

Effects of Exposure in Cognitive Behavior Therapy of Panic Disorder: Duration Matters!

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Keywords

Cognitive behavior treatment · Panic disorder · Exposure · Confrontation · Treatment trial · Group therapy

Summary

Background: A large number of empirical studies demonstrated the efficiency of cognitive behavioral therapy in the treatment of panic disorders. Treatment packages typically include components such as education, corrective information, cognitive restructuring and exposure to fear provoking stimuli. Treatment procedures range from simply providing a self-help manual with minimal therapeutic contact to intensive exposure training. Over the last 2 decades, cognitive therapy became more and more important in the treatment of panic disorders, and today is often regarded as even more important than exposure treatment. Other studies show that even minimal exposure interventions can lead to treatment effects. There is a lack of knowledge concerning if and how much exposure is needed for effective treatment. The aim of the present study is to assess the outcome of a group oriented cognitive behavior therapy (CBT) approach and the effect of increasing the time of exposure exercises. **Methods:** 2 groups of patients with panic disorder (diagnosed by structured interviews) were compared. Both groups took part in an inpatient standardized behavior group therapy program. One group (n = 81) received 1 day of therapist-accompanied exposure, the other group (n = 88) received 2 days. The course of symptomatic variables, level of depression and psychosocial impairment were assessed before and after treatment and 1 year later. **Results:** At the end of treatment both groups showed striking benefits and treatment response was comparable between the groups. However, the prolonged exposure group showed significantly more reduction of symptoms in the follow-up (1 year). **Conclusion:** Exposure is an essential component of CBT. The effects of increasing exposure can primarily be seen in the long term. It is assumed that extending exposure time facilitates generalization of treatment gain.

Schlüsselwörter

Kognitive Verhaltenstherapie · Panikstörung · Exposition · Konfrontation · Therapiestudie · Gruppentherapie

Zusammenfassung

Hintergrund: Eine beeindruckende Vielzahl an Therapiestudien belegt inzwischen die Effektivität kognitiver Verhaltenstherapie in der Behandlung von Panikstörungen. Die Behandlungsprogramme setzen sich meist aus psychoedukativen, kognitiven und behavioralen (Exposition) Therapieelementen zusammen. Der Anteil von Expositionsübungen innerhalb der untersuchten Programme variiert stark. Bisher ist unklar, welchen Nutzen Expositionsphasen in einer effizienten Behandlung bringen und wie zeitintensiv diese sein sollen. In dieser Untersuchung wird der Therapieerfolg eines kognitiv-verhaltenstherapeutischen Gruppenprogramms überprüft, insbesondere, ob eine Erhöhung des Anteils an Expositionsübungen zusätzliche Therapieeffekte bringt. **Methoden:** Verglichen wurden 2 Patientengruppen mit Panikstörungen. Beide Gruppen nahmen an einem stationären Gruppentherapieprogramm zur Angstbehandlung teil, das ein Expositionstraining beinhaltete. Für die 1. Behandlungsgruppe (n = 81) erfolgte ein Expositionstraining von einem Tag therapeutenbegleiteter Exposition, für die 2. Gruppe (n = 88) wurde die Expositionszeit verlängert und es erfolgten 2 Tage Exposition. Der Verlauf symptomspezifischer Variablen (Vermeidungsverhalten, ängstliche Bewertungen), depressiver Symptome und psychosozialer Beeinträchtigung wurde vor der Therapie, zu Therapiebeginn und -ende sowie in einer Katamnese (1 Jahr) erhoben. **Ergebnisse:** In beiden Gruppen zeigten sich signifikante Symptomreduktionen bei Abschluss der Therapie für die störungsspezifischen Selbsteinschätzungsverfahren (Zeiteffekt MANOVA mit Messwiederholung; $p < 0,001$). Beide Behandlungsgruppen sprachen in gleichem Ausmaß auf die Therapie an, in der Gruppe mit der verlängerten Exposition waren die erzielten Erfolge zum Katamnesezeitpunkt (1 Jahr) jedoch größer (signifikante Interaktionen Zeit \times Behandlungsgruppe; $p < 0,001$). **Schlussfolgerung:** Die Ergebnisse unterstützen die bisherige Praxis der Kombination kognitiver und verhaltenstherapeutischer Interventionsstrategien, wobei sie die Wirksamkeit der verhaltensorientierten Therapieelemente unterstreichen. Sie sprechen dafür, dass sich der erhöhte Expositionsaufwand lohnt und sich der Therapieerfolg bei Panikstörung durch eine Verlängerung der Expositionszeit verbessern lässt.

Introduction

The evidence of cognitive behavioral therapy's effectiveness for the treatment of panic disorder (with or without agoraphobia) has become quite impressive. The efficacy of the therapeutic approach has been confirmed both in the short term and also to some extent in multi-year follow-up studies [Bakker et al., 1998], and has been very well demonstrated in randomized controlled trials [Barlow et al., 2000; Hofmann and Smits, 2008]. In meta-analyses, cognitive behavioral programs achieved higher effect sizes than other psychotherapeutic treatments and pharmacotherapy [Borkovec et al., 1995; Gould et al., 1995; Ruhmland and Margraf, 2001; Mitte, 2005; Norton and Price, 2007; Stewart and Chambless, 2009].

There is still a lack of clarity, however, about which features are optimal and the efficacy of individual treatment components [Lang et al., 2009]. Most treatment programs for panic disorder combine behavioral and cognitive therapeutic strategies and are composed of psychoeducation, exposure to anxiety-provoking stimuli/situations and cognitive therapy elements.

If one compares the composition of the individual programs more precisely, one finds variation in the proportions of various treatment components. In recent years, cognitive therapy elements have definitely been in the foreground, while confrontational exercises increasingly remain in the background. Thus the proportion of confrontational exercises in the first studies of treatment for panic, with 20 h [Foa et al., 1980] or 48 h (sometimes more) [Fiegenbaum, 1988], is still very high, whereas it decreases in later studies, with less therapeutic effort. Exposure succeeds in part here not in the sense of *in vivo* exposure (actually exposing oneself to anxiety-provoking situations), but in smaller behavioral experiments, confrontation with interoceptive stimuli, or instructions for self-management of exposure. Since exclusively cognitive programs also yield good and stable long-term results [Clark et al., 1999], this trend in the composition of the treatment components seems well grounded, especially since in some studies there was no difference in treatment outcomes between purely cognitive therapy and therapy with interoceptive exposure or initially therapist-guided *in vivo* exposure [Bouchard et al., 1996; Arntz, 2002; Öst et al., 2004].

