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Temporal and specific pathways of change in cognitive behavioral therapy (CBT) and interpersonal psychotherapy (IPT) for depression

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ABSTRACT

Background: The present study investigated the specific and temporal role of putative mechanisms of change in cognitive-behavioral therapy (CBT) and interpersonal psychotherapy (IPT) for major depressive disorder (MDD).
Method: 200 patients were randomized to CBT weekly, CBT twice weekly, IPT weekly or IPT twice weekly. Outcome and putative mechanisms of change (i.e., dysfunctional thinking, behavioral activation, CBT skills, IPT skills, therapeutic alliance, compliance, motivation) were measured multiple times up to six months after the start of treatment. Latent change score models were used to investigate temporal relations and test mediation. Explorative analyses tested whether baseline working memory moderated the effect of mechanism change on outcome change.
Results: CBT skills and dysfunctional thinking mediated the relation between treatment modality and changes in depression. In both treatments, IPT skills and behavioral activation were related to subsequent change in depression while a decrease in depression led to subsequent improvement in therapeutic alliance and a decrease in autonomous motivation. Change in compliance was unrelated to change in depression. Baseline working memory was related to therapy skill improvement.
Conclusion: CBT skill improvement seems a specific mechanism of change leading to subsequent decrease in depression in CBT. Changes in IPT skills acted as a non-specific mechanism, subsequently reducing depression regardless of treatment modality. The specific role of cognitive change and behavioral activation remains unclear. Future studies should investigate the specificity and direction of the potential mechanisms of change throughout the course of therapy and investigate whether these mechanistic pathways differ between individuals.

1. Introduction

Multiple mechanisms of change have been hypothesized to explain the effects of psychotherapy for depression, but it is still unknown which exact mechanisms lead to a decrease in depression. Different psychotherapies for depression have comparable effects (Cuijpers et al., 2021), and it has been hypothesized that the comparable effectiveness implicates that different psychotherapies work through common mechanisms. Other studies have pointed to the different theoretical backgrounds of different forms of psychotherapies and hypothesized that the mechanisms through which psychotherapies achieve their effects are specific to the different psychotherapies. It is so far unclear whether specific or common mechanisms underlie effects of psychotherapy (Cuijpers, Reijnders, & Huibers, 2019). Progress in our knowledge on mechanisms of change in psychotherapy for depression seems to necessitate complex research designs that include multiple measurements of potential specific and common mediators (i.e., mediators can be defined as variables that represent the therapy processes that are mobilized in the patient by therapeutic procedures and, if accounting statistically for the relationship between the independent and dependent

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variables, can be seen as a potential mechanism of change (Bruijniks, DeRubeis, Hollon, & Huibers, 2019; Huibers, Lorenzo-Luaces, Cuijpers, & Kazantzis, 2021; Kazdin, 2007)), and additionally use modern statistical analyses to test causal and temporal relationships (Lemmens, Müller, Arntz, & Huibers, 2016).

Two of the most used and investigated psychotherapies for depression are cognitive-behavioral therapy (CBT; Beck, Rush, Shaw, & Emery, 1979) and interpersonal psychotherapy (IPT; Klerman, Weissman, Rounsaville, & Chevron, 1984). The most investigated potential specific mechanisms of change in CBT are changes in dysfunctional thinking and behavioral activation. Changes in dysfunctional thinking has been repeatedly related to subsequent change in depression and showed to mediate the relation between CBT and depressive symptom reduction (Cristea et al., 2015; Lemmens et al., 2016; Lorenzo-Luaces, German, & DeRubeis, 2015; Moreno-Peral et al., 2020). However, it is unclear whether change in dysfunctional thinking is specific to CBT and responsible for change in depression (Garratt, Ingram, Rand, & Sawalani, 2007; Longmore & Worrell, 2007). One recent study showed that in both a cognitive and non-cognitive intervention, changes in dysfunctional thinking mediated change in depressive symptoms, but that depressive symptoms also mediated changes in dysfunctional thinking (Hofheinz, Reder, & Michalak, 2020). Behavioral activation has been mostly investigated as a separate intervention that showed comparable effects in targeting depression to CBT (Jacobson et al., 1996). However, it is less clear whether behavioral activation also works as a mechanism of change through which CBT achieves its effects (for example by increasing responsiveness to reward; Forbes, 2020) or whether the behavioral procedures in CBT mostly induce changes in dysfunctional thinking that are responsible for the subsequent changes in depression (Lorenzo-Luaces, Keefe, & DeRubeis, 2015). Findings of studies that tested behavioral activation as a potential mediator in CBT are mixed (Seeley et al., 2019; Takagaki et al., 2016). Specific mechanisms in IPT have been investigated less extensively (Lipsitz & Markowitz, 2013). The ones that were done focused on the role of interpersonal functioning, but further studies are still necessary to confirm whether changes in interpersonal functioning lead to change in depression and are specific to IPT (Lemmens et al., 2017).

