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The Role of Safety Behaviors in Panic Disorder Treatment: Self-Regulation or Self-Defeat?

Katie Aafjes-van Doorn^{1,6} · Sigal Zilcha-Mano² · Kathryn Graham³ · Alyson Caldari³ · Jacques P. Barber³ · Dianne L. Chambless⁴ · Barbara Milrod⁵

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Abstract

Safety behaviors (SBs) are generally perceived as ‘dysfunctional’ emotion-regulation strategies that reduce physical symptoms and prevent unrealistic feared consequences of panic attacks. However, it is unclear whether all types of SBs are a hindrance or whether some may promote self-regulation in treatment. We propose that the type of SBs might explain some of the variability between panic disorder (PD) patients, and might help to predict why treatment is more successful for some than for others. In this secondary analysis of a subsample of 65 PD patients who received Cognitive Behavioral Therapy in a two-site randomized controlled trial, we examined the associations between type of SB and pre-treatment characteristics and their predictive value on trajectories of change in treatment process and outcome (panic symptoms, interpersonal problems, alliance). An observer-rating system for five types of SBs (avoidance/distraction/control-function and object/people-focus) was developed and applied to videotaped early treatment sessions, with high reliability. Patients with higher levels of people-focused SBs reported higher levels of panic symptoms pre-treatment at both treatment sites. These people-focused SBs predicted poorer treatment response on panic symptoms at one of two sites. Avoidance, control, or distraction-function and object-focused SBs were not associated with treatment process or outcomes. People-focused SBs may worsen PD symptoms, and possibly slow treatment progress, although this latter finding was not consistent across sites. This study differentiated between types of SBs and identified people-focused SBs as possible predictor of symptom change in CBT for PD—potentially relevant for efforts to improve treatment response.

Keywords Safety behaviors · Self-regulation · Panic disorder treatment · Alliance

Panic disorder (PD) is an anxiety disorder characterized by recurrence of unexpected panic attacks, in which an intense fear accompanied by a series of bodily and/or cognitive

symptoms develops abruptly, without an apparent external cause (American Psychiatric Association 2013). The cognitive theory of PD proposes that panic attacks occur as a result of an enduring tendency to misinterpret bodily sensations as a sign of imminent catastrophe such as a heart attack. Such catastrophic cognitions escalate the cycle wherein bodily sensations lead to panic, and persist due to PD patients’ tendency to avoid and/or escape situations in which panic occurs (Salkovskis et al. 1996). Panic disorder is common, with life-time prevalence of 3.7% (Kessler et al. 2006) and is associated with a poor of quality of life (e.g. Barrera and Norton 2009), and interpersonal difficulties and distress (e.g. Scocco et al. 2007). PD patients may present with agoraphobia and feel in need of the presence of another person for survival, resulting in a change in routines, decline in work performance and strained social relationships. Moreover, PD patients’ anxious attachment style

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and high separation anxiety likely compromise the ability to modulate stress with social supports (Milrod et al. 2014).

Although Cognitive-Behavioral Therapy (CBT) is reportedly the most efficacious psychotherapy for PD (Pompoli et al. 2016), approximately 40% of PD patients do not respond (Loerinc et al. 2015). Identifying sources of heterogeneity in PD patients might help in understanding how and for whom CBT might be most effective and guide treatment selection and tailoring. In addition to the therapeutic alliance, which has been shown to predict better outcome in CBT (e.g. Haug et al. 2016), a small number of studies on prognostic factors as outcome predictors in PD suggests that higher levels of pretreatment agoraphobic avoidance, depression, lower expectancy of change, and high levels of functional impairment predict a diminished response to CBT (see Porter and Chambless 2015 for a review). We hypothesized that the type of patients' SBs (their function and focus) might explain variability between patients with PD, and might also predict why CBT for PD is more successful for some than for others.

Safety Behaviors

Safety behaviors are unnecessary actions taken to prevent, escape from, or reduce the severity of a perceived threat (Telch and Lancaster 2012; Helbig-Lang and Petermann 2010). People with PD might use combinations of different types of idiosyncratic SBs that match their catastrophic cognitions (Salkovskis et al. 1999). For example, a PD patient might have a fear of losing control of his vehicle while driving, and then avoid driving or require a friend to be in the car.

