

# Research Article

## COGNITIVE MEDIATION OF CLINICAL IMPROVEMENT AFTER INTENSIVE EXPOSURE THERAPY OF AGORAPHOBIA AND SOCIAL PHOBIA

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**Background:** *The present study investigated cognitive mediation of clinical improvement in patients with agoraphobia (N = 427) or social phobia (N = 98) receiving high-density exposure therapy in a naturalistic clinical treatment setting.* **Methods:** *Patients were assessed before therapy, 6 weeks after the end of therapy, and 1 year thereafter, using a self-report assessment battery. Lower level mediation analyses provided support for the notion that cognitive changes partially mediate clinical improvement after exposure therapy.* **Results:** *Changes in cognitions relating to physical catastrophes mediated treatment outcome only for patients with agoraphobia, whereas changes in cognitions about loss of control mediated outcome for both agoraphobia and social phobia patients. Changes in relationship satisfaction did not mediate symptomatic improvement.* **Conclusions:** *The results extend previous findings by demonstrating mediation in an unselected clinical sample and by providing evidence for the specificity of mediation effects. They further support the importance of cognitive changes in cognitive-behavior therapy.* *Depression and Anxiety 27:294–301, 2010.* ©

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**Key words:** *cognitive-behavior therapy; cognitive mediation; agoraphobia; social phobia; panic disorder*

The efficacy of cognitive-behavior therapy (CBT) for anxiety disorders has been established in many randomized controlled trials (RCT),<sup>[1–4]</sup> and the available evidence suggests that CBT leads to significant and durable improvements in clinical symptoms. In a recent review of 16 meta-analyses<sup>[5]</sup> the authors conclude that CBT produces large effect sizes for all anxiety disorders and unipolar depression in adults.

The mechanisms by which CBT leads to clinical improvement are less clear. Current psychological models of panic disorder and agoraphobia see the patients' response to bodily sensations as central to this disorder.<sup>[6–11]</sup> Laboratory and field studies have

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established that these patients respond to normal bodily sensations (e.g., variations in heart rate or breathing) with catastrophic thoughts, resulting in a fear response to such sensations.<sup>[12,13]</sup> Furthermore, patients are concerned about the social consequences of showing anxiety symptoms in public and are afraid of going crazy or losing control.

Current models of social phobia<sup>[14,15]</sup> emphasize the patients' excessive concerns, that others will negatively evaluate their behavior and appearance and notice their anxiety or anxiety symptoms (e.g., sweating, blushing).

If these models are correct, improvement in clinical symptoms will necessitate a reduction in catastrophic cognitions, and the types of cognitions that need to change should vary with the disorder. There is initial evidence from RCTs to support the notion that changes in panic-related cognitions indeed mediate changes in panic-severity<sup>[16,17]</sup> and changes in the perceived probability and cost of social concerns mediate outcome in CBT of social phobia.<sup>[18,19]</sup>

Data on cognitive mediation are still sparse, however, and some authors have questioned the causal role of cognitive change in the clinical improvement with CBT. Longmore and Worrell<sup>[20]</sup> concluded from their review of "component analysis studies" that cognitive interventions do not add to treatment efficacy over and above exposure methods, and that this casts doubt on the importance of cognitive change as a mediator of treatment outcome. Nevertheless, Hofmann<sup>[21]</sup> pointed out that cognitions can change and mediate treatment outcome not only through direct cognitive challenges, but also through exposure, two techniques commonly used in CBT. This is in line with prominent theories of the effects of exposure.<sup>[22,23]</sup>

Nevertheless, more studies are needed to investigate the mediating role of cognitions in CBT. Furthermore, there is a need to study mediation in unselected patient populations, as the available evidence from RCTs may be limited to patients meeting trial inclusion criteria. The present study investigated the role of cognitive mediation on clinical outcome in patients with agoraphobia or social phobia drawn from an effectiveness study of a CBT program that uses in vivo exposure as its main treatment component.<sup>[24]</sup> Including patients with two different primary diagnoses allowed us to investigate the possible specificity of mediation effects. We hypothesized that changes in cognitions relating to physical catastrophes mediate treatment outcome in agoraphobia, but not in social phobia. As cognitions about loss of control are common to agoraphobia and phobia, we expected changes in these cognitions to mediate treatment outcome for both patient groups. In addition, we included a noncognitive, possible alternative mediator, i.e., the quality of relationship with the patients' partner. Interpersonal variables have been implicated in the etiology of agoraphobia and social phobia,<sup>[25-30]</sup> and may therefore also play a role in mediating treatment outcome. If cognitive variables are central

to treatment outcome, they should show a larger mediating effect than the quality of interpersonal relationships.