One potential specific mechanism of change that may play a role in both psychotherapies but that is specific to each type of psychotherapy is the therapy-specific skills. CBT skills can be defined as the skills of the patient to identify and evaluate dysfunctional thinking and to use behavioral activation to increase the experience of reward. It has been suggested that the development of skills may help the patient to cope with depression after treatment and protect against future relapse. In line with these hypotheses, CBT skills have been related to subsequent decrease of depression, better response and lower risk of relapse (Jarrett, Vittengl, Clark, & Thase, 2018; Murphy, Cheavens, & Strunk, 2020; Strunk, DeRubeis, Chiu, & Alvarez, 2007), were pointed out as a mediator between CBT and treatment outcome (Forand et al., 2018) and it was shown that CBT skill use was associated with subsequent change in depression and not the other way around (Hawley et al., 2016). It is yet not clear whether the development of CBT skills is specific to CBT. A scale to measure the therapy skills that are hypothesized to be developed during IPT was developed recently (Bruijniks, Peeters, Strunk, & Huibers, 2019) and was shown to mediate the relation between psychotherapies that were given in different session frequencies and depressive outcome, where a higher session frequency was related to better development of IPT skills leading to a subsequent decrease in depression, regardless of treatment modality (i.e., CBT versus IPT; (Bruijniks et al., 2021)). Whether the role of IPT skills in reducing depression is specific to IPT needs to be further investigated.

Besides these hypothesized specific mechanisms of change, research has also supported the role of common mechanisms of change in CBT and IPT for depression. Multiple studies have pointed to the role of therapeutic alliance in reducing depression, and its reversed relation, but findings have been mixed (from finding no relation to finding relations in both directions; Baier, Kline, & Feeny, 2020). Other potential mechanisms that are common across psychotherapies and that might play a role in reduction of depression are compliance and motivation. Compliance can be defined as the degree to which patients come to therapy (i.e., absence of drop-out) or the degree to which patients comply to the procedures and (homework) assignments during the course of psychotherapy. Drop-out is a phenomena seen equally across different psychotherapies (Cuijpers et al., 2021). Using the definition of compliance as the commitment to therapeutic procedures and homework, it has mostly been investigated and repeatedly related to symptom improvement in CBT, which is a homework-based therapy in contrast to IPT (Callan et al., 2018; Conklin & Strunk, 2015; Mausbach, Moore, Roesch, Cardenas, & Patterson, 2010). Motivation for therapy can be defined as the willingness or acceptability to participate in therapy for autonomous or external reasons (i.e., the latter one also called controlled motivation). While autonomous motivation can be defined as the extent to which patients experience treatment as a freely made choice, controlled motivation is defined as participating in treatment for external reasons that help to obtain reward or avoid punishment (McBride et al., 2010). In contrast to compliance, motivation was somewhat more extensive investigated in IPT compared to CBT. Autonomous motivation has shown to be predict better outcomes while controlled motivation was related to decreased treatment success in IPT (McBride et al., 2010; Zuroff et al., 2017). One study related motivation for therapy to subsequent better outcomes in low-intensity CBT (Knittle, Gellert, Moore, Bourke, & Hull, 2019). Conclusions of the temporal and causal relations between change in the potential common mechanisms of change and change in depression remain mixed and the temporal relation and potential reversed effects of compliance and motivation and change in depressive symptoms need to be further investigated.

The present study will investigate the specific and temporal effects of seven candidate mechanisms in CBT and IPT for depression: dysfunctional thinking, behavioral activation, CBT skills, IPT skills, therapeutic alliance, motivation, and compliance. Using RCT data (criteria 1) that compared CBT versus IPT (criteria 2: use of control group) in 200 patients with MDD (criteria 3: sample size $\geq$ 40) and included multiple measurements of both hypothesized potential specific and common mechanisms during the acute treatment phase (criteria 4: inclusion of multiple mediators and criteria 5: assessment of temporal relationships), the study complies to multiple criteria that have been established as a requirements in mechanism research (Kazdin, 2009; Lemmens et al., 2016). In addition, the present study will not only investigate the temporal effect of change in the proposed mechanism on subsequent change in depression but also test the reversed relationships (effect of change in depression on subsequent change in the proposed mechanism). Recently, the same dataset and methods were used to investigate the mechanistic pathways of change for different session frequencies in treatment for depression (Bruijniks et al., 2021). Findings pointed out that IPT skills mediated the relation between session frequency and change in depression, that an increase in CBT skills was related to subsequent improvement in depressive symptoms and a decrease in depressive symptoms was related to subsequent improvement in CBT skills, with the latter model showing better fit, and that a decrease in depression was related to subsequent decrease in motivation for therapy, and not in the reverse direction. A decrease in depressive symptoms was related to subsequent improvement in the therapeutic alliance, but a model with both directions included showed better fit and left no relations significant (Bruijniks et al., 2021). In addition, based on our recent studies that indicate that individual differences in learning capacity may moderate the success of therapy procedures in bringing about change in the putative mechanisms and outcome (Bruijniks, DeRubeis, et al., 2019; Bruijniks, van Grootheest, et al., 2020), in this paper we explored whether a baseline measure of working memory would affect change in the putative mechanisms and outcome. In our recent paper on the mechanistic pathways of change for different session frequencies (Bruijniks et al., 2021), we found that higher baseline

working memory scores were positively related to improvement in CBT skills and IPT skills during treatment but did not moderate the mediation of IPT skills. For the present paper, we expect that change in dysfunctional thinking, behavioral activation and CBT skills are mediators specific to CBT and lead to subsequent changes in depression (and not the other way around). In addition, we expect that change in IPT skills is specific to IPT and related to subsequent change in depression. We expect that improvements in the therapeutic alliance, motivation, and compliance relate to a subsequent decrease of depression, but that this relation does not differ between the two treatment modalities. In addition, we explored whether a baseline measure of working memory moderated the relation between change in the therapy processes and outcome.

