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EMPIRICAL PAPER

Does psychological process change during psychotherapy predict long-term depression outcome after successful cognitive therapy or interpersonal psychotherapy? Secondary analysis of a randomized trial

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Abstract

Objective Psychotherapies for depression are similarly effective, but the processes through which these therapies work have not been identified. We focus on psychological process changes during therapy as predictors of long-term depression outcome in treatment responders. **Method:** Secondary analysis of a randomized trial comparing cognitive therapy (CT) and interpersonal psychotherapy (IPT) that focuses on 85 treatment responders. Using mixed-effects models, changes during therapy (0–7 months) on nine process variables were associated with depression severity (BDI-II) at follow-up (7–24 months). **Results:** A decrease in dysfunctional attitudes was associated with a decrease in depression scores over time. Improved self-esteem was associated with less depression at follow-up (borderline significant). More improvement in both work and social functioning and interpersonal problems was associated with better depression outcomes in IPT relative to CT, while less improvement in work and social functioning and interpersonal problems was associated with better outcomes in CT relative to IPT. **Conclusions:** Less negative thinking during therapy is associated with lower depression severity in time, while changes during therapy in work and social functioning and interpersonal problems appear to predict different long-term outcomes in CT vs. IPT. If replicated, these findings can be used to guide clinical decision-making during psychotherapy.

Keywords: cognitive therapy; interpersonal psychotherapy; depression; therapy processes; prediction

Clinical or methodological significance of this article: This study shows that less negative thinking and increased self-esteem in the course of psychotherapy (cognitive therapy or interpersonal therapy) are associated with less depression after therapy has ended, while changes in work and social functioning and interpersonal problems during therapy appear to predict different long-term outcomes in cognitive therapy compared to interpersonal therapy. If replicated, these findings can be used to monitor individual progress and guide decision-making in psychotherapy.

Introduction

The effectiveness of psychotherapies such as cognitive (behavior) therapy (CT) and interpersonal psychotherapy (IPT) for depression is well demonstrated and appears to be similar (Cuijpers

et al., 2011; Cuijpers et al., 2014). However, individual responses to treatment vary greatly (Cohen & DeRubeis, 2018; Simon & Perlis, 2010) and to this date, the causal pathways of change through which these therapies exert their beneficial effects have

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not been identified in empirical research, despite the demonstrated association of processes and outcome, numerous theories and heated debates (Huibers & Cuijpers, 2015). CT and IPT stem from different theoretical backgrounds and are delivered according to different treatment protocols; CT puts emphasis on changes in dysfunctional thinking and avoidant behavior patterns (Beck et al., 1979), while IPT is believed to work through changes in interpersonal functioning (Klerman et al., 1984). Differential pathways of change are one explanation for their comparable effectiveness (DeRubeis et al., 2005), in opposition to the claim of the common factor theory stating that all therapies work through universal factors (Wampold, 2015).

In a recent systematic review, no solid evidence was found for specific (e.g., change in negative thinking) or common factors (e.g., therapeutic alliance) as empirically validated mechanisms of change that drive the effectiveness of psychotherapy (Cuijpers et al., 2019). A major limitation in most process-outcome studies is the analysis on the level of group means, ignoring important differences on the individual level. It was also concluded that most previous studies do not meet the methodological requirements for mechanism research, particularly the use of multiple measurement points to establish the temporality of changes, appropriate mediational analyses and the consideration of multiple candidate factors in mediational models to estimate the relative contributions these factors (Cuijpers et al., 2019; Lemmens et al., 2016). All this has hampered the development in the field, while insight into the therapeutic processes (and the role of individual differences in this regard) that lead to recovery is likely to be the way out of the deadlock that intervention science seems to be stuck in (Goldfried, 1980; Hofmann & Hayes, 2019; Huibers et al., 2020; Kazdin, 2007).

In this follow-up paper, we focus on changes in psychological processes during psychotherapy as *general* or *differential predictors* of depression outcome in the long term after the termination of CT or IPT, in a subgroup of patients who responded to treatment. The idea for this paper started with the notion that people who improve in therapy should also improve in the underlying psychological processes that drive or impact the depression, in order to stay well after they finished treatment. In that sense, we think that successful therapy can have long-term effects after the therapy has ended. Knowledge of these predictive change factors can provide insight into the underlying working mechanisms of a treatment (Kazdin, 2007). Unfortunately, prediction studies and more sophisticated mediational studies until now have generated surprisingly little knowledge on how CT, IPT and other forms of

psychotherapy actually work (Bernecker et al., 2017; Hamilton & Dobson, 2002; Lemmens et al., 2017; Van et al., 2008). Our research group for example investigated the role of five factors (dysfunctional thinking; interpersonal functioning; rumination; self-esteem; therapeutic alliance) as potential mediators of outcome in the acute phase of CT and IPT in the context of a randomized trial (Lemmens et al., 2015) and found no evidence for temporal relations (i.e., change in the process precedes change in depression) or mediational processes (i.e., change in the process accounts for the change in depression), except for a temporal relation between increased self-esteem and subsequently less depression (Lemmens et al., 2017).

Since relapse and recurrence are major problems in depression (Burcusa & Iacono, 2007; Van London et al., 1998), it is very relevant to identify markers of therapy progress that predict sustained improvement in the long term. Moreover, CT has proven to have prophylactic, enduring effects that are superior to pharmacotherapy (Cuijpers et al., 2013), which also implies that patients learn something in therapy that helps them to stay better in the long term and that associated therapy processes might be linked to long-term outcomes. In a recent paper, we reported on the long-term outcomes of this trial and found that symptom reduction in both CT and IPT was maintained up to 17 months after therapy, with the majority of treatment responders staying well over time (Lemmens et al., 2019).

Investigating within-therapy processes as general or differential predictors of subsequent outcome after therapy termination differs from prediction studies in which patient characteristics at baseline are associated with outcome in the acute phase or at follow-up. While the latter might inform us about what works for whom and thus can guide treatment selection (Cohen & DeRubeis, 2018), the former provides insight into (individual) process changes in the course of therapy that are associated with favorable outcomes afterwards, which bears great relevance for the monitoring of individual therapy progress in clinical practice. In that sense, the present paper combines the concept of a process-outcome study (pathways of change) with the methodology of a (time-lagged) prediction study. Only a few studies in the field of depression have modeled within-therapy processes as predictors of *subsequent* outcome in the long term, after therapy has ended. Strunk et al. found that both the development and the independent use of so-called cognitive therapy skills predicted a reduced risk of relapse in patients who responded to CT (Strunk et al., 2007). More recently, Gómez Penedo et al. applied Doss' 4-step model of psychotherapy to investigate

mechanisms of change and found that increased emotional processing during exposure-based cognitive therapy (EBCT) predicted better depression outcome in the long term, while increased cognitive restructuring within-therapy predicted better depression outcome in the long term in both EBCT and CT, although the mediational pathways that were hypothesized were not confirmed (Penedo et al., 2020). The present analysis adds to this literature.

We assessed nine process variables with the aim to capture the underlying mechanisms that may account for the effects of CT and IPT in the context of a randomized trial: four CT-specific variables (dysfunctional attitudes, cognitive reactivity, rumination, attributional style), two IPT-specific variables (interpersonal problems and work and social functioning) and three common factors (hopelessness, self-esteem and therapeutic alliance).