## METHOD

### PARTICIPANTS

Participants were 427 patients with a primary DSM-III-R<sup>[31]</sup> diagnosis of agoraphobia (94.6% panic disorder with agoraphobia, 5.4% agoraphobia without panic attacks) and 98 patients with a DSM-III-R diagnosis of social phobia, as determined by the German version of the Anxiety Disorders Interview Schedule-Revised.<sup>[32]</sup> The sample represents a random selection of the total treated population at several outpatient clinics (see<sup>[24,33]</sup> for detailed descriptions). Exclusion criteria were current alcohol or drug dependency, psychosis, or medical conditions not allowing exposure treatment (e.g., myocardial infarct). No other selection criteria were used.

Table 1 shows sociodemographic characteristics. The agoraphobia group was somewhat older than the social phobia group and had a later onset of the disorder. There were no differences in educational level, but a greater proportion of the social phobia group were students or apprentices, and fewer of them were married or had children. Almost all agoraphobia patients (92.8%) had received at least one previous course of treatment, and this percentage was significantly higher compared with the social phobia group (75.8%). Overall, the two patient samples are clinically representative for their respective disorder groups, although the average percentage of comorbid Axis I disorders recorded for both samples (32.4%) is lower than that previously reported.<sup>[34,35]</sup> This is probably due to the fact that at the beginning of standardized data collection little emphasis was placed on assessing comorbidity for either Axis I or Axis II disorders.<sup>[24]</sup> For clinical purposes, it seemed sufficient at the time to establish the primary diagnosis to decide on a treatment protocol. The current comorbidity prevalence rates may, therefore, underestimate the actual percentages.

Additional analyses tested whether the results remained the same if cases with comorbid agoraphobia and social phobia were excluded. These analyses led to identical results as those based on the total samples and are, therefore, not reported.

### TREATMENT

Treatment comprised high-density in vivo exposure (HDE), typically lasting 4-10 days; patients confronted their feared situations for several hours per day. Treatment is highly individualized and involves three phases<sup>[36]</sup>: psychological assessment (3-5 hr), diagnostic feedback and treatment rationale (1 week later, 1.5-2.5 hr), and HDE (for further details see<sup>[24]</sup>).

For the agoraphobia sample, the mean duration of direct therapist-patient contact was 30.1 hr,  $SD = 14.9$ ; the social phobia group had significantly fewer hours of contact with the therapist;  $M = 26.3$  hr,  $SD = 13.0$ ,  $P = .034$ . CBT interventions for phobias differ in how much of the exposure is done as homework or as therapist-assisted exposure. As the clinics used an intensive treatment format, much of the exposure was therapist-assisted. This may have somewhat increased the number of hours of direct therapist contact compared to weekly CBT programs used in some research protocols that rely heavily on homework, especially for the agoraphobia group. Nevertheless, the treatment duration is within the range previously reported for exposure therapies for these patient groups (agoraphobia: 24 hr;<sup>[37]</sup> social phobia: 30 hr<sup>[38]</sup>). Treatment was delivered by diploma-level psychologists (equivalent to a master's degree in clinical psychology) with specialist training in behavior therapy. An experienced cognitive-behavior therapist specializing in HDE closely supervised all therapists.

