Catastrophic misinterpretations as a predictor of symptom change during treatment for panic disorder

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Abstract

Objective—Cognitive models of panic disorder suggest that change in catastrophic misinterpretations of bodily sensations will predict symptom reduction. To examine change processes, a repeated measures design was used to evaluate whether the trajectory of change in misinterpretations over the course of 12-week cognitive behavior therapy is related to the trajectory of change in a variety of panic-relevant outcomes.

Methods—Participants had a primary diagnosis of panic disorder (N=43; 70% female; Mean Age: 40.14 years old). Race or ethnicity was reported as 91% Caucasian, 5% African-American, 2.3% Biracial, and 2.3% “Other.” Change in catastrophic misinterpretations (assessed with the Brief Body Sensations Interpretations Questionnaire) was used to predict a variety of treatment outcomes, including overall panic symptom severity (assessed with the Panic Disorder Severity Scale; PDSS), panic attack frequency (assessed with the relevant PDSS item), panic-related distress/apprehension (assessed by a latent factor, including peak anxiety in response to a panic-relevant stressor - a straw breathing task), and avoidance (assessed by a latent factor, which included the Fear Questionnaire-Agoraphobia subscale).

Results—Bivariate latent difference score modeling indicated that, as expected, change in catastrophic misinterpretations predicted subsequent reductions in overall symptom severity, panic attack frequency, distress/apprehension, and avoidance behavior. However, change in the various symptom domains was not typically a significant predictor of later interpretation change (except for the distress/apprehension factor).

Conclusions—These results provide considerable support for the cognitive model of panic and speak to the temporal sequence of change processes during therapy.

Keywords
panic disorder; catastrophic misinterpretations; cognitive behavior therapy; avoidance

While many people will experience a racing heart after climbing the stairs, far fewer individuals will interpret this increased heart rate as a sign that a heart attack is imminent. It is these latter individuals who are thought to be vulnerable to panic disorder (e.g., Beck, Emery, & Greenberg, 1985; Clark, 1986). The cognitive model of panic suggests that panic attacks occur because certain bodily sensations are misinterpreted as indicating a catastrophe, such as a heart attack or loss of control (Clark, 1986). In this model, the key feature to understanding panic disorder is the attribution of terrible consequences following bodily sensations, not the sensations themselves. Importantly, the model proposes that...
altering this cognitive bias is critical for symptom reduction: “According to the cognitive model of panic, change is attained through a shift in the way one interprets feared bodily and mental events” (Hoffart, 1998, p. 196; see also Clark, 1986; Hofmann et al., 2007). Thus, therapists are encouraged to work toward facilitating cognitive change in their patients, in addition to alleviating panic symptoms (Clark et al., 1999). As we describe below, there is compelling support for many aspects of the cognitive model of panic. However, a key prediction from the model - that cognitive change will precede and predict symptom change - has not been fully tested despite this temporal hypothesis being central to the model. The current study focuses on this open question by using a repeated measures design to examine how change in misinterpretations of bodily sensations over treatment predicts later reductions in a variety of measures tied to panic. While other factors are also important in the prediction of panic symptom reduction (e.g., thoughts regarding the likelihood of having a future panic attack; Cho, Smits, Powers, & Telch; 2007), we focus here on changes in misinterpretations of bodily sensations given their importance for evaluating cognitive models of panic.

Support for cognitive model of panic

Evidence in line with the cognitive model includes findings that panic disorder patients misinterpret bodily sensations in a catastrophic way significantly more than other anxiety disorder patients and non-anxious control participants do (e.g., Chambless & Gracely, 1989; Harvey, Richards, Dziadosz, & Swindell, 1993; McNally & Foa, 1987). Further, cognitive behavior therapies (CBTs), which focus on changing the negative interpretations of bodily sensations and helping patients get used to changes in autonomic sensations have been extremely effective (see Craske & Barlow, 2007, and meta-analysis by Gould, Otto, & Pollack, 1995). Also, anxiety in response to biological challenges that evoke panic sensations is reduced following CBT (e.g., Schmidt, Trakowski, & Staab, 1997), as are self-report measures of catastrophic misinterpretations and related cognitions (e.g., Clark et al., 1997; Clark et al., 1999; Poulton & Andrews, 1996; Wenzel, Sharp, Brown, Greenberg, & Beck, 2006). Importantly, when detailed instructions are given to patients with panic disorder regarding what symptoms to expect as a function of biological challenge agents like CO2 inhalation or lactate infusion, they experience significantly less intense somatic symptoms than patients who do not receive these instructions (see Rapee, Mattick, & Murrell, 1986; Clark, Salkovskis, & Anastasiades, 1990). As Clark (1993; p. 75) notes in his seminal review: “The cognitive theory of panic proposes that the challenge tests induced panic because they produce sensations that panic patients are prone to misinterpret and that it is the misinterpretation which is responsible for the induced attack.”

