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## Moderators of intensive CBT for adolescent panic disorder: the of fear and avoidance

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### Abstract

**Background**—Research supports the efficacy of intensive cognitive behavioral therapy (CBT) for the treatment of adolescent panic disorder with or without agoraphobia (PDA). However, little is known about the conditions under which intensive treatment is most effective. The current investigation examined the moderating roles of baseline fear and avoidance in the intensive treatment of adolescent PDA.

**Methods**—Adolescents with PDA (ages 11–17;  $N = 54$ ) were randomized to either an intensive CBT treatment ( $n = 37$ ) or a waitlist control condition ( $n = 17$ ). PDA diagnosis, symptom severity, and number of feared and avoided situations were assessed at baseline and 6-week post-treatment/post-waitlist. Hierarchical regression analyses examined the relative contributions of treatment condition, number of baseline feared or avoided situations, and their interactions in the prediction of post-treatment/waitlist PDA symptoms.

**Results**—The main effect of intensive CBT on post-treatment PDA symptoms was not uniform across participants, with larger treatment effects found among participants with lower, relative to higher, baseline levels of fear and avoidance.

**Conclusions**—Findings help clarify which adolescents suffering with PDA may benefit most from an intensive treatment format.

### Introduction

Panic disorder with or without agoraphobia (PDA) is a debilitating condition that commonly onsets in adolescence and early adulthood (Barlow, 2002; Beesdo, Knappe, & Pine, 2009; Grant et al., 2006; Kessler et al., 2012). Adolescents with PDA experience recurrent, unexpected panic attacks characterized by distressing physical and cognitive symptoms, including heart palpitations, nausea, difficulty breathing, dizziness, derealization, and fears of dying or losing control. These symptoms are associated with persistent fears that future panic attacks will occur, and are often accompanied by changes in behavior and daily routine – such as avoiding school, crowds, elevators, or exercise – to avoid the possibility of



The degree to which adolescents fear and avoid anxiety-provoking situations and stimuli are central aspects of PDA phenomenology. Gold-standard assessment measures of PDA symptoms and severity in youth (e.g. Silverman & Albano, 1997) emphasize a thorough evaluation of the extent of a child's fear and avoidance to inform PDA diagnostic impressions and decisions about clinical severity. Moreover, in the evidence-based treatment of PDA, fear and avoidance are central treatment targets for both adults (Barlow & Craske, 2000; Craske & Barlow, 2006) and children (Pincus, Ehrenreich, Mattis, & Barlow, 2008), and are addressed through the development of a fear and avoidance hierarchy that subsequently provides a roadmap for exposures across treatment. Given the centrality of fear and avoidance in the identification and treatment of youth with PDA, it is possible that heterogeneity across children's baseline levels of fear and avoidance are meaningfully linked to heterogeneity in treatment response. Thus, identifying whether baseline levels of fear and avoidance moderate treatment response can help clarify which youth may benefit most from intensive PCT-A.

The present study examines the moderating roles of baseline fear and avoidance on treatment response among adolescents receiving intensive PCT-A in the context of an RCT. We hypothesized that the extent of adolescents' baseline fear and avoidance would each moderate the effect of treatment on panic severity. Given that referrals to intensive programs often follow initial treatment failures (e.g., Storch et al., 2007), and given that concentrated exposure opportunities afforded by an intensive format may be particularly effective for severe cases, we specifically hypothesized that intensive PCT-A would have a significantly greater effect on youth with higher levels of baseline fear and avoidance than on youth with more moderate levels of baseline fear and avoidance.

## Method

### Participants

Participating youth were enrolled in an RCT investigating the feasibility and efficacy of intensive 8-day cognitive behavioral treatment for PDA. Main outcomes for the trial are reported elsewhere (Pincus et al., 2015). Treatment was conducted at a university-based anxiety specialty clinic. Adolescents with PDA were randomly assigned to immediate intensive PCT-A or a waitlist. Exclusion criteria for the trial were: (a) schizophrenia, pervasive developmental disorder, organic brain syndrome, mental retardation, or current suicidal ideation; (b) unavailability of a caregiver to bring the adolescent to treatment; (c) refusal to accept random assignment; and (d) refusal to accept medication stabilization requirements to remain on steady doses of current medications for the duration of the study. Finally, as all procedures were delivered in English, only English-speaking participants were enrolled.