**TABLE 1. Sociodemographic characteristics of patients with agoraphobia and social phobia**

	Agoraphobia			Social phobia			<i>t</i> -value/ $\chi^2$ ( <i>df</i> )	<i>P</i> -level
	Mean	( <i>SD</i> )	<i>N</i>	Mean	( <i>SD</i> )	<i>N</i>		
Age (yrs)	35.5	(9.07)	415	33.4	(9.92)	94	1.99	.047
Age at onset (yrs)	27.4	(9.16)	315	20.8	(8.53)	70	5.53	<.001
Duration of therapy (hr)	30.1	(14.89)	375	26.3	(12.77)	85	2.18	.030
Duration of disorder (yrs)	8.28	(7.31)	308	12.24	(8.83)	67	-3.73	<.001
<i>Highest educational level</i>								
Did not graduate	6 (1.5%)			2 (2.2%)			2.50 (4)	.64
Graduated after 8 years of school	80 (19.4%)			13 (14.0%)				
Graduated after 10 years of school	114 (27.6%)			25 (26.9%)				
Graduated after 12/13 years of school	108 (26.2%)			30 (32.3%)				
University degree	105 (25.4%)			23 (24.7%)				
<i>Employment</i>								
Blue-collar worker	11 (2.8%)			1 (1.1%)			21.0 (8)	.007
Skilled-labourer	14 (3.6%)			2 (2.3%)				
White-collar worker	127 (32.2%)			20 (23.0%)				
Professional	54 (13.7%)			13 (14.9%)				
Self-employed	56 (14.2%)			17 (19.5%)				
Homemaker	53 (13.5%)			3 (3.4%)				
Student/apprentice	53 (13.5%)			24 (27.6%)				
Unemployed	17 (4.3%)			6 (6.9%)				
Retired	9 (2.3%)			1 (1.1%)				
Received at least one previous course of treatment for the disorder	371 (92.8%)			73 (76.8%)			21.0 (1)	<.001
Has children	219 (54.8%)			32 (36.4%)			9.76 (1)	.002
With partner	360 (92.5%)			60 (77.9%)			15.5 (1)	<.001
Benzodiazepine use	84 (22.3%)			14 (14.4%)			2.94 (1)	.087
Antidepressant use	66 (17.6%)			14 (14.4%)			0.53 (1)	.47
Comorbid Axis I disorder	123 (30.7%)			30 (34.5%)			0.48 (1)	.49

## DESIGN AND MEASURES

Patients were assessed before therapy (baseline), 6 weeks after the end of therapy (post-treatment), and 1 year thereafter (follow-up), using the following measures:

**Diagnostic interview.** Diagnoses were established with the German version<sup>[39]</sup> of the Anxiety Disorders Interview Schedule-Revised.<sup>[32]</sup> This is a structured interview with well-established psychometric properties<sup>[40-43]</sup> and good acceptance in clinical practice and research settings,<sup>[44]</sup> allowing the assessment of Axis I disorders according to DSM-III-R.<sup>[31]</sup> Interviews were conducted by the therapists who had received intensive training in the use and scoring of the instrument.

**Mobility Inventory (MI).** The MI<sup>[45]</sup> (German version<sup>[46]</sup>) consists of 27 items assessing the patient's avoidance of the most common agoraphobic situations. Patients rate the avoidance of the situation twice, when being alone (MI-alone) and when accompanied by another person (MI-accompanied). Internal consistencies for the German version are .97 and .96, respectively. The MI-alone was used as the main outcome measure for agoraphobia. The internal consistency for the agoraphobia sample was .96 based on the entire sample for whom baseline data were available for all items ( $n = 523$ ).

**Symptom Checklist-90-Revised (SCL-90-R).** The SCL-90-R<sup>[47]</sup> (German version<sup>[48]</sup>) is a 90-item questionnaire assessing nine primary symptom dimensions and a Global Severity Index (GSI). It is frequently used as outcome parameter in studies evaluating clinical psychological interventions. The scale "interpersonal sensitivity" (9 items) was used as the main outcome measure for social phobia (SCL-IS). Internal consistency in the social phobia sample was .88, including all patients for whom baseline data were available for all items ( $n = 173$ ).

**Agoraphobic Cognition Questionnaire (ACQ).** The ACQ<sup>[49]</sup> (German version<sup>[46]</sup>) assesses typical agoraphobic cognitions. Each item is rated on a 5-point scale, ranging from 1 = *thought never occurs* to 5 = *thought always occurs*. Two subscales that have been validated with factor analyses in four independent samples of patients with anxiety disorders ( $N$ s between 88 and 1061)<sup>[46,49]</sup> were used for the analysis. The *physical crisis* subscale (ACQ-phys) (5 items) describes catastrophic thoughts relating to physical consequences of anxiety (e.g., "I will have a heart attack"); the *loss of control* subscale (ACQ-con) (7 items) describes catastrophic mental or socially unacceptable consequences (e.g., "I am going to go crazy"). Internal consistencies for the subscales were .65 (ACQ-phys,  $n = 744$ ) and .82 (ACQ-con,  $n = 733$ ) for the agoraphobia sample, and .72 (ACQ-phys,  $n = 170$ ) and .75 (ACQ-con,  $n = 168$ ) for the social phobia sample.