There is even some evidence that change from pre- to post-treatment in catastrophic misinterpretations of bodily sensations and associated panic-relevant beliefs predicts treatment response to CBT (e.g., Casey, Oei, & Newcombe, 2005; see also Hoffart, 1998). Additionally, Cho and colleagues (2007) demonstrated that the perceived consequences of panic predict a variety of outcomes associated with CBT for panic disorder. While there is less research directly testing cognitive mediation to evaluate the mechanisms of change in CBT (Oei, Llamas, & Devilly, 1999), recent findings have also been promising. For instance, Casey, Newcombe and Oei (2005) found that changes in the panic items from the Brief Bodily Sensations Interpretations Questionnaire (BBSIQ) explained the relationship between CBT (versus a waitlist condition) and reductions in panic symptoms. Analogous results (though mostly at the level of partial mediation) were observed by Smits, Powers, Cho and Telch (2004) using a measure of anxiety sensitivity as a mediator and by Hofmann et al. (2007) using a measure of catastrophic cognitions as a mediator.
These convergent lines of research, particularly the recent studies testing mediation, provide considerable support for the cognitive model of panic. Indeed, some researchers now believe that all current gold standard treatments for panic disorder, including exposure-based therapies, are cognitively mediated (e.g., Hofmann, 2008). However, because cognitive and symptom markers are typically only measured at pre- and post-treatment, these studies do not fully test the model since they cannot address temporal questions of change. As Smits et al. (2004) observed, “our design does not allow us to rule out the possibility that the [cognitive] change… was a consequence as opposed to a cause of panic disorder symptom reduction” (p. 650). This issue is problematic because the importance of cognitive change as a predictor of response to treatment has been questioned, with some researchers focusing more on strictly biological or behavioral hypotheses to explain the maintenance of panic attacks (e.g., Bouton, Mineka, & Barlow, 2001; Wolpe & Rowan, 1988). The possibility that cognitive change is simply an epiphenomenon of panic, and not meaningfully related to symptom reduction, needs to be addressed to better justify the argument that treatment should focus on altering biased cognitive processing (e.g., Clark et al., 1999). Moreover, even if panic-relevant cognitive change meaningfully influences change in other panic-relevant outcomes, it is possible that the reverse is true as well. For instance, Meuret, Roenfield, Hofmann, Suvak, and Roth (2009) found that breathing training focused on changing $pCO_2$ (i.e., carbon dioxide partial pressure) led to reductions in fears of bodily sensations; however, changing fears of bodily sensation did not predict changes in respiration. Thus, examining the order in which cognitive and symptom changes occur is paramount (see discussion in Casey, Newcombe, et al., 2005).

In the current study, we use a repeated measures design to investigate whether change in catastrophic misinterpretations of bodily sensations predicts later change in various panic-related outcomes over the course of CBT for panic disorder. In previous work (Teachman, Marker, & Smith-Janik, 2008), we found that changes in implicit, uncontrollable associations between the self and being panicked (versus calm) predicted subsequent reductions in overall panic severity using the Panic Disorder Severity Scale (PDSS). While this finding was congruent with the cognitive model of panic, the focus on implicit self-concept, rather than interpretations of bodily sensations, meant the findings did not directly speak to the model. A further limitation of the earlier study was the use of only a single outcome measure of panic symptoms (albeit one that assesses multiple dimensions of panic disorder). Given that panic involves multiple response systems (e.g., behavior, physiological mobilization, etc.; see Lang, Cuthbert, & Bradley, 1998) and the inherent limits of relying on a single indicator (see Shadish, Cook, & Campbell, 2002), the current study examines how change in catastrophic misinterpretations of bodily sensations predicts change in a variety of panic-relevant indicators. This allows us to use a multi-systems framework (Bradley & Lang, 2000) to test what responses related to panic are predicted by cognitive change.

### Establishing temporality within a multi-systems framework

Lang, Bradley and colleagues have described multiple systems by which fear can be expressed, and noted that it is not unusual for the different indicators to be desynchronous (i.e., a person may express high levels of distress but show minimal avoidance or physiological reactivity; Bradley & Lang, 2000; Lang, 1978; Lang et al., 1998). Given that desynchrony among the systems is not uncommon for emotional responding in general, it is important to consider whether such desynchrony also occurs in treatment. While the cognitive model of panic suggests that cognitive change will lead to symptom change, there has been little investigation of the differential impact of cognitive change on the various panic-relevant outcome indicators. In most cases, only a general panic severity indicator (such as the PDSS) has been used, and individual response systems have not been examined.

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Yet, there is good reason to wonder whether cognitive change will predict comparable changes across different panic-relevant indicators. Smits et al. (2004) found that change in anxiety sensitivity fully mediated the effects of CBT for a measure of global disability, but only partially mediated the effects for panic frequency, self-reported anxiety, and agoraphobic avoidance. Moreover, as Prins and Ollendick (2003) note, changes in cognitive processes are not consistently correlated with changes in behavior, despite this being an assumption of CBT models.

In the present study, we thus look at cognitive change as a predictor of not only reductions in overall panic symptom severity (using the PDSS), but also in key outcomes tied to panic, including frequency of panic attacks, associated distress and apprehension (including peak anxiety in response to a panic stressor), and reported avoidance. These outcomes were chosen because of evidence that all of these markers are closely tied to factors thought to maintain panic (see proposed model in White & Barlow, 2002). Moreover, there has been considerable consensus among panic experts that the primary outcomes relevant for panic disorder include panic attacks, panic-related anticipatory anxiety (involving both worry about future attacks and fear of bodily sensations), and phobic symptoms (i.e., avoidance and fear; see Shear & Maser, 1994). Thus, we evaluate each of these markers of panic separately in addition to the overall estimate of panic disorder severity (using the PDSS).

