation. *Psychophysiology*, *48*(3), 393–396. https://doi.org/10.1111/j.1469-8986.2010.01076.x

Lee, H., Turkel, J. E., Cotter, S. P., Milliken, J. M., Cougle, J., Goetz, A. R., & Lesnick, A. M. (2013). Attentional bias toward personally relevant health-threat words. *Anxiety, Stress & Coping*, *26*(5), 493–507. https://doi.org/10.1080/10615806.2012.713474

Leventhal, H., & Leventhal, E. A. (1993). Affect, cognition, and symptom perception. In *Current and emerging issues in cancer pain: Research and practice* (S. 153–173). Raven Press.

Longley, S. L., Broman-Fulks, J. J., Calamari, J. E., Noyes, R., Wade, M., & Orlando, C. M. (2010). A Taxometric Study of Hypochondriasis Symptoms. *Behavior Therapy*, *41*(4), 505–514. https://doi.org/10.1016/j.beth.2010.02.002

Lynn, S. K., & Barrett, L. F. (2014). "Utilizing" Signal Detection Theory. *Psychological Science*, *25*(9), 1663–1673. https://doi.org/10.1177/0956797614541991

Mallorquí-Bagué, N., Garfinkel, S. N., Engels, M., Eccles, J. A., Pailhez, G., Bulbena, A., & Critchley, H. D. (2014). Neuroimaging and psychophysiological investigation of the link between anxiety, enhanced affective reactivity and interoception in people with joint hypermobility. *Frontiers in Psychology*, *5*. https://www.frontiersin.org/articles/10.3389/fpsyg.2014.01162

Marcus, D. K., Gurley, J. R., Marchi, M. M., & Bauer, C. (2007). Cognitive and perceptual variables in hypochondriasis and health anxiety: A systematic review. *Clinical Psychology Review*, *27*(2), 127–139. https://doi.org/10.1016/j.cpr.2006.09.003

Mehling, W. E., Acree, M., Stewart, A., Silas, J., & Jones, A. (2018). The Multidimensional Assessment of Interoceptive Awareness, Version 2 (MAIA-2). *PloS One*, *13*(12), e0208034. https://doi.org/10.1371/journal.pone.0208034

Mehling, W. E., Todd, J., & Schuman-Olivier, Z. (2022). Multidisciplinary Assessment of Interoceptive Awareness, Version 2 (MAIA-2). In O. N. Medvedev, C. U. Krägeloh, R. J. Siegert, & N. N. Singh (Hrsg.), *Handbook of Assessment in Mindfulness Research* (S. 1–23). Springer International Publishing. https://doi.org/10.1007/978-3-030-77644-2_40-1

Millidge, B., Seth, A., & Buckley, C. L. (2022). *Predictive Coding: A Theoretical and Experimental Review* (arXiv:2107.12979). arXiv. https://doi.org/10.48550/arXiv.2107.12979

Mogg, K., & Bradley, B. P. (2002). Selective orienting of attention to masked threat faces in social anxiety. *Behaviour Research and Therapy*, *40*(12), 1403–1414. https://doi.org/10.1016/S0005-7967(02)00017-7

Mühlig, S., & Jacobi, F. (2011). Psychoedukation. In H.-U. Wittchen & J. Hoyer (Hrsg.), *Klinische Psychologie & Psychotherapie* (S. 477–490). Springer. https://doi.org/10.1007/978-3-642-13018-2_20

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). 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

Nanke, A., & Rief, W. (2003). Biofeedback-based interventions in somatoform disorders: A randomized controlled trial. *Acta Neuropsychiatrica*, *15*(4), 249–256. https://doi.org/10.1034/j.1601-5215.2003.00028.x

Newby, J. M., Hobbs, M. J., Mahoney, A. E. J., Wong, S. K., & Andrews, G. (2017). DSM-5 illness anxiety disorder and somatic symptom disorder: Comorbidity, correlates, and overlap with

DSM-IV hypochondriasis. *Journal of Psychosomatic Research*, *101*, 31–37. https://doi.org/10.1016/j.jpsychores.2017.07.010

Noyes, R., Kathol, R. G., Fisher, M. M., Phillips, B. M., Suelzer, M. T., & Woodman, C. L. (1994). One-Year Follow-up of Medical Outpatients With Hypochondriasis. *Psychosomatics*, *35*(6), 533–545. https://doi.org/10.1016/S0033-3182(94)71722-9

Olatunji, B. O., Deacon, B. J., & Abramowitz, J. S. (2009). Is hypochondriasis an anxiety disorder? *The British Journal of Psychiatry*, *194*(6), 481–482. https://doi.org/10.1192/bjp.bp.108.061085

Olatunji, B. O., Deacon, B. J., Abramowitz, J. S., & Valentiner, D. P. (2007). Body Vigilance in Nonclinical and Anxiety Disorder Samples: Structure, Correlates, and Prediction of Health Concerns. *Behavior Therapy*, *38*(4), 392–401. https://doi.org/10.1016/j.beth.2006.09.002

