

Behavioral Treatment of Panic Disorder

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We report the results of a long-term clinical outcome study testing variations of behavioral treatments for panic disorder without agoraphobic avoidance. Exposure to somatic cues combined with cognitive therapy was compared to relaxation therapy designed specifically for panic disorder. In a third treatment condition, these techniques were combined. All three treatments were superior on a variety of measures to a wait-list control group. In the two treatment conditions containing exposure to somatic cues and cognitive therapy, 85% or more of clients were panic free at post-treatment. These were the only groups significantly better than wait-list control on this measure. Relaxation, on the other hand, tended to effect greater reductions in generalized anxiety associated with panic attacks but was associated with high drop-out rates. These results suggest that we have a successful behavioral treatment for panic disorder, but leave questions on effective components and mechanisms of action unanswered.

In addressing the complex and disabling problem of panic disorder with agoraphobia, behavioral treatments traditionally attack agoraphobic avoidance using in-vivo exposure procedures (Mavissakalian & Barlow, 1981). Drug treatments, on the other hand, are intended to target panic attacks directly. Several studies have indicated that a variety of drugs may contribute to the treatment of panic disorder with varying degrees of agoraphobic avoidance (Ballenger, 1986; Ballenger et al., 1988; Zitrin, Klein, & Woerner, 1980; Mavissakalian & Michelson, 1986; Raskin, Marks, & Sheehan, 1983; Telch, Agras, Taylor, Roth, & Gallen, 1985). These studies have lead many clinicians to assume that drugs are the treatment of choice for panic attacks, while behavioral procedures are important in treating any agoraphobic avoidance that might be present. The implication of this assumption is that behavioral procedures would be ineffective for panic disorder without agoraphobic avoidance.

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Now, uncontrolled clinical series of cases reported from around the world suggest that we may have an effective behavioral treatment for panic disorder. For example, Gitlin et al. (1985) reported that 10 out of 11 patients receiving cognitive-behavioral treatment directed at panic attacks were not panicking by the end of treatment. Clark, Salkovskis, & Chalkley (1985), as well as Salkovskis, Jones, & Clark (1986) treated panic directly in a small number of patients suffering from panic either with or without agoraphobia using cognitive procedures and respiratory retraining. These patients were selected on the basis of a strong respiratory component to their panic attacks. Whether agoraphobic avoidance was present or not, the results indicate a nearly total elimination of panic attacks continuing to a follow-up of two years. Beck (1988), as well as Ost (1988) have also reported nearly total elimination of panic in patients suffering from panic disorder using either cognitive behavioral or behaviorally based relaxation treatments with gains maintained at follow-ups.

In the first controlled study (Barlow, Cohen et al., 1984), 11 subjects with panic disorder (as well as 9 with generalized anxiety disorder) were assigned to treatment or wait-list groups. None of the DSM-III panic disorder patients had more than minimal agoraphobic avoidance. Treatment consisted of an integration of EMG biofeedback, progressive relaxation training and cognitive therapy specifically designed to address panic disorder. Compared to controls, treated subjects improved significantly, and additional therapeutic gains were noted during the follow-up period. Beck (1988) has also compared his recent clinical series to a wait-listed group with similar results.

In this article we report the results of a long-term outcome study which began in 1983 evaluating several versions of a treatment developed at our Center for Stress and Anxiety Disorders to target panic attacks and the associated anxiety of panic disorder directly. At the heart of our newly developed treatment is exposure to somatic sensations associated with panic attacks. In this study, cognitive therapy derived from the work of Beck & Emery (1979) was combined with exposure and compared to an applied relaxation treatment similar in operation to that recently described by Ost (1988). Relaxation was included because it is a traditional behavioral approach to anxiety related disorders. In a third group, cognitive therapy and exposure was combined with relaxation. The effects of all three treatments were compared to a wait-list control group.

METHOD

Subjects

Subjects were selected from a large number of clients referred by mental health professionals, community agencies, or self-referred, to the Phobia and Anxiety Disorders Clinic, State University of New York at Albany. General exclusionary criteria were as follows: aged below 18 or above 65 years; current alcohol or drug dependency/abuse; primary diagnosis of major depression, and any signs of psychosis or organic brain syndrome. In addition, clients concurrently involved in other psychotherapy programs were assessed for suit-

ability only if the alternative therapy was not focused on anxiety management, and they had been in therapy for at least six months. Finally, subjects were excluded if they had begun benzodiazepines within the past three months or MAO inhibitors or tricyclic antidepressants within the past six months. Subjects on medications or receiving alternative psychotherapies for the requisite time, and who met suitability criteria, were included under the agreement that medication regime and psychotherapy contact were maintained at constant levels throughout.

All clients who participated met DSM III-R criteria for panic disorder with mild or no agoraphobic Avoidance. Diagnosis was established from responses during a structured interview: the Anxiety Disorder Interview Schedule-Revised (Di Nardo et al., 1983). Use of this diagnostic instrument has provided satisfactory interrater agreement coefficients for the DSM III diagnosis of panic disorder: kappa = .69. Interviewers were senior graduate students and psychologists who had met training criteria for interrater agreement on training trials. If subjects had not had a medical examination in the prior two years, they were recommended to do so before participating in the study in order to confirm a diagnosis of panic disorder.

The interviewers rated the severity of the disturbance on a 0 to 8 point scale (reflecting co-jointly distress and disability from the disorder), and only clients whose severity rating was at least 4 were included in the study. Finally, only subjects who reported the presence of at least one panic attack in a two week period prior to assessment were included following conventions established in studies of this type (e.g., Ballenger et al., 1988). After meeting the study criteria, subjects signed an informed consent statement and began pre-treatment assessments.

