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Agoraphobia

Michael J. Telch, Adam R. Cobb, and Cynthia L. Lancaster

Laboratory for the Study of Anxiety Disorders, The University of Texas at Austin

History of Agoraphobia

The term agoraphobia was first coined by Westphal (1871) in his description of three males who experienced intense anxiety when walking across open spaces. Westphal also noted the physiological symptoms of anxiety (i.e., palpitations, blushing, trembling, and sensations of heat) and the intense subjective anxiety that is elicited upon anticipating entering a feared situation. Today, agoraphobia remains one of the most disabling phobias and one of the most challenging to treat (Wittchen, Gloster, Beesdo-Baum, Fava, & Craske, 2010).

In the third edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-III*; American Psychiatric Association [APA], 1980), agoraphobia was characterized as a "marked fear and avoidance of being alone, or in public places from which escape might be difficult, or help not available in case of sudden incapacitation" (p. 227). However, even the *DSM-III* recognized the linkage between agoraphobia and panic attacks by stipulating that a diagnosis of agoraphobia with panic attacks should be coded if the onset of the disorder included recurring panic attacks. In the third revised edition of the *DSM* (*DSM-III-R*; APA, 1987) and subsequently in the fourth edition (*DSM-IV*; APA, 1994; *DSM-IV-TR*; APA, 2000), agoraphobia was reconceptualized as a common complicating feature of panic, thus relegating agoraphobia to a panic disorder "subtype" status. In the *DSM-IV*, the diagnosis "agoraphobia" no longer exists; rather, in cases of "pure" agoraphobia, clinicians are instructed to use the diagnosis "agoraphobia without history of panic disorder." It is interesting to note that the diagnostic criteria for agoraphobia in the *International Statistical Classification of Diseases and Related Health Problems* (10th ed.; *ICD-10*; World Health Organization, 1992)—the diagnostic system used in many other countries outside the United States—still recognizes agoraphobia as taking precedence over panic disorder.

There continues to be considerable controversy surrounding the current diagnostic status of agoraphobia. The crux of this controversy concerns whether agoraphobia

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should be conceptualized as a complication of panic attacks/panic disorder as outlined in the *DSM-IV-TR* or whether agoraphobia should be treated as a distinct, phobic syndrome independent of panic disorder as outlined in the *ICD-10*. The interested reader is referred to Wittchen et al. (2010) for an excellent review of this controversial issue, which has profound implications for both researchers and clinicians.

Epidemiology

Prevalence of Agoraphobia

Data from a community survey in Vermont predating the *DSM-III* (Agras, Sylvester, & Oliveau, 1969) estimated the prevalence of agoraphobia to be 6 per 1,000 individuals. Since that early report, numerous high quality epidemiological investigations using standard diagnostic criteria have appeared (Adler et al., 2006; Eaton, Kessler, Wittchen, & Magee, 1994; Kessler et al., 2006; Wittchen & Essau, 1991). Prevalence rates from these studies vary somewhat as a function of sample, diagnostic criteria, and diagnostic instrument, but a reasonably conservative estimate of the lifetime prevalence of agoraphobia with and without panic across studies is approximately 5%. Further, agoraphobia with and without panic disorder is about 2 and 1.3 times more likely to occur in women, respectively, and has a mean age of onset in the early 20s (Kessler et al., 2006).

First Generation Treatment Studies

The first series of research reports on the treatment of agoraphobia appeared almost 50 years ago. These first generation studies share several common features. First, they all predated the *DSM-III* and consequently it is not clear what proportion of the patients in these studies would have met current *DSM-IV* criteria for panic disorder with agoraphobia, or agoraphobia without panic disorder, or neither diagnosis. Second, the treatments included in this first group all targeted reductions in situational avoidance and phobic anxiety, as opposed to reductions in panic attacks, or fear of panic attacks. Third, despite a number of different treatment variations and labels, they all had a common procedural element, namely having the patient confront fear-eliciting situations repeatedly with the goal of eliminating the patients' phobic anxiety and avoidance. Finally, most would not meet the methodological standards of contemporary treatment outcome investigations; that is, the studies were underpowered, lacked treatment fidelity assessments, and focused their analyses on treatment completers only.

The specific treatments studied in these early investigations include systematic desensitization (Gelder & Marks, 1966; Gillan & Rachman, 1974), imaginal flooding (Gelder et al., 1973; Marks, Boulougouris, & Marset, 1971), reinforced practice (Agras, Leitenberg, & Barlow, 1968; Crowe, Marks, Agras, & Leitenberg, 1972), self-observation (Emmelkamp, 1974), group in vivo flooding (Hand, Lamontagne, & Marks, 1974; Stern & Marks, 1973; Teasdale, Walsh, Lancashire, & Mathews,

1977; Watson, Mullett, & Pillay, 1973), and participant modeling/guided mastery (Bandura, Jeffery, & Wright, 1974; Williams, 1990). As mentioned earlier, these treatments all shared the central procedural element of having the patient repeatedly confront fear-provoking situations. They differ mainly with respect to certain parameters of exposure, namely, mode of presentation (imaginal vs. in vivo), intensity (graded vs. ungraded), and mode of facilitation (therapist-aided, partner-aided, or self-directed).

Systematic Desensitization

The primary focus of systematic desensitization in the treatment of agoraphobia has been to teach the patient to produce inhibitory physiological responses (i.e., deep muscle relaxation) in order to inhibit the anxiety response to increasingly threatening situations. Gelder and Marks (1966) compared desensitization with attention placebo control in treating 20 inpatients with agoraphobia. Despite the trend in favor of desensitization, differences between the two groups at posttreatment and follow-up were not statistically significant. Similarly, Gelder, Marks, and Wolff (1967) found systematic desensitization only slightly more effective than individual or group psychotherapy in reducing phobic symptoms in 14 patients with agoraphobia. Further, Wolpe (1974) reported that desensitization is contraindicated in the treatment of agoraphobia except for those who suffer from a specific fear of open space.

Imaginal Flooding

Imaginal flooding involves exposing the patient in imagination to high levels of feared situations for prolonged durations. Research investigating its application in the treatment of agoraphobia first appeared in an article by Watson, Gaind, and Marks (1971) in which they reported significant reductions in phobic symptoms as measured by clinical ratings and heart rate response to phobic imagery among 10 agoraphobics. Other investigations of imaginal flooding have been conducted in the context of comparisons with systematic desensitization (Boulougouris, Marks, & Marset, 1971). Boulougouris et al., for instance, showed that imaginal flooding significantly outperformed imaginal desensitization in a mixed sample of patients with agoraphobia and specific phobias.

In an attempt to assess the role of anxiety experienced during flooding, Chambless, Foa, Groves, and Goldstein (1979) compared imaginal flooding alone, flooding plus a relaxant drug, and a control group with 27 outpatient agoraphobics. Results indicated that imaginal flooding decreased phobic symptoms as measured by client and therapist ratings, and physiological and behavioral measures. They found some support for the hypothesis that patients who experienced higher levels of anxiety during treatment benefited more from the treatment. This finding is in sharp contrast to results reported by Hussain and Nolan (1971), who treated 40 outpatients diagnosed with anxiety neurosis with either imaginal flooding with thiopental infusions or imaginal flooding with saline. Hussain and Nolan suggest that the use of a short-acting barbiturate (e.g., thiopental) protects against the possibility that exposure therapy may exacerbate anxiety.

Self-Observation

The self-observation procedure for treating agoraphobia was introduced by Emmelkamp and colleagues (Emmelkamp, 1974; Emmelkamp & Emmelkamp-Benner, 1975). Like successive approximation, self-observation requires patients to gradually enter feared situations. Upon experiencing undue anxiety, the patient is instructed to return immediately. This procedure is repeated for a number of trials, with the usual session length being approximately 90 minutes. Unlike successive approximation, however, patients are not given social reinforcement by the therapist. Instead, patients are provided with a stopwatch and instructed to record the time they spend outside. It should be noted that both self-observation and successive approximation differ from flooding in that they do not require the patient to experience a reduction in anxiety before terminating the trial.

Emmelkamp (1974) compared the relative effectiveness of self-observation, flooding, a combination of flooding and self-observation, and a wait-list control in treating 20 outpatient agoraphobics. Patients in the first three conditions received a total of 12 sessions (90 minutes each) over a 4-week period (three sessions per week). In the flooding sessions, patients received 45 minutes of flooding in imagination immediately followed by 45 minutes of flooding in vivo. Patients in the combined flooding/self-observation condition received flooding during the first three sessions and self-observation for the remaining nine sessions. Results indicated that patients in all three treatment conditions significantly improved on measures of phobic anxiety, phobic avoidance (rated by patient, therapist, and observer), and a behavioral in vivo measure. While no differences were found between self-observation and flooding, the combined flooding/self-observation treatment was shown to be more effective than either of the individual treatments. It is possible that the combined treatment proved more credible to the patients and thus increased their expectation for change. Unfortunately, credibility assessment was not carried out to test this hypothesis.

Everaerd, Rijken, and Emmelkamp (1973) compared self-observation and successive approximation in a cross-over design with 16 agoraphobic outpatients. Patients in both treatment conditions received six 90-minute sessions over a 3-week period (two sessions per week). Results indicated that both treatments produced significant improvement in phobic anxiety (rated by client and therapist) and in vivo measurement (number of minutes spent outside). Between-group comparisons yielded no significant differences on any of the measures. The findings suggest that social reinforcement administered by the therapist is not an essential component of in vivo treatments for agoraphobia.

Using a 2 x 2 factorial design, Emmelkamp and Emmelkamp-Benner (1975) tested the effects of historically portrayed modeling and group versus individual format on the outcome of self-observation treatment. Thirty-four agoraphobic outpatients were randomly assigned to one of the following four conditions: (a) video film plus individual treatment, (b) video film plus group treatment, (c) individual treatment (no film), and (d) group treatment (no film). Patients in all conditions received four 90-minute sessions of self-observation. Half of the patients were treated in small groups of 4 to 6 patients, while the other half were seen individually. The video film, which lasted 23 minutes, showed three ex-agoraphobics discussing their experiences with

self-observation treatment. The film stressed that clients had improved by practicing in the phobic situations. Patients in all conditions were instructed to carry out the procedure at home. Results showed a significant improvement for all conditions, as measured by in vivo client and observer ratings of phobic anxiety and phobic avoidance. Group treatment proved just as effective as individual treatment and the video film had no effect on treatment outcome. The present findings support the conclusion that self-observation treatment administered in a group setting is both effective and cost-efficient in treating agoraphobia.