Participants in the present study were 54 adolescents between the ages of 11 and 17 ( $M = 15.29$ ,  $SD = 1.68$ ) with a principal diagnosis of PDA. Participant diagnostic profiles were generated following semi-structured interviews conducted with children and parents. The majority of eligible participants received a diagnosis of panic disorder with agoraphobia ( $N = 53$ ); one participant was assigned a diagnosis of panic disorder without agoraphobia. Eight participants had co-principal diagnoses, including specific phobia of vomiting ( $N = 5$ ), social

anxiety disorder ( $N = 2$ ), and major depressive disorder ( $N = 1$ ). Participants were predominantly Caucasian/Non-Hispanic (86.8%), and 61% were female. Annual family income for participants ranged from \$25,000 to \$500,000, with a mean annual income of \$105,000. Nearly half of participants (46%) reported taking psychotropic medications at baseline. Reported medications included antidepressants ( $N = 11$ , 20.3%), antianxiety medications ( $N = 3$ , 5.5%), or multiple medications ( $N = 11$ , 20.3%).

A total of 103 adolescents were assessed in an initial phone screen. Forty-three participants were excluded because they did not meet diagnostic criteria for primary diagnosis of PDA. Three withdrew following the baseline evaluation due to unwillingness to participate in the study. (For a full CONSORT diagram detailing the flow of study participants, the interested reader is directed to Pincus et al., 2015).

## Measures

**Child diagnoses**—The Anxiety Disorders Interview Schedule for Diagnostic and Statistical Manual of Mental Disorders IV: Child and Parent Versions (ADIS-C/P; Silverman & Albano, 1997) was administered to inform clinician-generated diagnoses. The ADIS-C/P is a semi-structured diagnostic interview that assesses DSM-IV mood, anxiety, and disruptive behavior disorders. The ADIS-C/P is the most widely used diagnostic interview in clinical research with child anxiety populations, boasting strong reliability, validity, and sensitivity to change (Grills & Ollendick, 2003; Silverman & Ollendick, 2005; Silverman, Saavedra, & Pina, 2001; Wood, Piacentini, Berman, McCracken, & Barrios, 2002). Diagnosticians at the treatment site of the present study demonstrated good interrater agreement on primary diagnoses ( $= .87$ ), and 15% of study assessments were rated by two evaluators to ensure reliability.

**Fear and avoidance**—The child version of ADIS-C/P was used to collect baseline data on the extent of adolescents' fear and avoidance related to their PDA. Specifically, the Panic Disorder module of the ADIS-C includes a Fear Checklist and an Avoidance Checklist. Both checklists present situations commonly feared and/or avoided by youth with PDA, including classrooms, public transportation, elevators, etc., (total number of situations assessed = 20). When completing this checklist, the clinician inquires about whether the adolescent fears and/or avoids each of these situations due to panic. For endorsed items, adolescents rate the degree to which they fear and/or avoid that situation on a scale from 0–8, where 0 indicates no fear/avoidance, 4 indicates some fear/avoidance, and 8 signifies the greatest extent of fear/avoidance. As per ADIS-C/P administration guidelines, fear and avoidance ratings greater than or equal to 4 are considered clinically elevated. For the Fear and Avoidance Checklists, respectively, the number of all feared and avoided situations with a rating of 4 or above was summed to generate a baseline Total Number of Feared Situations and a baseline Total Number of Avoided Situations.

**Panic severity**—The Panic Disorder Severity Scale for Children (PDSS-C; Elkins, Pincus & Comer, 2014) is a 7-item self-report measure assessing the frequency and severity of PDA symptoms. The PDSS-C utilizes a 5-point scale (0 to 4) to assess each item, and responses to all items are summed to yield a total score ranging from 0 to 28 representing overall PDA

severity. The PDSS-C demonstrates strong reliability and validity, as well as sensitivity to treatment-related change (Elkins et al., 2014).

## Procedures

Potential participants and their parents completed an initial phone screen. Eligible participants completed assessments at baseline and 6-week post-waitlist/post-treatment administered by independent evaluators (IEs) who were blind to participants' study condition. IEs and study therapists were doctoral candidates and postdoctoral fellows in clinical psychology specializing in pediatric anxiety disorders. All IEs met internal certification and reliability procedures, developed in collaboration with one of the ADIS-C/P authors. IE assessments included the administration of the ADIS-C/P, including the Fear and Avoidance Checklists from the ADIS-C panic disorder module, and the PDSS-C self-report form. Demographic information was obtained from parent report.

