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RESEARCH ARTICLE

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What is the effect on comorbid personality disorder of brief panic-focused psychotherapy in patients with panic disorder?

John R. Keefe MA[1] | Barbara L. Milrod MD[2] | Robert Gallop PhD[3] | Jacques P. Barber PhD[4] | Dianne L. Chambless PhD[1]

[1]Department of Psychology, University of Pennsylvania, Philadelphia, PA, USA

[2]Department of Psychiatry, Weill Cornell Medical College, New York, NY, USA

[3]Department of Mathematics, West Chester University, West Chester, PA, USA

[4]Derner Institute of Advanced Psychological Studies, Adelphi University, Garden City, NY, USA

Correspondence
John R. Keefe, Department of Psychology, University of Pennsylvania, 425 S. University Avenue, Levin Building, 4th Floor, Philadelphia, PA 19104, USA.
Email: jack.keefe@gmail.com; jkeefe@sas.upenn.edu

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Background: No studies of psychotherapies for panic disorder (PD) have examined effects on comorbid personality disorders (PersD), yet half such patients have a PersD.

Methods: In a randomized trial for PD with and without agoraphobia comparing Cognitive-Behavioral Therapy (CBT) and Panic-Focused Psychodynamic Psychotherapy (PFPP), PersD was assessed pre-to-post treatment with the Structured Clinical Interview for the Diagnosis of Axis-II Disorders (SCID-II). For patients completing therapy ($n = 118$, 54 with PersD), covariance between panic and SCID-II criteria improvements was analyzed. SCID-II diagnostic remission and recovery were evaluated. Comparative efficacy of PFPP versus CBT for improving PersD was analyzed both for the average patient, and as a function of PersD severity.

Results: 37 and 17% of PersD patients experienced diagnostic PersD remission and recovery, respectively. Larger reductions in PersD were related to more panic improvement, with a modest effect size ($r = 0.28$). Although there was no difference between treatments in their ability to improve PersD for the average patient ($d = 0.01$), patients meeting more PersD criteria did better in PFPP compared to CBT ($P = .007$), with PFPP being significantly superior at 11 criteria and above ($d = 0.66$; 3 more criteria lost).

Conclusions: PersD presenting in the context of primary PD rarely resolves during psychotherapies focused on PD, and change in PersD only moderately tracks panic improvements, indicating non-overlap of the constructs. Patients receiving panic-focused psychotherapies may require additional treatment for their PersD. PFPP may be superior at improving severe PersD, but replication of this finding is required.

KEYWORDS
CBT, clinical trials, empirically supported treatments, panic attacks/agoraphobia, personality disorder, psychoanalytic/psychodynamic

1 | INTRODUCTION

Personality disorders (PersD) are common comorbidities in panic disorder (PD): roughly 50% of panic patients carry a PersD diagnosis, most often Cluster C (Friborg, Martinussen, Kaiser, Øvergård, & Rosenvinge, 2013). PersD comorbidity predicts substantially worse psychosocial impairment (Ansell, Sanislow, McGlashan, & Grilo, 2007; Penner-Goeke et al., 2015; Skodol et al., 2005), and is associated with worse longitudinal outcomes among patients with anxiety disorders (Ansell et al., 2011; Skodol, Geier, Grant, & Hasin, 2014). In treatment trials of Cognitive-Behavioral Therapy (CBT), PD patients with comorbid Cluster C PersD reportedly experience less panic symptom improvement, although the effect is small (Porter & Chambless, 2015).

A longstanding debate in the PersD literature concerns the extent to which PersD presenting in the context of active, symptomatic Axis I mood or anxiety disorders reflect truly separate "disorders" (Clark, 2007; Røysamb et al., 2011; Shea & Yen, 2003). Do PersDs underlie and predispose to acute psychiatric symptoms, are PersD symptoms rather a marker of severity or chronicity of primary mood or anxiety disorders, or do both share common vulnerabilities (Links & Eynan, 2013)? DSM-5 PersD criteria themselves may reflect a mixture of personality traits and state-like aggravations of trait-like personality features (McGlashan et al., 2005; Zanarini, Frankenburg, Hennen, & Silk, 2003).

