

“I don’t want to miss a symptom” –  
The role of biased interoception in somatic symptoms and  
illness anxiety

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## Summary

Somatic symptom disorder and illness anxiety disorder both involve preoccupation with signals from the body. The perception of somatic signals has recently been conceptualized in a predictive coding framework (Van den Bergh, Witthöft, Petersen, & Brown, 2017). Predictive coding theory assumes that the perception of somatic signals is guided by predictions about these signals, which add to the sensory characteristics. In the extreme, predictions alone can instigate the perception of somatic signals. Moreover, pathological forms of somatic symptoms have been linked to a “better safe than sorry” decision strategy (Van den Bergh, Brosschot, Critchley, Thayer, & Ottaviani, 2021). Supposedly, this (unconscious) strategy is intended to avoid potentially negative consequences of missing important somatic signals at the cost of overreporting these signals. Predictions may thus lead to the assumption that a somatic signal is present, even when sensory evidence is sparse or missing altogether. In the long run, this decision strategy may lead to persistent somatic symptoms that are uncoupled from actual physiological dysfunction.

Interoceptive tasks have been developed to measure the perception of somatic signals. Interoception refers to the sensing, interpretation, and integration of signals from within the body (Khalsa et al., 2018). Here, the individual ability to precisely monitor bodily signals, interoceptive accuracy, can be distinguished from the individual tendency to over- or underreport these signals. This tendency is referred to as response bias. A liberal response bias describes an overreporting of signals as part of the above described “better safe than sorry” decision strategy (Petersen, Van Staeyen, Vögele, von Leupoldt, & Van den Bergh, 2015). Whether such a liberal response bias goes along with reduced, increased, or unaltered interoceptive accuracy in pathological forms of somatic symptoms was not yet clear.

Against this background, the first article of this dissertation is a systematic review and meta-analysis of studies using interoceptive tasks in pathological and non-pathological somatic symptoms, illness anxiety, and related functional syndromes (Wolters, Gerlach, & Pohl, 2022). Results from 68 studies showed that interoceptive accuracy was reduced in functional syndromes, but not in somatic symptoms and illness anxiety. At the same time, a more liberal response bias was

consistently associated with somatic symptoms and illness anxiety in the eight included studies.

In order to additionally research the assumptions of the predictive coding view of somatic symptoms, we conducted two empirical studies with the somatic signal detection task (SSDT; Lloyd, Mason, Brown, & Poliakoff, 2008). In this task, response bias is assessed using weak tactile sensations. In the first study with healthy participants, it was attempted to manipulate predictions regarding bodily symptoms allowing to test whether tactile sensations are overreported under these circumstances (Wolters, Harzem, Witthöft, Gerlach, & Pohl, 2021). To this end, sham Wi-Fi exposure was used, given that many individuals believe that Wi-Fi exposure is able to induce physical symptoms. Indeed, participants tended to overreport sensations in the sham Wi-Fi as compared to a no-Wi-Fi condition, providing evidence for a predictive coding account of somatic symptom perception.

In a second empirical study, individuals with pathological illness anxiety were recruited to test response bias using the SSDT (Wolters et al., 2023). In addition to the original version of the SSDT, an adapted version with either neutral or illness words as additional stimuli was used. It was expected that participants with pathological illness anxiety would show a more liberal response bias than healthy controls, and that this liberalization would be stronger in trials including illness words. This liberalization was expected as a result of elicited “illness schemata” that lead to an overreporting of somatic sensations. Unexpectedly, response bias did not differ between groups in any of the conditions.

Taken together, the systematic review provided evidence of a more liberal response bias as part of a “better safe than sorry” strategy in various somatic symptoms and illness anxiety. The first empirical study showed that a “better safe than sorry” strategy can indeed be elicited in healthy participants when predictions regarding somatic signals are manipulated. Results of the second empirical study with a pathological sample were more equivocal and did not provide clear evidence of a “better safe than sorry” strategy in individuals with illness anxiety. Implications of the findings for clinical practice and future research are explicated in a general discussion.

## 1. Introduction

Somatic symptom disorder is characterized by an excessive preoccupation with distressing symptoms, while illness anxiety disorder is characterized by fear of having or getting a serious disease (American Psychiatric Association, 2013). Both disorders involve the preoccupation with signals from the body, and a tendency to interpret benign sensations as potentially threatening. A headache might be interpreted as “I have a brain tumor”, or a rumbling in the stomach as “Something is wrong with me”. Arguably, symptom perception is largely influenced by mostly unconscious expectations, which add to the sensory characteristics of body signals (Van den Bergh et al., 2017). In this vein, pathological forms of somatic symptoms have been linked to a “better safe than sorry” strategy, a response behavior that is characterized by avoiding potentially negative consequences of missing important signals: Even when sensory evidence is sparse, expectations may lead to the assumption that an aversive somatic signal is present (Van den Bergh et al., 2021). Over the course of time, this response behavior could lead to persistent symptoms that are unrelated to actual physiological dysfunction (van den Bergh, 2021, Henningsen, 2018). A “better safe than sorry” view on excessive somatic symptoms provides an overarching framework in researching the intersection of the perception of body signals, top-down mechanisms that affect such perceptions, and their role in the etiology of somatic symptom disorder and illness anxiety disorder.

### 1.1 A predictive coding perspective on somatic symptoms

Since Pennebaker’s book “The psychology of physical symptoms” (1982), several accounts have emphasized the role of attention, attributions, and interpretations that affect the perception of physical symptoms (e.g., Cioffi, 1991; Leventhal & Leventhal, 1993; Kirmayer & Taillefer, 1997; Barsky & Wyshak, 1990). While these accounts describe top-down influences on the perception of somatic symptoms, they all assume peripheral somatosensory input as an essential basis of the experience of somatic symptoms (for an overview of theories, see Van den Bergh et al., 2017). For instance, the theory of “somatosensory amplification” assumes that normal body sensations or (stress-related) physiological arousal are intensified and interpreted as threatening in a vicious cycle because of, for example, an increased attentional focus on them (Barsky & Wyshak, 1990).