Eligible participants were randomly assigned to receive either immediate intensive CBT with heavy parent involvement ( $N = 19$ ), immediate intensive CBT with minimal parent involvement ( $N = 18$ ), or a 6-week waitlist ( $N = 17$ ). Prior work (Pincus et al., 2015) found that the two active treatment conditions showed equivalent outcomes. Accordingly, data from these conditions were collapsed into a single intensive CBT condition (CBT;  $N = 37$ ) compared to a 6-week waitlist condition (WL;  $N = 17$ ).

Participants in the CBT condition received an intensive format of the manual-based PCT-A protocol, *Mastery of your Anxiety and Panic for Adolescents: Riding the Wave* (Pincus et al., 2008) adapted for delivery over eight consecutive days (Angelosante et al., 2009). As with standard weekly individual CBT for panic disorder, intensive treatment for adolescent PDA focused on targeting the cognitive distortions and associated behavioral avoidance related to each adolescent's symptoms, and incorporated well-established cognitive-behavioral treatment elements, such as psychoeducation, cognitive restructuring, interoceptive and in vivo exposures. Several steps were taken to individualize the treatment within fidelity to the treatment protocol to optimally address each adolescent's unique PDA presentation using a cognitive-behavioral approach. Specifically, therapists elicited information from each adolescent regarding the frequency, duration, and intensity of their panic symptoms; therapists and adolescents collaboratively created an individualized fear and avoidance hierarchy, which provided a guiding outline for later exposures; treatment addressed the cognitive distortions about panic particular to the adolescent; and in vivo exposures were tailored to address feared and avoided situations specific to each adolescent.

The first two days of treatment were devoted to rapport building, psychoeducation, developing an individualized fear and avoidance hierarchy, and cognitive restructuring. The third day was dedicated to practicing interoceptive exposures, and the fourth and fifth days were full-day sessions (6 to 8 hours) to allow for repeated therapist-assisted in vivo exposures, often conducted outside of the clinic to generalize treatment gains to "real life" settings. The adolescent and his or her family completed additional independent exposures over the weekend, and the final day in the clinic was devoted to review, relapse prevention, and planning for continued practice at home. Treatment included weekly 30-minute telephone check-ins for 1-month following the eighth day of treatment. These four phone

calls provided a forum for therapists and youth to collaboratively plan additional home-based exposure practices, troubleshoot problems as they arose, and facilitated the gradual transfer of responsibility for treatment to the adolescent; thus, post-treatment assessments for the CBT group occurred six weeks following the initial assessment. WL participants did not receive treatment, and were also assessed six weeks following their initial assessment.

### Analytic strategy

Hierarchical multiple regression analyses examined the relative contributions of treatment condition, number of baseline feared or avoided situations, and their interactions in the prediction of post-treatment PDA severity. Given that all data were normally distributed and assumptions of normality were not violated, generalized linear models were not appropriate for the present analyses. Two parallel analyses (one for baseline fear and one for baseline avoidance) were run in line with data analytic conventions for evaluating moderators (Baron & Kenny, 1986). Treatment condition (CBT vs. WL) was identified as the independent variable. As in previous analyses (Gallo, Cooper-Vince, Hardway, Pincus, & Comer, 2014), the dependent variable was PDSS-C Total Score at 6-week post-treatment/post-waitlist. Two proposed moderators were hypothesized: 1) number of Feared situations at baseline, and 2) number of Avoided situations at baseline (see Figure 1). For each model, treatment condition was entered into step 1 as a predictor of 6-week PDSS-C scores. The proposed moderator was then added as a centered predictor in step 2, and the product term of treatment condition  $\times$  the proposed moderator (the interaction term) was added as a centered predictor into step 3. Significance of the interaction term in step 3, after accounting for main effects in steps 1 and 2, is interpreted as evidence of significance moderation (Comer & Kendall, 2013). Evidence of significant moderation was followed-up with post-hoc analyses comparing simple slopes at different levels of fear and avoidance to clarify the direction of each moderation effect. Specifically, simple slopes were computed for youth showing  $>1$  SD and  $<1$  SD beyond the mean number of feared situations in the sample (i.e., high and moderate fear subgroups, respectively) and for youth showing  $>1$  SD and  $<1$  SD beyond the mean number of avoided situations in the sample (i.e., high and moderate avoidance subgroups, respectively). Youth in the present sample showing  $<1$  SD below the sample means were characterized as "moderate" rather than "low" given that all youth in the study presented with clinical levels of fear and avoidance.