No clinical trial of PD treatment(s) has yet examined whether improvement of PersD, either at diagnostic or trait level, corresponds to improvement in PD symptoms themselves (Markowitz et al., 2015). In addition, the ability of brief, targeted, panic-focused psychotherapies to alter PersD has rarely been evaluated. In the only trial of which we are aware, CBT for PD and imipramine were equivalently effective at improving self-reported PersD traits from the Wisconsin Personality Disorders Inventory, although PersD was not rigorously diagnosed, remission rates were not reported, and the overall within-group treatment effects were small (average $d = 0.28$) (Hofmann et al., 1998). Although some recovery from PersD has also been reported during short-term treatments for PTSD (Markowitz et al., 2015) and major depressive disorder (Cyranowski et al., 2004; Fava et al., 2002; Keefe, Webb, & DeRubeis, 2016), change in diagnostician-rated PersD has not been evaluated in PD treatment.

Understanding the degree to which PersDs are modified by successful treatment of PD might shed light on whether comorbid PersD reflects a syndrome meaningfully separate from acute PD. It is also clinically important to know whether PD patients presenting with comorbid PersD require additional treatment for the PersD. Furthermore, different treatments for PD, such as Panic-Focused Psychodynamic Psychotherapy (PFPP) (Milrod, Busch, Cooper, & Shapiro, 1997) and CBT for panic (Craske, Barlow, & Meadows, 2000), might have differential efficacy in treating comorbid PersD (Barber, Muran, McCarthy, & Keefe, 2013; Johansen, Krebs, Svartberg, Stiles, & Holen, 2011; Milrod, Leon, Barber, Markowitz, & Graf, 2007).

We examined these questions in the Cornell–Penn Study of Psychotherapies for Panic Disorder, a two-site randomized controlled trial that compared CBT, PFPP, and ART in a 2:2:1 ratio for 201 patients with primary DSM-IV PD with or without agoraphobia (Milrod et al., 2016). For the purposes of the present analysis, we eliminated the ART control group, for which data were sparse because this group was initially smaller and had a significantly higher (41%) drop-out rate relative to CBT and PFPP (25 and 21%, respectively). This rate of dropout was particularly pronounced among more severe panic symptomatic patients (69%), which was not the case for either CBT or PFPP. Moreover, patients with worse symptom trajectories tended to drop out of the trial significantly more. Completer ART patients were thus a relatively less symptomatic and (seemingly) more successful subsample, who would be unrepresentative for the present analyses.

We hypothesized *a priori* that PFPP would be superior to CBT in improving PersD criteria in patients with more severe PersD, as indexed by meeting more baseline PersD criteria. PFPP is designed to address some of the psychological processes that are hypothesized to underlie both PD and some aspects of PersD (Milrod et al., 2007). In particular, PFPP specifically targets dysregulated attachment that may sensitize panic patients to actual or imagined losses of attachment figures (Milrod et al., 2014), and the maladaptive defense use that prevents patients from experiencing and working with meanings surrounding panic (Busch, Shear, Cooper, Shapiro, & Leon, 1995). Both attachment dysregulation and defense use are especially severe in PersD (Levy, Johnson, Clouthier, Scala, & Temes, 2015; Perry & Bond, 2005). Furthermore, improvements in attachment, defense use, and insight into defense use have been observed to mediate symptomatic improvements in PersD therapy trials (Johansson et al., 2010; Perry & Bond, 2012; Rossouw & Fonagy, 2012) and naturalistic studies (Zanarini, Frankenburg, & Fitzmaurice, 2013).

Pursuant to answering these theoretical and clinical questions, our analyses were structured to investigate: (a) to what extent PersD improves alongside panic symptoms, indicating the degree of clinical overlap between the two constructs; (b) to what extent diagnostic remission and recovery from PersD is observed over the course of panic-focused treatment; and (c) to what extent PFPP and CBT exhibit differential effects on PersD improvement during panic-focused treatment.