**Partnerschaftsfragebogen (PFB [Partnership Questionnaire]).** The PFB<sup>[50]</sup> (English version<sup>[51]</sup>) is a 30-item instrument that measures partnership satisfaction on three subscales (Quarrelling, Tenderness, and Togetherness and Communication). The PFB total score (PFBT) was used as a measure of partnership satisfaction. Internal consistencies for the agoraphobia sample ( $n = 363$ ) and the social phobia sample ( $n = 79$ ) were .81 and .82, respectively.

## DATA REDUCTION AND ANALYSIS

We used a linear mixed model<sup>[52]</sup> with time (in weeks) and the two mediators (ACQ-phys, ACQ-con) as time-varying covariates<sup>[53]</sup> since both can vary within subjects (lower level mediation model<sup>[54]</sup>). Temporal trends across the three assessment points (baseline, post-treatment, follow-up) were expressed by a linear and a quadratic

polynomial. We focused on the linear polynomial, which, in the presence of a quadratic polynomial, is not constant but represents the instantaneous rate of change at a predefined time point. Here, we fixed this time point to mid-treatment (3.5 weeks) by centering the time variable accordingly. Thus, the linear polynomial in our study was a measure of the average linear temporal change of the outcome variable (MI-alone or SCL-IS) during intervention. Although the quadratic polynomial is contained in each of the three models tested (see below), these results are only reported when temporal trends for the intervention are described. Mediator effects were tested for both mediators simultaneously (two-mediator model).<sup>[55]</sup> In order to estimate total, direct, and mediated (i.e., indirect) effects, three models were set up<sup>[54]</sup>:

$$\text{Model 1: } Y_{ij} = \zeta_0 + c\text{WEEK}_{ij} + c_q\text{WEEK}_{ij}^2 + u_{0i} + \varepsilon_{ij}$$

$$\text{Model 2: } \text{MED}_{ij} = \zeta_1 + a\text{WEEK}_{ij} + a_q\text{WEEK}_{ij}^2 + u_{1i} + \varepsilon_{ij}$$

$$\text{Model 3: } Y_{ij} = \zeta_2 + c'\text{WEEK}_{ij} + c'_q\text{WEEK}_{ij}^2 + b_1\text{MED}_{1ij} + b_2\text{MED}_{2ij} + u_{2i} + \varepsilon_{ij}$$

$Y_{ij}$ ,  $\text{WEEK}_{ij}$ , and  $\text{MED}_{ij}$  denote the observed values of the outcome (MI-alone, SCL-IS), time (in weeks), and the mediator of concern (ACQ-con, ACQ-phys), respectively, of person  $i$  at time point  $j$ ;  $\zeta_0$  to  $\zeta_2$  denote the intercept,  $u_{0i}$  to  $u_{3i}$  the person specific intercept (deviation from  $\zeta_0$  to  $\zeta_2$ ), and  $\varepsilon_{ij}$  the error term. Nonmediated Model 1 tests for the total effect of time on the outcome. It contains a linear and quadratic polynomial (coefficients  $c$  and  $c_q$ ). Model 2 tests for temporal trends of the mediator of concern (coefficients  $a$  and  $a_q$ ). Model 3 tests for the temporal trend of the outcome (coefficients  $c'$  and  $c'_q$ ) in the presence of the two mediators,  $\text{MED}_1$  and  $\text{MED}_2$ , simultaneously (coefficients  $b_1$  and  $b_2$ ). All three models allow each participant to have their own intercept ( $u_{0i}$  to  $u_{3i}$ ).<sup>1</sup>

The following steps are required to establish mediation in the present study<sup>[57]</sup> (see Fig. 1): (1) the outcome variable declines over time ( $c$  is significantly smaller than 0); (2) both mediators decline over time ( $a_1$  and  $a_2$  are both significantly smaller than 0<sup>2</sup>); (3) the mediator of concern positively affects the outcome after controlling for time and the other mediator ( $b_1$  and  $b_2$  are significantly larger than 0); (4a) complete mediation: the outcome variable does not decline over time after controlling for the two mediators ( $c'$  is not significantly smaller than 0); (4b) partial mediation: the outcome variable declines less strongly over time after controlling for the two mediators than when not controlling for them ( $c'$  is significantly smaller than 0 but less negative than  $c$ ).