Participant Modeling/Guided Mastery

Participant modeling was first introduced by Bandura and his colleagues in a series of elegant experiments investigating cognitive change mechanisms governing the reduction of pathological fear (Bandura, Adams, Hardy, & Howells, 1980; Bandura, Jeffery, & Gajdos, 1975; Bandura et al., 1974). As in other exposure-based treatments, in participant modeling, later renamed guided mastery, the phobic patient confronts actual fear-provoking situations. However, in guided mastery, the therapist plays a very active role in incorporating specific mastery enhancing strategies to help the patient overcome his or her fear. These enhancement elements include: (a) the therapist modeling coping behavior in the feared situation, (b) the systematic introduction and subsequent fading of performance aids (e.g., the therapist sits next to the driving phobic patient and then gradually fades his or her presence), (c) setting proximal goals and mastering subtasks to help the patient manage challenging tasks (e.g., having the phobic patient drive only one exit on the highway prior to tackling multiple exits), (d) identification and elimination of defensive maneuvers (e.g., having the patient loosen his or her vice grip on the steering wheel), and (e) encouraging the patient to vary his or her performance (e.g., venture into different grocery stores).

The first controlled investigation of guided mastery in the treatment of agoraphobia was reported by Williams, Dooseman, and Kleifield (1984). Thirty-two patients displaying severe driving and height phobias were randomly assigned to one of three conditions: (a) guided mastery, (b) in vivo exposure alone, and (c) no-treatment control. Total amount of exposure time in the two active treatments was carefully controlled. At posttreatment, both active treatments outperformed no treatment; however, participants receiving guided mastery showed significantly greater improvement than those receiving in vivo exposure alone on multiple indices of outcome including performance on behavioral approach tests, and patient ratings of anxiety and coping self-efficacy. Subsequent studies of guided mastery have provided consistent support for its efficacy in the treatment of agoraphobia (Hoffart, 1995, 1998; Williams & Zane, 1989).

Self-Directed Exposure

For almost four decades, anxiety disorder researchers have speculated that exposure to feared situations is the crucial procedural element in the successful treatment of agoraphobia (Marks, 1978). If this assumption is true, agoraphobia sufferers should be able to achieve considerable therapeutic benefit on their own through

self-directed practice entering feared situations with guidance coming from a therapist, family member, or self-help manual. Several studies have examined the effects of simply providing agoraphobia patients with instructions for self-directed practice.

The first systematic evaluation of a self-directed home-based treatment program for agoraphobia was conducted by Mathews, Teasdale, Munby, Johnston, and Shaw (1977). Twelve married agoraphobia patients were seen at their homes and were provided with manuals which described (a) the development and maintenance of agoraphobia, (b) principles of target behavior selection, (c) self-monitored practice, and (d) panic management. In addition, patients' spouses were provided with a detailed manual describing the same material with additional sections covering the spouse's role in reinforcing phobic behavior and use of contingent attention to reinforce patients' practice. A therapist visited patients on eight occasions during the 4-week program. During the home visits, the therapist stressed the importance of daily practice, gave advice about overcoming specific difficulties encountered during practice, ensured that future targets had been agreed upon between partners, and encouraged the use of contingent reinforcement for achieving proximal goals. Results of the program were quite encouraging. Data obtained from patients' diaries revealed a twofold increase in the time spent out of the house. Significant improvement was also shown on ratings of phobic anxiety, phobic severity, and psychiatric ratings of overall improvement. Comparison of the present results with those achieved in earlier studies by the same authors using the same measures, therapists, and assessors (Mathews et al., 1976) revealed a similar or even greater effect for the home-based program. A notable finding was that patients showed further improvements on most measures during the follow-up.

A replication of the Mathews et al. home-based treatment program (Jannoun, Munby, Catalan, & Gelder, 1980) provided additional evidence for the efficacy of this self-directed exposure treatment. Twenty-eight women with agoraphobia were randomly assigned to the self-directed exposure program or a problem-solving control condition. Self-directed exposure led to a significantly greater increase in the number of weekly journeys out of the home compared to the problem-solving treatment. However, the authors also noted the unexpected improvement achieved in the problem-solving control treatment. This latter finding raises the question as to whether exposure to phobic situations is a crucial procedural component for fear reduction to occur as well as the possibility that both treatments may be mediated by a mechanism other than exposure-facilitated habituation to feared situations.

Several early studies have examined the efficacy of self-directed exposure to feared situations without the involvement of family members (Greist, Marks, Berlin, Gournay, & Noshirvani, 1980; McDonald et al., 1979). In McDonald et al., 19 patients with agoraphobia were randomly assigned to a self-exposure homework condition or a nonexposure discussion control. Results revealed a small but statistically significant superiority of the self-exposure condition on patients' ratings of phobic severity and assessors' ratings of target problems. It should be noted that the superiority of the self-exposure condition was obtained despite evidence from patients' diaries showing that the groups did not differ in the frequency of outings (McDonald et al., 1979).

Summary of Early First Generation Behavioral Treatment Studies

Results of these early behavioral treatment studies are of great historical significance because they provided compelling evidence, albeit without the rigor of today's randomized controlled trials (RCTs), that agoraphobics receiving treatments employing in vivo exposure to fear-provoking situations can achieve significant therapeutic benefit as measured by clinically meaningful reductions in situational avoidance and phobic anxiety. They also provide some very preliminary data to suggest that exposure treatments can be enhanced through the systematic addition of certain therapeutic strategies—a topic we address later in this chapter.

Second Generation Treatment Studies

This next group of treatment studies includes single-site RCTs in which patients meeting for agoraphobia with panic attacks (*DSM-III*) were randomly assigned to a psychological treatment that was compared to either another active treatment, a nonspecific treatment (attention/placebo control), or delayed treatment (wait-list control). As a group, the studies in this generation tend to be methodologically superior to those in the first generation by virtue of their (a) larger sample size, (b) use of structured diagnostic interviews to ensure patients met the threshold for agoraphobia, (c) use of psychometrically validated outcome measures, (d) greater attention to issues of treatment fidelity, (e) greater attention to patient dropouts in their outcome analyses, and (f) greater attention to the clinical significance of the changes brought about by the treatments. The treatments investigated in this generation of studies tend to be exposure-based treatments or attempts to enhance exposure treatments through one or more augmentation strategies. Representative studies in this generation (Michelson, Marchione, Greenwald, Testa, & Marchione, 1996; Öst, Thulin, & Ramnero, 2004; van den Hout, Arntz, & Hoekstra, 1994) are described later in this chapter in the section entitled, "Exposure Augmentation Strategies in the Treatment of Agoraphobia."

Third Generation Treatment Studies

This next group of treatment studies includes single-site RCTs in which patients met *DSM-III-R* or *DSM-IV* criteria for panic disorder with agoraphobia. As a group, the studies in this generation tend to be of high quality and share the same methodological strengths outlined above. Unlike second generation studies, which focused primarily on situational exposure treatments alone or in combination with other treatment augmentation strategies, the treatments investigated in this generation include therapeutic elements that specifically target panic attacks and panic-related apprehension. The three most widely researched treatments in this generation are panic-focused cognitive behavioral therapy (Barlow, Craske, Cerny, & Klosko, 1989; Craske et al., 2005; Margraf, Barlow, Clark, & Telch, 1993; Telch et al., 1993; Telch, Schmidt, Jaimez, Jacquin, & Harrington, 1995), cognitive therapy (Clark

et al., 1994; Clark et al., 1999), and applied relaxation training (Öst, 1987, 1988). Most studies of this generation include mixed samples of panic disorder with and without agoraphobia. To avoid duplication with Chapter 39 ("Panic Disorder"), we have limited this review to representative third generation treatment studies focusing on agoraphobia outcome.

In a comparative study of several widely established treatments for panic disorder with agoraphobia (PDA), Öst, Westling, and Hellstrom (1993) randomized 45 patients meeting *DSM-III-R* criteria for panic disorder with moderate to severe agoraphobia to applied relaxation, in vivo exposure, or cognitive therapy. Patients in all three conditions received self-exposure homework instructions. The three treatments yielded significant pre- to posttreatment improvements across behavioral and self-report measures of agoraphobia with no appreciable differences between the treatments. On a behavioral assessment of agoraphobia, 86.7% in the applied relaxation group, 80% in the in vivo exposure group, and 60% in the cognitive therapy group met criteria for clinically significant improvement at posttreatment. On a self-report assessment of agoraphobia, 53.3% in the applied relaxation group, 46.7% in the in vivo exposure group, and 60% in the cognitive therapy group met criteria for clinically significant improvement at posttreatment. Between-group comparisons revealed no statistically significant differences in the percentage of participants demonstrating clinically significant improvement. All three treatments maintained their gains at 1-year follow-up, although only patients assigned to cognitive therapy (26.7%) sought additional treatment during the follow-up period.

Craske, DeCola, Sachs, and Pontillo (2003) investigated the efficacy of augmenting panic control treatment (PCT) with in vivo exposure. Patients meeting *DSM-IV* criteria for panic disorder with moderate to severe agoraphobia were assigned to either PCT alone (in which they were encouraged to approach avoided situations, but were not provided with instruction or feedback) or PCT with formal in vivo exposure (in which they were encouraged to approach avoided situations and were provided with instruction and feedback). At posttreatment and at follow-up, both treatments were deemed equally effective for both panic disorder and agoraphobia. Clinically significant improvement at posttreatment was achieved in 42% of the PCT-only group and 32% of the PCT plus exposure group. At 6-month follow-up, 58% of the PCT-only group and 50% of the PCT plus exposure group met criteria for clinically significant improvement. There were no statistically significant between-group differences in the percentage meeting criteria for clinically significant improvement. Results overall suggest that adding formal in vivo exposure to standard PCT does not enhance therapeutic outcome in patients displaying moderate to severe agoraphobia. Unfortunately, the failure to include a treatment arm in which patients receive only in vivo exposure limits conclusions drawn from this study regarding the relative benefits of PCT versus in vivo exposure in the treatment of agoraphobia.