Brown (2004) was the first to postulate that peripheral input does not necessarily precede symptom perception, but that activated central nervous “symptom schemata” also may lead to conscious symptom experiences. This theory was further developed in a predictive coding framework (Van den Bergh et al., 2017). In this framework, the relationship between symptom report and bodily (dys)function is seen as highly variable both between and within individuals. Therefore, both medically unexplained somatic symptoms and symptoms of well-described diseases are viewed as functionally comparable. From this view, top-down processes influence not only how but also whether symptoms are experienced, implying that biased perception alone can lead to symptom report.

The main assumption of predictive coding theory in the context of somatic symptoms is that symptom perception results from a constructive neural process (Van den Bergh et al., 2017). The brain is assumed to estimate probabilities for certain outcomes and compare these with somatosensory input according to stochastic principles of Bayes (Van den Bergh et al., 2021). The “probability maps” incorporate past learning experiences in similar contexts. This learned knowledge about the world is represented by *priors*, which are adapted to the current context (Friston, 2005). Based on these priors, probabilistic *predictions* offer guidance when interpreting information from the body in a specific context (Van den Bergh et al., 2021). In the predictive coding model, the goal is to minimize *prediction errors*, which occur when there is a mismatch between predictions and the actual sensory input. The level of *precision* decides on how much confidence is attributed to predictions and prediction errors. Priors with a high level of precision based on previous experiences will lead to strong predictions. If, at the same time, the actual sensory input is imprecise (i.e., noisy or faint), these priors will gain more influence on perception and will be more resistant to updating (Van den Bergh et al., 2017).

The brain aims at reducing prediction errors in order to generate the best-fitting model of the real world, representing both external and internal stimuli. The most adaptive model is one that allows efficient evaluation of the sources of these stimuli as well as to predict what will happen in the future (Van den Bergh et al., 2021). The model resulting from the smallest prediction errors will then reach conscious perception (Hohwy, 2012).

Prediction errors can be reduced in three different ways (Van den Bergh et al., 2017; Barrett & Simmons, 2015; Seth, 2013). First, priors can be adapted to match



the actual input. Secondly, the body can be moved to initiate a sensory state that will match the prediction. The third way is by shifting attention, e.g., away from a painful perception (Hechler, Endres, & Thorwart, 2016). Here, modulation of the excitability of neurons biases the influence of incoming sensory signals (Barrett & Simmons, 2015).

Note that the highest goal in modeling the world is not necessarily accuracy but utility or adaptiveness. To this end, under some circumstances, accuracy may be sacrificed for the sake of more effective decision making (Lynn & Barrett, 2014). In the predictive coding framework, distorted perception will occur when the symptom report is part of the most adaptive model with the smallest prediction error. Symptom report can become gradually decoupled from actual sensory input when the presence of symptoms is predicted by highly precise priors (Van den Bergh et al., 2017). Alternative models might also be able to reduce prediction error, but to a lesser degree, or there might be alternative models that are even better at reducing prediction error but have not yet been learned. Therefore, the currently best model may be inaccurate and leave room for illusory perceptions (Hohwy, 2012).

These assumptions are supported by studies showing that symptoms can be acquired in an associative learning paradigm (Van Diest et al., 2006; Van den Bergh, Winters, Devriese, & Van Diest, 2002; Van den Bergh, Stegen, & Van de Woestijne, 1997; Meulders et al., 2010; Van den Bergh, Kempynck, van de Woestijne, Baeyens, & Eelen, 1995). In this paradigm, participants learn to anticipate symptoms induced by a respiratory challenge through CO<sub>2</sub> enriched air after they were paired with odors.

The predictive coding perspective has also been applied to pain perception (for reviews see Hechler et al., 2016; Büchel, Geuter, Sprenger, & Eippert, 2014; Wiech, 2016), showing that pain perception can be altered by the experimental modulation of predictions (e.g., Lim et al., 2020; Jepma, Koban, van Doorn, Jones, & Wager, 2018; Desmarteaux et al., 2021; Bräscher, Sütterlin, Scheuren, Van den Bergh, & Witthöft, 2020). For example, placebo effects lead to expectations for reduced pain and, in turn, lessen brain activation during painful stimulations in pain-associated brain regions as well as regions that are associated with emotions and valence more generally (for a meta-analysis, see Atlas & Wager, 2014).

Several factors influence how somatic signals are processed according to this generative model. First of all, adaption of the model is affected by characteristics of

the signal itself. More intense signals that are limited to a certain body part will produce more precise prediction errors (Van den Bergh et al., 2017). In other words, more weight will be put on more reliable sensory information (Den Ouden, Kok, & De Lange, 2012). As a consequence, priors are more likely to be adapted according to these signals (Van den Bergh et al., 2017).

In contrast, weaker and more widespread signals (such as fatigue) leave more room for priors to dominate the model. In this vein, the processing of signals can also be impaired by general interoceptive dysfunction, e.g., through stress (Schulz & Vögele, 2015). Secondly, attention modulates the relative weight of predictions and prediction errors. When attentional focus is directed to the body because a signal is expected, the salience of an actual signal can be intensified, and stronger signals have better precision (Hohwy, 2012). The resulting precise prediction errors can then foster an update of priors, leading into a self-perpetuating cycle (Van den Bergh et al., 2017). Thirdly, individual differences such as gender may influence the perceptual process. For example, it was suggested that priors might be more influential in women than in men (Van den Bergh et al., 2017). This suggestion is based on findings that women are less accurate than men at detecting physiological signals in laboratory environments (particularly in cardiac perception; Prentice & Murphy, 2022), but equally accurate in natural environments (Prentice, Hobson, Spooner, & Murphy, 2022; Harshaw, 2015; Van den Bergh et al., 2017). Women might compensate lower accuracy in naturalistic settings, where priors are more precise because of contextual cues (Van den Bergh et al., 2017).

Lastly, elevated sensitivity to threat as well as trait negative affectivity might be associated with increased symptom reporting. A specific processing strategy that is associated with the sensitivity to threat will be described in the following section.

