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A Comparison of Delivery Methods of Cognitive Behavioral Therapy for Panic

Disorder: An International Multi-center Trial

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Abstract

Cognitive behavior therapy (CBT) is the psychological treatment of choice for panic disorder (PD). But given limited access to CBT it must be delivered with maximal cost-effectiveness. Previous research has found that a brief computer-augmented CBT was as effective as extended therapist-delivered CBT. In order to test this finding 163 patients with PD across two sites in Scotland and Australia were randomly allocated to12 sessions of therapist delivered CBT (CBT12), 6 sessions of therapy either therapist-delivered (CBT6) or with computer augmentation (CBT6-CA), or a wait list control. At post treatment CBT12 was more effective than CBT6 but not different from CBT6CA, however CBT6 did not differ from CBT6CA. The active treatments did not differ statistically at 6-month follow up. The study provided some support for the use of computers as an innovative adjunctive therapy tool and merits further investigation.

A Comparison of Delivery Methods of Cognitive-Behavioral Therapy for Panic

Disorder: An International Multi-center Trial.

Substantial research evidence indicates that the psychological treatment of choice for panic disorder is cognitive-behavioral intervention (CBT) (Barlow, Gorman, Shear & Woods, 2000; Hofmann & Spiegel, 1999; Otto, Pollack & Maki, 2000.) As a result there has been a corresponding growth of demand for treatment, an increase in waiting times in some health care systems and, consequently, pressure for more accessible and efficient forms of treatment delivery.

This need is further highlighted by the high prevalence of panic disorder (Kessler, McGonagle, Zhao, Nelson, Hughes, Eshleman, et al, 1994), as well as the nature of the condition that often involves a level of agoraphobic avoidance. This may limit regular clinic attendance and access to conventional therapist-administered treatment (Côté, Gauthier, Laberge, Cormier & Plamondon, 1994). To date, one of the main alternatives to conventional CBT delivery has involved the use of written self-help materials or bibliotherapy.

Bibliotherapy (Dow, 1982) has proven to be as effective as eight sessions of group or individual CBT (Lidren, Watkins, Gould, Clum, Asterino, & Tulloch, 1994) although Power, Sharp, Swanson, and Simpson (2000) found a totally self-administered bibliotherapy condition to be significantly less effective on a range of outcome measures compared to 'standard' therapist delivered CBT. This may be related to inaccessibility and inconvenience of bibliotherapy during daily activities. One possible solution to the limits of bibliotherapy lies in computer-assisted therapy. Computers can increase patient access to treatment programs (Kenardy, McCafferty & Rosa, 2003), extend therapy to the patient's own environment and enhance cost-effectiveness with costs reduced to between one-third and one-sixth of conventional behavioral treatment (Kenardy & Adams, 1993, Newman, 2000.) Computer programs have been shown to be

effective adjuncts to more conventional treatment for a variety of anxiety disorders, including panic disorder, agoraphobia, social phobia, obsessive-compulsive disorder, and generalized anxiety disorder (Newman, 2000). With the advent of powerful, inexpensive hand-held computers, it has become possible to provide a realistic version of CBT that may be used in the patient's own environment

Preliminary studies by Kenardy, Fried, Taylor, and Kraemer (1992) on the use of hand held computers to aid monitoring of anxiety and coping ability among panic disorder patients showed that the computers were well accepted, led to increased compliance and more reliable self-monitoring. In a further pilot study, Newman, Kenardy, Herman and Taylor (1997) randomly assigned 18 patients to a standard (12session) CBT condition based on Panic Control Treatment, or a brief (4 session) computer-assisted CBT condition. The results showed that both treatments were equally effective at post treatment and at six months follow-up. The sample size, however, was small and the absence of a brief treatment comparison condition without a computer pre-empts any conclusion about the computer's effectiveness over and above that attributable to brief therapist contact alone. The present study therefore was designed to address these shortcomings by employing a development of the computerized CBT package of Newman, et al. (1997).

In order to assess the generalizability of the approach it was decided to conduct the study as an international multi-center trial, at the University of Queensland, Australia, and through Fife Healthcare, (now called Fife Primary Care NHS Trust) Scotland. The inclusion criteria permitted a wider range of patients to be included in the study than occurs in efficacy trials. Thus the aim was to frame the trial as an effectiveness study.

