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Coping Skills and Exposure Therapy in Panic Disorder and Agoraphobia: Latest Advances and Future Directions

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Abstract

Although cognitive-behavioral treatments for panic disorder have demonstrated efficacy, a considerable number of patients terminate treatment prematurely or remain symtpomatic. Cognitive and biobehavioral coping skills are taught to improve exposure therapy outcomes but evidence for an additive effect is largely lacking. Current methodologies used to study the augmenting effects of coping skills test the degree to which the delivery of coping skills enhances outcomes. However, they do not assess the degree to which acquisition of coping skills and their application during exposure therapy augment outcomes. We examine the extant evidence on the role of traditional coping skills in augmenting exposure for panic disorder, discuss the limitations of existing research, and offer recommendations for methodological advances.

Keywords

acceptance; cognitions; coping skills; exposure; mediation

Panic disorder with or without agoraphobia (PD/A) is a common emotional disorder with a lifetime prevalence estimate of approximately 4.7% in the United States (Kessler, Chiu, Demler, & Walters, 2005). It is associated with high levels of disability (Keller et al., 1994; Klerman, Weissman, Ouellette, Johnson, & Greenwald, 1991), considerable economic costs (Katon et al., 1990; Leon, Portera, & Weissman, 1995; Roy-Byrne et al., 1999), and high medical utilization (Deacon, Lickel, & Abramowitz, 2008).

The most empirically supported psychosocial treatment for PD/A is cognitive behavioral therapy (CBT), of which the central focus is repeated exposure to feared situations and sensations, supported by a set of control-based coping skills (see Craske & Barlow, 2008). These skills typically aim to change catastrophic appraisals and/or somatic symptoms. Patients are encouraged to apply the cognitive skills to control negative thoughts and somatic skills to control dysregulated physiology during exposure to feared sensations or

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situations. Although CBT for PD has clearly established itself as an effective treatment (Norton & Price, 2007; Westen & Morrison, 2001), effect sizes are smallest among the anxiety disorders (Andrews, Cuijpers, Craske, McEvoy, & Titov, 2010; Hofmann & Smits, 2008 but not Norton & Price, 2007). Also, a large percentage of completers are not panic free or do not reach responder status after treatment (Brown & Barlow, 1995). For example, in the largest randomized-controlled trial for PD to date (Barlow, Gorman, Shear, & Woods, 2000), only 32% assigned to CBT alone demonstrated strong treatment response 12 months after acute treatment. Together, these data indicate that there is room for improvement in PD/A treatment. Therapy optimization calls for a renewed focus on underlying mechanisms (i.e., why treatments work and for whom). The focus of this review is to examine the degree to which active ingredients of CBT (i.e., coping skill techniques) are implemented, augment exposure therapy, and mediate panic symptom reduction. To this end we (a) examine the extant evidence of the role of traditional coping skills in augmenting exposure, (b) discuss the limitations of existing research, and (c) offer recommendations for methodological advances. The latter will be discussed using examples of two emerging therapy approaches, acceptance and cognitive defusion, as employed in acceptance and commitment therapy (Hayes, Strosahl, & Wilson, 1999) and capnometry-assisted respiratory training (Meuret, Wilhelm, Ritz, & Roth, 2008).

Evidence for Additive Effects of Traditional Coping Skills

Coping skills traditionally included in CBT for PD/A are cognitive restructuring and either breathing retraining and/or relaxation. Presumably, the effects of exposure are augmented by applying the skills (e.g., disputing the probability of a harmful outcome while being exposed to a feared situation and showing that dysregulated physiology can be partially regulated). In the following, we review the evidence for the augmenting effects of traditionally taught cognitive and behavioral skills on exposure therapy in PD/A.

Cognitive skill training: description, efficacy, and evidence for augmenting exposure

Background—The cognitive theory of panic disorder (Clark, 1986) posits that panic attacks are caused by catastrophic beliefs about bodily sensations or situational contexts in which such sensations occur. In support, patients with PD/A have strong beliefs and fears of physical or mental harm arising from bodily sensations associated with panic attacks (e.g., Chambless, Caputo, Bright, & Gallagher, 1984; McNally & Lorenz, 1987). They are also more likely to interpret bodily sensations in a catastrophic fashion (Clark et al., 1988), and to allocate more attentional resources to physical sensations presented by words or heart rate feedback (e.g., Ehlers, Margraf, Davies, & Roth, 1988; Hope, Rapee, Heimberg, & Dombeck, 1990; Kroeze & van den Hout, 2000; Maidenberg, Chen, Craske, Bohn, & Bystritsky, 1996; McNally, Riemann, Louro, Lukach, & Kim, 1992). In addition, they are more likely to fear procedures that elicit panic sensations (Antony, Ledley, Liss, & Swinson, 2006; Blechert, Wilhelm, Meuret, Wilhelm, & Roth, 2010; Gorman et al., 1994; Jacob, Furman, Clark, & Durrant, 1992; Perna, Bertani, Arancio, Ronchi, & Bellodi, 1995; Rapee, 1986).

Skill Training—Cognitive skill training (CT) is aimed at recognizing cognitive errors and generating alternative, noncatastrophic explanations for the sensations that are feared during panic attacks. A rationale emphasizing the role of appraisals is followed by consideration of the evidence and logical empiricism to generate more evidence-based appraisals for recent and anticipated panic attacks and contexts that produce panic symptoms. During exposure, patients are encouraged to evaluate the degree to which elicited panic symptoms (via interoceptive or in vivo exposure) are indeed predictive of catastrophic outcome. Whereas bodily sensations are often cited as triggers of panic attacks, according to Clark (1986) and

McNally (1994), treatment success depends on the correction of the catastrophic interpretation of these sensations, not the sensations themselves. The extent to which biological factors that may elicit or sustain panic symptoms are without harm to the system remains unknown. As such, claims in either direction (harmful or nonharmful) presently lack an empirical basis.