Indications are that exposure is a very important and effective component of the therapy. Thus van den Hout et al. found that *in vivo* exposure, supplementing a cognitive therapy program, adds further treatment effects (especially with respect to avoidance behavior). According to the assumptions of learning theory, a treatment that directly promotes a process of counter-conditioning or extinction (exposure) leads to larger and more stable treatment outcomes [Bouton et al., 2001]. In the above-mentioned meta-analysis [Ruhmland and Margraf, 2001], which included various psychological therapies for panic disorder, the largest mean pre-post effect sizes for the main symptoms were obtained by confrontation *in vivo* (effect size

1.64 in short-term treatment effect), followed by cognitive behavioral therapy (effect size 1.19). Also from the results of the meta-analysis by Norton and Price [2007] and the review article by Lang et al. [2009], which evaluated the individual components of previously studied treatment programs for panic disorders (psychoeducation, cognitive techniques, exposure, relaxation/breathing exercises), the authors came to the conclusion that the combination of cognitive elements and exposure *in vivo* was superior to the rationales of most studies that were limited to the individual components.

It is unclear to what extent differential treatment effects of the individual components are to be expected, since also the different symptoms (anxiety about physical discomfort, avoidance, catastrophizing thoughts) influence one another, and the change of cognitive processes itself is associated with symptom changes [Hedley et al. 2001; Hoffart et al., 2008]. It remains an open question whether the greater therapeutic effort required by an exercise-oriented exposure treatment is justifiable, and what additional time is required for an effective anxiety treatment.

In addition, a point of criticism of the previous studies is that the results are not transferable to clinical practice. Most of the studies were conducted in research centers with a selected clientele, such that comorbid disorders, very severe conditions, and concomitant medication were mostly excluded or characterized a non-representative proportion of subjects. Epidemiological studies have shown that comorbidity with other mental disorders is very common in panic disorder [Yates, 2009]. With a diagnosis of panic disorder, there is an 83.1% risk (lifetime prevalence) that an additional comorbid mental disorder will be diagnosed according to DSM-IV [Kessler et al., 2006]. Thus many of the study results are applicable only to a minority of patients who are in normal practice, particularly since there is evidence of a different response to therapy by those who are taking medication at the same time or have comorbid depression [Barlow et al., 2000]. Looking at results of studies with other inclusion criteria, Rief et al. [2000] found that panic patients with comorbid depression also definitely benefit from the therapy, but have higher symptom scores than patients without comorbid depression. A greater likelihood of remission was shown in a treatment study with exposure for patients who had no comorbid depression and who took no psychotropic drugs during the treatment [Fava et al., 2001]. However Allen et al. [2010], in an analysis of data from a multi-center study, found no difference in response to a cognitive behavioral therapy treatment program as a function of comorbidity.

Based on these considerations, two questions are examined in the present study:

1. Are cognitive behavioral procedures also effective for panic disorder when used in routine care in an unselected sample?
2. Does increasing the exposure time improve treatment outcome?

Tab. 1. General characteristics of research groups

	1-day exposure (n = 81)		2-day exposure (n = 88)	
	Mean	SD	Mean	SD
Age, years	40.52	9.75	41.34	9.54
Duration of illness, years	8.56	7.55	9.49	8.06
Disability in the past year, weeks	20.74	26.79	13.99	24.47
Number of prior inpatient treatments	1.11	1.32	0.67	0.96
Number of prior outpatient treatments	0.99	1.43	1.29	1.22
Waiting time for hospital stay, weeks	32.48 *	15.64	39.05 *	23.69
Duration of inpatient treatment, weeks	9.50 **	3.51	8.00 **	2.06
Number of additional diagnoses	1.74	1.46	1.39	1.15
	n	%	n	%
Women	58	71.6	59	67
Married	49	60.5	53	60.2
Prior inpatient treatments	42	51.9	49	55.7
Prior outpatient treatments (> 5 sessions)	58	71.6	76	86.4
Agoraphobia	76	93.8	82	93.2
Major depression (at beginning of treatment)	36	44.4	37	42.0
Major depression (lifetime)	56	69.1	59	67.0
Medication taken during treatment	19	23.5	23	26.5

All continuous variables were tested by ANOVA, all dichotomous variables with a chi² test or t-test for differences between the groups.
*t = 3.41; df = 167; p < 0.01; **t = 3.41; df = 167; p < 0.001.

Methodology

Study Design

This is a natural longitudinal long-term study of patients who were consecutively admitted to the Roseneck medical-psychosomatic hospital. The patients received, as part of their hospital regime, a standardized treatment program for anxiety management. 2 patient groups in the group therapy program for anxiety management were compared; they had exposure training of different durations (1 day = ca. 8 h of treatment vs. 2 days = ca. 16 h of treatment). The distribution of participants in the group was consecutive: In the first survey period, patients received 1 day of exposure training; later the program was reorganized and patients who were accepted at a later stage received the same anxiety management program with 2 days of training. The first measurement was made at registration for the hospital (baseline); the second during the first week of hospitalization (beginning), the third in the last week of hospitalization (end), and the follow-up study ca. 1 year after discharge (FU). The waiting time for hospital admission (baseline – beginning) was an average of 35.9 weeks (SD = 20.44; range = 0–99); the duration of treatment (beginning – end) was 8.72 weeks (SD = 2.93; range = 3.71–21); and the follow-up period (end – FU) extended to 74.87 weeks (SD = 21.70; range = 42–148). The follow-up period is somewhat longer for the first group (1 day of exposure, an average of 16 weeks), since in each survey wave an attempt was made to contact patients who had not previously been reached. Thus, the response in the first group studied is a little higher.

Patients

The study included 169 patients, chosen on the basis of a written report filed in the registration process that described evidence of a panic disorder. The International Diagnostic Checklist (IDCL) [Hiller et al., 1995] was used with these patients at the time of admission (the beginning) to verify the diagnosis of panic disorder according to DSM-IV. Table 1 shows selected sample characteristics of the subjects. The two samples did not differ significantly with regard to age, gender, or duration of illness, which was an average of ca. 9 years. Slightly less than half of the total

group had previously received inpatient treatment for the main symptoms (46.1%) and ca. three quarters (73.3%) had had outpatient psychotherapy (outpatient treatment was only counted if there were more than 5 sessions). Additional data indicate that this was a sample characterized by high chronicity and unsuccessful prior treatment (e.g., high degree of work disability in the year prior to admission) and that for many patients, in addition to the index disorder (panic disorder), additional mental disorders were diagnosed (93% with agoraphobia, 44% with current major depression, and 25% with a lifetime diagnosis of major depression, but with no evident acute depression at the start of therapy). There were slight qualitative differences in the pattern of comorbidity. The average number of additional diagnoses did not differ significantly (overall average 1.56). A significant group difference was found for the duration of treatment (t = 3.41; df = 167; p < 0.01). The group with the prolonged exposure had a significantly shorter duration of treatment (8 vs. 9.5 weeks), which was caused by the rising cost pressure of the sequential study design. These data for the respective samples are shown in table 1. Thus, the patient group was characterized by chronicity and some patients had been treated several times without success, as is often found in routine hospital care in Germany, particular when combined with long work disability.

