Journal of Consulting and Clinical Psychology
2004, Vol. 72, No. 4, 646–652

0022-006X/04/$12.00 DOI: 10.1037/0022-006X.72.4.646

Mechanism of Change in Cognitive–Behavioral Treatment of Panic Disorder: Evidence for the Fear of Fear Mediational Hypothesis

Jasper A. J. Smits, Mark B. Powers, Yongrae Cho, and Michael J. Telch
University of Texas at Austin

Numerous clinical trials have demonstrated the efficacy of cognitive–behavioral treatment (CBT) for panic disorder. However, studies investigating the mechanisms responsible for improvement with CBT are lacking. The authors used regression analyses outlined by R. M. Baron and D. A. Kenny (1986) to test whether a reduction in fear of fear (FOF) underlies improvement resulting from CBT. Pre- and posttreatment measures were collected from 90 CBT-treated patients and 40 wait-list control participants. Overall, treatment accounted for 31% of the variance in symptom reduction. The potency of FOF as a mediator varied as a function of symptom facet, as full mediation was observed for the change in global disability, whereas the effects of CBT on agoraphobia, anxiety, and panic frequency were partially accounted for by reductions in FOF. Clinical implications and future research directions are discussed.

Fear of fear (FOF), or the tendency to respond fearfully to benign bodily sensations, figures prominently in several theoretical accounts of panic disorder (Barlow, 1988; Beck, Emery, & Greenberg, 1985; Bouton, Mineka, & Barlow, 2001; Clark, 1986; Goldstein & Chambless, 1978; Wolpe & Rowan, 1988). Several lines of research have provided evidence consistent with the FOF hypothesis. First, descriptive studies consistently show that compared with psychiatric and nonpsychiatric control participants, panic disorder patients score significantly higher on self-report measures tapping fear of bodily sensations such as the Body Sensations Questionnaire (BSQ; Chambless, Caputo, Bright, & Gallagher, 1984; Chambless & Gracely, 1989) and the Anxiety Sensitivity Index (ASI; Peterson & Reiss, 1987; Taylor, Koch, & McNally, 1992; Telch, Jacquin, Smits, & Powers, 2003). Second, evidence from laboratory challenge studies using numerous panic provocation agents suggests that those who score high on measures tapping FOF display heightened emotional responding to challenge compared with those who score low on these same FOF measures (M. Brown, Smits, Powers, & Telch, 2003; Eke & McNally, 1996; Holloway & McNally, 1987; McNally & Eke, 1996; Rapee & Medoro, 1994; Telch et al., 2003). Furthermore, anxious responding to biological challenges is significantly reduced following cognitive–behavioral treatment (CBT; Jaimez & Telch, 2003; Schmidt, Trakowski, & Staab, 1997). Third, findings from several prospective studies suggest that people who score high on the ASI are at greater risk for developing naturally occurring panic attacks (Schmidt, Lerew, & Jackson, 1997; Schmidt, Lerew, & Joiner, 1998). Similarly, causal modeling studies of learning history suggest that some early learning experiences may influence the development of anxiety sensitivity, which in turn results in a higher risk of panic attacks (Stewart et al., 2001).

CBTs of panic disorder share the strategic aim of providing patients with corrective information and experiences designed to eliminate patients' faulty emotional responding to harmless cues of stress and arousal. Specific procedural components contained in contemporary CBT manuals for panic disorder include (a) education about the nature and physiology of panic and anxiety, (b) breathing retraining designed to assist patients in learning to control hyperventilation, (c) cognitive restructuring aimed at teaching patients to identify and correct faulty threat perceptions that contribute to their panic and anxiety, (d) interoceptive exposure aimed at reducing patients' fear of harmless bodily sensations associated with physiological activation, and (e) fading of maladaptive defensive behaviors such as avoidance of external situations (Barlow, Craske, Cerny, & Klosko, 1989; Clark et al., 1994; Telch et al., 1993).

The efficacy of CBT for panic disorder has been examined in numerous controlled randomized trials. The findings indicate that CBT results in significant and durable improvement in panic disorder symptoms (Barlow, Gorman, Shear, & Woods, 2000; Clum, Clum, & Surls, 1993; Gould, Otto, & Pollack, 1995) as well as changes in patients' quality of life (Telch, Schmidt, Jaimez, Jacquin, & Harrington, 1995). Moreover, preliminary findings suggest that these treatments are as effective when delivered in the real world (Stuart, Treat, & Wade, 2000; Wade, Treat, & Stuart, 1998).

As the evidence supporting the efficacy of CBT accumulates, there are surprisingly few studies investigating the mechanism of action of CBT. On the basis of contemporary psychological theories of panic disorder, it makes sense to ask whether the changes resulting from CBT are mediated by changes in FOF. Indeed, several findings implicate change in FOF as a mediator of treatment outcome. First, CBT results in significant reductions on

Jasper A. J. Smits, Mark B. Powers, Yongrae Cho, and Michael J. Telch, Laboratory for the Study of Anxiety Disorders, Department of Psychology, University of Texas at Austin.

