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# Cognitive Vulnerability in the Context of Panic: Assessment of Panic-Related Associations and Interpretations in Individuals with Varying Levels of Anxiety Sensitivity

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## Abstract

**Background** Cognitive models of panic disorder (PD) highlight the role of panic-related associations and interpretations. However, results are mixed and rely on specific measures. This study examined panic-related associations and interpretations using established and new paradigms in individuals varying on anxiety sensitivity (AS).

**Methods** Associations were measured using a priming task and a novel Single Target Implicit Association Test (STIAT); interpretations were assessed using the Interpretation Bias Questionnaire (IBQ) and a novel Scrambled Sentences Task (SST). Symptoms were assessed via a provocation task (Straw Breathing Task, SBT).

**Results** Panic-related interpretations correlated with AS and other PD-related measures. Of the association tasks, only the priming task correlated with one of the other PD-related measures. Panic-related interpretations assessed via the SST, but not priming, STIAT, and IBQ, predicted SBT reactivity. The relationship between AS and SBT reactivity was mediated by panic-related interpretations.

**Conclusions** Our data provide support for panic-related interpretations as an important cognitive mechanism.

**Keywords** Panic disorder · Anxiety sensitivity · Automatic associations · Interpretations · Cognitive-behavior therapy

## Introduction

Panic disorder (PD) is a prevalent and often disabling anxiety disorder (Barlow et al. 2000; Olesen et al. 2012). Several theories have been developed, postulating strong cognitive components in the pathogenesis of PD (e.g., Clark 1986; Margraf and Ehlers 1989). In brief, these accounts

assume that people with PD are hypervigilant to their bodily reactions, and once attention is paid to these reactions, panic-related threat associations (e.g., fear) are immediately triggered. These are then followed by more complex, panic-related interpretations (e.g., a catastrophizing interpretation). This, in turn, increases anxiety, triggers additional anxiety-related bodily reactions, and ultimately escalates into a vicious cycle of panic. To illustrate, if someone with PD e.g., attends to their heartbeat, a fear association is activated immediately, followed by a highly dysfunctional interpretation, e.g., “I am having a heart attack”. This, in turn, produces both more anxiety symptoms and additional bodily reactions, which are then interpreted as additional evidence for the imminent threat. A likely ending of this cognitive, downward spiral is a full-blown panic attack (for additional support, see e.g., Beck 1988; Margraf and Ehlers 1989). Following this, panic-related associations and interpretations should thus be regarded as two different cognitive manifestations of an underlying vulnerability that have different operational properties. This theorizing is in line with hypotheses of dual-process models of anxiety (e.g., Ouimet et al. 2009). That is, panic-related associations are activated

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automatically and unintentionally, and therefore represent a first, quick evaluation of the threatening stimulus. In contrast, panic-related interpretations are activated slowly, and rely on relatively reflective and deliberate processing of the stimulus. From a procedural perspective, however, the two processes do not operate in isolation in that the activated panic-related associations are thought to have a biasing influence on panic-related interpretations (for a critique on assumptions put forward by dual processing models, see Gladwin and Figner 2014).

PD models have often been studied using an analogue approach that compares samples with high versus low anxiety sensitivity (AS), a disposition involving persistent concerns about possible negative consequences of symptoms associated with anxiety (Reiss and McNally 1985). AS is elevated in PD and has been shown to be a risk factor for PD development and maintenance (cf. Olatunji and Wolitzky-Taylor 2009). For example, Ehlers (1995) showed that AS is associated with the persistence of PD, the occurrence of panic attacks, and the onset of panic attacks in patients with simple phobias. Further, elevated levels of AS are associated with stronger panic-related associations and interpretations (e.g., Richards et al. 2001; Steinman and Teachman 2010; Teachman 2005). Accordingly, AS provides a useful PD-analogue when studying panic-related cognitive processes, circumventing limitations inherent to clinical samples, like comorbidity and (side-)effects of psychoactive medication.

A large body of research has aimed at advancing the scientific understanding of panic-related associations and interpretations, in both people with PD and samples with varying levels of AS. For assessing panic-related associations, computerized tasks, such as priming paradigms (e.g., Fazio et al. 1986), the Implicit Association Test (IAT; Greenwald et al. 1998), or the Extrinsic Affective Simon Task (EAST; De Houwer 2003) have been used. All three tasks require participants to assign stimuli into categories, and since strongly associated stimuli can be processed more quickly, reaction times constitute a reliable behavioral index of associative strength. To illustrate, the priming study by Hermans et al. (2010) used a priming task consisting of bodily symptom primes and catastrophic outcome targets (e.g., palpitations—dying). Results showed that people with PD, compared to anxious controls (e.g., with obsessive-compulsive disorder or social phobia), reacted quicker during those panic trials than during control trials. However, this study seems an exception, since a number of studies did not show the expected priming effects (e.g., Cloitre et al. 1992; McNally et al. 1997; Schniering and Rapee 1997), or only found the expected results when priming effects were calculated for ideographically selected stimuli (Schneider and Schulte 2007). Teachman et al. (2007) employed an IAT and found that people with PD, compared to healthy controls, had stronger associations between concepts relating to

the *self* and *panic*. In contrast, the IAT measuring *alarming* associations regarding *bodily changes* did not show a significant group difference (see also Teachman 2005; Teachman et al. 2008). Finally, Woud et al. (2016) applied an EAST and expected people with PD, compared to controls, to show stronger negative than positive automatic associations for both panic-related symptoms and agoraphobia-related situations. However, results did not confirm these expectations. Results are also mixed in the context of AS. To illustrate, when using a priming paradigm that included fear trials with fear-triggers, for example, “elevator” as prime words, and fear symptoms, for example “dizziness” as targets, participants high in AS, compared to low in AS, paradoxically reacted more quickly to neutral targets and slower to fear-symptom targets (Yang et al. 2016). When using an EAST, however, high- compared to low-AS participants automatically associated fearful consequences with panic-related symptoms (Lefaivre et al. 2006). Similarly, using the IAT, Teachman (2005) showed that high- compared to low-AS participants automatically associated themselves with panic (for a review about the role of automaticity in anxiety, see Teachman et al. 2012).

The Interpretation Bias Questionnaire (IBQ; McNally and Foa 1987) is the most widely used self-report measure to assess panic-related interpretations. It includes ambiguous scenarios that are panic-related vs. panic-unrelated, and participants interpret these scenarios using e.g., a multiple choice answering format. Here, results showed that people with PD/ agoraphobia interpreted panic-related scenarios more often as threatening compared to treated people with PD/agoraphobia and healthy controls (McNally and Foa 1987, see also Clark et al. 1997). Further, Woud et al. (2014) found that panic-related interpretation biases were predictive of new onsets of PD. In the context of AS, it has been shown that participants with high, compared to participants with low levels of AS, interpret panic-related bodily sensations as more aversive (McNally 1999) and show stronger catastrophic misinterpretations (Hilchey and Clark 2014, for additional finding see Olthuis et al. 2012).

