



Don't panic: Interpretation bias is predictive of new onsets of panic disorder



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ABSTRACT

Psychological models of panic disorder postulate that interpretation of ambiguous material as threatening is an important maintaining factor for the disorder. However, demonstrations of whether such a bias predicts onset of panic disorder are missing. In the present study, we used data from the Dresden Prediction Study, in which an epidemiologic sample of young German women was tested at two time points approximately 17 months apart, allowing the study of biased interpretation as a potential risk factor. At time point one, participants completed an Interpretation Questionnaire including two types of ambiguous scenarios: panic-related and general threat-related. Analyses revealed that a panic-related interpretation bias predicted onset of panic disorder, even after controlling for two established risk factors: anxiety sensitivity and fear of bodily sensations. This is the first prospective study demonstrating the incremental validity of interpretation bias as a predictor of panic disorder onset.

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1. Introduction

A pounding heart, hot flashes, lightheadedness – these could merely be signs that one is falling in love. However, individuals suffering from panic disorder often interpret these bodily sensations as signifying an imminent catastrophe such as a heart attack. Psychological models of panic disorder postulate that such biased interpretations serve to maintain the disorder (e.g., Beck, Emery, & Greenberg, 1985; Clark, 1986; McNally, 1994). In particular, these models postulate that patients suffering from a panic disorder automatically interpret bodily sensations as threatening, inciting a vicious circle that can culminate in panic.

Modifying a measure by Butler and Mathews (1983), McNally and Foa (1987) developed an Interpretation Questionnaire containing ambiguous scenarios that were panic-related or panic-unrelated. They found that patients suffering from agoraphobia and panic interpreted panic-related scenarios as threatening more often than did treated agoraphobia/panic patients and healthy control subjects. Other investigators replicated and extended these findings. Harvey, Richards, Dziadosz, and Swindell (1993) found

that relative to social phobia patients and healthy control subjects, panic patients exhibited an interpretation bias specific for the ambiguous panic scenarios, whereas both anxiety groups exhibited a threatening interpretation bias for the panic-unrelated scenarios. Results of Clark et al. (1997) further clarified this issue, demonstrating that patients suffering from panic disorder are more likely to believe their (biased) interpretations compared to other anxiety patients and healthy controls. Finally, Rosmarin, Bourque, Antony, and McCabe (2009) showed that panic patients exhibited a self-referential, not a global interpretation bias for threat.

Extending this work, Teachman, Smith-Janik, and Saporito (2007) studied the role of dysfunctional panic-related interpretations by combining a scenario based assessment with a reaction time (RT) based assessment. The scenario based assessment (Brief Body Sensation Questionnaire, BBSQ; Clark et al., 1997) included ambiguous panic-related scenarios as well as ambiguous scenarios describing generally threatening situations. The RT assessment involved the Implicit Association Test (IAT; Greenwald, McGhee, & Schwartz, 1998), a computerized categorization task using RTs as indices for the strength of memory associations. The IAT results showed that panic patients, compared to healthy controls, had stronger associations of concepts related to the self and panic.¹

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¹ Please see Teachman et al. (2007) for outcomes of a second IAT assessing different panic-related associations.

The BBSIQ results showed a panic-related interpretation bias in patients, but not in healthy subjects.

It remains unclear whether this interpretation bias is a consequence of panic disorder or a predictor, and possible causal risk factor, for the disorder (Kraemer et al., 1997). To (partly) investigate this question, Schneider, Unnewehr, Florin, and Margraf (2002) administered the Anxiety Interpretation Questionnaire for Children (AIQ-C), based on McNally and Foa's Interpretation Questionnaire, to children of panic patients, children of parents with animal phobia, and children of healthy subjects. The AIQ-C included three types of ambiguous scenarios, i.e., descriptions of panic-related and panic-unrelated body sensations as well as animal-related situations. Results demonstrated that children of parents who suffered from a panic disorder exhibited a panic-related interpretation bias, but only after they had been primed with panic-relevant but not with panic-irrelevant material.

Another way to investigate this issue is to study people who are at risk of developing panic disorder. For example, cross-sectional and longitudinal research shows that anxiety sensitivity predicts the onset of panic attacks (e.g., Cox, Endler, Swinson, & Norton, 1991; Schmidt, Lerew, & Jackson, 1997) and anxiety disorders (Schmidt, Zvolensky, & Maner, 2006). Hence, examining panic-related interpretation biases in people scoring high on anxiety sensitivity may provide valuable information. Teachman (2005) found that individuals high on anxiety sensitivity exhibited a panic-related interpretation bias (see also Richards, Austin, & Alvarenga, 2001).