Jasper A. J. Smits is now at the Department of Psychology, Southern Methodist University; Yongrae Cho is now at the Department of Psychology, Hallym University, Chunchon, South Korea.

This research was supported by National Institute of Mental Health Grant MH74-600-203.

Correspondence concerning this article should be addressed to Michael J. Telch, Department of Psychology, SEA 3.208, 1 University Station Stop A8000, University of Texas at Austin, Austin, TX 78712. E-mail: telch@mail.utexas.edu

measures broadly tapping FOF (Bouchard et al., 1996; Clark et al., 1997; Poulton & Andrews, 1996). Second, modifying patients' catastrophic misinterpretations of bodily sensations results in significant reductions in panic (Taylor, 2000). Similarly, posttreatment measures of faulty threat appraisals of body sensations predict outcome status at follow-up (Clark et al., 1994, 1999). Third, in a clinical trial comparing cognitive therapy with guided mastery therapy for panic disorder, changes in catastrophic cognitions predicted differential change in panic disorder symptoms (Hoffart, 1998).

The overarching objective of the present study was to shed light on the mechanism of action of CBT. To this end, we applied the analytic steps outlined by Baron and Kenny (1986) to test whether the short-term effects of CBT were mediated by changes in FOF. To reduce mono-operation bias (see Shadish, Cook, & Campbell, 2002), we examined multiple outcome measures of treatment (i.e., panic attacks, anticipatory anxiety, panic-related avoidance, and global disability) separately. The inclusion of multiple outcome measures also allowed us to test the mediational specificity of FOF across the four major outcome measures.

Method

Participants

The sample consisted of 130 participants (99 women and 31 men). All participants were referred to our laboratory from physicians and mental health professionals in the Austin, TX, area as part of several panic disorder treatment outcome studies (Telch et al., 1993, 1995). Further details of the participant recruitment and screening are provided elsewhere (Telch et al., 1993, 1995). All participants met the following entry criteria: (a) principal Axis I diagnosis of panic disorder with agoraphobia as determined by the Structured Clinical Interview for *DSM–III–R* (SCID; Spitzer, Williams, Gibbon, & First, 1992); (b) at least one panic attack during the past 30 days; (c) age 18–65 years; (d) no recent change in psychotropic medications; and (e) negative for current psychosis, bipolar disorder, and substance abuse disorder. Demographic characteristics are presented in Table 2 (appearing later).

Treatment

Of the 130 participants, 40 were randomly assigned to a waitlist condition, and 90 participants received treatment previously described by Telch (Telch et al., 1993, 1995). This multicomponent group CBT treatment consists of four major treatment components: (a) education and corrective information concerning the nature, causes, and maintenance of anxiety and panic; (b) cognitive therapy techniques aimed at helping the patient identify, examine, and challenge faulty beliefs of danger and harm associated with panic, anxiety, and phobic avoidance; (c) training in methods of slow diaphragmatic breathing to help patients eliminate hyperventilation symptoms and reduce physiological arousal; (d) interoceptive exposure exercises designed to reduce patients' fear of somatic sensations through repeated exposure to various activities (e.g., running in place) that intentionally induce feared bodily sensations (e.g., heart racing); and (e) self-directed exposure to patients' feared situations designed to reduce agoraphobic avoidance.

Treatment sessions were led by an experienced doctoral level clinician and co-led by one of several advanced doctoral student clinicians. Treatment consisted of twelve 2-hr highly structured sessions conducted over an 8-week period. Sessions were conducted twice weekly for the first 4 weeks and then once each week for the remaining 4 weeks. Participants were required to tape-record each session and were encouraged to listen to the tape between sessions. Skill-building home practice was assigned in each session and participants completed home practice monitoring forms to track their adherence. A 65-page treatment manual (Telch & Schmidt, 1990) describes the specific goals and strategies for each session.

Adherence to the treatment manual was rated by independent evaluators on a random sample of videotaped sessions. Compliance with the treatment manual was high (i.e., 177 of 180 exercises rated as completed, 177 of 177 exercises rated as consistent with manual description) across all sessions assessed ($N = 36$).

Measures

Assessment of clinical status and FOF occurred at Week 1 (pretreatment) and Week 10 (posttreatment). Participants in the wait-list control condition were offered CBT after completion of posttreatment assessment.

Clinical Status

Texas Panic Attack Record Form. Panic attacks were assessed with a prospective self-monitoring approach similar to that used in the Upjohn Cross-National Collaborative Panic Study (Ballenger et al., 1988). Participants were provided with daily panic diary forms. For each panic episode, participants were instructed to record the (a) date, (b) time, (c) duration, (d) severity, (e) symptoms experienced, and (f) setting parameters (e.g., place, activity, presence of others). Panic attacks with three or fewer symptoms (i.e., limited symptom attacks) were not included in the panic attack count. The importance of immediate recording was emphasized to increase the accuracy of participants' recollection of the panic attack.