Measurement Methods Used

At the beginning of treatment, a detailed diagnostic workup was performed using the IDCL. At the follow-up point (1 year after treatment), patients were surveyed by telephone, using an expanded form of the IDCL to check to what extent panic attacks were still occurring and whether the diagnosis of panic disorder could still be made. In addition, a follow-up questionnaire was filled out, for assessment of the therapy and to provide other data about the follow-up period. At all 4 measurement points, the following self-assessment procedures were used:

The questionnaire on body-related anxieties, cognitions, and avoidance (AKV) [Ehlers and Margraf, 1993], which is the German-language edition of 3 English-language inventories from Dianne Chambless's working group on the symptom clusters of panic disorder. It comprises the following questionnaires:

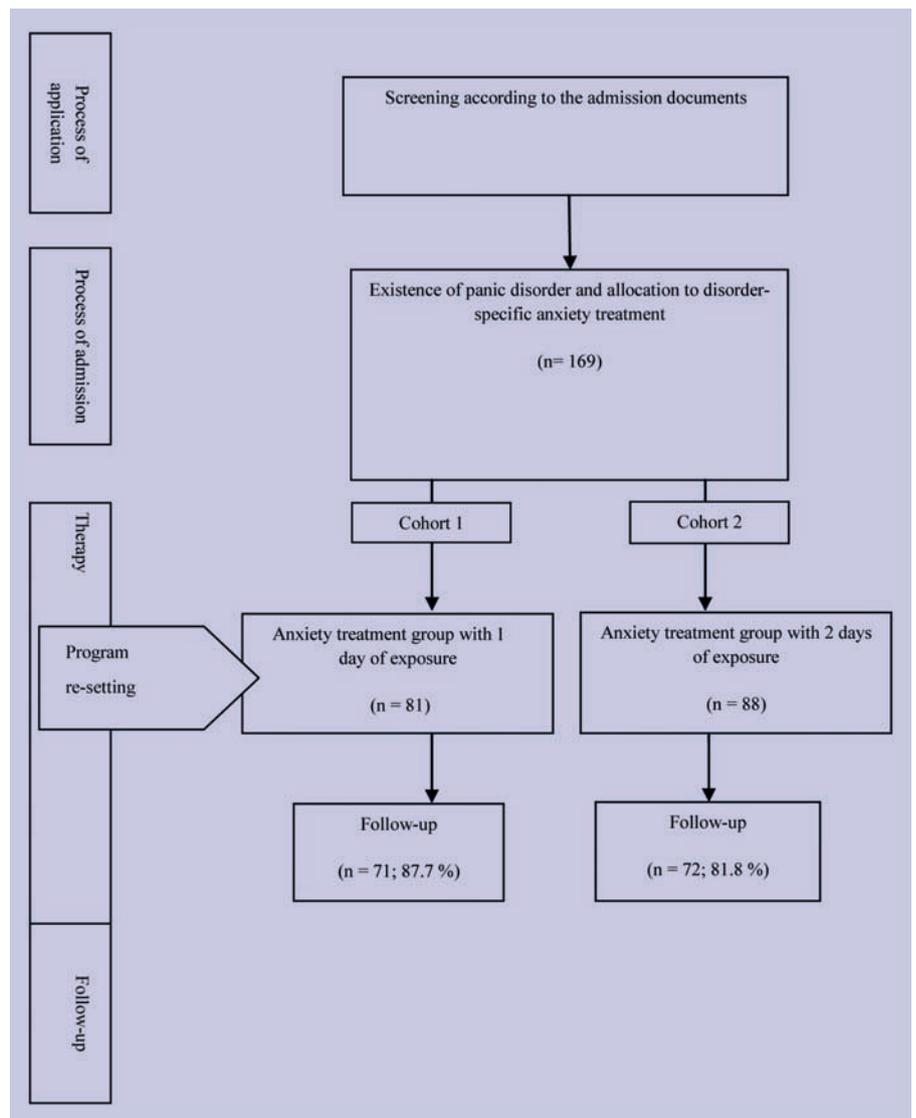


Fig. 1. Flow chart for patients included in the study.

- The Body Sensations Questionnaire (BSQ) [Chambless et al., 1984]. It uses 17 items to assess anxiety about bodily sensations such as dizziness, heart palpitations, or tingling. This anxiety can be assessed from 1 ('not worried or anxious about this feeling') to 5 ('extremely anxious about this feeling').
 - The Agoraphobic Cognitions Questionnaire (ACQ) [Chambless et al., 1984], which uses 14 items to assess the frequency of typical anxiety-related cognitions, such as 'fear of having a heart attack' or 'fear of going crazy'. The response categories range from 1 ('the thought never occurs to me') to 5 ('I think about it constantly').
 - The Mobility Inventory (MI) [Chambless et al., 1985] contains 27 typical agoraphobic situations (e.g., standing in line, being far from home, traveling by train) or places (cinemas, elevators), which the patient has to rate in terms of avoidance (0 = 'never avoid' to 5 = 'always avoid'). The extent of avoidance can be specified in two contexts: when they are exposed to the situation alone (MI-A) and when they are exposed to the situations accompanied by someone else (MI-B).
- Patients also estimated the extent of their impairment caused by the symptoms on a 3-item scale (BE) in the areas of work/education, leisure/social life and family/domestic duties [cf. Margraf and Schneider, 1990]. The estimates from 0 ('not at all impaired') to 4 ('very serious impairment') may vary and an average is determined for the evaluation.

To assess depression, we used the general depression scale (ADS,

the German version of the CES-D) [Hautzinger and Bailer, 1993]. The presence of current depressive symptoms during the prior 7 days was recorded (from 0 = 'not at all/rarely' to 3 = 'most of the time/all the time').

Inclusion and Drop-Out

The inclusion criteria were the presence of panic disorder as well as participation in anxiety management therapy. Thus all of the 169 patients enrolled in the studies had gone through the treatment program. Figure 1 is a flow chart of the patients enrolled. The follow-up interview could be given to 84.6% of patients, which can be considered high for studies under routine clinical conditions.