Evidence for Efficacy From Clinical Trials—CT is often intermingled with behavioral techniques (e.g., "behavioral experiments," "hypothesis testing," "instructions" involving exposure), which complicate the direct testing of efficacy of CT in its "pure" form (e.g., Hoffart, Sexton, Hedley, & Martinsen, 2008; Hofmann et al., 2007; Öst, Westling, & Hellström, 1993; Teachman, Marker, & Smith-Janik, 2008). Nonetheless, there is some evidence that training in cognitive procedures in full isolation from exposure and behavioral procedures is efficacious in reducing aspects of panic (Beck, Stanley, Baldwin, Deagle, & Averill, 1994; Meuret, Rosenfield, Seidel, Bhaskara, & Hofmann, 2010; Salkovskis, Clark, & Hackmann, 1991; Van den Hout, Arntz, & Hoekstra, 1994). Similarly, in a study by Bouchard et al. (1996), exposure therapy was as effective in reducing panic symptoms as cognitive restructuring. In comparison to in vivo exposure, some studies have shown that CT alone was less effective for agoraphobia (Williams & Falbo, 1996). Hoffart (1995) found that CT targeting misappraisals of bodily sensations was as effective as guided mastery exposure delivered intensively over 6 weeks for individuals with moderate to severe agoraphobia, although some elements of exposure (e.g., hyperventilation tests to elicit sensations) were included in the CT condition.

Evidence for an Exposure-Augmenting Effect—A few studies have evaluated the effects of CT combined with exposure in comparison to exposure alone or in combination with other coping skills. Most often, CT plus exposure does not yield an additional benefit over exposure in vivo alone (Öst, Thulin, & Ramnero, 2004; van den Hout et al., 1994). One exception was a study by Murphy, Michelson, Marchione, Marchione, and Testa (1998), in which those receiving CT + graded exposure outperformed those receiving graded exposure alone or graded exposure + relaxation training. Furthermore, a recent meta-analysis, albeit across different anxiety disorders, indicated no differences across CT, exposure therapy, or their combination (Norton & Price, 2007). In the only published study to date that has experimentally evaluated initial training in CT followed by in vivo exposure, van den Hout and colleagues randomized clients with moderate to severe agoraphobia to four sessions of CT or attention control followed by eight sessions of exposure therapy. Initial CT resulted in reductions in panic frequency, but not avoidance behavior or other panic-related symptoms. The latter were only reduced with the addition of exposure. Attention control did not change panic symptoms or avoidance, but after adding exposure, avoidance behavior was reduced to the same extent as the CT condition. No differences were observed between CT + exposure or attention control plus exposure during the exposure phase in panic symptoms (behavioral and self-report measures). Hence, CT did not potentiate exposure effects in this study.

Taken together, the extant data indicates that the delivery of CT alone is partially effective for PD/A, but there is little evidence suggesting CT augments the effects of exposure alone. As discussed earlier, the lack of data on successful acquisition and application of cognitive skills renders premature any conclusions regarding their augmenting effect upon exposure. Thus, we can currently conclude that *delivery* of CT as a part of an exposure-based treatment for PD/A does not confer significantly greater benefit, but conclusions regarding the degree to which actual use of CT during exposure enhances outcome remains unknown.

Breathing training: description, efficacy, and evidence for augmenting exposure

Background—Respiratory abnormalities have been postulated as an important factor in the development or maintenance of PD/A (Gorman et al., 1988; Klein, 1993; see Meuret & Ritz, 2010, for a review) and has led to speculations about a causal relationship between respiratory regulation, in particular PCO_2 and panic. According to Ley (1985) panic attacks are caused by acute states of hypocapnia, which may not be limited to the attack itself, but may precede and follow it, giving rise to moderate sustained hypocapnia. Hyperventilation according to Klein is viewed as a compensatory or secondary reaction to an overly sensitive "suffocation alarm system" in these patients. When a patient's PCO_2 rises, the system starts firing at an abnormally low threshold and/or responds with greater sensitivity to increments in CO_2. This leads to disproportional dyspnea (sensations of air hunger, breathlessness, suffocation), which due to its distressing nature initiates a cascade of panic symptoms. In this context, chronic hyperventilation is interpreted as an adaptation to a lowered suffocation alarm threshold, in that it keeps PCO_2 sufficiently low to avoid triggering the suffocation alarm. Evidence for both postulations has been found in a recent ambulatory study tracing cardio respiratory changes in the hour before out-of-the-blue attacks (Meuret et al., in press) and decades of experimental studies (Blechert et al., 2010; Caldirola, Bellodi, Caumo, Migliarese, & Perna, 2004; Dager et al., 1995; Gorman, Martinez, Coplan, Kent, & Kleber, 2004; Gorman et al., 1988; Wilhelm, Gerlach, & Roth, 2001). Consistently, breathing training (BRT), with the purpose of modifying pathogenic breathing, is part of many CBT packages for PD/A (Barlow, Craske, Cerny, & Klosko, 1989; Telch et al., 1993).