To conclude, the evidence concerning panic-related associations does not provide a consistent and robust picture, for both the clinical and analogue studies, and apart from a few exceptions, the majority of studies did not find the expected effects. Further, findings for panic-related interpretations mainly rely on one measure, the IBQ. To the best of our knowledge, only one study has studied both panic-related associations and interpretations at the same time (see Teachman et al. 2007). Given the fundamental role of these cognitive processes in cognitive models of panic that have widely been adopted in clinical practice, additional work is clearly needed. On the one hand, it is needed to refine our understanding of both the cognitive models and the tasks used in earlier studies. On the other

hand, it is needed for testing novel measures for cross-validation and triangulation of results (cf. Munafò and Davey Smith 2018). Accordingly, the present study had two primary aims: (1) implementing tasks that had previously shown the expected result patterns (priming and IBQ) as a further test of their potential utility, and (2) expanding the field using promising novel tasks (STIAT and SST). To do so, we selected a sample with varying levels of AS, assessed by the Anxiety Sensitivity Index (ASI; Reiss et al. 1986).

Regarding panic-related associations, the well-established priming task by Hermans et al. (2010) was selected for the current study. As a novel, parallel task, we used a Single Target Implicit Association Test (STIAT; Wigboldus et al. 2004), a modified version of the IAT (Greenwald et al. 1998). Various studies successfully applied the STIAT in the context of psychopathology, for example, fear of spiders (Woud et al. 2011) or generalized anxiety disorder (Reinecke et al. 2010a, b). The choice to use the STIAT instead of the IAT or EAST was supported by the following arguments: First, the STIAT does not require two opposing target categories such as the IAT or EAST; second, the extent to which the target is associated with the two attribute dimensions can be measured independently of the association with another target category; third, the psychometric properties of the STIAT are at least equally reliable as the IAT (Karpisnki and Steinmann 2006), but clearly better compared to those of the EAST (e.g., Bluemke and Friese 2008; De Houwer and De Bruycker 2007; Reinecke et al. 2015).

Regarding panic-related interpretations, the well-established IBQ (McNally and Foa 1987) was employed as a computerized version, as well as a computerized version of the Scrambled Sentences Task (SST; Wenzlaff and Bates 1998; Rude et al. 2001) as a novel paradigm. During the SST, participants are asked to sort a string of six words into a grammatically correct sentence, leaving out one word. The unscrambled sentence can be positive or negative in valence, depending on which word is omitted. The SST is an established measure of dysfunctional interpretations, for example, in depression research (e.g., Rude et al. 2001), but has not been applied in panic research. It therefore is a promising, innovative tool for assessing panic-related interpretations. Furthermore, we employed the Straw Breathing Task (SBT, see Taylor and Rachmann 1994; Teachman et al. 2007), a task that induces panic-related bodily sensations and assesses the propensity to react with panic-related symptoms to breathing restriction. This allows further examining the external validity of the cognitive test-battery for predicting panic propensity. Before and after the SBT, the 13 panic symptoms according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5, see American Psychiatric Association 2013) were assessed, as an index of (changes in) panic-related symptomatology (i.e., SBT reactivity). Hence,

SBT reactivity is derived from changes in panic symptoms experienced before versus after performing the SBT.

To summarize, our tasks and their conceptualization were derived from predictions of cognitive models of PD, and AS was operationalized as a risk factor for panic. The functional relationship between these three elements (i.e., AS, cognitive models, and our tasks) as a rationale for our study set-up is as follows: Individuals with elevated levels in anxiety sensitivity experience fear regarding anxiety-related symptoms (Reiss and McNally 1985). This, in turn, biases subsequent information-processing, in such that anxiety symptoms are misinterpreted as being dangerous. Accordingly, AS represents a cognitive vulnerability here. Cognitive models of panic incorporate such biased information-processing styles, in such that these models predict that cognitive biases are responsible for the development and maintenance of pathological anxiety reactions, i.e., panic attacks. In this study, these biases are operationalized via the computer tasks, which require participants to react to panic-related stimuli, whereby participants' associations or interpretations were indexed e.g., via reaction times or probability ratings, respectively, depending on the task employed.

In line with predictions of cognitive models of PD, our main expectation was that the higher the levels of AS, the faster the categorization times for panic-related association trials, both during the priming task and the STIAT. In addition, we expected that the higher the levels of AS, the more often panic-related scenarios would be interpreted in a panic-related manner on the IBQ, and the more panic-related sentences would be generated on the SST. Further, we expected that more panic-related responses on these four cognitive tasks would uniquely predict higher levels of SBT reactivity, over and above other relevant predictors. The Agoraphobic Cognitions Questionnaire (ACQ, Chambless et al. 1984) and Body Sensation Questionnaire (BSQ; Chambless et al. 1984) were additionally applied to test for generalization to other PD-related traits, expecting a similar pattern as with the ASI. Finally, we hypothesized that panic-related associations and interpretations would mediate the relationship between AS and the experimentally provoked panic symptom reactivity in the SBT. With these hypotheses, we partly follow recommendations put forward by Kraemer et al. (1997) of how to structurally investigate a potential causal risk factor of psychopathology. That is, and in line with our analogue, correlational design, we first examine panic-related associations and interpretations as a correlate and unique predictor (i.e., over and above other predictors) of experimentally induced panic-related symptomatology. Second, we investigate whether panic-related associations and interpretations help to better understand the processes underlying anxiety sensitivity and panic-related symptomatology by investigating the pattern of shared and unique variance via mediation analyses.



## Method

### Procedure

We advertised that we were recruiting participants for a study that investigated the relationship between cognitive thinking styles and bodily sensations. Via the online screening, participants completed the ASI and were then invited to the lab session. Participants were assessed individually in a one-hour session. During the assessment, participants first completed the self-report measures, that is, the ACQ, BSQ, DASS-21, STAI-S, STAI-T, and the first self-ratings of the DSM-5 panic symptoms. After that, they completed the computer tasks, that is, the Priming, STIAT, SST, and IBQ, followed by the second rating of the DSM-5 panic symptoms and STAI-S. Next, the SBT was performed, after which participants completed the third panic symptom ratings and the STAI-S. Finally, all participants were debriefed, reimbursed, and thanked for their participation.

### Recruitment, Online Screening, and Participants

Participants were students recruited from Ruhr University Bochum (Germany) via social media, posters, and flyers. Interested participants contacted the research team via e-mail and were then sent an online screening. This screening assessed demographics (age, gender) and included the Anxiety Sensitivity Index (ASI; Reiss et al. 1986; Ehlers 1986). Regarding the ASI, we aimed to recruit a sample with a large variance in ASI scores, including sufficient participants with low ( $\leq 16$ ) versus high ( $\geq 17$ ) scores (for cut-offs, see e.g., Blechert et al. 2013). Post-hoc inspection of our sample indeed matches results of other experimental-analog studies using ASI scores. The distribution of our sample was as follows: 26 participants had low ASI scores ( $M = 10.23$ ,  $SD = 3.49$ ) and 28 participants had high ASI scores ( $M = 24.11$ ,  $SD = 4.86$ ), resembling findings of Blechert et al. (2013) (mean of the low AS group:  $M = 9.11$ ,  $SD = 5.85$ ; mean of the high AS group:  $M = 25.3$ ,  $SD = 3.58$ ). Since PD often develops during late adolescence/early adulthood (see e.g., Juul and Nemeroff 2012), we aimed to recruit a specific and consistent age range, namely participants between 18 and 35 years.