2. Methods

2.1. Design and participants

The study was conducted in context of a randomized trial that investigated the effects of session frequency and mechanisms of change in cognitive-behavioral therapy (CBT) and interpersonal psychotherapy (IPT) for major depressive disorder (MDD) (Bruijniks et al., 2015). Patients with MDD were randomized to CBT weekly ($n = 49$), CBT twice weekly ($n = 49$), IPT weekly ($n = 55$), IPT twice weekly ($n = 47$), all receiving an equal number of sessions. Patients were adult out-patients referred to one of nine Dutch specialized mental healthcare centers located across the Netherlands. Patients were included if they received a primary diagnosis of DSM-IV major depressive disorder (including chronic depression), were aged 18 to <65 years, had a pre-treatment score ≥20 on the Beck Depression Inventory-II (BDI-II), had sufficient knowledge of the Dutch language and had access to internet facilities. Patients were excluded if they showed acute risk for suicide, had planned to start antidepressants, or changed their dosage in the past 3 months, had a diagnosis of drug or alcohol dependence, a diagnosis of a cluster A or B personality disorder was present or if participants received more than five sessions of adequate CBT or IPT in the previous year. Results of the RCT showed that twice weekly sessions led to better depressive outcomes compared to weekly sessions, but there were no differences between CBT versus IPT (Bruijniks, Lemmens, et al., 2020). Further details on the design, participants, procedures and outcomes can be found in the protocol- and main outcome paper of the study (Bruijniks et al., 2015, Bruijniks, Lemmens, et al., 2020). Results on mechanistic pathways of change between the different session frequencies can be found in Bruijniks et al. (2021). All patients signed informed consent. The study was approved by the Medical Ethical Committee of VU Medical Centre Amsterdam (registration number 2014.337).

2.2. Measurement instruments

2.2.1. Outcome

Depression: Beck Depression Inventory II (BDI-II)

The BDI-II is a 21-item self-report instrument assessing symptoms of depression during the last two weeks. A score 0–13 indicates minimal depression, 14–19 mild depression, 20–28 moderate depression and 29–63 severe depression. Reliability and validity have been supported (Beck, Steer, & Brown, 1996; Beck, Steer, & Carbin, 1988).

2.2.2. Potential therapy-specific mechanisms of change

Cognitive change: Cognition Checklist (CCL)

The CCL investigates automatic negative thoughts and cognitions related to anxiety and depression (Steer, Beck, Clark, & Beck, 1994). The scale consists of 26 items that are rated on a 5-point Likert-type scale ranging from 1 (never) to 5 (always). Reliability and validity have been supported (Steer et al., 1994).

Behavioral activation: Behavioral Activation for Depression Scale (BADS)

The BADS is a 25-item self-report scale that intends to measure patients' avoidance behavior and activity level during the past week. Items are rated on a 7-point scale. Validity and reliability showed to be adequate (Raes, Hoes, Van Gucht, Kanter, & Hermans, 2010).

CBT skills: Cognitive Therapy Scale-Self Report (CCTS-SR)

The CCTS-SR is a 29-item questionnaire designed to assess patients' use of CBT skills during the past 2 weeks. Items were rated on a scale of 1 (not at all) to 7 (completely). The CCTS-SR has shown sufficient validity and reliability (Bruijniks, Peeters, et al., 2019; Strunk et al., 2007; Strunk, Hollars, Adler, Goldstein, & Braun, 2014).

IPT skills: Interpersonal Psychotherapy Skills Scale–Self-Report (IPSS- SR)

The IPSS-SR consists of 25 items measured on a 7-point Likert Scale 1 (not at all) to 7 (completely) and assesses patients' use of IPT skills during the past two weeks. The IPSS-SR consists of four scales measuring communication skills and social support, understanding of own feelings, coping with grief and major life change, and understanding the feelings of others. Initial psychometric properties have been supported (Bruijniks, Peeters, et al., 2019).

2.2.3. Potential common mechanisms of change

Therapeutic alliance: Working Alliance Inventory (WAI)

The WAI measures tasks (e.g., behaviors and cognitions that form the therapeutic process), bonds (e.g., positive personal attachments between patient and therapist) and goals (e.g., therapist and patient mutually endorsing and valuing the goals) as components of the therapeutic alliance. The questionnaire consists of 12 items rated on a 5-point Likert scale and was filled out by the patient. Reliability and validity have been supported (Horvath & Greenberg, 1989; Stinckens, Ulburghs, & Claes, 2009; Vertommen & Vervaeke, 1990).

Motivation for therapy: Autonomous and Controlled Motivation for Treatment Questionnaire (ACMTQ)

The ACMTQ includes two six-item subscales in order to assess autonomous (for example: 'I personally believe it is the most important aspect of becoming well') motivation for therapy and controlled (for example: 'Others would be upset if I didn't') motivation for therapy. Items were rated on a 7-point rating scale and a total score was computed by combining the questionnaires. Both the total scores as well as the subscales were investigated separately in the analyses. Initial reliability and validity have been demonstrated (McBride et al., 2010; Zuroff, Koestner, Moskowitz, McBride, & Bagby, 2012).