Skill Training—The rationale of BRT assumes a central role for hypocapnia in panic symptom production (Ley, 1985), postulating a positive feedback loop between increasing anxiety and increasing hyperventilation. Amelioration of panic symptoms is expected when patients achieve reductions in transient and sustained hypocapnia. The descriptions of the therapeutic strategies and outcomes for BRT are sparse and mixed (see Meuret, Wilhelm, Ritz, & Roth, 2003, for a review). Most manuals and studies describe instructions in abdominal breathing as their central techniques. Other techniques include pacing aids (e.g., recorded audio tones) or breathe counting. Furthermore, target respiratory rates as well as duration and frequency of between-session exercises vary largely across studies. Most surprisingly, the central tenet of BRT, the correction of hypocapnic breathing, is neither measured nor targeted in traditional BRT. Given the lack of such data, bold claims such as, "There is no evidence that breathing therapy works by normalizing pCO_2" (Bass, 1997, p. 425) technically are accurate.

Evidence for Efficacy From Clinical Trials—Traditional BRT has rarely been tested in isolation but is intermingled with either cognitive (de Beurs, van Balkom, Lange, Koele, & van Dyck, 1995; de Ruiter, Rijken, Garssen, & Kraaimaat, 1989) or behavioral (de Beurs, Lange, van Dyck, & Koele, 1995) techniques.1 There are only three studies that have tested the effects of traditional BRT in isolation (Clark, Salkovskis, & Chalkley, 1985; Rapee, 1985; Salkovskis, Jones, & Clark, 1986), all of which indicate decreases in panic symptom severity, but also all lack control comparison groups. In-session PCO_2 was assessed in only one study (Salkovskis et al., 1986) with evidence of normalization from initial hypocapnic to normocapnic levels at posttreatment.

[1]Studies testing the efficacy of BRT in patients diagnosed with hyperventilation syndrome (HVS; Kraft & Hoogduin, 1984; Folgering, Lenders, & Rosier, 1980; Grossman, de Swart, & Defares, 1985; Han, Stegen, de Valck, Clement, & Van de Woestijne, 1996; van Doorn, Folgering, & Colla, 1982), even though promising, are not included here as the diagnostic entity and relationship of HVS to PD remains debated (Bass, 1997; Spinhoven, Onstein, Sterk, & le Haen-Versteijnen, 1993).

Evidence for Exposure-Augmenting Effects—Only two controlled studies tested the additive effects of BRT upon exposure. In the study by Hibbert and Chan (1989), PD/A patients were randomly assigned to receive either 2 weeks of BRT or supportive therapy followed by 3 weeks of in vivo exposure. The interventions were equally effective in the first 2-week phase, but BRT yielded greater improvement in clinician (but not self-report) ratings than supportive therapy following the additional exposure training. Bonn, Redhead, and Timmons (1984) alternately allocated patients with agoraphobia to receive either two sessions of BRT followed by 7 weekly sessions of in vivo exposure or in vivo exposure alone for 9 weeks. While BRT plus exposure was equally effective as exposure alone at posttreatment, BRT plus exposure yielded superior outcome 6 months later. Other studies have attempted to identify the degree to which BRT exerts an effect as part of a multicomponent exposure-based protocol using comparative and dismantling designs. For instance, Craske, Rowe, Lewin, and Noriega-Dimitri (1997) compared CT + interoceptive exposure (IE) + in vivo exposure to CT + BRT + in vivo exposure. Group differences at posttreatment suggested that treatments were equally effective on most of the 27 measures related to anxiety and distress, such as panic apprehension, panic fear and avoidance, agoraphobic fear and avoidance, and general distress. A dismantling study by Schmidt and colleagues (2000) examined the differential efficacy of group CBT +/− breathing retraining. No significant condition differences were found, thus questioning the additional additive benefit of BRT to CBT. Although these studies provide an important foundation for studying the additive effect of coping skills, such as BRT, the use of multicomponent treatment protocols for both groups, as well as the lack of outcome assessment after the delivery of each component and/or assessment regarding the degree to which the coping skills are used, limits our ability to fully assess the contribution of BRT over and above other components. As noted by White and Barlow (2002), “An important limitation of this study [Schmidt et al., 2000], however, is the lack of assessment of each patient's true use of each treatment component […] Such evaluation would benefit from a thorough assessment that identifies what treatment techniques were used or not used by patients […]” (p. 371).

Taken together, BRT has been rarely tested in isolation from other therapeutic strategies in the treatment of PD/A, and studies examining the potentiation of BRT upon exposure are limited and yield mixed results. Most problematically, it remains unknown whether traditional BRT actually reverses hypocapnic breathing relative to control conditions.

Relaxation skill training: description, efficacy, and evidence for augmenting exposure

Because traditional relaxation is used less often in recent approaches to treating PD/A, this section will only briefly review the historical significance of this coping skill in the treatment of PD/A, and the research contributions that have furthered our understanding of this technique.

Background—Progressive muscle relaxation (PMR) was first described by Jacobson (1934) and derived from his theory that negative emotional states were caused by “neuromuscular hypertension” (Jacobson, 1938). PMR was later implemented in behavior therapy by Wolpe (1958), who trained patients in this relaxation strategy as part of systematic desensitization. In his protocol, the primary goal was to use relaxation as an antagonistic response to anxiety that would reciprocally inhibit anxiety and eventually become a conditioned inhibitor. Later, Bernstein and Borkovec (1973) formalized and standardized PMR training. PMR as a training for PD/A was typically taught to reduce general tension to achieve a body state that lowers the risk for stressors to elicit panic.

Skill Training—In the most widely studied approach to PMR (Bernstein & Borkovec, 1973), patients learn to tense and relax a series of muscle groups (starting with 16), and

gradually reduce the number of muscle groups (typically from 8 to 4). Patients are taught to (a) focus their attention on a specific muscle group, (b) tense that muscle group, (c) maintain the muscle contraction for 5 to 7 seconds, (d) then relax the muscle group upon cue for 20 seconds, and (e) focus on the feelings and sensations of relaxation in the muscle group.