Sheehan Patient-Rated Anxiety Scale (SPRAS). The SPRAS (Sheehan, 1983) is a 35-item self-report scale for assessing the intensity of anxiety symptoms. Each of the 35 symptoms (e.g., shaking or trembling) is rated on a 5-point scale ranging from 0 (*not at all distressing*) to 4 (*extremely distressing*). The instructions were modified so that symptom ratings were based on a 1-week time frame. The total score was computed by summing the responses to the 35 items. The SPRAS has demonstrated adequate psychometric properties (Sheehan, 1983).

Fear Questionnaire–Agoraphobia subscale (FQ-Ago). The Fear Questionnaire (Marks & Mathews, 1979) was used to assess level of agoraphobia. The questionnaire consists of 15 items representing three separate phobia types (agoraphobia, blood-injury phobia, and social phobia). For each item, the participant rates the degree of avoidance to the object or situation. The 5-item FQ-Ago has demonstrated adequate psychometric properties and is the most widely used self-report measure for assessing agoraphobia in treatment outcome research (Jacobson, Wilson, & Tupper, 1988).

Sheehan Disability Scale (SDS). The SDS is a four-item self-report measure of global impairment created by the presenting problem. The SDS was used in the Upjohn Cross-National Collaborative Panic Study (Ballenger et al., 1988). Three items assess impairment: (a) work activities, (b) social life and leisure activities, and (c) family life and home responsibilities. Each item is rated on an 11-point Likert-type scale (0 = *not at all*, 1–3 = *mild*, 4–6 = *moderate*, 7–9 = *marked*, 10 = *severe*). One item assesses overall (i.e., global) work and social disability and is scored on a 5-point scale.

FOF

ASI. The ASI (Peterson & Reiss, 1987) is a 16-item self-report instrument designed to assess one's tendency to respond fearfully to anxiety-related symptoms. Respondents are presented with statements expressing concerns about possible negative consequences of anxiety such as "When I am nervous, I worry that I might be mentally ill." For each statement, respondents rate each item on a Likert-type scale ranging from 0 (*very little*) to 4 (*very much*). The ASI total score is computed by summing responses across the 16 items. Data on the reliability and validity of the

ASI scales have been favorable (Peterson & Heilbronner, 1987; Telch, Shermis, & Lucas, 1989).

BSQ. The BSQ (Chambless et al., 1984) is a 17-item self-report instrument tapping the fear of bodily sensations. Each item represents an anxiety-related bodily sensation (e.g., heart palpitations). Each item is rated on a 1 (*not frightened or worried by this sensation*) to 5 (*extremely frightened by this sensation*) Likert-type scale. The total score is computed by averaging the responses to the 17 items. The scale has demonstrated high internal consistency and test–retest reliability (Chambless et al., 1984).

Statistical Analyses

We examined baseline differences between CBT-treated participants and wait-list control participants on demographic characteristics, panic-related features, and FOF measures using one-way analyses of variance (ANOVAs) for continuous variables and chi-square tests for categorical variables. We computed residualized change scores for each of the clinical status and FOF measures. This was done by regressing the posttreatment scores on the pretreatment scores for all study participants. The FOF score was defined as a change in FOF from pre- to posttreatment and was obtained through summation of the *z* scores of the residualized change scores of the ASI and BSQ.

The hypothesis that the effects of CBT would be mediated by changes in FOF was tested in accordance with the analytic steps outlined by Baron and Kenny (1986). In Step 1, we tested the effects of treatment on the proposed mediator by performing an ANOVA with treatment group (CBT vs. wait list) as the grouping factor and FOF score as the dependent variable.

In Step 2, we tested for the presence of a treatment effect by performing a series of univariate ANOVAs with treatment group (CBT vs. wait list) as the grouping factor and residualized change scores of the four major clinical status measures (i.e., panic attack frequency, anxiety, agoraphobic avoidance, and overall disability) as the dependent variables.

In Step 3, the relationship between the proposed mediator and the four major clinical status measures was examined. Specifically, this step was tested by performing a series of analyses of covariance with treatment group (CBT vs. wait list) as the grouping factor, residualized change scores of clinical status measures as the dependent variables, and the FOF score as the covariate.

The final step tested the relationship between treatment and change in panic disorder symptom facets after controlling for the effects of the proposed mediator. According to Baron and Kenny (1986), evidence for full mediation exists when the relationship between treatment and outcome is no longer significant after controlling for the effects of the mediator, whereas evidence for partial mediation exists when the relationship between treatment and outcome is significantly attenuated (but still significant) after controlling for mediator effects. This final step was tested by comparing the effect of treatment in the third step with the effect of treatment in the second step.