## **1.2 “Better safe than sorry” – a proposed processing strategy in the perception of bodily symptoms**

A proposed processing strategy associated with the perception of somatic symptoms was labeled “better safe than sorry” (Van den Bergh et al., 2021; Petersen et al., 2015). This processing strategy is thought to be associated with dispositional negativity, a personality factor that plays a role in different forms of psychopathology. Dispositional negativity is defined as “the propensity to experience and express more frequent, intense, or enduring negative affect” (Shackman et al., 2016, p. 3). The

“better safe than sorry” strategy supposedly is associated with processing heuristics that lead to different phenomenal characteristics of dispositional negativity, including increased somatic symptom report (Van den Bergh et al., 2021). Elevated symptom reporting and negative affectivity, a related construct of dispositional negativity, are principally linked (Van Diest et al., 2005) and more specifically linked in situations in which the experience of symptoms is particularly likely (e.g., during symptom inductions; Bogaerts et al., 2015; Constantinou, Bogaerts, Van Diest, & Van den Bergh, 2013). Furthermore, it was shown that a negative affective framing led to increased symptom perception in high symptom reporters (Constantinou et al., 2013) and patients with functional syndromes (Van den Bergh et al., 1997; Van Den Houte et al., 2017). Increased symptom perception after presentation of negative valence cues in a conditioning paradigm was also mediated by individual levels of negative affectivity (Devriese et al., 2000).

The proposed processing heuristic is particularly relevant in response to (assumed) threat: Individuals with a “better safe than sorry” strategy more readily classify perceived signals as threatening, at the cost of more detailed somatosensory processing. From a predictive coding perspective, threat-related priors are highly precise, while the processing of signals and resulting prediction errors are unprecise. This results in a stagnated error-reduction process, in which prediction errors have limited impact. Reduced detail in signal processing in turn leads to insufficient updating of priors and chronic uncertainty. Following such a “better safe than sorry” processing heuristic, perception relies more on threat-related priors than actual signals (Van den Bergh et al., 2021).

In relation to somatic symptom perception, a “better safe than sorry” strategy is associated with precise symptom-related priors and an influential affective-motivational component in experiencing symptoms, while sensory-perceptual processing is unprecise. Empirical evidence of impaired sensory-perceptual processing can, for example, be found in lower accuracy of respiratory symptom perception in individuals with high negative affectivity and in negative affective framings (Bogaerts et al., 2005; Van den Bergh et al., 2004). Also implying less precise sensory-perceptual processing, patients with clinical and non-clinical somatic symptoms show reduced memory specificity regarding health cues and symptom episodes (Walentynowicz et al., 2018; Walentynowicz, Raes, Van Diest, & Van den Bergh, 2017). A series of studies with fibromyalgia patients implies impaired learning

of fear of pain: Patients showed reduced differential acquisition of pain-related fear (Meulders, Boddez, Blanco, Van Den Houte, & Vlaeyen, 2018; Meulders, Jans, & Vlaeyen, 2015), and more non-differential fear generalization and slower extinction of pain generalization than healthy controls (Meulders et al., 2015; Meulders, Meulders, Stouten, De Bie, & Vlaeyen, 2017). Increased susceptibility to symptom-related priors was also shown by increased symptom report in healthy participants after negative affect induction and reading a symptom questionnaire (Van Den Houte et al., 2017). Similarly, high vs. low somatic symptom reporters reported more symptom complaints when the context was symptom-related as compared to neutral (Bogaerts et al., 2008).

### 1.3 Interoceptive bias as a measure of processing symptoms

When following the proposed “better safe than sorry” processing strategy, bodily signals are more readily appraised as threatening. This in turn leads to an overreporting of these signals, which prevents that potentially threatening signal might be missed. Such a tendency to overreport signals can be determined in interoceptive tasks. Interoception refers to the process by which the nervous system senses, interprets, and integrates signals from within the body (Khalsa et al., 2018). This process comprises several facets, including interoceptive attention (observing body sensations), sensibility (the self-reported tendency to focus on body signals), and insight (the metacognitive evaluation of interoceptive performance; Khalsa et al., 2018). Interoceptive performance can be measured in *accuracy* or *sensitivity* tasks<sup>1</sup>, in which correct and precise monitoring of body signals is assessed based on the extent to which self-report and behavioral measures of body signals match. Independent of their level of accuracy, individuals can show a tendency to over- or underreport signals. This tendency is referred to as interoceptive bias, or *response bias*. A liberal response bias implies an overreporting of signals along a “better safe than sorry” decision strategy, while a conservative response bias implies an underreporting of signals as part of a “wait and see” approach (Petersen et al., 2015).

The assumptions of a “better safe than sorry” decision strategy in populations with pathological somatic symptoms thus suggest a more liberal response bias in

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<sup>1</sup> Accuracy is used as an umbrella term for tasks that measure performance on objective behavioral tests (Garfinkel, Seth, Barrett, Suzuki, & Critchley, 2015). Sensitivity is used as a more specific term for accuracy in signal detection tasks. Here, sensitivity is measured separately from response bias and refers to how well signal and noise can be distinguished (Stanislaw & Todorov, 1999).

these samples. Assumptions regarding interoceptive accuracy from a predictive coding perspective have not yet been developed, but it could be argued that either diminished or unimpaired accuracy are more likely because of unprecise sensory-perceptual processing in the context of a “better safe than sorry” strategy. Empirical evidence of altered interoceptive accuracy and response bias in somatic symptoms and illness anxiety will be summarized in the following section.