Evidence for Efficacy From Clinical Trials—Evidence for the efficacy of PMR for PD/A is sparse and mixed, which is perhaps why it is infrequently used as a treatment component in modern CBT approaches to PD/A. One study (Marks et al., 1993) compared (a) alprazolam + in vivo exposure (combined treatment), (b) alprazolam + PMR (used as a psychological placebo), (c) pill placebo + in vivo exposure, and (d) pill placebo + PMR (double placebo). All four treatment conditions showed improvement in panic measures, with no differences between them on most panic symptom measures during treatment or throughout the follow-up period. However, percentages of those classified as “much/very much improved” on the Clinical Global Improvement Scale (CGI) at follow-up were lower for PMR + placebo (25%) compared to the other groups (51% for alprazolam + PMR, 71% for alprazolam + exposure, and 71% for placebo + exposure). Thus, PMR (plus placebo) fared less well than the other conditions when using clinician measures. In another study, Öst (1988) found that PMR alone resulted in large reductions of panic symptom severity, although it was less effective than the combination of PMR + interoceptive exposure (i.e., applied relaxation).

Evidence for Exposure-Augmenting Effects—The majority of PMR study designs do not test augmenting effects due to the intermingling effect of additional components. For example, in the study by Öst and Westling (1995), the authors examined the efficacy of applied relaxation (i.e., PMR + in vivo exposure) and CBT (which included “behavioral experiments”). The contribution of either technique over and above exposure only cannot be tested with such design because the inclusion of some exposure strategies prevents the parsing out of components and comparing their effects directly. In another study, Öst and colleagues (1993) assessed differential outcome among three coping skill trainings for patients with PD/A: applied relaxation (AR), in vivo exposure, and CT. Again, CT was intermingled with exposure elements, whereas the in vivo exposure “only” training appeared to be confounded by “instructions for coping with panic during exposure” (p. 387), thus impeding comparative testing. Nonetheless, the results indicated very few differences between in vivo exposure and AR on panic-related measures. On a behavioral measure of fear, AR outperformed CT, whereas in vivo exposure alone did not, suggesting that AR may have augmented exposure to some degree. Other studies have evaluated the effects of applied PMR (i.e., training in PMR combined with instructions to use PMR during in vivo exposure) for PD/A (e.g., Barlow et al., 1989; Milrod et al., 2007), but did not evaluate the additive effects of PMR to in vivo exposure.

Finally, earlier studies (albeit none specifically examining PD/A samples) that compared graduated imaginal exposure with versus without the addition of PMR generally found no differences between the two conditions (e.g., Dawson & McMurray, 1978; Waters, McDonald, & Koresko, 1972; Yates, 1975; see Kazdin & Wilcoxon, 1976; McGlynn, Solomon, & Barrios, 1979, for reviews). These studies provided the basis for abandoning Wolpe's (1958) systematic desensitization approach in favor of more fear-activating approaches to exposure.

In sum, studies that directly test the efficacy of PMR in augmenting are largely absent from the literature. Thus, the degree to which acquisition of PMR skills and their application during exposure therapy augment exposure therapy remains unknown.

Shortcomings in current coping skill research

In light of the reviewed studies, one may conclude that traditional coping skills either bear no augmenting effect over exposure or their effects upon exposure are unknown in the treatment for PD/A. Constructive, dismantling, and component analysis designs have made important contributions to a preliminary understanding of what treatment components are most and least efficacious in the treatment of PD/A. However, despite their strengths, these studies, which typically fail to show that coping skills augment exposure, are limited not only in number, but in the conclusions that can be drawn using these methodologies. Specifically, the methodologies used to study the augmenting effects of coping skills test the degree to which the *delivery* of coping skills enhances outcomes; they have not assessed the differential degree to which *acquisition* of coping skills, and/or their *application during exposure therapy* enhance outcomes. The extant reliance on the *delivery* of coping skills training detracts from important questions about the degree to which acquisition and application takes place and the validity of their proposed mechanisms.

To advance our understanding on the potent contributors of change in CBT, there is a need for methodological designs that fully evaluate the role of coping skills training above and beyond the effects of exposure therapy alone. Furthermore, successful *delivery* of coping skills does not guarantee that the recipient successfully acquires and applies the skills. That is, unless we evaluate the degree to which a skill is actually learned and correctly applied during exposure, it is premature to draw conclusions about its potency. Proper testing of augmenting effects warrants a multiphase approach in which a particular skill is first acquired and then tested in the context of exposure therapy. Only if the skill training is administered in a “pure” format (i.e., not mixed with other skill trainings) can the *unique* contribution of this skill to exposure be determined. Additionally, the combined treatment needs to be contrasted with an “exposure only” treatment, ideally with a preceding placebo to account for time. Up to this point we have reviewed the additive effect of coping skills to exposure (i.e., improved efficacy), which is only part of the question when looking at augmenting effects. Mediational analyses allow us to look at the relationship between changes in psychological constructs of interest (such as catastrophic misinterpretations) and outcomes.

Exploring Mechanism of Therapy Success in PD

Kazdin (2007) cogently outlined the importance of mechanism research, including the potential to optimize the way in which treatment is delivered and thereby enhance outcomes. However, despite the invocation for mechanism research, less than a handful of psychosocial intervention studies have tested mediation properly. In the following we examine the meditational evidence for traditional coping skills in PD.

Mechanistic evidence for cognitive reappraisal strategies

Cognitive strategies are assumed to facilitate exposure by the development of explicit nonthreat appraisals about the mental, physical, or social consequences of panic attacks and related sensations, which in turn encourage approach behavior and lessen distress (e.g., Craske & Barlow, 2008). Thus, both the purported mediator and skill in CT is the ability to reappraise previously feared bodily sensations as nonthreatening.