Compliance: Before each session, patients rated their effort they put in the treatment between the sessions by answering two questions on a 0–100 scale: 1. 'How much time have you spent on what was discussed in the last session?' and, 2. 'How well did these activities fit into what was discussed in the previous session?'. A total compliance score was computed as the average on both questions. Compliance ratings were completed during the session. Because session frequencies differed between patients, the ratings were matched to standardized time points, i.e. after week 2, month 1, 2 and 3 (i.e., in the once-weekly conditions the ratings of session 2, 4, 8 and 12 were used, for twice-weekly condition ratings of session 4, 8, 16 and 20 were used).

2.2.4. Potential moderator

Working memory: n-back task (Braver et al., 1997)

Working memory was measured with the n-back task (Braver et al., 1997). The exact same version was used as reported in one of our previous studies (Bruijniks, Sijbrandij, et al., 2019. During the n-back task participants were asked if a letter on the screen matched a letter previously (1-back, 2- back, 3-back) presented for 500 ms with an interval of 2000 ms. After running a test trial where they got elaborate feedback about the incorrect responses ('The previous letter was X, this indicated you had to press the button'), the participants completed a 1-back trial (2 min) and a 2-back trial (two parts of 2.5 min). Only when the participants performed well on the 2-back (i.e., 2/3 correct responses; a correct response means a correct press or a correct no-press), were they

forwarded to the 3-back part of the task that also took 5 min (two parts of 2.5 min). WM load increased as the task progressed from 1-back to 3-back. The number of n-backs (i.e., potential hits) in each condition was 33%. Feedback was given after a correct response (marked by a green V) or a miss (marked by a black X). The task took a maximum of 12.5 min and was completed at baseline. Validity of the n-back task has been supported (Wilhelm, Hildebrandt, & Oberauer, 2013).

2.3. Procedure

Outcomes and potential mechanisms of change were measured extensively throughout the study. A summary of measurements is given in Table 1.

2.4. Data analyses

2.4.1. Main analyses

Data were analyzed according to the intention-to-treat principle, indicating that all patients were analyzed according to their randomized condition. First, descriptives (mean, standard deviations, within-group and between-group effect sizes) on the outcome and on all putative mechanisms at each time-point and correlations between change in depression and change in the putative mechanisms were described for the whole group and per treatment modality. To facilitate the interpretation of the correlations, change in depression on the BDI-II was recoded so that positive correlations indicated that improvement on the putative mechanisms is related to improvement in the outcome. Descriptives and correlations were computed using SPSS Version 27 for Windows.

Second, to investigate whether change in the putative mechanism was related to change in the outcome, Latent Change Score (LCS) models were analyzed using Mplus (Grimm, Ram, & Estabrook, 2017). In LCS models, change is presented by a latent variable and it is possible to separate the model change in the putative mechanisms and outcome between and across the different time points (Castro-Schilo & Grimm, 2018; McArdle, 2009). A certain latent variable presented the change in the raw scores of a certain variable between two measurement moments, this means that a positive latent difference score points to an increase in the raw variable score while a negative latent difference score means a decrease in the raw score of the variable. For our models, this means that positive latent difference scores indicate worsening of depression or dysfunctional thinking (i.e., as higher BDI-II scores indicate worse depression and a higher score on the CCL indicates worsening of dysfunctional thinking), but improvement in any of the other putative mechanisms (i.e., as for these variables higher raw scores indicate improvement of the putative mechanism). Thus, a positive relationship between change in the putative mechanism and change in the outcome indicated that improvement in the mediator (except for the CCL where this points to worsening of dysfunctional thinking) was associated with a worsening of depression. In contrast, a negative relationship indicated that improvement in the putative mechanism was associated with improvement of depression.

Before change in the putative mechanism was linked to change in the outcome, it was determined how change could be best modeled for each variable separately by fitting single change models for each putative mechanism (models that were tested were: no change, constant change, proportional change, dual change or dual change with dynamic error). Subsequently, using these resulting models, each putative mechanism was linked to the outcome in an LCS model to test temporal relations between change in the putative mechanism and change in the outcome. A temporal relation indicated that change in the putative mechanism preceded subsequent change in the outcome. To control for reversed causality, we subsequently ran the model with the direction the other way around (i.e., change in the outcome to change in the putative mechanism), the directions modelled in both ways and compared model fit. Note that the temporal relations of change in CBT skills, IPT skills, therapeutic alliance and compliance with change in depression were already tested and reported in (Bruijniks et al., 2021).

Third, mediation (treatment → change in the putative mechanism → change in depression) was tested by adding treatment to the model and testing indirect effects using non-symmetric confidence intervals following the approach from MacKinnon and colleagues (Mackinnon, Lockwood, West, & Sheets, 2002; MacKinnon & Fairchild, 2010). In case the model with reversed causality (i.e., change in the outcome linked to subsequent change in the putative mechanism) showed similar or better fit compared to the initial model, mediation was also tested in the reversed direction. Raw and standardized betas of the significant pathways were reported. Standardized pathways indicated change in standard deviations of the therapy process when treatment modality would change with one standard deviation (pathway a) and change in depression change in standard deviations when the therapy process would change with one standard deviation (pathway b). As an indicator of the effect size of the mediation, the partially standardized indirect effect (Miočević, O'Rourke, MacKinnon, & Brown, 2018) was reported. The partially standardized indirect effect could be interpreted as the change in standard deviations of the outcome (depression) resulting from changing from CBT to IPT through change in the therapy process.