MEASURES

Interview data. Several measures were recorded from responses during the ADIS-R, including the interviewer's rating of severity (0 to 8). Consensus case conferences and provision for independent second interviews in the case of uncertainty or if the interviewer's confidence rating was less than 70% were implemented. In addition, the Hamilton Anxiety and Depression Scales (Hamilton, 1959; 1960), which are embedded in the ADIS-R were recorded. The number of months from the first panic that was recalled at the time of the diagnostic evaluation was recorded, as was the current use of medication. This interview was repeated at post-treatment and at the various follow-up assessments by a blind, independent rater. A second independent rater reviewed the responses for the post and follow-up assessments to provide a consensus severity rating. An average of the two raters' severity scores was used unless there was wide disagreement (2 points or more), in which case consensus was reached through case conference discussion. In fact, raters scores are the same or within one point in 97% of all cases rated. Independent ratings were obtained because post and follow-up interviews were less detailed than the initial interview.

Standardized self-report data. A battery of questionnaires was administered

at each assessment point. These included: the Trait Scale of the State-Trait Anxiety Inventory (Spielberger, Gorsuch, & Lushene, 1970), which was included to determine the effect of treatment on trait anxiety; the Cognitive-Somatic Anxiety Questionnaire (Schwartz, Davidson, & Goleman, 1978) which has separate subscales for cognitive and somatic anxiety; the Fear Questionnaire (Marks & Mathews, 1979), from which 0 to 8 point self-rating of phobic distress was analyzed; the Beck Depression Inventory (Beck, Ward, Mendelson, Mock, & Erbaugh, 1961); the Psychosomatic Rating Scale (Cox, Freundlich, & Meyer, 1975), which entails rating the frequency and intensity of 17 somatic symptoms, such as nausea and headaches, from which an overall score is derived, and the Subjective Symptom Scale, which entails 0 to 8 point ratings of interference with five different areas of daily functioning (such as work, leisure, home management, etc.) due to the anxiety. The latter is a modification of scales introduced by Hafner & Marks (1976). The Life Experiences Survey (Sarason, Johnson, & Siegel, 1978) was administered at pre-treatment, and at the various follow-up assessments.

Self monitoring records. To provide detailed information of the daily fluctuations in anxiety and depression and the occurrence of panic attacks, clients were asked to monitor daily, beginning two weeks before treatment and continuing two weeks beyond the end of treatment. They also monitored for two week periods at the different follow-up assessment points.

Clients monitored their current levels of anxiety, depression and pleasantness on 0 to 8 point scales, four times a day (morning, afternoon, evening and bedtime). Any time their anxiety reached a level of 4 or higher on the 0 to 8 point scale, they recorded the following information: time of onset and offset; maximum level of anxiety experienced (0 to 8); whether it was a panic or not (clients were trained to differentiate panic attacks from more insidious episodes of generalized anxiety); the duration of the panic, and whether the anxiety episode and/or the panic were associated with a stressful event or not (in order to distinguish uncued or spontaneous from cued panic attacks). Unfortunately, the duration measurement was rarely completed and, therefore, duration data were not analyzed. The maximum level of anxiety experienced reflected the intensity of both anxiety and panic episodes. Number and intensity of anxiety and panic episodes per week and mean daily ratings of anxiety, depression and pleasantness were averaged over the two week assessment intervals to reflect frequency and intensity per week. Subjects also monitored the amount and type of medication used each day.

Finally, clients underwent a standard physiological assessment, the results of which will not be reported here.

Composite Criteria

Two composite measures of clinically significant change were developed to assess each client's response to treatment, using guidelines established by Himadi, Boice, & Barlow (1986). One measure is concerned with the degree of change during treatment (e.g., Barlow et al., 1984) and the other with the client's end state functioning (e.g., Mavissakalian & Michelson, 1983).

Treatment responder. This composite based criterion specifies a 20% im-

provement in at least three of the following four measures: (1) clinical rating of severity (at least 2 points); (2) client's self-rating from the Fear Questionnaire (at least 2 points); (3) number of panic attacks per week, and (4) Subjective Symptom Scale total score (at least 8 points). A decrement criterion was also included in the determination of post-treatment responder status. A client was considered a treatment non-responder if a deterioration of 20% or greater occurred on any one of the four measures from pre- to post-treatment, irrespective of the degree of improvement obtained on the other measures. Responder status was determined if data from three different measures were present and all three reflected positive or negative responding. Responder status could not be determined if more than one of the four measures were missing.

End state functioning. This criterion reflected absolute level of functioning at post-treatment and was applied only to treatment responders. They were assigned to either low end state (LES) or high end state (HES) categories, depending on their level of functioning (in contrast, responder and nonresponder categories reflected degree of improvement). At least three of the following five criteria had to be obtained for high end state status: (1) score of 2 or less on the clinician's rating of severity; (2) score of 2 or less for the client's self-rating; (3) zero panic attack per week; (4) score of 2 or less for the mean anxiety rating, and (5) score of 10 or less for the Subjective Symptom Scale total score. End state functioning was determined if data from only three different measures were present but all three reflected positive or negative responding. End state status could not be determined if more than two of the five measures were missing.

Treatment Conditions. Clients were randomly assigned to one of four treatment conditions: wait list (WL); applied progressive muscle relaxation (R); exposure and cognitive restructuring (E & C), and relaxation combined with exposure and cognitive restructuring (combined). In the wait-list condition, subjects were instructed to continue their monitoring for a period of 15 weeks, after which time they would receive treatment. Therapists phone-contacted clients once every two to three weeks to provide general feedback regarding their weekly records. Clients were informed that help would be available in the event of a crisis. No other intervention took place.