In total, 54 people (29 female, 25 male) with an age range between 20 and 31 years ( $M = 24.02$ ,  $SD = 2.5$ ) (see Table 1 for sample characteristics) were included in the analysis.

## Clinical Measures<sup>1</sup>

### Anxiety Sensitivity Index (ASI)

The ASI (Reiss, et al. 1986; German translation: Ehlers 1986) is a 16-item questionnaire measuring concerns about possible negative consequences of symptoms associated with anxiety. The ASI consists of three first-order factors, that is, physical concerns, cognitive concerns, and social concerns. Participants indicate their responses on a 5-point Likert scale, ranging from 0 = "Very little" to 4 = "Very much".

### Agoraphobic Cognitions Questionnaire (ACQ)

The ACQ (Chambless et al. 1984; German translation: Ehlers et al. 1993a, b) is a 14-item questionnaire in which participants indicate how often specific anxiety-related cognitions occur. The ACQ consists of two subscales, that is, loss of control and physical concerns. Participants indicate the frequency of each anxiety-related cognitions on a 5-point Likert scale ranging from 1 = "Never" to 5 = "Always".

### Body Sensations Questionnaire (BSQ)

The BSQ (Chambless et al. 1984; German translation: Ehlers et al. 1993a, b) includes 17 items reflecting specific bodily sensations commonly associated with panic (e.g., palpitations, dizziness). Participants indicate the degree to which they experience anxiety related to these sensations by means of a 5-point Likert scale, ranging from 1 = "Not at all" to 5 = "Extremely".

### Depression-Anxiety-Stress Scale – 21 item version (DASS-21)

The DASS-21 (Lovibond and Lovibond 1995; German translation: Nilges and Essau 2015) is a 21-item questionnaire and measures negative affective states experienced during the past seven days. Participants indicate to which extent they experience each symptom on a 4-point Likert scale ranging from 0 = "Did not apply to me at all" to 3 = "Applied to me very much, or most of the time".

### Spielberger State-Trait Anxiety Inventory (STAI)

The trait anxiety scale (STAI-T) (Spielberger et al. 1970; German translation: Laux et al. 1981) measures a stable tendency to experience anxiety and to perceive stressful

<sup>1</sup> An overview of the main questionnaires and computer tasks used in the study can be found in Table 1 in the supplementary material.

**Table 1** Sample characteristics

Measure (total possible range)	Frequency	<i>M</i>	<i>SD</i>	Range
Gender				
Female	29			
Male	25			
Age		24.02	2.50	20–31
ASI (0–64)		17.43	8.17	5–33
ACQ (15–75)		20.89	4.76	15–40
BSQ (0–68)		17.35	11.12	0–43
DASS-21 (0–63)		11.31	7.36	0–35
STAI-T (20–80)		38.56	8.27	25–62
STAI-S (20–80)				
Assessment 1 <sup>1</sup>		34.52	7.64	21–58
Assessment 2 <sup>2</sup>		34.91	6.93	22–50
Assessment 3 <sup>3</sup>		37.93	8.95	23–60
Subjective ratings of DSM-5 panic symptoms				
Panic symptoms (13–130)				
Assessment 1 <sup>1</sup>		8.87	15.11	0–83
Assessment 2 <sup>2</sup>		6.33	9.25	0–48
Assessment 3 <sup>3</sup>		16.91	17.66	0–88
General anxiety (1–10)				
Assessment 1 <sup>1</sup>		.65	1.48	0–8
Assessment 2 <sup>2</sup>		.33	1.13	0–7
Assessment 3 <sup>3</sup>		.67	1.33	0–7
Frequency of panic attacks				
Assessment 1 <sup>1</sup>	0			
Assessment 2 <sup>2</sup>	0			
Assessment 3 <sup>3</sup>	1			
Priming				
Panic prime–Panic target		641.48	143.27	
Panic prime–Neutral target		647.43	126.96	
Neutral prime–Panic target		659.49	131.61	
Neutral prime–Neutral target		628.93	125.93	
Panic difference score		18.01	84.20	
Neutral difference score		18.49	67.67	
STIAT				
D-Score <sup>a</sup>		.07	.34	
SST				
Ratio		.25	.17	
IBQ				
Panic scenario–Panic explanation		20.53	13.48	
Panic scenario–Neutral explanation		66.18	11.59	
Threat scenario–Threat explanation		44.79	14.62	
Threat scenario–Neutral explanation		56.46	12.12	
SBT				
Participants adhering to 2 min time limit	23	120.00	0	
Participants terminating the SBT early	31	47.74	24.70	

Priming task values and STIAT task values are reported in milliseconds. For all questionnaires and tasks, *N* = 54, unless stated otherwise

*ASI* Anxiety Sensitivity Index, *ACQ* Agoraphobic Cognitions Questionnaire, *BSQ* Body Sensations Questionnaire, *DASS-21* Depression-Anxiety-Stress Scale – 21 item version, *STAI-T* State-Trait Anxiety Inventory: trait anxiety scale, *STAI-S* State-Trait Anxiety Inventory: state anxiety scale, *Panic difference score* latencies of Panic prime—Panic target trials subtracted from latencies of Neutral prime—Panic target trials, *Neutral difference score* latencies of Neutral prime—Neutral target trials subtracted from latencies of

**Table 1** (continued)

Panic prime – Neutral target trials, *STIAT* Single Target Implicit Association Test, *SST* Scrambled Sentences Task, *Ratio* division of panic sentences by the sum of all correctly unscrambled sentences, *IBQ* Interpretation Bias Questionnaire, *PS* panic scenario, *PE* panic explanation, *NE* neutral explanation, *TS* threat scenario, *TE* threat explanation, *D-Score* subtracting latencies of combined compatible block during the *STIAT* from the combined compatible block, *SBT* Straw Breathing Task

<sup>1</sup>This assessment was prior to the completion of the computer tasks

<sup>2</sup>This assessment was after the completion of the computer tasks

<sup>3</sup>This assessment was after the completion of the SBT

<sup>a</sup>53 participants

situations as threatening. The state anxiety scale (STAI-S; Spielberger et al. 1970; German translation: Laux et al. 1981) assesses participants' current feelings of anxiety. Both scales consist of 20 items and are rated on a 4-point Likert scale ranging from 1 = "Not at all" to 4 = "Very much".

### Subjective Ratings of DSM-5 Panic Symptoms

A 15-item symptom checklist was used to assess panic- and anxiety related symptoms (for a similar procedure, see Wilhelm et al. 2001). This checklist included the 13 panic symptoms described in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association 2013) and assessed the general level of anxiety. Answers were given via a 10-point Likert scale ranging from 1 = "Not present" to 10 = "Very present". In addition, the occurrence of a panic attack could be indicated on a dichotomous item ("Yes" vs. "No").