Treatment Program

The treatment program was designed for a total duration of 5–8 weeks. The focus of inpatient treatment for the research sample was a manualized anxiety management program. It combined 8 double group therapy sessions and in vivo exposure. The group sessions were held twice a week, and contained classic elements of cognitive behavioral therapy: psychoeducation ('components of anxiety', the vicious circle model, a hyperventilation exercise as an illustrative behavioral experiment), working through the role of avoidance and safety behaviors and the therapeutic rationale for exposure. After the 5th group session, exposure exercises were per-

Tab. 2. Mean values and standard deviation of symptom-specific variables

Variable	Point in time	1-day exposure		2-day exposure		Differences (group comparisons)		
		Mean	SD	Mean	SD	df	F	p
Impairment (BE)	baseline	2.89	0.65	2.68	0.82	1.164	3.41	0.067
	beginning	2.55	0.88	2.53	0.79	1.151	0.03	0.862
	end	1.86	0.95	1.69	1.05	1.137	0.94	0.333
	1 year (FU)	1.97	1.12	1.45	1.03	1.137	7.94	0.006
	effect size ^a	1.04		1.33				
Avoidance when alone (MI-A)	baseline	3.36	1.03	3.33	0.95	1.144	0.04	0.836
	beginning	3.18	1.13	3.19	1.05	1.135	0.00	0.948
	end	2.17	0.91	2.03	0.82	1.134	0.98	0.324
	1 year (FU)	2.35	1.09	2.04	0.94	1.125	2.97	0.087
	effect size ^a	0.95		1.37				
Avoidance when accompanied (MI-B)	baseline	2.77	0.98	2.62	0.94	1.138	0.86	0.356
	beginning	2.55	1.03	2.50	0.95	1.128	0.08	0.778
	end (FU)	1.71	0.68	1.64	0.73	1.130	0.28	0.596
	1 year	1.94	0.97	1.62	0.81	1.125	4.15	0.044
	effect size ^a	0.85		1.14				
Agoraphob. cognitions (ACQ)	baseline	2.33	0.58	2.31	0.64	1.152	0.04	0.840
	beginning	2.28	0.73	2.32	0.69	1.146	0.10	0.754
	end (FU)	1.99	0.73	1.86	0.75	1.145	0.96	0.328
	1 year	2.07	0.82	1.84	0.72	1.137	3.18	0.077
	effect size ^a	0.37		0.67				
Anxiety about physical symptoms (BSQ)	baseline	3.01	0.67	2.91	0.62	1.156	1.02	0.315
	beginning	3.02	0.75	2.94	0.69	1.141	0.53	0.468
	end (FU)	2.45	0.83	2.30	0.89	1.140	0.97	0.326
	1 year	2.60	0.89	2.26	0.78	1.136	5.85	0.017
	effect size ^a	0.53		0.93				
Depression (ADS)	baseline	32.35	11.30	30.80	11.05	1.163	0.76	0.383
	beginning	28.53	11.12	28.83	11.76	1.151	0.03	0.873
	end (FU)	19.96	11.86	18.22	12.89	1.146	0.72	0.396
	1 year	26.31	14.04	21.59	14.10	1.141	4.03	0.047
	effect size ^a	0.48		0.73				
Panic attacks (prior week)	1 year	1.79	5.56	1.43	4.11			

^a $(M_{\text{Baseline}} - M_{\text{Follow-up}}) / SD_{\text{pooled}}$.

formed under guidance/supervision for either 1 day (about 8 h of treatment) or 2 days (approximately 16 h of treatment). After explaining the rationale of the therapy, patients were instructed to practice independently as much as possible, to tolerate the anxieties, not to quit and not to perform any safety behaviors. On the practice days, the patients were accompanied by therapists (usually one) in anxiety-provoking situations, received instructions for anxiety management (with a review of the rationale of the group), and were supposed to master such situations themselves during the progression of the exercises. All exercises (accompanied/alone) were extensively discussed both before and afterwards. If, as in most cases, the first exposure was accompanied by the therapist, it was directly followed by an exposure exercise in which the patient practiced alone. Among the situations presented on practice days were a train ride to a neighboring big city, going shopping, climbing up into church steeples, subway rides, a ride in a chairlift, or a trip to the movies. The anxiety-provoking situations were selected according to the individual's particular constellation of problems. On the day with additional exposure, the group that was having only 1 day of exposure participated in their regular therapy program at the hospital. The exposure treatments were conducted only by 1–2 experienced psychologists and 1–2 co-therapists

(nurses). The psychotherapists had either completed a course in behavioral therapy training or were advanced in their course. All the therapists received additional specialized education in preparation for the program and had guided exposure therapy at least twice before as co-therapists. After the exposure phase, the group program held a retrospective analysis of the exercises, including motivating the patients to keep practicing, and with additional interventions to check any dysfunctional thoughts. The overall concept of anxiety management therapy is based upon existing, mostly outpatient, therapy programs [Margraf and Schneider, 1990; Telch et al., 1993], and has been adapted by Rief [1993] for the inpatient setting in a group therapy approach.

In another treatment program as part of their hospitalization, patients were given individual therapy sessions once or twice a week and participated 2 to 3 times a week in a general problem-solving group (a double session). Complementary therapy modules were selected depending on the individual circumstances, including assertiveness training, progressive muscle relaxation, ancillary somatic medicine treatment, or sports therapy. There was no complete standardization of treatment because this is a study in routine care, although the treatment groups did not differ systematically in accessory elements of therapy.