In a study designed to address whether cognitive therapy, exposure therapy, and their combination vary in efficacy depending on the patient's level of agoraphobia, Williams and Falbo (1996) randomized 48 panic patients with varying levels of agoraphobic avoidance to one of four conditions: (a) cognitive therapy, (b) guided performance mastery, (c) combined cognitive therapy plus guided mastery, and (d) wait-list. Between-group comparisons of the three active treatments for the full

sample showed equally large effects across the primary measures of panic attacks, and agoraphobic avoidance. However, comparison of patients with high and low levels of agoraphobia revealed that all three treatments were significantly less effective for reducing panic attacks for those with high levels of agoraphobia (88% vs. 39%, respectively, at the 2-year follow-up). Accordingly, Williams et al. suggest that panic disorder treatment studies that exclude patients with agoraphobia may be overestimating the efficacy of cognitive behavioral therapy (CBT) for panic attacks and argue that exposure-based treatments that do not directly target panic attacks are as effective for reducing panic as cognitive therapy.

Investigation of Exposure Parameters in the Treatment of Agoraphobia

Because in vivo exposure is a cornerstone therapeutic strategy in the treatment of agoraphobia, it makes sense to examine the parameters of exposure that optimize its efficacy. In this next section we review studies examining several distinct parameters of exposure therapy implementation.

Massed versus Spaced Exposure Sessions

What is the optimal frequency of exposure therapy sessions? Are sessions conducted weekly more effective than sessions occurring every day? In the first study to address this issue, Foa, Jameson, Turner, and Payne (1980) used a counterbalanced crossover design to compare the effects of 10 daily sessions with 10 weekly sessions in a small sample of agoraphobics ($N = 11$). At posttreatment, the massed condition outperformed the weekly spaced condition on independent assessor ratings of phobic anxiety and avoidance.

In the only other study to compare massed versus spaced exposure treatment for agoraphobia, Chambless (1990) used a between-subjects design to compare massed versus spaced therapist-assisted in vivo exposure. Agoraphobic patients ($N = 19$) received 10 daily or 10 weekly sessions of in vivo exposure along with several anxiety control strategies including respiratory control training, thought-stopping, and paradoxical intention. Exposure homework was not given due to the obvious advantage that would give to patients assigned to the spaced condition. Results revealed no significant differences in outcome at either posttreatment or 6-month follow-up. Moreover, they found no evidence to support the claim that massed sessions would lead to more dropouts and significantly higher relapse relative to spaced sessions. However, it should be noted that the failure to find differences may have been due to insufficient statistical power as a result of the relatively small sample size.

Brief versus Standard Treatments for Agoraphobia

Reducing length of treatment has several potential advantages including lower treatment offset costs and increased accessibility of care. However, these potential

advantages hinge on the assumption that standard empirically supported treatments for panic disorder with agoraphobia can be condensed without a loss of therapeutic efficacy. Fortunately, there is now converging evidence across laboratories that brief CBT confers significant therapeutic benefit over control conditions, including wait-list (Clark et al., 1999) and nondirective treatment (Craske, Maidenberg, & Bystritsky, 1995). Moreover, studies comparing brief versus standard CBT also suggest that brief treatments tend to be as effective overall as standard length treatments (Côté, Gauthier, Laberge, Cormier, & Plamondon, 1994; Gould, Clum, & Shapiro, 1993; Hecker, Losee, Fritzler, & Fink, 1996).

One limitation of the above studies is that patients exhibited minimal or no agoraphobia, and thus they do not directly address the efficacy of brief treatments for agoraphobia symptoms per se. However, there is encouraging evidence that the efficacy of condensed CBT interventions can also benefit patients with agoraphobia. Goisman et al., (1987) randomly assigned 40 patients with agoraphobia to receive self-exposure instructions from a psychiatrist, a self-help book, or a computer. All three groups improved substantially and continued to maintain those gains through a 6-month follow-up (Goisman et al., 1987). These data are encouraging and suggest that providing exposure instructions, regardless of the delivery modality, affords major therapeutic benefits despite only brief contact with a clinician.

In a more ambitious study, Roberge, Marchand, Reinharz, and Savard (2008) randomized 100 patients meeting *DSM-IV* criteria for panic disorder with agoraphobia to 14-session standard CBT ($n = 33$), 14-session group CBT ($n = 35$), or 7-session brief CBT ($n = 32$). Patients received a self-study manual and were assigned weekly readings and exercises. The results indicate that regardless of the treatment condition, CBT for moderate to severe panic disorder with agoraphobia is beneficial in the intermediate and long term. To this effect, all three treatment conditions significantly improved quality of life and reduced the intensity of symptoms, producing large within-group effect sizes (d ranging from 1.13 to 1.68) on the Panic and Agoraphobia Scale (Bandelow, 1995), and on a clinician-rated index of global severity (d ranging from 1.41 to 1.65) at 3-month follow-up. A 2-year follow-up report revealed large within-group effect sizes ($d = 1.67$ to 1.89) on the primary agoraphobia outcome measure across the three treatments, which supports the durability of treatment gains (Marchand, Roberge, Primiano, & Germain, 2009). Not surprisingly, patients receiving brief individual CBT and group CBT had superior cost-effectiveness relative to standard individual CBT. The implication of these findings is clear—CBT can be delivered in more cost-effective formats without reduced efficacy. Future research will hopefully address two important follow-up questions: (a) Could group CBT also be delivered in fewer sessions to improve its efficiency? and (b) What are the patient prognostic factors that predict differential response to brief versus group CBT?

Group versus Individually Administered Treatment

Although several investigators have demonstrated the efficacy of group behavioral treatment of agoraphobia (Telch, Agras, Taylor, Roth, & Gallen, 1985; Telch et al., 1993; Telch et al., 1995), few studies have conducted a head-to-head comparison of individual- versus group-administered treatments for agoraphobia. Sharp, Power,

and Swanson (2004) compared group with individual CBT in 97 patients meeting *DSM-IV* criteria for panic disorder either with or without agoraphobia. On the major index of agoraphobia treatment outcome, both groups showed statistically equal symptom reduction at 3-month follow-up; 40% of the participants receiving group CBT and 58% of the participants receiving individual CBT met criteria for clinically significant improvement. However, two additional findings are worth noting. First, 47% of the participants assigned to the group treatment condition dropped out of the study, which is four times higher than that observed in previous group administered CBT (Telch et al., 1985; Telch et al., 1993; Telch et al., 1995). Second, when wait-listed patients were given the choice of receiving group or individual treatment, the majority chose individual treatment.

Therapist-Assisted versus Self-Directed Exposure

Does the presence of the therapist during in vivo exposure to agoraphobic situations offer advantages over therapist-unaccompanied exposure? Those working directly with agoraphobics know full well the tremendous dread that many display while anticipating and performing in vivo exposure procedures. There are several reasons to believe that therapeutic outcome might be enhanced for patients when the therapist is present to offer instructions, guidance, and moral support, and to assist the patient in problem-solving obstacles encountered during in vivo exposure. Until recently, there have been few data that speak directly to this important issue. Fortunately, an impressive eight-site clinical trial has been completed that directly addresses the impact of therapist assistance during in vivo exposure (Gloster et al., 2011). Patients ($N = 369$) meeting *DSM-IV* criteria for panic disorder with moderate to severe agoraphobia were randomized to a wait-list control group or to group CBT in which they either (a) completed all situational confrontations as homework, or (b) had a therapist present for one-third of the situational confrontations. For sessions involving in vivo exposure in the latter condition, the therapist accompanied the participant for one in vivo exposure and then assigned two independent exposures for homework. Results suggest that both CBT interventions were beneficial for patients; however, those who received therapist-assisted in vivo exposure exhibited superior outcomes, particularly for agoraphobic avoidance (Cohen's $d = 0.32$). This finding supports the conclusion that the presence of a therapist during the initial exposures to feared situations enhances the effectiveness of exposure therapy for agoraphobia.

Exposure Augmentation Strategies in the Treatment of Agoraphobia

In this next section we provide a brief overview of research examining efforts to enhance the efficacy of exposure-based treatments for agoraphobia by integrating additional procedural elements. For an excellent in-depth review of the research on exposure augmentation in agoraphobia, see Meuret, Wolitzky-Taylor, Twohig, and Craske (2012).

Cognitive Strategies

Several studies have investigated whether cognitive restructuring interventions enhance the efficacy of exposure-based therapies for agoraphobia (Michelson et al., 1996; Öst et al., 2004; van den Hout et al., 1994). In a well-crafted, two-phase design by van den Hout et al. (1994), 24 agoraphobia patients were randomized to one of two groups: Group 1 received four sessions of cognitive therapy (CT) without exposure followed by eight sessions of CT plus exposure. Group 2 received four sessions of a placebo psychotherapy ("associative therapy") followed by exposure without CT. At the conclusion of the first 4-week phase, CT resulted in reductions in panic, but not avoidance, whereas those assigned to the attention control showed no significant change in panic or avoidance. At the conclusion of 8 weeks of either exposure therapy or exposure therapy plus CT, no differences were observed, thus showing that CT did not enhance the effects of exposure.

Öst et al. (2004) randomized 73 patients meeting *DSM-IV* criteria for panic disorder with agoraphobia to (a) in vivo exposure alone, (b) in vivo exposure plus CT, or (c) wait-list control. The two active treatments were equated for both number of sessions (12–15) and duration of each session (45–90 minutes). Both active treatments showed large pre-to-post effect sizes and maintenance of improvement at the follow-up assessment. Comparisons between the two active treatments were consistent with the earlier findings of van de Hout et al. (1994) showing that those receiving the combination of CT plus exposure therapy fared no better than patients receiving exposure therapy alone. The percentage of patients no longer meeting criteria for a diagnosis of panic disorder with agoraphobia at the end of treatment was 76% among those receiving CT plus exposure, 62% receiving exposure alone, and 0% among wait-listed patients. At follow-up, 86% of patients receiving exposure alone and 74% receiving exposure plus CT no longer met *DSM-IV* criteria for panic disorder with agoraphobia (follow-up results include wait-list patients who had been randomized to an active treatment condition).