Safety Behaviors as Hindrance

At first blush, SBs appear to be adaptive because they mitigate anxiety; however, SBs may actually be harmful in the long term (Blakey and Abramowitz 2016). In addition to misattribution of safety to the behavior, SBs prevent the occurrence of disconfirming learning experiences and impede extinction (Blakey and Abramowitz 2016). For example, by sitting down, the PD patient never experiences that he would not have fainted had he remained standing. Support for the argument that SBs may be a hindrance comes from theories on emotional processing (e.g., Foa and Kozak 1986), and information processing (Richards et al. 2014) that suggest that SBs promote safety misattributions, attenuate negative expectancy violation, contextualize inhibitory learning, and dampen distress tolerance. Moreover, research consistently implicates SBs in the development and maintenance of anxiety disorders (Helbig-Lang and Petermann 2010).

Patients' use of SBs in daily life and during treatment is seen as a barrier to symptom reduction that undermines the effectiveness of CBT (e.g., Craske et al. 2006, p. 83; Wolf and Goldfried 2014), and has been shown to be harmful especially during exposure exercises (Helbig-Lang et al. 2014; Salkovskis et al. 1999). Some patients may come to therapy with rigid and dysfunctional interpersonal coping strategies (e.g., avoidance of people or extreme dependence) that interfere with the establishment of a strong working alliance (Scocco et al. 2007). In turn, therapists can feel frustrated when patients are unwilling to give up their SBs (Chambless et al. 2010; Zalaznik et al. 2016). Therapists help patients realize that they are at little risk for danger even if they do not engage in SBs, and help them to process their exposures (Korte et al. 2018). In the context of CBT, patients might initially use SBs or therapists might serve as a safety signal themselves, but then encourage patients to eventually eliminate SBs (e.g., Craske and Barlow 2008).

Safety Behaviors as Self-Regulation

In contrast to the hindrance hypothesis, some have argued that despite their link with psychopathology, SBs might not be detrimental in treatment (Goodson and Haefel 2018). SBs may serve as helpful coping strategies to enhance the person's perception of control over the environment and the potential threat (Hofmann and Hay 2018) and to regulate the somatic stress response (Hamm et al. 2016). This attempt at self-regulation may be useful in treatment, not only in tolerating the anxiety provoked in exposure tasks, but also because many PD patients are fearful of establishing an alliance with the therapist (Chambless et al. 2010; 1997). Advocates of the judicious use of SBs in treatment (i.e. careful use of SBs for a limited period in the early stages of treatment initiated by the patient or by the therapist to help overcome barriers to exposures) highlight positive consequences, such as enhanced treatment acceptability, approach behavior, sense of mastery and self-efficacy (e.g., Deacon et al. 2010; Levy and Radomsky 2014; Rachman et al. 2008). In support of this self-regulation hypothesis, recent empirical treatment studies have shown that SBs may not interfere with emotional and cognitive changes during treatment and can even enhance treatment outcomes (Deacon et al. 2010; Hood et al. 2010; Milosevic and Radomsky 2008; Sy et al. 2011), and that SB use during everyday life is related to greater symptom reduction after PD treatment (Helbig-Lang et al. 2014). Overall, these discrepant conceptualization of SBs and mixed empirical findings (for a review, see Meulders et al. 2016), reflect the complexities in defining maladaptive SBs and distinguishing them from coping. In order to disentangle the hindering and self-regulating effects of SBs on PD treatment outcome within a CBT framework, in which behaviors are highlighted, it might be important to explore

the specific types of SBs in more detail (e.g., Blakey and Abramowitz 2016). In contrast to SBs that function as avoidance and may hinder treatment, other more 'restorative' SBs may serve to dampen excessive anxiety and facilitate a sense of safety and self-regulation in treatment (e.g., Goodson and Haefffel 2018).

Measuring Safety Behaviors in Panic Disorder

Given the potential importance of SBs in the etiology and treatment of PD, it is surprising that there are so few validated measures (see Telch and Lancaster 2012 for a review on SB measures). Three measures of panic specific SBs exist (Borden et al. 1988; Funayama et al. 2013; Kamphuis and Telch 1998). Using these measures, previous studies examined the self-reported frequency of SBs in daily life as PD treatment outcome (e.g., Manjula et al. 2009), or in-session use of SBs during exposure therapy (e.g. Funayama et al. 2013). Self-report measures like these arguably have limited validity. Patients might under-report their SBs due to social desirability or unfamiliarity with the term 'SB,' or might not identify with the limited examples provided on a pre-designed questionnaire or they are not immediately aware of them. Moreover, instead of categorizing SBs based on a topological description of behavior it is important to understand their idiosyncratic functions for the individual (Thwaites and Freeston 2005). To address these limitations, we developed an observer-rating system of types of SBs used in the patient's life that are described by the patient or therapist in treatment.