### Straw Breathing Task (SBT; Taylor and Rachman 1994).

The SBT required participants to breathe through a thin straw with a diameter of about 2 mm while wearing a nose clip to reduce airflow. The duration of this task was 2 min, but participants could stop the task at any time. Participants stood during the SBT and received a time update every 20 s. The SBT is supposed to trigger harmless symptoms relevant in PD, such as temporary breathlessness, dizziness, and light-headedness (e.g., Antony et al. 2006; Teachman et al. 2007; Teachman et al. 2010). Hence, this task represents a valid tool to trigger panic symptoms as specified in the DSM-5.

## Computer Tasks<sup>2</sup>

### Priming Task

The priming task is based on the task used in Hermans et al. (2010). Regarding the stimuli, 10 panic primes and 10 panic targets were used, representing bodily sensations

usually experienced during a panic attack and the negative consequence associated with the respective sensation, respectively. In addition, 10 associatively related neutral primes and targets were included, and 20 (pronounceable) non-words.<sup>3</sup> Participants were instructed to sort target words as word or non-word by pressing the corresponding keys (D or L). Before a target word appeared, a prime word was presented. Participants were instructed to look at the prime without responding to it. For each trial, a fixation cross was presented for 500 ms, and 500 ms after the fixation cross disappeared, the prime word was shown for 200 ms, followed by an inter-stimulus interval of 50 ms. Thereafter, the target appeared and remained on the screen until the participant responded, or, if no response was given, disappeared after 2000 ms. In case of an incorrect response, participants did not receive any feedback and the next trial started by the presentation of the fixation cross. The trial order was assigned randomly (for further details, see Hermans et al. 2010). The task started with a practice phase, consisting of 20 trials, using both neutral primes and targets. Here, 10 trials included existing target words, and the other 10 trials included non-existing target words. Next, the experimental trials started. We used the following prime-target combinations resulting in a total of 80 trials: 10 panic prime–panic target (P–P; e.g., breathlessness—suffocate), 10 panic prime–neutral target (P–N; e.g., breathlessness—car), 10 neutral prime–panic target (N–P; e.g., book—danger), 10 neutral prime–neutral target (N–N; e.g., flower—harvest), 20 panic prime–non-word target (P–NW; e.g., breathlessness—balizisi), and 20 neutral prime–non-word target (N–NW; e.g., car—balizisi).

<sup>2</sup> For an overview of the complete stimulus material per computer task, see Tables 2 to 5 in the supplementary material.

<sup>3</sup> Hermans et al. (2010) removed one particular neutral word pair ("groceries – shopping") from the original stimulus set from the analyses as this word pair elicited significantly more fear in people with PD and was related to agoraphobia. We modified this word pair ("groceries – arrange") to create a neutral valence. In addition, we modified another original word pair, i.e., "meal – prepare" to "vacation – prepare" since the original one could be associated with vomiting or nausea, which in turn is represented in the DSM 5 panic criteria.



### Single Target Implicit Association Test (STIAT)

The STIAT used in this study was conceptually based on the IAT as used by Teachman et al. (2007). The attribute category labels of the STIAT were “alarming” versus “meaningless”, and the target category label was “bodily reaction”. The stimuli included 4 attribute words for each attribute category (e.g., alarming: scary, dangerous; meaningless: trivial, insignificant) and there were 4 target words, describing bodily changes associated with PD<sup>4</sup> (e.g., rapid pulse, dizzy). Participants were asked to sort stimuli according to the category labels presented on the screen by means of two response keys (D or K). The latency between the stimuli presentation was 250 ms. The STIAT’s procedure was as following: First, during the attribute practice phase, participants practiced categorizing the attribute words according to their emotional valence (20 trials). Next, the first combined STIAT block was introduced, that is, the target category label appeared on the screen and participants were instructed to sort both target and attribute words into their corresponding categories. First, there was a 20-trial practice phase, followed by a 40-trial test phase. During this phase, targets shared a response key with “alarming” attributes (compatible block). During the subsequent block, the assignment was reversed, that is, targets shared a response key with the “meaningless” attributes (incompatible block). Again, this started with a 20-trial practice and 40-trial test phase. In case of an incorrect word categorization, a red X appeared and participants were required to re-categorize the word into the correct category.

### Scrambled Sentences Task (SST)

For the novel panic-related SST, 24 scrambled sentences were generated, each containing six words. Stimuli were based on the 13 DSM-5 symptoms of PD. The present study used a computerized version of the SST (see also Sanchez et al. 2015). All trials started with presenting a fixation cross for 500 ms, and 500 ms after that, the scrambled sentence appeared. Using the computer mouse, participants were instructed to sort the words into a grammatically correct statement, using only five words, which allowed for a panic-related or a neutral solution, depending on which word was omitted (e.g., “palpitations symptoms insignificant bodily dangerous are”, panic-related interpretation: “palpitations are dangerous bodily symptoms”, neutral interpretation: “palpitations are insignificant bodily symptoms”). When

<sup>4</sup> In contrast to the original stimulus material by Teachman et al. (2007), we included the target word “shortness of breath” instead of the original item “sweating” as the former is more specifically related to the cardiovascular symptoms of PD.

a word was assigned per click, a white number appeared above the word, indicating its position within the sentence. The word order was not changeable after the selection. The sentences were displayed individually, for 10 s in total. If this time was exceeded, the next sentence appeared. A practice trial containing five neutral scrambled sentences was presented first, followed by the experimental trial. In line with suggestions by Wenzlaff and Bates (1998), participants were shown a 6-digit number for 10 s at the beginning of the task, which they had to keep in mind during the task and reproduce at the end of the task (cognitive load), assuming that such a cognitive load reduces the potential impact of cognitive control processes during the task.

### Interpretation Bias Questionnaire (IBQ)

Instead of the original paper- and pencil questionnaire (McNally and Foa 1987; German translation: Ebert 1993), we used a computerized version of the IBQ. There were nine scenarios describing ambiguous, panic-related situations, and nine scenarios describing ambiguous, general, threat-related situations. There were three explanations per scenario. For panic-related situations (e.g., “You’re feeling dizzy. Why?”), there were two panic-unrelated explanations (e.g., “You didn’t get enough sleep last night”/ “You should eat something”) and one panic-related explanation (e.g., “You are going to faint”). For threat-related situations, there were two threat-unrelated explanations and one threat-related explanation. For each explanation, participants had to rate the likelihood of the presented explanation on a visual analogue scale with the two endpoints “Very unlikely” (0) and “Very likely” (100). The task started with three practice trials presenting ambiguous, neutral scenarios and neutral explanations, followed by the experimental trials. The general procedure was as follows: First, the scenario appeared for 5000 ms and disappeared automatically afterwards. Then, 100 ms after that, one out of the three explanations was shown for 3000 ms, and then disappeared automatically as well. Again, 100 ms later, the rating scale appeared and disappeared after entering the response. There was an inter-trial pause of 2000 ms before the next scenario appeared. The explanations per scenario appeared consecutively and in random order.