Total effects are represented by  $c$ , direct effects by  $c'$ , mediated effects by the product  $a_1b_1$  and  $a_2b_2$ , and total mediated effects by the term  $a_1b_1 + a_2b_2$ . In addition, the proportion of the total mediated effect is presented. Preliminary analyses revealed that this proportion remained almost constant when centering the time variable either to the start or the end of treatment, or the end of follow-up, rather than to mid-treatment. To obtain standard errors of mediated effects and of total mediated effects we used equations 5.7.<sup>[55]</sup> Mediation effects were tested for statistical significance by dividing estimates by their standard error, assuming normal distribution of results. Outcome variables (MI-alone,

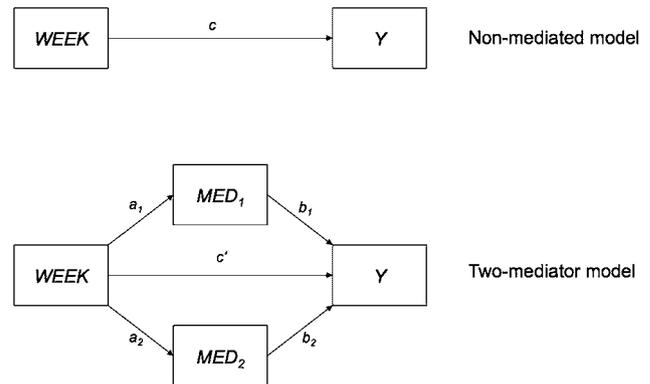


Figure 1. Path diagram of the nonmediated (top) and mediated (bottom) intervention effect on the outcome.  $c$  denotes the effect of WEEK on  $Y$  in the absence of  $\text{MED}_1$  and  $\text{MED}_2$ ,  $c'$  denotes the effect of WEEK on  $Y$ , corrected for  $\text{MED}_1$  and  $\text{MED}_2$ ,  $a_1$  and  $a_2$  denote the effects of WEEK on  $\text{MED}_1$  and  $\text{MED}_2$ , respectively, and  $b_1$  and  $b_2$  denote the effect of  $\text{MED}_1$  and  $\text{MED}_2$  on  $Y$ , corrected for WEEK. Note that only the linear but not the quadratic polynomial of WEEK is shown here for simplicity.

SCL-IS) were square-root transformed in order to better meet model assumptions. All analyses were carried out using SPSS, rel. 14.0.

## RESULTS

### ATTRITION AND MISSING VALUES

The agoraphobia sample included 427 patients who had completed at least one of the two post-baseline assessments (post-treatment, follow-up). Data were missing for 20 patients at baseline, 40 at post-treatment, and 126 at follow-up. Of the total attending initial assessment ( $n = 767$ ), 23% did not start exposure treatment, 8% dropped out during treatment, and 13% failed to return the post-treatment measures. Analyses of outcome data suggested that post-data followed a “missing-completely-at-random pattern” (MCAR)<sup>[58]</sup> with respect to the preceding measurements of MI-alone: whether MI-alone data was missing at post-treatment or at follow-up did not depend on baseline values;  $t_{721} = -1.05$ ,  $P = .29$  for post-treatment;  $t_{618} = -.26$ ,  $P = .80$  for follow-up (two-sample  $t$ -test). Also, missing data of MI-alone at follow-up did not depend on MI-alone at post-treatment,  $t_{227} = -.65$ ,  $P = .52$ .