Aims

The aims of this study were: (1) to develop an observer-rated measure of types of SBs to examine the patterns that underlie PD patients' idiosyncratic SBs, (2) to test SBs' associations with pre-treatment characteristics and their predictive value on trajectories of change in CBT process and outcome (PD symptoms, interpersonal problems, and alliance).

Methods

Patients

The present study is a secondary analysis of data from a randomized controlled trial (RCT) by Milrod et al. (2016) comparing CBT, panic focused psychodynamic psychotherapy (PFPP), and applied relaxation training (ART) among patients with primary DSM-IV PD with or without agoraphobia. The study is registered with ClinicalTrials.gov (NCT00353470) and was approved by the institutional review boards of both sites. Patients were recruited at two

sites: Weill-Cornell Medical College ("Cornell") and University of Pennsylvania ("Penn") and given written informed consent. Treatment was provided gratis and took place twice weekly for 12 weeks. Therapists had, on average, 13 years of post-degree experience and at least one year of experience with PD. The CBT treatment produced a 63% overall response rate. For a detailed report of study outcomes, see Milrod et al. (2016).

Specifically, we focus on a subsample of 65 patients of the 81 patients randomized to CBT in the RCT who had available pre-treatment baseline data and an available video-recording of an early treatment session (2nd session week 1). This 2nd session was deemed early enough in treatment to be uninfluenced by a possible treatment effect. The CBT manual guides therapists to use this 2nd session to assess the patients' SBs and other coping strategies. Therefore, we could expect that the therapist would introduce the topic of SB and that the patient would have the opportunity to share examples of different types of SBs. Only the CBT patients were included in this pilot study because the CBT treatment for PD specifically focuses on SBs while the other therapies in the RCT do not.

Excluded patients did not differ from the 65 included patients on gender, age, agoraphobia, ethnicity, or baseline panic severity (all $ps > .20$). Of these 65 PD patients, 36 were treated at Cornell, and 29 were treated at Penn. In line with the original RCT treatment outcomes, this subsample of 65 patients showed a significant improvement of panic symptoms [$F(2.744, 123.478) = 71.128, p < .0001$] and of interpersonal problems [$F(2, 58) = 19.974, p < .0001$] and no change in alliance [$F(1.497, 41.924) = 1.015, p = .351$] across treatment. There were no differences between the two sites on change in alliance [$F(1.527, 41.226) = 1.545, p = .226$], or interpersonal functioning [$F(2, 56) = 1.722, p = .188$] during treatment. However, the level of panic symptoms showed a significant site difference [$F(2.905, 127.807) = 3.496, p = .019$], indicating a higher score for Penn at baseline, $t(63) = 2.853, p < .006$. Most patients were diagnosed with comorbid Agoraphobia ($n = 52; 80%$), and 23 patients had a comorbid diagnosis of Major Depressive Disorder (35.4%). The mean age was 39 ($SD = 13$), 38 patients were male (58.5%), 42 self-identified as White/Caucasian (64.6%), 17 as African American (26.2%), 5 as Asian (7.7%), and 1 as "other".

Treatment

Therapists in the CBT arm followed the panic control therapy protocol (Barlow et al. 2000), as modified to fit the 24-session, 45-min per session format of the RCT. Following the first introductory educational session, in the second session, the therapist is instructed to ask patients to elaborate on their experience of PD and their coping strategies, and to

help patients to identify their SBs. The CBT sessions were highly structured, and included psychoeducation about anxiety and panic; identification and correction of maladaptive thoughts about panic; training in diaphragmatic breathing; and in-session exposure to bodily sensations designed to mimic those experienced during panic (interoceptive exposure). All sessions were followed by homework assignments. In vivo exposure via homework assignments was introduced at session 17 for those with significant agoraphobic avoidance, and session 24 focused on review and relapse prevention.