### Data Cleaning and Preparation

#### Priming

The data preparation and analysis was based on the procedure used by Hermans et al. (2010). First, error trials were excluded from the analysis (4.10%) as well as latencies varying more than 2.5 SD from the participant’s mean response time per prime-target combination (2.15%). Next, mean response times were calculated, per participant, per

prime-target combination. Of main relevance for the analyses were the following combinations: panic prime–panic target (P–P), panic prime–neutral target (P–N), neutral prime–panic target (N–P), neutral prime–neutral target (N–N). These combinations were used to create two difference scores. First, a panic-related difference score was created whereby response latencies of P–P trials were subtracted from response latencies of N–P trials, with higher scores indicating faster categorization times for panic targets when primed by a panic compared to a neutral prime. Second, a neutral difference score was calculated whereby response latencies of N–N trials were subtracted from response latencies of P–N trials, with higher scores indicating faster categorization times for neutral targets when primed by a neutral compared to a panic prime.

### STIAT

The data aggregation and analysis were based on the procedure used by Bluemke and Frieze (2008). Data aggregation only included trials of the combined blocks, that is, practice and test phase. First, incorrect responses were omitted (6.33%), and response times below 300 ms and above 3000 ms were recoded to these latencies. In order to control for individual differences, each individual reaction time was turned into a z-score. Finally, a d-score was calculated by subtracting response latencies of the combined compatible block from the combined incompatible block, whereby a positive d-score is indicative of faster response latencies for “bodily reactions” and “alarming” compared to “bodily reactions” and “meaningless”. Participants with an error rate of 20% or more in any individual block were excluded which was true for one participant (mean error rate after exclusion: 6.08%).

### SST

Data from the SST were inspected manually and sentences that were not generated within the 10 s time limit (10.19%) or were grammatically incorrect (15.12%) were excluded (for similar error rates see Viviani et al. 2018). Next, sum scores per participants were created, that is, a sum score for all correct neutral sentences, and a sum score for all correct panic-related sentences. These sum scores were then used to create a ratio score by dividing panic-related sentences by the sum of all correctly unscrambled sentences. Hence, the higher the ratio, the more panic-related sentences were generated.

**Table 2** Correlations between panic-related associations and interpretations and panic-unrelated self-report measures

Computer Tasks	DASS-21	STAI-T	STAI-S <sup>b</sup>
Priming			
Panic difference score	.220	.077	.157
STIAT			
D-Score	–.041 <sup>a</sup>	.097 <sup>a</sup>	.188 <sup>a</sup>
SST			
Ratio	.574**	.541**	.466**
IBQ			
PS-PE	.498**	.597**	.460**
TS-TE	.447**	.610**	.382**

*DASS-21* Depression-Anxiety-Stress Scale – 21 item version, *STAI-T* State-Trait Anxiety Inventory: trait anxiety scale, *STAI-S* State-Trait Anxiety Inventory: state anxiety scale, *Panic difference score* Latencies of Panic prime–Panic target trials subtracted from latencies of Neutral prime–Panic target trials, *STIAT* Single Target Implicit Association Test (D-Score), *SST* Scrambled Sentences Task, *IBQ* Interpretation Bias Questionnaire, *PS* panic scenario, *PE* panic explanation, *TS* threat scenario, *TE* threat explanation. For all questionnaires and tasks, N = 54, unless stated otherwise

\*\* $p < .01$

<sup>a</sup>53 participants

<sup>b</sup>Assessment 1 prior to the completion of the computer tasks

### IBQ

Unlike previous studies that used a multiple choice answering format, requiring participants to select the most likely explanation (e.g., Woud et al. 2014), the present study required participants to rate the probability of each presented explanation, enabling us to assess a more nuanced interpretation. Accordingly, we created two mean scores, one for the ratings of panic-related explanations, and one for the ratings of neutral explanations (i.e., collapsed across the two neutral explanations).

### Subjective Ratings of DSM-5 Panic Symptoms

First, a sum score for the ratings of all 13 panic symptoms was calculated. For the main analyses (SBT reactivity), a difference score was created by subtracting the sum score post SBT (third assessment) from the sum score pre SBT (second assessment), with a positive score indicating higher levels of fear after the symptom provocation task.

### Statistical Analysis

Data was analyzed using SPSS version 25.0 (IBM 2012). Pearson correlations were used to examine the relationship between the cognitive test battery outcome markers, the ASI, the panic-related questionnaire scores (i.e., ACQ

and BSQ), and the SBT-reactivity.<sup>5</sup> Generally, there were no outliers and overly influential data points (visual inspection of box plots and scatter plots).<sup>6</sup> Regression analyses were conducted to explore the predictive validity of panic-related associations and interpretations for changes in SBT reactivity. That is, we wanted to find unique predictors of change when controlling for general factors (age, gender), ASI, and panic-specific symptom severity (BSQ). For this regression, the ASI and BSQ were chosen as predictors. The ASI was chosen because it represents the operationalization of AS, which in turn is an important risk factor in the context of PD. The BSQ was chosen because it specifically assesses panic-relevant symptoms that were also triggered during the symptom provocations task. As such, unlike the ACQ, there was close conceptual match. Following standard guidelines (e.g., Backhaus et al. 2003), a minimum of 10 cases per predictor is recommended to have sufficient statistical power for regression analyses. Accordingly, we planned to conduct four separate multiple regressions, that is, one per cognitive task, each including 5 predictors. For each regression, we used the following step-wise approach: the dependent variable was SBT reactivity. Predictors of Step 1 were age and gender. In Step 2, ASI and BSQ scores were added, to test whether these panic-specific measures had predictive value above the demographic data. In Step 3, the concept of interest, that is, a score on a computer task, was entered, to test potential specificity of the corresponding predictor. The models' statistics,  $R^2$ , and changes in  $R^2$ , as well as Betas,  $p$ -values per step and per predictor, respectively, are reported (see Tables 3, 4). Regression analyses were only computed if we found a significant correlation between the concept of interest and changes in SBT reactivity (Warner 2012). Finally, we examined whether panic-related interpretations mediated the relationship between AS and SBT reactivity using PROCESS version 3 for SPSS by Hayes (2013). Effect sizes, standard errors, and confidence intervals are reported. Similar to the regression analyses, we performed the mediation analyses separately for each task. The analyzed dataset can be obtained via the open science framework via the following link: [https://osf.io/4nbtv/?view\\_only=c64f327c4d314664bc493a9e7d4d718d](https://osf.io/4nbtv/?view_only=c64f327c4d314664bc493a9e7d4d718d)

<sup>5</sup> Only the analyses for the main hypotheses will be reported in the text, but the correlation analyses of the remaining variables (i.e., DASS-21, STAI-T and STAI-S) are presented in Table 2.

<sup>6</sup> One participant scored more than three interquartile ranges from the nearer edge of the boxplot on the ACQ. When removing this case, the correlations between the ACQ score and priming and IBQ scores remained equally strong. Further, the correlation between the ACQ score and the STIAT score remained non-significant. However, the correlation between the ACQ score and the SST score was no longer significant.