Studies on patients undergoing cognitive behavior therapy (CBT) suggest that reduction in interpretation biases over the course of therapy predicts reduction in symptom severity and panic frequency (Teachman, Marker, & Clerkin, 2010). Similarly, reduction in the strength of automatic panic associations predicts symptom reduction during CBT (Teachman, Marker, & Smith-Janik, 2008). Though longitudinal, these studies could not test whether premorbid interpretation biases predict the onset of panic disorder.

Accordingly, in this study we used a prospective design to test whether a version of McNally and Foa's Interpretation Questionnaire predicted new onset of panic disorder in an epidemiologic study of young German women tested at two time points over an approximately 17-month time interval. We hypothesized that women who interpret ambiguous panic-related scenarios in a threatening manner at baseline are more likely to develop panic disorder at follow-up than are women who have benign interpretations of these scenarios at baseline. In addition, we expect that the panic-related interpretation bias retains its predictive significance, even after controlling for levels of anxiety sensitivity and for fear of bodily sensations, which are two established correlates of panic disorder.

2. Method

2.1. Participants

Participants were 1538 German women who took part in the Dresden Predictor Study (DPS; Trumpf et al., 2010). The study involved two assessments. The baseline assessment occurred between July 1996 and September 1997, and the follow-up assessment occurred about 17-months after that ($M = 16.9$ months, $SD = 6$, range = 7–30 months). During both assessments, participants completed a diagnostic interview and a battery of self-report questionnaires including the Interpretation Questionnaire (see Trumpf et al., 2010). This article includes the data of participants who completed the diagnostic interview at both time points.

Participants were female residents drawn randomly from the population register of Dresden whose age the time of the initial

interview ranged between 18 and 25 years old. There were 5203 eligible women, and 2068 of them completed the baseline diagnostic interview and 997 of these participants completed only the questionnaires for a response rate of 58.9%. Of those who completed the diagnostic interview, 1538 (74.4%) completed the interview at follow-up.

2.2. Diagnostic interview

At both assessments, a trained interviewer administered the "Diagnostisches Interview bei psychischen Störungen – Forschungsversion" (F-DIPS; translation: Diagnostic Interview for Mental Disorders – Research Version; Margraf, Schneider, Soeder, & Becker, 1996). The F-DIPS is an extended version of the Anxiety Disorders Interview Schedule (ADIS-IV-L; Di Nardo, Brown, & Barlow, 1995) that assesses DSM-IV Axis I disorders. Baseline interviews assessed 7-day information and lifetime and point prevalence. Follow-up interviews also assessed 7-day information plus the time interval since baseline (for details about procedure, training of interviewers, and reliability ratings see Trumpf et al., 2010).

2.3. Anxiety Sensitivity Index (ASI; Ehlers, 1986; Reiss, Peterson, Gursky, & McNally, 1986)

The ASI is a 16-item self-report questionnaire measuring fear and concerns regarding anxiety-related symptoms such as "It scares me when my heart beats rapidly". Items are rated on a five-point Likert scale (0 = "Very little" to 4 = "Very much").

2.4. Body Sensations Questionnaire (BSQ; Chambless, Caputo, Bright, & Gallagher, 1984; Ehlers, Margraf, & Chambless, 1993)

The BSQ includes 17 items that reflect specific bodily sensations (e.g., heart palpitations, dizziness). Participants are asked to indicate the degree to which they experience anxiety related to these sensations by means of a five-point Likert scale (1 = "Not at all" to 5 = "Extremely").

2.5. Interpretation Questionnaire

The Interpretation Questionnaire consisted of 18 brief scenarios used in earlier studies (Ebert, 1993); 14 were translated from the Interpretation Questionnaire of McNally and Foa (1987). Nine items described panic-related situations (e.g., "You feel discomfort in your chest area. Why?"), and the other nine described general, threat-related situations (e.g., "You smell smoke"). Below each scenario, three interpretations appeared, one threatening. To illustrate, for the first example the following explanations were presented: (1) Something is wrong with your heart, (2) You have a sore muscle, and (3) You have indigestion. Participants had to indicate the interpretation (explanation) most likely to come to mind if they were to experience the sensation in the scenario. Panic-related and general threat-related scenarios were presented alternating, and the order of threatening and non-threatening explanations was randomized across scenarios. All participants received the same order of scenarios.