Most studies of mediation of CT for PD/A merely measure change in purported mediators (i.e., reappraisal) as well as outcomes (i.e., panic symptom reduction) across the same interval of time, from pre- to posttreatment (e.g., Hofmann et al., 2007; Meulenbeek, Spinhoven, Smit, van Balkom, & Cuijpers, 2010; Smits, Powers, Cho, & Telch, 2004; Vögele et al., 2010) or without complete mediation models of analysis (e.g., Clark et al., 1994, 1999; Forman, Herbert, Moitra, Yeomans, & Geller, 2007; Schmidt & Bates, 2003).

Among the few studies fulfilling the criteria for mediational analyses is one by Bouchard and colleagues (2007), who found that changes in daily ratings of beliefs about panic preceded and were associated with changes in apprehension about future panic attacks. In another study by Hoffart et al. (2008), fear of bodily sensations influenced catastrophic beliefs, which in turn influenced avoidant behavior. A reduction in the latter decreased the fear of bodily sensations. Finally, evidence for modality-specific pathways was supported in a recent study by Meuret, Rosenfield, et al. (2010). In patients assigned to 4 weeks of exclusive training in cognitive skills, reductions in symptom appraisal mediated improvements in perceived control and panic symptom severity, and vice versa.

These studies, however, relied upon retrospective self-report measures of thoughts and beliefs, which are likely to be confounded by responder biases and demand characteristics, and unlikely to match ongoing, moment-to-moment cognition (Jarrett, Vittengl, Doyle, & Clark, 2007). Additionally, measures such as the Anxiety Sensitivity Index (ASI; Reiss, Peterson, Gursky, & McNally, 1986) capture dispositional characteristics, but not occurrent responding (Fridhandler, 1986). For instance, a person scoring high on the ASI is likely to respond fearfully to bodily sensations and is more likely to catastrophize about them. Notwithstanding, the ASI does not lend evidence to whether such thoughts and feelings are actually occurring in real time. Here, further research on approaches such as the think-aloud paradigm (Davison, Vogel, & Coffman, 1997; Davison, Williams, Nezami, Bice, & DeQuattro, 1991; Williams, Kinney, Harap, & Liebmann, 1997) will allow testing of symptom appraisal in real time. An example for capturing “in-the-moment” appraisals during cognitive skill training and exposure, using the think-aloud technique, is described below (see “Think-Aloud Paradigm”).

Mechanistic evidence for breathing and relaxation strategies

PMR and BRT are presumed to decrease anxiety by reducing heightened physiological arousal observed in PD/A. Specifically, the purported mediator for BRT is PCO_2, which serves as an index of the degree of hyperventilation. The commonly used coping skill is slow, deep, and/or abdominal breathing with the purpose of restoring normal levels of PCO_2. For PMR, the purported mediator is muscle tonus, and the coping skill is to “physically relax” with the purpose of restoring a “normal” level of muscle tension. These strategies are assumed to facilitate exposure by physical correction of hyperventilation or muscle tension/autonomic arousal that subsequently attenuate disturbing sensations, thereby encouraging further approach behavior and less distress. Given that the proposed mediators for PMR and BRT are physiological indices, they are subject to objective and direct assessment. However, with the exception of one uncontrolled study (Salkovskis et al., 1986), PCO_2 has not been assessed in traditional BRT. In addition to speculations of BRT acting as an impediment to treatment success by inhibiting necessary arousal to facilitate learning during exposure (Craske et al., 1997; Schmidt et al., 2000), experimental research suggests an actual hyperventilation-enhancing effect from traditional breathing techniques. That is, the slowing of respiratory rate, one of the core techniques of traditional BRT, can lead to compensatory deeper breathing that perpetuates/exacerbates hyperventilation in persons with PD/A (Conrad et al., 2007; Ley, 1991; Meuret et al., 2003, 2008). Compensatory overventilation is likely attributable to an exaggerated perception of sensations of “air hunger” (i.e., dyspnea) in patients with PD/A (Klein, 1993).

The few studies that have assessed physiological activity as an outcome measure in PMR generally have not found support for the association between decreased physiological arousal and improvement on psychological outcome measures for PD/A (Beck et al., 1994) or chronic anxiety (Leboeuf & Lodge, 1980). Furthermore, although some studies have found PMR to result in decreased physiological arousal, these decreases are not unique to those treated with PMR. For example, Michelson et al. (1990) observed heart rate

decrements after both PMR and in vivo exposure for the treatment of agoraphobia, with no differences between the two treatments. The only studies that have actually evaluated muscle tonus throughout exposure therapy utilized imaginal exposure. In those cases, PMR was associated with *increased* rather than reduced autonomic arousal (Borkovec & Sides, 1979; Levin & Gross, 1985). However, these studies were not conducted in samples with PD/A, and none of the above studies met criteria for proper meditational testing. Taken together, research elucidating the presumed physiological mediators driving symptom reduction is greatly lacking.

In summary, direct evaluation of the degree to which coping skills are *acquired* and the degree to which they are *applied* when confronted with feared situations or sensations, or the degree to which such acquisition and application mediate outcomes from exposure therapy is lacking. Furthermore, there are very few studies in which purported mediators are fully assessed. Consequently, extant data may misrepresent the impact of coping skills in the treatment of PD/A, because outcomes from exposure therapy may indeed be augmented as a function of degree of acquisition and/or application of coping skills. Such measurement would permit evaluation of not only the ‘”augmentation potential”’ of coping skills, but also a thorough evaluation of the degree to which individual differences moderate skill acquisition and application, and thereby outcomes. In the following, we introduce strategies aimed at addressing the above-discussed methodological shortcomings.