Our goal was to test whether a theoretically-derived cognitive variable (catastrophic misinterpretations of bodily sensations) is predictive of various forms of panic-relevant symptom change. As Kazdin and Nock (2003) note, this involves using a repeated-measures design to assess process and symptom variables at multiple time points throughout therapy to demonstrate both an association between cognitive and symptom change, and temporal precedence (i.e., that cognitive change predicts subsequent symptom change). To this end, we followed an approach used by Barber, Connolly, Crits-Christoph, Gladis and Siqueland (2000), which involves evaluating changes within a treatment group, rather than comparing across treatment conditions (see Teachman et al., 2008, for further detail). Our overall measure of panic severity (the PDSS) was assessed at each session throughout therapy, and our process variable (catastrophic misinterpretations, measured with the BBSIQ) and other panic-relevant outcomes (e.g., avoidance using the agoraphobic avoidance subscale of the Fear Questionnaire and peak anxiety during a panic stressor) were assessed five times over the course of 12-week group CBT. This allowed us to model the change trajectories for catastrophic misinterpretations and each of the outcome variables, and then use structural equation modeling (SEM) to test whether change in catastrophic misinterpretations predicted later changes in the different panic-related outcomes, and/or whether change in the panic-related outcomes predicted later change in catastrophic misinterpretations. Given the previous demonstrations of cognitive mediation and broad substantiation of the cognitive model of panic, it was hypothesized that change in catastrophic misinterpretations would predict subsequent changes in overall panic severity.

Making specific predictions for the different panic-relevant outcomes was challenging because determining covariation across fear response modalities is not well understood (see Zinbarg, 1998). With respect to panic attack frequency, it was hypothesized that changes in catastrophic misinterpretations would predict less frequent future panic attacks given the basic assumption in the cognitive model that the negative interpretation of bodily sensations fuels the ‘fear of fear’ cycle that leads to the escalation of symptoms into a full-blown panic attack.

1Note, this approach was not designed to test the efficacy of CBT for panic disorder or to conduct a standard test of mediation that looked at change in cognition from pre- to post-treatment to explain differences between treatment conditions, because both of these important questions have already been evaluated (see Craske & Barlow, 2007; Hofmann et al., 2007).
Regarding predictions for the measure of distress/apprehension associated with panic (operationalized in this study as reported distress during panic, anticipatory anxiety about future attacks, and peak anxiety during a panic stressor), CBT models certainly suggest that changes in cognition will result in changes in affect. Further, the “cognitive primacy hypothesis” put forth by Beck and colleagues in their early models of emotion dysregulation (e.g., Beck et al., 1985) suggests that cognitive responding will occur in advance of the affective reaction. At the same time, there is evidence that state anxiety might impede cognitive change and interfere with integrating new information that would reduce cognitive biases (e.g., certain cognitive biases are stronger under conditions of elevated state anxiety; Chen & Craske, 1998). Moreover, while Foa and Kozak (1986) emphasize the importance of evoking anxiety to effectively reduce symptoms, they also suggest that, “persistent high levels of arousal during exposure interfere with encoding and integration of disconfirming information” (p. 29). This suggests that reducing state anxiety to some extent first may be more likely to engender cognitive change (see Craske & Pontillo, 2000). This fits with the “affect-as-information” hypothesis that one’s subjective mood influences judgment and other forms of information processing (see Clore, Gasper, & Garvin, 2001). Rather than viewing these two paths as incompatible, we suspect that a bidirectional relationship between changes in catastrophic misinterpretations and changes in affect is likely.

Finally, with respect to behavioral change, there is some mixed evidence regarding how strongly catastrophic beliefs relate to avoidance behavior (see Craske & Barlow, 1988; Telch, Brouillard, Telch, Agras, & Taylor, 1989), but in reviewing the evidence as a whole, Barlow (2002) argues that cognitive symptoms are useful for predicting avoidance. Also, using latent variable path modeling, Hoffart, Sexton, Hedley, and Martinsen (2008) found that catastrophic beliefs were related to increased avoidance. Thus, we expected that change in catastrophic misinterpretations would predict later reductions in avoidance behavior.

Together, the opportunity to model trajectories of change in catastrophic misinterpretations and in a series of panic-relevant outcomes allows for a more direct and comprehensive test of the temporal predictions underlying the cognitive model of panic.

**Methods**

**Participants**

As described in Teachman, Smith-Janik and Saporito (2007) and Teachman et al. (2008), participants with panic disorder were recruited through a variety of media (e.g., newspaper, television, radio) and flyers inviting individuals who had experienced panic attacks to contact our phone line. Interested individuals were then screened by phone to do a preliminary assessment of criteria for panic disorder and confirm occurrence of a panic attack over the past month. Additional inclusion criteria assessed during the phone screen included: (1) minimum 18 years of age, (2) mastery of written and spoken English, and (3) no history of completing a prior course of CBT for panic. The screener also asked about substance abuse or dependence within the past year, and unmanaged manic symptoms or current psychosis, because these were exclusion criteria given their probable influence on treatment response. Other comorbidity, including current mood and additional anxiety disorders, and prior or current medication (or psychosocial treatments not specific to panic) were not grounds for exclusion. If another treatment was current, we asked that participants be stable in their treatment course for at least six weeks.