Cognitive change as measured by an improvement in *dysfunctional attitudes* is assumed to be a central mechanism of CT (Beck et al., 1979) and has been associated with an improvement in depression as a result of CT (Cristea et al., 2015). *Cognitive reactivity* refers to the underlying psychological vulnerability after initial treatment response and was found to predict future relapse in both CT and antidepressant medication (Segal et al., 2006). *Rumination* is defined as repetitive thinking about the causes, meanings and implications of feeling depressed and is considered a key process in CT (Watkins et al., 2011). An individual's *attributional style* refers to the explanations one gives why certain events happen and was found to predict outcome in CT and not in pharmacotherapy (DeRubeis et al., 1990).

Interpersonal problems are the key focus in IPT and are assumed to be a central change mechanism (Klerman et al., 1984), although empirical evidence is scarce in this area (Lipsitz & Markowitz, 2013). *Work and social functioning* was found to be a non-specific predictor of outcome in IPT and pharmacotherapy (Frank et al., 2011), but it might also be a proxy for an IPT-specific process of change.

Hopelessness was defined by Beck as generalized negative future expectations as part of the dysfunctional belief system (Beck et al., 1974) and was found to be more associated with suicidality than to depression (Beck et al., 1985). Although conceptualized as part of the cognitive theory, there is no evidence that it is a therapy-specific process. *Self-esteem* and depression are strongly associated (Sowislo & Orth, 2013), but there is no evidence that a positive change in self-evaluations is restricted to a certain type of psychotherapy.

Finally, the *therapeutic alliance* has been associated with psychotherapy outcome in numerous trials

(Fluckiger et al., 2012) and is generally considered to be the most important common factor.

The aim of the present study is to investigate whether change in these specific and common factors during therapy is predictive of depression outcome in the long term, particularly in those patients that show improvement in therapy (i.e., therapy responders) and whether this differs between CT and IPT. We hypothesized, according to theory, that change in CT-specific process factors (i.e., less dysfunctional thinking, less cognitive reactivity, less rumination, and a less dysfunctional attributional style) during therapy would predict depression outcome after successful CT, while IPT-specific process factors (e.g., less interpersonal problems and better work and social functioning) during therapy would predict depression outcome after successful IPT. We hypothesized that changes in common factors during therapy would be predictive of long-term outcome in both CT and IPT.

Methods

Design and Participants

Data came from a randomized controlled trial into the effectiveness and mechanisms of change of individual CT and IPT for major depressive disorder (MDD). More details about the methods can be found in the original protocol paper (Lemmens et al., 2011). 182 Adult outpatients (18–65 years) were recruited from the mood disorder unit of the Academic Community Mental Health Centre Maastricht. Inclusion criteria were a primary diagnosis of MDD (confirmed with the Structured Clinical Interview for DSM-IV Axis I disorders; First et al., 1995), internet access, an email address, and sufficient knowledge of the Dutch language. Individuals with bipolar or highly chronic depression (current episode > 5 years) were excluded from the study. Other exclusion criteria were a high acute suicide risk, concomitant pharmacological or psychological treatment, drugs and alcohol abuse/dependence, and insufficient cognitive capacities for psychotherapy. After providing written informed consent, participants were randomly assigned to CT ($n = 76$), IPT ($n = 75$), or a 2-month waiting-list control followed by treatment of choice ($n = 31$).

Treatments

Treatment consisted of 16–20 individual 45-min sessions ($M = 17$, $SD = 2.9$) that were planned weekly and were allowed to be less frequent towards the

end of therapy. CT was carried out following the guidelines by Beck et al. (1979), IPT was based on the manual by Klerman et al. (1984). Therapists were ten licensed psychologists, psychotherapists and psychiatrists (five in each condition) with substantial clinical experience ($M=9.1$ years, $SD=5.4$). For both CT and IPT, treatment quality was rated by independent assessors as “(very) good” to “excellent” (Lemmens et al., 2015). During follow-up, individuals were free to seek additional treatment for MDD. Additional treatment was defined as psychological support (one or more sessions with a general practitioner or a mental health care professional) and/or the use of antidepressant medication.

35 patients (41.2% of 85 responders) were still in treatment at the end of the acute phase (month 7). Of these 35 patients, 16 were assigned to CT and 19 to IPT. The mean number of sessions in this group at this time point was 14.11 ($SD=2.74$) and on average these patients had a total of 17.29 ($SD=2.74$) sessions, comparable to the group that finished within 7 months. Most of these patients started on time but did not manage to complete therapy because of planning problems. Instead of weekly sessions, these patients sometimes received biweekly sessions or had even longer intervals between sessions (because of holidays of the patient or the therapist). Since we consider these patients treatment completers in the final stage of therapy at the time of 7-month assessment we included them in the analyses.

Measures

Primary outcome: Primary outcome was depression severity measured with the Beck Depression Inventory, second edition (BDI-II, Beck et al., 1996) during follow-up (7–24 months). The BDI-II is a 21 item self-report questionnaire with items rated on a 4-point Likert scale (0–3) with higher scores indicating higher levels of depression severity (range is 0–63). The BDI has strong psychometric properties (Beck et al., 1996; Van der Does, 2002a).

Specific CT Processes

Dysfunctional attitudes—The presence and intensity of dysfunctional beliefs or attitudes were assessed with the 17-item Dysfunctional Attitudes Scale (form A) Revised (DAS-A17); (de Graaf et al., 2009). Respondents rate the extent to which they agree with a series of dysfunctional assumptions. Items are rated on a 7-point Likert scale (1 = fully disagree to 7 = fully agree). Higher scores reflect

more negative and absolute thinking (range is 17–119). Psychometric properties of the DAS-A17 are good (de Graaf et al., 2009). Cronbach’s α in this study at baseline was 0.89 and 0.91 post-treatment (month 7).

Cognitive reactivity—The Leiden Index of Depression Sensitivity (LEIDS; Van der Does, 2002b) was included as a measure of cognitive reactivity (i.e., the relative ease with which negative patterns of thinking can be reactivated by minor triggers such as subtle mood fluctuations). The LEIDS assesses whether and how patients expect their thinking patterns to change when they experience mild dysphoria. The 34 items of this questionnaire are rated on a 4-point Likert scale ranging from “not at all” to “very strongly”. Psychometric properties are good (Van der Does, 2002b). Cronbach’s α in this study at baseline was 0.87 and 0.89 post-treatment (month 7).

Rumination—The Ruminative Response Scale (RRS-NL; Raes et al., 2003) was used to obtain a measure of rumination. The RRS-NL includes 22 items describing responses to depressed mood. Participants read each item and indicate how often they think or do this when they feel sad or depressed. Items are rated on a 4-point Likert scale ranging from almost never (1) to almost always (4). The total score is the sum of the 22 items (range is 22–88). Reliability and validity have found to be satisfactory (Raes et al., 2003). Cronbach’s α in this study at baseline was 0.86 and 0.93 post-treatment (month 7).

Attributional style—Attributional style—a persons’ explanation of why events happen—was measured with the Attributional Style Questionnaire (ASQ; Peterson et al., 1982). The ASQ presents respondents with 12 hypothetical events.¹ Respondents are asked to carefully read the events, imagine themselves in every scenario, and decide on the major cause in case this would happen to them. After that, they rate this cause along a 7-point Likert scale for three causal dimensions: personal, permanent and pervasive. The psychometric properties of the Dutch translation of the ASQ are comparable to those of the original ASQ (Peterson et al., 1982), which suggests that the ASQ can be used in the Dutch population (Cohen et al., 1986). Cronbach’s α in this study at baseline was 0.71 and 0.78 post-treatment (month 7).