Method

Participants

In Scotland patients were recruited via referrals from general practitioners to the Adult Clinical Psychology Service in Fife and were seen for all treatment sessions in local outpatient clinics, health centers or surgeries. In Australia patients were recruited via referrals from general practitioners and through the media, and were seen for all treatments in the Psychology Clinic at the University of Queensland. Diagnostic status was confirmed using the Structured Clinical Interview for DSM - IV Axis I Disorders (SCID - I, First, Spitzer, Gibbon & Williams, 1997.) Ethical approval was obtained through the relevant Ethics Committees. Patients entered the study if they provided written informed consent and conformed to the following entry requirements: DSM-IV (American Psychiatric Association, 1994) Panic Disorder with or without Agoraphobia; current episode duration of at least three months; age 18 to 60 years inclusive; consider panic their main problem; willing to accept random allocation, including the waiting list condition; no depressive disorder severe enough to require urgent treatment; no cognitive-behavior therapy for the current episode; no evidence of organic mental disorder, schizophrenia, alcohol or drug dependence, cardiovascular disease, asthma, epilepsy, pregnancy or intention to become pregnant during the course of the study. Concurrent Axis II personality disorder was not a reason for exclusion unless the personality disorder was clearly the primary problem. All patients taking medication at the time of entry must have been on a stable dose for three months and must have been willing and able to remain on a stable regime for three months during the course of treatment.

Patients who failed to receive at least three sessions of their respective course of treatment or provide adequate pre-treatment and end-point data were defined as dropouts. Patients who dropped out were replaced.

Treatments

Therapy was conducted by licensed psychologists with extensive experience of CBT. Each therapist was assigned patients randomly which resulted in each therapist treating approximately equal proportions of patients in each of the three treatment conditions. In the brief treatment conditions the time allocated to cover content was reduced from 12 to 6 one-hour sessions.. This was equivalent to the time allocation for brief CBT for panic disorder evaluated by Clark et al (1999), and to the time allocation in our pilot outcome study (Newman et al, 1997.) It was determined through the pilot study that six hours was sufficient time to deliver the content of the standard protocol. Based on client feedback, it was decided that, instead of being delivered over four sessions (six hours contact) (Newman et al, 1997), the therapy would be over six sessions, each of one hour. The manuals provided specific detail of content to be covered within each session including session agendas, information to be presented, homework exercises, and specific therapeutic procedures (e.g. interoceptive exposure, relapse prevention.) The CBT approach was based on Panic Control Treatment (Barlow et al, 1989) that incorporated the cognitive and behavioral theories of panic (e.g. Barlow et al, 1989; Clark, 1986) and standard cognitive and behavioral techniques. The protocol was adapted from Panic Control Treatment protocols but also included a graded exposure component. Graded exposure was introduced after the second session. Patients were encouraged to engage in selfdirected exposure as part of homework, and progress was monitored throughout treatment

All sessions for all treatment conditions were tape-recorded and a random selection (20%) of tapes were exchanged between sites and rated by JK and MD to ensure adherence to treatment protocols and therapeutic competence. There were no significant effects for Site, Treatment, or Site X Treatment on protocol adherence or therapeutic adequacy. Therapists also completed a separate checklist for each therapy session to evaluate adherence to the protocol. The correlation between therapist-rated and externally rated protocol adherence was 0.92 (p<.001). No significant differences were found on therapist-rated treatment protocol compliance across Site or Treatment, or for Site X Treatment. Overall, there was 97.1 % protocol adherence.

CBT12, or standard treatment, involved 12 weekly 1-hour individual sessions with the therapist. Average number of sessions completed was 10.5. The six-week treatment protocols, CBT6 and CBT6-CA constituted a condensed version of the standard CBT 12 regime including individual sessions with the therapist, the same content and the same supplementary handouts. Total therapist contact time, however, for the brief treatments (CBT6 and CBT6-CA) was 6 hours (i.e. six weekly one hour contacts). This was equal to the contact time of the brief treatment condition in Newman et al (1997). On average patients completed 5.9 therapy sessions in CBT6-CA and 5.9 sessions in CBT6. In the CBT6-CA condition, patients continued to carry the palmtop computer for the remaining 6 weeks, after which it was returned.