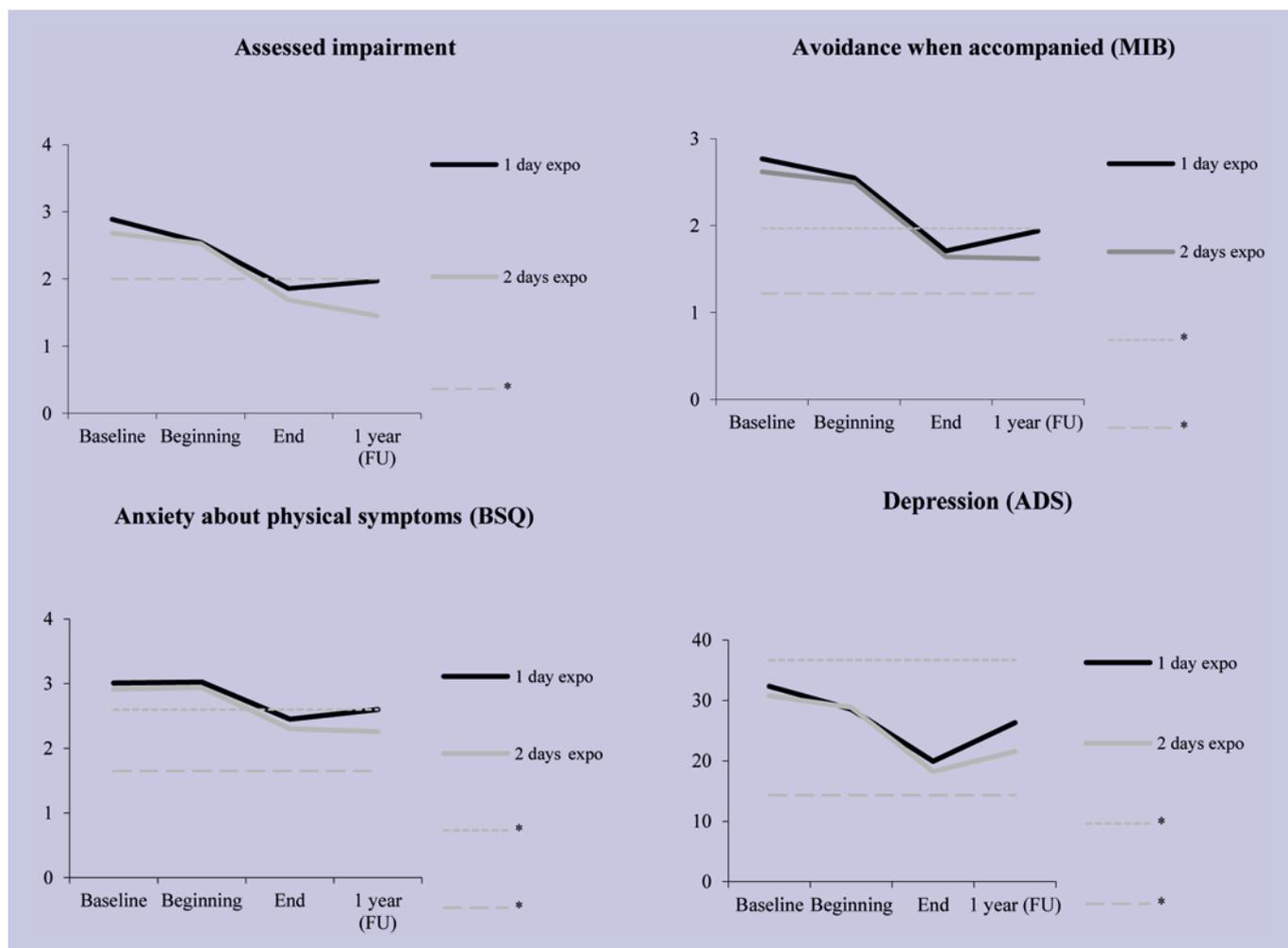


Fig. 2. Progression of some disorder-specific variables (mean values) of treatment groups in 1 day versus 2 days of exposure. *The dotted lines give the orientation to comparison values and norm samples. The mean scale value is drawn for the assessed impairment. For avoidance when accompanied, anxiety about physical symptoms, and depression, the top lines represent the mean value of the clinical comparison group and the bottom lines the healthy control group from the test manuals.

Statistical Analyses

A multivariate analysis of variance (MANOVA) with repeated measures (4 measurement points) was first performed for analysis of the quantitative variables. The dependent variables were related self-assessment procedures (MI, ACQ, BSQ, CES, BE). Subsequently univariate analyses of variance were added to the individual measurement points. To avoid the risk of an increased alpha error, the univariate testing was performed only if there were significant results in the multivariate analysis.

To evaluate the treatment effects, effect sizes were also calculated as Cohen's *d* [Cohen, 1988], where the changes between the registration point and the 1-year follow-up were put in relation to the mean distribution ($M_{\text{baseline}} - M_{\text{follow-up}} / SD_{\text{pooled}}$).

A significance test (t-test) or a χ^2 test was used to check whether the 2 treatment groups differed with respect to the occurrence of panic attacks at follow-up and the presence of a panic disorder.

A measure of clinically significant improvement was also defined, which allows a comprehensive assessment of symptoms of the condition at follow-up. The variable 'impairment from the illness' was chosen as the superordinate measure. A finding was rated as clinically significant if there was improvement between baseline and follow-up of at least one standard deviation or a value of 2 at the most (on the average, no more

than moderate impairment from the illness according to item coding). Both surveys were done at times when the patients were in their home environments, so that there would be no distortions as a result of the hospital environment.

Intent-to-treat analysis: Despite the high response rate at the 1-year follow-up, an 'intent-to-treat' analysis was also performed as a conservative test. Repeated measure analyses of variance were done once again for the self-assessment procedure, and a χ^2 test was calculated for the presence of panic disorder and responder rates, so that for all subjects who had no follow-up value, the follow-up value was equated with the baseline value.

Results

With the repeated measure MANOVA, which included all symptom-specific self-assessment procedures, there was a consistently significant time effect ($F = 64.71$; $df = 1.63$; $p < 0.001$) as well as significant values for interaction time \times treat-

Tab. 3. Diagnosed panic disorder and response rate^c 1 year after therapy

	Total		1-day exposure		2-day exposure	
	n = 142	%	n = 63	%	n = 79	%
Proportion without panic disorder	76	55.3	29	46.0	47	59.4
No depression at the beginning	48	63.2	15	51.7	33	70.2
	n = 139	%	n = 67	%	n = 72	%
Proportion of responders ^a	93	66.9	38	56.7	55	76.4
No depression at the beginning ^b	60	64.5	21	55.3	39	70.9

^aSignificant differences: overall response rate: $\chi^2(1, n = 139): 6.07; p < 0.05$.
^bResponders without depression: $\chi^2(df = 1, n = 139): 10.24; p < 0.05$.
^cChange in evaluation of the disorder because of impairment (BE) > one standard deviation or < 2.

ment group ($F = 4.73; df = 1.63; p < 0.05$) and symptoms \times time ($F = 32.74; df = 1.63; p < 0.001$). The group effect was not significant ($F = 1.66; df = 1.63$).

In the univariate test of group differences regarding disorder-specific measurements at the individual measurement points, there were no statistically significant differences between the groups at the registration, admission, and discharge points. At the follow-up (1 year after treatment), there were statistically significant group differences in the following variables: assessment of impairment caused by the symptoms (BE), avoidance behavior (MI-B), anxiety about physical symptoms (BSQ), and depression (ADS). The mean symptom assessments of the group with prolonged exposure (2 days) were consistently lower. Descriptive and inferential statistical values for the self-assessment procedure for individual measurement points are shown in table 2, and figure 2 is a graphic illustration of the symptoms over time for the 4 variables with significant differences at follow-up (impairment, avoidance behavior when accompanied, anxiety about physical symptoms, and depression).

Effect Sizes

To facilitate comparison of treatment effects in the treatment group, effect sizes were calculated for the disorder-specific self-assessment measures (BE, MI-A, MI-B, ACQ, BSQ, ADS), whereby the change between baseline and follow-up was put in relation to the mean distribution. Table 2 shows that the group with 2 days of exposure (with d between 0.57 and 1.12) consistently achieved higher effect sizes (with d in the group with 1 day of exposure lying between 0.17 and 0.65).