Future Directions in the Implementation, Assessment, and Evaluation of Current and Novel Coping Skills in Augmenting Exposure

There is a pressing need for both objective and online measurement of purported mediators, and evaluation of the degree to which change in those indices are predictive of change in subsequent symptom outcomes. Below we illustrate the implementation of online assessments using examples of two recently developed therapeutic approaches. The first exemplifies the direct manipulation and assessment of dysfunctional respiration, and the second illustrates a novel approach of assessing online thought processes.

Capnometry-assisted respiratory training: description, efficacy, and evidence for augmenting exposure

Background and Description—In contrast to traditional BRT, capnometry-assisted respiratory training (CART) targets respiratory dysregulation, in particular hypocapnia (Meuret et al., 2008; Meuret, Rosenfield, et al., 2010). CART is a brief, 4-week training that uses immediate feedback of end-tidal PCO_2 to teach patients how to raise their subnormal levels of PCO_2 (hyperventilation) and thereby gain control over dysfunctional respiratory patterns and associated panic symptoms (e.g., shortness of breath, dizziness). In this respect, CART substantially differs from traditional BRT because it focuses directly on the proposed mediator, PCO_2 (see Meuret et al., 2003, for a review). Most importantly for the current review, CART takes advantage of novel technologies that allow the precise assessment and monitoring of core respiratory variables. The device, a portable capnometer, offers breath-by-breath feedback of expired carbon dioxide and rate of breathing (both measured via a nasal canula). Compliance and skill acquisition and application can be assessed by means of electronic data storage. Between-session data are downloaded during the treatment session and presented and discussed with patients. This allows for a unique way to determine whether patients are willing and able to adapt new skills.

Evidence for Efficacy From Clinical Trials—Due to the novelty of CART, randomized controlled trials are limited but promising. In a first randomized controlled study, Meuret and colleagues (2008) tested the efficacy of 4 weeks of CART (n = 20)

compared to a delayed wait-list (WL) control group (WL, $n = 17$). CART, but not WL, led to sustained increases in PCO_2 levels and reduced panic severity and frequency. Reductions in panic symptom severity (PDSS; Shear et al., 1997) were comparable to standard CBT and improvements were maintained at 12-month follow-up. In a second study, patients with PD/A were randomly assigned to receive either 4 weeks of CART ($n = 21$) or CT ($n = 20$). An initial 4 weeks of skills training was followed by three sessions of in vivo exposure and a fourth session at a 2-month follow-up. Respective skill acquisition trainings led to significant and comparable reductions in panic symptom severity and panic-related cognitions, regardless of modality. However, only CART, but not CT, led to a correction of hypocapnic levels of PCO_2 (Meuret, Rosenfield, et al., 2010). Similarly, although improvements in panic severity across exposure sessions were large and independent of previously acquired coping skills, normalization in PCO_2 was only observed for patients undergoing prior training CART, but not CT (Seidel, Rosenfield, Bhaskara, Hofmann, & Meuret, 2009). Also, PD/A patients (Meuret et al., 2008) and patients with asthma in another capnometry-assisted study (Meuret, Rosenfield, Hofmann, Suvak, & Roth, 2009) demonstrated high compliance with the assigned 17-min, twice-daily homework exercises. The compliance also moderated improvement in panic symptom reduction (Meuret, Hofmann, & Rosenfield, 2010).

Mechanistic Evidence for CART—Like traditional BRT, PCO_2 is presumed to be the primary mediator of CART. Preliminary evidence for this thesis comes from longitudinal mediation analyses indicating that changes in PCO_2, measured continuously during between-session exercises, indeed mediated and preceded changes in fear of bodily sensations (Meuret et al., 2009) and cognitive reappraisal of symptoms and perceived control (Meuret et al., 2010) in CART but not CT. Although significantly reduced, reductions in rate of breathing neither mediated reductions in panic fear of bodily sensations (Meuret et al., 2009) nor panic symptom severity or cognitions (including perceived control) (Meuret et al., 2010). Mediation analysis examining changes during exposure showed bidirectional relations for cardiorespiratory changes mediating changes in physical symptom and for cardiac changes mediating changes in cognitive symptoms (Seidel et al., 2009); these pathways were significant and consistent across all exposure sessions. As expected, levels of PCO_2 during exposure were significantly greater in CART compared to CT (Seidel et al., 2009).

These findings strengthen the idea that panic symptom reduction can be achieved through different mechanisms. However, an evaluation of the degree to which CART augments exposure therapy (relative to exposure therapy alone) a waits testing. Most importantly, the measurement of changes in PCO_2 provides direct, ongoing measurement of purported mechanisms that permits evaluation of the degree to which CART skills are acquired and then applied during in vivo exposure, and the degree to which such acquisition and application mediate symptom outcomes.

Assessment of Cognitive Appraisal/Acceptance Skills: Think-Aloud Paradigm

In a recent pilot study, we tested the feasibility of a modified and extended version of the think-aloud paradigm (Davison et al., 1991, 1997; Williams et al., 1997). The paradigm is aimed at assessing concurrent, situation-specific, and participant representative thoughts both during skill acquisition and application. This online method of recording verbalizations provides a sample of thinking that differs from the constraints of forced-choice formats and retrospective judgments (e.g., questionnaires), and appears to be less susceptible to responder biases inherent to retrospective judgments. Think-aloud methodologies have been

used to evaluate thoughts during experimental exposure to feared situations (Williams et al., 1997) and are considered valid indicators of covert verbalizations when derived from instructions to "say in a continuous stream whatever one is saying to oneself at that moment" (vs. report upon what one thinks one has been saying over a past interval) and limited to brief snippets of time.