The social phobia sample comprised 98 patients who had completed at least one of the two post-baseline assessments. There were no missing data at baseline, 3 were missing at post-treatment, and 41 at follow-up. Of a total of 177 patients attending initial assessment, 18% did not start exposure treatment, 5% dropped out during exposure, and 22% failed to return the post-treatment questionnaires. Data again appeared to follow an MCAR pattern with respect to the preceding measurements of SCL-IS: whether SCL-IS data was missing at post-treatment or follow-up did not depend on baseline values;  $t_{170} = -.52$ ,  $P = .60$  for post-treatment;  $t_{114} = -.29$ ,  $P = .77$  for follow-up. Missing

<sup>1</sup>All models initially considered the additional term  $u_{1i}\text{WEEK}_{ij}$ , allowing participants to have their own slope parameter. Nevertheless,  $u_{1i}$  was not significantly different from 0 in neither of the models and was hence not included in the analyses. This facilitates the computation of standard errors of mediated effects as the covariance between  $a$  and  $b$  equals 0, i.e., they can be assumed to be fixed.<sup>[54,56]</sup>

<sup>2</sup>If either  $a_1$  or  $a_2$  is not significantly smaller than 0 then the corresponding mediating variable is not a mediator.

SCL-IS at follow-up did not depend on SCL-IS at post-treatment,  $t_{85} = .28, P = .78$ .

**MEDIATOR EFFECTS**

In the agoraphobia sample correlations between mediators at baseline were generally low<sup>[59]</sup> (ACQ-con and ACQ-phys,  $r = .20, P < .001, n = 419$ ; ACQ-con and PFBT,  $r = -.01, P = .88, n = 343$ ; ACQ-phys and PFBT,  $r = .02, P = .76, n = 345$ ). The corresponding correlations in patients with social phobia were generally higher but never large ( $r = .38, P < .001, n = 95$ ;  $r = -.04, P = .77, n = 51$ ;  $r = .29, P = .040, n = 52$ ).

**MEDIATION OF TREATMENT OUTCOME IN AGORAPHOBIA PATIENTS (TABLE 2, MAIN COLUMN 1)**

MI-alone significantly decreased during intervention and then remained almost constant until follow-up ( $c$ , quadratic polynomial  $c_q > 0, P < .001$ ). ACQ-con and ACQ-phys also showed a significant reduction from baseline to post-treatment and little change to follow-up ( $a$ , quadratic polynomial  $a_q > 0, P < .001$ , for both ACQ-con and ACQ-phys). Both ACQ-con and ACQ-phys mediated treatment outcome, as the indirect effects for both mediators ( $a_1b_1, a_2b_2$ ) and their total indirect effect ( $a_1b_1 + a_2b_2$ ) were all significantly different from 0. ACQ-con accounted for 16% and ACQ-phys for 13% of the total effect; combined they explained 29% of the total intervention effect. The direct effect remained significant after accounting for the

effect of the two mediators ( $c'$ ), suggesting partial mediation by ACQ-con and ACQ-phys.

**MEDIATION OF TREATMENT OUTCOME IN SOCIAL PHOBIA PATIENTS (TABLE 2, MAIN COLUMN 2)**

SCL-IS, and ACQ-con and ACQ-phys all decreased significantly during treatment and showed little change to follow-up (SCL-IS:  $c$ , quadratic polynomial  $c_q > 0, P < .001$ ; ACQ:  $a$ , quadratic polynomial  $a_q > 0, P < .001$  for both ACQ-con and ACQ-phys). ACQ-con mediated treatment outcome, as the indirect effect ( $a_1b_1$ ) was significantly different from 0 and the proportion of the total mediated effect on SCL-IS was 45%. In contrast, ACQ-phys did not mediate treatment outcome (neither  $b_2$  nor  $a_2b_2$  differed significantly from 0) and accounted for only 6% of the total effect. The total mediated effect ( $a_1b_1 + a_2b_2$ ) was significant, and both mediators together accounted for 50% of the total intervention effect. The direct effect remained significant after accounting for the mediator effect of the two mediators ( $c'$ ), indicating partial mediation, for which mainly ACQ-con was responsible.

**MEDIATION BY PARTNERSHIP SATISFACTION (TABLE 2, MAIN COLUMNS 3 AND 4)**

As information on partnership satisfaction was not available for all patients, the analysis involving PFBT was based on smaller samples compared with the

**TABLE 2. Direct, total and mediated effects of intervention on MI-alone and SCL-IS with mediators ACQ-con, ACQ-phys, and partnership satisfaction.**