Constants across the three active treatment conditions were as follows: individual therapy sessions, conducted once per week for 15 weeks, and the application of anxiety-management skills to real life anxiety producing events, through the assignment of practices between sessions, from the sixth session to the fifteenth session. The progressive muscle relaxation treatment condition was based on procedures outlined by Bernstein & Borkovec (1973) in their modification of the Jacobson relaxation procedure. The essence of the actual exercise was a focusing of attention on particular muscle groups, tensing for 5–10 seconds, with attention to the sensations, relaxing of the muscle group with attention to the sensations, and suggestions of relaxation, heaviness and warmth. The number of muscle groups was gradually reduced from 16 to 8 to 4. Discrimination training was included. Relaxation by recall was then practiced, followed by cue-controlled relaxation established through repetition of the association between the relaxed state and the word "relax." Home practice

of the exercise was required two times a day (compliance issues and their relationship to the success of treatment will be addressed in a separate paper). The relaxation skill was applied to everyday anxiety and panic provoking situations, arranged in a graduated manner on the basis of an individualized 10 item hierarchy. After the sixth session, subjects were required to approach one situation three times a week with the use of muscle relaxation as a coping skill.

The interoceptive exposure and cognitive restructuring treatment condition consisted of the cognitive therapy for anxiety modified from Beck & Emery (1979), as well as exposure to interoceptive stimuli. A skills training approach was implemented in which cognitive skills were acquired for coping with anxiety and for re-evaluating beliefs and appraisals about environmental and internal physiological cues. The treatment proceeded through two phases; the first involved the exploration of the role of cognitions and their significance for individual client's anxiety reactions, using procedures such as analysis of faulty logic, reattribution, exploring alternatives, decatastrophizing, hypothesis testing and self-instruction. The cognitive skills were then applied (from the sixth session) to anxiety provoking situations and sensations, in the form of an individualized 10 item hierarchy. Some of the items in the hierarchy involved interoceptive exposure to feared sensations through exercises such as visualization of anxiety scenes, overbreathing and spinning. Breathing retraining was implemented in one session in the middle of treatment. Finally, the combined treatment condition represented a combination of progressive muscle relaxation and cognitive skills with emphasis upon exposure to interoceptive cues. Most emphasis was given to relaxation in the initial sessions with progressively more attention given to cognitive therapy and exposure procedures. The combined treatment protocol has been described in detail elsewhere (Barlow & Cerny, 1988).

Therapists

Therapists were senior graduate students and psychologists who had been trained in the use of each of the three therapeutic procedures (from observation and practice with corrective feedback). Treatment manuals which detailed the techniques and information per session were used and supervision was provided on a weekly basis to insure correct application of therapeutic procedures. Clients were randomly assigned to available therapists for the different treatment conditions. During the multi-year course of the study, more than 10 therapists participated.

Treatment Integrity

Treatment delivery was examined by means of ratings of the content of therapy sessions from periodic spot checks of audiotapes (all therapy sessions were audiotaped to avoid the possibility of response bias in the therapists verbal behavior during spot checking). Thirty-five tapes were randomly selected, with the stipulation that each therapist and each treatment phase of each treatment condition were represented in the sample. Two randomly selected five minute segments (excluding the first and last five minutes of the session and

including at least three minutes of therapist talk) were rated from each tape. Therapists rated other therapists on several dimensions. Verbalizations were checked as belonging to one of the following set of categories: information and rationale; encouragement and support; assigning/discussing behavioral tasks; challenging cognitions; cognitive coping; visualization instruction; questioning about anxiety producing situations identifying cognitions/symptoms/antecedents to anxiety, and instruction in, and discussion of self-monitoring. In addition, raters recorded any verbalization that was inappropriate (e.g., off-target, alternative therapeutic techniques). Raters also judged the particular treatment condition and from which of the three phases the sample came – the introductory phase (sessions 1 and 2), the rehearsal phase (sessions 3 to 6), or the application phase (sessions 7 to 15).

Eight tapes were sampled from the E & C condition, 14 from the R condition and 13 from the combined condition. In all cases, raters identified correctly the treatment condition represented by the sample. Judgments of the treatment phase from which the sample came were correct in 31 of the 35 cases; two misjudgements were from the E & C condition and two from the R condition. There were only two instances of inappropriate material; both of which referred to nontargeted problem areas and not to inappropriate treatment technique.

Subjects also completed a treatment credibility questionnaire at the end of the first treatment session (following treatment rationale and description). The questionnaire was based on an instrument developed by Borkovec & Nau (1972). Subjects rated (on 0 to 8 point scales) how logical the treatment seemed, how confident they were that the treatment would eliminate their anxiety problems, how confident they would be in recommending the treatment to anxious friends, and how successful they thought the treatment would be in reducing other problems involving anxiety, such as headache.

Assessments were conducted at pre-treatment and post-treatment. Active treatment group subjects were also assessed 3 months, 6 months, 12 months and 24 months after treatment completion. However, the follow-up assessments are still in progress.

RESULTS

Dropouts

One subject dropped from the WL condition, five from the R condition, one from the E & C condition and four from the combined condition. The number of subjects who completed each condition were (in respective order) 15, 10, 15 and 20. However, 4 subjects who completed the combined condition were excluded from the analysis since they were “washed out” from drugs before treatment began, as part of the requirements for another study leaving 16 completers in this group. The percentage of dropouts for each condition were, therefore, 6%, 33%, 6%, and 17%. Seventeen percent refers to 4 dropouts out of the original 24 subjects who began the combined condition (see subject section). Tests of differences between proportions of subjects dropping out demonstrate that a significantly greater number of subjects in the R group

dropped compared to E & C and WL ($Z = 1.90$, $p < .04$ in both comparisons) but not compared to the combined group. The reasons for attrition were as follows: other time commitments (2), began alternative treatment (1), panic free (1), moved to a different city (1), unknown (6). The range of sessions completed for those who dropped extended from 2 to 9, and the mean number of sessions completed by that group of people was 4.1.