#### **1.4 Empirical evidence of altered interoceptive accuracy and bias in somatic symptoms and illness anxiety**

Findings of previous studies differed considerably depending on samples and interoceptive tasks. Several studies using a heartbeat perception task showed diminished interoceptive accuracy in somatic symptom disorder (Lee et al., 2018; Pollatos et al., 2011; Weiss, Sack, Henningsen, & Pollatos, 2014; Sachse, 1994; Schonecke, 1995), while others showed unimpaired accuracy in such samples (Schröder, Gerlach, Achenbach, & Martin, 2015; Schäfer, Egloff, & Witthöft, 2012) as well as samples with illness anxiety disorder (Barsky, Brener, Coeytaux, & Cleary, 1995; Krautwurst, Gerlach, & Witthöft, 2016).<sup>2</sup> When determining the threshold at which participants are able to sense weak tactile stimuli, accuracy was diminished in a sample with somatic symptom disorder (Katzer, Oberfeld, Hiller, Gerlach, & Witthöft, 2012) but not in a sample with illness anxiety disorder (Haenen, Schmidi, Schoenmakers, & van den Hout, 1997). Unimpaired accuracy was also shown in a sample with somatic symptom disorder when using the rubber hand illusion paradigm, in which participants were asked to estimate the distance between their own hidden hand and a rubber or virtual hand (Perepelkina, Romanov, Arina, Volel, & Nikolaeva, 2019).

Moreover, patients with somatic symptom disorder were *more* accurate than healthy participants in a muscle perception task (Scholz, Ott, & Sarnoch, 2001). Increased accuracy was also shown in a sample with illness anxiety disorder, using a signal detection task that measured the perception of physiological changes indicated by spontaneous changes in skin conductance (Krautwurst et al., 2016).

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<sup>2</sup> Please note that the DSM-5 terms somatic symptom disorder and illness anxiety disorder are used for former diagnostic classifications as well (e.g., somatoform disorder, hypochondriasis), although these diagnoses are not completely congruent. For non-clinical forms, the terms excessive somatic symptoms and illness anxiety will be used accordingly (instead of e.g., somatoform symptoms, medically unexplained symptoms, health anxiety).

Only few studies have examined response bias in pathological samples. Krautwurst et al. (2016) found a more liberal response bias in a sample with illness anxiety disorder compared to healthy controls in the aforementioned signal detection task. Another study provided restricted evidence of a more liberal response bias in a sample with somatic symptom disorder when using a tactile detection task (Katzer et al., 2012). A more liberal response bias was also found in a sample with somatic symptom disorder when using a heartbeat discrimination task (Schäfer et al., 2012). However, Schröder et al. (2015) did not find a difference in response bias in this task when comparing patients with noncardiac chest pain and healthy controls. Additionally, three studies found evidence of a more liberal response bias in non-pathological samples using signal detection tasks (Krautwurst, Gerlach, Gomille, Hiller, & Witthöft, 2014; Katzer et al., 2011; Brown, Brunt, Poliakoff, & Lloyd, 2010), while one study using a muscle tension perception task did not (Sarnoch, Adler, & Scholz, 1997).

When summarizing empirical findings of interoceptive accuracy and bias, it should be noted that not all interoceptive tasks are able to distinguish between these two facets. For example, one of the most frequently used tasks to determine accuracy, the heartbeat mental tracking task (Schandry, 1981), has been criticized because accuracy and response bias are intertwined and underreporting of heartbeat mainly accounts for differences in accuracy (Zamariola, Maurage, Luminet, & Corneille, 2018; Pohl et al., 2021). Interoceptive tasks grounded on signal detection theory overcome this issue: here, sensitivity and response bias can be determined separately for each participant (Stanislaw & Todorov, 1999). Signal detection tasks are therefore suitable to test the overreporting of signals as part of a “better safe than sorry” strategy. A signal detection task of tactile stimuli that has been repeatedly used in the context of somatic symptoms will be introduced in the following section.

### **1.5 Experimental operationalization of a “better safe than sorry” strategy**

The somatic signal detection task (SSDT) was designed to create illusory sensations as an analogue for medically unexplained symptoms (Lloyd et al., 2008). Based on the observation that sensations of touch are induced when visual stimuli are presented (Johnson, Burton, & Ro, 2006), vibration and light stimuli are combined in this paradigm. Before starting the actual task, individual thresholds for

detecting vibration stimuli are determined. Thresholds are adjusted so that 40-60% of tactile stimuli are correctly detected (Lloyd et al., 2008). In the main task, tactile and light stimuli are each presented in half of the trials, resulting in four different types of trials: trials with only a tactile stimulus, trials with only a light stimulus, trials with both a tactile and a light stimulus, and trials with no stimulus. After each trial, participants are asked whether they have felt a vibration or not. From participants' answers across the different trials, the signal detection theory test statistics  $d'$  and  $c$  can be calculated. Individual sensitivity is captured with the  $d'$  index, with a higher score implying higher sensitivity. For response bias  $c$ , a score below zero indicates a liberal response bias, and a score above zero indicates a conservative response bias. Alterations of these parameters in trials with light stimuli are of particular interest here, because the light stimuli are assumed to affect bias. Sensitivity in no-light trials is not assumed to differ between participants, because the preceding thresholding procedure should result in similar levels of sensitivity.

Studies using the SSDT consistently showed that response bias was indeed more liberal in trials with light stimuli (Lloyd et al., 2008; Brown et al., 2010; McKenzie, Lloyd, Brown, Plummer, & Poliakoff, 2012; Brown et al., 2012; Katzer et al., 2011; Katzer et al., 2012). In most of these studies, sensitivity was also increased in light trials (Katzer et al., 2012; Brown et al., 2010; McKenzie et al., 2012; Brown et al., 2012).

These studies provide first evidence of a more liberal response bias in the SSDT in excessive somatic symptoms and illness anxiety. In healthy subjects, a more liberal response bias was associated with the tendency to experience pseudoneurological symptoms (Brown et al., 2010), more symptom report in general, and higher illness anxiety scores (Katzer et al., 2011). Symptom report was also associated with a higher false alarm rate in healthy participants and in a sample with medically unexplained and medically explained gastroenterological symptoms (Brown et al., 2012). Interestingly, there were no differences in false alarm rates between participants with medically unexplained and medically explained symptoms (Brown et al., 2012). Another study showed a more liberal response bias in participants with somatic symptom disorder, but only in the first half of the SSDT and in trials without light stimuli (Katzer et al., 2012). In this study, false alarms were associated with the report of somatic symptoms, and particularly pseudoneurological symptoms. No group differences or correlations of somatic symptoms or illness

anxiety with  $d'$  were found (Katzer et al., 2011; Katzer et al., 2012; Brown et al., 2010).