### Results

Means and standard deviations across study variables are presented in Table 1. At baseline, no demographic or clinical group differences were noted between CBT and WL youth: age ( $t[52] = -1.62, p = 0.11$ ), gender ( $\chi^2[1] = 0.14, p = 0.71$ ), medication status ( $\chi^2[1] = 0.01, p = 0.94$ ), baseline PDSS-C Total scores, ( $t[48] = .67, p = .51$ ), baseline numbers of feared situations ( $t[52] = .71, p = 0.48$ ), and baseline number of avoided situations ( $t[52] = .45, p = 0.66$ ). Across the full sample, baseline fear and avoidance both showed small, negative associations with post-treatment panic severity ( $r = -.17, p = .32$ , and  $r = -.13, p = .44$ , respectively). Among youth receiving CBT, baseline fear and avoidance both showed small, positive associations with post-treatment panic severity ( $r = .25, p = .23$ , and  $r = .32, p = .13$ , respectively).

### Moderating effect of baseline fear on treatment outcome

Table 2 presents the results of the hierarchical multiple regression analysis evaluating the relative contributions of treatment condition, number of feared situations at baseline, and their interaction in the prediction of treatment outcome, as measured by the PDSS-C Total score at post-treatment/post-waitlist. In the prediction of treatment outcome, the main effect of treatment condition provided a significant contribution to the model,  $F(1, 37) = 11.48$ ,  $p < .01$ , indicating significantly greater reductions in panic severity at six weeks among youth treated with intensive CBT than among youth in the WL group. Adding the main effect of baseline fear as a predictor did not improve the predictive utility of the model,  $F_{\text{change}}(1, 36) = .09$ ,  $p = .77$ . However, after accounting for main effects, the interaction of Treatment Condition  $\times$  Fear added a significant contribution to the prediction of six week panic symptoms,  $F_{\text{change}}(1, 35) = 4.61$ ,  $p = .04$ , indicating that the extent of baseline fear moderates the effect of intensive CBT on panic severity.

To probe the direction of this moderation effect, post-hoc analyses compared simple slopes among high ( $n = 11$ ) and moderate ( $n = 10$ ) fear youth – defined as those with fear scores one standard deviation above and below the sample mean, respectively. The effect of treatment condition on 6-week PDSS-C scores was significant among moderate fear youth ( $B = 20$ ,  $SE = 4.12$ ,  $\beta = .93$ ,  $p < .01$ ), whereas there was no condition effect on 6-week PDSS-C scores among high fear youth ( $B = 2.20$ ,  $SE = 4.63$ ,  $\beta = .19$ ,  $p = .65$ ).

### Moderating effect of baseline avoidance on treatment outcome

Hierarchical regression procedures examined the moderating effect of baseline avoidance on treatment outcome (see Table 3). As with baseline fear analyses, results indicated a main effect of Treatment Condition in step 1,  $F(1, 37) = 11.48$ ,  $p < .01$ . Adding the main effect of baseline avoidance as a predictor in step 2 did not add a significant contribution to the prediction of 6-week panic severity,  $F_{\text{change}}(1, 36) = .07$ ,  $p = .79$ . However, after accounting for main effects, the interaction of Treatment Condition  $\times$  Avoidance significantly contributed to the prediction of post-treatment panic symptoms,  $F_{\text{change}}(1, 36) = 5.51$ ,  $p = .03$ , indicating that the extent of baseline avoidance also moderates the effect of intensive CBT on panic severity.

Post-hoc analyses compared simple slopes among high ( $n = 9$ ) and moderate ( $n = 10$ ) avoidance youth – defined as those with avoidance scores one standard deviation above and below the sample mean, respectively). Similar to the baseline fear analyses, the effect of treatment condition on 6-week PDSS-C scores was significant among moderate avoidance youth, ( $B = 17.53$ ,  $SE = 4.69$ ,  $\beta = .86$ ,  $p = .01$ ), whereas there was no condition effect on 6-week PDSS-C scores among high avoidance youth ( $B = 1.75$ ,  $SE = 5.12$ ,  $\beta = .15$ ,  $p = .75$ ).