Those who dropped from the study (total of 11) were compared to all other subjects who completed their respective programs on major pre-treatment variables, using one-way ANOVAS. The dropouts did not differ from other subjects in terms of age, duration of the disorder (number of months since the first panic to the time of the diagnostic evaluation), Hamilton Anxiety or Depression scores, treatment credibility scores (although the number of those who completed this rating form from the dropout group was very minimal – 4), nor with respect to any of the standardized self-report questionnaires or self-monitoring data. However, at pre-treatment, the dropout group were assigned on average a lower clinical severity rating: $F(1, 65) = 5.53$, $p < .03$. The dropout group average severity was 4.7 (S.D. = 0.7) compared to 5.4 (SD = 0.9) for study completers. In addition, 82% (9) of the subjects who dropped out reported the use of medication (anxiolytic, antidepressant or beta blockers) at pre-treatment assessment in comparison to 46% (26) of the subjects who completed: a chi-square analysis of the frequency distribution was significant ($\chi^2(1) = 4.61$, $p < .05$).

For the study completers, data were missing at post-test for several variables due to non-compliance. The number of missing data points ranged from 1 to 4 variables within each group. Missing data were not replaced by averages.

Pre-Treatment Differences

Pre-treatment scores were compared between the completers of the four groups, using one-way ANOVAS. The groups did not differ in terms of subject characteristics – age, duration of the disorder, or sex. Also, they did not differ in terms of any outcome measure – interview scores, standardized self-report questionnaire scores or self-monitoring data. Nor did they differ in terms of the number of stressful events occurring in the six months prior to treatment. While more of the WL group reported the use of anxiolytic medication at pre-assessment in comparison to each of the treatment groups, a chi-square was not significant: $\chi^2(3) = 6.32$, $p < .10$. In addition, the use of self report of anxiolytics at preassessment as a covariate did not alter the pattern of results from those examined without a covariate. Therefore, covariance methods were not reported for the remainder of the statistical analyses. In addition, the groups did not differ in terms of the credibility ratings for each treatment. A summary of pre-treatment characteristics of the sample is presented in Table 1. Additional axis 1 diagnoses (of secondary severity) for the entire sample were as follows: generalized anxiety disorder ($n = 1$); social phobia ($n = 1$); simple phobia ($n = 7$); dysthymia ($n = 10$), and major depressive episode ($n = 3$). These comorbid diagnoses were distributed randomly across treatment groups.

TABLE 1
SAMPLE CHARACTERISTICS

	Wait list group (N = 15)	Relaxation group (N = 10)	Exposure and cognitive group (N = 15)	Combined group (N = 16)
Age	36.1 (12.5)	38.0 (22.8)	36.1 (6.8)	31.7 (8.3)
Sex				
Females	14	7	10	12
Males	1	3	5	4
Number of months since first panic	71.7 (52.0)	102.2 (121.4)	88.2 (69.8)	76.1 (99.4)
Positive life events	6.6 (6.5)	6.1 (5.7)	3.2 (3.4)	4.7 (6.7)
Negative life events	10.1 (9.6)	21.8 (36.3)	10.4 (9.9)	15.4 (15.3)
Frequency (percent) using anxiolytic medication	10 (67)	6 (60)	6 (40)	4 (25)
Treatment Credibility (0-9)	—	6.5 (1.7)	6.8 (2.0)	7.9 (1.4)

Composite Score Analyses

Using the composite score criteria methods described previously, responder status could not be established due to insufficient data for 3 of the WL, 4 of the R, 3 of the E & C, and 3 of the combined group. On the basis of the remaining data, responder frequency and percentage for each group respectively were 2 (17%), 5 (83%), 7 (58%), and 8 (62%). These percentages are depicted in Figure 1.

Tests of differences between proportions were conducted for each pair of groups. The proportion of responders from the WL group was significantly lower than the proportion of responders from the E & C group ($Z = 2.05$, $p < .05$), the R group ($Z = 2.60$, $p < .01$) and the combined group ($Z = 2.30$, $p < .05$). The proportions did not differ significantly between the active therapy groups.

Endstate functioning could not be determined for 3 of the WL group, 4 of the R group, 4 of the E & C group, and 3 of the combined group due to insufficient data. From the remainder of the data, the following frequencies and percentages of high endstate were obtained: 0 (0%), 3 (50%), 5 (46%), and 6 (46%). Those patterns are depicted in Figure 2. The proportion of high endstate functioners from the WL group was significantly lower than the proportion of high end state functioners from the R group ($Z = 2.67$, $p < .05$), the E & C group ($Z = 2.66$, $p < .05$) and the combined group: ($Z = 2.69$, $p < .05$). The proportions did not differ between the active therapy groups.

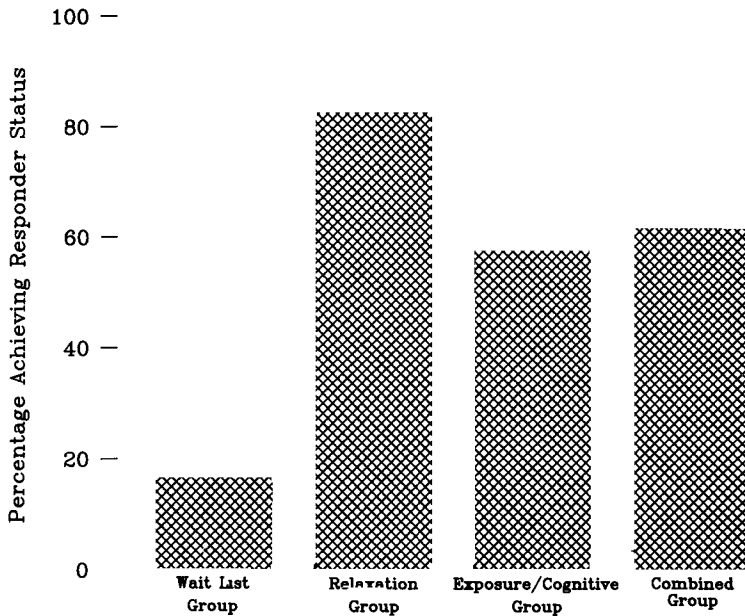


FIG. 1. Percentage of each group achieving responder status at post-treatment assessment.