**Table 3** Stepwise regression analysis predicting changes in SBT reactivity with main predictor SST

Predictive variables	B	Sig	$R^2$	$\Delta R^2$	Sig
Step 1					
Age	-.359	.589			
Gender	-4.722	.155			
Step 2					
Age	-.102	.875	.160	.115	.043*
Gender	-2.985	.356			
ASI	.048	.836			
BSQ	.359	.043*			
Step 3					
Age	.004	.995	.240	.079	.030*
Gender	-3.107	.319			
ASI	-.004	.986			
BSQ	.257	.142			
SST	21.840	.030*			

Dependent variable: change in anxiety pre-post SBT. For all questionnaires and tasks N = 54

SST Scrambled Sentences Task (Ratio), ASI Anxiety Sensitivity Index, BSQ Body Sensations Questionnaire, SBT Straw Breathing Task

\* $p < .05$

**Table 4** Stepwise regression analysis predicting changes in SBT reactivity with main predictor IBQ

Predictive variables	B	Sig	$R^2$	$\Delta R^2$	Sig
Step 1					
Age	-.359	.589			
Gender	-4.722	.155			
Step 2					
Age	-.102	.875	.160	.115	.043*
Gender	-2.985	.356			
ASI	.048	.836			
BSQ	.359	.043*			
Step 3					
Age	.224	.744	.191	.030	.187
Gender	-2.709	.400			
ASI	-.042	.862			
BSQ	.264	.161			
IBQ	.211	.187			

Dependent variable: change in anxiety pre-post SBT. For all questionnaires and tasks N = 54

IBQ Interpretation Bias Questionnaire (Panic scenario—Panic explanation), ASI Anxiety Sensitivity Index, BSQ Body Sensations Questionnaire, SBT Straw Breathing Task

\* $p < .05$

## Results

### Manipulation Check Straw Breathing Task

During the SBT, 31 participants terminated the task early (mean seconds spent on the task for this sub-sample:  $M=47.74$ ,  $SD=24.70$ ). To test whether the SBT induced an increase in SBT reactivity, a paired sample  $t$ -test was conducted using the subjective panic ratings pre-to-post SBT. Results indeed showed a significant increase,  $t(53)=6.46$ ,  $p<0.001$  ( $M_{pre}: 6.33$ ,  $SD: 9.25$ ,  $M_{post}: 16.91$ ,  $SD: 17.67$ ). A similar pattern was found for the STAI-S scores,  $t(53)=3.43$ ,  $p=0.001$  ( $M_{pre}: 34.91$ ,  $SD: 6.93$ ,  $M_{post}: 37.93$ ,  $SD: 8.95$ ), and general levels of anxiety,  $t(53)=3.06$ ,  $p<0.01$  ( $M_{pre}: 0.34$ ,  $SD: 1.13$ ,  $M_{post}: 0.67$ ,  $SD: 1.33$ ).

### Correlational Analyses

#### Panic-Related Associations

**Priming Task** We did not find a significant correlation between the priming task and the ASI score ( $r=0.239$ ,  $p=0.082$ ) and SBT reactivity ( $r=-0.073$ ,  $p=0.600$ ). Regarding the generalization of effects to the ACQ, we found a significant correlation with the priming score, indicating that faster categorization times for P-P trials were associated with higher levels of dysfunctional cognitions ( $r=0.389$ ,  $p=0.004$ ). However, we did not find a significant relationship between the priming score and the BSQ score ( $r=0.080$ ,  $p=0.568$ ).

**STIAT** There was neither a significant association between the STIAT score and the ASI score ( $r=0.120$ ,  $p=0.394$ ), nor between the STIAT score and SBT reactivity ( $r=0.019$ ,  $p=0.893$ ). Further, the STIAT score did not generalize to other panic-related self-report measures (ACQ:  $r=-0.058$ ,  $p=0.681$ ; BSQ:  $r=0.225$ ,  $p=0.105$ ).

#### Panic-Related Interpretations

**SST** We found a significant correlation between the SST score and the ASI score ( $r=0.294$ ,  $p=0.031$ ), and between the SST score and SBT reactivity ( $r=0.404$ ,  $p=0.002$ ), indicating that the more panic-related sentences were generated, the higher the levels of AS and the more SBT reactivity was reported. Regarding the generalization effects, the SST score correlated with the ACQ score ( $r=0.455$ ,  $p=0.001$ ) and the BSQ score ( $r=0.379$ ,  $p=0.005$ ), that is, generating more panic-related sentences was associated with higher levels of dysfunctional cognitions and fear of bodily sensations.

**IBQ** There was a significant correlation between the IBQ score and the ASI score ( $r=0.514$ ,  $p<0.001$ ) as well as SBT reactivity ( $r=0.361$ ,  $p=0.007$ ), indicating that the higher the mean ratings of panic interpretations on the IBQ, the higher the levels of AS and the higher the SBT reactivity. Further, we found generalization effects, that is, the IBQ score correlated with the ACQ score ( $r=0.550$ ,  $p<0.001$ ) and BSQ score ( $r=0.566$ ,  $p<0.001$ ), indicating that the higher the mean ratings of panic interpretations, the higher the levels of dysfunctional cognitions and fear of bodily sensations.

#### Prediction of SBT Reactivity

**SST** The BSQ score significantly predicted SBT reactivity, however, the ASI score was not significant. Most importantly, results showed that the SST score was a statistically significant predictor of SBT reactivity (see Table 3 for a full overview).

**IBQ** The BSQ score significantly predicted SBT reactivity, however, the ASI score was not significant. Unexpectedly, however, the IBQ score was not a significant predictor of SBT reactivity (see Table 4 for a full overview).

### Validation of Computer Tasks

Analyses revealed that the priming difference score did not correlate with the STIAT score ( $r=-0.077$ ,  $p=0.581$ ), the SST score ( $r=0.069$ ,  $p=0.620$ ), or the IBQ score ( $r=0.073$ ,  $p=0.599$ ). Additionally, the STIAT score neither correlated significantly with the SST score ( $r=-0.029$ ,  $p=0.839$ ) nor with the IBQ score ( $r=0.152$ ,  $p=0.278$ ). However, there was a significant correlation between the SST score and IBQ score ( $r=0.402$ ,  $p=0.003$ ). That is, generating more panic-related sentences was associated with a higher propensity for panic-related explanations.