Olatunji, B. O., Kauffman, B. Y., Meltzer, S., Davis, M. L., Smits, J. A. J., & Powers, M. B. (2014). Cognitive-behavioral therapy for hypochondriasis/health anxiety: A meta-analysis of treatment outcome and moderators. *Behaviour Research and Therapy*, *58*, 65–74. https://doi.org/10.1016/j.brat.2014.05.002

Ormel, J., Rosmalen, J., & Farmer, A. (2004). Neuroticism: A non-informative marker of vulnerability to psychopathology. *Social Psychiatry and Psychiatric Epidemiology*, *39*(11), 906–912. https://doi.org/10.1007/s00127-004-0873-y

Palser, E. R., Palmer, C. E., Galvez-Pol, A., Hannah, R., Fotopoulou, A., & Kilner, J. M. (2018). Alexithymia mediates the relationship between interoceptive sensibility and anxiety. *PLOS ONE*, *13*(9), e0203212. https://doi.org/10.1371/journal.pone.0203212

Pauli, P., & Alpers, G. W. (2002). Memory bias in patients with hypochondriasis and somatoform pain disorder. *Journal of Psychosomatic Research*, *52*(1), 45–53. https://doi.org/10.1016/S0022-3999(01)00295-1

Paulus, M., Feinstein, J., & Khalsa, S. (2019). An Active Inference Approach to Interoceptive Psychopathology. *Annual Review of Clinical Psychology*, *15*, 97–122. https://doi.org/10.1146/annurev-clinpsy-050718-095617

Petersen, S., Schroijen, M., Mölders, C., Zenker, S., & Van den Bergh, O. (2014). Categorical Interoception: Perceptual Organization of Sensations From Inside. *Psychological Science*, *25*(5), 1059–1066. https://doi.org/10.1177/0956797613519110

Pohl, A., Hums, A.-C., Kraft, G., Köteles, F., Gerlach, A. L., & Witthöft, M. (2021). Cardiac interoception: A novel signal detection approach and relations to somatic symptom distress. *Psychological Assessment*, *33*(8), 705–715. https://doi.org/10.1037/pas0001012

Quigley, K. S., Kanoski, S., Grill, W. M., Barrett, L. F., & Tsakiris, M. (2021). Functions of Interoception: From Energy Regulation to Experience of the Self. *Trends in Neurosciences*, *44*(1), 29–38. https://doi.org/10.1016/j.tins.2020.09.008

Rief, W., Hiller, W., & Margraf, J. (1998). Cognitive aspects of hypochondriasis and the somatization syndrome. *Journal of Abnormal Psychology*, *107*(4), 587–595. https://doi.org/10.1037/0021-843X.107.4.587

Ring, C., & Brener, J. (2018). Heartbeat counting is unrelated to heartbeat detection: A comparison of methods to quantify interoception. *Psychophysiology*, *55*(9), e13084. https://doi.org/10.1111/psyp.13084

Schaefer, M., Egloff, B., Gerlach, A. L., & Witthöft, M. (2014). Improving heartbeat perception in patients with medically unexplained symptoms reduces symptom distress. *Biological Psychology*, *101*, 69–76. https://doi.org/10.1016/j.biopsycho.2014.05.012

Shackman, A. J., Tromp, D. P. M., Stockbridge, M. D., Kaplan, C. M., Tillman, R. M., & Fox, A. S. (2016). Dispositional negativity: An integrative psychological and neurobiological perspective. *Psychological bulletin*, *142*(12), 1275–1314. https://doi.org/10.1037/bul0000073

Simon, G. E., Gureje, O., & Fullerton, C. (2001). Course of hypochondriasis in an international primary care study. *General Hospital Psychiatry*, *23*(2), 51–55. https://doi.org/10.1016/S0163-8343(01)00115-3

Sørensen, P., Birket-Smith, M., Wattar, U., Buemann, I., & Salkovskis, P. (2011). A randomized clinical trial of cognitive behavioural therapy versus short-term psychodynamic psychotherapy

versus no intervention for patients with hypochondriasis. *Psychological Medicine*, *41*(2), 431–441. https://doi.org/10.1017/S0033291710000292

Sugawara, A., Terasawa, Y., Katsunuma, R., & Sekiguchi, A. (2020). Effects of interoceptive training on decision making, anxiety, and somatic symptoms. *BioPsychoSocial Medicine*, *14*(1), 7. https://doi.org/10.1186/s13030-020-00179-7

Tang, X., Wu, J., & Shen, Y. (2016). The interactions of multisensory integration with endogenous and exogenous attention. *Neuroscience & Biobehavioral Reviews*, *61*, 208–224. https://doi.org/10.1016/j.neubiorev.2015.11.002

Tiller, J., Pain, M., & Biddle, N. (1987). Anxiety disorder and perception of inspiratory resistive loads. *Chest*, *91*(4), 547–551. https://doi.org/10.1378/chest.91.4.547