	Effect on MI-alone in agoraphobia patients (n = 426)		Effect on SCL-IS in social phobia patients (n = 97)		Effect on MI-alone in agoraphobia patients (n = 253)	Effect on SCL-IS in social phobia patients (n = 56)
	Two mediators		Two mediators		One mediator	One mediator
	ACQ-con	ACQ-phys	ACQ-con	ACQ-phys	Partnership satisfaction	Partnership satisfaction
$a_1, a_2, a$ [ $\times 100$ ] <sup>a</sup>	-9.93 (0.492)***	-9.77 (0.451)***	-8.11 (1.08)***	-2.48 (0.555)***	-23.0 (8.11) <sup>b</sup>	-18.3 (19.9) n.s.
$b_1, b_2, b$ [ $\times 100$ ] <sup>c</sup>	11.5 (1.06)***	9.89 (1.20)***	28.3 (3.43)***	11.3 (7.09) n.s.	-0.162 (0.077) <sup>a</sup>	-0.346 (0.283) n.s.
$a_1b_1, a_2b_2, ab$ [ $\times 100$ ]	-1.14 (0.122)***	-0.937 (0.124)***	-2.29 (0.414)***	-0.281 (0.187) n.s.	-0.0373 (0.0219) n.s.	-0.0633 (0.0856) n.s.
Mediated proportion (%) <sup>d</sup>	16	13	45	6	0.50%	-1.2%
$a_1b_1 + a_2b_2$ [ $\times 100$ ]	-2.07 (0.191)***		-2.58 (0.418)***			
Total mediated proportion (%) <sup>b</sup>	29		50			
$c$ [ $\times 100$ ]	-7.23 (0.199)***		-5.11 (0.566)***		-6.89 (0.276)***	-5.44 (0.799)***
$c'$ [ $\times 100$ ]	-5.15 (0.222)***		-2.50 (0.602)***		-6.85 (0.277)***	-5.48 (0.796)***

Estimated values of the terms  $a_1b_1 + a_2b_2 + c'$  (two-mediator model) or  $ab + c'$  (one-mediator model) were very close to the value of  $c$  (absolute deviations  $\leq 0.68\%$  for any term), but not identical as found in ordinary regression analysis (McKinnon, 2008).

<sup>a</sup> $a_1$  or  $a_2$  for two-mediator model,  $a$  for one-mediator model.

<sup>b</sup>Sum of the two-mediated proportions (for two-mediator model only).

<sup>c</sup> $b_1$  or  $b_2$  for two-mediator model,  $b$  for one-mediator model.

<sup>d</sup>Proportion of the total effect  $c$ , that is mediated, i.e.  $a_1b_1/c$  or  $a_2b_2/c$  (two-mediator model) or  $ab/c$  (one-mediator model).

\*\*\* $P < .001$ .

analyses regarding the ACQ-con and ACQ-phys as mediators. In order to test for possible mediation by PFBT we used a single mediator model.<sup>[55]</sup> Partnership satisfaction did not mediate treatment outcome in either group, as shown by the nonsignificant indirect effects (*ab*) and the very low respective proportions of mediated to total effect for both MI-alone and SCL-IS.

## DISCUSSION

The main aim of the present study was to investigate whether cognitive changes mediate treatment effects of exposure therapy in agoraphobia and social phobia. As in previous reports from the participating clinics<sup>[24,33]</sup> and disorder-specific meta-analyses,<sup>[60,61]</sup> measures of clinical outcome strongly and significantly improved in both patient samples between baseline and post-treatment. This effect was maintained at 1-year follow-up, suggesting lasting improvements in response to high-density exposure-based CBT.

The results support the notion that cognitive changes mediate outcome in CBT in unselected patients with agoraphobia or social phobia. ACQ-scores were significant mediators of symptom change. As the treatment was exposure-based and did not include cognitive interventions except for the treatment rationale it can be concluded that cognitive changes occur even without explicit cognitive challenges, in line with information processing theories of the effects of exposure.<sup>[23]</sup>

The results further pointed to specificity of the mediation effects. Changes in cognitions relating to physical catastrophes mediated treatment outcome only for patients with agoraphobia, whereas cognitions about loss of control significantly mediated outcome for both agoraphobia and social phobia patients. This disorder-related specificity of the type of cognitions that mediate CBT outcome supports cognitive models of agoraphobia<sup>[6-11]</sup> and social phobia.<sup>[14,15]</sup> We included partnership satisfaction as an alternative mediator to test the hypothesis that treatment outcome is mediated by other, noncognitive factors. Although partnership satisfaction increased between baseline and post-treatment, it did not mediate treatment outcome in either patient sample. This confirms previous reports on cognitive changes as mediators of symptom improvement<sup>[16-19]</sup> and further supports the central role of cognitive changes in CBT outcome.