To confirm a diagnosis of panic disorder with or without agoraphobia, check for suicidal intent (an additional exclusion criterion), and assess other Axis I disorders, interested persons who met the initial criteria were invited to our clinic to complete the Structured Clinical Interview for DSM-IV (SCID; First, Spitzer, Gibbon & Williams, 1995). Details on
training of the assessors as well as inter-rater reliability are described in Teachman et al. (2008). Further, this paper includes a Consolidated Standards of Reporting Trials (CONSORT) figure that reports data on and reasons for participant exclusion and attrition during initial stages of the study. Teachman et al. (2008) also includes a description of the sequential assignment design used to preferentially allocate individuals to an immediate treatment condition (N=35), relative to a delayed waitlist condition (N=8; these participants waited approximately 12 weeks, and then joined the next available treatment group).

The final sample (those who started treatment from either condition; N=43; 70% with agoraphobic avoidance) was 70% female, mean age was 40.14 years old (SD=15.17, Range=18-71), and 91% were Caucasian, 5% were African-American, 2.3% described themselves as biracial, and 2.3% indicated “other”. Mean duration between participants’ first reported panic attack and intake was 175.51 months (SD=185.08, Range=2–732 months). Based on participant’s report of current interference and/or symptom severity, panic disorder was the primary diagnosis in all cases; however, the sample was highly comorbid. As listed in Teachman et al. (2008), current comorbid Axis I diagnoses at intake included: 35% had other anxiety disorders (Specific Phobia, Generalized Anxiety Disorder, Obsessive Compulsive Disorder, Social Phobia, Post Traumatic Stress Disorder), 26% had mood disorders (21% Major Depressive Disorder, 2.3% Bipolar I Disorder, and 2.3% Bipolar II Disorder), 7% had eating disorders (Binge Eating Disorder and Eating Disorder NOS) and 2% had Trichotillomania. In addition, 61% reported current psychotropic medication use at intake: 44% on antidepressants, 2% on antipsychotics, 30% on benzodiazepines, 2% on beta-blockers, and 9% on mood-stabilizers. Also, 21% reported ongoing psychosocial treatment at intake.

### Materials

#### Measures of Panic Severity and Related Outcomes

**Panic Disorder Severity Scale (PDSS; Shear et al., 1997):** This 7-item scale provides a composite severity score of frequency, distress, and impairment associated with panic attacks (scores range from 0-28). Although this measure was designed as a clinician-administered instrument, several prior studies have successfully had participants complete it as a self-report measure (e.g., Otto, Pollack, Penava, & Zucker 1999; Penava, Otto, Maki, & Pollack, 1998; Teachman, 2005). The PDSS was modified slightly for this study by adding a description of panic attacks to the instructions so that it could be more easily completed in a self-report format. The full scale was used to evaluate overall symptom severity, while the item assessing frequency of attacks per week was used to measure attack frequency, and the distress, apprehension and avoidance items were used to create latent factors as described below.

**Panic-related distress/apprehension:** To reflect a variety of the ways panic disorder results in distress and apprehension (a general negative affect construct), a latent factor was created, which included the PDSS items measuring distress during panic attacks (item 2) and anticipatory anxiety about future attacks (item 3), along with peak anxiety during a panic stressor. Specifically, participants were asked to breathe through a thin straw for up to two minutes while pinching their nostrils shut to reduce airflow. This is a harmless activity, based on the interoceptive exposure used in Taylor and Rachman (1994), which typically produces some very temporary dizziness and lightheaded feelings. Participants were explicitly told they could stop the task at any point and that we did not expect everyone to complete the task. The task ended when participants had either reached the two-minute point

2The assessments reported here are part of a larger study evaluating a range of cognitive biases in panic disorder. For a complete listing of measures, please contact the first author.
or reported that they did not wish to proceed further. Immediately after the task ended, participants were asked to report their peak level of anxiety during the task using a Subjective Units of Distress Scale (SUDS) ranging from 0 (very low) to 100 (very high). Note, validity of the straw breathing stressor was established in an earlier study that showed that persons with panic disorder report more distress and spend less time on the task than do healthy control participants (Teachman et al., 2007). Further, the straw breathing task was never recommended to participants during therapy to separate this measure from the treatment procedures.

**Panic-related avoidance:** To capture a range of the different types of avoidance behavior exhibited by persons with panic disorder and so that we would not rely solely on a measure of agoraphobia (given that not all participants met criteria for agoraphobia), a latent factor was created to assess avoidance. The factor included the PDSS items assessing panic-related avoidance of particular situations (item 4) and panic-related avoidance of sensations (item 5), as well as the Fear Questionnaire - Agoraphobia subscale (FQ-Agoraphobia; Marks & Mathews, 1979). The 5-item FQ-Agoraphobia subscale measures level of phobic avoidance toward common agoraphobic situations, such as crowded shops. The subscale is internally consistent and effectively distinguishes among persons with panic disorder with agoraphobia, and individuals with other anxiety difficulties or non-clinical panic, supporting its reliability and validity (Cox, Swinson, & Shaw, 1991).