### Mediation

#### Panic-Related Interpretations

Regarding the relationship between ASI scores and SBT reactivity, the total effect of the bootstrapped mediation analyses was not significant, i.e., for both the analyses of the SST and IBQ. Adding the SST or the IBQ score to the model yielded no significant direct effects. However, the indirect effects, i.e., the pathway of ASI scores on SBT reactivity via the SST or the IBQ score, were significant, and thus provide evidence for the SST and the IBQ score to serve

**Table 5** Estimated coefficients for mediation effect of panic-related interpretations

Variable	Total effect <sup>a</sup>			Direct effect <sup>b</sup>			Indirect effect <sup>c</sup>		
	c	SE	95% CI	c'	SE	95% CI	Ab	SE	95% CI
SST									
SBT reactivity	0.339	0.200	[- 0.060, 0.738]	0.180	0.196	[- 0.214, 0.573]	<b>0.160</b>	0.112	[0.002, 0.451]
IBQ									
SBT reactivity	0.339	0.200	[- 0.060, 0.738]	0.090	0.224	[- 0.360, 0.539]	<b>0.250</b>	0.146	[0.014, 0.596]

Confidence intervals of the indirect effects generated with bias corrected and bootstrapping ( $N=10,000$ ). All findings presented in bold are significant

SST Scrambled Sentences Task (Ratio), IBQ Interpretation Bias Questionnaire (Panic scenario–Panic explanation), SBT Straw Breathing Task. For all questionnaires and tasks  $N=54$ , unless stated otherwise

<sup>a</sup>Effect of Anxiety Sensitivity Index (ASI) on SBT reactivity

<sup>b</sup>Effect of ASI controlling for respective cognitive task, i.e., SST or IBQ

<sup>c</sup>Indirect path via respective cognitive task, i.e., SST or IBQ

as mediators between ASI scores and SBT reactivity (see Table 5 for complete results of all mediation analyses).

## Discussion

The primary aim of this study was to deepen the understanding of panic-related associations and interpretations in the context of AS, a prominent risk factor for PD. We expected that the higher the levels of AS, the stronger panic-related associations and interpretations, and the more SBT reactivity after a behavioral panic-induction task would be reported. Further, we expected a similar pattern with two other clinical trait measures relevant in the context of PD, namely the ACQ and BSQ. We also expected that panic-related associations and interpretations would have a unique predictive validity for panic-related symptomatology when controlling for other panic-related measures. Finally, we expected that the relationship of AS and SBT reactivity would be mediated by the cognitive tasks.

Contrary to our expectation, we did not find the predicted correlations between the ASI and panic-related associations. Regarding panic-related interpretations, we found the expected relationship between the ASI and panic-related interpretations. That is, the higher levels of AS, the more panic-related sentences were generated on the SST, and the higher the mean ratings for panic-related explanations on the IBQ. These results are in line with earlier findings regarding the IBQ (McNally and Foa 1987; Woud et al. 2014), and support the validity of our newly developed task, the SST. Regarding outcomes on the SBT, we did not find a correlation between panic-related associations and SBT reactivity. However, we did find the expected pattern for panic-related interpretations. That is, the higher the levels of SBT reactivity, the more panic-related sentences on the SST were generated, and the higher the mean ratings for panic interpretations on the IBQ. When exploring the other two panic-related self-report

measures, the ACQ and BSQ, we found a similar pattern as described above: both interpretation tasks correlated with either self-report measure, indicating that the higher the levels of catastrophic, panic-related cognitions, the stronger the panic-related interpretations. With regard to panic-related associations, only the ACQ was associated with scores on the priming task. The higher the levels of dysfunctional cognitions, the faster panic-panic trials were categorized. A speculative explanation could be that the ACQ, unlike the BSQ and ASI, contains concepts that were better captured by the priming task. If indeed such a subtle association was true, this would require fine-grained follow-up work.

For the regression analyses, results showed that the SST but not the IBQ predicted an increase in panic symptoms over and above the other measures. That is, the more panic-related sentences were generated, the higher the levels of SBT reactivity, even when controlling for age, gender, ASI, and BSQ. This result further supports the validity of the novel panic SST, and makes an important contribution to the prediction of behavioral reactivity via panic-related interpretations. Here, our results are in line with Teachman et al. (2010), who found that changing panic-related misinterpretations predicted decreased reactivity after a behavioral activation task post treatment. Finally, results of the mediation analyses showed that panic-related interpretations, assessed via the SST and the IBQ, were significant mediators for the relationship between ASI and SBT reactivity, indicating that the relationship between AS and changes in SBT reactivity can be explained via levels of panic-related interpretations.

To conclude, results of panic-related association tasks do not concur with our expectations. However, we found a stable pattern regarding the results of panic-related interpretations. The tasks' validation data further support this since we only found a correlation between the SST and IBQ. There are a number of explanations that could account for our findings regarding panic-related associations. First, since



cognitive models of PD assume that associations are activated very quickly, not all tasks may be sensitive enough to capture such subtle processes. This reasoning is in line with a review by Teachman et al. (2012), putting forward that there is merely moderate support for automatic, emotional information processing biases in PD. Second, it is possible that our tasks were operationalized sub-optimally. To illustrate, the STIAT only included a small number of stimuli, and this homogeneity may have limited the task's validity. Further, the priming task used prime-target combinations such as "breathlessness—suffocate" and "headache—brain tumor". That is, the prime represented a bodily sensation and the target the negative interpretation. Such an operationalization, however, may not adequately capture the processes relevant here, in such that the first response following a potential threat-related cue (i.e., a bodily sensation) may be a pure threat-related association (e.g., "breathlessness – fear"). Put differently, the operationalization of our priming task already included a rather elaborated interpretational process, which may have complicated a simple associative assessment. This is in line with assumptions put forward by dual-process models, which assume that a bodily sensation initially activates a general fear association and not necessarily a specific psychopathologic association (Ouimet et al. 2009). Hence, follow-up work is needed to further disentangle this, for example, by including priming tasks that present bodily sensations followed by 'simple' fear associations, and then examining whether the potential associative pattern is related to panic-related measures and symptoms. The sub-optimal operationalization of the priming task is also reflected in the missing correlation among the two association tasks, i.e., priming and STIAT. There are at least two explanations that account for this. First, the STIAT includes a homogenous whereas the priming a heterogeneous set of stimuli. As such, the two measures may not have shared much variance. Second, the tasks are operationalized differently. The STIAT assesses the associative strength between a panic-related stimulus and a simple, valenced attribute dimension. In contrast, the priming assesses the associative strength between a panic-related stimulus and a (more or less) complex, interpretational outcome. These differences in operationalization could have also been meaningful. A last critical thought is related to the sequence of events described in the cognitive models of panic. That is, it is very likely that the movement through the stages does not follow a simple linear path as described in the model. To illustrate, it is possible that there are stage-dependent and reinforcing feedback loops, e.g., between the cognitive appraisal and anxiety stages, respectively. For example, threat associations could themselves trigger anxiety, and this could initiate the vicious circle in the first place. However, it seems also likely that there are internal feedback loops within the broader cycle, in such that the anxiety triggered via the fear associations

feeds-back to the interpretational stage. Neither our study design nor our data offers a satisfying way to address such speculations, but it would be useful for future research to pursue this hypothesis further to advance our understanding of the temporal mechanisms underlying cognitive models of PD.