3. Results

3.1. Participant characteristics

At baseline (i.e., T1), 45 of the 1538 women met criteria for lifetime panic disorder with or without agoraphobia, and 114 women diagnosed with another lifetime psychological disorder served as a comparison group. Within this latter group, 70 suffered from a mood disorder, 19 from a somatoform disorder, 10 from a substance

Table 1

Demographic data per diagnostic group for all four predictors, i.e., Interpretation Questionnaire (IB): IB panic, IB general threat; levels of anxiety sensitivity (ASI); and fear of bodily sensations (BSQ).

Diagnostic group	Measure	No diagnosis at T1 and T2 <i>M (SD)</i> <i>N</i>	No diagnosis at T1 but at T2 <i>M (SD)</i> <i>N</i>
Panic	IB panic	0.70 (1.02) 1376	1.67 (1.74) 21
	IB threat	2.80 (1.70) 1377	3.70 (1.89) 20
	ASI	12.42 (7.35) 1400	20.41 (9.84) 22
	BSQ	1.80 (0.61) 1389	2.14 (0.69) 23
Other psych. disorders	IB panic	0.60 (0.93) 744	0.48 (0.73) 52
	IB threat	2.71 (1.70) 748	2.51 (1.65) 53
	ASI	11.56 (6.84) 756	10.39 (7.70) 54
	BSQ	1.73 (0.57) 754	1.82 (0.64) 54

use disorder, and 31 from an eating disorder.² However, this group did not include any participants with anxiety disorders at baseline or follow-up as panic attacks occur frequently in other anxiety disorders, too (Barlow, 2002). At follow-up (i.e., T2), there were 26 new onsets of panic disorder, and 32 had remitted from panic disorder. Within the comparison group, there were the following new onsets: 37 suffered from a mood disorder, 13 from a somatoform disorder, 9 from a substance use disorder, and 9 from an eating disorder. At follow-up, 6 participants in the comparison group had remitted from a mood disorder, 2 from a somatoform disorder, 1 from a substance use disorder, and 4 from an eating disorder.

Please find an overview of the group's means and standard deviations of the Interpretation Questionnaire, levels of anxiety sensitivity (ASI) and fear of bodily sensations (BSQ) in Table 1.

3.2. Interpretation Questionnaire

Data preparation and statistical approach. First, participants' scores were recoded: All threatening explanations were coded with '1' (e.g., when a panic-related interpretation was checked for a panic scenario), all non-threatening ones with '0' (e.g., when a panic-unrelated interpretation was checked for a panic scenario). Second, scores were collapsed into a sum score per participant for both panic- and general threat-related scenarios. Out of the 1538 women, we had the complete data of 1418. Sixty-eight women did not complete the questionnaire. The missing data of the remaining sample ranged from 1 to 11 items. For analyses, we used only complete data sets (see Table 1 for means and standard deviations of bias indices and *ns*).³

We conducted several logistic regressions. The dependent variable in each regression was new onset of the respective disorder (0 = absent, 1 = present). The small sample size in the panic group precluded an analysis including all 4 predictors (i.e., panic- and threat-related bias, ASI, BSQ). Indeed, standard guidelines (e.g., Backhaus, Erichson, Plinke, & Weiber, 2003) specify a minimum of $N = 10$ per predictor, and hence a minimum of $N = 40$ for a full

analysis in our case. However, our total sample included between 19 and 23 participants (see Table 2 for a detailed overview per predictor/predictor combination). Accordingly, the maximum number of predictors per analysis was two, and therefore we conducted several multiple regressions involving two predictors (e.g., panic-related interpretation bias with ASI). The sample size of new onsets of psychological disorders was slightly larger, but still insufficient for full analyses. Hence, we again conducted several multiple regressions.