1.1 | Methods

201 patients (aged 18–70 years) were recruited at Weill Cornell Medical College ("Cornell") and the University of Pennsylvania ("Penn")[1] and randomized to treatment: PFPP, CBT, or ART in a 2:2:1 ratio. Of these, 118 patients completed CBT or PFPP and are the focus of this manuscript. All patients provided informed, written consent. Patients received study treatment gratis. Both sites' institutional review boards approved the protocol (ClinicalTrials.gov identifier: NCT00353470).

Patients were included in the trial if they experienced one or more spontaneous panic attacks for the month before trial entry, and qualified for a DSM-IV PD diagnosis with or without agoraphobia determined as per the ADIS-IV Lifetime version (Brown, DiNardo, & Barlow, 2004). Cross-site agreement on ADIS ratings for panic severity (with "4″ indicating diagnostic threshold) was excellent ($ICC = 1.00$). Assessors from both sites rated two cases together annually to prevent drift, in addition to within-site reliability meetings.

Non-study psychotherapy was prohibited. Medications were permitted if stable for at least two months at presentation, and were recorded, held constant, and monitored during the trial. Exclusion criteria were: active substance dependence (less than 6 month's remission), history of psychosis or bipolar disorder, acute suicidality, or organic mental syndrome (Milrod et al., 2016).

1.2 | Treatments

PFPP is based on the central assumption that panic symptoms have a partly unconscious psychological meaning. It explores feelings and subjective content of panic episodes, so the patient can begin to address these meanings rather than experiencing conflicts physically as somatic anxiety leading to panic (Milrod et al., 1997). The therapy helps patients understand and alter core conflicts (e.g., regarding attachment and dependency) to avert future panic vulnerability. CBT for PD followed a modified version of the Panic Control Therapy protocol (Craske et al., 2000), entailing education about panic, correction of maladaptive thoughts about anxiety and body sensations, and both in-session and homework interoceptive exposures to bodily sensations designed to mimic those experienced during panic (Craske et al., 2000). Both psychotherapies comprised 24 sessions delivered twice weekly (12 weeks). Additional information on treatments, including training, supervision, and adherence monitoring, can be found in Milrod et al. (2016).

1.3 | Measures

Structured Clinical Interview for Diagnosis for Axis-II Disorders (SCID-II) (First, Gibbon, Spitzer, Williams, & Benjamin, 1997). This structured clinical interview assesses presence of PersD criteria and diagnoses as defined by DSM-IV. Primary analyses of relationships between change in PersD, panic improvement, and treatment condition employed the number of criteria met rather than PersD diagnosis for reasons of statistical power (MacCallum, Zhang, Preacher, & Rucker, 2002), following research suggesting that DSM-IV PersD reflects a continuum of illness rather than categorical taxonomies (Harford, Chen, & Grant, 2014; Harford et al., 2013; Haslam, Holland, & Kuppens, 2012). For descriptions of PersD diagnostic recovery, we examined both remission (defined as an individual falling under diagnostic threshold), and a stricter PersD "recovery" criterion defined by the Collaborative Longitudinal Personality Disorders Study as meeting two or fewer criteria in originally diagnosed PersDs (Gunderson et al., 2011). Trained, independent masters' level diagnosticians blinded to treatment condition administered the interviews. Cross-site inter-rater reliability for number of PersD criteria scored as present on the SCID-II was excellent (*ICC* = 0.92), and good for PersD Clusters A, B, and C, respectively ($ICC_A = 0.82$ / $ICC_B = 0.87$ / $ICC_C = 0.86$).

Panic Disorder Severity Scale (PDSS) (Shear et al., 1997). The primary outcome measure of the study was the PDSS, a diagnosis-based, composite, global rating of PD severity that has acceptable psychometric properties (Shear et al., 1997). Inter-rater reliability was excellent (*ICC* = 0.95). Analyses for this manuscript employed pre-to-post treatment change scores.

1.4 | Analyses

All statistical analyses were conducted within the *R* statistical computing language (R Core Team, 2016). All regression analyses were accomplished using robust regressions as implemented in the *R* package "robustbase" (Cantoni & Ronchetti, 2001; Huber & Ronchetti, 2009; Koller & Stahel, 2016; Maechler et al., 2016). As per Huber and Ronchetti, robust regression was used for its superior properties of robustness against multivariate outliers and deviation from homoscedasticity (Huber & Ronchetti, 2009).