Number of Panic Attacks and Diagnoses of Panic Disorder at Follow-Up

In the follow-up telephone interview, patients were asked to what extent they had had panic attacks during the previous week. On average, the group with 1 day of exposure exercises had 1.79 attacks ($SD = 5.56$), and those who had 2 days of exposure had 1.43 attacks ($SD = 4.11$). The t -test showed no statistically significant difference. The proportion of those for whom panic disorder was no longer diagnosed at follow-up

(using the IDCL) was 53.5% in the whole group and was higher, 59.4%, in the group with 2 days of exposure (compared to 46.0% in the group with 1 day of exposure) (table 3), but the difference was not statistically significant ($\chi^2 = 2.55; df = 1; n = 142$). Looking at the groups separately for the presence or absence of depression at the start of therapy, we find 70.2% without panic disorder at follow-up in the group without depression after prolonged exposure (51.7% in the group with 1 day of exposure).

Clinically Significant Improvement

The total sample had a response rate of 66.9% (55.0% with the valuation of drop-outs as non-responders). Comparing both treatment groups, there occurred responder rates of 76.4% (53.9% with the evaluation of drop-outs as non-responders) in the group with 2 days of exposure and 56.7% (39.2%) in the group with 1 day of exposure. The differences between the groups are statistically significant ($\chi^2 = 6.0; df = 1; p < 0.05$). If the responders are divided again into those with or without diagnosed depression at the start of therapy, the proportion of responders without depression at the start of therapy is 70.9% in the group with prolonged exposure and 55.3% in the group with 1 day of exposure.

Questions at Follow-Up

In the follow-up survey, the groups did not differ in their disability over the previous 12 months (in the group with 1 day of exposure, the average was 6.82 weeks, $SD = 13.38$; in the group with 2 days of exposure, 5.08 weeks, $SD = 11.93$; t -test: $t = 0.70; df = 104$). Patients were asked how often they visited certain doctors (family doctor, neurologist, psychiatrist, psychotherapist, other specialist doctors, counseling centers, support groups). In the group with 1 day of exposure, doctor visits were consistently more frequent; e.g., patients reported an average of 11.78 visits ($SD = 14.97$) to the psychotherapist within the prior 12 months in the group with 1 day of exposure, and 7.36 visits ($SD = 13.53$) in the group with 2 days of exposure. The proportion of patients who had additional outpatient psychotherapy as of the follow-up point (number of visits to the psychotherapist > 5, thus more than the proba-

tional number of sessions = preliminary therapy sessions allowed by statutory insurance regulations in German clinical practice) amounted to 32.8% for the group with 1 day of exposure ($n = 22$) and 9.0% for the group with 2 days ($n = 6$) ($\chi^2 = 11.56$; $df = 1$; $p < 0.001$). On the question of whether, in retrospect, the individual treatment components were seen as helpful, 72.2% of the patients said that the anxiety management therapy was indeed helpful (there was a similarly good rating only for individual psychotherapy, 74.2%; the helpfulness of the other therapeutic components was evaluated at between 16.0% and 56.8%). 81.1% of patients also indicated that they are continuing to use the strategies they had learned in the anxiety therapy for coping with the illness (the proportion of those who are in individual psychotherapy is 70.5%, and in other therapies 28.8%).

Intent-to-Treat Analysis

The results of the intent-to-treat analysis confirm most of the previously described results: the MANOVA with repeated measures for the disorder-specific self-assessment procedures showed a consistently significant time effect ($F = 63.27$; $df = 1.81$; $p < 0.001$) and a significant effect for interaction time \times symptoms ($F = 32.74$; $df = 1.63$; $p < 0.001$). The interaction of treatment group \times time ($F = 4.73$; $df = 1.81$) and the group effect ($F = 0.14$; $df = 1.63$) did not achieve statistical significance. In the univariate testing of group differences in disorder-specific measures, the differences in BE ($F = 8.13$; $df = 1.158$; $p < 0.05$), MI-B ($F = 3.69$; $df = 1.146$; $p < 0.05$), and BSQ ($F = 4.50$; $df = 1.156$; $p < 0.05$) remained significant at the follow-up (1 year after treatment). The symptom assessments in the group with the prolonged exposure (2 days) were consistently below those of the group with the shorter exposure time (1 day).

Discussion

We investigated the question of whether cognitive behavioral therapy for panic disorder is effective in routine care with an unselected sample and whether increased exposure improves the treatment outcome. Our results lead us to the following conclusions:

Cognitive behavioral therapy methods result in a moderate to high reduction of disorder-specific measurements in the treatment groups studied. The treatment outcome was definitely stronger and more stable in the group with prolonged exposure. The tested sample overall showed high chronicity, multiple comorbidities, and a considerable degree of impairment, but responded well to treatment (response rate of 66.9%, 1 year after treatment). The effect sizes were lower than those of other studies [Ruhmland and Margraf, 2001; Stewart and Chambless, 2009], which was to be expected in an unselected, highly impaired sample. Peikert et al. [2004] found a rate of 40.3% panic-free patients at the end of treatment, in

another inpatient treatment group. They found effect sizes for reduction of the main symptoms over time (within the self-assessment process of the AKV) from 1.16 to 1.86. In comparison, the efficacy of therapy in our study (53.5% of patients were no longer diagnosed with panic disorder at follow-up and effect sizes were 0.57–1.22) can be considered positive, especially since in Peikert et al. there were no follow-up data.

But the results of increasing the exposure time are even more striking. Both groups had benefited equally from the treatment at the end of therapy. This is at first a sobering result, given the doubling of the duration of confrontational therapy. But in the long term, there were definitely more stable therapeutic results from prolonged exposure: The effect sizes were consistently higher and the measures of the severity of the disorder and the extent of impairment were found to yield consistently lower values in the group with longer exposure, with partly statistically significant differences at follow-up.

Evidence for further stabilization and improvement in the treatment outcome at follow-up was also shown in a long-term study of cognitive behavioral group treatment by Martinsen et al. [1998]. Since cognitive behavioral treatment methods tend to be aimed at long-term changes, effects may be delayed, so differences in treatment results are clearly also possible at a later date. Since anxiety management therapy is regarded retrospectively by both groups at the follow-up as particularly helpful, and the patients say that they are still using the elements of this therapy to overcome their problem, this effect is likely due to the intensive exposure treatment. Additional data from treatment or follow-up give no indication that this difference was caused by later treatments that occurred, especially since the amount of additional therapeutic treatment received by the group with 1 day of exposure was greater than that received by the 2-day group, and it cannot be assumed that additional treatment reduces the treatment effect. The treatment effect in the 2-day group, because of its lower proportion in the treatment during the follow-up period, is therefore hardly being overestimated. According to a study by Brown and Barlow [1995] of the symptom progression of panic patients after 2 years of cognitive behavioral therapy, additional treatment likewise provided no additional treatment effects. However, the authors also discuss how this might be related to the fact that chronic patients and non-responders are seeking further treatment. There is no indication that such patients were unsystematically allocated to the evaluated groups, because their initial values were quite similar.