Individual Variable Analyses

Repeated measures ANOVAS were conducted to compare the four groups in terms of pre- to post-treatment change. Means and standard deviations for each dependent variable are presented in Table 2. Multivariate analyses were not conducted due to the restrictive cell sizes, but the alpha level was set to .01 to reduce Type 1 error rate. Statistical analyses were not conducted on the last two variables (intensity of panic and anxiety episodes) because when those who do not experience panic or anxiety episodes at pre- and post-assessment are excluded from these analyses, cell sizes often fall below an n of 5.

A significant group by time effect was apparent for the clinician's rating of severity of panic disorder, $F(3,47) = 10.56, p < .001$. Subsequent simple effects analyses indicated that each of the active treatment groups evidenced significant reductions in the clinical severity rating, in comparison to the WL group. For each of the three active treatment groups, the probability levels were less than .0001. It should be noted, however, that there was a trend for the WL group to improve somewhat $F(1,47) = 4.21, p < .05$. In addition, Duncan's tests of post-assessment data showed that the clinicians rating of severity was significantly higher on average for the WL group in comparison to each of the active treatment groups.

The group by time interaction was significant for the Hamilton Anxiety Score also: $F(3,48) = 5.10, p < .01$. Subsequent simple effects analyses indicated that each of the active treatment groups exhibited significant reductions in

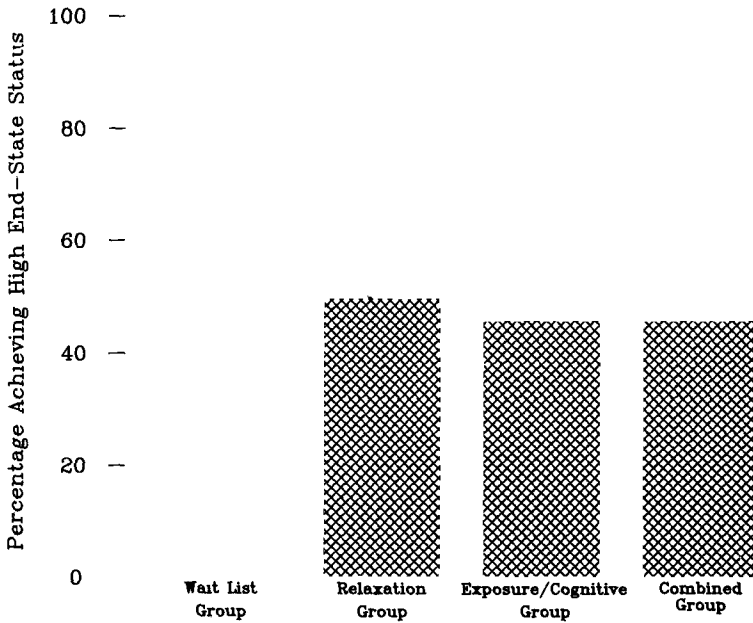


FIG. 2. Percentage of each group achieving high-end state at post-treatment assessment.

the Hamilton Anxiety score, unlike the WL group whose scores on that variable tended to remain stable. For each group of the active treatment groups, the probability levels were less than .001. Also Duncan's paired comparison tests of post-assessment data indicated that both the R and combined groups' ratings were lower than the WL group's ratings.

Ratings on the Psychosomatic Symptoms Scale also yielded a significant interaction: $F(3,45) = 4.4, p < .01$. Subsequent simple effects analyses indicated that the R group only evidenced a reduction in the report of general psychosomatic symptoms: $F(1,45) = 7.15, p < .01$. Similarly, at post-assessment, only the R group was significantly lower than the WL group.

Other rating scale or questionnaire measures, including the Hamilton Depression Scale, the Beck Depression Inventory, the Trait Scale of State-Trait Anxiety Inventory, and the CSAQ, were not significantly different among groups. Finally, of those subjects who continued to report panic at post-treatment, the intensity of the panics tended to be less in the active treatment groups (pre average = 6.08, post average = 5.11) in comparison to a slight increase in the WL group (pre average = 6.00, post average = 6.35). However, Group X Time statistical analyses were prevented by the small numbers of subjects in the active treatment groups who reported panic at post-assessment. The number of panics (total or situational) did not result in a significant interaction. However, the percentages of each group reporting zero panics at post treatment differed significantly. At post treatment, 5 out of 14 or 36% of the