## 1.6 Key research goals

In the previous sections, a “better safe than sorry” decision strategy regarding somatic signals as part of the predictive coding framework was presented, where the tendency to overestimate signals was proposed as a potential mechanism in excessive somatic symptoms and illness anxiety. The overestimation of signals can be captured with an index representing a response bias in interoceptive tasks such as the SSDT.

Until now, empirical evidence regarding response bias is sparse, but points to a more liberal response bias in excessive somatic symptoms and illness anxiety. Findings regarding interoceptive accuracy in pathological and non-pathological somatic symptoms and illness anxiety are inconsistent, with some evidence showing regular accuracy, some evidence showing diminished accuracy, and a few studies even showing better accuracy in somatic symptoms and illness anxiety. The first research goal was therefore to summarize previous findings regarding interoceptive accuracy and response bias in pathological and non-pathological somatic symptoms and illness anxiety in a systematic review and meta-analysis.

The second research goal was to test assumptions of a predictive coding view of excessive somatic symptoms: here, the aim was to examine whether response bias can be liberalized by influencing expectations. From a predictive coding view, the prediction of a somatic signal leads to a liberalization of responses. A liberalization of responses regarding somatic stimuli through a manipulation of predictions would strengthen a predictive coding view on excessive somatic symptoms.

The third research goal was to examine response bias in the SSDT in a sample with pathological illness anxiety for the first time. The aim was to test whether response bias is generally more liberal in this sample than in healthy controls, and whether this potential liberal response style is further intensified when predictions are manipulated.



## **2. Original publications**

### **2.1 Study 1 – Interoceptive accuracy and bias in somatic symptom disorder, illness anxiety disorder, and functional syndromes: A systematic review and meta-analysis**

This study was published under the following reference:

Wolters, C., Gerlach, A.L., & Pohl, A. (2022). Interoceptive accuracy and bias in somatic symptom disorder, illness anxiety disorder, and functional syndromes: A systematic review and meta-analysis. *PLoS One*, 17(8):e0271717.

doi:10.1371/journal.pone.0271717. PMID:35980959; PMCID:PMC9387777.

#### **Individual contribution to this study**

My own contribution to this study, based on CRediT (Contributor Roles Taxonomy), was as follows: conceptualization, data curation, formal analysis, investigation, methodology, project administration, visualization, writing – original draft.

## **2.2 Study 2 – Somatosensory illusions elicited by sham electromagnetic field exposure: Experimental evidence for a predictive processing account of somatic symptom perception**

This study was published under the following reference:

Wolters, C., Harzem, J., Witthöft, M., Gerlach, A.L., & Pohl, A. (2021).

Somatosensory Illusions Elicited by Sham Electromagnetic Field Exposure: Experimental Evidence for a Predictive Processing Account of Somatic Symptom Perception. *Psychosomatic Medicine*, 83(1), 94-100. doi: 10.1097/PSY.0000000000000884. PMID:33141791.

### **Individual contribution to this study**

My own contribution to this study, based on CRediT (Contributor Roles Taxonomy), was as follows: conceptualization, data curation, formal analysis, investigation, methodology, visualization, writing – original draft.

### **2.3 Study 3 – Symptom perception in pathological illness anxiety: tactile sensitivity and bias**

This study was published under the following reference:

Wolters, C., Slotta, T., Ratayczak, J., Witthöft, M., Gerlach, A.L., Pohl, A. (2023). Symptom Perception in Pathological Illness Anxiety: Tactile Sensitivity and Bias. *Psychosomatic Medicine* 85(1), 79-88. doi:10.1097/PSY.0000000000001154. PMID:36516317.

#### **Individual contribution to this study**

My own contribution to this study, based on CRediT (Contributor Roles Taxonomy), was as follows: conceptualization, data curation, formal analysis, investigation, methodology, visualization, writing – original draft.

### 3. Conclusions and outlook

#### 3.1 Main findings from the three publications

The systematic review and the two empirical studies presented above were conducted to answer three central research goals. The first goal was to shed light on inconsistent findings regarding interoceptive accuracy and bias in excessive somatic symptoms and illness anxiety in the literature. The systematic review and meta-analysis showed reduced interoceptive accuracy across 68 studies. However, moderator analysis revealed that this effect was substantially affected by type of diagnosis in the respective studies: Accuracy was indeed reduced in studies assessing functional syndromes, but not in studies assessing pathological and non-pathological somatic symptoms or illness anxiety. Eight studies have assessed response bias in such samples, and consistently showed a more liberal bias.

The second research goal was to test whether response bias can be liberalized by manipulating expectations in an analogue sample. Expectations were influenced using a sham Wi-Fi exposure when conducting the SSDT to measure response bias. Indeed, participants showed a more liberal response bias in classifying tactile sensations when the Wi-Fi was simulated to be switched on as compared to when it was not. At the same time, sensitivity did not differ between these two runs.

The third research goal was to examine whether individuals with pathological illness anxiety show a more liberal response bias in classifying tactile stimuli, and whether response bias is affected when illness words are presented as a manipulation of predictions. In this study, results were more equivocal. Unexpectedly, response bias did not differ between participants with pathological illness anxiety and healthy controls. Instead, there was a group difference in sensitivity, depending on trial type: Participants with pathological illness anxiety showed higher sensitivity in trials with an auxiliary light stimulus vs. no light stimulus, but lower sensitivity in trials with auxiliary illness words vs. neutral words when compared to healthy controls. Follow-up analyses did not show group differences in either version of the SSDT.

### **3.2 Better safe than sorry? A theoretical and empirical integration of findings**

First, the finding of a more liberal response bias in the systematic review and meta-analysis confirms the assumption of a “better safe than sorry” strategy in excessive somatic symptoms and illness anxiety, so that somatic signals are more readily reported as present. The eight included studies had examined both pathological and non-pathological samples and were mixed regarding the interoceptive tasks and body domains. Because only tasks without any targeted manipulation of response bias were selected, it can also be concluded that this processing strategy does not depend on specific contextual factors, such as threatening cues. Additionally, the variety of body domains used in the study tasks (touch sensations of the hand, breathing, skin conductance, heartbeat) implies that this processing strategy is not restricted to specific body parts. Instead, a more general processing strategy seems to characterize participants with pathological and non-pathological illness anxiety and somatic symptoms. However, based on the studies in the systematic review, it cannot be concluded whether an activation of threat-related priors may intensify this strategy.