Outcome Measures

Panic Symptoms

The Panic Disorder Severity Scale (PDSS; Shear et al. 1997) provides a composite severity score of frequency, distress, and impairment associated with panic attacks (Houck et al. 2002), based on 7 items, scored from 0 (none) to 4 (extreme). The PDSS demonstrated good reliability and validity (Shear et al. 1997). In the RCT, the PDSS was used as primary outcome measure, and was assessed by trained diagnosticians, with excellent interrater reliability (ICC [2,1] = .95) at baseline (week 0), early treatment (week 1), mid-treatment (week 5), late-treatment (week 9), and at termination (week 12).

Interpersonal Problems

The Inventory of Interpersonal Problems-Circumplex Scales (IIP-64; Horowitz et al. 2000) is a 64-item self-report questionnaire of interpersonal difficulties and distress. Patients rate interpersonal behaviors that are “hard for you to do” (e.g., “it is hard for me to let other people know when I am angry”) and that “you do too much” (e.g., “I am too afraid of other people”) on a 5-point scale, ranging from 0 (not at all) to 4 (extremely). The IIP-64 has demonstrated good psychometric properties and sensitivity to change in psychotherapy (e.g. Ruiz et al. 2004). The IIP-64 was one

of the secondary outcome measures in the RCT, and was assessed at baseline (week 0), mid treatment (week 5) and at termination (week 12).

Working Alliance

The Working Alliance Index-Short Form (WAI-SF; Tracey and Kokotovic 1989) is a 12-item patient self-report scale used to assess the therapeutic relationship. Each item is rated on a 1 (never) to 7 (always) Likert scale. In the RCT, the WAI-SF was administered early treatment (week 1), mid-treatment (week 5) and late-treatment (week 9). In the current study the internal reliability for the three time points was .91–.94.

Safety Behavior Measure

Development of the Safety Behavior Scale

A detailed observer-rating system of SBs was developed to get a general sense of the type of SB that is typical for each patient. The two developers of this coding system were licensed clinical psychologists with over 10 years of clinical experience. They relied on definitions of SBs more generally provided in the clinical literature: “Safety behaviors are unnecessary actions taken to prevent, escape from, or reduce the severity of a perceived threat (Telch and Lancaster 2012) that are maintained by negative reinforcement (Helbig-Lang and Petermann 2010).”

Based on a random sample of 15 videotapes of PD treatment sessions, specific types of SBs were extracted from the clinical data (data-driven), that repeated themselves across different individuals and thus served as our rating categories. Five categories were identified (as outlined in Table 1); three function categories (the specific function of the SB) and two focus categories (the specific focus of the SB). The two developers relied on their clinical expertise and reached consensus about which SBs belonged in which category. Examples of SBs and their assigned category of

Table 1 Summary of the observer-rating manual of safety behaviors

Types of safety behaviors	
Function	
Avoidance	<i>Avoidance</i> of feelings, sensations, situations or locations (e.g. no caffeine, no parties, not getting out of breath, no exercise, no arguments with partner)
Distraction	<i>Distraction</i> or doing things to not think about the anxious situation (e.g. keeping busy, listening to music/talking to people)
Control	<i>Gaining control</i> to avoid catastrophe (e.g. acquisition/taking things like water bottle/pills/money or checking the location of hospitals/exits)
Focus	
People	<i>People</i> focused on affiliation (e.g. ask for support or reassurance, talk to people)
Object	<i>Object</i> focused on things (e.g. lucky charms, places, exit)

SB focus and function, include: Avoid drinking caffeine due to fear of palpitation (Avoidance-function SB); Reading a book when feeling overwhelmed in the subway (Distraction-function SB); Drinking alcohol to reduce anxiety in public situations (Control-function SBs); Seeking reassurance from loved ones to ensure that the fears are unwarranted (People-focused SB); Wearing a lucky charm (Object-focused SB);

Function

Patients' SBs tended to serve one of three functions: (1) direct avoidance of certain feelings, situations, sensations (e.g., getting out of breath, caffeine), or escape to a 'safe' area; (2) distraction by doing other things to not think about the anxious situation (e.g., listening to music, keeping busy, talking to people). Distraction may be used to avoid confronting phobic objects or reactions or as a tool to demonstrate that one can elect to divert attention away from the phobic object without placing oneself at risk (Craske et al. 2006, p. 42); or (3) gaining control over negative emotional and bodily reactions by the acquisition of things or subtle behaviors (e.g., sitting near the exit, bringing a water bottle) to prevent a feared catastrophe (Craske and Barlow 2008). These three SB functions are similar to previously identified categories in self-report measures of SBs in PD patients (e.g., subtle preventative behaviors, avoidance, and escape; Salkovskis et al. 1996; avoidance, distraction, escape, and use of a companion; Helbig-Lang et al. 2014; Kamphuis and Telch 1998).

