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Short-term psychotherapy for depression

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Therapist-rated outcomes
in a randomized clinical trial comparing
cognitive behavioral therapy and
psychodynamic therapy
for major depression

Abstract

Background: The efficacy of psychodynamic therapy (PDT) for depression is debated due to a paucity of high-quality studies. We compared the efficacy of short psychodynamic supportive psychotherapy (SPSP) to cognitive behavioral therapy (CBT) and used therapist-rated outcomes to examine how the course of change during treatment could be best represented and to compare treatment efficacy, hypothesizing non-significant differences.

Methods: 341 Adults meeting DSM-IV criteria for a depressive episode and with Hamilton Depression Rating Scale (HAM-D) scores ≥ 14 were randomized to 16 sessions of individual manualized CBT or SPSP within 22 weeks. Severely depressed patients (HAM-D>24) received additional antidepressant medication. After each session, therapists rated the Clinical Global Impression Scale subscales 'Severity of Illness' (CGI-S) and 'Global Improvement' (CGI-I) and DSM-IV Axis V Global Assessment of Functioning Scale (GAF). Data were analyzed with mixed model analyses using intention-to-treat samples.

Results: CGI-S and GAF indicated a linear symptom decrease, while CGI-I suggested an S-shaped curve with relative more improvement the first and last phases than in the middle phase of treatment. No significant post-treatment differences were found. Post-treatment differences were less pronounced when controlling for therapist gender and profession.

Limitations: Therapists were not specifically trained for CGI and GAF assessment, treatment adherence was not assessed objectively and allocation sequence was known to the research staff enrolling participants.

Conclusions: These findings add to the evidence-base of PDT for depression and show that therapist characteristics need to be taken into account when interpreting therapist-rated outcomes.

Trial registration: Current Controlled Trials ISRCTN31263312 (http://www.controlled-trials.com)

Introduction

The efficacy of psychodynamic therapy (PDT) for depression remains controversial due to a scarcity of adequately conducted trials (American Psychiatric Association [APA], 2010; National Institute for Health and Clinical Excellence [NICE], 2009; Driessen et al., 2010). In a randomized clinical trial comparing the efficacy of PDT with cognitive behavioral therapy (CBT) in a large group of patients with a major depressive episode treated in non-academic routine outpatient clinics (Driessen et al., 2007), we found no significant treatment differences on observer-rated and patient-rated outcomes (Driessen et al., 2012).

Therapist-rated outcome measures can provide additional information to observer-rated and patient-rated measures, since they are based on clinician's judgment. Therapist-rated measures as the Clinical Global Impression Scales (CGI; Guy, 1976) and DSM-IV Axis V Global Assessment of Functioning Scale (GAF; APA, 2000) have a one-item structure that provides the benefit of a quick and easy assessment of patient symptom level, but that also might be more at risk for bias, because their subjective ratings can be based on different information and because in psychotherapy efficacy research it is by definition impossible to conduct blind therapist-ratings. However, therapist-rated measures can provide valuable information regarding patient functioning from a clinician's perspective and are often used as efficacy measures in clinical practice.

In our study, therapist-rated outcomes were assessed after each session in order to examine how the course of change during treatment could be best represented and to compare CBT and PDT with regard to these measures. We expected symptom decrease during treatment, but did not specify hypotheses regarding curves. We hypothesized no significant differences between conditions on all therapist-rated outcome measures.

Methods

Methods have been described in detail elsewhere (Driessen et al, 2007; Driessen et al., 2012) and will only be summarized here.

Design
This study is a randomized clinical trial (RCT) with an allocation ratio CBT:PDT of 1:1. The Dutch Union of Medical-Ethic Trial Committees for mental health organizations approved the study design.