Among CBT and PFPP trial completers ($n = 118$), 4 patients (3.4%) were missing baseline SCID-II criteria data, and 25 patients were missing termination SCID-II criteria data (21.2%). Apart from assessor error, missing termination SCID-IIs among completers were missing because collection of the trial's primary outcome measure (the PDSS) was prioritized over secondary measures in subjects for whom it was difficult to complete the full termination assessment. Thus, for treatment completers both baseline and termination SCID-II missingness was presumed to be missing at random.

For the treatment completers ($n = 118$) a multiple-imputation based approach to the missing baseline and termination SCID-II data was undertaken using the *R* packages "mice" and "CALIBERrfimpute." We employed multiple imputations by chained equations using draws from a random-forest developed distribution, creating 100 iterations of 50 imputed datasets, with analyses pooled together using Rubin's rule (Shah, Bartlett, Carpenter, Nicholas, & Hemingway, 2014; van Buuren & Groothuis-Oudshoorn, 2011). All analyses were repeated using only completer patients providing completely observed data, and in no instances did results between the multiple imputation and complete data approaches substantively differ (i.e., significant results becoming nonsignificant, or vice-versa).

All analyses controlled for baseline number of SCID-II criteria met, baseline PDSS score, and a main effect of site. Analyses that included treatment condition used CBT as the reference group. Site was originally included as an interaction term with the focal predictors in all following analyses (e.g., did the relationship between PDSS and SCID-II change differ by site), but it was ultimately removed in analyses for which it lacked statistical significance ($P < 10$) in order to conserve power and retain interpretability. However, the main effect of site was maintained throughout all analyses.

2 | RESULTS

2.1 | Description of sample

Fifty-four of 118 completers (45.8%) qualified at baseline for a PersD diagnosis, comparable to the diagnosis rate in the full CBT/PFPP sample (48.0%). Among all CBT and PFPP patients, treatment completion was unrelated to baseline PersD criteria ($B = -0.03$ [95% CI: −0.08 to 0.03], $z = -1.05$, $P = .296$), and this relationship did not differ based on treatment condition ($z = 1.13$, $P = .260$).

Baseline demographic/clinical information and PersD criteria endorsements for PersD and non-PersD patients are presented in Tables 1 and 2, respectively. The average completer with a PersD met criteria for 1.6 (SD 0.8) PersD diagnoses. There were no site or site by treatment differences in PersD (Milrod et al., 2016). Among completers with an SCID II PersD, the most common criteria endorsements were Cluster C (mean 6.1), followed by Clusters B (3.7) and A (2.5). Rates of individual PersD diagnoses (see Table 3) were comparable to those found in the only other PD psychotherapy trial (to our knowledge) that employed the SCID-II to formally diagnose PersD (Milrod et al., 2007).

2.2 | Correlation between PersD criteria change and panic symptom change

Patients who experienced larger reductions in PersD criteria during treatment tended to have more panic symptom improvement on the PDSS ($B = -0.26$ [95% CI: −0.45 to −0.08], $t[93.4] = -2.79$, $P = .006$), with a moderate effect size ($r = 0.28$). The correlation between improvements in panic symptoms and PersD did not differ as a function of baseline PersD severity on a criteria level ($B = 0.00$ [95% CI: −0.02 to 0.02], $t[100.3] = -0.24$, $P = .808$) or of treatment group ($B = -0.17$ [95% CI: −0.50 to 0.15], $t[95.2] = 1.06$, $P = .294$).

We examined whether the relationship between improvement in panic symptoms and PersD differed by PersD cluster (A, B, or C). Only improvements in Cluster C PersD criteria uniquely correlated

TABLE 1 Demographic and clinical differences between PersD and non-PersD patients