All parameter estimates were assessed by using bias-corrected 95% bootstrap confidence intervals (CI) with 1000 bootstrap samples. If zero was not contained in the confidence intervals we concluded that the indirect effect was significant. Model fit was compared based on how well the model captured the observed data (the root-mean-square error of approximation (RMSEA), cut- off value $<.08$, and even better <0.05, the standardized root mean square residual (SRMR) cut- off value

Table 1
Measurement of outcome and potential mechanisms.

	Baseline	Week 2	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6
Outcome								
BDI-II	X	X	X	X	X	X	X	X
Potential therapy-specific mechanisms								
CCL		X	X	X	X	X	X	X
BADS	X	X	X	X	X	X	X	X
CCTS-SR	X	X			X			X
IPSS-SR	X	X			X			X
Potential common mechanisms								
WAI		X	X	X	X	X	X	X
ACMTQ	X	X	X	X	X	X	X	X
Compliance		X	X	X	X			
Potential moderator								
N-back task	X							

Note: ACMTQ = Autonomous and Controlled Motivation for Treatment Questionnaire; BADS = Behavioral Activation for Depression Scale; BDI-II = Beck Depression Inventory II; CCL = Cognition Checklist; CCTS-SR = Competencies of Cognitive Therapy Scale-Self Report; IPSS-SR = Interpersonal Psychotherapy Skills Scale–Self-Report; WAI = Working Alliance Inventory.

<0.08, and even better <0.05; the Comparative Fit Index (CFI), fit is considered adequate if the value is > 0.90 and good if > 0.95, the Tucker-Lewis index (TLI) fit is considered adequate if the value is > 0.95) (Hu & Bentler, 1999). The Akaike Information Criterion (AIC) was used for model comparison, with a lower AIC reflecting better model fit (Vrieze, 2012). Lower AIC by > 2 was considered reflecting a better model (Burnham & Anderson, 2004). A maximum likelihood (ML) estimation algorithm was used for the analyses, using all available data of each participant. ML uses all available information under the assumption that the incomplete data are missing at random, therefore missing values were not imputed.

2.4.2. Explorative analyses: the role of working memory in therapy process change

First, correlations between baseline working memory and change in putative mechanisms and outcome were computed. Second, in case of a significant mediation pathway of a therapy process between treatment modality and change in the outcome, moderation of working memory of the relation between change in the putative mechanism and change in depression was tested. Moderation was tested using bias-corrected 95% bootstrap confidence intervals (CI) with 10000 bootstrap samples with a model where baseline depression, treatment modality, baseline working memory, baseline putative mechanism, change in the putative mechanism (i.e., change in the putative mechanism between the specific measurement points where mediation was found) and the interaction between baseline working memory and treatment modality (the moderator) as independent variables, and change in depression (between the specific measurement points where mediation was found) as a dependent variable.

3. Results

3.1. Descriptive statistics

Tables 2 and 3 show the descriptive statistics and the within- and between group effect sizes on the putative mechanisms and outcome. The temporal correlations between change in the putative mechanisms and change in the outcome for the whole group and per treatment modality can be found in data supplement 1.

3.2. Multivariate latent change score models

The multivariate LCS models investigated the relations between change in the therapy process and change in depression. Change in all variables was best modelled using a constant change factor, except for therapeutic alliance and cognitive change where a dual change model (i.e., modelling both a constant change and a proportional change between measurement moments) showed the best fit. Change in depression was best modelled using constant change (when all time points were included) or dual change (when baseline, week 1, months 3 and 6 were

Table 2
Means and standard deviations (SD) of therapy processes and the outcome on each measurement point for the whole group (n = 200).