Specific IPT Processes

Interpersonal problems—Interpersonal problems were assessed with the 64-item version of the Inventory of Interpersonal Problems (IIP-64; Horowitz et al.,

1988). The IIP is a self-report measure that describes the types of problems that people experience in their relationships with others, and the level of distress associated with this. Items are rated on a 5-point Likert scale (0–4) with higher scores indicating more interpersonal problems (range is 0–256). Psychometric properties are good (Horowitz et al., 1988). Cronbach's α in this study at baseline was 0.92 and 0.96 post-treatment (month 7).

Work and social functioning—To measure the experiential impact of the disorder, the Work and Social Adjustment Scale (WSAS; Mundt et al., 2002) was used. This 5-item self-report scale examines to what extent the disorder impairs a person's everyday functioning in five domains. Items are rated on a 9-point Likert scale, with higher scores indicating more severe impairment. Psychometric properties of the WSAS are good (Mataix-Cols et al., 2005; Mundt et al., 2002). Cronbach's α in this study at baseline was 0.76 and 0.89 post-treatment (month 7).

Non-specific Processes

Hopelessness—The Beck Hopelessness Scale (BHS; Beck et al., 1974) is a self-report instrument that determines the extent of positive and negative beliefs about the future over the previous 7 days using 20 true-false statements. All statements are scored 0 or 1 with the total being calculated by summing the pessimistic responses for the items. The BHS has been shown to have good psychometric properties for application in clinical samples (Beck & Steer, 1988; Dyce, 1996). Cronbach's α in this study at baseline was 0.88 and 0.91 post-treatment (month 7).

Self-Esteem—The Self-Liking and Self-Competence Scale Revised (SLSC-R; Tafarodi & Swann, 2001) is a self-report measure of self-competence and self-liking, two dimensions of self-esteem. The SLSC-R contains eight items each rated on a 5-point Likert scale, for each of the two dimensions. Subscale scores can range from 8 to 40, with higher scores indicating higher self-competence or higher self-liking. A total score is calculated by summing the score of the two subscales. Psychometric properties are good (Vandromme et al., 2007). Cronbach's α in this study at baseline was 0.90 and 0.92 post-treatment (month 7).

Therapeutic alliance—The observer-rated version of the Working Alliance Inventory—Short (WAI-O-S; Tichenor & Hill, 1989) was used to obtain a measure of the quality of the therapeutic alliance, based on videotapes of the therapy sessions. The WAI-O-S is based on the assumption that a

strong alliance forms if a therapist and client (a) agree on the *goals* of therapy, (b) agree on the *tasks* needed to meet those goals, and (c) have a *bond* between them that will facilitate this process. Each of the 12 items of the scale (4 for each subscale) are rated on a 7-point scale (1 = never, to 7 = always) and a higher score indicates a stronger alliance. A total score is obtained by summing up all item scores (range is 12–84).

In order to obtain a measure of alliance comparable to the fixed assessment points of the self-report data, we selected videotaped therapy sessions that were closest to the assessment points at baseline and 7 months. Eight students and four experts rated the alliance. The number of tapes per rater ranged from 1 to 4. The intraclass correlation coefficient (ICC) for the subscales and total scale for the tapes that were rated twice ranged (129 out of 261 in total) from 0.705 to 0.847, which is considered to be good. Further details on the rating of therapeutic alliance can be found elsewhere (Lemmens et al., 2017). Psychometric properties are good (Horvath, 1994). Cronbach's α in this study at baseline was 0.94 and 0.94 post-treatment (month 7).

Procedure

Study protocol was approved by The Medical Ethics Committee of Maastricht University and registered at The Netherlands Trial Register (ISRCTN 67561918). Participants were recruited during regular intakes at our clinical site between 2007 and 2014. The main assessment points for the BDI-II in the original RCT were baseline, 3, 7, 9, 12 and 24 months. Process measures were assessed at baseline, 3 and 7 months. All assessments were administered on a computer. Pre- and post-treatment assessments (baseline and 7 months) were administered at the research center. Mid-treatment (3 months) and follow-up assessments (9–24 months) took place online.

For the current analyses, we mainly focused on the 85 treatment responders (i.e., patients whose BDI-II scores had decreased by at least 9 points by the end of therapy in combination with a post-treatment BDI-II score lower than 20 or patients with a post-treatment BDI-II score lower than 10; CT $n = 45$, IPT $n = 40$) out of 134 patients who were randomized to one of the active conditions (CT/IPT) and provided post-treatment data (88.7% of 151). The choice to focus on responders follows from our study aim to investigate whether improvement in therapy can be linked to certain changes in therapy processes and subsequent outcome at follow-up. Pre- to post-treatment change (from month 0, 3

and 7) on nine psychological process variables and outcome data from the post-treatment follow-up phase (from month 7, 9, 12 and 24) were used in the analyses.

Data Analysis

We computed *psychological process change variables* for all non-missing psychological process measures by subtracting the post-treatment score from the baseline score. We then compared the baseline, post-treatment and change scores on the psychological process scales between responders ($n = 85$) and non-responders ($n = 49$) using paired t -tests.

To examine the impact of psychological process change during treatment on BDI-II change throughout follow-up, mixed-effects (multilevel) models were applied. First, rates of change of the psychological process measures during treatment were estimated for each individual. This was done by building mixed-effects models with the repeated psychological process measures (at 0, 3 and 7 months) as dependent outcome, and time as independent outcome. From these models, individual slopes were extracted indicating the rate of change of the various psychological process measures for each individual. Second, we built separate univariable models to explore the impact of psychological process variables with repeated follow-up BDI-II scores (measured at 7, 9, 12 and 24 months) as dependent variable and the following fixed effects as independent variables: time, treatment (CT or IPT), time-by-treatment interaction, and the slope of the psychological process variable together with its interactions with treatment, time and treatment-by-time. As the factor of individual therapists did not impact the acute and follow-up depression severity change (Lemmens et al., 2015; Lemmens et al., 2019), we did not include this in our current analysis.

Because of sample size, it was decided to build separate multivariable models for general and differential predictors. The psychological process variables (slopes) were carried through to this next step depending on their significance level ($p < 0.05$) in the univariable models and were either included in the *multivariable general predictor model* (i.e., main effects) or the *multivariable differential predictor model* (i.e., main effect interactions with treatment). Both multivariable models used the repeated follow-up BDI-II scores as the dependent variable and time, treatment, selected psychological process variables (slopes), and their interactions with time as independent variables. The independent variables of multivariable differential predictor model included time, treatment, time-by-treatment, selected psychological

process variables (slopes), and their interactions with treatment, time and treatment-by-time. The significance level in the *multivariable general predictor model* was set at $p = 0.05$ and at $p = 0.10$ in the *multivariable differential predictor model* (because of the sample size and the two- and three-way interactions).

Model assumptions (i.e., testing the model residuals for normality and homoscedasticity) were checked. Standardized health-related quality of life (EQ-5D-3L utility score; EuroQolGroup, 1990) was added as a covariate to all univariable and multivariable mixed-effect models, since this baseline measure differed between CT and IPT (albeit not significant, see Lemmens et al., 2015) in the original randomized trial. The Dutch value set was used to translate response patterns into utilities (Lamers et al., 2006). All models were also adjusted for the slope of the BDI-II between 0 (baseline) and 7 months (post-treatment), to assess the association of process changes with outcome independent of depression change. Since “additional psychological and/or pharmacological treatments received during follow-up” did not impact long-term depression outcome (Lemmens et al., 2019), we chose not to control for it in the current analyses. Time was modeled as a linear function with the endpoint (month 24) coded as zero, which was considered the best fit compared to other transformations of time (quadratic, loglinear) using visual inspection and fit indices. In all models, intercepts and slopes were random and were allowed to be correlated. For the residuals, an autoregressive covariance structure was applied to take the correlation between consecutive measurements points into account. The treatment variable was centered (CT = -0.5 or IPT = 0.5).