Smits et al.<sup>[16]</sup> for example, followed a similar approach by using lower level mediation analyses in the investigation of the effects of an exposure-based treatment in a homogeneous sample of patients with fear of public speaking. In line with the current results, cognitive changes (in probability and cost estimates)-mediated symptom improvement (fear reduction). Nevertheless, cross-lagged panel analyses suggested that only one type of cognitive changes (reductions in probability bias) resulted in fear reduction, whereas the other (reduction in cost bias) was only a consequence of

symptom reduction. This finding suggests that even within an anxiety disorder such as social phobia, some of the cognitive biases may be of particular importance for mediating CBT outcome and should, therefore, be targeted in exposure-based treatments.

There are several possibilities how changes in cognitions may lead to clinical improvement, and these concepts are not mutually exclusive. From a cognitive perspective,<sup>[6,12,14]</sup> changes in cognitions would be expected to affect clinical symptoms directly and indirectly. If agoraphobic patients no longer believe that palpitations presage a heart attack, this will directly decrease their anxiety levels and likelihood of panic attacks. Similarly, if patients with social phobia no longer believe that other people will evaluate them negatively, this will directly decrease their anxiety in social interactions. The belief changes will also decrease the patients' motivation for behaviors that maintain the disorders (e.g., situational avoidance, safety seeking behaviors). From an emotional processing perspective,<sup>[23]</sup> the belief change presents new information that is incorporated into the patients' fear memory structures so that the strength of association between innocuous stimuli (e.g., feeling one's heart beating) and fear responses is reduced and the stimuli therefore no longer trigger anxiety.

Finally, the effects of exposure therapy are often interpreted within the conceptual framework of extinction of learned fear responses. Specifically for panic disorder, enhanced resistance to extinction of fear conditioning has recently been shown experimentally.<sup>[62]</sup> This raises the question of how cognitive change may affect such acquired responses. In a recent review Hofmann<sup>[63]</sup> discusses several learning theories that are relevant to exposure treatments such as conditioning, preparedness theory, or modern learning theories. One mechanism whereby cognitions may affect learned fear responses is by changing CS-US expectancies. Exposure therapy can be interpreted as an intervention that changes CS-US expectancies, i.e., the expectation that something bad will happen if the individual encounters the feared stimuli.<sup>[63]</sup>

The current study has several limitations. First, the study design and statistical procedure do not allow for the timeline between the mediator and the outcome to be established. As mediators and outcomes were assessed at the same time, it cannot be ruled out that symptom change may have preceded or occurred concurrently with cognitive changes. Nevertheless, it can be argued that the current results provide a line of evidence from a naturalistic setting, which converges with other lines of evidence, e.g., from RCTs.<sup>[16-19]</sup> Second, outcomes were entirely based on self-report measures. The inclusion of independent blind assessor ratings may be desirable from a methodological point of view. Nevertheless, effect sizes based on blind assessor ratings have been shown to exceed those for self-report.<sup>[64]</sup> The use of self-report data in the current study may, therefore, have painted a more

negative but also more realistic picture. Third, this study shares the challenges to internal validity that are characteristic of an open clinical follow-up study including the unavailability of reliability data for diagnoses or formal treatment adherence or competency measures. Fourth, it remains to be tested whether noncognitive factors other than partnership satisfaction mediate treatment outcome of HDE.

Despite these limitations the current results provide further support for the mediating role of cognitive changes for outcome in exposure therapy for agoraphobia and social phobia.<sup>[16–19]</sup> The study extends previous findings by demonstrating mediation in an unselected clinical sample and by providing evidence for the specificity of mediation effects. These results may have important clinical implications as they suggest that cognitive change is a key mechanism of improvement with exposure therapy of agoraphobia and social phobia. Patients who do not show improvement with exposure therapy might benefit from the assessment of behavioral and cognitive strategies that prevent cognitive changes (e.g., subtle and covert forms of avoidance, such as distraction from bodily sensations, proximity to safety cues etc.) and their modification through challenging them directly.

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