Subjective symptom scale	15.8 (7.1)	13.3 (7.4)	14.0 (7.7)	8.3 (4.6)	12.3 (10.3)	6.2 (6.0)	14.4 (7.1)	9.9 (10.1)
Self-rating fear (0-8) questionnaire	3.8 (2.4)	3.2 (1.9)	4.8 (2.3)	2.3 (0.8)	4.8 (2.2)	2.3 (0.9)	5.0 (2.0)	2.6 (2.1)
Beck depression inventory	14.9 (6.7)	10.6 (4.6)	12.3 (6.4)	7.2 (4.4)	13.5 (8.9)	11.3 (7.2)	12.6 (6.4)	8.3 (3.2)
Average daily anxiety	2.3 (1.2)	2.1 (1.2)	1.7 (0.8)	0.9 (0.7)	1.9 (1.0)	2.0 (2.2)	2.0 (1.0)	1.3 (1.1)
Average daily depression	1.0 (1.0)	1.0 (1.0)	1.4 (0.9)	0.5 (0.8)	1.7 (0.8)	1.3 (0.9)	1.1 (1.2)	0.7 (1.0)
Average daily pleasantness	2.6 (1.3)	2.5 (1.5)	2.3 (1.1)	3.1 (2.2)	2.7 (1.5)	2.9 (1.5)	2.1 (1.4)	2.5 (1.9)
Average number of anxiety episodes per week	3.0 (3.4)	2.9 (5.7)	1.2 (1.1)	0.4 (0.5)	2.1 (1.5)	1.3 (1.6)	1.6 (1.5)	0.4 (0.7)
Average number of panic attacks per week	2.5 (2.8)	1.4 (2.5)	1.3 (1.0)	0.6 (0.9)	1.2 (1.0)	1.0 (2.6)	1.9 (2.4)	0.1 (0.3)
Average number of stress related panics per week	1.7 (2.6)	1.0 (2.6)	0.7 (0.7)	0.2 (0.4)	0.7 (0.7)	0.4 (1.1)	0.9 (0.5)	0.1 (0.3)
Intensity of anxiety episodes (excluding 0)	4.8 (1.1)	5.8 (1.3)	3.5 (2.1)	4.0 (0.0)	5.3 (0.9)	4.1 (1.1)	5.4 (0.5)	3.9 (0.9)
Intensity of panic attacks (excluding 0)	6.0 (1.3)	6.4 (0.9)	6.3 (1.2)	4.8 (1.1)	6.4 (0.1)	4.8 (1.2)	5.5 (0.7)	5.8 (1.8)

* p < .01.

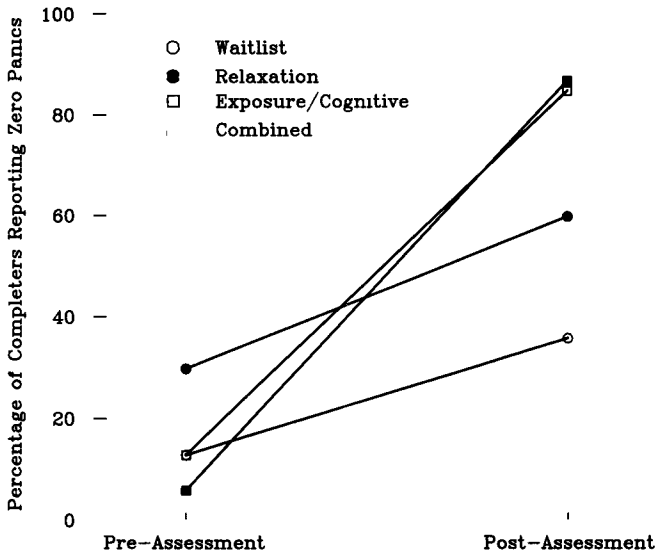


FIG. 3A. Percentage of study completers who self monitored zero panic attacks over a two week interval at pre and post assessment.

WL, 6 out of 10 or 60% of the R group, 11 out of 13 or 85% of the E & C group and 13 out of 15 or 87% of the combined group reported no panic attacks. Tests of differences between proportions of subjects reporting zero panic attacks at post-treatment were conducted between each pair of groups. Both the E & C ($Z = 2.58, p < .05$) and the combined ($Z = 2.83, p < .05$) groups differed from the wait-list. No other differences were found. The percentages of completers in each group who reported no panic attacks at pre- and post-assessment are depicted in Figure 3A. It should be noted that several subjects self monitored no panic attacks in the two weeks prior to treatment, despite the interview report of at least one panic (and on average, 10 panic attacks) in the two weeks prior to assessment.

If one makes the conservative assumption that dropouts were continuing to panic, the percentage of the total sample in each group who were panic free after treatment changes to 33% in the WL group; 40% in the R group; 79% in the E & C group; and 74% in the combined group. These percentages are presented in Figure 3B. Now tests of differences between proportions indicates that both E & C and the combined group are significantly better than R ($Z = 2.12, p < .03$; $Z = 2.06, p < .03$) and WL ($Z = 2.57, p < .02$; $Z = 2.47, p < .02$) groups.

No other significant differences were observed on self-monitored anxiety, depression or pleasant mood. Patterns of medication use (based on self-monitoring data) are presented in Table 3. Statistical comparisons among the groups in terms of the number of subjects using medication could not be con-

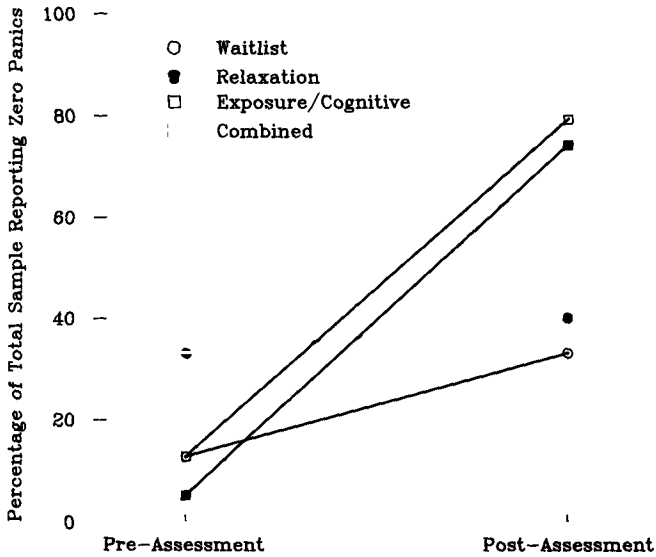


FIG. 3B. Percentage of total sample who self monitored zero panic attacks over a two week interval at pre and post assessment.

ducted due to restrictive cell sizes. Overall, 67% of the WL group used anxiolytic medication at pre compared to 60% at post, while 39% of the treated subjects used anxiolytic medication at pre compared to 22% at post. In addition, 2 of the WL group and 3 of the R group increased their use of medication from pre- to post-assessment.