Results

Missing Data, Baseline Characteristics and Change Scores

Scores on the WSAS, SLSC and IIP each had 1 value missing (0.005% of the total values). On the WAI, however, 53 values were missing, mostly because videotapes of the sessions were not available. The impact of these missing values was partly handled by using estimated slopes in the mixed-effect models based on at least two data values measured at 0, 3 and 7 months, resulting in only 24 missing slopes (28.2%). Of the BDI-II outcomes at 7, 9, 12 and 24 months, 31 values were missing (5.2%). Missing values were not imputed because multilevel models can deal with them (through pairwise deletion), however, all observations were used.

Table I. Baseline characteristics, pre-treatment, post-treatment and change score comparisons of psychological process measures between responders ($n = 85$) and non-responders ($n = 49$).

	Baseline		Post-treatment		Change scores				<i>t</i> -value	<i>p</i> -value
	Responders	Non-responders	Responders	Non-responders	Responders	Range	Non-responders	Range		
Female sex, <i>n</i> (%)	56 (65.9)	35 (71.4)	–	–	–	–	–	–	–	–
Age in years	41.6 (11.3)	42.6 (13.4)	–	–	–	–	–	–	–	–
Education, <i>n</i> (%)										
Low	18 (21.2)	8 (16.3)	–	–	–	–	–	–	–	–
Medium	48 (56.5)	28 (57.1)	–	–	–	–	–	–	–	–
High	19 (22.3)	13 (26.6)	–	–	–	–	–	–	–	–
Partner, yes, <i>n</i> (%)	54 (63.5)	31 (69.4)	–	–	–	–	–	–	–	–
Active employment, yes, <i>n</i> (%)	55 (64.7)	24 (49.0)	–	–	–	–	–	–	–	–
Depression severity (BDI-II)	27.8 (9.0)	31.9 (8.0)	–	–	–	–	–	–	–	–
Recurrent depression, <i>n</i> (%)	44 (51.8)	21 (42.9)	–	–	–	–	–	–	–	–
Dysfunctional Attitudes (DAS), <i>m</i> (<i>SD</i>)	59.8 (16.6)	64.8 (15.1)	47.6 (14.2)	62.7 (14.5)	–12.2 (14.7)	–56 to 25	–2.1 (14.0)	–36 to 35	3.91	0.0001
Cognitive Reactivity (LEIDS), <i>m</i> (<i>SD</i>)	48.0 (17.1)	50.7 (14.2)	33.8 (17.0)	47.8 (11.6)	–14.2 (17.0)	–74 to 19	–2.9 (10.9)	–22 to 20	4.18	0.0001
Rumination (RRS), <i>m</i> (<i>SD</i>)	49.8 (9.1)	51.8 (8.9)	37.3 (9.4)	50.3 (10.3)	–12.5 (10.7)	–39 to 10	–1.5 (10.4)	–18 to 33	5.79	<0.0001
Attributional Style (ASQ), <i>m</i> (<i>SD</i>)	0.003 (1.1)	0.1 (1.1)	0.7 (1.0)	0.2 (1.0)	0.7 (1.1)	–2.3 to 4.1	0.1 (1.0)	–2.1 to 2.9	–2.89	0.0045
Hopelessness (BHS), <i>m</i> (<i>SD</i>)	11.3 (5.1)	12.5 (4.4)	4.4 (3.3)	12.3 (4.5)	–6.9 (5.2)	–18 to 3	–0.2 (4.2)	–9 to 11	7.67	<0.0001
Work and Social Functioning (WSAS), <i>m</i> (<i>SD</i>)	22.1 (7.2)	24.2 (8.1)	11.6 (9.0)	21.9 (8.1)	–10.4 (10.7)	–32 to 14	–2.3 (6.9)	–14 to 11	4.77	<0.0001
Self-esteem (SLSC-R), <i>m</i> (<i>SD</i>)	38.6 (10.4)	38.9 (9.3)	47.4 (11.4)	38.7 (8.7)	8.8 (9.1)	–7 to 34	–0.2 (7.0)	–13 to 25	–6.04	<0.0001
Interpersonal Problems (IIP), <i>m</i> (<i>SD</i>)	82.0 (29.2)	90.6 (31.9)	55.1 (34.8)	88.1 (30.4)	–27.0 (32.3)	–117 to 34	–2.5 (19.8)	–47 to 52	4.81	<0.0001
Therapeutic Alliance (WAI-O-S), <i>m</i> (<i>SD</i>)	66 (8.4)	64.4 (6.8)	70.9 (8.9)	63.4 (10.6)	6.2 (6.9)	–7 to 24	–0.8 (10.7)	–26 to 18	–2.96	0.0046

SD = standard deviation, BDI-II = Beck Depression Inventory II, DAS = Dysfunctional Attitudes Scale, LEIDS = Leiden Index of Depression Sensitivity, RRS = Ruminative Response Scale, ASQ = Attributional Style Questionnaire, BHS = Beck Hopelessness Scale, WSAS = Work and Social Adjustment Scale, SLSC-R = Self Liking and Self Competence Scale Revised, IIP = Inventory of Interpersonal Problems, WAI-O-S: Observer rated version of the Working Alliance Inventory—Short.

Table I shows the baseline characteristics and pre-treatment (baseline) scores, post-treatment scores and change scores on the psychological process variables over the course of psychotherapy (0–7 months), stratified per response category. Responders had significantly lower BDI-II scores at baseline than non-responders ($p = 0.008$). All other baseline characteristics and process variables did not differ significantly at baseline between responders and non-responders. Average pre-post-treatment change scores were significantly different between responders and non-responders on all process variables ($p < 0.01$), with responders showing the greater change in the favorable direction.

Univariable Analyses

Changes on the LEIDS, ASQ, BHS and WAI during therapy were not associated with depression scores at follow-up. The slopes of the SLSC and the RSS demonstrated a main effect on outcome, meaning that change in these variables was associated with BDI-II scores at the end of follow-up (24 months). The slope of the DAS showed a main effect interaction with time, meaning that a decrease in the DAS predicted a decrease in BDI-II scores during the follow-up. The slopes of the WSAS and the IIP demonstrated three-way interactions with main effects, time and treatment (CT or IPT), which means that the change in BDI-II scores predicted by these variables differed between CT and IPT. It should be noted that this was borderline significant for the WSAS ($p = 0.59$) but we decided to carry it through to the differential predictor model anyway, together with the IIP.

The SLSC, DAS and RRS were therefore selected as potential predictors for the multivariable general predictor analysis. The WSAS and IIP were selected as potential predictors for the multivariable differential predictor analysis.

Multivariable General Predictor Analysis

The results of the multivariable predictor analysis are displayed in Table II. Of the three candidate predictors, only change on the DAS (i.e., less dysfunctional thinking) during therapy (0–7 months) predicted a decrease in BDI scores over time (7–24 months). The slope of the SLSC displayed the main effect (albeit borderline significant), showing that change on the SLSC (i.e., more self-liking and self-competence) during therapy was associated with lower BDI-scores at the end of follow-up (since lower order effects reflect the effect of that variable at the

Table II. Results of the multivariable mixed-effect model estimating the impact of the general predictors selected from the univariable analyses.