**Measure of Catastrophic Misinterpretations of Bodily Sensations**

*Brief Body Sensations Interpretation Questionnaire – panic items (BBSIQ; Clark et al., 1997):* The seven ‘panic’ items from the BBSIQ that refer to events consistent with a catastrophic misinterpretation of bodily sensations were used in the present study (with very minor wording modifications to make the measure more prototypic of American rather than British English). Participants were presented with ambiguous events and then asked to rate three alternative explanations for why the event might have occurred. One option is always negative, whereas the other responses are either neutral and/or positive. An example of a panic item is, “You notice that your heart is beating quickly and pounding.” The three alternative explanations are, “because you have been physically active,” “because there is something wrong with your heart,” or “because you are feeling excited.” Participants rated the extent to which they believed each of the explanations on a 0-8 Likert scale – only endorsement of the negative explanation (e.g., “because there is something wrong with your heart” in this example) was used in order to tap into catastrophic misinterpretations of bodily sensations.

**Treatment**—The widely used Panic Control Treatment manual (Barlow & Craske, 1994) was followed, modified slightly to fit a group format. Treatment involved 12, 90-minute weekly sessions, which covered: 1) psychoeducation about the nature of anxiety and the fear of fear cycle, 2) diaphragmatic breathing and progressive muscle relaxation training, 3) cognitive restructuring to identify and re-evaluate panic-relevant beliefs, and 4) exposure exercises. Exposures involved interoceptive exercises to learn to tolerate feared bodily sensations as well as homework assignments to reduce agoraphobic avoidance. Each of the nine groups, which ranged in size from 4-6 participants, was co-led by a pair of advanced-level graduate students, following extensive training in CBT techniques, the panic treatment protocol, and review of training tapes. Every session was either observed (via one-way mirror) or reviewed through audio tape recordings by the first author, and therapists received weekly supervision.

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3The explanations were also ranked but these data are not reported here because of our interest in using a continuous measure of negative interpretations.
Procedure—Informed consent was obtained in advance of the SCID interview. At the outset of every therapy session (and at intake), participants completed the PDSS as a measure of overall panic severity. Assessment of catastrophic misinterpretations (using the BBSIQ) and the other panic outcome measures (FQ-agoraphobia, peak anxiety during straw breathing) were completed at testing sessions held immediately prior to session 1 of treatment, and then following sessions 3, 6, 9, and 12. Order of the BBSIQ and the questionnaire set (FQ-Agoraphobia, PDSS) was counterbalanced, while order within the questionnaire set was randomized. The straw breathing task was completed last due to concerns that residual anxiety from the task could contaminate the other measures.

Results

Descriptive statistics are listed in Table 1. Specifically, means and standard deviations are noted for the main assessment points for the measure of misinterpretations, and for the observed and latent indicators of treatment outcome.

Statistical Procedure

A series of bivariate latent difference score (LDS) models were used to evaluate how the measure of catastrophic misinterpretations and the various treatment outcome variables interacted across the course of treatment in terms of whether one variable was a leading indicator of change in the other variable. Due to space limitations, a complete description of LDS models is not possible here; however, interested readers are referred to McArdle and Nesselroade (2002) as the current procedures are based on their methods (for further technical details, see McArdle, 1988; McArdle & Hamagami, 2001; for other practical examples, see Hawley, Ho, Zuroff, & Blatt, 2006; 2007; for a review of LDS, see Ferrer & McArdle, 2010). The LDS model is an alternative method for the structural modeling of longitudinal data that integrates features of latent growth curve models and cross-lagged regression models. LDS was especially useful for examining the present questions because one can simultaneously model overall change across time and lagged relationships, allowing us to estimate whether change in one process (i.e., misinterpretations) predicts later change in outcome, while controlling for overall change in both.

Prior to fitting the bivariate models, we completed univariate latent growth curve models for each of the key measures to determine the best pattern of univariate change (e.g., linear or some type of non-linear growth), and modeled whether the slopes of the catastrophic misinterpretations variable and the given treatment outcome variable correlated, indicating that the change processes were related. The univariate latent models were then combined to create the bivariate latent difference score models. Models with each variable’s change affecting the other variable were created to determine whether change in catastrophic misinterpretations (measured by the BBSIQ) led to later change in overall panic symptom severity (captured in this study by the overall PDSS score), and the specific panic domains identified by the consensus panel (see Shear & Maser, 1994). These included: a) panic attacks (evaluated with the specific PDSS item measuring frequency of panic attacks), b) panic-related distress/apprehension (measured by the distress and anticipatory anxiety PDSS items, and peak anxiety reported during the straw breathing task), and c) panic-related avoidance (measured by the FQ-Agoraphobia and two avoidance-related PDSS items).