3.3. Relationship of interpretation bias with new onsets of panic disorder and psychological disorders at follow-up

An overview of the results appears in Table 2. Analyses revealed that a panic-related interpretation bias significantly predicted new onsets of panic disorder even after we controlled statistically for anxiety sensitivity and for fear of bodily sensations in two separate regressions. In contrast, a general threat-related interpretation bias was a non-significant predictor of new onsets of panic disorder after we controlled for anxiety sensitivity, and a marginally significant predictor when we controlled for fear of bodily sensations. Finally, results showed that levels of anxiety sensitivity also significantly predicted new onsets of panic disorders after we controlled for a panic- and general threat-related interpretation bias as well as for fear of bodily sensations. Fear of bodily sensations, however, was only predictive in the regression controlling for the threat-related interpretation bias. Regarding the prediction of onset of other psychological disorders, results showed that only anxiety sensitivity and fear of bodily sensations were significant predictors, but only when these were combined in one analysis.

4. Discussion

To the best of our knowledge, this is the first longitudinal study to investigate whether new onsets of panic disorder are predictable by a panic-related interpretation bias. As hypothesized, analyses revealed that women who interpreted ambiguous panic-related scenarios in a threatening manner at baseline were more likely to develop panic disorder at follow-up than were women who had benign interpretations of these scenarios. Strikingly, interpretation bias for panic-related (but not other) scenarios retained its predictive significance after we controlled for anxiety sensitivity and for fear of bodily sensations – two established correlates of panic disorder. Neither of the two bias measures predicted new onsets of other psychological disorders. However, when combined in one analysis, anxiety sensitivity and fear of bodily sensations were significant predictors for onset of psychological disorders.

One may explain our findings as follows. Women who interpreted ambiguous panic-related cues as threatening are more often exposed to panic-related threat. Hence, they might experience increased stress, fear, and worry in their daily life, and may regard the world as generally dangerous, thereby developing a panic-specific memory schema. This panic-specific memory schema is hypersensitive (i.e., easily activated) regarding panic-related information, and thus could, in turn, reinforce the dysfunctional processing of ambiguous panic-related cues. Having such a vulnerability increases the likelihood of their developing panic disorder.

We also found that a general threat-related bias is a marginally significant predictor of developing a panic disorder. This is not surprising, as it is very likely that there is some overlap in panic- and threat-related memory schemata, respectively. Hence, activation of one memory schema will likely activate associated concepts. Findings of cross-sectional studies partly support this, showing that panic patients are also likely to misinterpret general threat-related ambiguous information (e.g., Harvey et al., 1993).

² From now on, we no longer point out that these data relate to lifetime prevalence.

³ See Trumpf et al. (2010) for attrition analyses. Analyses of missing values within the present data revealed that there was differential attrition within both panic groups. However, this is most likely due to the large sample sizes. Furthermore, effects sizes were extremely low.

Table 2
Prediction of new onsets rates of panic disorder and psychological disorders by means of Interpretation Questionnaire (IB): IB panic, IB general threat; levels of anxiety sensitivity (ASI); and fear of bodily sensations (BSQ).

Diagnostic group	Predictor(s) in regression	N	p	Statistics	
				OR	CI
Panic disorder	IB panic	21 vs. 1376	<0.001	1.678	1.297–2.171
	IB threat	20 vs. 1377	0.02	1.315	1.044–1.656
	ASI	22 vs. 1400	<0.001	1.109	1.063–1.157
	BSQ	23 vs. 1398	0.009	2.189	1.213–3.951
	IB panic	20 vs. 1357	0.023	1.445	1.051–1.988
	IB threat		0.26	1.161	0.896–1.504
	IB panic	20 vs. 1373	0.036	1.380	1.022–1.863
	ASI		<0.001	1.092	1.040–1.146
	IB panic	21 vs. 1372	0.002	1.552	1.176–2.049
	BSQ		0.106	1.715	0.891–3.3
	IB threat	19 vs. 1343	0.249	1.159	0.902–1.49
	ASI		<0.001	1.102	1.051–1.156
	IB threat	20 vs. 1373	0.093	1.230	0.966–1.565
	BSQ		0.043	1.972	1.020–3.811
	ASI	22 vs. 1396	<0.001	1.116	1.052–1.184
	BSQ		0.757	0.879	0.389–1.989
Other psychological disorders	IB panic	52 vs. 744	0.373	0.855	0.605–1.207
	IB threat	53 vs. 748	0.396	0.929	0.783–1.102
	ASI	54 vs. 756	0.231	0.975	0.934–1.017
	BSQ	54 vs. 754	0.289	1.285	0.808–2.045
	IB panic	52 vs. 738	0.587	0.902	0.620–1.310
	IB threat		0.487	0.935	0.773–1.130
	IB panic	52 vs. 741	0.563	0.901	0.633–1.283
	ASI		0.245	0.974	0.931–1.018
	IB panic	52 vs. 740	0.295	0.829	0.585–1.177
	BSQ		0.284	1.304	0.803–2.119
	IB threat	53 vs. 745	0.564	0.95	0.797–1.132
	ASI		0.346	0.979	0.937–1.023
	IB threat	53 vs. 744	0.257	0.903	0.756–1.078
	BSQ		0.187	1.381	0.855–2.228
	ASI	54 vs. 752	0.015	0.93	0.877–0.986
	BSQ		0.014	2.212	1.176–4.161