The existence of acute depression at the beginning of treatment adversely affects the outcome of therapy in the sample studied. There is a greater proportion of responders without depression. This is consistent with results of Fava et al. [2001]. Surprisingly, among those with comorbid depression at the beginning of treatment, there is also no advantage to the 2-day exposure, but rather a significant contrary trend. Under certain circumstances, the frequently shorter treatment time

for the cohort of those with a 2-day exposure has a more negative effect on those with comorbid depression than on those without comorbid depression, or perhaps the more prolonged intensive exposure phase was more difficult for them because of impairments related to depression. Because of the naturalistic design, however, there is no point in speculating further here.

Learning theory offers a good explanation of the more stable treatment outcome in the group with more exposure: The processes of extinction are heavily dependent on context [Rescorla, 1986]. Applied to the use of exposure for treatment of anxiety, this means that anxiety management training often leads to better extinction of anxiety and transfer of what has been learned to the various conditions of everyday life [Bouton, 1988]. In the present study, the patients in the 2-day group exposed themselves to additional anxiety-provoking situations. This may have contributed to an extension of the contextual conditions for stabilization of therapeutic outcome. Otto and Deveney [2005] also derive from previous research findings that good cognitive behavioral therapy should routinely ensure that anxiety reduction takes place in multiple contexts.

Overall, the results obtained are consistent with a study by van den Hout et al. [1994], in which the frequency of panic attacks was reduced by cognitive therapy and exposure had greater influence on agoraphobic avoidance behavior. In other comparative studies, there was no additional treatment effect from exposure [e.g., Hoffart, 1995; Bouchard et al., 1996]. This contradiction to the findings of the study presented here could be partly explained if we take a closer look: Exposure conditions that involve confrontation with bodily signals (hyperventilation and other interoceptive exercises) are used more in cognitive behavioral experiments intended to clarify cognitive explanatory models. In our view, this type of exposure is better classified as a cognitive intervention strategy and therefore provides no additional effects. The findings of the meta-analysis by Ruhmland and Margraf [2001], however, are consistent with our results: The largest effect sizes of the follow-up studies were achieved after in vivo confrontation (main symptom = 1.76; overall impairment = 0.90).

The validity of the present study is limited by the fact that the effects of concomitant medication were not controlled, the interviewers at follow-up were not blinded, the response rate in the group with 1 day of exposure was slightly higher, and there was no randomized assignment to the treatment groups. The sequential group comparison study, which was chosen for its ease of implementation, may have had confounding effects. The experience of the therapist or improvements in the manual can be excluded as factors, however, because the therapists for the anxiety management group were changed in each phase of the study and the manual remained the same. Al-

though obviously high-quality and even randomized designs are possible in routine care, in an inpatient setting it is difficult to change treatment conditions and there are numerous transfer effects among patients with different treatment conditions, which would have made such a study much more difficult.

A small defect in the present study is the fact that the group with more exposure also actually received more therapy in the anxiety management program. On the other hand, their total duration of treatment in the inpatient setting was shorter, despite more exposure therapy. The biggest limitation in the validity of this study arises from the naturalistic setting, in which not all influential factors can be controlled or recorded. Duration of therapy, therapeutic program, treatment after hospitalization, concomitant treatment with medication, waiting time, and follow-up period can all vary greatly. Aside from the follow-up period, however, it is not likely that they do so systematically in favor of one of the experimental conditions, although this naturally restricts the validity of the results.

Overall, the results support the previous practice of combining cognitive and behavioral therapeutic intervention strategies, underscoring the effectiveness of the behavioral therapy elements. The results suggest that the increased exposure time with guidance from a therapist is definitely worthwhile and has positive effects on the stability of therapeutic outcome. Thus it is recommendable to schedule a certain number of in vivo exposure exercises. It remains an open question what the optimal duration should be. To what extent a further condensation of the treatment period, by raising the proportion of time spent with exposure, could lead to further optimization, and to what extent comorbid depression requires a different approach, cannot be decided based on the available data, and the answer to these questions is left for future studies. But it is to be assumed that treatment outcome will not rise indefinitely by raising the proportion of confrontational exercises. Other specific questions about the mechanisms of exposure treatment, especially the need for therapist guidance and training in the exercises, are addressed in a large randomized study, whose results are expected soon [Arolt et al., 2009; Gloster et al., 2009; initial results: Gloster et al., 2011].

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Disclosure Statement

The authors declare that they have no conflicts of interest regarding this work.