The clinical application was tested in a small sample of patients undergoing a brief training in acceptance therapy (Hayes et al., 1999; Segal, Williams, & Teasdale, 2002) followed by six sessions of exposure (Meuret, Twohig, Rosenfield, Hayes, & Craske, submitted for publication). Acceptance-based skill training differs to traditional coping skill training as the emphasis is not on control (e.g., of physiology or thoughts) but rather the acceptance of panic-related sensations and cognitions as they occur from moment to moment. Patients are asked to pay nonjudgmental attention to thoughts, feelings, images, and bodily sensations and learn to see thoughts as an ongoing process distinct from self rather than an event with literal meaning (cognitive defusion). Empirical evidence for the efficacy of acceptance approaches for PD/A has been demonstrated (e.g., Forman et al., 2007; Levitt, Brown, Orsillo, & Barlow, 2004); however, as with cognitive and behaviorally based treatments, both acquisition/application and mechanistic validation of acceptance skills is lacking.

During the first 4 weeks of training, patients were asked to practice willingness to experience internal sensations and apply these techniques using audio-guided exercises. During the twice-daily 15-min between-session exercises, patients recorded whatever was on their mind at prompted, 30-sec intervals (minute: 3, 7, 11), using a digital voice recorder. Recordings, with date and time stamps, were downloaded during the sessions and discussed with the therapist. Think-aloud samples were also recorded, in addition to cardiorespiratory physiology (see Figure 1) during exposures with the instruction to verbalize whatever they were saying to themselves in a continuous stream using a digital voice recorder. The results of this feasibility trial were promising and indicated high compliance with homework exercises and significant improvements in symptom appraisal, mindfulness, and panic symptom severity. The think-aloud paradigm provided valuable data regarding the degree to which patients acquired and applied acceptance-based skills. Notably, the think-aloud paradigm would be equally suitable for cognitive coping skills. In the following, we provide sample data for the physiological and "think-aloud" recordings collected during this pilot trial.

Examples for ongoing recording during skills training and during in vivo eexposure

Overall, patients were very receptive to and compliant with the recording devices for their physiology and their verbalizations. Figure 2 illustrates extracts from the prompted verbalizations during the first 4 weeks of acceptance skills training. Data of this type offers much needed insight into the acquisition and application of coping skills and warrants proper meditational testing. Patient 1 offered some dialogue of increased willingness to experience panic sensations and interest in practicing acceptance while having a panic attack. Patient 2 showed a greater grasp of acceptance as taught in this pilot study. These examples illustrate variation in acceptance skills acquisition (at least as verbalized) across patients. Data such as these will be informative for testing the degree to which coping skills acquisition and subsequent application during exposure actually mediate outcomes. Furthermore, they will permit evaluation of which individual difference variables moderate acceptance skill acquisition, and eventual treatment outcomes.

Conclusion

Empirical support for an augmenting effect of traditional coping skills (cognitive and biobehavioral) on exposure is lacking. However, the extant reliance on *delivery* of coping

skills detracts from examining the degree to which *acquisition* of coping skills and their *application during exposure therapy* enhance outcomes. At present, implementation of appraisal techniques (as taught in CT) are largely assessed retrospectively; likewise the assessment of core physiological processes (i.e., PCO_2 in BRT and muscle tonus in PMR) both during skill training (i.e., between-session exercises) and application (i.e., exposure) is lacking. Furthermore, concurrent testing of various coping skills clouds the testing of their additive effect on exposure. Thus, it is premature to draw conclusions as to whether they augment exposure alone because it remains unclear whether patients learn and apply the taught skills.

In this review, we advocate improved methodologies for examination of augmenting effects of coping skills. In particular, multiphase intervention designs are warranted, in which skill acquisition training precedes exposure, in order to dissect both the potency of the skill training and its contribution to exposure. Additionally, we posit mediational testing to ascertain that the skill in question indeed exerts its effect by means of its proposed mechanism. We have outlined recently developed methodologies and preliminary evidence for objective, online measurements of cognitive (i.e., think-aloud technique) and physiological processes (i.e., therapeutic capnography) to warrant proper assessment of their mechanism and efficacy testing. Understanding how these strategies work will allow researchers to develop more potent and efficacious treatment protocols for PD/A and will inform practicing clinicians about which coping skill will be most effective for which patient, and thereby improve treatment outcomes.

The findings from this review also offer clinical and applied suggestions. The general cognitive-behavioral treatment package is well supported in the treatment of PD/A, and is considered the first-line psychosocial treatment for PD/A. The choice to focus on cognitive distortions, ineffective breathing patterns, or neither could very reasonably be based on the presentation of the patient. Whatever choice the therapist and patient make, it is also suggested that some method to track the psychological process of change, in addition to outcomes, be utilized. This review suggests that these augmentation techniques are trained, but that their adoption and implementation are generally not tracked. It would behoove therapists to dually focus on what is being learned in the exposure exercises in addition to the outcomes that are being achieved. This can be accomplished with standardized measures, biomedical technology, or by using think-aloud techniques as described herein.