Mean (SD) or number (%)	No personality disorder ($n = 64$)	Personality disorder ($n = 54$)
Baseline PDSS†	13.2 (3.2)	14.4 (3.6)
Baseline SDS* (Leon, Shear, Portera, & Klerman, 1992)	13.3 (6.3)	17.1 (7.4)
Baseline HAM-D** (Hamilton, 1960)	9.1 (4.0)	12.1 (5.1)
Baseline IIP** (Horowitz, Alden, Wiggins, & Pincus, 2000)	1.0 (0.4)	1.3 (0.5)
Baseline mobility inventory agoraphobic avoidance (Alone) (Chambless et al., 2011)	2.0 (0.8)	2.3 (0.8)
Age*	36.7 (12.9)	42.2 (13.3)
Gender (Female)	41 (64.1%)	34 (63.0%)
Concurrent psychopharmacology (Yes)	19 (30.0%)	14 (25.9%)
Age of first panic onset* (Years)	23.9 (11.3)	28.9 (11.9)
Childhood trauma sum* (Lizardi et al., 1995)	3.0 (1.1)	3.6 (1.7)
Baseline BBSIQ (Clark et al., 1997)	1.9 (0.4)	1.9 (0.3)
Baseline RF (Rudden, Milrod, & Target, 2005)	4.3 (1.2)	4.2 (1.3)
Baseline PSRF (Rudden, Milrod, Target, Ackerman, & Graf, 2006)	3.4 (1.1)	3.6 (1.2)

Notes:†$P < .10$; *$P < .05$; **$P < .01$.
BBSIQ = Brief Bodily Sensations Interpretation Questionnaire; HAM-D = Hamilton Rating Scale for Depression; IIP = Inventory of Interpersonal Problems; PDSS = Panic Disorder Severity Scale; PSRF = Panic Specific Reflective Functioning; RF = Reflective Functioning; SDS = Sheehan Disability Scale.

TABLE 2 Baseline SCID-II PersD criteria endorsed by PersD and non-PersD patients

Mean (SD)	No personality disorder ($n = 64$)	Personality disorder ($n = 54$)
Avoidant**	0.7 (1.0)	2.0 (1.9)
Dependent**	0.3 (0.7)	1.1 (1.7)
Obsessive–compulsive**	1.1 (1.0)	3.0 (1.8)
Paranoid**	0.4 (0.8)	1.9 (2.0)
Schizotypal	0.1 (0.3)	0.2 (0.5)
Schizoid†	0.1 (0.4)	0.3 (0.6)
Histrionic*	0.1 (0.3)	0.5 (0.8)
Narcissistic**	0.3 (0.6)	1.5 (2.0)
Borderline **	0.4 (0.7)	1.6 (2.0)
Antisocial*	0.0 (0.0)	0.1 (0.4)

Notes:†$P < .10$; *$P < .05$; **$P < .01$.

TABLE 3 PersD diagnoses at baseline and after treatment for completers ($n = 118$)

Disorder	Baseline (Percentage diagnosed)	Post-treatment (Percentage remission)
Avoidant PersD	14 (11.9%)	9 (35.7%)
Dependent PersD	6 (5.1%)	4 (33.3%)
Obsessive–compulsive PersD	27 (22.9%)	22 (18.5%)
Paranoid PersD	17 (14.4%)	7 (58.8%)
Narcissistic PersD	7 (5.9%)	3 (57.1%)
Borderline PersD	7 (5.9%)	5 (28.6%)
PersD—not otherwise specified	7 (5.9%)	6 (14.3%)

with amelioration of panic symptoms ($B = -0.42$ [95% CI: −0.73 to −0.11], $t[94.1] = 2.73$, $P = .008$, $r = 0.27$).[2] Improvements in Clusters A ($B = -0.30$ [95% CI: −0.75 to 0.15], $t[89.3] = 1.33$, $P = .187$, $r = 0.14$) and B ($B = -0.15$ [95% CI: −0.51 to 0.21], $t[90.4] = 0.83$, $P = .407$, $r = 0.09$) were not significantly related to panic symptom change, controlling for change in Cluster C.

2.3 | Treatment-related changes in PersD

2.3.1 | Remission of PersDs

Overall, 37.0% (95% CI: 24.6 to 51.3%) of PersD patients fell below SCID-II diagnostic criteria for all PersDs by the end of treatment ($n = 20$). Neither PFPP nor CBT showed superiority in promoting remission ($B = -0.14$ [95% CI: −1.34 to 1.06], OR = 0.87, $z = -0.24$, $P = .814$). Remission rates were not statistically distinguishable across sites ($B = -0.59$ [95% CI: −0.67 to 1.85], OR = 1.81, $z = 0.94$, $P = .351$). Table 3 shows remission rates on a per-PersD basis.