Because the change process could go in either direction - change in catastrophic misinterpretations could predict subsequent change in a panic outcome domain, or vice versa - we simultaneously estimated a parameter for each direction (i.e., for change in catastrophic misinterpretations as the predictor and for change in a panic outcome as the predictor). Note, all paths are presented as standardized beta coefficients.
Markov Chain Monte Carlo (MCMC) estimation was used for all analyses with Mplus software (Muthén & Muthén, 2010; Asparouhov & Muthén, 2010). This type of Bayesian estimation, which uses prior distributions on all parameters and simulation-based estimation, is especially suited for small sample sizes and incomplete data. Furthermore, all models were also estimated with full information maximum likelihood estimation (Muthén & Muthén, 2008) and results were similar. This procedure estimates the model parameters using all available information rather than deleting cases with incomplete data (Enders, 2001). Thus, people who did not have all sessions completed were still utilized in these analyses. This decision was made to maximize power and to be conservative in our approach (by not only examining treatment completers). Analogously, our focus was on creating a reliable parameter estimate for change in each variable as a predictor of the dynamic change in the other variables, rather than on estimating all possible curvilinear growth parameters. Thus, we only estimate growth parameters for a linear pattern of change in the bivariate latent difference score models in order to keep the tests highly focused and not raise the risk of Type I error by estimating many parameters with a relatively small sample size. Notably, other curvilinear modeling approaches (e.g., a proportional change model) were also examined, but these models did not provide substantively better estimates of fit than the linear models so are not reported here.

Finally, the number of participants attending each of the main assessment sessions was: Session 1 = 43, 3 = 35, 6 = 33, 9 = 32, 12 = 32. To help address the impact of attrition on the results, we conducted an analysis of incomplete data (see Little & Rubin, 2002). As part of this analysis, we examined variables that might predict patterns of missingness with new procedures in Mplus (based on Collins, Schafer, & Kam, 2001; Enders, 2010; Graham, 2003). Initial levels of panic severity (using the PDSS), agoraphobic avoidance (using the FQ-agoraphobia subscale), and peak anxiety during the straw breathing task were not found to be significant predictors of incomplete data. Baseline BBSIQ score was also not a significant predictor.

Model 1: Catastrophic misinterpretations and overall panic symptoms

The univariate models established that change occurs in each of the variables: catastrophic misinterpretations on the BBSIQ and panic symptoms on the PDSS. Next, a dual latent growth curve model indicated that the slope of panic symptoms is related to the slope of misinterpretations, establishing that change in one variable is significantly correlated with change in the other variable. However, this model does not clarify which variable’s change process, if any, predicts subsequent change in the other variable (see supplement). Thus, we attempted to model the leading indicators of change using bivariate latent difference score modeling.

Model 1 attempts to determine whether change in catastrophic misinterpretations (BBSIQ) leads to later change in panic symptom severity (total PDSS) and/or whether change in symptoms leads to later change in catastrophic misinterpretations. Figure 1 presents a simplified diagram showing this relationship with the bivariate latent difference score model (all 12 PDSS time points were used in this model for better reliability of change parameters). Most arrows have parameters that are set to one (approach modeled off of McArdle & Nesselroade, 2002), while the arrows labeled with the $\alpha$ (alpha) parameters are used to estimate the change in each variable over time. The arrows labeled with $\gamma$ (gamma) predict the relationship between variables (i.e., whether change in one variable predicts later change in the other variable, reported with standardized beta coefficients). The $\alpha$ and $\gamma$ parameters

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4These steps were followed for each of the main outcome variables (before they were combined into the latent factors). Details about this series of initial models (e.g., model fit indices, etc.) that preceded the bivariate latent difference score model are not listed due to space constraints, but are described in a supplement posted at the journal’s web site.
are constrained to be equal across time (i.e., we constrain the change process to be the same over time). In sum, we focused our analysis on the specific question of whether one change process was a leading indicator of another change process, but this test cannot address the question of exactly when in treatment the change was most predictive. As hypothesized, change in the misinterpretations of bodily sensations predicted later change in panic symptoms ($\gamma_{\text{BBSIQ}} = .18$; 95% C.I. = 0.09, 0.28; $p < .05$). However, change in symptoms did not predict later change in misinterpretations ($\gamma_{\text{PDSS}} = .01$; 95% C.I. = -0.18, 0.20; $p > .05$).

**Model 2: Catastrophic misinterpretations and panic attack frequency**

Given the centrality of panic attack frequency on impairment tied to panic disorder, Model 1 was rerun looking at the PDSS item assessing this outcome. While using a single indicator to operationalize a construct is inherently limited, these analyses provide an opportunity to examine the specificity of the relationship between the change processes in misinterpretations and various aspects of panic symptom severity. The results indicated that there was a small significant effect for change on the BBSIQ to predict later change in frequency of panic attacks (item 1 on the PDSS; $\gamma_{\text{BBSIQ}} = 0.08$; 95% C.I. = 0.03, 0.11; $p < .05$). There was not a significant effect for change in panic frequency to predict later change on the BBSIQ ($\gamma_{\text{PDSS1}} = 0.06$; 95% C.I. = -0.14, 0.27; $p > .05$; all 12 PDSS time points were used in this model for better reliability of change parameters).