Focus

Idiosyncratic SBs varied in generating dependence upon people or objects. Whereas some patients attributed the absence of harm to other people (e.g. "I did not lose control of the car because my husband was with me"), others attributed their current safety to objects (e.g. lucky charms). Arguably, the absence or presence of interpersonal focus (also identified by Craske et al. 2006) might be relevant to the interpersonal difficulties and distress associated with PD, as well as the interpersonal nature of the alliance in psychotherapy.

We measured the presence, rather than the frequency of each of these five SB categories. A score of 0, 1 or 2 was given for each of the five SB categories; 0 = no implicit or explicit reporting of this category appears to be present; 1 = 1 SB example in this category is discussed or is implicitly reported; 2 = at least 2 distinct examples of this category of SBs are clearly present in patient's life. These ratings thus reflect past and current behaviors in the patient's life in and outside the session, discussed by patient or therapist. Different SB categories might overlap, in that a SB example could be coded within a function category and a focus category

at the same time (e.g., compulsively bringing a cell phone/money may be object-focused & have a control-function; talking to strangers may be people focused & have a distraction function). Please contact the first author for a more detailed SB observer-coding manual.

Training Procedures

Two raters (psychology undergraduates who worked as research assistants) were trained in the identification of PD-related SBs within videotaped treatment sessions during a one-day workshop. The main premise for the raters was to be able to first identify SBs in psychotherapy process, and then gain agreement as to which category and how much (i.e., degree) certain types of SBs were discussed. The raters were unaware of study hypotheses, patients' baseline characteristics and treatment outcomes. The raters read selected clinical papers on SBs in anxiety disorders as well as the developed coding manual prior to the initial training. The first and second author, the developers of the rating system who were experienced in the identification of SBs, coded the sessions of the first 15 patients to determine expert ratings. Then together with the first author, the raters watched these initial 15 sessions, stopped the tape and talked through their scoring decisions after each session. Scoring discrepancies across SB categories were identified and closely examined.

Following this initial training phase, both raters completed the ratings for each of the remaining 50 CBT patients in this PD sample, individually. On the few occasions (four times in total) that their ratings were discrepant, the first author also reviewed the video-recording and consensus was reached among the three raters to determine the final rating for that session. In line with psychotherapy process coding recommendations (Stein et al. 2010), the two raters rated around three tapes per week for 16 weeks, and regular group meetings with the first author were held every 4 weeks to examine any systematic inconsistencies in ratings and address issues of rater drift. Subsequent interrater reliabilities were calculated based on the raters' scores on all 65 tapes. The consensus ratings per session were used as final ratings in the reported analyses.

Analyses

Correlations and group comparison analyses were conducted using SPSS 24.0 (IBM Corp 2016) and multi-level modeling was done with SAS version 9.4 (Littell et al. 2007). The SB categories were not normally distributed (skewness and kurtosis more than twice the standard error), therefore non-parametric tests were used in subsequent analyses. We adjusted *p* values using the Benjamini–Hochberg correction (which yields more power than the traditional Bonferroni correction that controls for family-wise error; Benjamini

and Hochberg 1995) to control for the false discovery rate of multiple correlations at an alpha of .05. Each calculated adjusted p value is unique to an individual analysis, and thus individually reported. Two-tailed tests of significance were applied throughout, in line with the exploratory nature and non-directional hypotheses in this study. Due to a site-by-treatment interaction reported in the primary outcome paper (Milrod et al. 2016), as well as the differences in panic symptoms at baseline in our subsample of 65 CBT patients, we examined whether the SB scores interacted with site to predict outcomes. The use of an existing dataset and observer-ratings meant that there were no missing SB scores.

Sample sizes for correlations that involved outcome data, ranged from 51 to 65, due to participant or interviewer error in collecting treatment data. Little's MCAR test (1988) showed that the missing longitudinal data were missing at random, $\chi^2(25, N = 65) = 33.10, p = .129$.

Power Analysis

Based on prior research (e.g., Goodson and Haefel 2018), we expected a moderate effect of SBs on therapy outcomes. With an estimated power of .80, and alpha of .05, the multi-level regression analysis was able to detect a moderate effect (Cohen's f^2 of .18).