Participants
Participants were referred by their general practitioner to one of three outpatient mental health clinics in Amsterdam, The Netherlands. Inclusion criteria were: 1) presence of a depressive episode according to DSM-IV criteria (APA, 2000) as assessed

with the *MINI-International Neuropsychiatric Interview – Plus* (MINI-Plus; Sheehan et al., 1998), 2) *Hamilton Depression Rating Scale* (HAM-D; Hamilton, 1960) scores ≥ 14, 3) age between 18 and 65 years, and 4) written informed consent.

Interventions
Short psychodynamic supportive psychotherapy (SPSP; de Jonghe et al., in press; de Jonghe, Kool, van Aalst, Dekker, & Peen, 2001; de Jonghe et al., 2004; Dekker et al., 2005; Dekker et al., 2008) constituted PDT in this study. Both SPSP and CBT encompassed 16 individual sessions within 22 weeks and were conducted according to published treatment manuals (de Jonghe, 2005; Molenaar, Don, van den Bout, Sterk, & Dekker, 2009).

Psychotherapists in both conditions were trained (resident) psychiatrists or psychologists. No differences were found between conditions with regard to years of psychotherapist experience (CBT: 7.5, range=1-30; SPSP: 7.4, range=0-32; U=13,711.00, z=-0.148, p=.88), but CBT was conducted more often by psychologists (CBT: 62.8%, SPSP: 15.6%), while psychodynamic therapy was more often conducted by (resident) psychiatrists (CBT: 8.9%, SPSP: 56.0%, χ^2(1)=109.80, p<.001). Furthermore, CBT was conducted more often by a female therapist (CBT: 73.3%, SPSP: 53.0%, χ^2(1)=15.91, p<.001). All psychotherapists met bi-weekly (residents weekly) for supervision sessions chaired by a study supervisor in which audio-taped material was discussed and manual adherence was checked without using an adherence measure. With regard to protocol adherence, CBT therapists reported a mean score of 7.1 (scale=0-10) over 1218 CBT sessions.

Severely depressed patients (HAM-D>24 at baseline; n=129) and moderately depressed patients at baseline that developed severe symptoms during treatment (n=21) were offered additional antidepressant medication administrated by (resident) psychiatrists according to a protocol starting with extended-release venlafaxine 75 mg/day.

Outcome measures
Therapist-rated outcome measures included the seven-step CGI (Guy, 1976) subscales 'Severity of Illness' (CGI-S) and 'Global Improvement' (CGI-I). CGI-S rates depression severity at the moment of contact from "normal, not at all ill" (0) to "among the most extremely ill patients" (7). CGI-I rates the therapist's clinical impression of the improvement or deterioration when compared to treatment start form "very much improved" (0) to "very much worse" (7). GAF (APA, 2000), which scores range 0 to 100 with higher scores indicating better levels of functioning, constituted the third measure. All three outcome measures were rated after each psychotherapy session by the therapist, who was unaware of observer-rated and patient-rated depression scores.

Statistical Methods
Given the hierarchical data-structure, linear mixed model analyses were conducted according to a three-level structure (therapist, patient, repeated measures) using an

intention-to-treat sample. Location was included as a covariate in one of the sensitivity analyses, rather than a level, because of the small number of categories (*n*=3). Mixed model analyses were performed with MLwiN (version 2.22).

Growth curves were fitted by starting with a model including a random intercept and a main effect for treatment (fixed slope) to which time was added. If time was a significant predictor, a higher order time-polynomial was added until the added time-polynomial was no longer a significant predictor. The last added non-significant time-polynomial was then removed from the model and time-by-treatment interactions were next added for all time-polynomials included. Finally, a random slope was added to the time-polynomials to see if this resulted in a model improvement. The resulting model constituted the basic model. In order to control for (possible) confounders, we added the following sets of covariates to the basic model: 1) therapist profession and therapist gender, 2) clinic and number of patients with baseline HAM-D>24, 3) demographic variables (patient age, gender, cultural background, marital status, living situation, educational level, job status, and income), 4) depression characteristics (duration present episode, prior treatment, number of prior depressive episodes, and comorbid dysthymia). Finally, we checked the p-values of the treatment main effect and time-by-treatment interactions for significant effects (*p*<.05).