Results

Group Comparisons on Demographic Characteristics, Clinical Status, and Proposed Mediator Variables at Baseline

As can be seen in Table 1, the clinical status measures and FOF measures were significantly correlated. Because the distribution of panic frequency scores was skewed, we performed a square root transformation and used these transformed scores in the subsequent analyses. Participants in the two groups did not differ significantly on any of the demographic variables at intake (see Table 2). Means and standard deviations for each of the clinical status measures are presented in Table 3. The two groups did not differ significantly at baseline on any of the treatment outcome indices with the exception that compared with participants assigned to the wait-list condition, those receiving CBT showed higher baseline scores on the SPRAS ($p < .05$). As can be seen in Table 3, the two groups did not differ significantly on the BSQ at baseline, but the CBT-treated participants scored higher on the ASI than the wait-list control participants ($p < .05$).

Table 1
Intercorrelations Between Clinical Status Measures and Indices of Fear of Fear at Baseline

Measure	1.	FQ-Ago 2.	SPRAS 3.	SDS 4.	ASI 5.	BSQ 6.
1. Panic frequency	—	.18*	.36**	.18*	.28**	.21*
2. FQ-Ago		—	.37**	.44**	.37**	.37**
3. SPRAS			—	.49**	.57**	.58**
4. SDS				—	.39**	.45**
5. ASI					—	.64**
6. BSQ						—

Note. FQ-Ago = Fear Questionnaire–Agoraphobia subscale; SPRAS = Sheehan Patient-Rated Anxiety Scale; SDS = Sheehan Disability Scale, average of first three subscales; ASI = Anxiety Sensitivity Index; BSQ = Body Sensations Questionnaire; Panic frequency = number of panic attacks during the last week.
* $p < .05$. ** $p \leq .01$.

Effects of Treatment on the Proposed Mediator (Mediation Test—Step 1)

Effect sizes for the indices of FOF are presented in Table 4. CBT-treated participants displayed significantly greater improvement in FOF as indexed by the FOF score relative to the wait-list control participants, $F(1, 128) = 93.08$, $p < .01$. These data confirm that the first condition for mediation was met.

Effects of Treatment on the Major Clinical Status Measures (Mediation Test—Step 2)

Significantly greater improvement was observed among CBT-treated participants relative to wait-list control participants on all clinical status measures (all *p*s $< .01$). The percentage of variance accounted for by treatment ranged from 17% for change in panic attack frequency to 43% for change in anxiety as measured by the SPRAS (see Figure 1). As can be seen in Table 4, the mean within-subject effect size across the major clinical status measures for CBT-treated participants was 1.52 ($SD = 0.45$), whereas wait-list control participants showed only a modest improvement from pre- to posttreatment (M within-subject effect size = 0.22, SD within-subject effect size = 0.07). These data confirm that the second condition for mediation was met.

Relationship Between Change in the Proposed Mediator and Treatment Outcome (Mediation Test—Step 3)

Results revealed significant covariation between residualized change in the FOF index and each of the four clinical status change score measures after controlling for treatment: panic frequency,

Table 2
Demographic Characteristics of CBT-Treated and Wait-List Control Participants

Demographic characteristic	CBT (n = 90)	WL (n = 40)	Total (N = 130)
Age (years)			
M	32.80	34.43	33.93
SD	8.48	9.68	9.32
Gender (%)			
Women	76.67	75.00	76.15
Men	23.33	25.00	23.85
Ethnicity (%)			
White	82.22	80.00	81.54
Hispanic	8.89	5.00	7.69
Black	4.44	7.50	5.38
Asian	1.11	2.50	1.54
No response	3.33	5.00	3.85
Marital status (%)			
Never married	23.33	35.00	26.92
Married	60.00	50.00	56.92
Divorced or separated	16.67	15.00	16.15
Education (%)			
Less than high school	12.22	12.50	12.31
High school	10.00	12.50	10.77
Part college	44.44	37.50	42.31
College graduate or beyond	32.22	30.00	31.54
No response	1.11	7.50	3.08
Employment status (%)			
Employed	57.78	62.50	59.23
Unemployed	32.22	20.00	28.46
Student	8.89	12.50	10.00
Homemaker	0.00	2.50	0.78
No response	1.11	2.50	1.54
Chronicity (years)			
M	6.81	9.51	7.63
SD	6.68	9.72	7.79

Note. CBT = cognitive–behavioral treatment; WL = wait-list control.

$F(1, 127) = 4.30$, $p < .05$; anxiety, $F(1, 127) = 78.00$, $p < .01$; agoraphobia, $F(1, 127) = 42.79$, $p < .01$; global disability, $F(1, 127) = 64.69$, $p < .01$. These data confirm that the third necessary condition for mediation was met.