Computer

The palmtop computer used in the CBT6-CA was the Hewlett Packard 200LX, which weighs about 300 g and when folded measures 16 x 2.5 x 8.5 cm. It unfolds into two sections: a QWERTY keyboard with function keys, and a screen (16 lines by 40 characters). The computer was programmed to signal the subject five times daily - at 800am; 1100am; 4.00pm; 7.00pm and 9.00pm to prompt the practice of the therapy

components. The computer program included a self-statement module, a breathing control module, and a new exposure module incorporating both situational exposure and interoceptive exposure. The exposure included goal setting and specification of exposure tasks. In the case of interoceptive exposure specific tasks, such as hyperventilation, were presented in relation to concern about particular salient somatic symptoms, such as difficulty breathing.

Measures

The primary measures comprised a comprehensive battery of panic and anxiety measures, comparable to that employed by Clark and colleagues (Clark, et al, 1994; 1999). Secondary outcome measures assessed disability and quality of life. These were completed pre-treatment, post-treatment, and at 6-months follow-up. Frequency of panic attacks over the last 2 weeks was assessed using a 5-point (0-4) scale. In addition, panic-related distress/disability was rated on a 9-point scale, where 0 represented 'not at all disturbing and/or disabling', 2 'slightly', 4 'definitely', 6 'markedly' and 8 'very disturbing/disabling'. Phobic avoidance was assessed by the Fear Questionnaire (Marks & Mathews, 1979.) Patients also completed the Mobility Inventory for Agoraphobia (Chambless, Caputo, Jasin, Gracely & Williams, 1985) which yields an average score for situational avoidance, both when accompanied and alone; the Body Sensations Questionnaire (BSQ; Chambless, Caputo, Bright & Gallagher, 1984) which assesses degree of anxiety and selective attention to physical symptomatology and sensations; and the Agoraphobic Cognitions Questionnaire (ACQ; Chambless et al, 1984) which was used as an additional measure of panicrelated cognition. General anxiety was assessed using the State-Trait Anxiety Inventory-Form X Trait Scale (STAI-T; Spielberger, Gorsuch & Lushene, 1970.) Depression was assessed by the Beck Depression Inventory (BDI; Beck, Steer & Garbin, 1988). The Medical Outcomes Survey Short Form 36 (SF-36; Ware & Sherbourne, 1992) was used as a general measure of Quality of Life and broad health status. Two standardized Component scores, Mental and Physical, are derived from the SF-36.

At the first treatment session patients not in the wait-list condition completed a four-item scale of treatment outcome expectancy. Items were rated on a 5-point scale from 'not at all' (1) to 'extremely' (5) and scores were summed to give a total score. Patients in the CBT6-CA condition also completed a question on satisfaction with the computer using the same five-point scale.

Statistical Analysis

To ensure initial equivalence among groups across sites, pre-treatment/wait scores for the three treatment groups and waitlist were compared by separate two-way analyses of variance (ANOVAs) for each measure. For the outcome analyses between site and group differences pre- to post-treatment and pre- to follow-up were examined by means of repeated-measures analyses of variance (ANOVAs). Planned comparisons were used to identify significant between-group differences. These were Waitlist vs. active treatments, CBT12 vs. CBT6CA, CBT12 vs. CBT6 and CBT6CA vs. CBT6. These were chosen to test the study hypotheses. The main analysis was based on a single unweighted composite panic-anxiety measure (Clark et al 1994; Connors, Epstein, March, Angold, Wells, Klaric et al, 2001). Additional analyses were conducted on individual panic/anxiety measures if significant between-group differences were found. The composite score was calculated by the procedure recommended by Connors, Epstein, March, Angold, Wells, Klaric et al, (2001).

Effect size is calculated using the formula $ES = (X_{comp} - X_{ref}) / SD_{ref}$ (Gould et al, 1995), where X_{comp} is the mean of the comparison group, X_{ref} is the mean of the

reference (or control) group, and SD_{ref} is the standard deviation of the reference group. To determine clinical significance the reliable change index (RCI) was calculated for each variable using norms and test-retest reliability estimates, and then a cut-off score of 1.96 standard deviation units was applied. (Newman et al, 1997). The outcome was defined as clinically significant when the RCI exceeded the cut-off score so that the mean was closer to a functional population. Panic-free status and Clinically Significant Change status were analyzed using binary logistic regression analyses. A coding system was used in which one category was designated a reference category (Tabachnick & Fidell 1996). Sample size was based on a mean effect size for CBT for panic disorder of 0.68 (Gould, et al, 1995), and calculated based on 80% power, two-tailed $\alpha = 0.05$, and a drop-out rate of 10-15%.