Interestingly, while the response bias overall was more liberal, samples with excessive somatic symptoms and illness anxiety did not differ with regard to interoceptive accuracy. A “better safe than sorry” processing strategy is assumed to be low in sensory-perceptual detail, while threat-related priors are driven by the affective-motivational component of symptom experience (Van den Bergh et al., 2021). Based on the findings of the systematic review, sensory-perceptual detail, as operationalized by interoceptive accuracy, was not lower in samples with excessive somatic symptoms and illness anxiety than in control populations. Again, it should be mentioned that interoceptive accuracy was measured in a variety of tasks and body domains in the studies that were included into the systematic review. Importantly, the majority of tasks did not distinguish between accuracy and response bias (60 out of 67 studies did not report any measure of response bias), resulting in accuracy scores that might be latently affected by response bias. Note, however, that it is not yet clear whether accuracy is diminished in situations associated with threat or in individuals with high negative affectivity, which single studies point to (e.g., Bogaerts et al., 2005; Van den Bergh et al., 2004).

In the two empirical studies, it was shown that priors regarding somatic signals can liberalize response bias in healthy participants, but neither sensitivity nor response bias were altered in a sample with pathological illness anxiety. The results of the sham Wi-Fi study fit in well with findings of an earlier study showing that healthy participants rate tactile sensations as more intense under sham Wi-Fi radiation (Bräscher, Raymaekers, Van den Bergh, & Witthöft, 2017). The present study provided evidence that higher intensity ratings were not fostered by increased sensitivity but a liberalization of response bias. This finding is in line with the assumption that a “better safe than sorry” processing strategy is applied when somatic signals are expected. Again, the findings do not support the assumption of lower sensitivity (i.e., lower detail sensory-perceptual processing) as a premise for priors to exert influence on decision strategies.

A liberal response bias in tactile tasks was also found in healthy participants with elevated levels of illness anxiety and somatic symptoms (Brown et al., 2010; Katzer et al., 2011) as well as somatic symptom disorder (Katzer et al., 2012). Taken together, these findings imply that 1) response bias in tactile tasks may be liberalized in a context where the perception of somatic signals is expected, 2) this response behavior characterizes participants with pathological and non-pathological forms of elevated symptom report as well as healthy participants with elevated illness anxiety.

The question whether response bias of tactile stimuli is affected in clinical forms of illness anxiety was tackled in the second empirical study. Surprisingly, no differences regarding response bias were found. This result contradicts findings of a more liberal response bias in non-specific skin conductance fluctuations in pathological and non-pathological illness anxiety (Krautwurst et al., 2014; Krautwurst et al., 2016).

The unexpected finding could be due to methodological issues: The comparison between the two versions of the SSDT showed that the adapted word version of the SSDT lowered sensitivity and rendered response bias more conservative in both groups. The two versions were presented in randomized order. Arguably, when the adapted version of the SSDT was presented first, the more conservative response bias carried over to the original version of the SSDT as well. This order effect was not found for sensitivity. Interestingly, the only group effect was found with regard to sensitivity. In the pathological illness anxiety group, sensitivity increased from no-light to light trials in the original SSDT but slightly decreased from

neutral to illness words in the adapted SSDT. Control participants showed a less steep increase in sensitivity from no-light to light trials, and an increase in sensitivity from neutral to illness words. Lower sensitivity in illness word trials could be interpreted as lower detail sensory-perceptual processing when the affective-motivational component, elicited by threatening illness words, is activated. However, this finding cannot be interpreted as indicator of a “better safe than sorry strategy”, because there was no change in the processing strategy as measured by response bias. Also, follow-up analyses of the adapted version of the SSDT did not confirm group differences with regard to word stimuli. Therefore, group differences with regard to trial types should be seen as diverging reactions to the context in which somatic signals are presented, rather than consequences of a specific processing strategy in pathological illness anxiety.

Differences in the findings from the Krautwurst et al. (2014) study could be due to the use of different interoceptive tasks or to the selection of the sample: In their study, comorbid diagnoses of DSM-IV somatoform disorder (except for undifferentiated somatoform disorder) were excluded. In the present study, diagnosis of pathological illness anxiety was based on either DSM-5 illness anxiety disorder or somatic symptom disorder. Response behavior might differ between illness anxious individuals with impairing somatic symptoms and those without. On the other hand, Katzer et al. (2012) found a more liberal response bias in the SSDT in a sample with somatoform disorders. Interestingly, they did not find any association between response bias and levels of illness anxiety within that sample. Up to now, evidence is too sparse to confidently argue that differences regarding response bias are due to different subgroups with illness anxiety or somatic symptoms, different tasks, or methodological issues. Findings from the patient study therefore remain inconclusive with regard to a potential underlying “better safe than sorry” strategy.

A secondary finding from this third study (with the clinical sample) was that there were no group differences in accuracy scores in the heartbeat mental tracking task. This results provides further evidence that accuracy is not generally lower in individuals with pathological illness anxiety. Here, the absence of group differences in heartbeat perception scores is in line with findings from the systematic review and meta-analysis, which did not support the assumption of lower interoceptive accuracy in illness anxiety and excessive somatic symptoms.

In sum, findings of the systematic review and the empirical study with the analogue sample underpin the assumptions of a “better safe than sorry” processing strategy, with no measurable deficits in interoceptive accuracy or sensitivity. Results of the study with the pathological illness anxiety sample were inconclusive and await further clarification.