## Discussion

Intensive treatment formats may play a crucial role in the expansion of evidence-based treatment options for anxiety-disordered youth (Ollendick, 2014). Data on intensive treatment formats for adolescent PDA have been encouraging (Chase et al., 2012; Gallo et al., 2013; Pincus et al. 2015), but despite the great value of identifying treatment moderators

for informing patient-centered care (see Comer & Kendall, 2013; Kazdin, 2002), research has yet to evaluate which adolescents are most likely to benefit from this promising treatment format.

The present findings offer the first data-based portrait of presenting clinical characteristics in the context of response to intensive treatment for adolescent PDA. Within the present RCT, the main effect of intensive treatment on post-treatment panic symptoms was not uniform across participants. Indeed, treatment effects were moderated by the extent of baseline fear and avoidance, with treatment effects stronger among adolescents with more moderate, relative to higher, levels of fear and avoidance. These results suggest that data on baseline fear and avoidance can provide compelling prognostic information regarding the conditions under which intensive treatment for adolescent PDA is most effective.

Although significant moderators of treatment response were identified, contrary to hypotheses, more moderate levels of baseline fear and avoidance predicted more favorable outcome. All participating youth presented with elevated symptoms, but the present findings suggest that intensive treatment may be best suited for youth with more moderate, relative to severe, fear and avoidance patterns. Although intensive treatments are often recommended for more severe patients who have not responded to standard weekly treatment (e.g. Storch et al., 2007), the present data suggest that in the case of adolescent PDA, prescribing intensive treatments for severe cases may be somewhat misguided. It may be that for adolescents with relatively high fear and avoidance, asking them to confront their symptoms in the condensed span of eight days may be less productive than weekly treatment formats or medication management. In contrast, the present findings suggest that adolescents with moderate degrees of fear and avoidance benefit most from intensive treatment. Given the role of intensive approaches to help overcome barriers in the availability of expert care (see Comer & Barlow, 2014), it is encouraging that the more moderate cases, which constitute the majority of the adolescent PDA population, appear to be well served by intensive treatment alternatives to traditional weekly treatment formats.

The present analysis has several limitations. First, the study was conducted at an urban university-based outpatient clinic specializing in the treatment of anxiety disorders. As a result, although participants traveled from across the country, findings may not be fully representative of youth with PDA. Similarly, the sample was English-speaking, predominantly Caucasian, and of relatively high economic means. Given these limitations, future work is needed to examine cultural and socioeconomic variations in the extent to which fear and avoidance moderates treatment outcome. Second, many participants were concurrently taking psychotropic medications, which could have impacted symptom presentations and treatment response. However, as adolescents with PDA are five times more likely to be treated with antidepressants than adolescents without PDA, and are also more likely to be taking anxiolytic, mood stabilizing, or stimulant medications (Olfson, He, & Merikangas, 2012), restricting the trial to medication-naïve youth would have considerably limited the generalizability of findings. Third, although significant results were identified, the results of the present study may have been influenced by the sample size, and it is possible that a larger sample size may have yielded different results. Future work would do well to recruit larger sample sizes to increase the power to detect clinically significant



moderators of treatment outcome for youth receiving intensive CBT for PDA. Fourth, although fear and avoidance are conceptualized throughout the literature as related but distinct predictors of PDA presentation, it is possible that fear and avoidance as presently measured did not assess distinct symptom dimensions in the present study.

As the present trial utilized a waitlist control rather than an active treatment comparison, the extent to which baseline fear and avoidance specifically moderate intensive treatment formats, as opposed to all active treatments, remains unclear. Future controlled evaluations are needed in which youth are either (a) randomly assigned to intensive or weekly formats, or (b) randomly assigned to varying sequences of intensive and weekly formats (Barlow & Comer, 2013). Finally, although we examined baseline fear and avoidance, there are a number of features of PDA that could be considered when identifying diagnostic severity (e.g., intensity of physiological panic symptoms, reliance on safety behaviors). Future work may do well to consider other features of PDA that may additionally inform the identification of sub-populations of PDA youth who would benefit from intensive treatment.

Despite the development of well-tolerated, evidence-based treatments for children's mental health problems, serious gaps persist between treatment available in experimental settings and services broadly available in the community (Sandler et al., 2005). The present findings add to a growing body of literature suggesting that intensive treatment options at expert care facilities may be an important alternative to standard weekly care—particularly for youth presenting with more moderate severity—when local professional expertise is lacking (Comer & Barlow, 2014). Given the promising role that intensive treatment formats may play in the expansion of evidence-based care for youth, continued empirical efforts are needed to identify the benefits of intensive treatment options and to clarify for whom such formats are most effective.