An intention-to-treat analysis was also conducted in which all cases with available pre-treatment data were carried forward. Since most of the pre-treatment dropouts did not have complete data available for calculation of the composite, it was decided to use panic-free status as the outcome variable as data were available for all subjects at pre-treatment. The intention-to-treat analysis was limited to 3-month posttreatment since it was judged that extrapolation of pre-treatment data to the 6-month follow-up was untenable.

Results

In total 186 patients met the above entry criteria and were offered and accepted a place in the study. Of these 163 patients (87.6%) commenced treatment (waitlist n = 41, CBT6 n = 39, CBT6-CA n = 41, CBT12 n = 42.) Twenty-three patients (14.1%) failed to receive at least three sessions of their respective course of treatment or provide adequate data and were classified as drop-outs. A further 13.1% (n = 14/107) of completers in the active treatment conditions were lost to follow-up. This left 93

patients who had adequate 9-month data to allow for follow-up analysis.. No differences were found between dropouts and completers on the main outcome measures or duration of disorder.

The mean age of the sample was 36.8 years (*SD* = 10.00), with 75.5% female. The majority of patients had a diagnosis of Panic Disorder with Agoraphobia (76.1%.) Patients in Scotland had a significantly greater mean duration current episode compared to the Australian patients, 40.2 months compared to 114.9 months, *F* (1,163) = 34.11, *p*<.001. Overall 52 (33.1%) patients had completed at least some post-secondary education, and there was also a significant difference between sites on education level with 47.4% of the Australian patients having completed some postsecondary education compared to 23% of the Scottish patients, χ^2 (2, *N* = 163) = 16.67, *p*<.001. Significantly more of the Australian patients, 14.1%, χ^2 (1, N = 163) = 21.01, p<.001.

Main Outcomes

Table 1 shows the mean composite and individual measure scores before treatment/wait, at post-treatment/wait and at 6 months follow-up. The results of a series of two-way (Site X Treatment) ANOVAs to compare pre-treatment/waiting list scores for the composite and all individual outcome measures for treatment commencers revealed significant differences for Site on the two Mobility Inventory subscales, Alone F (1, 155) = 4.40, p<.05, Australia M = 2.91 (SD = 1.07) vs. Scotland M = 3.28 (SD = 1.14); Accompanied F (1, 155) = 4.60, p<.05, Australia M = 2.20 (SD = 0.93) vs. Scotland M = 2.53 (SD = 0.98). No other differences were found.

In order to examine pre- to post-treatment outcome a three-way repeatedmeasures ANOVA with Site (Australia, Scotland) X Treatment (Waitlist, CBT6, CBT6-CA, CBT12) X Time (Pre-, Post-) as independent variables was conducted on composite scores. No significant Site X Treatment X Time or Site X Time interaction was found. The Treatment X Time interaction was highly significant (Table 1). Planned comparisons on the pre- to post-treatment composite scores revealed that all treatment conditions were significantly better than wait-list, that CBT12 was significantly better than CBT6, but that CBT6-CA did not differ significantly from either CBT12 or CBT6. Effect sizes (ES) between the treatment conditions and the wait-list calculated on the post-treatment composite scores (Gould et al, 1995.) The treatments were all more effective than the wait-list, with large effect sizes overall, CBT6 ES = 1.51, CBT6CA ES = 1.96, CBT12 ES = 2.16. However, a significant difference between treatment conditions in effect size was found only for CBT12 and CBT6 at post- treatment ES = 0.82, p < .01.

For the individual measures, the only significant Site X Treatment X Time effect was for STAI-T, F(3, 140) = 4.28, p < .005. There was a significantly greater reduction in trait anxiety in the CBT6-CA condition in Australia than in Scotland, t(33) = 2.29, p < .05. Planned comparisons between treatment conditions on all individual measures comprising the composite score showed all treatments to be significantly superior to the waiting list (Table 1). While differences between CBT12 and CBT6 conditions were not uniformly significant, there was nevertheless a consistent trend favoring CBT12 over the CBT6 condition, with CBT6-CA occupying an intermediate position on each outcome measure. The same pattern of results was found for Beck Depression Inventory, F(3, 132) = 10.08, p < .001, SF-36 Mental Component F(3, 118) = 6.71, p < .001, and SF-36 Physical Component F(3, 118) = 4.27, p < .01. Clinically Significant Change and Panic-free Status

The main outcome variables were also analyzed using clinically significant change. Table 2 presents the results of those analyses. No significant Site or Treatment X Site effects were found on any outcome variable. Significant Treatment effects were found on all outcome variables except the FQ-Ag and FQ-Soc. These effects, however, were only found for CBT12 and CBT6CA with reference to the waiting list condition, with no significant difference between CBT6 and waiting list.