	Fixed effects		
	β	SE	<i>P</i>
Intercept	9.37	6.05	0.121
Depression (BDI-II)	-5.95	0.90	<0.001
Baseline health-related quality of life (EQ-5D-3L)	-1.07	0.50	0.032
Time	0.16	0.37	0.663
Condition	0.92	2.15	0.669
Condition * time	-0.17	0.14	0.901
Dysfunctional Attitudes (DAS)	4.66	1.44	0.001
Dysfunctional Attitudes (DAS) * time	0.23	0.09	0.016
Rumination (RRS)	1.38	2.81	0.624
Rumination (RRS) * time	-0.08	0.18	0.659
Self-esteem (SLSC-R)	-5.54	3.18	0.082
Self-esteem (SLSC-R) * time	0.09	0.21	0.644

SE = Standard Error, BDI-II = Beck Depression Inventory II, EQ-5D-3L = EuroQol Utility Score, Condition = Cognitive Therapy or Interpersonal Psychotherapy, DAS = Dysfunctional Attitudes Scale, RRS = Ruminative Response Scale, SLSC-R = Self-Liking and Self-Competence Scale—Revised.

intercept and we centered the time variable at the end of follow-up).

Figure 1 displays the association over time based on two subgroups (median split on the slope): responders who showed a high improvement in dysfunctional attitudes ($n = 43$) had lower depression scores at follow-up compared to responders who showed low improvement in dysfunctional attitudes ($n = 42$). As can be seen, the difference in BDI scores between the subgroups grew over time.

Figure 2 shows the same approach for the SLSC. Responders with a high improvement in self-liking and self-competence ($n = 43$) had somewhat lower depression scores at follow-up compared to responders who showed low improvement in self-liking and self-competence ($n = 42$), but the difference between the subgroups was not large and remained more or less constant over time.

Multivariable Differential Predictor Analysis

The results of the multivariable differential predictor analysis are displayed in Table III. For the WSAS, an interaction between main effect and treatment (and no longer with time) was found, which indicates different associations of the WSAS and outcome at follow-up in CT and IPT. The IIP showed an interaction between main effect, treatment and time, indicating that the IIP predicted different change patterns of depression scores in CT and IPT.

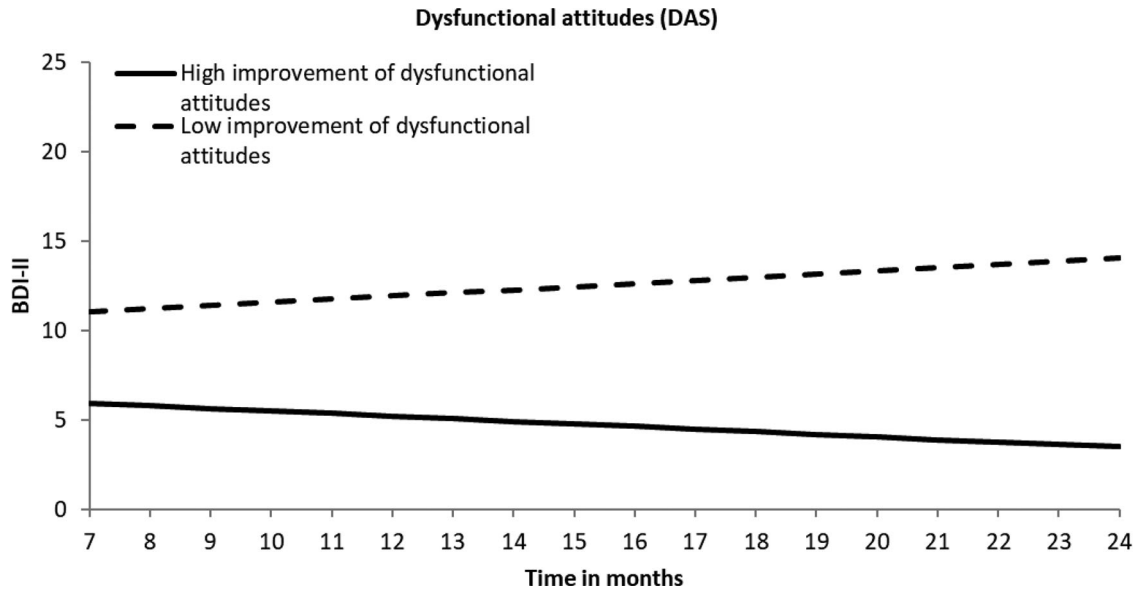


Figure 1. Estimated means of the average BDI-II scores at follow-up (7–24 months) of individuals with high improvement in dysfunctional attitudes ($n = 43$) and with low improvement in dysfunctional attitudes ($n = 42$).

Figure 3 illustrates the moderated effect on the WSAS. First, high improvement in work and social functioning during therapy was associated with better depression outcomes at follow-up in IPT relative to CT, while low improvement in functioning was associated with (somewhat) better outcomes in CT relative to IPT. Second, change on the WSAS had a strong predictive value in the IPT group. Patients who showed high improvement during IPT ($n = 19$) had on average lower and decreasing BDI-II scores during the follow-up, while those with low

improvement during IPT ($n = 21$) had on average higher and (somewhat) increasing BDI-II scores during the follow-up. So, for IPT high improvement in functioning is associated with a better outcome, while low improvement in functioning is associated with a worse outcome. The WSAS had also some predictive value in CT, with a similar pattern but far less pronounced compared to IPT.

Figure 4 displays similar patterns for the IIP, but noticeably stronger compared to the WSAS. Those with low improvement in interpersonal problems

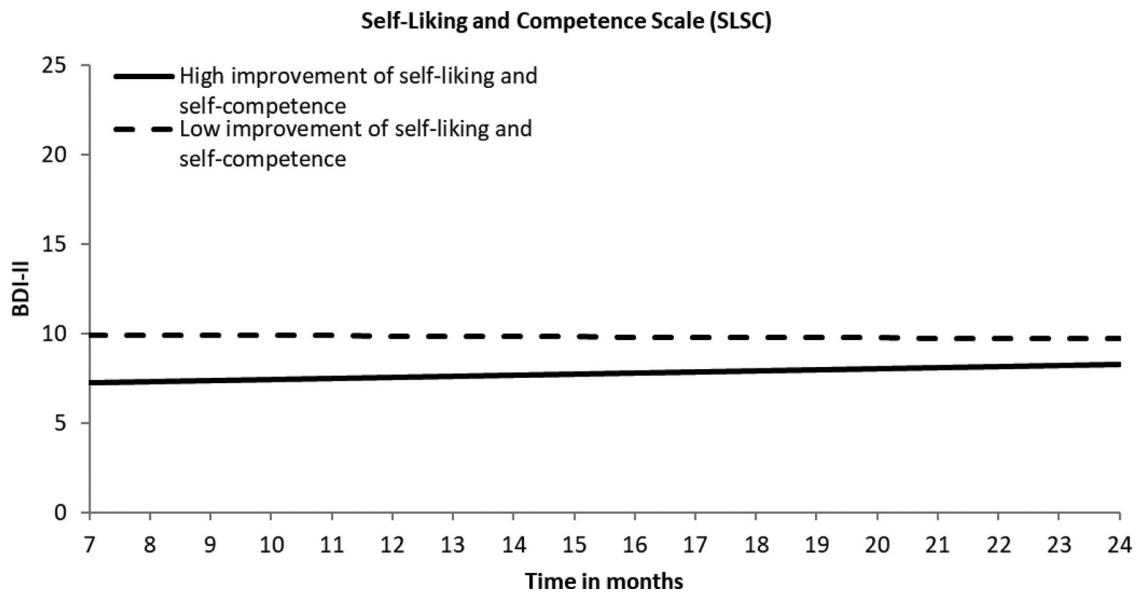


Figure 2. Estimated means of the average BDI-II scores at follow-up (7–24 months) of individuals with high improvement in self-liking and self-competence ($n = 43$) and with low improvement in self-liking and self-competence ($n = 42$).