In the only study to show a significant exposure enhancement effect of cognitive therapy, Michelson et al. (1996) randomized 92 patients meeting *DSM-III* criteria for agoraphobia with panic attacks to one of three treatment arms: (a) group-administered graded exposure (GE) alone, (b) GE plus CT, and (c) GE plus relaxation training (RT). Experienced doctoral-level clinicians delivered the treatments and total treatment time (48 hours) was equated across the three conditions. Results revealed that patients assigned to CT plus GE were significantly more likely to achieve high end-state functioning (44% at posttreatment; 71% at follow-up) relative to GE alone (22% at posttreatment; 38% at follow-up) or GE plus RT (22% at posttreatment; 33% at follow-up). The observed enhancement effect brought about by CT in this study raises the obvious question: Why did CT enhance the effects of exposure in this study but not in the two studies reviewed above (Öst et al., 2004; van den Hout et al., 1994)? One possibility, although unlikely, is that the increased sample size led to greater statistical power to detect a CT enhancement effect. A more likely possibility is that the markedly increased "dose" of CT used by Michelson et al. (i.e., at least a threefold increase in therapy hours over other studies) was responsible for the observed exposure enhancement effects of CT.

Respiratory Training

For over 25 years, aberrant respiratory functioning has been implicated in the pathogenesis of panic disorder with agoraphobia (Klein, 1993; Ley, 1985). Reduced levels of pCO2 (i.e., partial pressure of CO2) brought about through hyperventilation can lead to a positive feedback loop in which heightened levels of anxiety lead to increased respiration resulting in further lowering of pCO2 and panic-like symptoms. Consequently, many of the CBT packages for panic disorder with agoraphobia have included a breathing retraining component (BRT) designed to normalize pCO2 levels, thus reducing somatic perturbations and, presumably, anxiety and panic. Several studies have examined whether adding BRT enhances the efficacy of exposure treatment for panic disorder with agoraphobia (Bonn, Readhead, & Timmons, 1984; Hibbert & Chan, 1989) or whether BRT contributes to the efficacy of multicomponent CBT interventions for panic/agoraphobia (Schmidt et al., 2000).

In the study by Bonn et al. (1984), patients with panic disorder with agoraphobia received either two sessions of BRT followed by seven weekly sessions of in vivo exposure, or nine weekly sessions of in vivo exposure with no BRT. Findings at posttreatment showed no differences, but an advantage of BRT-augmented exposure emerged at the 6-month follow-up. In the Hibbert and Chan (1989) study, patients with panic and agoraphobia received 2 weeks of BRT followed by 3 weeks of in vivo exposure, or 2 weeks of supportive therapy followed by 3 weeks of in vivo exposure. At the end of the in vivo exposure treatment, patients receiving BRT showed greater improvement on clinician ratings of improvement, but not on patient self-report ratings.

In a dismantling study of group CBT, Schmidt et al. (2000) randomized panic disorder patients with and without agoraphobia to CBT either with or without BRT. At the end of the trial there were no significant differences in outcome, suggesting that BRT did not significantly contribute to the efficacy of group CBT. These findings are in accord with those reported by Craske, Rowe, Lewin, and Noriega-Dimitri (1997), who found no differences on measures of agoraphobic avoidance between an individual-administered CBT treatment consisting of cognitive restructuring (CR), interoceptive exposure, and in vivo exposure relative to a treatment package combining CR plus BRT plus in vivo exposure. Taken together, these findings provide little evidence that BRT enhances the efficacy of either exposure treatment or multicomponent CBT interventions for panic disorder with agoraphobia.

Involvement of Spouses in Treatment

Several studies have explored whether involving spouses in treatment enhances the outcome of exposure therapy for agoraphobia. Theoretically, involving spouses in therapy may augment the effectiveness of interventions for two reasons: (a) spouses can reinforce the development of skills for managing anxiety and the completion of exposure exercises, and (b) spouses can be educated about actions they can take to stop reinforcing or perpetuating agoraphobic symptoms (Byrne, Carr, & Clark, 2004; Oatley & Hodgson, 1987).

In one of the earlier investigations in this area, Cobb, Mathews, Childs-Clarke, and Blowers (1984) assigned patients to receive home-based exposure therapy with or without the participation of their spouse. Therapists visited the homes of clients for each session and provided a total of 5 hours of therapy over the course of treatment. The group without spouse involvement received a therapeutic manual during the first session, and completed one therapist-assisted in vivo exposure session. Additional sessions were spent planning and discussing independent in vivo exposure assignments. In this group, spouses only attended the first therapy session and were otherwise uninvolved in therapy. The group with spouse involvement differed in that spouses attended each session of therapy, received a therapy manual, were instructed to assist clients in completion of homework assignments, and were told to promote self-help in lieu of dependence from the client. Results indicated that both treatments led to improvements on agoraphobic symptoms that were maintained at 6-month follow-up; however, between-group comparisons did not reveal an advantage for involvement of spouses. Thus, the authors concluded that while the involvement of a spouse is not detrimental, it also does not appear to enhance outcome.

Similarly, Emmelkamp et al. (1992) randomized agoraphobia patients to receive in vivo exposure therapy with or without the involvement of their spouse. In the spouse-assisted condition, spouses attended each treatment session and received a manual describing how to support the client. However, the authors explicitly stated that relationship problems were not discussed until after the experimental trial, which may suggest that any communication skills regarding coping with agoraphobic symptoms were not actively discussed during treatment. Though overall both treatments improved agoraphobic symptoms, there was no clear advantage of spouse-assisted treatment. However, other studies have produced conflicting results.

In contrast to the above findings, Barlow, O'Brien, and Last (1984) found a treatment enhancement effect for including spouses in treatment. In their study, women with agoraphobia were randomly assigned to a group CBT intervention consisting of coping skills training, in vivo exposure, and cognitive restructuring, with or without the attendance of their husbands. The spouse-assisted condition included discussion of methods for the husband to assist the client in anxiety management and reduction of avoidance behaviors, and discussion about the possible roles of spouses in maintaining agoraphobia. Additionally, husbands were instructed to assist with in vivo exposure exercises, but to allow the client to complete at least one exposure independently for each feared situation. Furthermore, partners worked on strategies for communicating when the client was anxious or panicked and agreed upon strategies for managing anxiety in these situations. Results indicated that significantly more participants in the spouse versus no spouse group (i.e., 12 out of 14 vs. 6 out of 14, respectively) were classified as treatment responders at posttreatment based on a composite index of treatment outcome. Furthermore, the advantage of spouse involvement was maintained at 2-year follow-up (Cerny, Barlow, Craske, & Himadi, 1987).

Similarly, research by Arnow, Taylor, Agras, and Telch (1985) also suggests that the involvement of spouses can enhance treatment outcomes. In contrast to previous studies, in which the partner primarily supported the client in completing a course of exposure therapy, this study also included a component of therapy that specifically

focused on the development of communication skills in the relationship. Couples' communication skills training emphasized the modification of interactions that may play a role in maintaining agoraphobic symptoms. In this study, female agoraphobia patients received exposure plus couples relaxation training or exposure plus couples communication skills training. All participants first received 4 weeks of exposure to feared situations. Exposure was delivered in a group format that included the participation of partners. Couples were then assigned to receive 8 weeks of either relaxation training or communication skills training. The relaxation group served as a comparison group with similar situational exposure, partner involvement, and overall therapy time. Participants who received exposure plus communication skills training demonstrated more improvement in relationship communication skills and better posttreatment outcomes on behavioral and self-report measures of agoraphobia. Further, the superiority of the communication skills group was maintained, with no significant differences found on outcome measures between posttreatment and 8-month follow-up. It is noteworthy that both studies providing support for the involvement of spouses included communication skills development either as a primary focus of therapy (Arnow et al., 1985) or as a component of therapy (Barlow et al., 1984). Future research should further examine the role of improved relationship communication skills in enhancing outcomes of exposure-based therapy for agoraphobia.

Fading of Safety Behaviors

Human beings are hardwired to engage in protective actions when faced with perceived threats. Examples of such actions include wearing seat belts while driving, wearing warm clothing when venturing outside on a winter's day, and using condoms with a sexual partner. However, engaging in such protective actions when no real threat exists appears to actually contribute to the development of new forms of pathological anxiety (Olatunji, Etzel, Tomarken, Ciesielski, & Deacon, 2011) or maintain pathological anxiety that already exists. Several putative causal pathways through which safety behaviors exert their anxiety-maintaining effects are discussed elsewhere (see Telch & Lancaster, 2012).

In the case of agoraphobia, Kamphuis and Telch (1998) factor analyzed safety behavior data from 105 panic disorder patients (with or without agoraphobia) recruited from the community. Based on their analyses of the 50 items of the Texas Safety Maneuver Scale (TSMS; Kamphuis & Telch, 1998), five interpretable factors emerged. These five factors were named (a) classic agoraphobic avoidance—such as avoidance of crowded stores, and avoidance of public transportation; (b) relaxation techniques—such as meditation or yoga to relieve anxiety; (c) avoidance of stressful encounters—such as arguments with loved ones or stress at work; (d) avoidance of somatic perturbations—such as avoidance of caffeine or rigorous exercise; and (e) use of distraction techniques—such as listening to music, or staying busy in order to avoid anxiety or panic symptoms.