References

- Allen L, White K, Barlow D, Shear M, Gorman J, Woods S: Cognitive-behavior therapy (cbt) for panic disorder: Relationship of anxiety and depression comorbidity with treatment outcome. *J Psychopathol Behav Assess* 2010;32:185–192.
- Arntz A: Cognitive therapy versus interoceptive exposure as treatment of panic disorder without agoraphobia. *Behav Res Ther* 2002;40:325–341.
- Arolt V, Zwanziger P, Ströhle A, Hamm A, Gerlach A, Kircher T, Deckert J: The research network PANIC-NET: improving the treatment of panic disorder – from a better understanding of fear circuit mechanisms to more effective psychological treatment and routine care. *Psychother Psychosom Med Psychol* 2009;59:124–131.
- Bakker A, van Balkom A, Spinhoven P, Blaauw B, Dyck R: Follow-up on the treatment of panic disorder with or without agoraphobia: A quantitative review. *J Nerv Ment Dis* 1998;186:414–419.
- Barlow DH, Gorman JM, Shear MK, Woods SW: Cognitive-behavioral therapy, imipramine, or their combination for panic disorder: A randomized controlled trial. *JAMA* 2000;283:2529–2536.
- Borkovec TD, Abel JL, Newman H: Effects of psychotherapy on comorbid conditions in generalized anxiety disorder. *J Consult Clin Psychol* 1995;63:479–483.
- Bouchard S, Gauthier J, Laberge B, French D, Pelletier M-H, Godbout C: Exposure versus cognitive restructuring in the treatment of panic disorder with agoraphobia. *Behav Res Ther* 1996;34:213–224.
- Bouton ME: Context and ambiguity in the extinction of emotional learning: Implications for exposure therapy. *Behav Res Ther* 1988;26:137–149.
- Bouton ME, Mineka S, Barlow DH: A modern learning theory perspective on the etiology of panic disorder. *Psychol Rev* 2001;108:4–32.
- Brown TA, Barlow DH: Long-term outcome in cognitive-behavioral treatment of panic disorder: Clinical predictors and alternative strategies for assessment. *J Consult Clin Psychol* 1995;63:754–765.
- Chambless DL, Caputo GC, Bright P, Gallagher R: Assessment of fear of fear in agoraphobics: The body sensation questionnaire and the agoraphobic cognition questionnaire. *J Consult Clin Psychol* 1984;52:1090–1097.
- Chambless DL, Caputo GC, Jasin SE, Gracely EJ, Williams C: The mobility inventory for agoraphobia. *Behav Res Ther* 1985;23:35–44.
- Clark DM, Salkovskis PM, Hackmann A, Weels A, Ludgate J, Gelder M: Brief cognitive therapy for panic disorder: A randomized controlled trial. *J Consult Clin Psychol* 1999;67:583–589.
- Cohen J: *Statistical Power Analysis for the Behavioral Sciences*. Hillsdale, NJ, Lawrence Erlbaum Associates, 1988.
- Ehlers A, Margraf J: Fragebogen zu körperbezogenen Ängsten, Kognitionen und Vermeidung. Weinheim, Beltz, 1993.
- Fava GA, Rafanelli C, Grandi S, Conti S, Ruini C, Mangelli L, Belluardo P: Long-term outcome of panic disorder with agoraphobia treated by exposure. *Psychol Med* 2001;31:891–898.
- Fiegenbaum W: Long-term efficacy of ungraded versus graded massed exposure in agoraphobics; in Hand I, Wittchen HU (eds): *Panic and Phobias II*. Berlin, Springer, 1988.
- Foa EB, Jameson JS, Turner RM, Payne LL: Massed versus spaced exposure sessions in the treatment of agoraphobia. *Behav Res Ther* 1980;18:333–338.
- Gloster A, Wittchen H, Einsle F et al.: Mechanism of action in cbt (mac): Methods of a multi-center randomized controlled trial in 369 patients with panic disorder and agoraphobia. *Eur Arch Psychiatry Clin Neurosci* 2009;259:155–166.
- Gloster AT, Wittchen HU, Einsle F, Lang T, Helbig-Lang S, Fydrich, T, et al.: Psychological treatment for panic disorder with agoraphobia: A randomized controlled trial to examine the role of therapist-guided exposure in situ in CBT. *J Consult Clin Psychol* 2011;79:406–20.
- Gould RA, Otto MW, Pollack MH: A meta-analysis of treatment outcome for panic disorder. *Clin Psychol Rev* 1995;15:819–844.
- Hautzinger M, Bailer M: *Allgemeine Depressions-skala (ADS)*. Deutsche Form der Center for Epidemiological Studies Depression Scale. Weinheim, Beltz, 1993.
- Hedley LM, Hoffart A, Sexton H: The change process in a cognitive-behavioral therapy: Testing a cognitive, a behavioral, and an integrated model of panic disorder with agoraphobia. *Psychother Res* 2001;11:401–413.
- Hiller W, Zaudig M, Mombour W: *IDCL-P. Internationale Diagnosen Checkliste für Persönlichkeitsstörungen nach ICD-10 und DSM-IV*. Bern, Hans Huber, 1995.
- Hoffart A: A comparison of cognitive and guided mastery therapy of agoraphobia. *Behav Res Ther* 1995;33:423–434.
- Hoffart A, Sexton H, Hedley LM, Martinsen EW: Mechanisms of change in cognitive therapy for panic disorder with agoraphobia. *J Behav Ther Exp Psychiatry* 2008;39:262–275.
- Hofmann SG, Smits JAJ: Cognitive-behavioral therapy for adult anxiety disorders: A meta-analysis of randomized placebo-controlled trials. *J Clin Psychiatry* 2008;69:621–632.
- Kessler RC, Chiu WT, Jin R, Ruscio AM, Shear K, Walters EE: The epidemiology of panic attacks, panic disorder, and agoraphobia in the national comorbidity survey replication. *Arch Gen Psychiatry* 2006;63:415–424.
- Lang T, Helbig-Lang S, Petermann F: Was wirkt in der kognitiven Verhaltenstherapie der Panikstörung mit Agoraphobie? *Zeitschrift für Psychiatrie, Psychologie und Psychotherapie* 2009;57:161–175.
- Margraf J, Schneider S: *Panik. Angstanfälle und ihre Behandlung*, 2. überarbeitete Aufl. Berlin, Springer, 1990.
- Martinsen EW, Olsen T, Toenset E, Nyland KE, Aarre TF: Cognitive-behavioral group therapy for panic disorder in the general clinical setting: A naturalistic study with 1-year follow-up. *J Clin Psychiatry* 1998;59:437–442.
- Mitte K: A meta-analysis of efficacy of psycho- and pharmacotherapy in panic disorder with and without agoraphobia. *J Affect Disord* 2005;88:27–45.
- Norton PJ, Price EC: A meta-analytic review of adult cognitive-behavioral treatment outcome across anxiety disorders. *J Nerv Ment Dis* 2007;195:521–531.
- Öst LG, Thulin U, Ramnerö J: Cognitive behavior therapy vs exposure *in vivo* in the treatment of panic disorder with agoraphobia. *Behav Res Ther* 2004;42:1105–1127.
- Otto MW, Deveney C: Cognitive-behavioral therapy and the treatment of panic disorder: Efficacy and strategies. *J Clin Psychiatry* 2005;66:28–32.
- Peikert G, Wagner G, Tauber R, Gruhn U, Sobanski T: Effektivität stationärer Verhaltenstherapie bei schwerer Panikstörung und Agoraphobie. *Verhaltenstherapie* 2004;14:253–263.
- Rescorla RA: Extinction of facilitation. *J Exp Psychol: Anim Behav Process* 1986;12:16–24.
- Rief W: Stationäre Behandlung von Angst- und Panikpatienten: Darstellung eines Therapiekonzeptes; in Baumgärtel F, Wilker F-W (Hrsg): *Klinische Psychologie im Spiegel der Praxis*. Bonn, Deutscher Psychologen Verlag, 1993.
- Rief W, Trenkamp S, Auer C, Fichter MM: Cognitive behavior therapy in panic disorder and comorbid major depression. *Psychother Psychosom* 2000;69:70–78.
- Ruhmland M, Margraf J: Effektivität psychologischer Therapien von Panik und Agoraphobie: Metanalyse auf Störungsebene. *Verhaltenstherapie* 2001;11:41–53.
- Stewart RE, Chambless DL: Cognitive-behavioral therapy for adult anxiety disorder in clinical practice: A meta-analysis of effectiveness studies. *J Consult Clin Psychol* 2009;77:595–606.
- Telch MJ, Lucas JA, Schmidt NB, Hanna HH, Jaimez TL, Lucas RA: Group cognitive-behavioral treatment of panic disorder. *Behav Res Ther* 1993;31:279–287.
- van den Hout M, Arntz A, Hoekstra R: Exposure reduced agoraphobia but not panic, and cognitive therapy reduced panic but not agoraphobia. *Behav Res Ther* 1994;32:447–451.
- Yates WR: Phenomenology and epidemiology of panic disorder. *Ann Clin Psychiatry* 2009;21:95–102.