As expected, rates of recovery from PersD (i.e., having two criteria or less) were much lower than SCID-II remission rates. Only 16.7% (95% CI: 8.4 to 29.8%) of patients ($n = 9$) experienced recovery from all baseline PersDs. SCID-II PersD "remission" thus often reflected falling just under threshold for PersD diagnosis, rather than experiencing pronounced improvement.

2.3.2 | Changes in PersD criteria

Patients experienced equivalent improvement in PersD criteria in CBT and PFPP ($B = 0.03$ [95% CI: −1.39 to 1.45], $t[80.4] = 0.04$, $P = .967$, $d = 0.01$), corresponding to an average decline of 2.7 PersD criteria for patients without a baseline PersD and a decline of 6.3 PersD criteria for patients with a PersD. This was true across all PersD clusters ($ps = 0.670$ to 0.261). There was no significant site by treatment interaction ($t[75.0] = 1.05$, $P = .295$), yet there were significant site differences: patients in either treatment at the Penn site experienced less PersD criteria improvement than patients treated at Cornell ($B = 2.07$ [95% CI: 0.55 to 3.59], $t[70.0] = 2.71$, $P = .008$).

Consistent with our hypotheses, there was a significant interaction between baseline PersD criteria and treatment condition, such that patients with more PersD criteria at baseline experienced greater PersD criteria improvement in PFPP than CBT ($B = -0.32$ [95% CI: −0.55 to −0.09], $t[91.2] = -2.77$, $P = .007$; see Figure 1). This pattern showed no site by treatment interaction ($B = 0.24$ [95% CI: −0.23 to 0.70], $t[93.5] = 1.02$, $P = .310$). When each PersD criteria cluster was

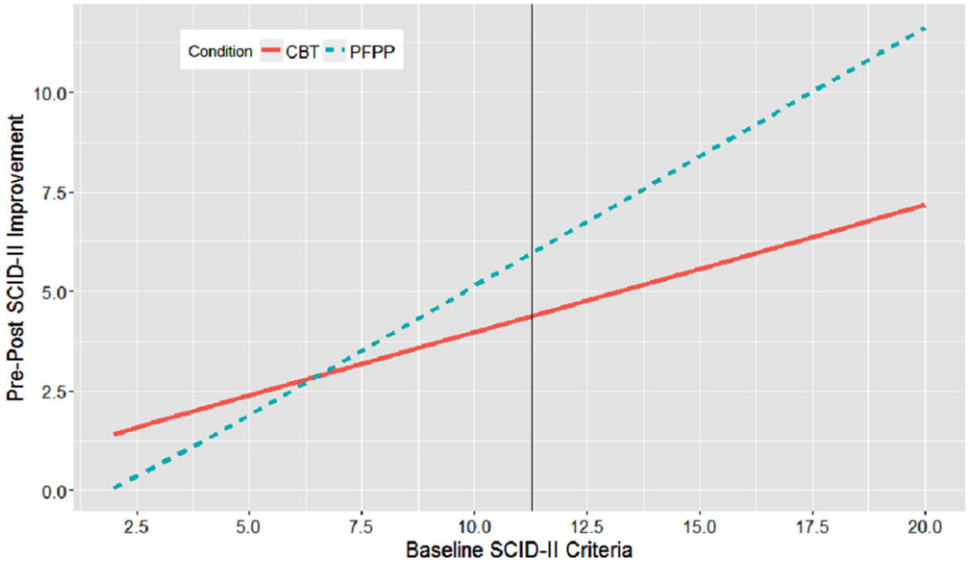

FIGURE 1 Model estimates for improvement in SCID-II PersD criteria as a function of treatment condition and baseline PersD criteria met. As a patient qualified for more PersD criteria at baseline, their PersD criteria improved more in PFPP as compared to CBT ($P = .007$). The vertical black line represents the critical point estimated by the Johnson–Neyman technique, wherein PFPP becomes significantly superior to CBT in PersD improvement (11 criteria), which was 25% of the analyzed sample.