The first empirical evidence supporting the utility of fading safety behaviors during exposure therapy with agoraphobia patients was reported by Salkovskis, Clark, Hackmann, Wells, and Gelder (1999). They randomized participants with panic

disorder and moderate to severe avoidance to receive 15 minutes of in vivo exposure therapy, with or without instructions to reduce safety behaviors. Though both treatment groups reported similar anxiety levels during exposure, the group instructed to reduce safety behaviors had superior outcomes. More recently, this same group (Salkovskis, Hackmann, Wells, Gelder, & Clark, 2006) replicated their earlier finding. In this study, agoraphobia patients underwent 3.25 hours of exposure therapy with a habituation rationale, or exposure therapy with a threat disconfirmation rationale and the fading of safety behaviors. At the conclusion of treatment, patients assigned to the exposure plus safety behavior fading arm showed markedly greater improvement (between-group effect sizes [Cohen's *d*] ranging from 1.7 to 2.7) on self-report measures of anxiety and situational avoidance, and completed significantly more steps on a standardized behavioral approach test. These data are consistent with findings from a recent review showing that out of eight controlled trials investigating safety behavior fading in anxiety disorders, all eight have shown significant enhancement effects (see Telch & Lancaster, 2012). Accordingly, there is compelling evidence suggesting that clinicians should assist their agoraphobic patients in eliminating safety behaviors when encountering fear-provoking situations.

Intensive Treatment Programs for Agoraphobia

The development of more efficient interventions, including high-density and brief exposure-based treatments, has been a tradition in clinical research, with successful applications to the treatment of agoraphobia. For instance, Hahlweg, Fiegenbaum, Frank, Schroeder, and von Witzleben (2001) provided high-density exposure to a large community health center-based sample ($N = 416$) of patients all meeting *DSM-III-R*- criteria for panic disorder with agoraphobia. Treatment consisted of 4 to 10 days of in vivo exposure with each session lasting several hours per day. At 6-week and 1-year follow-ups, patients showed significant reductions in measures of anxiety, depression, general symptomatology, and agoraphobic avoidance. Within-group effect sizes (Cohen's *d*) ranged from 0.93 to 1.82 (mean = 1.23) at posttreatment, and ranged from 0.92 to 1.7 (mean = 1.24) at follow-up. Despite several limitations (i.e., reliance on self-report measures and a lack of treatment integrity data), this study offers evidence that high-density exposure can be successfully translated from research to applied settings.

An intensive eight-session treatment program for patients presenting with moderate to severe agoraphobia was developed in David Barlow's Center at Boston University. Coined Sensation-Focused Intensive Treatment (SFIT; Morissette, Spiegel, & Heinrichs, 2006), this approach incorporates cognitive restructuring and massed interoceptive and situational exposure. During Days 1 to 3, patients receive standard CBT components including psychoeducation, interoceptive exposure, and cognitive restructuring. On Days 4 and 5, patients receive two full days of ungraded, massed therapist-accompanied exposure to their most fear-provoking situations. This is followed by two full days of unaccompanied intensive self-exposure, and a final session

focusing on maintenance of treatment gains and relapse prevention. A small proof-of-concept study (Bitran, Morissette, Spiegel, & Barlow, 2008) with 40 patients all meeting criteria for panic disorder with moderate to severe agoraphobia revealed that the program led to large pre-to-post improvements in panic, agoraphobic avoidance, anxiety sensitivity, and self-efficacy. Gains were maintained at follow-up (1 to 6 months posttreatment) on all measures, and further gains emerged for measures of anxiety sensitivity and agoraphobic avoidance.

Innovative Agoraphobia Treatment Delivery Systems

In the last decade, a number of new treatments for panic disorder and agoraphobia have emerged, prompted by barriers to dissemination, as well as a need to augment existing treatments and boost their economic appeal. With a foundation rooted in established cognitive behavioral techniques and driven by technological innovations, these treatments reflect two major movements in the extant research. The first movement aims to improve patient access through efficacy and effectiveness trials of teletherapy and Internet-based treatments. The second movement, driven by advances in virtual reality (VR) technologies, aims to enhance exposure-based treatments through incorporating VR components in the therapist's arsenal of effective techniques. Here we review these innovative and emerging treatments, which have shown promising preliminary results.

Teletherapy and Internet-Based Treatments

Both the isolative nature of agoraphobia and advances in telecommunication technology have prompted a number of investigators to examine the efficacy of teletherapy and Internet-based variants of established cognitive behavioral treatments. The obvious benefit of these techniques addresses significant barriers to treatment; namely, that patients suffering from agoraphobia often do not have access to evidence-based treatments either because of prominent avoidance behaviors or because of a lack of access to clinicians skilled in their implementation.

Prior to the advent of videoconferencing capabilities, the question of whether anxiety disorders, generally, were amenable to telephone-delivered therapies was being explored; however, very few studies examined applying distance-therapies to the treatment of agoraphobia, despite its obvious appeal. One early study by McNamee, O'Sullivan, Lelliott, and Marks (1989) investigated the efficacy of exposure versus relaxation techniques administered via telephone to 23 patients with panic disorder with agoraphobia, 14 of whom were assessed at 32 weeks posttreatment. While psychotherapeutic contact was very brief relative to standard CBT protocols (i.e., patients spent just 2 hours dispersed over 12 weeks consulting with therapists), the exposure-based intervention was found to be significantly more effective than the relaxation-based intervention in improving phobia and social functioning.

Another seminal study by Swinson, Fergus, Cox, and Wickwire (1995) investigated the effectiveness of an 8-week course of telephone-delivered, exposure-based behavior therapy administered to 42 patients with panic disorder with agoraphobia relative to

a wait-list control. Results revealed significant reductions in phobic avoidance, fear, and anticipatory anxiety; furthermore, treatment gains were maintained at 3- and 6-month follow-ups.

It has been noted that videoconferencing is qualitatively different from telephone-based treatments (e.g., Bouchard et al., 2004), and so results based on telephone-delivered therapies may not generalize to videoconferencing treatments. For instance, teletherapy may not have the same potential for establishing a strong therapeutic alliance if one considers the importance of face-to-face contact in patient–therapist interactions; further, teletherapy may limit the capacity to clinically monitor symptoms and the integrity of therapist-assisted, self-administered interventions.

In an early pilot investigation, Bouchard et al. (2000) examined the efficacy of administering 12 sessions of CBT via videoconferencing to 8 adults suffering from panic disorder with agoraphobia. Despite having a very small sample, significant results were found for all outcome measures (with large within-group effect sizes [*r*] ranging from 0.71 to 0.89), including panic frequency and apprehension, self-efficacy, and global measures of panic and agoraphobia, anxiety, and disability. Bouchard's group later extended these results experimentally by comparing CBT administered either face-to-face or via videoconferencing to a sample of 21 patients with panic disorder with agoraphobia (Bouchard et al., 2004). The two modalities were comparable in effectiveness; for both groups, clinically significant reductions were found on all measures, with no significant differences between conditions. Furthermore, therapeutic alliances were readily established in the videoconferencing group, a finding that refutes a common criticism of teletherapy, namely, that rapport and working alliance may be diminished relative to that achieved in face-to-face therapies.

Internet-Based Self-Help Treatments

In addition to increasing access and affordability of treatment through the use and development of teletherapy, other avenues have been pursued, including evidence-based self-help programs administered via the Internet. Derived from the tradition of bibliotherapy and aided by the increased capabilities of dissemination afforded by the World Wide Web, research suggests that these programs are at least marginally effective. While the evidence is scant in regards to applying such programs to the treatment of agoraphobia, considering the potential benefits of increased accessibility, their continued use and empirical development is warranted.

Contributing to this line of research, Carlbring, Ekselius, and Andersson (2003) investigated the efficacy of Internet-based self-help treatment with minimal therapist contact for panic disorder in a sample of 22 patients (of whom over 90% met criteria for agoraphobia). Participants were randomized to either applied relaxation or a multicomponent treatment based on CBT. Although both groups improved, counter to expectations, participants receiving applied relaxation showed a greater clinical response than those receiving CBT. The authors note that one possible factor accounting for the observed advantage shown for the applied relaxation treatment was the fact that this group had materials they could take home to use (i.e., a CD with relaxation instructions), and they perhaps enjoyed more frequent rewards as they progressed through shorter modules. Importantly, a major limitation of this study,

and perhaps a potential pitfall of Internet-administered therapies generally, is that only 56% of the treatment materials were completed. The authors provide some possible explanations for such low engagement, including that participants complained the treatment was too impersonal, and that treatment credibility was lower relative to previous studies. Importantly, the authors report they have had greater success in terms of homework completion in previous studies (i.e., up to 90%).

In a similar study with minimal therapist contact, Wims, Titov, Andrews, and Choi (2010) assessed the efficacy of clinician-assisted, Internet-based CBT administered to patients with panic disorder with and without agoraphobia. While controlling for pretreatment symptom severity, those assigned to the Internet CBT group ($n = 32$) exhibited significantly less posttreatment symptoms of panic, fear of body sensations, and agoraphobic cognitions relative to controls ($n = 27$). Furthermore, remission rates were 31% and 8% for the treated versus control groups, respectively. Note however, that, posttreatment measures targeting symptoms of phobic avoidance revealed no group differences. Overall, these results suggest that Internet-based CBT for panic disorder achieves about half the level of improvement on panic disorder severity relative to therapist-delivered CBT interventions, but does not exert an appreciable effect on agoraphobia symptoms specifically.

Virtual Reality Exposure Therapy

Another developing, innovative therapy bolstered by the advancement of technology is virtual reality exposure therapy (VRET), which has been lauded as an alternative to in vivo and imaginal exposure (Krijn, Emmelkamp, Olafsson, & Biemond, 2004). Certainly, the ability to sensorially immerse a patient in a virtual environment has enormous appeal in the treatment of anxiety disorders. Among the many conceivable benefits are increased acceptability (especially for severely phobic patients), greater control over graduated exposures, improved cost-effectiveness, the ability to tailor treatment precisely to the individual patient, and the possibility of repeating exposures as frequently as desired. In the early 1990s, the first conceptions and investigations of applying VR exposure to anxiety disorders were underway (e.g., North, North, & Coble, 1998), despite the fact that the technology was in its infancy. Technological advances, improved virtual environments, and the ability to manipulate those environments and to integrate multiple sensory inputs have allowed the construction of more convincing virtual worlds. This important feat, in turn, has afforded a greater sense of "presence" in patients immersed in virtual environments, which has been identified as an important variable in creating viable, evocative stimuli (Jang, Ku, Shin, Choi, & Kim, 2000), and in invoking emotion in VR exposures (Krijn et al., 2004). Moreover, invoking emotion during exposure (e.g., activation of fear structures) is held as a theoretically important mechanism underlying the effectiveness of exposure therapies (Foa & Kozak, 1986). To date, research on VR exposure for anxiety disorders supports the use of this technology for fear of heights and fear of flying (see Krijn et al., 2004, for a review); however, findings for its efficacy in treating other anxiety disorders are inconclusive, and there is a paucity of clinical studies applying this technique to agoraphobia.