	Baseline	Week 2	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6
Outcome								
Depression	34.71 (9.96)	31.76 (10.54)	30.82 (11.94)	27.61 (13.17)	25.66 (12.85)	24.04 (13.92)	22.68 (14.74)	22.12 (14.70)
CBT	35.84 (9.98)	31.08 (9.96)	30.37 (11.74)	28.12 (12.60)	26.65 (12.76)	24.38 (13.79)	23.58 (14.67)	22.86 (13.98)
IPT	33.62 (10.75)	32.48 (11.18)	31.23 (12.18)	27.11 (13.78)	24.65 (12.95)	23.67 (14.16)	21.73 (14.86)	20.37 (15.44)
Therapy process								
Cognitive change	44.53 (17.43)	44.91 (16.72)	45.23 (17.92)	43.33 (19.61)	40.38 (20.04)	40.13 (19.33)	38.83 (21.71)	35.3 (21.53)
CBT	44.25 (16.31)	43.71 (16.26)	44.45 (16.9)	43.97 (18.10)	40.61 (19.51)	40.11 (19.78)	40.23 (22.6)	37.3 (20.56)
IPT	44.80 (18.5)	46.24 (17.27)	45.95 (18.88)	42.69 (21.12)	40.15 (20.71)	40.16 (18.97)	37.42 (20.85)	33.26 (22.24)
Behavioral activation	68.46 (19.99)	71.05 (21.23)	72.86 (21.51)	76.92 (24.72)	80.74 (24.81)	84.26 (23.38)	85.94 (25.50)	88.09 (25.91)
CBT	68.67 (18.48)	72.22 (20.42)	74.14 (21.54)	75.61 (23.43)	78.55 (26.64)	85.14 (23.55)	84.66 (26.46)	86.74 (24.36)
IPT	68.26 (21.43)	69.77 (22.21)	71.69 (21.56)	78.22 (26.04)	82.99 (22.74)	83.2 (23.33)	87.25 (24.64)	89.52 (27.57)
CBT skills	80.79 (22.35)	87.68 (22.76)			105.03 (27.06)			107.31 (30.06)
CBT	78.43 (18.97)	86.69 (22.16)			106.61 (28.85)			106.58 (27.41)
IPT	83.03 (25.04)	88.75 (23.54)			103.44 (25.22)			108.06 (32.71)
IPT skills	91.03 (20.29)	93.95 (19.28)			99.31 (20.53)			102.61 (22.69)
CBT	91 (21.53)	93.61 (18.49)			100.04 (21.12)			101.35 (21.76)
IPT	91.06 (19.15)	94.31 (20.25)			98.58 (20.05)			103.88 (23.69)
Therapeutic alliance		28.67 (10.41)	29.21 (9.39)	29.79 (10.31)	31.48 (10.01)	32.44 (9.52)	32.20 (9.84)	30.53 (10.16)
CBT		30.5 (10.58)	28.81 (10.3)	31.07 (9.86)	32.22 (10.19)	33.87 (8.87)	32.42 (10)	30.41 (10.83)
IPT		26.69 (9.95)	29.58 (8.52)	28.49 (10.66)	30.75 (9.85)	30.80 (10.03)	31.98 (9.75)	30.64 (9.52)
Motivation for therapy	51.61 (9.76)	54.27 (10.41)	53.22 (10.13)	52.77 (11.01)	54 (10.55)	53.33 (10.94)	52.59 (10.53)	51.69 (10.99)
CBT	51.54 (8.88)	53.4 (9.85)	51.9 (9.15)	52.74 (9.03)	53 (9.8)	53.36 (9.96)	51.59 (10.08)	50.83 (10.59)
IPT	51.67 (10.58)	55.21 (11)	54.43 (10.88)	52.81 (12.77)	55.02 (11.23)	53.29 (12.04)	53.63 (10.95)	52.54 (11.38)
Autonomous motivation	32.35 (4.51)	33.76 (5.04)	33.62 (4.72)	33.32 (5.65)	34.39 (4.94)	33.66 (5.72)	33.18 (5.76)	33.01 (5.99)
CBT	32.79 (3.84)	33.80 (4.62)	33.59 (3.88)	33.57 (4.37)	34.16 (4.69)	33.73 (4.86)	32.88 (5.38)	32.23 (5.92)
IPT	31.93 (5.06)	33.73 (5.50)	33.65 (5.40)	33.06 (6.73)	34.63 (5.21)	33.59 (6.62)	33.50 (6.14)	33.79 (6.00)
Controlled motivation	19.25 (7.60)	20.50 (7.59)	19.60 (7.60)	19.45 (8.00)	19.60 (8.18)	19.66 (8.05)	19.40 (7.87)	18.67 (7.83)
CBT	18.74 (7.38)	19.60 (7.50)	18.31 (7.22)	19.16 (7.18)	18.83 (7.82)	19.63 (7.76)	18.71 (7.68)	18.60 (7.61)
IPT	19.74 (7.81)	21.48 (7.63)	20.77 (7.80)	19.75 (8.78)	20.39 (8.52)	19.69 (8.43)	20.12 (8.07)	18.75 (8.09)
Compliance		5.16 (2.35)	5.71 (2.25)	6.21 (2.43)	6.39 (2.41)			
CBT		5.62 (2.46)	6.15 (2.20)	6.73 (2.28)	6.65 (2.57)			
IPT		4.72 (2.15)	5.29 (2.23)	5.71 (2.48)	6.15 (2.24)			

Note that the following data was missing: Behavioral activation (BADS), baseline: $n = 1$, week 2: $n = 89$, month 1: $n = 47$, month 2: $n = 48$, month 3: $n = 60$, month 4: $n = 70$, month 5: $n = 73$, month 6: $n = 64$; Depression (BDI-II), week 2: $n = 84$, month 1: $n = 43$, month 2: $n = 47$, month 3: $n = 57$, month 4: $n = 64$, month 5: $n = 69$, month 6: $n = 54$; Cognitive change (CCL), baseline: $n = 1$, week 2: $n = 86$, month 1: $n = 45$, month 2: $n = 48$, month 3: $n = 58$, month 4: $n = 69$, month 5: $n = 71$, month 6: $n = 57$; CBT skills (CCTS-SR), baseline: $n = 1$, week 2: $n = 86$, month 3: $n = 57$, month 6: $n = 55$; IPT skills (IPSS-SR), baseline: $n = 1$, week 2: $n = 89$, month 3: $n = 58$, month 6: $n = 63$; Motivation for therapy (ACMTQ): week 2: $n = 86$, month 1: $n = 45$, month 2: $n = 47$, month 3: $n = 57$, month 4: $n = 67$, month 5: $n = 68$, month 6: $n = 54$; Therapeutic alliance (WAI), week 2: $n = 85$, month 1: $n = 44$, month 2: $n = 49$, month 3: $n = 56$, month 4: $n = 65$, month 5: $n = 69$, month 6: $n = 53$. ACMTQ = Autonomous and Controlled Motivation for Treatment Questionnaire, BADS = Behavioral Activation for Depression Scale, BDI-II = Beck Depression Inventory II, CCL= Cognition Checklist, CCTS-SR = Cognitive Competencies of Cognitive Therapy Scale-Self Report, IPSS-SR = IPT Skill Scale-Self Report, WAI = Working Alliance Inventory.