At post treatment, using a logistic regression analysis, there was a significant prediction of panic free status. While neither Site nor Site X Treatment significantly predicted high panic free status, Treatment was a significant predictor at all levels with reference to the waiting list condition, CBT12 OR = 32.22 (7.92 - 131.03), CBT6-CA OR = 21.82 (5.46 - 87.14), and CBT6 OR = 8.89 (2.27 - 34.79). CBT12 and CBT6-CA produced similar outcomes (Figure 1). In contrast, fewer patients in the CBT6 treatment reached panic-free status at the end of treatment. Using CBT12 as the reference category CBT6-CA did not differ from CBT12, OR = 0.68 (0.24 -1.90), but CBT6 was significantly worse than CBT12, OR = 0.28 (0.10 - 0.76.) Similar results were found with an intention-to-treat analysis.

Follow-up

To assess whether treatment effects were sustained over the course of the follow-up period, a three-way repeated-measures ANOVA with Site (Australia, Scotland) X Treatment (CBT6, CBT6-CA, CBT12) X Time (Pre-, Follow-up) as independent variables was conducted on the composite scores. The only significant effect was for Time, F(1, 87) = 255.55, p < .001, indicating a significant improvement from pre-treatment to follow-up across all treatment conditions. ANOVA's performed on variables that made up the composite found a main effect for Time in the direction

of improvement [Panic frequency F(1, 87) = 128.57, p<.001; Panic severity F(1, 87) = 150.21, p<.001; BSQ F(1, 87) = 150.99, p<.001; ACQ F(1, 87) = 125.32, p<.001; STAI-T F(1, 87) = 95.16, p<.001; MI-Al F(1, 87) = 84.37, p<.001; MI-Ac F(1, 87) = 43.40, p<.001; FQ-Ag F(1, 87) = 96.23, p<.001; FQ-Soc F(1, 87) = 71.54, p<.001; FQ-BI F(1, 87) = 46.70, p<.001.] The only significant Time X Treatment interaction was for FQ-BI, F(2, 87) = 4.18, p<.05) where there was greater improvement in CBT6 compared to CBT6-CA. In summary, treatment gains were sustained over the follow-up period, and there was little evidence of differential improvement between treatment conditions.

No significant differences were found for outcome expectancy. Positive treatment outcome expectancy predicted improvement on the composite at post-treatment (r = .29, p < .001), but not at follow-up. Satisfaction with the computer significantly predicted improvement on the composite pre- to post-treatment (r = 0.46, p < .05) but not post-treatment to follow-up. Concurrent use of anxiolytic or antidepressant medication did not predict improvement on the composite pre- to post-treatment or maintenance post-treatment to follow-up. When the primary analysis of the composite score was repeated including only those patients who were medication free, this yielded the same pattern of results as for the whole sample.

Discussion

This is the first randomized, multi-site international trial involving CBT. It is also significant given the relatively large number of patients involved in the study, the use of sites from two different countries, and the liberal inclusion criterion. The results of the primary analysis are complex. While they indicate that the most favorable outcome at post-treatment is obtained from a standard duration treatment,, a brief version, when augmented with a computer, is not significantly different in effectiveness. Furthermore, a brief version without computer augmentation performs significantly worse than the standard duration treatment at post-treatment, but is no different from brief, computer-augmented treatment. Thus, there is some evidence, albeit mixed, that the brief computer-augmented treatment does impact positively on post-treatment outcome since, on all variables, it is associated with better outcomes than the brief condition alone. At six-months follow-up the picture changes with CBT delivered in the standard or in a shorter version with or without computer, resulting in similar level of significant improvement in all patients. The more conservative intention-to-treat and clinically significant change analyses mirror this result. Thus the impact of length of treatment fails to carry through to follow-up, where all treatments cannot be distinguished statistically. This replicates, with a greatly increased sample size, the findings of Newman, et al (1997). However, more power may have helped to detect differences between the conditions. While not statistically significant, apparent improvement from post-treatment to follow-up in the brief therapy condition may be explained, in part, by differential attrition. For example panic-free status in post-treatment to follow-up drop-outs was 33.3% (2/6) in the brief therapy condition compared to 80% (4/5) in the brief computer-aided therapy condition. Also, dropouts in the brief therapy condition had a more chronic history (111.8 mo.) than in the brief computer-aided therapy condition (46.4 mo.).