**Model 3: Catastrophic misinterpretations and panic-related distress/apprehension**

Model 3 attempted to determine whether change in catastrophic misinterpretations (BBSIQ) led to later change in panic-related distress/apprehension (represented by a latent variable of PDSS items 2 and 3 and peak anxiety during the straw breathing task)\(^5\) or whether the reciprocal relationship existed. As expected, change in misinterpretations predicted later change in distress/apprehension ($\gamma_{\text{BBSIQ}} = 0.05$; 95% C.I. = 0.03, 0.07; $p < .05$). Notably, change in distress/apprehension also predicted later change in misinterpretations ($\gamma_{\text{distress}} = 0.06$; 95% C.I. = 0.01, 0.11; $p < .05$).

**Model 4: Catastrophic misinterpretations and panic-related avoidance**

Model 4 attempted to determine whether change in catastrophic misinterpretations (BBSIQ) led to later change in avoidance symptoms (represented by a latent variable of PDSS items 4 and 5 and FQ-Agoraphobia)\(^6\) or whether the reciprocal relationship existed. As expected, change in misinterpretations did significantly predict later change in avoidance ($\gamma_{\text{BBSIQ}} = 0.13$; 95% C.I. = 0.03, 0.23; $p < .05$). In contrast, the change in reported avoidance did not predict later change in misinterpretations ($\gamma_{\text{Avoidance}} = -0.09$; 95% C.I. = -0.21, 0.05; $p > .05$).

**Discussion**

To evaluate the prediction from cognitive models of panic disorder that change in catastrophic misinterpretations of bodily sensations predicts subsequent symptom reduction, the slope of change in misinterpretations over the course of CBT was examined as a predictor of reductions in overall symptom severity, panic attack frequency, panic-related distress and apprehension, and avoidance. The reciprocal relationships, with change in

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\(^5\)The latent variable was created by weighting the straw breathing anxiety and PDSS items 2 and 3 equally with a factor loading of one. Although the PDSS was administered weekly, only those assessment points that corresponded to the straw breathing anxiety measurements were used (i.e., initial, weeks 3, 6, 9, and 12).

\(^6\)Similar to the distress/apprehension factor, the latent avoidance variable was created by weighting the FQ-Agoraphobia and PDSS items 4 and 5 equally with a factor loading of one.
panic-relevant outcomes predicting later change in misinterpretations, were also tested. As expected, change in catastrophic misinterpretations predicted subsequent reductions in overall symptom severity, panic attack frequency, distress and apprehension, and avoidance. However, change in the various symptom domains did not significantly predict later interpretation change, except for the distress/apprehension factor. Overall, results provide considerable support for the cognitive model of panic and offer evidence that cognitive change occurring in advance of symptom change can predict better treatment outcome.

More generally, the current findings add a piece to the puzzle regarding the importance of cognitive change in reducing panic symptomology. Specifically, arguments that cognitive biases are an epiphenomenon or consequence of panic (e.g., Wolpe & Rowan, 1988), rather than being functionally related, seem less plausible given that changes in catastrophic misinterpretations predict later changes in multiple panic-relevant outcomes. While our design does not test causality or all elements of mediation, adding the temporal prediction piece strengthens the contention that reduction of catastrophic misinterpretations is important for achieving maximum alleviation of symptoms (Clark et al., 1999).

Changes in misinterpretations on the BBSIQ predicted decreases in overall panic severity on the PDSS, in panic attack frequency and in the latent distress/apprehension and avoidance factors. Yet, in most cases, the reciprocal relationships did not reach significance, with the exception of the distress/apprehension factor. For some of the panic outcomes, low power may be an issue (e.g., the effect size for change in panic attack frequency as a predictor was comparable to some of the other effects that did reach significance in other models). This points to a possible cyclical relationship, with a strong role for cognitive change influencing symptom change, and then the changes in symptoms, especially self-reported distress and apprehension, may have some impact on further reducing misinterpretations. Future research with a larger sample size that can enable examination of interactive change processes across multiple time points during therapy will be helpful, as opposed to examining only one overall change process as a predictor of the other overall change process as was required in the current study. Nonetheless, the significant effects for change in catastrophic misinterpretations as a predictor are in line with the assumptions guiding the cognitive model of panic (see Clark, 1986) and the idea of cognitive primacy (Beck et al., 1985), whereby change in cognition precedes symptom reduction.