In an early study investigating the use of VRET with 60 university students who expressed the presence of agoraphobic symptoms on a general measure of agoraphobic attitudes, North, North, and Coble (1996) demonstrated significant reductions in subjective distress across eight (or fewer) sessions of exposure to anxiety-provoking, interactive virtual environments, and significant reductions on a (nonvalidated) measure of agoraphobia administered posttreatment. While these results suggest an effective therapeutic manipulation when considering the significant habituation observed across sessions, the results do not speak to the ecological validity of this technique; that is, the question remains as to whether results would generalize outside laboratory settings to truly clinical populations.

Another notable investigation by Jang et al. (2000) demonstrated the importance of the design of virtual environments, and the environmental conditions under which such manipulations are administered. A sample of 45 patients diagnosed with panic disorder with agoraphobia, all of whom identified the same scene as most distressing (i.e., being in a traffic-jammed tunnel), were later subjected to this scene using a VR head-mounted display. Due to insufficient patient immersion in the virtual environment, the authors discontinued use of VRET with patients after just two sessions, and no viable data were obtained. They cite a number of issues that may have prevented proper immersion in the virtual scene, including having a burdensome apparatus with a limited field of view (i.e., 50 degrees), having multiple physiological sensors, having the therapist present and actively reassuring distressed patients, and having the external environment interfere with engagement with the virtual scenes (e.g., bright light flooding in through the crevice of the head-mounted display). The authors note the importance of creating realistic virtual scenes; however, they suggest that preparing the environmental conditions under which patients will engage with these scenes may be a more prominent factor in eliciting patients' presence in virtual scenes.

With a more refined protocol, more promising results were achieved by Vincelli et al. (2003), who developed and tested a new treatment called experiential-cognitive therapy (ECT), which combines VR exposure and traditional cognitive behavioral techniques. Twelve patients with panic disorder with agoraphobia were assigned to receive either eight sessions of ECT or 12 sessions of standard CBT, or to a wait-list control group. Results revealed significant improvement in the number of panic attacks, the level of depression, and state and trait anxiety, but no significant differences were found between the two treatment groups. While this suggests comparable efficacy, the authors interpret this finding as indicative that ECT can produce its effects in 33% fewer sessions (i.e., eight vs. 12 sessions) relative to standard CBT, boosting its economic appeal and justifying the addition of VR techniques to established treatment protocols.

In a sample of 40 patients with panic disorder with agoraphobia, Choi et al. (2005) showed similar effectiveness of ECT, compared to a more established panic control program (PCP). Both groups showed significant improvement with no differences in high end-state functioning and medication discontinuation at posttreatment, but more patients discontinued medication in the PCP group at 6-month follow-up, which the authors take as evidence that ECT may be relatively less effective in the long term.

Botella et al. (2007) compared nine weekly sessions of VRET, in vivo exposure, or a wait-list control administered to 37 patients with panic disorder with agoraphobia (82.9% of the sample) or without agoraphobia (17.1% of the sample). At posttreatment and 9-month follow-up, VRET showed similar efficacy relative to the in vivo exposure treatment, with no significant differences on any outcome measures, whereas both active treatments were significantly superior to the wait-list control condition on all outcome measures (with effect sizes [partial eta squared] ranging from 0.35 to 0.8, and most measures obtaining medium to large pre-to-post effects).

Treating a sample of 29 panic disorder patients with or without agoraphobia, Perez-Ara et al. (2010) compared the efficacy of virtual reality interoceptive exposure (VRIE), in which patients were simultaneously exposed to arousal-inducing audio and visual effects in virtual agoraphobic situations, to a traditional interoceptive exposure (IE) treatment. Results revealed significant reductions in primary outcome measures at posttreatment which were maintained or even improved at 3-month follow-up, but no differences were found between treatment conditions. While these data suggest that VRIE is comparable to traditional, gold standard IE in the absence of VR components, the authors argue that VR may be more palatable for some patients, and conclude that the incorporation of multisensory stimulation in VR may enhance the ecological validity of exposure situations.

In a recent study, Pelissolo et al. (2012) compared the effects of 12, hour-long sessions of VRET, CBT, and a wait-list control, administered to 92 patients with panic disorder with agoraphobia. Results revealed no significant differences between groups, providing evidence that VRET is at least as effective as traditional CBT. Despite a lack of statistical difference between groups (and curiously, this study did not show significant differences between the active treatment groups and wait-list groups, perhaps due to relatively high rates of attrition), treatment effects were impressive, with a mean reduction of around 50% in measures of agoraphobia and panic at 9 months posttreatment.

In sum, the evidence supporting the use of VR exposure for the treatment of agoraphobia is inconclusive. Some authors suggest that its use is as effective (Botella et al., 2007; Pelissolo et al., 2012; Perez-Ara et al., 2010) or more efficient (Vincelli et al., 2003) compared to traditional CBT, while others demonstrate that traditional techniques are superior (e.g., Choi et al., 2005). Still, considering the potential benefits of applying VR technology to the treatment of agoraphobia, and notable advances in the technology and refined protocols that may directly boost treatment effects, continued empirical development appears warranted.

Alternatives to Cognitive Behavioral Therapy: Other Psychosocial Treatments for Agoraphobia

Though CBT is currently the gold standard treatment for agoraphobia, several alternative approaches are available for patients seeking treatment. It is vital to the well-being of agoraphobia patients that researchers actively investigate alternative treatments being employed in the field, and that practitioners, in turn, consider research outcomes when selecting treatment approaches. Therefore, this section will

provide a brief review of literature related to three alternative approaches to treating panic disorder with agoraphobia: psychodynamic approaches, interpersonal therapy, and acceptance and commitment therapy.

Psychodynamic Treatment Approaches

Psychodynamic therapy has been tested as a possible approach for the treatment of agoraphobia (Hoffart & Matinsen, 1990). This approach assumes that intrapsychic conflicts from childhood, reactivated by adult stressors, play an important role in the pathogenesis of agoraphobia. The principal therapeutic goals are to assist the patient in developing autonomy by addressing suppressed inner conflicts, guided by experiences that arise during exposure. Hoffart and Matinsen (1990) compared the effectiveness of psychodynamic therapy alone with a program that integrated psychodynamic therapy with exposure therapy administered to an inpatient agoraphobic sample. The exposure component included graduated in vivo exposure combined with cognitive restructuring. At 1-year follow-up, results demonstrated superior outcomes for the integrated treatment group on assessments of ability to approach agoraphobic-related situations alone, agoraphobic-related cognitions, and several other measures of anxiety. Although the group receiving psychodynamic treatment alone demonstrated posttreatment improvements, gains were not maintained through 1-year follow-up. Overall, results of this study suggest that psychodynamic therapy alone has little therapeutic benefit, whereas there is preliminary support for combining psychodynamic therapy and exposure treatment. However, conclusions should be interpreted with caution given notable weaknesses in study design (e.g., no random assignment, and the clinician-rated assessments were conducted by the therapist for most patients in the study). Furthermore, the integrated treatment should be compared with a control group (i.e., psychological placebo or wait-list control) and the gold standard treatment (i.e., CBT) before drawing conclusions about its effectiveness in the treatment of agoraphobia.

Milrod and her colleagues (Milrod et al., 2001; Milrod et al., 2007) have developed and tested a 24-session manualized panic-focused psychodynamic treatment for panic disorder with and without agoraphobia. The treatment consists of three distinct phases: (a) initial evaluation and early treatment, (b) panic vulnerability, and (c) termination (see Milrod et al., 2007, for a detailed overview of the clinical strategies used in each of the phases). To examine the effectiveness of this approach, a well-executed small-scale comparative study was conducted in which 49 patients with panic disorder with and without agoraphobia (the proportion of those with agoraphobia was not specified) were randomized to either psychodynamic treatment or applied relaxation. Intent-to-treat clinical response rates in the two treatments based on a 40% reduction in the total score on the Panic Disorder Severity Scale (Shear et al., 1997) were 73% for psychodynamic therapy versus 39% for applied relaxation. Subject attrition in the applied relaxation condition was significantly higher (34%) than in the psychodynamic treatment (7%) which speaks to the favorable tolerability of the treatment. Nevertheless, the differential dropout rates make interpretation of the

between-group differences problematic, and, unfortunately, specific outcome indices for agoraphobic avoidance were not reported.

Interpersonal Psychotherapy

Given data suggesting that interpersonal stressors may contribute to the onset and maintenance of panic and agoraphobia (Faravelli & Pallanti, 1989), it is reasonable to expect that psychotherapy aimed at correcting interpersonal problems may confer significant benefits to patients presenting with agoraphobia. Interpersonal psychotherapy (IPT) is a time-limited, manualized, structured treatment originally developed for the treatment of depression (Klerman, Weissman, Rounsaville, & Chevron, 1984), which has been adapted and shown to be efficacious for a range of problems including major depression, bipolar disorder, bulimia, and substance use disorders (see Markowitz & Weissman, 2012, for a review). Encouraging preliminary findings were reported from an open pilot trial of IPT in 12 patients meeting *DSM-IV* criteria for panic disorder (Lipsitz et al., 2006).