The level of effectiveness of the standard therapy and brief therapy is consistent with that found in the literature (Gould, et al, 1995). The effect sizes on the composite score were comparable to those found by Clark, et al (1994). While the difference in the effect size for the composite score at post-treatment between brief and standard therapy was significant, the effect size compared to wait-list for brief therapy was still large. If the standard therapy were augmented with the computer, it might be possible to produce a more powerful treatment than the standard treatment. Future research could explore this possible development.

The superiority of the full implementation of CBT over the brief treatment at post-treatment contrasts with Clark, et al (1999) who found no differences between brief and full implementation of CBT for panic disorder. However, in their brief therapy these authors conducted five brief cognitive therapy sessions (total therapist contact time 6.5 hours) over a three-month period, whereas in the current study, six sessions (6 hours) were conducted across 6 weeks. Further Clark et al. included self-study modules that were comparable to bibliotherapy. Differences in sample characteristics may have been important since our patients had higher levels of depressive symptoms and a more chronic presentation than patients in the Clark et al. study. One limitation of the present study was the use of self-report outcomes. This meant that evaluation of diagnosis was not possible at post-treatment or follow-up.

Consistent with previous work (Newman et al, 1996; 1997) the computer was well accepted. This is particularly impressive given that 26% of the Scottish and 36% of the Australian sample using the computer had a post-secondary education.. On average each computer received 84 weeks of constant use. This has implications for the cost of the use of the computer as an adjunct to treatment. Since one reason for using the computer in this study was to improve treatment efficiency and reduce cost, it is worthwhile examining relative costs of the treatments. Based on an average fee for service of \$100 per therapist contact hour, palmtop computer hardware costs, software costs and base station costs (distributed over seven patients), the relative costs are \$1200 for the standard therapy, \$600 for the brief therapy, and \$680 for the computer-assisted brief therapy. This is the first international multi-site study and by far the largest study to examine the effectiveness of CBT for panic disorder (although

Marks, Swinson, Basoglu, Kuch, Noshirvani, O'Sullivan, et al., (1993) conducted a trial of exposure versus alprazolam for panic disorder in Canada and the United Kingdom.) Matched studies of CBT in different cultures with different health care systems are rare and much may be learned from these detailed comparisons. Important differences were found in concurrent medication usage, and chronicity of the disorder. In the United Kingdom there has been a significant reduction in the frequency of prescription of benzodiazepines with rates in general practice of approximately 4% (Holden, Hughes, and Tree, 1994). In contrast in Australia the rate of prescription in primary care for anxiety is about 50% (Mant, Mattick, de Burgh, Donnelly, & Hall, 1995.) Greater chronicity in the Australian patients may reflect the reduced accessibility to health care professionals who can deliver effective treatment for anxiety disorders in the United Kingdom than in Australia. In contrast to the United Kingdom where clinical psychology services are provided as part of the National Health Service via referral from primary care, no such scheme exists in Australia. This means that patients with anxiety disorders are more likely to receive CBT earlier in the course of the disorder than in Australia. In spite of these differences, it can be concluded from the similarity of the results in the two countries, that CBT for panic disorder is equally effective in both, and hence that treatment effectiveness is robust to cultural differences. Perhaps more relevant to the use of computers was the educational differences found between the Scottish and the Australian samples. However, adding hand held computers to brief CBT did not appear to be associated with any differential attrition, treatment outcomes or satisfaction with treatment.

Conclusion

This study, conducted at relatively low cost but involving an international group of investigators and a large number of patients demonstrates the feasibility of international collaborative efforts examining psychological therapies. Although the investigators met yearly, the meetings were brief and much of the communication occurred via the Internet. The availability of standardized measures, diagnostic criteria and standard protocols and procedures were critical in this effort. Multi-site studies conducted in this way allow effectiveness trials to be conducted more rapidly and less expensively; and have the added benefit of expanding the generalizability and importance of the findings. The use of computers as an innovative adjunctive therapy tool received some support and merits further investigation.