Results

Participants
From April 2006 to December 2009, 4866 patients were screened for eligibility, 341 of which were randomized (CBT: 164, SPSP: 177). Patient characteristics are described in Chapter 7 (Table 1). No significant differences were found between the conditions in terms of demographic and clinical characteristics and with regard to proportions of patients not completing treatment (CBT: 31.1%, psychodynamic: 25.9%; Driessen et al., 2012). Respectively, 48 (14.1%), 50 (14.7%), and 55 (16.1%) patients were excluded from CGI-S, CGI-I and GAF analyses due to missing therapist data.

Therapist-rated outcomes
Observed mean scores during treatment are plotted in Figure 1, which indicate better functioning over the course of treatment in both conditions on all three outcome measures. Outcomes of the mixed-model growth curve analyses are presented in Table 1. CGI-S and GAF scores during treatment were both best predicted by a random regression model including a first-order time-polynomial with random slope, indicating a linear relationship between time and therapist-rated depression scores. CGI-I scores were best predicted by a model including a third-order time-polynomials with random slopes, resulting in an S-shaped curve with relatively sharper decreases of symptoms during the first and last weeks of treatment than in the middle weeks of treatment.

Time was consistently found to be a significant predictor of therapist-rated outcome. No significant time-by-treatment interactions were found for any of the outcome measures under all different models. Treatment condition was not found to

Table 1: Regression coefficients for time, treatment and time×treatment interactions for the basic model of analysis and when corrected for different sets of covariates.

Outcome measure	Basic model			Model 1			Model 2			Model 3			Model 4		
	β	SE		β	SE		β	SE		β	SE		β	SE	
CGI-S															
Treatment (week 22)	0.350	0.191	t	0.219	0.205		0.385	0.189	*	0.306	0.189		0.366	0.192	t
Time	-0.090	0.006	**	-0.090	0.006	**	-0.090	0.006	**	-0.090	0.006	**	-0.091	0.006	**
Time x Treatment	0.013	0.008		0.013	0.008		0.013	0.008		0.013	0.008		0.013	0.008	
CGI-I															
Treatment (week 0)a	-0.022	0.065		-0.017	0.077		-0.017	0.065		-0.019	0.067		-0.006	0.067	
Time	-0.171	0.026	**	-0.173	0.026	**	-0.171	0.026	**	-0.171	0.026	**	-0.171	0.026	**
Time2	0.010	0.003	**	0.010	0.003	**	0.010	0.003	**	0.010	0.003	**	0.010	0.003	**
Time3	$-2.5 \cdot 10^{-4}$	$9.5 \cdot 10^{-5}$	*	$-2.6 \cdot 10^{-4}$	$9.4 \cdot 10^{-5}$	**	$-2.6 \cdot 10^{-4}$	$9.5 \cdot 10^{-5}$	**	$-2.5 \cdot 10^{-4}$	$9.4 \cdot 10^{-5}$	**	$-2.7 \cdot 10^{-4}$	$9.6 \cdot 10^{-5}$	**
Time x Treatment	0.044	0.037		0.045	0.037		0.045	0.037		0.047	0.036		0.044	0.037	
Time2 x Treatment	-0.003	0.004		-0.003	0.004		-0.003	0.004		-0.003	0.004		-0.003	0.004	
Time3 x Treatment	$4.2 \cdot 10^{-5}$	$1.3 \cdot 10^{-4}$		$4.1 \cdot 10^{-5}$	$1.3 \cdot 10^{-4}$		$4.4 \cdot 10^{-5}$	$1.3 \cdot 10^{-4}$		$5.0 \cdot 10^{-5}$	$1.3 \cdot 10^{-4}$		$5.2 \cdot 10^{-5}$	$1.3 \cdot 10^{-4}$	
GAF															
Treatment (week 22)	-1.497	1.402		-0.446	1.504		-1.634	1.390		-1.271	1.379		-1.673	1.417	
Time	0.555	0.045	**	0.559	0.045	**	0.559	0.045	**	0.552	0.045	**	0.550	0.045	**
Time x Treatment	-0.055	0.060		-0.060	0.060		-0.057	0.060		-0.047	0.061		-0.047	0.061	