More recently, Vos, Huibers, Diels, and Arntz (2012) completed an RCT comparing IPT and CBT in 91 patients meeting *DSM-IV* criteria for panic disorder with moderate to severe agoraphobia. The major treatment components included in the IPT protocol were (a) characterizing panic disorder in terms of the medical model, (b) determining the focus of treatment (e.g., role conflict, transition, grief, or skills deficit), (c) exploration and improvement of interpersonal problems, and (d) treatment termination. CBT included cognitive therapy, interoceptive exposure, and in vivo exposure. Relative to IPT, CBT produced significantly greater improvement in panic attack frequency (i.e., from baseline to 1-month follow-up, within-group effect sizes [Cohen's *d*] were 0.74 and 0.51 for the CBT and IPT groups, respectively), but more importantly, CBT was also superior on multiple measures of agoraphobic dysfunction (i.e., from baseline to 1-month follow-up, effect sizes based on a composite agoraphobia score were 1.05 and 0.58 for the CBT and IPT groups, respectively). The authors concluded that IPT appears to have limited value in the treatment of moderate to severe agoraphobia.

Acceptance and Commitment Therapy

While conventional forms of CBT conceptualize the goal of therapy as changing maladaptive behavior and cognitions, acceptance and commitment therapy (ACT) was designed to promote a balance of acceptance and change. One might conceptualize CBT as a therapy that promotes judging certain cognitions and emotions as in need of elimination. In contrast, ACT suggests that clients should accept the experience of cognitions or emotions without judging them, and commit to act in a way that is consistent with their values. The literature regarding the treatment of agoraphobia with ACT is still in its infancy, with only a few case studies currently available.

For example, Carrascoso López (2000) reported the case study of an individual diagnosed with panic disorder with agoraphobia treated with ACT. Though therapy incorporated some techniques employed in CBT, such as in vivo exposure homework

and interoceptive exposure, these techniques were framed in terms of ACT goals and objectives (e.g., learning to abandon the attempt to control bodily sensations, rather than striving to habituate fear response to bodily sensations). A comparison of baseline to posttreatment scores revealed a significant decrease in panic and agoraphobia symptoms. The patient also exhibited a reduction in escape and avoidance behaviors observed during the session and in self-reported agoraphobic symptoms. However, the inclusion of exposure treatment for this case precludes drawing conclusions about the specific contribution of ACT.

Codd, Twohig, Crosby, and Enno (2011) reported the outcome of another case in which panic disorder with agoraphobia was treated with ACT. In contrast to Carrascoso López (2000), the authors specifically avoided conducting any in-session exposure therapy to reduce the overlap of ACT with previously established treatments for panic and agoraphobia. At posttreatment, the patient demonstrated a clinically significant decrease in clinician-rated symptoms of panic disorder and no longer met diagnostic criteria for panic disorder with agoraphobia. Furthermore, self-reported reductions in daily ratings of avoidance behaviors were noted after the first couple of sessions and maintained through the end of treatment. Interestingly, while the client's diagnostic status and avoidance behaviors changed, her mean anxiety level remained somewhat constant throughout therapy. The authors note that this pattern of findings suggests that the change process in ACT alters the function of anxiety in one's life, rather than altering the severity of anxiety experienced.

The case studies reviewed herein provide preliminary support for the feasibility of ACT as a treatment for panic disorder with agoraphobia; however, additional empirical support is needed before conclusions can be drawn regarding the efficacy of ACT in treating panic with agoraphobia. RCTs are needed to determine the efficacy of ACT relative to CBT. Furthermore, research exploring predictors of treatment outcome may help identify subsets of patients most amenable to this approach.

Predictors of Treatment Outcome

Research aimed at identifying factors that influence agoraphobia patients' response to treatment has important implications for clinical management. As more data emerge on patient and treatment variables that impact treatment outcome, clinicians are in a better position to prescribe more individualized treatment regimens for their patients. Despite such clear advantages, identifying prognostic factors has been traditionally less prominent as an investigational aim relative to establishing, comparing, and augmenting treatment efficacy. Furthermore, only recently have the sample sizes in panic/agoraphobia treatment studies been large enough to provide sufficient statistical power to investigate the relationship between various patient prognostic factors and response to cognitive behavioral treatment. Methodologies have also generally improved; for example, while many of the early studies relied solely on self-report measures as indices of outcome, more modern studies have utilized clinician-based assessments, and other more objective assessments, the sensitivity of which allows evidence of predictors to emerge more reliably from the data. In this

section, we review those studies that examine one or more patient prognostic factors on measures of agoraphobia treatment outcome.

Psychiatric Comorbidity Predicting Treatment Outcome

Patients with agoraphobia often present with one or more co-occurring psychiatric conditions such as depression, other anxiety disorders, and substance use disorders (Kessler et al., 2006). The fact that psychiatric comorbidity is more the rule than the exception raises the important question: How does the presence of a comorbid psychiatric condition impact patients' response to cognitive behavioral treatment? Probably the best data available on the impact of comorbid anxiety and depression on patients' level of improvement in agoraphobia symptoms during cognitive behavioral treatment come from a recent report by Allen et al. (2010) using data from a large multisite treatment study of panic disorder and agoraphobia (Aaronson et al., 2008). The investigators tested whether the presence of a comorbid anxiety disorder, comorbid depression, or comorbid anxiety and depression resulted in less improvement in panic and agoraphobia symptoms, relative to patients without any comorbid diagnoses. The results of this study are presented in Figure 40.1. Consistent with early reports (Brown, Antony, & Barlow, 1995; McLean, Woody, Taylor, & Koch, 1998), patients presenting with comorbid anxiety and depression diagnoses at baseline showed greater severity of panic disorder and agoraphobia at baseline. The only baseline comorbid condition associated with a poorer treatment response was adult separation anxiety disorder. The good news, however, is that with the

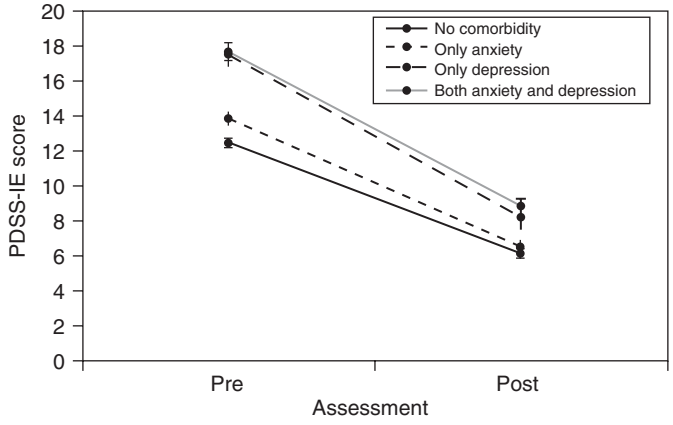

Figure 40.1 PDSS-IE scores (with standard errors) across treatment for participants with no comorbidity, only anxiety comorbidity, only depression comorbidity, and both anxiety and depression comorbidity. *PDSS-IE* Panic Disorder Severity Scale—Independent Evaluator Version, *Pre* pretreatment, *Post* posttreatment. With kind permission from Springer Science+Business Media: Laura B. Allen (2009), Cognitive-behavior therapy (CBT) for panic disorder: Relationship of anxiety and depression comorbidity with treatment outcome, *Journal of Psychopathology and Behavioral Assessment, 32*, 185–192.

exception of adult separation anxiety disorder, patients who have panic disorder with agoraphobia and comorbid anxiety and depression seem to benefit just as much from CBT as those without comorbid conditions. This latter finding is generally consistent with earlier reports (Brown et al., 1995; Tsao, Mystkowski, Zucker, & Craske, 2005). The other positive finding is that patients also showed significant reductions in comorbid conditions, which is consistent both with earlier reports (e.g., Brown et al., 1995) and with a more recent naturalistic study of changes in comorbid conditions following CBT treatment for anxiety disorders (Davis, Barlow, & Smith, 2010).

Axis II Comorbidity Predicting Treatment Outcome

Personality disorder comorbidity is frequently cited as a factor implicated in poor treatment response to both pharmacotherapy (Slaap & den Boer, 2001) and psychosocial treatments (Reich & Green, 1991). Although not studied systematically, personality dysfunction may negatively affect agoraphobia treatment outcome through its potential influence on other moderators of treatment outcome such as patient dropout (Grilo et al., 1998), compliance with treatment regimens (Schmidt & Woolaway-Bickel, 2000), the therapeutic alliance, or motivation for treatment (Persons, Burns, & Perloff, 1988).

Despite claims that agoraphobia patients displaying comorbid Axis II pathology respond less favorably to cognitive behavioral treatment (Mennin & Heimberg, 2000), evidence from controlled prospective studies is inconclusive due to the small number of prospective studies and the methodological limitations of the existing studies (i.e., small sample size, use of questionnaires to assess personality dysfunction, and failure to control for baseline severity of Axis I pathology; Dreessen, Arntz, Luttels, & Sallaerts, 1994). In the largest study to date to examine whether personality disorders interfere with patients' responses to treatment, Telch, Kamphuis, and Schmidt (2011) investigated the influence of personality pathology assessed both dimensionally and categorically on acute clinical response to cognitive behavioral treatment in a sample of 173 outpatients diagnosed with panic disorder with or without agoraphobia. Results revealed that approximately one-third of the sample met criteria for one or more personality disorders, with the majority meeting criteria for an "Anxious or Fearful" Cluster C diagnosis. Consistent with earlier reports (Friedman, Shear, & Frances, 1987; Reich & Chaudry, 1987), patients presenting with personality disorders were significantly more likely to show extensive agoraphobia relative to patients without personality disorders. Without controlling for pretreatment panic severity, patients presenting with one or more personality disorders showed greater posttreatment symptoms on the continuous panic outcome measures and were significantly less likely (39% vs. 65% for patients with and without personality disorders, respectively) to achieve clinically meaningful change at posttreatment. However, after controlling for pretreatment panic/agoraphobia severity, the results showed that the presence of personality disturbance, whether assessed via dimensional or categorical indices, conferred a very modest, albeit statistically significant, deleterious effect on treatment outcome (see Figure 40.2).