Table 3
Within group and between group effect sizes (Cohen's d).

	Within-group	Between-group
Depression		
Total	1.26	.06
CBT	1.30	
IPT	1.23	
Cognitive change		
Total	.52	.19
CBT	.42	
IPT	.62	
Behavioral activation		
Total	.98	.01
CBT	.97	
IPT	.99	
CBT skills		
Total	1.18	.48
CBT	1.48	
IPT	.99	
IPT skills		
Total	.57	.18
CBT	.48	
IPT	.66	
Therapeutic alliance		
Total	.17	.38
CBT	.01	
IPT	.39	
Motivation for therapy		
Total	.01	.00
CBT	.08	
IPT	.08	
Autonomous motivation		
Total	.14	.22
CBT	.14	
IPT	.36	
Controlled motivation		
Total	.07	.10
CBT	.01	
IPT	.12	
Compliance		
Total	.52	.24
CBT	.41	
IPT	.66	

Note. Within-group effect sizes were computed as: (M T0 – M T6)/SD T0. Between group effect sizes were computed by taking the difference of the within-group effect sizes of the treatment modalities.

included), and the simplest model (i.e., constant change only) was chosen to use in the analyses. Fit parameters of the original (change in the putative mechanism on subsequent change in the outcome) and reversed model (change in the outcome on subsequent change in the putative mechanism) can be found in data supplement 2. Fit parameters of the final models can be found in Table 4. Model estimates of the final multivariate latent change score models can be found in Table 5.

3.2.1. Cognitive change

An increase in dysfunctional thinking between month 3 and 4 and month 4 and 5 was related to a significant subsequent reduction in depression between month 4 and 5 and month 5 and 6 (see Table 5). Running the reversed model (change in depression to change in dysfunctional thinking) did slightly improve model fit (see data supplement 2) and showed that reduction of depression between week 2 and month 1, month 1 and 2, month 3 and 4, month 4 and 5 was related to subsequent decrease in dysfunctional thinking on the subsequent timepoints (decrease in dysfunctional thinking between month 1 and 2, month 2 and 3, month 4 and 5 and month 5 and 6) (see Table 5). A model including effects in both directions did not converge.

3.2.2. Behavioral activation

An increase in behavioral activation between month 4 and month 5 had a significant effect on subsequent increase in depression between month 5 and month 6 (see Table 5). Running the reversed model (change in depression to change in behavioral activation) did not improve model fit (see data supplement 2) and did not point to any significant relations. Running the model with both directions included did not improve model fit.

3.2.3. Cognitive-behavioral therapy skills

Change in CBT skills between baseline and week 2 had a significant

Table 4
Estimates of the final multivariate LCS models linking change in the therapy process to subsequent change in depression.

	X^2	df	RMSEA	SRMR	TLI	CFI	AIC
Cognitive change							
Depression - > cognitive change	301.74	129	.08	.07	.95	.94	16651.69
Treatment - > cognitive change - > depression	328.59	140	.08	.06	.94	.94	16669.63
Behavioral activation							
Behavioral activation - > depression	271.04	129	.07	.08	.94	.94	17527.40
CBT skills							
Depression - > CBT skills	73.44	25	.09	.08	.91	.92	9754.14
Treatment - > CBT skills - > depression	87.75	31	.09	.07	.89	.90	9756.15
IPT skills							
IPT skills - > depression	54.94	25	.07	.06	.95	.96	9247.67
Therapeutic alliance							
Depression <–> Alliance	172.64	91	.07	.07	.96	.96	13211.31
Motivation for therapy							
Depression - > motivation for therapy	278.23	129	.07	.08	.94	.93	16171.98
Autonomous motivation for therapy							
Depression <–> motivation for therapy	280.19	123	.08	.13	.92	.92	14798.56
Controlled motivation for therapy							
Depression <–> motivation for therapy	253.21	123	.07	.06	.94	.94	15340.09
Compliance							
Depression - > compliance	27.60	25	.02	.05	.99	.99	6699.77

Note. The root-mean-square error of approximation (RMSEA), cut- off value is <0.08, and better is < 0.05; the standardized root mean square residual (SRMR) cut- off value <0.08, and even better <0.05; the Comparative Fit Index (CFI), fit is considered adequate if the value is > 0.90 and good if > 0.95); the Tucker-Lewis index (TLI) fit is considered adequate if the value is > 0.95.

Table 5
Model estimates of the multivariate LCS models linking change in the therapy process to subsequent change in depression.