Effects of Treatment on Panic Disorder Symptoms After Controlling for the Effects of the Proposed Mediators (Mediation Test—Step 4)

As can be seen in Figure 1, the effects of CBT on panic disorder symptom reduction were reduced considerably after controlling for changes in FOF. Analyses revealed that changes in FOF fully mediated the effects of treatment on global disability, $F(1, 127) = 2.45$, $p = .12$, whereas partial mediation was observed for panic frequency, $F(1, 127) = 7.23$, $p = .01$; anxiety, $F(1, 127) = 13.89$, $p < .01$; and agoraphobia, $F(1, 127) = 7.67$, $p = .01$. These findings indicate that the fourth condition for mediation was also met.

Discussion

In the present study we sought to clarify the mechanism governing change in panic disorder symptoms following CBT. On the basis of previous research findings implicating heightened FOF in the pathogenesis of panic disorder, we tested whether the symptom changes brought about by CBT were mediated by reductions in FOF. Our test of mediation used the multistep analytic strategy proposed by Baron and Kenny (1986).

As reported elsewhere, group-administered CBT led to statistically significant and clinically meaningful improvement across the major symptom facets of the disorder. Although the treatment effects were large, they varied somewhat as a function of symptom facet. The most potent treatment effects were observed for anxiety (43% of variance accounted for by treatment), and the least potent effects were observed for panic attack frequency (17% of variance explained by treatment). Likewise, CBT was associated with significant improvement in the proposed mediator (i.e., FOF), and the magnitude of improvement is similar to that reported in previous clinical trials (e.g., T. A. Brown & Barlow, 1995).

The mediation analyses provide support for the hypothesis that CBT exerts its effects on panic disorder symptoms by reducing FOF and are consistent with contemporary theories implicating the fear of bodily sensations in the pathogenesis of panic disorder (Barlow, 1988; Beck et al., 1985; Bouton et al., 2001; Clark, 1986; Goldstein & Chambless, 1978; McNally, 1994; Wolpe & Rowan, 1988). Our demonstration that FOF significantly mediates the effects of CBT across each of the four well-accepted but loosely correlated outcome measures (i.e., panic attack frequency, anxiety, agoraphobic avoidance, and global disability) reduces the threat of mono-operation bias (cf. Shadish, Cook, & Campbell, 2002) and provides further confidence in the fidelity of the mediational findings.

An interesting finding was that the potency of the mediational effects varied as a function of symptom facet. In the case of global disability, change in FOF fully mediated the effects of CBT; whereas for panic frequency, anxiety, and agoraphobic avoidance, FOF partially mediated the effects of CBT. We can only speculate as to why the mediational effects of FOF were strongest for global disability.

Which specific procedural components of CBT are responsible for reduction in FOF? Although this question has not been addressed directly, data from dismantling studies of CBT of panic disorder provide some insights. For example, in one dismantling study, Schmidt et al. (2000) found that the breathing retraining component of CBT for panic disorder did not add to CBT's overall treatment efficacy or change in fear of somatic sensations. Future dismantling studies that include measures tapping FOF will likely clarify the specific procedural components that are responsible for FOF change.

Our test of FOF as a potential mediator of treatment outcome in panic disorder hinges on the assumption that FOF is not merely a symptom of panic disorder. Several lines of evidence provide compelling support for this assumption. First, heightened FOF has been reported among patients with various anxiety disorders (Taylor et al., 1992). Second, heightened FOF is present in nonclinical populations with no history of panic disorder or panic attacks (Taylor, 1999). Third, evidence from biological challenge studies and longitudinal risk studies suggests that heightened anxiety sensitivity (FOF) among nonclinical participants with no history of panic may increase the risk for challenge-induced panic (Telch, Silverman, & Schmidt, 1996) or the subsequent development of naturally occurring panic attacks (Schmidt et al., 1997). Finally, it

Table 3
Pre- and Posttreatment Means and Standard Deviations for the Treatment Outcome and Proposed Mediator Variables

	CBT (n = 90)				WL (n = 40)			
	Pretreatment		Posttreatment		Pretreatment		Posttreatment	
Variable	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*
				Outcome				
Panic frequency	2.44	2.65	0.49	1.04	3.00	5.13	2.18	4.26
FQ-Ago	17.00	10.19	5.53	5.70	16.03	7.76	13.98	8.97
SPRAS	64.03	24.80	20.39	17.48	53.52	26.45	49.30	26.07
SDS	5.28	2.12	1.96	1.78	4.71	2.09	4.02	2.27
				Mediators				
ASI	37.32	11.04	13.93	8.88	33.13	10.78	30.40	10.21
BSQ	2.92	0.77	1.75	0.65	2.75	0.72	2.56	0.78

Note. CBT = cognitive–behavioral treatment; WL = wait-list control; panic frequency = number of panic attacks during the last week; FQ-Ago = Fear Questionnaire–Agoraphobia subscale; SPRAS = Sheehan Patient-Rated Anxiety Scale; SDS = Sheehan Disability Scale, average of first three subscales; ASI = Anxiety Sensitivity Index; BSQ = Body Sensations Questionnaire.

should be noted that heightened FOF is not recognized as a symptom of panic disorder in the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.; American Psychiatric Association, 1994). Taken together, these observations argue strongly against the position that heightened FOF is merely a symptom of panic disorder.