Note. Basic model.: basic model including treatment, time and time*treatment interactions; Model 1: basic model with therapist gender and profession added as covariates; Model 2: basic model with number of patients with baseline HAM-D>24 and clinic added as covariates; Model 3: basic model with demographic variables (patient age, gender, cultural background, marital status, living situation, educational level, job status, and income) added as covariates; Model 4: basic model with depression characteristics (duration present episode, prior treatment, number of prior depressive episodes, and comorbid dysthymia) added as covariates

t = non-significant trend (>.05 p ≤ .10)

a In the CGI-S and GAF models the variable time-minus-22 was used to estimate treatment differences at week 22. However, for CGI-I including this variable did not result a valid model, likely because the addition of a variable with negative signs to three time polynomials with all random slopes resulted in a model to complex to be calculated. We therefore report the model including the regular time variable that did result in valid outcomes and estimated treatment differences at week 0.

Figure 1: Therapist-rated observed mean scores during treatment
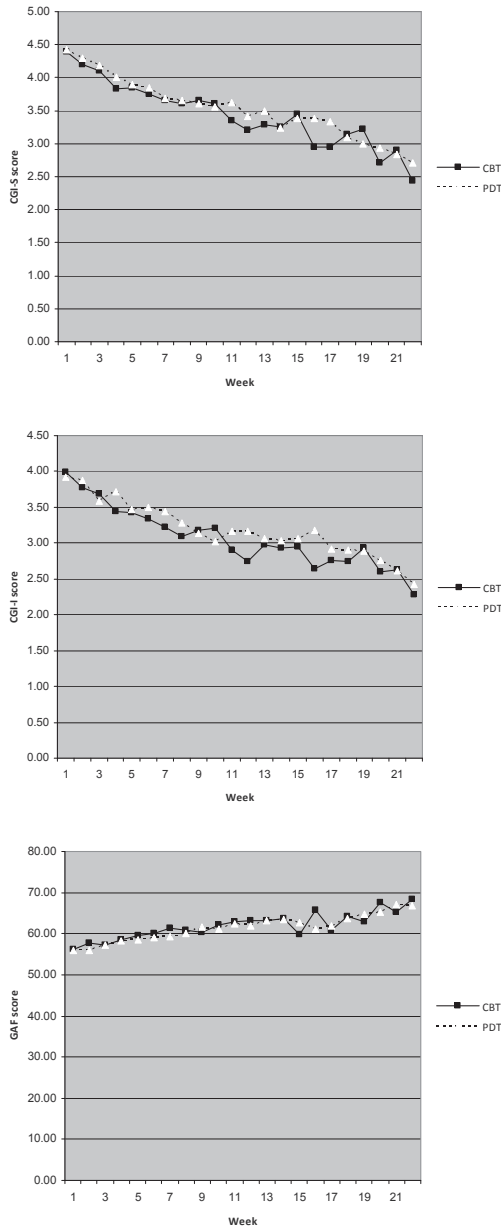
CBT = cognitive behavioral therapy, CGI-I = Clinical Global Impression, Improvement subscale, CGI-S = Clinical Global Impression, Severity subscale, GAF = DSM-IV Global Assessment of Functioning scale, PDT = psychodynamic therapy.

be a significant predictor of post-treatment CGI-I and GAF scores, nor was it found a significant predictor of post-treatment CGI-S score when controlling for therapist gender and therapist function.