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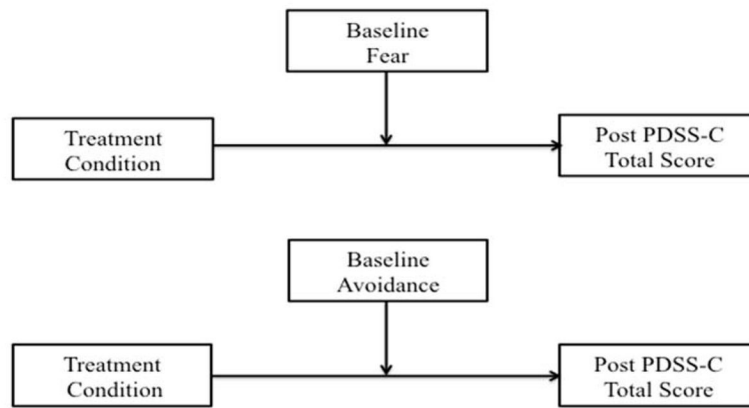
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### Key Practitioner Message

- Intensive cognitive behavioral therapy (CBT) has shown considerable efficacy in the treatment of adolescent panic disorder (PDA). However, it is important to clarify which patients are most likely to benefit from this approach.
- Considering the degree to which adolescents fear and avoid common situations and settings at baseline may inform whether a given adolescent will benefit from intensive treatment for PDA.
- Results indicate that adolescents with more moderate fear and avoidance at baseline may benefit most from intensive CBT.
- The present findings add to the literature suggesting that intensive treatment may be an important alternative to standard weekly care for many affected youth, particularly those presenting with more moderate severity.



**Figure 1.**  
Model of proposed moderators of panic disorder severity

**Table 1**

Baseline characteristics of participants, by condition (N =54)

	Total Sample		CBT Youth (N = 37)		WL Youth (N = 17)		Significance test
	N	%	N	%	N	%	
Female	33	61.1	22	59.5	11	64.7	$\chi^2 (1) = .14, p = .71$
Taking psychotropic medication	25	46.3	17	45.9	8	47.1	$\chi^2 (1) = .01, p = .94$
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	Significance test
Age, years	15.29	1.7	15.04	1.8	15.82	1.3	$t(52) = -1.62, p = .11$
Baseline # feared situations	6.42	4.2	6.70	4.2	5.82	4.5	$t(52) = .71, p = .48$
Baseline # avoided situations	5.46	3.8	5.62	3.6	5.12	4.2	$t(52) = .45, p = .66$
Baseline PDSS-C Total	13.46	5.25	13.82	5.5	12.77	4.8	$t(48) = .67, p = .51$

Note: CBT = Youth assigned to intensive cognitive-behavioral therapy; WL = Youth assigned to waitlist control; PDSS-C = Panic Disorder Severity Scale for Children

**Table 2**

Hierarchical regression examining moderating role of baseline feared situations in predicting treatment response (N = 54)

Variable Entered	<i>B</i>	<i>SE(B)</i>	$\beta$	<i>t</i>
Step 1.				
Treatment condition (CBT vs. WL)	6.62	1.95	.49	3.39**
Step 2.				
Treatment Condition	6.47	2.05	.48	3.16**
Baseline Fear	-.07	.23	-.05	-.30
Step 3.				
Treatment Condition	5.91	1.97	.44	3.01**
Baseline Fear	1.27	.66	.83	1.92
Treatment Condition $\times$ Baseline Fear	-.97	.45	-.94	-2.15*

Note:

\*  $p < .05$ ,

\*\*  $p < .01$

**Table 3**

Hierarchical regression examining moderating role of baseline avoided situations in predicting treatment response (N = 54)

Variable Entered	<i>B</i>	<i>SE(B)</i>	$\beta$	<i>t</i>
Step 1.				
Treatment condition (CBT vs. WL)	6.62	1.95	.49	3.39**
Step 2.				
Treatment Condition	6.52	2.01	.48	3.24**
Baseline Avoidance	-.07	.26	-.04	-.26
Step 3.				
Treatment Condition	6.41	2.00	.47	3.38**
Baseline Avoidance	1.59	.75	.92	2.13*
Treatment Condition $\times$ Baseline Avoidance	-1.14	.49	-1.01	-2.35*

Note:

\*  $p < .05$ ,

\*\*  $p < .01$