### **3.3 Clinical implications of the findings**

Some clinical implications can be drawn from the idea of a “better safe than sorry” strategy in samples with excessive somatic symptoms and illness anxiety that has been partially confirmed by the present studies. For example, Van den Bergh et al. (2021) suggest tailoring interventions to dissolve the stagnated error-reduction process that is associated with this processing strategy. Specifically, to overcome stagnated error-reduction, aversive information needs to be processed in detail, especially with regard to sensory-perceptual components. Prediction errors should then modify threat-related priors, and these more adaptive priors may in turn predict new input. As part of active inference, defensive-action programs are initiated to confirm predictions. Via signals to the motor system, the body is moved to generate the predicted sensations (Barrett & Simmons, 2015). Effective treatments should thus target the way that threatening information is processed at these different response levels, and train patients to disengage from defensive-action tendencies (Van den Bergh et al., 2021).

Exposure based interventions are a standard technique in behavioral therapy and effective in illness anxiety disorder (e.g., Bouman & Visser, 1998; Visser & Bouman, 2001; Weck, Neng, Richtberg, Jakob, & Stangier, 2015) and functional syndromes such as irritable bowel syndrome (Craske et al., 2011). Exposure therapy tackles avoidance behavior and places patients in situations where they are likely to produce prediction errors (Paulus, Feinstein, & Khalsa, 2019). Arguably, exposure to aversive stimuli will give patients an opportunity to adjust their priors and form a new, adaptive model. Paulus et al. (2019) give the example of a hyperprecise prior that sensing one’s heartbeat can lead to a heart attack. This prior could then be modified towards a non-catastrophic prior when the individual does not experience a heart attack after sensing their heartbeat.



Exposure therapy is usually assumed to work by collecting corrective information that will modify cognitive structures that hold (unrealistic) information about the fear stimuli, fear responses, and their meaning (Foa & Kozak, 1986). Defensive responses will then become redundant when cognitive structures are changed and it is no longer expected that the feared stimulus will appear. From a predictive coding perspective, this process is conceptualized somewhat differently: Here, exposure therapy is assumed to train the disengagement from defensive responses *during* the processing of threatening information (Van den Bergh et al., 2021). This disengagement supposedly reduces threat and changes associated psychophysiological and motor responses. In turn, the weight of threat-related priors will also be reduced. A more detail-oriented sensory-perceptual processing will in turn update prior beliefs. This processing style has been described as a “wait-and-see approach” (Van den Bergh et al., 2021).

How these considerations can be used to actually improve exposure-based interventions remains an open question. As a specific form of exposure therapy, interoceptive exposure enhances treatment effects in a variety of mental disorders, but has been mainly studied in panic disorder (Gerlach & Neudeck, 2012). In interoceptive exposure, symptoms of anxiety and panic are induced using either biochemical substances such as CO<sub>2</sub> inhalation, or provocation procedures such as hyperventilation (Gerlach & Neudeck, 2012). In line with these considerations, it has been suggested to tailor interoceptive exposure therapy to individual somatic symptoms (Khalsa & Lapidus, 2016). New provocation methods such as the provocation of gastrointestinal disturbance in irritable bowel syndrome (Craske et al., 2011) could be seminal for the improvement of treatments in somatic symptom disorder.

Another approach to tackle interoceptive bias in practice is through mindfulness techniques (Farb et al., 2015). Practicing mindfulness may help to shift attention toward perceptible bodily signals. This practice is thought to broaden the distribution of priors because a variety of visceral sensations are experienced, thereby minimizing prediction errors. This type of training might also help individuals to refrain from automatic responses to interoceptive experiences, such as avoidance in response to aversive experiences (Farb et al., 2015). Indeed, a short body scan meditation training increased sensitivity towards tactile stimuli and decreased false alarm rates in the SSDT, while it did not result in significant changes of response bias

scores (Mirams, Poliakoff, Brown, & Lloyd, 2013). In contrast, no differences in heartbeat perception scores were found after a week-long body scan training (Parkin et al., 2014) or between individuals with and without meditation experience (Khalsa et al., 2008; Melloni et al., 2013). Beneficial effects of mindfulness were shown in experimentally induced pain (Gard et al., 2012; Zeidan, Gordon, Merchant, & Goolkasian, 2010), and these effects went along with increased sensory processing in the brain (Gard et al., 2012). Patients with diabetes who reported more mindfulness during difficulties were more accurate in estimating their blood glucose levels (Kiken, Shook, Robins, & Clore, 2018). Mindfulness-based cognitive therapy led to an increase in several aspects of body awareness in a sample with chronic pain and acute depression (de Jong et al., 2016). Pilot studies for the implementation of body awareness therapy in fibromyalgia have to date yielded inconclusive results (Mannerkorpi & Arndorw, 2004; Kendall, Brolin-Magnusson, Sören, Gerdle, & Henriksson, 2000) and need further investigation. Innovative forms of therapy such as Floatation-REST (Reduced Environmental Stimulation Therapy), which is supposed to increase muscle relaxation and attention to the body by attenuating external sensory input, showed first positive effects in the treatment of anxiety (Feinstein et al., 2018a; Feinstein et al., 2018b; Jonsson & Kjellgren, 2016).

In sum, the implementation of mindfulness and related interventions to reduce interoceptive bias and symptom distress is promising, but research regarding the link between these aspects is still in its infancy.

A more specific method to increase the processing of sensory-perceptual details of bodily states is biofeedback. For example, cardiac feedback training is able to increase heartbeat perception performance (Meyerholz, Irzinger, Witthöft, Gerlach, & Pohl, 2019; Schandry & Weitkunat, 1990; Weisz, Báalazs, & Ádám, 1988; Sugawara, Terasawa, Katsunuma, & Sekiguchi, 2020; but see Rominger, Graßmann, Weber, & Schwerdtfeger, 2021). Heartbeat discrimination training reduced somatic symptoms in healthy participants (Sugawara et al., 2020). Patients with somatic symptom disorder showed lower symptom distress after a heartbeat perception training procedure, even though heartbeat perception was not improved (Schäfer, Egloff, Gerlach, & Witthöft, 2014). Nanke and Rief (2003) conducted a biofeedback training in patients with somatic symptom disorder, which included surface electromyography, skin conductance level, peripheral skin temperature, and blood volume pulse amplitude. They found a decrease in catastrophizing somatic

sensations and an increase in the acceptance of psychosocial causes of symptoms (Nanke & Rief, 2003). Pilot studies of heart rate variability biofeedback have shown symptom reductions in patients with somatic symptom disorder (Krempel & Martin, 2022), chronic pain (Hallman, Olsson, von Schéele, Melin, & Lyskov, 2011; Weeks, Whitney, Tindall, & Carter, 2015), fibromyalgia (Hassett et al., 2007), and chronic fatigue syndrome (Windthorst et al., 2017). Again, causal pathways of symptom reductions through different forms of biofeedback are still up for research.