When controlling for therapist gender and therapist function, estimated CGI-S differences between treatments were smaller (0.22) than under the basic model and the other models that controlled for patient characteristics (0.31-0.39), and treatment condition was not a significant predictor of post-treatment CGI-S scores, while it was found to predict post-treatment CGI-S scores at the level of a non-significant trend under the basic model (p=.05-.10; Table 1). GAF differences between treatments were also smaller when controlling for therapist gender and function (-0.45) than under the basic model and the models that controlled for patient characteristics (-1.27--1.67).

Discussion

We conducted a large RCT comparing PDT and CBT for patients with a major depressive episode treated in non-academic routine outpatient clinics and used therapist-rated outcomes to examine how the course of change during treatment could be best represented and to compare treatment efficacy. We found linear symptom decreases for the two therapist-measures rating severity, while the one measure rating improvement compared to treatment start suggested an S-shaped curve indicating relative more improvement the first and last phases of treatment when compared to the middle of treatment. We speculate that when rating improvement compared to treatment start, therapists notice relatively larger gains during the first and last phases of treatment, while gains are reported in a relative more steady pace when rating symptom severity at a given moment.

We found no significant treatment effects or time-by-treatment interactions when analyses were controlled for differences between conditions in terms of therapist gender and function. These findings are in line with the observer-rated and patient-rated outcomes of the same study that also showed no significant differences between treatment conditions at post-treatment and with meta-analyses (Driessen et al., 2012; Cuijpers, van Straten, Andersson, & van Oppen, 2008; Leichsenring, 2001) that reported no significant post-treatment differences between individual CBT and PDT. These findings add to the evidence-base of PDT for depression.

Post-treatment differences were smaller in CGI-S and GAF models controlling for therapist function and gender than in the other models examined, suggesting that differences in therapist pools might have augmented post-treatment differences between conditions. These findings underline that therapist-ratings can be influenced by therapist characteristics and indicate that it is important to check and control for differences in therapist pools when using this kind of measures. Furthermore, possible rating differences between severity and improvement measures might be taken into account when implementing therapist-rated measures in outcome studies.

Strengths of this study include efforts to increase external validity, such as providing treatment in non-academic routine outpatient clinics by a large number of therapists

with different experience levels and the inclusion of patients with relatively low social-economic statuses. Furthermore, in terms of sample size this study is a large addition to the field of PDT for depression outcome research, including 341 participants compared to a total of 421 participants across all 6 CBT-PDT RCTs included in a PDT for depression meta-analysis (Driessen et al., 2010). However, these study's findings must also be considered in the light of the following methodological limitations (see also Driessen et al., 2012): 1) a substantial number of patients did not complete treatment or was lost to assessment, 2) psychodynamic therapy adherence was not assessed by means of an adherence measure, 3) research assistants enrolling participants were aware of the allocation sequence, and 4) no control group was included. Although we applied statistical measures robust to missing data, treatment adherence was monitored by means of intensive supervision and no significant differences were found between treatment conditions at baseline, we cannot rule out the possibility that selection bias affected our findings. Another important limitation is that therapists were not specifically trained for CGI and GAF assessment, which might have affected the reliability of the assessment. They were, however, provided with written instructions.

In conclusion, therapist-rated severity measures in a large sample of patients treated for a major depressive episode in routine non-academic outpatient clinics suggested a linear symptom decrease, while improvement was best represented by an S-shaped curve indicating relative more improvement the first and last phases of treatment than in the middle of treatment. No statistically significant post-treatment differences on therapist-rated outcome measures were found between PDT and CBT, which extends the evidence-base of psychodynamic therapy for depression. Therapist-rated outcomes can provide a quick and simple summary score of general patient functioning from a clinician's perspective, but possible differences between improvement and severity measures need to be taken into account when implementing these measures in outcome research and differences in therapist characteristics need to be taken into account when interpreting their outcomes.

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