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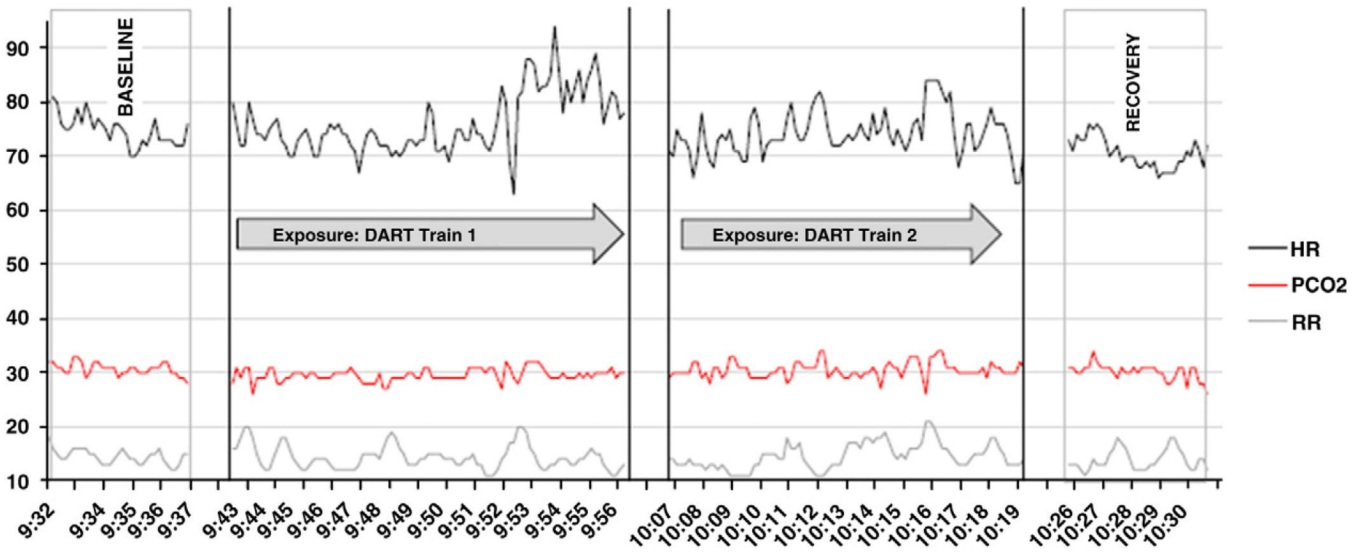

FIGURE 1.

Ambulatory data of heart rate (HR), end-tidal PCO_2, and respiration rate (RR) during real-life exposure. Measurement interruptions indicate periods of physical activity.

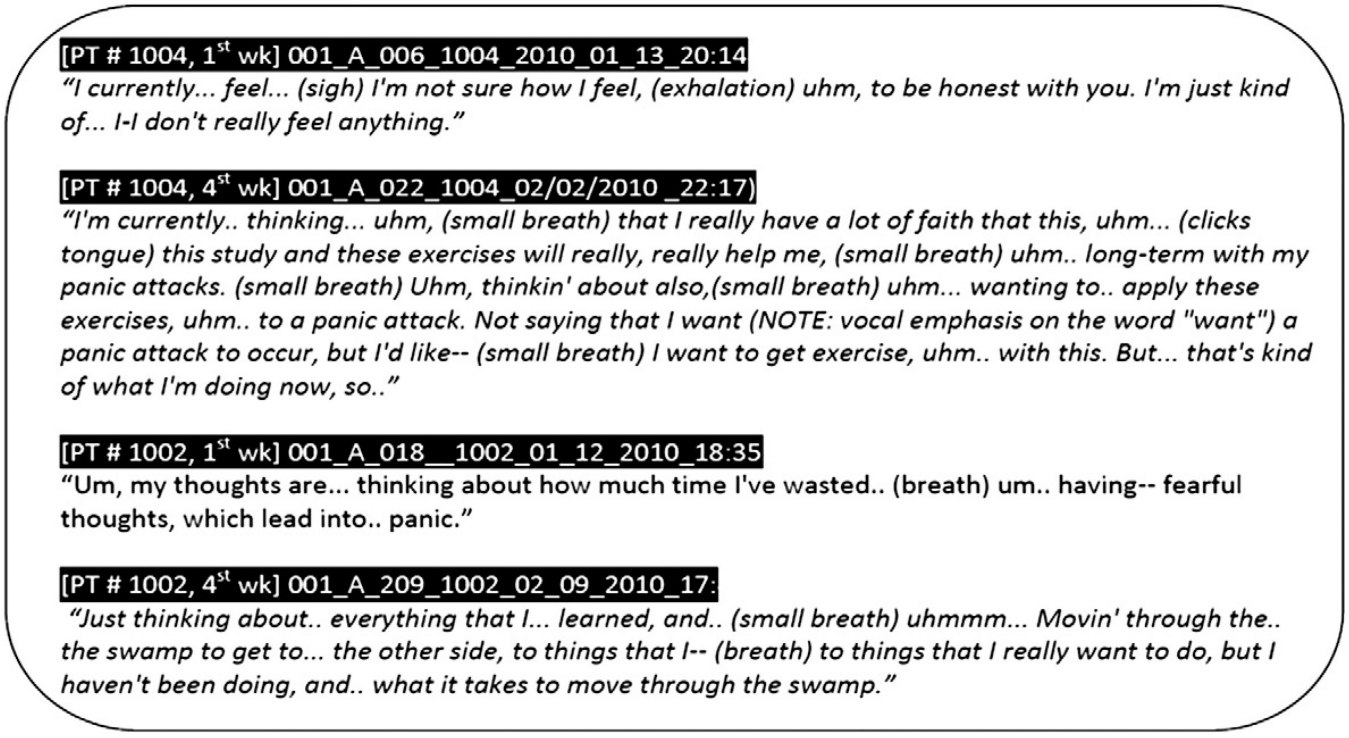

FIGURE 2.
Sample transcripts from "think-aloud" recordings during the first and last weeks of acceptance skill training.