Overall, there was considerable consistency in the findings in terms of the range of panic outcomes that were predicted. At the same time, the discrepant effect sizes across the models (i.e., change in the various panic outcomes were not all predicted to the same degree by the change in catastrophic misinterpretations) and variability in the extent that the relationships were reciprocal also suggest that change processes over the course of treatment can be desynchronous. Consistent with expectations from a multi-systems framework, uncoupling of anxiety response systems is common even when evaluating change over treatment (Lang, 1978). Evidently, there are multiple paths that can lead to symptom reduction and these paths may differ depending upon the panic-relevant system being modified. Thus, rather than concluding that a cognitive versus behavioral versus biological model is the “right” model, it seems more appropriate to consider integrated models (see Barlow, 2002) and ask how change in each panic response can best be enhanced. In most cases, the field cannot yet match specific treatment processes to particular patients to determine a priori which type of change process will be most helpful for a given patient’s presenting symptoms (e.g., Project MATCH found few clear predictors from baseline patient characteristics to suggest which substance abuse treatment would be most helpful for that patient; Project Match Research Group, 1997). However, further studies that assess multiple change processes, either across treatments or within a given therapy, may help us move in that direction.
The present findings need to be understood in light of a number of limitations. In particular, the sample size was relatively small, which limited power and required us to constrain the number and nature of the tests being conducted to maximize the reliability of the results. Importantly, using this approach, convergence (number of iterations to find the results) was relatively quick and the same results were achieved with different estimation procedures, suggesting that the results are reliable. Furthermore, while a variety of panic-relevant outcome measures were included, it would be helpful in future work to include direct measures of physiological change over treatment. Also, measuring each of the panic-relevant variables at every session, as opposed to every three sessions, would be useful to examine more specific questions about the temporal lag between change on one variable and subsequent change on another variable. Moreover, the straw breathing task may have been a somewhat insensitive measure of fear responding given that some patients with panic disorder do not experience problems in this specific domain. Additionally, our primary focus was on within-subject change processes, so a control group was not needed to examine these questions. However, adding an untreated control group that followed the same repeated measures assessment sequence as the treated group would have been helpful to address the possibility that factors unrelated to treatment might explain the change trajectories in panic outcomes. Finally, it is important to acknowledge that one of the limitations of the cognitive model of panic is that it can be difficult to test. For instance, Roth, Wilhelm, and Pettit (2005) note that catastrophic cognition theories can seem unfalsifiable because of the abstract nature of concepts like catastrophic misinterpretations, which are challenging to effectively measure.

Despite these limitations, this study offers some new evidence consistent with cognitive models of panic by establishing the temporal relationship between change in catastrophic misinterpretations and subsequent reductions in overall panic symptom severity, panic attack frequency, panic-related distress and apprehension, and avoidance. More clearly establishing the mechanisms by which cognitive change predicts change in various panic symptoms, as well as evaluating interactive change processes across multiple time points throughout therapy, will be exciting next steps.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1.
Bivariate latent difference score model of the Panic Disorder Severity Scale (PDSS) and Brief Body Sensations Interpretation Questionnaire (BBSIQ). Previous change on the BBSIQ is a significant predictor of later change on the PDSS. However, previous change on the PDSS is not a significant predictor of later change on the BBSIQ.

Note. The role of the latent intercepts and slopes is to describe change in a manner similar to a latent growth curve model (i.e., to take into account the starting point and overall linear change process for each measure separately, as we look at our primary question of how the change processes across variables are predictive of one another). The $\alpha$ refers to alpha (estimate to model straight-line growth), and the $\gamma$ refers to gamma (estimate to model change process across time). All 12 PDSS time points were used in the analyses, but only a subset of the time points are shown here for readability. The estimates are reported as standardized betas.
Table 1

Descriptive statistics (means with SD in parentheses) for the measures of misinterpretations and treatment outcome.

<table>
<thead>
<tr>
<th>Treatment Session</th>
<th>Catastrophic Misinterpretations (BBSIQ)</th>
<th>Overall Panic Symptoms (PDSS)</th>
<th>Peak Anxiety During Straw Breathing (0-100)</th>
<th>Agoraphobic Avoidance (FQ-Avoid)</th>
<th>Latent Avoidance Factor (FQ-Avoid and PDSS items 4 &amp; 5)</th>
<th>Latent Distress/Apprehension Factor (Straw Anxiety and PDSS items 2 &amp; 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-treatment</td>
<td>2.58 (1.97)</td>
<td>13.42 (4.26)</td>
<td>60.95 (27.51)</td>
<td>10.51 (9.32)</td>
<td>7.62 (4.39)</td>
<td>19.97 (10.65)</td>
</tr>
<tr>
<td>3</td>
<td>2.10 (1.32)</td>
<td>8.20 (4.33)</td>
<td>44.20 (28.35)</td>
<td>8.40 (7.29)</td>
<td>5.27 (3.76)</td>
<td>18.74 (10.09)</td>
</tr>
<tr>
<td>6</td>
<td>1.57 (1.35)</td>
<td>7.18 (3.95)</td>
<td>40.77 (26.31)</td>
<td>6.84 (6.35)</td>
<td>4.89 (3.51)</td>
<td>18.46 (11.95)</td>
</tr>
<tr>
<td>9</td>
<td>1.58 (1.47)</td>
<td>6.88 (4.38)</td>
<td>39.73 (29.93)</td>
<td>7.22 (5.91)</td>
<td>4.76 (3.56)</td>
<td>15.74 (10.91)</td>
</tr>
<tr>
<td>Post-treatment</td>
<td>1.44 (1.20)</td>
<td>5.75 (4.29)</td>
<td>31.10 (26.58)</td>
<td>5.00 (3.56)</td>
<td>3.32 (3.29)</td>
<td>10.13 (9.06)</td>
</tr>
</tbody>
</table>

Note. BBSIQ = Brief Body Sensations Interpretation Questionnaire, PDSS = Panic Disorder Severity Scale, FQ-Avoid = Fear Questionnaire - agoraphobic avoidance subscale