Several limitations of the current study should be noted. First, although the current findings are consistent with the hypothesis that reductions in FOF mediate the effects of CBT in panic disorder, our design does not allow us to rule out the possibility that the change in FOF was a consequence as opposed to a cause of panic disorder symptom reduction. Future studies examining FOF as a mediator should include multiple assessments during the course of treatment so that more powerful analytic techniques (e.g., autoregression techniques) might demonstrate temporal precedence of the mediator. Second, our study design does not address the important question of whether changes in FOF mediate improvement observed from alternative treatments with established efficacy such as pharmacotherapy. Future studies are needed

Table 4
Effect Sizes for the Treatment Outcome and Proposed Mediator Variables

	Effect size		
	Within[a]		
Variable	CBT	WL	Between[b]
	Outcome		
Panic frequency	0.97	0.17	0.55
FQ-Ago	1.39	0.24	1.12
SPRAS	2.03	0.16	1.30
SDS	1.70	0.32	1.01
	Mediators		
ASI	2.33	0.26	1.72
BSQ	1.64	0.25	1.13

Note. CBT = cognitive–behavioral treatment; WL = wait-list control; panic frequency = number of panic attacks during the last week; FQ-Ago = Fear Questionnaire–Agoraphobia subscale; SPRAS = Sheehan Patient-Rated Anxiety Scale; SDS = Sheehan Disability Scale, average of first three subscales; ASI = Anxiety Sensitivity Index; BSQ = Body Sensations Questionnaire; pre = pretreatment; post = posttreatment.

[a] Within-subject effect size = $(M_{pre} - M_{post})/SD_{pooled}$, where

$$SD_{pooled} = \sqrt{(SD_{pre}^2 + SD_{post}^2)/2}.$$

[b] Between-subjects (controlled) effect size = $(M_{CBT\text{-}post} - M_{WL\text{-}post})/SD_{pooled}$, where

$$SD_{pooled} = \sqrt{(SD_{CBT\text{-}post}^2 + SD_{WL\text{-}post}^2)/2}.$$

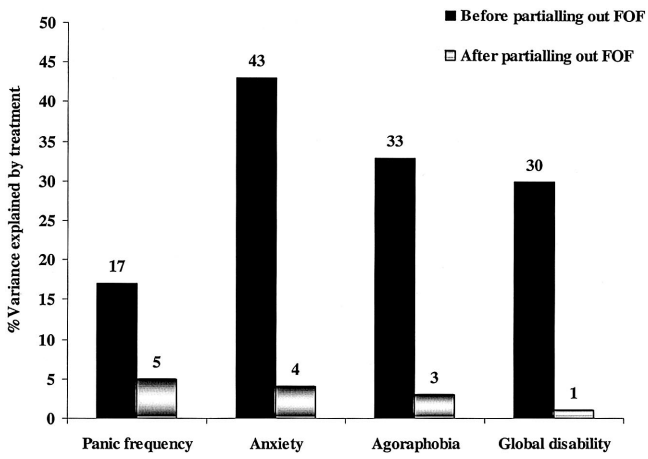

Figure 1. Percentage of variance in symptom change accounted for by treatment before and after controlling for fear of fear (FOF).

to determine the mediational specificity of FOF in governing treatment response in panic disorder.

References

American Psychiatric Association. (1994). *Diagnostic and statistical manual of mental disorders* (4th ed.). Washington, DC: Author.

Ballenger, J. C., Burrows, G. D., DuPont, R. L., Lesser, I. M., Noyes, R., Pecknold, J. C., et al. (1988). Alprazolam in panic disorder and agoraphobia: Results from a multicenter trial: I. efficacy in short-term treatment. *Archives of General Psychiatry, 45,* 413–422.

Barlow, D. H. (1988). *Anxiety and its disorders.* New York: Guilford Press.

Barlow, D. H., Craske, M. G., Cerny, J. A., & Klosko, J. S. (1989). Behavioral treatment of panic disorder. *Behavior Therapy, 20,* 261–282.

Barlow, D. H., Gorman, J. M., Shear, M. K., & Woods, S. W. (2000). Cognitive–behavioral therapy, imipramine, or their combination for panic disorder: A randomized controlled trial. *Journal of the American Medical Association, 283,* 2529–2536.

Baron, R. M., & Kenny, D. A. (1986). The moderator–mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. *Journal of Personality and Social Psychology, 51,* 1173–1182.

Beck, A. T., Emery, G., & Greenberg, R. (1985). *Anxiety disorders and phobias: A cognitive perspective.* New York: Basic Books.