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Table 1 presents means and standard deviations (in brackets) for the analysis of composite and outcome variables for each time point.

Variable	Time	A.W/L	B.CBT6	C.CBT6- CA	D.CBT12	Treatment X Time and planned comparisons
Composite	Pre-	0.08	0.02	-0.11	-0.08	-
	treatment	(0.64)	(0.65)	(0.59)	(0.57)	
	Post-	0.04	-1.02	-1.33	-1.47	$F(3,132) = 34.05^{***}$
	treatment	(0.70)	(0.77)	(0.69)	(0.55)	A>B,C,D; B>D
	6 month	N/A	-1.21	-1.21	-1.52	
	follow-up		(0.76)	(0.76)	(0.70)	
Panic	Pre-	2.55	2.35	2.49	2.50	
frequency	treatment	(0.87)	(1.07)	(0.70)	(1.25)	
(client rated)	Post-	2.55	0.91	0.66	0.35	F(3,132) = 18.06***
(0-4)	treatment	(1.20)	(1.03)	(1.14)	(0.68)	A>B,C,D; B>D
	6-month	N/A	0.72	0.77	0.69	
	follow-up		(1.14)	(1.12)	(1.15)	
Panic Severity	Pre-	5.09	5.07	4.77	4.93	
(client rated)	treatment	(1.53)	(1.86)	(1.61)	(1.62)	
(0-8)	Post-	4.83	2.24	2.00	1.68	F(3,132) = 12.00 * * *
	treatment	(1.94)	(1.79)	(1.95)	(1.79)	A>B,C,D
	6-month	N/A	1.75	1.95	1.37	
	follow-up		(2.51)	(2.13)	(1.78)	
Body	Pre-	3.28	3.32	3.23	3.17	
Sensations	treatment	(0.79)	(0.61)	(0.86)	(0.89)	
Ouestionnaire	Post-	2.99	2.22	1.85	1.67	F(3,132) = 11.94 * * *
(BSO)	treatment	(0.92)	(0.78)	(0.72)	(0.68)	A>B,C,D;B>D;C>D
	6-month	N/A	2.21	2.08	1.64	
	follow-up		(0.77)	(0.72)	(0.69)	
Agoraphobic	Pre-	2.71	2.81	2.70	2.55	
Cognitions	treatment	(0.67)	(0.76)	(0.82)	(0.76)	
Ouestionnaire	Post-	2.59	1.92	1.68	1.56	F(3,132) = 10.31 * * *
(ACO)	treatment	(0.82)	(0.79)	(0.62)	(0.46)	A > B C D B > D
$(\Pi \cup \chi)$	6-month	(0.0 _) N/A	1.80	1 76	1 49	11 0,0,0,0 0
	follow-up	1011	(0.72)	(0.60)	(0.56)	
State-Trait	Pre-	55 88	58 09	55 55	55 92	
Anxiety	treatment	(9.70)	(10.60)	(9.04)	(11 41)	
Inventory-	Post-	54 90	47.86	42.22	41 10	F(3 132) = 13 16***
Trait	treatment	(11 44)	(12.31)	(10.84)	(13.14)	A > B C D B > D
(STAL-T)	6-month	N/A	45 54	44 30	38 71	
(51111)	follow-up	1 1/1 1	(11.74)	(10.79)	(14,78)	
Mobility	Pre-	3 10	3 01	2 95	3 16	
Inventory-	treatment	(1 12)	(1 14)	(1 18)	(1.04)	
Alone (MI-Al)	Post-	3 21	2.41	2.03	1 97	F(3 132) = 17 10
	treatment	(1.06)	(1.16)	(1 04)	(0.74)	A > B C D
	6-month	N/A	2.26	2.13	1 89	
		1 1/ I I	 0	<u> </u>	1.07	