### 3.4 Outlook

Interoception is increasingly recognized as a factor in the development and maintenance of mental disorders (Paulus et al., 2019; Khalsa et al., 2018; Brewer, Murphy, & Bird, 2021), and both interoceptive processes and interoception-based interventions are increasingly studied (for reviews see Khalsa & Lapidus, 2016; Khoury, Lutz, & Schuman-Olivier, 2018). Interoceptive phenomena are used to describe the symptomatology of disorders such as somatic symptom disorder (American Psychiatric Association, 2013), but are still underrepresented in the nosology of mental disorders (Paulus et al., 2019). Even in dimensional classification systems such as the Research Domain Criteria (RDoC; Kozak & Cuthbert, 2016) or the Hierarchical Taxonomy of Psychopathology (HiTOP; Kotov et al., 2017), interoception is not included, albeit providing a direct link between biological and psychological processes in several mental disorders (Paulus et al., 2019). Instead, interoceptive processes are provisionally assigned to other categories such as internalization (e.g., in Van den Bergh et al., 2021), or linked to existing categories (e.g., linking self-reported interoceptive abilities to the internalizing and somatoform spectra within the HiTOP model; Brand, Petzke, & Witthöft, 2022). Potential reasons for the limited amount of attention that has been paid to interoceptive biomarkers include insufficient conceptual understanding, a lack of reliable assessment tools, and vague terminology (Paulus et al., 2019).

To advance research on interoceptive processes, theoretical models such as the predictive coding model have to be translated into testable hypotheses (Van den Bergh et al., 2017). This suggestion was brought to fruition in the present empirical studies by measuring response bias. Findings of these and previous studies on response bias in excessive somatic symptoms and illness anxiety are difficult to

compare because they have not only used heterogeneous assessment tools but also heterogeneous diagnostic criteria. Current DSM-5 criteria, particularly with regard to the distinction between somatic symptom disorder and illness anxiety disorder, have been up for debate (Bailer et al., 2016; Rief & Martin, 2014; Newby, Hobbs, Mahoney, Wong, & Andrews, 2017). Additionally, a myriad of terms such as somatization, functional symptoms or medically unexplained symptoms has been in use, and it is difficult to find consensus (Creed et al., 2010).

Future studies should pay particular attention to both common and distinctive features of somatic symptom disorder and illness anxiety disorder. An example is anxiety sensitivity, a transdiagnostic factor that describes the fear of arousal-related sensations (Taylor et al., 2007). Anxiety sensitivity is associated with illness anxiety disorder and somatic symptom disorder (e.g., Axelsson, Hedman-Lagerlöf, Hedman-Lagerlöf, Ljótsson, & Andersson, 2020; Bailer et al., 2016), and has been conceptualized within the predictive coding framework (Paulus et al., 2019). Additionally, anxiety-specific cognitive processes such as worrying could play a role in the prediction of interoceptive states (Paulus & Stein, 2010). Future studies could examine if such cognitive processes play a role in interoceptive bias in somatic symptoms and illness anxiety as well.

To date, only few assessment tools are available that measure interoceptive bias, and these tools commonly measure harmless sensations in a resting state (such as the tactile stimuli in the empirical studies presented here). Paulus et al. (2019) raised concerns that important facets of symptom variability might be ignored when using resting state assessments, because clinically or emotionally significant events are usually associated with arousal and homeostatic deviations. They propose using assessment tools that include perturbations of interoceptive systems, because these methods would be more naturalistic, may show effects that are not present during resting states, and avoid floor-effects that are typical for some tasks such as the heartbeat mental tracking task (Paulus et al., 2019). Engaging the interoceptive system under naturalistic conditions to measure its dysfunction could be seen as equivalent to a cardiac stress test (Khalsa et al., 2018). Perturbations could be produced using noninvasive methods such as the Trier social stress test (Kirschbaum, Pirke, & Hellhammer, 1993) but it would be preferable to use tasks in which the predictability and controllability of sensory input vary (Paulus et al., 2019). The use of breathing restrictions (Petersen et al., 2015) is an example of how to

assess both interoceptive accuracy and response bias under perturbation of an interoceptive system. Ideally, bottom-up perturbation approaches should be combined with top-down assessments, so that more than one interoceptive feature can be captured within the same task (Khalsa et al., 2018). Paulus and Stein (2010) suggest that it may even be possible to distinguish individuals with a predominant bottom-up dysregulation and those with a predominant top-down dysfunction.

This type of combined assessment could be particularly interesting for the further investigation of a “better safe than sorry” strategy in the perception of somatic symptoms. Possibly, this strategy is only applied when sensory stimuli are perceived as relevant, or even threatening. In a study using breathing stimuli which were sometimes followed by unpredictable electrocutaneous stimuli, this context of threat affected how breathing stimuli were perceived (Zacharioudakis, Vlemincx, & Van den Bergh, 2020). In an elegant study design, Hoskin et al. (2019) showed how expectations of pain and uncertainty in these expectations can be manipulated to test assumptions of the predictive coding model. An interoceptive paradigm that allows for an effective manipulation of variables such as expectations and uncertainty could greatly advance empirical testing of a “better safe than sorry” strategy in excessive somatic symptoms and illness anxiety.

Hopefully, future studies will further advance research of symptom perception from a predictive coding view. Empirical evidence of a “better safe than sorry” could shed more light on the complex interplay between top-down and bottom-up mechanisms of symptom perception in somatic symptom disorder and illness anxiety disorder. Ultimately, these findings could pave the way for improved diagnostic and therapeutic applications in individuals suffering from these disorders.

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