entered into the same regression testing the interaction with treatment condition, number of baseline Cluster B PersD criteria predicted the difference between CBT and PFPP in improvement across PersD criteria ($t[94.3] = -3.18$, $P = .002$), whereas baseline number of criteria in Clusters A ($t[95.3] = -1.20$, $P = .233$) and C ($t[91.3] = -1.67$, $P = .099$) did not. In addition, the overall interaction of PersD criteria count (across all Clusters) with treatment condition predicted an advantage of PFPP with increasing severity primarily for improvement in Cluster B PersD criteria ($t[91.6] = -3.25$, $P = .002$), but not significantly for improvement in Clusters A ($t[91.7] = -0.24$, $P = .813$) or C ($t[89.5] = -1.39$, $P = .168$).

Using the Johnson–Neyman technique (Johnson & Fay, 1950), we probed for the regions of significance of the continuous interaction, to identify what threshold of baseline PersD criteria was associated with PFPP's superiority to CBT. PFPP was estimated as significantly superior to CBT for patients entering the trial meeting at least 11 PersD criteria. This included 25.4% ($n = 30$) of the total analyzed subsample, and 56% of patients with a PersD diagnosis. The median patient in this subsample had two PersD diagnoses, and all had at least one PersD diagnosis. Among these more severely personality-disordered patients, PFPP was superior to CBT in improving PersD, with a medium effect size advantage ($d = 0.66$) of an average of 3.0 additional criteria lost in PFPP. By contrast, there was no point at which CBT was estimated to be significantly superior to PFPP in improving PersD criteria.

One possibility is that these differential changes in PersD traits were confounded with declines in acute panic symptomatology. As a statistical check, we re-ran all PersD criteria outcome analyses using a measure of PersD criteria change that had been residualized on (i.e., controlling for) PDSS panic symptom change. The chief interaction between PersD criteria and treatment condition remained statistically significant ($P = .009$). Estimated declines in residualized PersD criteria folded across the two treatments were marginally smaller, at 1.3 criteria for patients without PersD, and 5.0 criteria for patients with PersD.

3 | DISCUSSION

Comorbid PersD that presents in the context of primary PD with or without agoraphobia only partially resolves during brief, 12-week PD psychotherapies. Over 80% of patients did not recover from their PersD over the course of 3 months of biweekly panic-focused psychotherapy, indicating that short-term panic-focused psychotherapies are insufficient to treat comorbid PersD.

Although patients lost more PersD criteria after experiencing improvement in panic symptoms compared to those who did not experience improvement, the effect size of this relationship was moderate, suggesting that a patient could experience a full remission of PD yet continue to suffer from PersD. The modest correspondence between amelioration of PD and PersD indicates that only a limited proportion of PersD improvement in this trial can be attributed to amelioration of panic symptoms. This finding, in conjunction with low observed rates of PersD recovery, indicates substantial non-overlap of PD and PersD, which constitutes an important nosological finding regarding PersD comorbidity in the context of a primary Axis I anxiety disorder.

Change in Cluster C PersD criteria uniquely correlated with improvement of PD symptoms, whereas change in Clusters A and B did not. This may be because Cluster C, the "anxious" Cluster, encompasses a set of syndromes partly contiguous with symptoms of anxiety disorders (Marques et al., 2012; Torvik et al., 2016) that may improve with targeted anxiety treatment. In the Collaborative Longitudinal Personality Disorders Study, the six-month stability of schizotypal and borderline PersD did not substantively differ from that of avoidant and obsessive-compulsive PersD (Sanislow et al., 2009), and remission

from Cluster C PersDs over time was only marginally swifter than that of borderline PersD (Gunderson et al., 2011). Thus, the higher correlation we observed between PD and Cluster C criteria improvement may not reflect a greater tendency of Cluster C PersD to remit relative to other PersDs, but rather syndrome overlap between PD and Cluster C. On the other hand, levels of Cluster A and B PersD criteria in this trial were lower than Cluster C, which may have attenuated correlations between change in these Clusters and panic improvement.