Mobility	Dro	2.48	2 22	2.22	2.24	
Inventory	FIC-	2.40	2.32	(1, 00)	(0.02)	
A a a a men a mia d	treatment	(1.00)	(0.99)	(1.00)	(0.93)	
Accompanied	Post-	2.61	1.80	1.59	1.55	$F(3,132) = 9.79^{***}$
(MI-Ac)	treatment	(0.99)	(0.85)	(0.80)	(0.51)	A>B,C,D
	6-month	N/A	1.79	1.71	1.50	
	follow-up		(0.87)	(0.90)	(0.53)	
Fear	Pre-	20.57	19.18	16.80	16.84	
Questionnaire-	treatment	(12.15)	(9.87)	(11.39)	(10.73)	
Agoraphobia	Post-	19.92	11.40	8.02	7.05	F(3,132) = 8.33***
(FQ-Ag)	treatment	(11.09)	(9.55)	(8.88)	(7.91)	A>B,C,D; B>D
	6-month	N/A	8.79	8.80	6.46	
	follow-up		(7.09)	(9.55)	(8.47)	
Fear	Pre-	19.53	16.62	16.69	15.89	
Questionnaire-	treatment	(8.92)	(9.05)	(9.18)	(8.37)	
Social Phobia	Post-	19.78	12.53	9.80	9.03	F(3,132) = 9.14 ***
(FQ-Soc)	treatment	(8.69)	(8.27)	(7.11)	(7.96)	A>B,C,D
	6-month	N/A	10.75	10.97	6.97	
	follow-up		(7.74)	(6.72)	(7.27)	
Fear	Pre-	16.40	17.18	12.66	13.62	
Questionnaire-	treatment	(9.33)	(8.89)	(9.08)	(8.15)	
Blood/injury	Post-	17.38	12.62	8.96	9.30	F(3,132) = 6.50 * * *
(FQ-BI)	treatment	(9.51)	(9.13)	(6.83)	(7.00)	A>B,C,D
	6-month	N/A	9.36	10.47	8.31	
	follow-up		(6.38)	(8.45)	(7.51)	

***p<.001 Note: Only significant planned comparisons are reported.

Variable	Time	W/L	CBT6	CBT6CA	CBT12	$\chi^{2}(7)$
Body	Post-	6.1	38.2	45.7§	51.4§	28.42, p<.001
Sensations	treatment [§]					
Questionnaire	6-month	N/A	32.1	30.0	55.9	
	follow-up					
Agoraphobic	Post-	20.6	50.0	64.78	55.38	20.54, p=.005
Cognitions	treatment§			0	0	, <u>1</u>
Questionnaire	6-month	N/A	60.7	48.3	54.3	
	follow-up					
State-Trait	Post-	5.9	48.5	60.0§	60.5§	43.87, p<.001
Anxiety	treatment [®]				<i></i>	
Inventory-Trait	6-month	N/A	48.1	46.7	60.0	
N (- 1- 11:4	follow-up	2.0	$\mathcal{D}(\mathbf{F})$	EA E 8	(0.5%	20.95 < 001
Inventory	Post- trootmont [§]	2.9	20.3	54.58	60.58	39.83, p<.001
Alone	6-month	N/A	393	44 8	60.0	
<i>i</i> none	follow-up	1 1/2 1	57.5	11.0	00.0	
	· · · I					
Mobility	Post-	2.9	32.4	36.4§	47.4§	25.57, p=.001
Inventory-	treatment [§]					
Accompanied	6-month	N/A	39.3	41.4	48.6	
	follow-up		•••		42 2	10.00
Fear	Post-	14.7	38.2	37.1	43.2	10.28, p=.173
Questionnaire-	treatment [°]	NI/A	20.2	267	17 1	
Agoraphobla	follow-up	1N/A	39.3	30.7	4/.1	
Fear	Post-	88	20.6	28.6	32.4	6.92 n=44
Ouestionnaire-	treatment [§]	0.0	20.0	20.0	52.1	0.9 2 , p
Social Phobia	6-month	N/A	27.9	30.0	47.1	
	follow-up					
Fear	Post-	8.8	44.1	42.9§	45.9§	19.66, p=.006
Questionnaire-	treatment§					
Blood/injury	6-month	N/A	65.5	28.7	38.7	
	follow-up					

Table 2 Percentage meeting conjoint criteria for clinically significant change*

*Conjoint criteria represents the percentage of individuals who reliably improved (reliable change index > 1.96) and whose mean placed them closer to the mean of the functional population than the mean of the dysfunctional population. \$Differ significantly from W/L at p<.05





Figure Captions

Figure 1 Top Panel: Percentage panic-free post-treatment and 6-month follow-up. Bottom Panel: Percentage panic-free at post-treatment using Intention-to-Treat analysis.