Table III. Results of the multivariable mixed-effect model estimating the impact of the differential predictors selected from the univariable analyses.

	Fixed effects		
	β	SE	<i>P</i>
Intercept	2.03	4.47	0.649
Depression change score (BDI-II)	-4.42	0.71	<0.001
Baseline health-related quality of life (EQ-5D-3L)	-0.31	0.48	0.509
Time	-0.34	0.24	0.162
Condition	18.66	7.52	0.013
Condition * time	0.85	0.48	0.079
Work and Social Functioning (WSAS)	2.63	2.86	0.359
Work and Social Functioning (WSAS) * time	-0.21	0.18	0.233
Work and Social Functioning (WSAS) * condition	9.95	5.65	0.078
Work and Social Functioning (WSAS) * time * condition	0.27	0.36	0.449
Interpersonal Problems (IIP)	0.55	0.59	0.261
Interpersonal Problems (IIP) * time	-0.01	0.03	0.843
Interpersonal Problems (IIP) * condition	0.97	1.19	0.416
Interpersonal Problems (IIP) * time * condition	0.013	0.07	0.095

SE = Standard Error, BDI-II = Beck Depression Inventory II, EQ-5D-3L = EuroQol Utility Score, Condition = Cognitive Therapy or Interpersonal Psychotherapy, WSAS = Work and Social Adjustment Scale, IIP = Inventory of Interpersonal Problems.

during therapy showed increasing BDI scores at follow-up in the IPT group ($n = 22$) but decreasing BDI scores at follow-up in the CT group ($n = 20$). In those with high improvement, the pattern was reversed: those who received CT ($n = 25$) showed increasing BDI scores over time while those in the IPT group ($n = 18$) showed decreasing BDI scores. The IIP had therefore strong predictive value in both the IPT and CT group.

Full Sample Analyses

We repeated these analyses in the full sample (134 responders and non-responders) as a sensitivity and specificity analysis. The results and a brief discussion can be found in the online supplementary material.

Discussion

Main Findings

In this paper, we investigated nine psychological process change measures as potential predictors of long-term depression severity in treatment responders, and found that changes in dysfunctional attitudes, rumination, work and social functioning,

self-esteem and interpersonal functioning during therapy univariably predicted subsequent outcome, while changes in cognitive reactivity, attributional style, hopelessness and therapeutic alliance did not.

Change in dysfunctional attitudes during therapy emerged as a significant predictor in the multivariable general predictor analysis. It was found that a stronger decrease in dysfunctional attitudes during therapy was associated with a further decrease in depression in the long term. Increased self-esteem was associated with lower depression scores at the end of follow-up, but the significance was borderline. In the multivariable differential predictor analysis, change in work and social functioning and change in interpersonal problems both emerged as predictors (also called moderators). It was found that high improvement in work and social functioning and in interpersonal problems during therapy was associated with better depression outcomes at follow-up in IPT relative to CT, while less improvement in these processes was associated with better outcomes in CT relative to IPT. Work and social functioning had some predictive value in responders who received CT, but considerably less than the predictive value in responders who received IPT. Interpersonal problems on the other hand had strong predictive value in both IPT and CT.

Our hypotheses were partly confirmed. A CT-specific process factor (dysfunctional attitudes) predicted subsequent depression outcome in both CT and IPT, while two IPT-specific process factors (work and social functioning and interpersonal problems) predicted differential outcome in IPT vs CT. Self-esteem, a common factor, was associated with long-term depression outcome in both CT and IPT.

Interpretation of Findings

The predictive value of dysfunctional attitudes or negative thinking is in line with previous studies that showed that changes in dysfunctional attitudes and depression are strongly associated in the context of psychotherapy. Lorenzo-Luaces et al. (2015) reviewed the literature and found that cognitive change (i.e., less negative thinking) contributes to depression symptom change. In a meta-analysis, Cristea et al. (2015) also found a strong association between treatment effects on dysfunctional thinking and depression, in CT but in other psychotherapies and pharmacotherapy as well. Moreover, we found a temporal relation, with change in negative thinking predicting subsequent depression outcome after the correction for change on the BDI, which speaks to the specificity of cognitive change as an important