N: new onsets vs. no onsets; p: significance; OR: odds ratio, CI: 95% confidence interval. Significant p-values are printed in italics.

Taking together, these findings support the incremental, predictive validity of panic-related interpretation biases, thereby deepening our understanding of the role of panic-related interpretation biases. As of yet, there is evidence showing that high levels of anxiety sensitivity are positively associated with panic-related interpretation biases (e.g., Richards et al., 2001; Teachman, 2005) and with having future panic attacks (e.g., Schmidt et al., 1997). Moreover, although Schmidt et al. (2006) found that anxiety sensitivity predicted new onsets of Axis I disorders in general, they did not find that it specifically increased risk for new onsets of panic disorder per se. However, in our epidemiologic sample, we found that anxiety sensitivity predict new onsets of panic disorder, not merely panic attacks. As far as we know, this is the first demonstration of anxiety sensitivity as a predictor of panic disorder onset.

The present study is not without limitations. First, the sample of main interest (i.e., new onsets of panic) was small, so analyses including all four predictors as well exploratory analyses including for example participants' pre-existing (panic-related) psychopathologies were impossible. Second, our design included two assessments so (individual) change trajectories could not be examined. Hence, a multi-wave design including three or more time points would have been preferable. Third, maintaining a constant time interval between baseline and follow-up was impossible. Therefore, the 17 months is not an a priori planned interval, and we do not know whether this affected our results. Fourth, the inclusion of control explanations in the Interpretation Questionnaire (e.g., neutral, positive) would have been a more optimal approach and would have strengthened our conclusions. Finally, the results have a limited generalizability. The sample included only well-educated

women scoring relatively high on socioeconomic status. Furthermore, we only tested young women.

To summarize, the present data provide new insights regarding the development of panic disorder. This becomes even more important when taking into consideration that the anxiety literature does not provide many demonstrations of the predictive power of interpretation biases. The evidence we found is restricted to studies involving (preschool) children and adolescents, and focused on anxiety in general (e.g., Creswell, Shildrick, & Field, 2011; Muris, Jacques, & Mayer, 2004; Pury, 2002). However, as of yet we do not know whether a panic-related interpretation bias should be also considered as a causal risk factor (Kraemer et al., 1997). Teachman et al. (2010) found that changes in catastrophic interpretations predicted positive panic-relevant treatment outcomes. We found that a panic-related interpretation bias is predictive of new onsets of panic disorder. Although these findings clearly demonstrate the important role of panic-related interpretation biases in panic disorder, what is needed now are investigations manipulating this factor, for example via cognitive bias manipulation procedures (cf. Koster, Fox, & MacLeod, 2009). To illustrate, research on social anxiety has shown that interpretation biases seemingly play a causal role in increasing anxiety proneness (e.g., Mathews & Mackintosh, 2000). Hence, investigating whether an experimentally induced panic-related interpretation bias affects the appraisal of potential panic symptoms would be a next step, bearing in mind the ethical requirements of such an approach.

Moreover, it is also important to think of ways to prevent the development of a panic disorder. In this context, the study of Woud,

Postma, Holmes, & Mackintosh (2013) provides a promising line of research. Their study successfully employed appraisal training as a 'cognitive prophylaxis' in the context of analogue trauma. Hence, developing a preventative tool for panic disorder offers an interesting challenge. Finally, research is needed that extends present findings regarding panic-related biases in information processing. To illustrate, panic patients do also suffer from panic-related attentional biases (e.g., Beck, Stanley, & Averill, 1992; Ehlers, Margraf, Davies, & Roth, 1988). Therefore, it would be worthwhile to start examining the functional relationship between panic-related interpretation and attentional biases, respectively.

In conclusion, our findings provide strong support for a role of panic-related interpretation biases in the development of panic disorder.

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