Bouchard, S., Gauthier, J., Laberge, B., French, D., Pelletier, M. H., & Godbout, C. (1996). Exposure versus cognitive restructuring in the treatment of panic disorder with agoraphobia. *Behaviour Research and Therapy, 34,* 213–224.

Bouton, M. E., Mineka, S., & Barlow, D. H. (2001). A modern learning theory perspective on the etiology of panic disorder. *Psychology Review, 108,* 4–32.

Brown, M., Smits, J. A. J., Powers, M. B., & Telch, M. J. (2003). Differential sensitivity of the three ASI factors in predicting panic disorder patients' subjective and behavioral response to hyperventilation challenge. *Journal of Anxiety Disorders, 17,* 583–591.

Brown, T. A., & Barlow, D. H. (1995). Long-term outcome in cognitive–behavioral treatment of panic disorder: Clinical predictors and alternative strategies for assessment. *Journal of Consulting and Clinical Psychology, 63,* 754–765.

Chambless, D. L., Caputo, G. C., Bright, P., & Gallagher, R. (1984). Assessment of fear of fear in agoraphobics: The Body Sensations Questionnaire and the Agoraphobic Cognitions Questionnaire. *Journal of Consulting and Clinical Psychology, 52,* 1090–1097.

Chambless, D. L., & Gracely, E. J. (1989). Fear of fear and the anxiety disorders. *Cognitive Therapy and Research, 13,* 9–20.

Clark, D. M. (1986). A cognitive approach to panic. *Behaviour Research and Therapy, 24,* 461–470.

Clark, D. M., Salkovskis, P. M., Hackmann, A., Middleton, H., Anastasiades, P., & Gelder, M. (1994). A comparison of cognitive therapy, applied relaxation, and imipramine in the treatment of panic disorder. *British Journal of Psychiatry, 164,* 759–769.

Clark, D. M., Salkovskis, P. M., Hackmann, A., Wells, A., Ludgate, J., & Gelder, M. (1999). Brief cognitive therapy for panic disorder: A randomized controlled trial. *Journal of Consulting and Clinical Psychology, 67,* 583–589.

Clark, D. M., Salkovskis, P. M., Ost, L. G., Breitholtz, E., Koehler, K. A., Westling, B. E., et al. (1997). Misinterpretation of body sensations in panic disorder. *Journal of Consulting and Clinical Psychology, 65,* 203–213.

Clum, G. A., Clum, G. A., & Surls, R. (1993). A meta-analysis of treatments for panic disorder. *Journal of Consulting and Clinical Psychology, 61,* 317–326.

Eke, M., & McNally, R. J. (1996). Anxiety sensitivity, suffocation fear, trait anxiety, and breath holding duration as predictors of response to carbon dioxide challenge. *Behaviour Research and Therapy, 34,* 603–607.

Goldstein, A. J., & Chambless, D. L. (1978). A reanalysis of agoraphobia. *Behavior Therapy, 9,* 47–59.

Gould, R. A., Otto, M. W., & Pollack, M. H. (1995). A meta-analysis of treatment outcome for panic disorder. *Clinical Psychology Review, 15,* 819–844.

Hoffart, A. (1998). Cognitive and guided mastery therapy of agoraphobia: Long-term outcome and mechanisms of change. *Cognitive Therapy and Research, 22,* 195–207.

Holloway, W., & McNally, R. J. (1987). Effects of anxiety sensitivity on the response to hyperventilation. *Journal of Abnormal Psychology, 96,* 330–334.

Jacobson, N. S., Wilson, L., & Tupper, C. (1988). The clinical significance of treatment gains resulting from exposure-based interventions for agoraphobia: A reanalysis of outcome data. *Behavior Therapy, 19,* 539–554.

Jaimez, L. T., & Telch, M. J. (2003). *Treatment response to a 35% CO_2 challenge: A comparison of CBT, educational/supportive treatment, and delayed treatment control.* Manuscript in preparation.

Marks, I. M., & Mathews, A. M. (1979). Brief standard self-rating for phobic patients. *Behaviour Research and Therapy, 17,* 263–267.

McNally, R. J. (1994). *Panic disorder: A critical analysis.* New York: Guilford Press.

McNally, R. J., & Eke, M. (1996). Anxiety sensitivity, suffocation fear, and breath-holding duration as predictors of response to carbon dioxide challenge. *Journal of Abnormal Psychology, 105,* 146–149.

Peterson, R. A., & Heilbronner, R. L. (1987). The anxiety sensitivity index: Construct validity and factor analytic structure. *Journal of Anxiety Disorders, 1,* 117–121.

Peterson, R. A., & Reiss, S. (1987). *Anxiety Sensitivity Index.* Palos Heights, IL: International Diagnostic Systems.