Although PFPP and CBT were on average equally effective in improving PersD criteria for completers, patients with more PersD criteria (estimated at ≥11 criteria; median 2 PersD diagnoses, minimum 1) experienced significantly greater improvement in PersD criteria in PFPP than CBT, with a medium-to-large effect size ($d = 0.66$, average of 3 additional criteria lost). Although past PersD treatment trials comparing psychodynamic therapies to CBT and the related dialectical behavioral therapy have typically detected no differences in efficacy between these modalities for primary PersD (Barber et al., 2013), these investigations have employed forms of CBT tailored specifically to treat PersD, not the panic-focused CBT utilized in this study.

Baseline number of Cluster B criteria best predicted differential PersD treatment response on the criteria level. In addition, Cluster B criteria improved the most in PFPP among patients with the most PersD symptomatology. If these exploratory findings are replicated, PFPP may be indicated for PD patients meeting a high number of Cluster B criteria, as severe Cluster B criteria do not appear to improve as well in CBT for panic. However, further research into treatment selection in PD, balancing efficacy in treatment of PD versus comorbid conditions, is necessary.

3.1 | Limitations

The analysis of PersD outcomes, although planned, was not the primary focus of this trial. In addition, these analyses are limited to change during acute treatment, and do not include follow-up results. As such, all findings should be viewed as preliminary results that can best serve for hypothesis-generation for future treatment trials, in which recruitment and stratification can balance presence of primary anxiety disorders with PersDs across treatments.

Furthermore, due to power considerations concerning the relatively small absolute number of completer patients with PersD diagnoses ($n = 54$), our analyses of differential treatment efficacy concerned PersD criteria rather than PersD diagnostic remission. Although these analyses were statistically optimal, this limits the clinical utility of our findings for those who approach PersD categorically or prototypically rather than dimensionally (Shedler et al., 2010; Spitzer, First, Shedler, Westen, & Skodol, 2008; Westen, Shedler, & Bradley, 2006). Relatedly, although the SCID-II is a gold-standard instrument in the assessment of diagnostic PersD and PersD criteria counts have dimensional psychometric properties (Harford et al., 2014; Harford et al., 2013), it may not be the best tool to employ to measure PersD as a continuous spectrum. Other scales such as the Personality Inventory for DSM-5 (Hopwood, Thomas, Markon, Wright, & Krueger, 2012) may have been more appropriate, although there remains much debate about the best way(s) to measure PersD traits.

In this trial, we did not collect data on possible mediators of PersD improvements, such as attachment or defense mechanism use (Levy et al., 2015; Perry & Bond, 2005). As such, although we would hypothesize that the reason why PFPP was superior to CBT for improving more severe PersD was because PFPP better targeted these personality facets, our results do not directly address this hypothesis. A trial including repeated measurements of both PersD symptoms and putative mediators during treatment would be revelatory on this question.

4 | CONCLUSION

In the context of PD treatment, PD and PersD appear to be clinically dissociable diagnoses. Although PersD generally improves during psychotherapy for PD, a majority of completers with PersD retain at least one PersD diagnosis following treatment, and less than 20% meet PersD recovery criteria. Patients with more severe PersDs, especially Cluster B, may experience more PersD improvement in PFPP as compared to CBT, a preliminary finding that requires replication.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

ENDNOTES

[1] The primary outcome paper for this trial indicated that treatment attrition was not missing at random (NMAR), such that patients with worse panic symptom outcome trajectories were more likely to drop out of treatment (Milrod et al., 2016). Due to the NMAR dropout pattern, an imputation-based approach to missing data for trial dropouts would result in biased estimates. As the SCID-II was only administered before and after treatment, statistical methods to account for NMAR dropout could not be employed. Moreover, due to its high rates of dropout, this means that ART trial completers were particularly likely to represent an unusually successful and mildly ill subgroup of patients from this treatment, further speaking to its exclusion from these analyses. Thus, only CBT and PFPP patients fully completing the trial were used for the following analyses ($n = 118$).

[2] When entered into the same regression, improvement in the criteria for each Cluster C diagnosis significantly correlated with improvements in panic symptoms ($P < .05$), suggesting that general improvement in Cluster C was correlated with symptom change on the PDSS.

ORCID

John R. Keefe MA http://orcid.org/0000-0001-7250-8960

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