Follow-up Assessments

As insufficient data were available to analyse treatment group interaction effects at follow-up assessments, data from the three active groups were combined in the following set of descriptive statistics. It should be noted that data are missing for reasons of both attrition, as well as incomplete data from some subjects. The follow-up data are still being collected. These data were based primarily on 6 month data, but when 6 month data were missing, 3 month data ($n = 2$) or, 12 month data if 3 month data were missing, ($n = 4$) were used. The five variables used to determine endstate functioning were examined: clinical severity rating ($n = 24$), number of panic attacks ($n = 18$), self rating of distress ($n = 20$), average daily anxiety ($n = 18$) and subjective symptom scale scores ($n = 19$). Means, standard deviations and patterns of change are presented in Table 4. Repeated measures t-tests indicated that none of the variables significantly changed from post- to follow-up assessment, although daily functioning evidenced a positive trend ($t(18) = 1.11, p < .10$). Fully 68% of clients who were followed demonstrated improvement in the areas of work, social, and leisure function.

TABLE 3
 REPORTED MEDICATION USE—FREQUENCIES (PERCENTAGES)

	Wait list group	Relaxation group	Exposure and cognitive group	Combined group
Anxiolytic				
Pre	10 (67)	6 (60)	6 (40)	4 (25)
Post	9 (60)	5 (50)	2 (13)	2 (13)
Anti-depressant				
Pre	2 (13)	0 (0)	1 (7)	0 (0)
Post	0 (0)	0 (0)	0 (0)	0 (0)
Beta blockers				
Pre	1 (7)	0 (0)	0 (0)	1 (6)
Post	1 (7)	0 (0)	0 (0)	1 (6)

DISCUSSION

The results clearly indicate that all three variations of treatment were successful in the treatment of panic disorder. Panic attacks were eliminated in a very large percentage of patients, and overall improvement in associated anxiety and general functioning were apparent. Results were maintained over time in those patients followed, although follow-up will continue for two years post-treatment to determine if follow-up is affected by treatment group assignment.

Some differences or trends emerged between groups. Generally, fewer patients among completers in the relaxation group reported complete elimination of panic at post-test (60% vs 85% and 87%). Only the E & C and combined group were significantly better than the WL group on this measure. On the other hand, scores on the psychosomatic symptom checklist were significantly better for the R group only. Greater reductions in average daily anxiety were noted in the two groups receiving relaxation. This accounts for the slightly (but nonsignificantly) higher percentage of patients receiving high end-state functioning status at post-treatment in the relaxation group. This suggests that relaxation, as administered in this treatment protocol, is a less specific treatment for panic attacks than the other treatment conditions. The fact that a greater percentage of patients increased rather than decreased daily anxiety at the follow-up assessments suggests that relaxation may not fare as well when adequate numbers of clients are available for treatment group interaction effects at follow up. This remains to be seen.

Despite the positive results reported in the current study, it is worth noting that the almost total elimination of panic does not necessarily correlate with high endstate functioning. In the exposure and cognitive therapy, as well as in the combined group, nearly 90% of the patients were panic free, and yet only approximately 50% reached a criteria of high endstate functioning. The data suggests that these patients are left with some residual anxiety, as well as some continuing impairment in daily functioning at post-test which precludes

TABLE 4
SUMMARY OF FOLLOW-UP DATA MAJOR VARIABLES

	Post assessment	Follow-up assessment	Increase	Percentage decrease	Unchanged
Clinical severity rating (N = 24)	2.67 (1.34)	2.23 (1.58)	13	50	38
Number of panic attacks per week (N = 18)	0.25 (0.65)	0.25 (0.52)	22	17	61
Frequency (percent) reporting zero panic attacks	16 (83)	13 (72)			
Self rating-fear questionnaire (N = 20)	2.84 (1.30)	2.25 (1.80)	15	45	40
Average daily anxiety (N = 18)	1.63 (1.12)	1.68 (0.98)	50	44	6
Subjective symptom scale (N = 19)	9.58 (7.75)	7.90 (6.11)	16	68	16

* $p < .01$.

high end-state functioning status, although they are improved on these measures. Follow-up data suggests that gains in all areas are largely maintained. In fact, work and social functioning as measured by the SSS shows a trend towards further improvement from post-test to follow-up with fully 68% of treated patients evidencing further improvement. This change accounts, in part, for an increase in high end-state functioning status at follow-up from 48% (averaged across all treatment groups) to 60%. Nevertheless, careful attention to individual patients with less than optimal functioning will be required to determine if residual anxiety and interference with daily functioning remain a problem despite elimination of panic attacks.

Dropout rates from this study are also noteworthy despite the rather limited sample from which to generalize in this study. Dropout rates from the relaxation group, as well as the combined group, are higher than those typically observed in most psychological treatments and approach dropout rates reported from drug studies (Barlow, 1988). In this study, several factors were associated with high dropout rates. First, a significantly higher proportion of those who entered our program already on medications dropped from treatment. It has been observed previously that pharmacological interventions, particularly benzodiazepines, may interfere with the effects of psychological treatments (Barlow, 1988). It is possible that faced with a treatment clearly requiring the evocation of anxiety, some patients already on anxiolytics judged this to be antithetical to their treatment goals. However, we have not noticed this problem before in other treatment outcome studies where dropout rates have been very low whether patients were on drugs before beginning treatment or not (e.g., Barlow,

O'Brien, & Last, 1984). In addition, all patients clearly met the criteria for panic disorder at the beginning of the study despite their pharmacological regimens and, therefore, were motivated to seek additional relief.