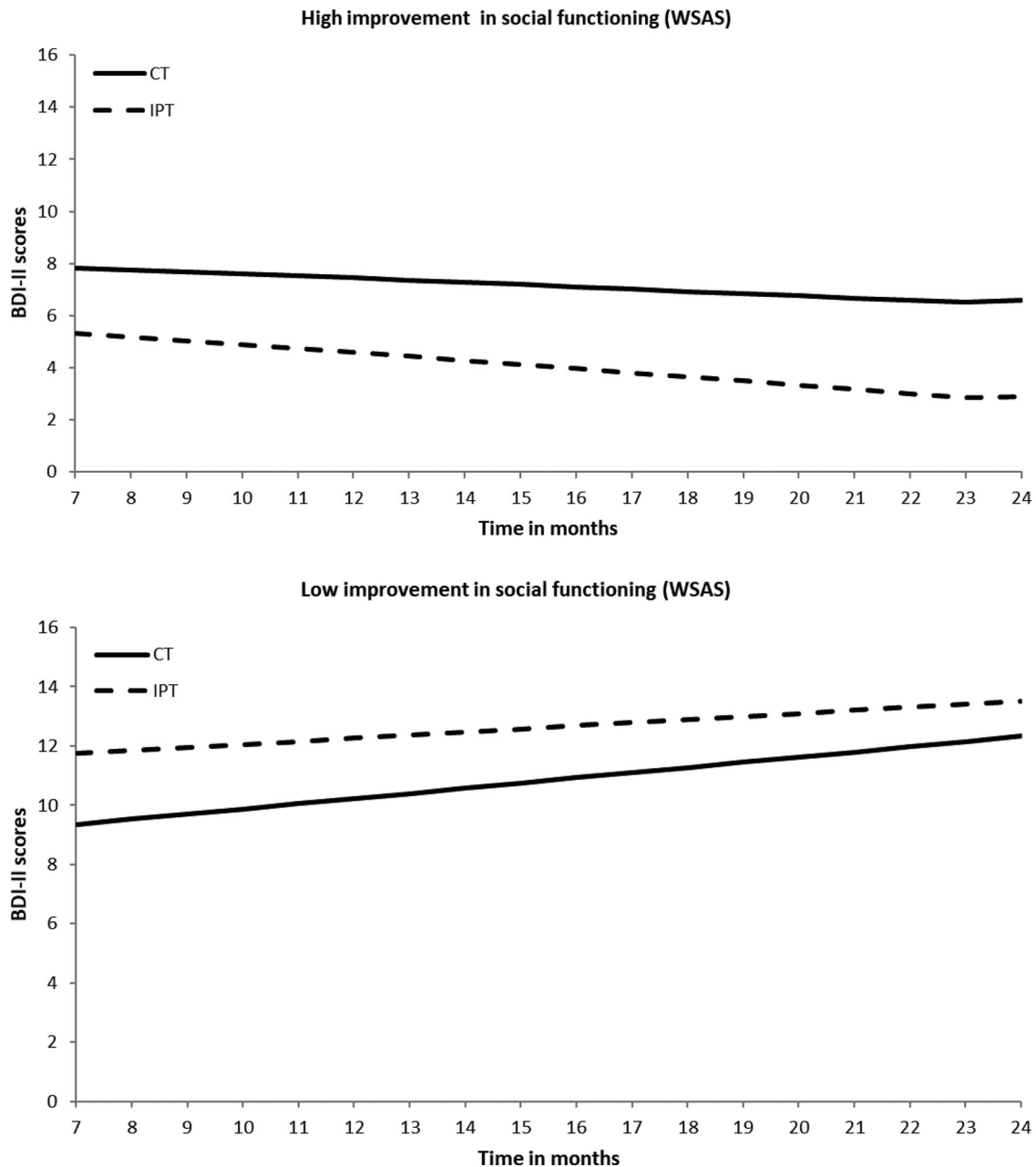


Figure 3. Estimated means of the average BDI-II scores at follow-up (7–24 months) of individuals with high improvement in social functioning who received CT ($n = 24$) and IPT ($n = 19$) and of individuals with low improvement in social functioning who received CT ($n = 21$) and IPT ($n = 21$).

therapy process. This is in line with a recent study by Schmidt et al. (2019), who applied a fine-grained session-to-session analysis to demonstrate that the relation between immediate cognitive change in a previous CT session and subsequent depression change in the following session was mediated by the sustained cognitive change measured at the beginning of the following session. Moreover, both immediate and sustained cognitive change predicted subsequent symptom change, and the only variable that predicted

immediate cognitive change was therapist adherence to cognitive methods. The Schmidt et al. study not only reveals that cognitive change predicts symptom change, but also highlights cognitive change as an important mechanism of change, at least in CT. In another analysis of the same sample, it was found that the predictive relation between cognitive change and symptom change was moderated by self-perceived social skills and the level of interpersonal problems (with a stronger prediction in those with fewer skills and greater

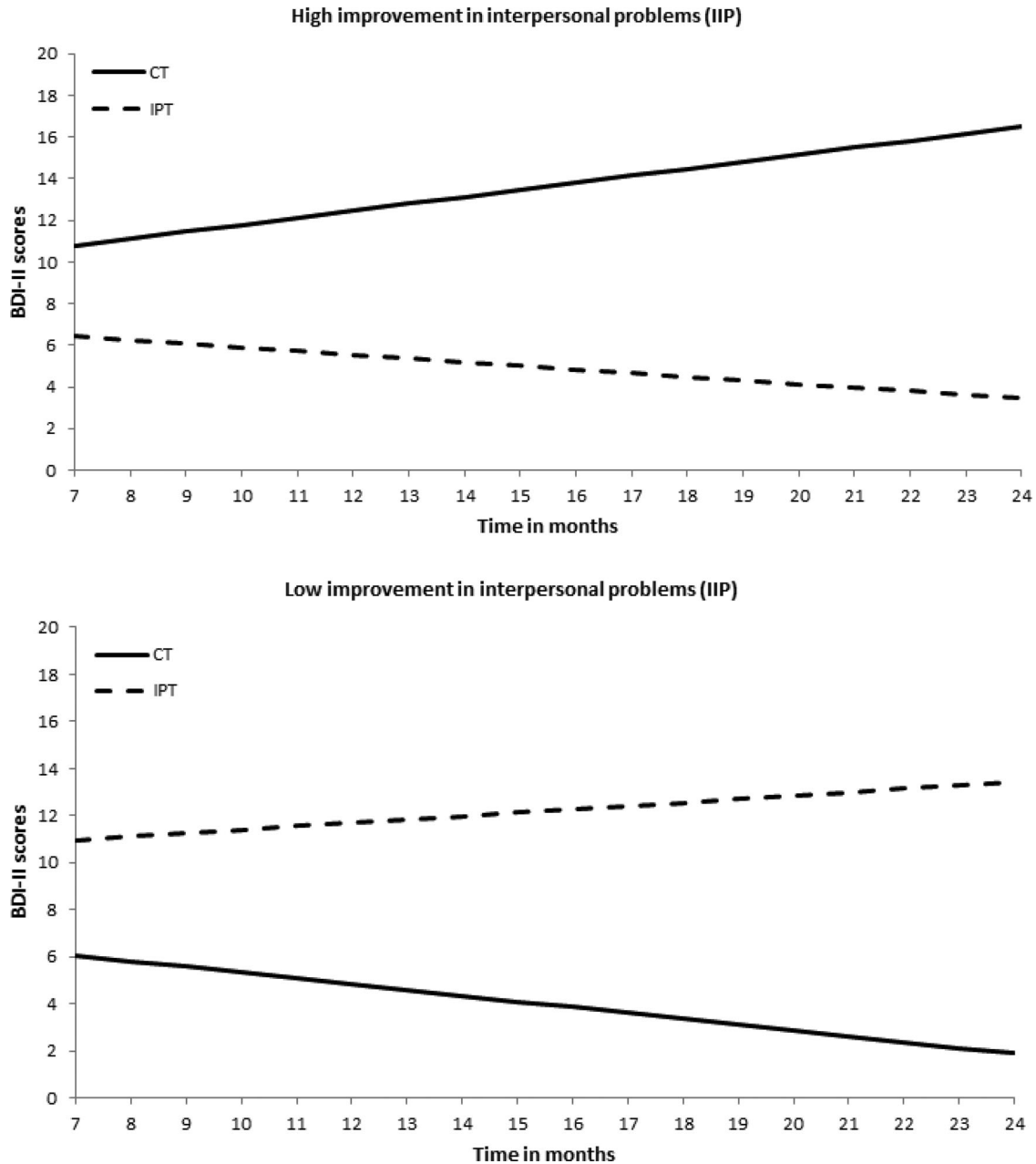


Figure 4. Estimated means of the average BDI-II scores at follow-up (7–24 months) of individuals with high improvement in interpersonal problems who received CT ($n = 25$) and IPT ($n = 18$) and of individuals with low improvement in interpersonal problems who received CT ($n = 20$) and IPT ($n = 22$).

problems), which is interesting in the context of the current analysis (Fitzpatrick et al., 2020).

Self-esteem has been associated with depression in numerous studies (Sowislo & Orth, 2013). For example, in a narrative review of 62 studies from a prospective cohort study (NESDA) with 2981 participants, low self-esteem was found to be a risk factor for depression and anxiety, while implicit self-esteem predicted the persistence and recurrence of depression and anxiety (Struijs et al., 2021). We could not find studies in which change in self-

esteem was evaluated as a predictor of (differential) response in CT and IPT for depression.

Less is known about the role of work and social functioning (WSAS) and interpersonal problems as specific process factors in CT or IPT, compared to dysfunctional attitudes. In theory, work and social functioning and interpersonal problems are particularly important in IPT with its focus on interpersonal relations. Studies have shown that interpersonal functioning changes in the course of IPT (Ravitz et al., 2019). Bernecker et al. for example

investigated several cognitive and interpersonal changes during IPT, and found that only reduced romantic functioning was related to post-treatment depression reduction (Bernecker et al., 2014). Interpersonal problems as measured with the IIP is a typical process measure for IPT, but the suitability of the IIP as a theory-specific mediator has been questioned (Lemmens et al., 2017). Interestingly, both the IIP and the WSAS were retained in the multivariable analysis, even though they seem to slightly suppress each other's effect (which might also indicate that they tap into the same construct). It should also be noted that the WSAS measures *beliefs* about the impact on one's depression. In CT and IPT, patients might be learning different ways of thinking about their depression—with patients in IPT being encouraged to adopt the “sick role”—and this may in part explain the differential predictive value.