Results

Psychometrics of Safety Behavior Rating System

Table 2 shows the frequencies of ratings and intraclass correlation (ICC) estimates with two raters across 65 ratings, calculated based on a mean-rating ($k = 2$), absolute-agreement, 2-way random-effects model. The ICCs ranged from .91 to .98, with all ICC ($2, 2$) $> .91$, indicating excellent reliability (Shrout and Fleiss 1979). Avoidance-function SBs were negatively correlated with distraction-function SBs ($rs(63) = -.260; p = .036$). Object-focused SBs were positively related to control-function SBs ($rs(63) = .347;$

$p = .005$). The other SB categories were not significantly associated with each other (all p 's $> .379$).

Safety Behaviors and Baseline Characteristics

There was no significance difference in SB ratings for patients with different pre-treatment characteristics, including patient or therapist gender, race, income, educational level, marital status, or employment (all $ps > .071$). Patients with or without Agoraphobia (all $ps > .264$) and with or without comorbid MDD (all $ps > .679$) did not differ in terms of SBs. However, Mann–Whitney U-tests showed that there was a significant effect of treatment site, with higher levels of control-function SBs at Penn [$U(63) = 288, z = -3.31, p = .001$] and higher levels of object-focused SBs at Cornell [$U(63) = 359, z = -2.48, p = .013$]. The other three SB categories were not significantly different at the two treatment sites (all $ps > .075$).

Partial correlation coefficients with treatment site as covariate variable, were conducted for the five SB categories measured at session 2 (week 1) with baseline symptom levels on the PDSS (week 0) and IIP-64 (week 0) and ratings of alliance (week 1). Patients who reported using people-focused SB strategies to cope with their panic symptoms showed a higher level of panic symptoms on the PDSS at baseline [$rs(62) = .408; p = .001$, critical adjusted $p = .002$]. The other SB categories were not associated with baseline panic symptoms. None of the SB categories were related to scores on the IIP-64 at baseline (all $ps > .153$) or alliance ratings in week one (all $ps > .473$).

Safety Behaviors and Trajectories of Change

The data were hierarchically nested on three levels: Assessments nested within patients nested within therapists. To account for the correlation between within-patient session observations and observations from patients of the same therapist, we added both the random intercept and random slope of time of patients nested within therapists, and the random intercept of therapists to the model using the SAS

Table 2 Mean scores and intra class correlations of the five safety behavior categories

Safety behavior category	Mean (SD)	n (%) Score 0	n (%) Score 1	n (%) Score 2	ICC
Function					
Avoidance	1.46 (.81)	13 (17%)	9 (12%)	43 (55%)	.976
Distraction	1.09 (.81)	18 (23%)	23 (30%)	24 (31%)	.960
Control	.82 (.79)	29 (37%)	19 (24%)	17 (22%)	.925
Focus					
People	.60 (.75)	36 (46%)	19 (24%)	10 (13%)	.907
Object	.55 (.77)	40(52%)	14 (18%)	11 (14%)	.945

ICC intra class correlations

PROC MIXED procedure for multilevel modeling (Littell et al. 2007). Analyses were conducted within a three-level hierarchically nested model and were controlled for baseline levels of PDSS, IIP, or WAI respectively. One predictor (people-focused SBs) was correlated with PDSS baseline scores, thus risking a spurious relationship with slope because of the steeper slope evinced by patients who started with higher PDSS scores. To reduce the likelihood of artefactual findings, we regressed this predictor on baseline PDSS scores and used residualized predictor variables.

To investigate the moderating effect of site on the association between SBs and individual trajectories of change in PDSS, IIP and WAI we conducted a series of two models for each of these three variables: the first model including two 3-way interaction effects of site by week by people-focused SBs and of site by week by object-focused SBs. The second model included three 3-way interaction effects of site by week by avoidance-function SB, of site by week by distraction-function SBs, and of site by week by control-function SBs. These two models were repeated for each of the three variables (PDSS, IIP, & WAI), resulting in six multilevel models in total. The only significant interaction was of site by week by people-focused SBs for the PDSS, $F(1275) = 12.96$, $p = .0004$ and suggests that people-focused SBs can predict the trajectory of change in PDSS at Penn ($\beta = .04$, S.E. = .01, $t = 2.70$, $p = .009$) but not at Cornell ($\beta = -.02$, S.E. = .01, $t = -1.45$, $p = .15$). Thus, at Penn, patients who reported people-focused SBs had worse outcomes on the PDSS than those who did not.