Van den Bergh, O., Brosschot, J., Critchley, H., Thayer, J. F., & Ottaviani, C. (2021). Better safe than sorry: A common signature of general vulnerability for psychopathology. *Perspectives on Psychological Science*, *16*(2), 225–246. https://doi.org/10.1177/1745691620950690

Van den Bergh, O., & Walentynowicz, M. (2016). Accuracy and bias in retrospective symptom reporting. *Current Opinion in Psychiatry*, *29*(5), 302–308. https://doi.org/10.1097/YCO.0000000000000267

Van den Bergh, O., Witthöft, M., Petersen, S., & Brown, R. J. (2017). Symptoms and the body: Taking the inferential leap. *Neuroscience and Biobehavioral Reviews*, *74*(Pt A), 185–203. https://doi.org/10.1016/j.neubiorev.2017.01.015

Vanden Bogaerde, A., Derom, E., & De Raedt, R. (2011). Increased interoceptive awareness in fear of flying: Sensitivity to suffocation signals. *Behaviour Research and Therapy*, *49*(6–7), 427–432. https://doi.org/10.1016/j.brat.2011.03.011

Visser, S., & Bouman, T. K. (2001). The treatment of hypochondriasis: Exposure plus response prevention vs cognitive therapy. *Behaviour Research and Therapy*, *39*(4), 423–442. https://doi.org/10.1016/S0005-7967(00)00022-X

Walentynowicz, M., Bogaerts, K., Stans, L., Van Diest, I., Raes, F., & Van den Bergh, O. (2018). Retrospective memory for symptoms in patients with medically unexplained symptoms.

Journal of Psychosomatic Research, *105*, 37–44. https://doi.org/10.1016/j.jpsychores.2017.12.006

Warwick, H. M. C., & Salkovskis, P. M. (1990). Hypochondriasis. *Behaviour Research and Therapy*, *28*(2), 105–117. https://doi.org/10.1016/0005-7967(90)90023-C

Watson, D., & Pennebaker, J. W. (1989). Health complaints, stress, and distress: Exploring the central role of negative affectivity. *Psychological Review*, *96*(2), 234–254. https://doi.org/10.1037/0033-295X.96.2.234

Weck, F., Richtberg, S., & M.B. Neng, J. (2014). Epidemiology of Hypochondriasis and Health Anxiety: Comparison of Different Diagnostic Criteria. *Current Psychiatry Reviews*, *10*(1), 14–23.

Weerdmeester, J., Rooij, M. M. van, Engels, R. C., & Granic, I. (2020). An Integrative Model for the Effectiveness of Biofeedback Interventions for Anxiety Regulation: Viewpoint. *Journal of Medical Internet Research*, *22*(7), e14958. https://doi.org/10.2196/14958

Weigel, A., Hüsing, P., Junge, M., & Löwe, B. (2023). Helpful explanatory models for persistent somatic symptoms (HERMES): Results of a three-arm randomized-controlled pilot trial. *Journal of Psychosomatic Research*, *172*, 111419. https://doi.org/10.1016/j.jpsychores.2023.111419

Wells, A. (2005). Detached Mindfulness In Cognitive Therapy: A Metacognitive Analysis And Ten Techniques. *Journal of Rational-Emotive and Cognitive-Behavior Therapy*, *23*(4), 337–355. https://doi.org/10.1007/s10942-005-0018-6

Werner, N. S., Duschek, S., Mattern, M., & Schandry, R. (2009). Interoceptive sensitivity modulates anxiety during public speaking. *Journal of Psychophysiology*, *23*(2), 85–94. https://doi.org/10.1027/0269-8803.23.2.85

Woud, M. L., Zhang, X. C., Becker, E. S., Zlomuzica, A., & Margraf, J. (2016). Catastrophizing misinterpretations predict somatoform-related symptoms and new onsets of somatoform disorders. *Journal of psychosomatic research*, *81*, 31–37.

Zacharioudakis, N., Vlemincx, E., & Van den Bergh, O. (2020). Categorical interoception and the role of threat. *International Journal of Psychophysiology*, *148*, 25–34. https://doi.org/10.1016/j.ijpsycho.2019.12.009

Zacharioudakis, N., Vlemincx, E., & Van den Bergh, O. (2023). Categorical interoception: The role of disease context and individual differences in habitual symptom reporting. *Psychology & Health*, *38*(1), 39–57. https://doi.org/10.1080/08870446.2021.1952586

Zamariola, G., Vlemincx, E., Corneille, O., & Luminet, O. (2018). Relationship between interoceptive accuracy, interoceptive sensibility, and alexithymia. *Personality and Individual Differences*, *125*, 14–20. https://doi.org/10.1016/j.paid.2017.12.024

Zou, Y., Li, P., Hofmann, S. G., & Liu, X. (2020). The Mediating Role of Non-reactivity to Mindfulness Training and Cognitive Flexibility: A Randomized Controlled Trial. *Frontiers in Psychology*, *11*. https://www.frontiersin.org/articles/10.3389/fpsyg.2020.01053