The current study also provides interesting findings regarding the ACQ and BSQ, which both capture highly relevant concepts in the context of PD. Specifically, the ACQ and BSQ correlated positively with panic-related interpretations (i.e., the SST and IBQ), and the ACQ correlated with the priming task. Further, when looking at Step 2 of the regression analyses, the BSQ but not the ASI significantly predicted SBT reactivity. Here, results of McNally and Eke (1996) are similar to ours, in such that the Suffocation Fear Scale (SFS; Rachman and Taylor 1994) was a better predictor of the reaction to a respiration challenge than the ASI. The authors postulated that this might be due to the increased conceptual similarity between the SFS and the respiration challenge compared to the ASI and the respiration challenge, and such a conceptual match seems also relevant for our results. Further, both McNally & Eke's results and ours are relevant for recent discussions related to the ASI. Specifically, the ASI is a multifaceted measure (Deacon et al. 2003), and previous studies have shown that the ASI items assessing anxiety-related cognitions are not sufficiently differentiated (Deacon and Valentiner 2001). However, since anxiety-related cognitions assessed by the ACQ were related to reactions on the priming task, it is possible that the underrepresentation of cognitive items on the ASI is at least in part responsible for the non-significant findings regarding panic-related associations in our study. Further, there is some debate about the factor structure underlying the ASI, and there is evidence for e.g., a two-, three- or four-factor structure (Rodriguez et al. 2004). Recent consensus supports a three-factor structure, including physical, cognitive, and social concerns. For example, in the Anxiety Sensitivity Index-3 (ASI-3; Taylor et al. 2007), these three facets are considered different scales and can be analyzed separately. In the present study, the standard version of the ASI was used to foster comparability with previous studies. However, present results indicate that the relationship between AS and panic-related associations and interpretations is more subtle and nuanced, in such that, for example, mainly the somatic consequences of bodily sensations may be of relevance. Hence, AS might act as a general risk factor for PD (Schmidt et al. 1997, 1999), but may only correlate with some of its clinical characteristics. Another critical aspect in this context is the lack of specificity of AS as a risk factor for PD. That is, there is accumulating evidence indicating that AS is associated with both various anxiety disorders and general psychopathology. To illustrate, meta-analyses have found that cognitive concerns are related with

general levels of psychopathology (Olatunji and Wolitzky-Taylor 2009; Naragon-Gainey 2010). For anxiety disorders in particular, similar results have been found in such that the three different AS dimensions correspond to distinct anxiety disorder symptoms, e.g., the dimension ‘social concern’, i.e., fear of negative social consequences, is most strongly related to social phobia (Olatunji and Wolitzky-Taylor 2009). As such, caution is needed when describing AS as a specific risk factor for PD, which in turn clearly limits the extent to which we can draw PD -specific conclusions from our results. In fact, the same is true when looking at the results of our interpretation tasks (i.e., SST and IBQ). Here, we found that these measures also correlated with levels of depression and distress (e.g., on the Depression-Anxiety-Stress Scale, DASS-21). This indicates that also these measures may not be as specific as initially expected. Therefore, future research should further investigate the specific and potentially trans-diagnostic role of panic-related interpretation biases in the general context of emotional psychopathology.

### Limitations and Future Directions

There are several limitations to the present study. The first limitation is the small sample size, which limited our statistical power and affected our analytical approach. Second, during the SBT, the experimenter communicated the elapsed time, which could have made the end of the task predictable. This, in turn, is in direct contrast to the experience of unexpected panic attacks. Therefore, participants could have perceived the panic-like symptoms as less aversive. This is in line with studies showing that contextual factors, for example, the predictability may modulate anxious responses to symptom provocations (Benke et al. 2015). Further, participants in this study were healthy students. Although anxiety sensitivity/ fear of bodily symptoms were used as reference constructs to PD, results of this non-clinical sample cannot be generalized to a clinical population. In line with this is another important note: Our results relate to between-person differences that might index vulnerability and cannot be used to make inferences about how panic-related processes dynamically unfold within an individual, which would be a valuable route for future research. Fourth, we modified the administration of the IBQ, since providing probability ratings of each explanation seemed to represent a more sensitive measurement than asking participants to choose the most likely explanation. However, this clearly limits both the comparability to other studies and the generalization of our results. Accordingly, a follow-up study is required, comparing both IBQ versions. Finally, the cross-sectional nature of the design restricts any causal interpretations of the data. That is, we cannot make any valid conclusion about the direction of the observed effect (e.g., whether the experience of panic attacks is followed by dysfunctional

interpretations or vice versa). Given others and our promising results regarding panic-related interpretations, however, lab-based, experimental studies could clearly delineate their causal mechanisms. Indeed, current cognitive bias modification (CBM; Koster and MacLeod 2009; Woud and Becker 2014) studies have made first attempts to understand this relationship better. To illustrate, a study by Steinman and Teachman (2010), testing a sample with heightened ASI scores, showed that positive CBM training, i.e., a training to reduce panic-related interpretations, compared to negative CBM training, a training to induce panic-related interpretations, or no training, successfully reduced panic-related interpretations. Another study by MacDonald et al. (2013), also using a sample with heightened ASI scores, showed that a positive CBM training compared to a sham condition resulted in lower ASI scores and less panic-related interpretations. However, neither study showed an effect of positive CBM training on reduced subjective anxiety or avoidance of bodily symptoms after a symptom provocation. When interpreting these findings from the perspective of AS being a specific, cognitive vulnerability factor, these results in fact provide some support for the pathogenic and unique role of AS in the context of PD. However, additional studies are needed to both further disentangle the potential causal role of panic-related interpretations and the specific role of AS. Finally, it may also be important to use more aversive symptom provocations to induce the different symptoms of PD even better, for example, via inhalation of CO<sub>2</sub> (e.g., Blechert et al. 2013). During the CO<sub>2</sub> induction, participants wear a breathing mask through which the CO<sub>2</sub> mixture is delivered, rendering it impossible to make the task ‘milder’, and therefore increasing the chance of triggering more severe panic symptoms. Relatedly, studies showed that caffeine administration resulted in heightened subjective fear and panic-related symptoms (e.g., Benke et al. 2015; Charney et al. 1985; Pané-Farré et al. 2015). Such an induction could also be advantageous over the SBT, since it allows for blinding participants whether they are administered a caffeinated drink or not.

### Conclusion

To conclude, our data provide additional evidence that panic-related interpretations but not associations, assessed in the context of a non-clinical sample with varying levels of AS, are a correlate and unique predictor of experimentally induced, panic-relevant symptoms, and mediate (in a statistical sense) the relationship between levels of anxiety sensitivity and panic-relevant symptomatology. This, in turn is not only important for theory refinement and development, but also for clinical application. Present cognitive-behavioral treatment approaches highly rely on cognitive techniques

(such as cognitive restructuring), informed by insights from fundamental research on cognitive processes in PD. Hence, in order to continuously integrate these insights into, and by this improve, therapeutic interventions, a precise understanding of the relevant (cognitive) processes of the disorder is needed (Holmes et al. 2014), e.g., by studying (cognitive) risk and vulnerability factors like the present study did. Given the potential for developing further refined association tasks as outlined above, future research should not give up on the theoretically well-founded investigation of panic-related associations and continue examining their specific role of panic-related associations and interpretations in PD.

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## Compliance with Ethical Standards

**Conflict of Interest** Lisa Zahler, Katharina Sommer, Andrea Reinecke, Frank H. Wilhelm, Jürgen Margraf and Marcella L. Woud declare that they have no conflict of interest.

**Ethical Approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee of the Faculty of Psychology at the first author's University (ethical approval number: 354) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Animal Rights** No animal studies were carried out by the authors for this article.

**Informed Consent** All participants provided written informed consent.

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