Discussion

We hypothesized that SBs were a potential factor to explain heterogeneity among PD patients treated with CBT. In this study, we aimed to: 1) Develop an observer-rated measure that assesses types of idiosyncratic SBs present in the patient's life; and 2) Test SBs' associations with pre-treatment characteristics and with the trajectories of change in CBT process and outcome (PD symptoms, interpersonal problems, alliance).

First, we identified five broad SB categories from a dataset of PD patients; SBs that serve the *function* of avoidance, distraction, or control, and SBs that *focus* on other people or on objects. These SB categories resembled previously identified categories in self-report measures of SBs in PD patients (e.g., Craske et al. 2006; Helbig-Lang et al. 2014; Salkovskis et al. 1996). An observer coding manual based on these categories was developed. Videos of early sessions in a manualized CBT treatment of 65 PD patients were coded by two independent raters. The excellent interrater reliability suggests that SBs might be identifiable early in treatment by trained observers. Avoidance-function SBs

and distraction-function SBs were negatively related with one another in this sample. The fact that object-focused SBs were positively related to control-function was unsurprising given that patients with PD frequently use objects to gain a sense of control over a feared consequence (Craske et al. 2006). This newly developed SB observer rating system is innovative, in that it examines patients' underlying pattern of types of idiosyncratic SBs rather than frequency of SBs per se. Also, it might be a good teaching tool for students and supervisees because it can be applied to video-recorded therapy sessions. Another advantage of this SB rating system is that it is data driven ("bottom up") in that the categories are based on what PD patients reported rather than a priori assumptions about categories proposed by theorists.

Second, SBs' associations with baseline characteristics suggested that patients with more severe panic symptoms reported higher levels of people-focused SBs to cope with their panic symptoms. It is possible that the more severely ill patients had more need for SBs to cope; alternatively that these SBs were a hindrance, rather than a facilitative self-regulation tool (Goodson and Haeffel 2018). Although these correlations cannot clarify causality, these findings are congruent with previous findings from the three self-report measures of SBs (e.g., (Funayama et al. 2013; Helbig-Lang et al. 2014; Kamphuis and Telch 1998), adding to the validity of the observer rating system.

Additionally, in further support of a hampering effect, we found that high levels of people-focused SBs predicted worst trajectories of change in PD symptoms over treatment in one of the two treatment sites. More specifically patients who used higher levels of people-focused SBs improved at a slower rate at Penn but not at Cornell. These interaction effects might reflect unidentified patient variables or other, as yet unmeasured, site or population differences. It is unlikely that the relatively lower level of education reported by patients at Penn was responsible for a slower rate of improvement, because education level was not significantly related to people-focused SBs. Also, in the original outcome study, outcome analyses revealed site-by-treatment interactions in speed of PDSS change over time ($p = .013$) (Milrod et al. 2016). In our subsample, people-focused SBs were correlated with initial panic disorder severity on the PDSS, which was higher at the Penn site. However, this is unlikely to account for the observed interaction because we controlled for initial panic disorder severity in our analyses. Alternatively, given the large number of analyses and relatively small samples per site, the site difference might reflect a Type I error.

Our findings suggest that people-focused SB use in daily life, as identified in an early treatment session, may potentially hinder the progress in CBT for PD, leading to slower symptom reduction during treatment. The patients' absence or presence of an interpersonal focus (also identified by

Craske et al. 2006) might be relevant to the interpersonal difficulties and distress associated with PD (e.g., strained social relationships, anxious attachment style and high separation anxiety; Milrod et al. 2014), as well as the interpersonal nature of psychotherapy. It is possible that others reinforce the patients' SBs and hence their symptoms, and that during treatment, these people-focused SB undermine exposure tasks conducted in between sessions treatment. For example, in the case of obsessive-compulsive disorder, Amir et al. (2000) showed that relatives' accommodation of patients' symptoms was related to poorer treatment outcome.