Poulton, R. G., & Andrews, G. (1996). Change in danger cognitions in agoraphobia and social phobia during treatment. *Behaviour Research and Therapy, 34,* 413–421.

Rapee, R. M., & Medoro, L. (1994). Fear of physical sensations and trait anxiety as mediators of the response to hyperventilation in nonclinical subjects. *Journal of Abnormal Psychology, 103,* 693–699.

Schmidt, N. B., Lerew, D. R., & Jackson, R. J. (1997). The role of anxiety sensitivity in the pathogenesis of panic: Prospective evaluation of spontaneous panic attacks during acute stress. *Journal of Abnormal Psychology, 106,* 355–364.

Schmidt, N. B., Lerew, D. R., & Joiner, T. E., Jr. (1998). Anxiety sensitivity and the pathogenesis of anxiety and depression: Evidence for symptom specificity. *Behaviour Research and Therapy, 36,* 165–177.

Schmidt, N. B., Trakowski, J. H., & Staab, J. P. (1997). Extinction of panicogenic effects of 35% CO_2 challenge in patients with panic disorder. *Journal of Abnormal Psychology, 106,* 630–638.

Schmidt, N. B., Woolaway-Bickel, K., Trakowski, J., Santiago, H., Storey, J., Koselka, M., & Cook, J. (2000). Dismantling cognitive–behavioral treatment for panic disorder: Questioning the utility of breathing retraining. *Journal of Consulting and Clinical Psychology, 68,* 417–424.

Shadish, W. R., Cook, T. D., & Campbell, D. T. (2002). *Experimental and quasi-experimental designs for generalized causal inference.* Boston: Houghton Mifflin.

Sheehan, D. (1983). *The anxiety disease.* New York: Scribner.

Spitzer, R. L., Williams, J. B., Gibbon, M., & First, M. B. (1992). The Structured Clinical Interview for *DSM–III–R* (SCID). I: History, rationale, and description. *Archives of General Psychiatry, 49,* 624–629.

Stewart, S. H., Taylor, S., Jang, K. L., Cox, B. J., Watt, M. C., Fedoroff, I. C., & Borger, S. C. (2001). Causal modeling of relations among learning history, anxiety sensitivity, and panic attacks. *Behaviour Research and Therapy, 39,* 443–456.

Stuart, G. L., Treat, T. A., & Wade, W. A. (2000). Effectiveness of an

empirically based treatment for panic disorder delivered in a service clinic setting: 1-year follow-up. *Journal of Consulting and Clinical Psychology, 68,* 506–512.

Taylor, S. (1999). *Anxiety sensitivity: Theory, research, and treatment of the fear of anxiety.* Mahwah, NJ: Erlbaum.

Taylor, S. (2000). *Understanding and treating panic disorder: Cognitive–behavioural approaches.* New York: Wiley.

Taylor, S., Koch, W. J., & McNally, R. J. (1992). How does anxiety sensitivity vary across the anxiety disorders? *Journal of Anxiety Disorders, 6,* 249–259.

Telch, M. J., Jacquin, K., Smits, J. A. J., & Powers, M. B. (2003). Respiratory hypersensitivity as a predictor of agoraphobia status among individuals suffering from panic disorder. *Journal of Behavior Therapy and Experimental Psychiatry, 34,* 161–170.

Telch, M. J., Lucas, J. A., Schmidt, N. B., Hanna, H. H., Jaimez, T. L., & Lucas, R. A. (1993). Group cognitive–behavioral treatment of panic disorder. *Behaviour Research and Therapy, 31,* 279–287.

Telch, M. J., & Schmidt, N. B. (1990). *Cognitive–behavioral treatment for panic disorder and agoraphobia: Panic inoculation treatment manual.* Unpublished manuscript.

Telch, M. J., Schmidt, N. B., Jaimez, T. L., Jacquin, K. M., & Harrington, P. J. (1995). Impact of cognitive–behavioral treatment on quality of life in panic disorder patients. *Journal of Consulting and Clinical Psychology, 63,* 823–830.

Telch, M. J., Shermis, M. D., & Lucas, J. A. (1989). Anxiety sensitivity: Unitary personality trait or domain-specific appraisals? *Journal of Anxiety Disorders, 3,* 25–32.

Telch, M. J., Silverman, A., & Schmidt, N. B. (1996). Effects of anxiety sensitivity and perceived control on emotional responding to caffeine challenge. *Journal of Anxiety Disorders, 10,* 21–35.

Wade, W. A., Treat, T. A., & Stuart, G. L. (1998). Transporting an empirically supported treatment for panic disorder to a service clinic setting: A benchmarking strategy. *Journal of Consulting and Clinical Psychology, 66,* 231–239.

Wolpe, J., & Rowan, V. C. (1988). Panic disorder: A product of classical conditioning. *Behaviour Research and Therapy, 26,* 441–450.

Received September 3, 2002
Revision received September 23, 2003
Accepted October 4, 2003 ■