A second factor correlated with dropout rates is the presence of the relaxation component of treatment. Neither the E & C treatment condition alone nor the wait-list control group evidenced the rate of dropouts present in the two treatment conditions where relaxation was a component. Fully 33% of the R group dropped from treatment. Previously we had demonstrated that relaxation in the early stages can be anxiogenic and even panicogenic (Adler, Craske, & Barlow, 1987a & 1987b). It is possible that some of these patients experienced increased anxiety and panic during the early stages of relaxation although, since our therapists are sensitized to this issue, it should have been observed and handled appropriately.

Finally, dropouts as a group were rated as less severe than completers at the beginning of the study. It is possible that this less severe group of dropouts did not possess the requisite motivation to complete three months of therapy, particularly relaxation training with its extensive practice requirements. Therefore, these less severe patients might be candidates for drug treatment.

While each of the three variations of treatment was generally effective for panic disorder, mechanisms of action are not clear. When this clinical outcome study was originated in the early 1980s, theoretical attention was directed to cognitive versus somatic aspects of anxiety and panic, with panic conceptualized as an extreme form of somatic anxiety (Barlow et al., 1984). Since then, conceptualizations have changed considerably and uncontrolled clinical trials reviewed above have approached panic disorder from three somewhat different perspectives. One tradition espoused by Lum (1976) and Ley (1985) attributes panic to the effects of chronic hyperventilation. While there is much evidence disputing this view (Barlow, 1988) there is little question that hyperventilatory episodes are a prominent feature of at least some panic attacks. Based on this tradition, treatment involves breathing retraining such that hyperventilatory episodes are precluded (e.g., Kraft & Hooguin, 1984). A second school of thought focuses on the catastrophic misinterpretation of otherwise normal somatic events as the cause of panic. Treatment then involves the correction of these cognitive distortions (e.g., Beck & Emery, 1985). Several clinical investigators have combined these rationales. For example, Clark et al., (1985) and Rapee (1985) suspect that at least some patients (approximately 50%) may be vulnerable to hyperventilatory episodes which are then misattributed. Thus, breathing retraining would be combined with cognitive therapy in these patients but the emphasis is clearly on cognitive distortions. Finally, in our Center, pure exposure to somatic cues associated with panic which may be occasioned by any number of panic provocation procedures such as hyperventilation or CO₂ inhalation or a variety of idiosyncratic exercises is conceptualized as a crucial component for treatment. An expanded number of those exercises for eliciting interoceptive sensations forms the basis of our most current treatment approach for panic disorder (Barlow & Craske, 1988). These exposure based treatments may prevent the escapist action tendencies which

seem such a prominent part of panic attacks, as well as allow the development of a sense of control over these events (Barlow, 1988).

At the present time, it is difficult to untangle these different explanations for the success of treatment since most case studies and clinical replication series, as well as the treatment groups described above, typically include all three components. For example, clinicians emphasizing exposure to somatic events typically also employ cognitive procedures in which patients are educated about the source of their somatic symptoms. Breathing retraining and exposure to interoceptive cues would also seem to be a part of the relaxation condition since a reduction in breathing rate is inherent in relaxation training and relaxation produces interoceptive cues that are anxiogenic and panicogenic in some cases (Heide & Borkovec, 1983; 1984; Adler et al. 1987). Thus, current treatment protocols quite purposely include a combination of breathing retraining, cognitive therapy and interoceptive exposure. An important future step will be to dismantle these treatment packages in an attempt to identify the essential components.

One obvious question concerns the efficacy of these new treatments compared to better established drug treatments. The first study comparing these treatments has now appeared (Klosko, 1987; Klosko, Barlow, Tassinari, & Cerny, 1988). A combined treatment condition identical to the treatment described above, was administered to an overlapping group of patients and compared to a wait-list control group. These two groups were compared to groups receiving alprazolam (xanax) or a placebo administered in a double-blind fashion. In this study, cognitive behavioral (combined) therapy was significantly better than placebo or wait-list on most measures, but not significantly different than alprazolam. Only for intensity of panic symptoms, as well as the important symptom of dyspnea, was the therapy group significantly better than the alprazolam group. Fully 86% of the therapy group was panic free compared to 50% of the alprazolam group, although this difference was not statistically significant. Nevertheless, the therapy group demonstrated a broader pattern of positive therapeutic change than the alprazolam group.

An obvious step is to explore a combination of pharmacological and behavioral treatments. It is possible that an additive effect exists, particularly in terms of the pattern of therapeutic results. For example, when alprazolam works, it tends to work quickly, often within the first week of administration. Therapy on the other hand lasts three months with important changes occurring only after a substantial part of treatment has been experienced. Furthermore, preliminary results from follow-ups indicate that the effects of cognitive behavior therapy are long lasting. Clinical experience with alprazolam, on the other hand, suggests that relapse is common if withdrawal is successfully completed which, in and of itself, has proven a difficult task (e.g., Fyer et al., 1987; Fontaine, Chouinard, & Annable, 1984). Thus it might be beneficial to start patients on alprazolam, particularly those experiencing intense panic attacks that preclude normal functioning, with a therapeutic contract to withdraw them from alprazolam as cognitive behavior therapy progresses. On the other hand, benzodiazepines may interfere with the effects of behavior therapy for

a variety of reasons (Barlow, 1988). Of course, many patients in this study were on medication when treatment began and had been for some time. But the dosages were small and probably not therapeutic for the most part as reflected in pre-treatment severity scores. Thus the contribution of these agents would seem minimal.

In any case, it seems clear that effective behavioral treatments for panic disorder now exist. Whether it will prove beneficial or not to combine these treatments with drugs for some clients is a question for future research. In the meantime, clients and therapists have a choice of drug or behavioral treatments for panic disorder.

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