High improvement on the WSAS predicted a better outcome in IPT compared to CT, although outcomes in both CT and IPT responders in this subgroup of WSAS improvers remained well below an average mean of 10 on the BDI, the cut-off point for depression. In the subgroup whose WSAS scores demonstrated low improvement in functioning during therapy, BDI scores at follow-up were lowest in CT responders but the difference with IPT responders was not very large. This also illustrates that WSAS change scores had predictive power mostly in IPT, with very different BDI outcomes for those with high and low functioning. It could mean that improvement in work and social functioning in therapy is needed to keep IPT responders well after therapy, while less improvement might indicate that important issues were not dealt with properly—in or outside therapy—with less favorable depression outcomes at follow-up despite an initial response post-treatment. In IPT it appears that WSAS change scores can be seen as indicators of therapy progress, which might bear relevance for clinical practice. In contrast, change in interpersonal problems had strong predictive value in both CT and IPT and could be valuable as a monitoring tool in both therapies. However, it should be noted that administration of the IIP is considerably more time-consuming than the WSAS, which might limit its usability.

The four process factors that did *not* show any association with depression outcome were therapeutic alliance (WAI), attributional style (ASQ), hopelessness (BHS) and cognitive reactivity (LEIDS). Therapeutic alliance has been shown to predict subsequent depression in CT in recent studies (Lorenzo-Luaces et al., 2014; Lorenzo-Luaces et al., 2016; Webb et al., 2011). Although

the change score in this paper differed significantly between responders and non-responders, we previously reported that the overall change in therapeutic alliance was small in our sample (Lemmens et al., 2017), mainly because the average alliance was already high at the start of therapy. Cognitive reactivity as measured with the LEIDS was shown to predict relapse in treatment responders in several studies (Figuroa et al., 2015; Segal et al., 2006). A logical explanation for the lack of association in this study (besides other study differences) is that we did not look at relapse specifically but at depression outcome in general, which are related but not equivalent constructs. A statistical explanation for the lack of association of the LEIDS, but also the ASQ and BHS with subsequent depression outcome is that these constructs overlap to great extent with depressive symptomology and are suppressed when controlling for BDI change.

In line with our mediation analysis (Lemmens et al., 2017), we did not find evidence for differential pathways of change for CT and IPT, except for the differential prediction effect of work and social functioning and interpersonal problems. Unraveling the mechanisms of change requires highly sophisticated designs and is extremely challenging (Huibers et al., 2020) and few studies up to date meet the necessary criteria for this kind of research (Cuijpers et al., 2019). Our study could be considered as preliminary evidence for the specificity of work and social functioning and interpersonal problems as process factors in IPT, in the absence of a large sample size, experimental tests and replication. However, while the WSAS and the IIP emerged as differential predictors, the DAS and the SLSC were general predictors of outcome in both therapies, which could be interpreted as preliminary evidence that not only self-esteem but dysfunctional thinking too is in fact a *common factor* in both therapies, regardless of how this change comes about.

Strengths and Limitations

Strengths of the current study include the temporal design, the multiple process variables that were examined in a multivariable analysis, and the two-year follow-up.

A major limitation is the relatively small sample size of the responder sample. We included 182 patients in the original randomized trial, but in the primary analysis only 85 therapy responders out of 151 patients in the active conditions could be included. To visualize the predicting and moderating effects of DAS, SLSC, WSAS and IIP, we used

subgroup analyses, with even smaller numbers. The statistical power was therefore modest and our results should be interpreted with caution, also because we chose not to correct for multiple testing. It has also led to a restriction of range in the outcome variable (BDI), but we think this is outweighed by the specificity of the process-outcome associations in this subgroup of patients. This is essentially an explorative study with a correlational design. Although our results may shed some light on potential causal pathways, the lack of an experimental design involving the process factors does not permit any claims or conclusions in that area.

The results of the WAI should be interpreted with even more caution as we only had complete baseline and post-treatment ratings for approximately 50% of the participants, and only 50% of the available tapes were rated twice, which could have introduced a form of selection bias.

A commonly heard criticism about the association between dysfunctional thinking and depression is that dysfunctional thinking is part of the construct and measurement of depression symptoms and might therefore be nothing more than another proxy for depression. However, it should be noted that the DAS predicted BDI-II scores at follow-up after adjustment for the slope of the BDI-II scores during therapy, which suggests that DAS change scores contributed uniquely to the prediction of depression.

Another limitation is that regression to the mean cannot be ruled out in these data, as the process variables display large between-person variation at baseline. However, since we merely report associations of process change and outcome as markers for therapy progress that do not allow causal inferences, regression to the mean might be less of a problem.

Finally, some authors have argued that it is equally important to ask “*who* works best for whom?” (Constantino et al., 2017). Indeed, therapist effects have often been neglected as potential predictors in the research literature (Delgado et al., 2020; Spielman & Fluckiger, 2018). However, since we did not find a therapist effect in the effectiveness analysis (Lemmens et al., 2015) we chose not to include it in the current analysis.

Clinical Implications and Future Directions

Several process variables were found to be (univariably) associated with outcome after therapy and can be seen as indicators of good or bad therapy progress. In other field of medicine and health care, terms like “green” and “red” flags are used for

measurements that facilitate the monitoring of treatments. Based on our findings, individual patient scores on the DAS, SLSC, WSAS and IIP during therapy may “generate” a green flag that encourages the therapist to continue her treatment strategy, or a red flag and a clear indication that the therapist should explore what is hampering progress and adapt whatever she is doing in therapy. It should be noted that our analysis left out therapy non-responders, and it is unclear whether DAS and WSAS changes are also signs of therapy progress in this more difficult to treat group. Unfortunately, the small sample of non-responders ($n = 49$) did not allow such an analysis.

However, our findings align with the outcome feedback literature that has demonstrated that providing feedback to therapists on individual patient outcomes in the course of therapy is an effective way to deal with non-response and improve the effectiveness of psychotherapy (Knaup et al., 2009; Lambert, 2017). If replicated, process factors like the DAS, SLSC, WSAS and IIP can be used to track individual progress and guide clinical decision making in psychotherapy, for example as part of the individual patient data that therapists receive feedback on. However, predictive value does not constitute proof of a causal relation and caution is warranted. Experimental tests should confirm whether process factors like these are not only predictors of outcome but actual mechanisms of change.

Conclusion

Less negative thinking in the course of therapy is associated with less depression in the long term in both CT and IPT, while changes during therapy in work and social functioning and interpersonal problems appear to predict different outcomes in CT vs IPT. If replicated, these findings can be used to guide the monitoring of individual progress and clinical decision-making during psychotherapy.

Note

¹ Because of missing data on scenarios 11 and 12, we excluded these from the current analyses. As a result, our calculations are based on only 10 scenarios.

Disclosure Statement

No potential conflict of interest was reported by the author(s).

Supplemental data

Supplemental data for this article can be accessed here <https://doi.org/10.1080/10503307.2022.2064251>

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