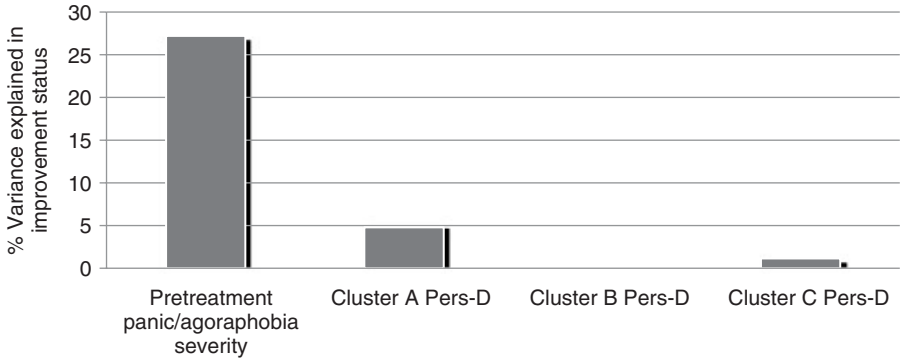

Figure 40.2 Proportion of variance in clinically significant change explained by pretreatment panic disorder/agoraphobia severity, and the presence of Cluster A, B, and C personality disorders (pers-d).

Cognitive and Family Relationship Variables Predicting Agoraphobia Treatment Outcome

Cognitive variables as well as relationship variables have each been posited as potential mediators of change in behavioral and cognitive behavioral treatments for agoraphobia. Using structural equation modeling, Renshaw, Chambless, and Steketee (2003) examined the relationship between perceived criticism in the family and treatment outcome in 67 patients with either obsessive compulsive disorder or panic disorder with agoraphobia. Results indicated that pretreatment levels of perceived family criticism significantly predicted posttreatment symptom severity while controlling for pretreatment symptom severity. Although subanalyses by disorder were not presented, their findings hint at the importance of perceived family criticism as a negative prognostic factor in behavioral treatment of obsessive compulsive disorder and panic disorder with agoraphobia.

Using mediational analyses outlined by Baron and Kenny (1986), Smits, Powers, Cho, and Telch (2004) examined whether changes in fear of fear (FOF) mediate improvement in CBT treatment of panic disorder with agoraphobia. Although treatment effects were quite large and statistically significant across all symptom facets (i.e., global disability, anxiety, agoraphobic avoidance, and panic attacks), CBT accounted for greater symptom change on measures of panic-related anxiety and agoraphobia than for panic attacks. Mediational analyses revealed that change in FOF, as assessed by a composite of two widely used FOF indices (i.e., the Body Sensations Questionnaire and the Anxiety Sensitivity Index), met Baron and Kenny criteria for treatment mediation across each of the four symptom facets of panic disorder with agoraphobia. However, the strength of mediation also varied as a function of symptom facet; full mediation for FOF was demonstrated for change in global disability, whereas partial mediation effects of FOF were found for measures of agoraphobia, anxiety, and panic frequency.

Cho, Smits, Powers, and Telch (2007) examined pre- to posttreatment change in three panic appraisal dimensions (anticipated panic, panic consequences, and panic

coping) in predicting panic disorder with agoraphobia patients' clinical status at a 6-month follow-up. Patients ($N = 120$) undergoing group-administered CBT were administered the Panic Appraisal Inventory (PAI; Telch, Brouillard, Telch, Agras, & Taylor, 1989) at three time points (pre, post, and 6-month follow-up), along with a standard outcome assessment battery indexing panic-related anxiety, agoraphobic avoidance, panic attack frequency, and global impairment. When entered together, pre- to posttreatment changes in the three panic appraisal dimensions accounted for 28% of the variance in agoraphobia severity at follow-up. Perceived panic consequences emerged as the most consistent predictor of anxiety, global impairment, and agoraphobic avoidance at 6-month follow-up. Change in anticipated panic also uniquely predicted anxiety and agoraphobic avoidance but not global impairment.

Van Apeldoorn et al. (2010) compared the long-term effectiveness of CBT, selective serotonin reuptake inhibitor medication, or a combination of the two for 150 patients with panic disorder with or without agoraphobia. For the entire mixed sample (i.e., patients with and without agoraphobia), results demonstrated slight superiority of the combined treatment over either individual treatment alone at posttreatment, but these differences were not maintained at 6- and 12-month follow-up. Consistent with findings reported earlier by Telch et al. (1989), the more severely agoraphobic patients endorsed less confidence in their ability to cope with future panicogenic situations relative to their less agoraphobic counterparts. Unfortunately, formal mediational analyses were not conducted to test whether changes in patients' panic appraisals mediated change over the course of treatment.

Utilizing a large sample of patients with agoraphobia (with or without panic disorder; $N = 427$) and a sample of patients with social phobia ($N = 98$), Vögele et al. (2010) conducted mediational analyses of cognitive change on clinical improvement following a course of high-density exposure in a community-based treatment setting. Results demonstrated strong, significant, and maintained clinical improvement in both groups. Cognitive mediation was demonstrated differentially for the two groups. Cognitive change related to physical catastrophes mediated outcome only for patients with agoraphobia, whereas changes in cognitions related to control mediated outcome for both groups. Changes in relationship satisfaction were not found to mediate outcome in either group. Based on these results, the authors conclude that cognitive change is an important mechanism, even in purely exposure-based interventions.

In a recent study investigating the differential effectiveness of guided mastery alone, interoceptive exposure alone, or their combination in the treatment of panic disorder with agoraphobia, Reilly, Gill, Dattilio, and McCormick (2005) found that all three treatments were equally effective for both panic and agoraphobia. Further, in predictive analysis, they found that changes in FOF, anticipated panic, panic coping efficacy, and agoraphobic self-efficacy all predicted improvement in panic frequency, whereas only changes in agoraphobia self-efficacy and anticipated panic predicted improvement in agoraphobia.

Predicting Long-Term Outcome

Using survival analysis on a relatively large sample ($N = 200$) meeting *DSM-III-R* and *DSM-IV-TR* criteria for panic disorder with agoraphobia, Fava et al. (2001) examined

long-term outcome up to 14 years posttreatment with a standard protocol that emphasized regular, non-therapist-assisted situational exposure. The probability of remitting was found to increase with younger age, but lessen with the presence of a personality disorder, high levels of pretreatment depression, persisting agoraphobic avoidance at posttreatment, and concurrent use of antidepressants and benzodiazepines. Importantly, patients who entirely overcame agoraphobic behaviors at posttreatment exhibited better outcomes, indicating that a primary aim of treatment should be the elimination of agoraphobic avoidance and not simply the elimination of panic.

Future Directions

In this final section we provide some recommendations for advancing research and treatment for agoraphobia.

First, there is a need for research on the nature and treatment of individuals presenting with pervasive situational avoidance (agoraphobia) without a history of panic disorder/panic attacks. Evidence from epidemiological studies suggests that almost 50% of adults meeting diagnostic criteria for agoraphobia have no history of panic disorder or panic attacks that predate the onset of their agoraphobia (Wittchen et al., 2010). Unfortunately, with the exception of large-scale epidemiological studies, virtually all agoraphobia research studies (intervention and nonintervention) conducted over the past 25 years have restricted their samples to adults with agoraphobia and panic disorder/panic attacks. This state of affairs has created a tremendous knowledge gap in our understanding of the nature and treatment of individuals disabled by pervasive situational avoidance without panic disorder/panic attacks.

Second, there is a need for treatment matching research aimed at identifying factors that predict differential treatment response to pharmacological, exposure, cognitive, and combined therapies. Our review of the research studies examining predictors of agoraphobia treatment outcome suggests that we have yet to identify specific patient factors that predict differential clinical response to one treatment modality relative to another. To meet this objective, we need a large-scale multisite trial with the following features: (a) a sufficient number of treatment arms to accommodate the treatment matching objective, (b) a thoughtfully selected battery of putative moderator variables, and (c) recruitment of research participants who display pervasive situational avoidance with and without a history of panic disorder/panic attacks.

Third, research should test new strategies for increasing compliance with exposure therapy regimens. Despite its established clinical efficacy, a sizeable minority of patients make only minimal progress or show significant return of fear due to poor compliance with exposure treatment prescriptions, and continued use of subtle forms of avoidance such as excessive use of safety aids during exposure outings. We also know that compliance with exposure homework predicts treatment outcome in PDA patients (Schmidt & Woolaway-Bickel, 2000).

The possible causes of poor compliance with exposure therapy are numerous but usually fall into one of three major classes: (a) strategic errors on the part of the therapist—examples include poor choice of exposure target, inadequate patient training in the execution of exposure, and insufficient monitoring of patients' exposure

homework; (b) patient factors—these may include comorbid health problems, low distress tolerance, high anxiety sensitivity, and faulty assumptions about exposure therapy, and (c) environmental stressors, including relationship, family, or work stressors.

Given the prominent status of exposure to fear-eliciting targets as a central therapeutic element in the treatment of agoraphobia (not to mention most other anxiety disorders), research aimed at improving our understanding of exposure noncompliance and strategies for its amelioration should be given high research priority.

Conclusions

Based on our qualitative review of the literature spanning the past 35 years, the following conclusions can be drawn with a reasonable degree of confidence:

1. Exposure techniques, whether administered alone or in combination with panic-focused education, cognitive restructuring, and relaxation/breathing retraining techniques, provide the most consistent evidence for clinical efficacy.
2. Agoraphobia patients achieve greater improvement from in vivo exposure when therapists accompany patients into the field for at least some of their exposure outings.
3. More cost-effective CBT delivery systems including group treatments, brief treatments, and computer/Internet-based treatments outperform no treatment or attentional control interventions and thus appear promising for delivering CBT to a broader range of agoraphobia sufferers.
4. Agoraphobia patients presenting with significant Axis I or Axis II comorbidity show greater baseline severity of their agoraphobia and panic symptoms but appear to benefit as much from CBT as those without significant psychiatric comorbidity.
5. Research on change mechanisms governing symptom improvement among agoraphobia patients receiving CBT has provided the most consistent support for cognitive change variables including coping self-efficacy, panic appraisal, and anxiety sensitivity.

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