Overall, our exploratory findings are most congruent with the hindrance hypothesis (i.e., seen as barriers to symptom reduction that undermine the effectiveness of CBT; Craske et al. 2006, p. 83; Wolf and Goldfried 2014) and are in line with other empirical studies that identified SB use during everyday life (using self-report measures) as barriers to symptom reduction that undermine the CBT treatment (Helbig-Lang et al. 2014; Salkovskis et al. 1999). Notably, these tentative results fit with the current clinical CBT guidelines for PD, which encourage patients to eliminate SBs (e.g. Craske and Barlow 2008). However, given that we obtained these effects only at one site, conclusions cannot be made.

Limitations and Future Research

Several limitations with this set of exploratory analyses should be kept in mind when interpreting our preliminary data. Safety behaviors were assessed in the first week of therapy. It cannot be ruled out that information provided during the intake procedures or first session might have changed patients' appraisals of their behavior. In this second treatment session, the therapist specifically inquired about the patients' SBs and other helpful and unhelpful coping strategies. It is possible that different types of SBs might have come up at other sessions, however, there was no way of predicting when a given patient-therapist dyad would discuss SBs at subsequent sessions. This highlights a potential limitation to this method.

Also, our observer ratings of SBs reflected SB use at the beginning of treatment and, although frequent SB use in daily life is associated with SB use during exposure exercises (see Helbig-Lang et al. 2014), it is unclear whether the patients actually experienced hindrances in their CBT treatment. Similarly, this method of assessing SBs focuses on the presence of SBs more generally, rather than the frequency of use of various SBs. It is possible that the frequency of its use is related to treatment outcome. Frequency of SB use might be more appropriately assessed using self-report or interview methods. Another limitation of this observer-rated method is its time-consuming nature, which limits its use in clinical practice. This SB observer-coding system was developed specifically for this sample of PD patients

in CBT treatment and, so far, has only been used in this pilot study. The CBT based protocol itself might have influenced the way therapists initiated the topic of SBs and the type of responses and examples elicited and thus might have shaped the development of the categories in the rating system. Therefore, more research is needed to establish its validity and reliability in different patient samples and treatments. To increase its construct validity, it will be important to relate scores on other existing self-report measures of SBs with this observer-rated measure within the same sample and same therapy session. Our observer-rated method adds the benefit of therapist guidance and clarification. However, it still relies on patients' self-reports of their experiences and does not eliminate the possibility of patients' misunderstanding SBs or misrepresenting their use of them. This should be noted. Content validity could be improved by sharing this measure with experts in the field of SBs for people with PD, asking them for feedback in order to revise it. Although the authors strived to truly let the data guide the development of the SB coding system, it is likely that the authors also had SB categories and definitions from the existing literature in mind to some extent when determining the SB categories for this observer rated coding system. Assessment of interrater reliability among new groups of trained raters will improve its usefulness as research tool. Future studies should add to the knowledge gained from this study, in order to increase replicability of the SB codings. For example, systematic qualitative methods, like Consensual Qualitative Research (CQR; Hill 2012) that uses a larger team of collaborators, who work together to reach consensus, could ensure that they draw similar conclusions from the data.

Finally, the study findings were limited by the small sample size with limited power. Future research into the change of SBs during treatment could, for example, indicate whether PD patients still cling to SBs later in treatment and whether people-focused SBs change when exposure exercises become a more prominent part of treatment (Craske et al. 2006). Future research into predictors of treatment outcome could have considerable clinical utility (Porter and Chambless 2015). If predictors turn out to be unrelated to treatment outcome, this information may increase therapists' confidence in their patients' ability to change. Likewise, the identification of predictors of poorer outcome (e.g., people-focused SBs at one site) could be used to refine treatments to improve their efficacy. Identified predictors are candidates for potential moderators to be examined in future studies that compare symptom improvement in CBT to other PD treatments (Porter and Chambless 2015).

In sum, this study examined the unique effects of different types of safety-seeking behaviors in PD, not just as unhelpful patterns that reflect the patient's level of suffering, but also as a possible hindering factor in CBT treatment. In particular, we identified people-focused SBs as a possible

additional predictor of slower CBT treatment progress for PD at one of two treatment sites. If our findings are replicated in larger-scale studies in the future, this could suggest that patient's level of people-focused SBs might be more important to consider than other types of SBs and could be systematically assessed and addressed throughout treatment to maximize PD symptom improvements (Blakey and Abramowitz 2016).

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Compliance with Ethical Standards

Conflict of interest All authors declare that they have no conflicts of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of retrospective study formal consent is not required.

Informed Consent Informed consent was obtained from all participants included in the study.

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