	Cognitive change	Behavioral activation	CBT skills	IPT skills	Therapeutic alliance[a]	Therapeutic alliance[b]	Motivation for therapy	Compliance
Correlations								
Baseline depression and change in the therapy process	.76 (−1.81/ 3.53)	−1.85 (−7.02/3.42)	2.80 (−14.20/ 20.73)	−3.95 (−14.76/ 5.19)	.008 (−9.62/15.73)		−1.90 (−5.12/1.14)	.09 (−1.80/ 2.13)
Baseline therapy process and change in depression	.99 (−4.13/ 6.38)	.71 (−6.89/7.97)	−1.83 (−16.53/ 14.70)	.04 (−12.1/ 14.33)	−9.40 (−16.01/.40)		−1.63 (−4.24/.87)	−1.84* (−3.21/- .53)
Change parameters								
Constant change depression	−1.84 2.14/-1.55)*	−2.30 (−3.26/-1.42)*	−4.31 (−5.00/- 3.60)*	−2.75 (−3.93/- 1.67)*	−1.30* (−1.97/-.39)		−1.81 (−2.10/-1.50)*	−2.07* (−2.60/- 1.52)
Constant change therapy process	.84 (−.59/2.37)	2.81 (2.24/3.35)*	6.33 (3.69/ 8.98)*	3.56 (2.45/ 4.62)*	−1.10 (−25.33/10.83)		1.14 (−.03/2.24)	.59* (.33/.86)
Proportional change depression	NA	NA	NA	NA	NA		NA	NA
Proportional change therapy process	NA[a]	NA	NA	NA	.06 (−.38/.93)		NA	NA
Coupling parameters								
Δ baseline – week 2-> Δ week 2 – month 3			−1.87 (−2.98/- .86)*	-.83 (−1.59/- .19)*				
Δ week 2 – month 3 -> Δ month 3 – month 6			-.03 (−.90/.89)	-.39 (−.80/.07)				
Δ baseline – week 2 -> Δ week 2 – month 1	.64 (−.58/1.80)	.32 (−.15/.79)					.64 (−.21/.1.48)	
Δ week 2 – month 1 -> Δ month 1 – month 2	1.38 (.48/2.34)*	-.03 (−.58/.44)			−1.32 (−4.40/.46)	.30 (−.92/1.86)	.63 (−.19/1.38)	.06 (−.14/.31)
Δ month 1 – month 2 -> Δ month 2 – month 3	1.49 (.43/2.79)*	.16 (−.22/.61)			−1.09 (−4.09/1.07)	-.16 (−1.90/.61)	.68 (−.13/1.45)	.17 (−.01/.39)
Δ month 2– month 3 -> Δ month 3 – month 4	.86 (−.10/1.98)	.21 (−.22/.61)			-.46 (−1.64/.50)	.60 (−.54/2.31)	.85 (.06/1.62)*	
Δ month 3 – month 4 -> Δ month 4 – month 5	2.00 (1.02/3.00)*	.28 (−.13/.74)			−2.47 (−10.79/1.12)	.25 (−.79/2.16)	.97 (.17/1.75)*	
Δ month 4 – month 5 -> Δ month 5 – month 6	1.96 (1.05/3.01)*	.38* (.02/.75)			.29 (−2.53/4.23)	1.33 (−.78/5.82)	.73 (−.04/1.45)	

Note. [a] Note that the multivariate model with the CCL and BDI-II using a dual change model for the CCL could not be estimated and therefore the CCL scores were included with only constant change parameters in the models. *Significant estimates using bias corrected 95% bootstrap confidence intervals (CI) with 1000 bootstrap samples. Note that coefficients for the model with the best fit were reported: 1. Change in depression - > cognitive change, 2. Change in behavioral activation - > change in depression, 3. change in depression - > change in CBT skills, 4. Change in IPT skills - > change in depression, 5a. Alliance - > Depression, 5b. Depression - > Alliance, 6. Change in depression - > change in motivation for therapy, 7. Change in depression - > change in compliance. Note that 5a and 5b were estimated in one model.

effect on subsequent change in depression between week 2 and month 3, indicating that improvement in CBT skills was related to a subsequent decrease in depression. Running the reversed model (change in depression to change in CBT skills) improved model fit (see data supplement 2) and pointed to a significant relation between change in depression from baseline to week 2 on change in CBT skills from week 2 to month 3 (where a decrease in depression is related to improvement in CBT skills) (see Table 5). Running the model with both directions included did not improve model fit.

3.2.4. Interpersonal psychotherapy skills

Change in IPT skills between baseline and week 2 had a significant effect on subsequent change in depression between week 2 and month 3, indicating that improvement in IPT skills was related to a decrease in depression (see Table 5). Running the reversed model (change in depression to change in IPT skills) did not improve model fit and did not point to significant relations (see data supplement 2). Running the model with both directions included did not improve model fit.

3.2.5. Therapeutic alliance

Change in therapeutic alliance was not related to subsequent change in depression. Running the reversed model (change in depression to subsequent change in therapeutic alliance) showed similar model fit (see data supplement 2) and relations between the initial scores at week 2 and subsequent changes in depression over time and pointed to a significant relation between change in depression from month 1 to month 2 on subsequent change in therapeutic alliance from month 2 to month 3, indicating that a decrease in depression was related to subsequent improvement in the therapeutic alliance. Because both models did not differ in model fit, the model with both directions included, was considered as the best model. No relations remained significant when both directions were included in the model (see Table 5).

3.2.6. Motivation for therapy

Change in motivation for therapy was not related to subsequent change in depression. Running the reversed model (change in depression to subsequent change in motivation for therapy) showed similar to better model fit (see data supplement 2) than the model testing the relation between change in motivation for therapy and subsequent change in depression and pointed to significant relations between change in depression between month 2–3 on change in motivation for therapy between month 3–4 and change in depression between month 3–4 on change in motivation for therapy between month 4–5, all indicating that a decrease in depression is related to a decrease in motivation for therapy (see Table 5). Running the model with both directions included did not improve model fit. When motivation was split into autonomous motivation versus controlled motivation, results showed that change in controlled motivation was not related to subsequent

change in depression or the other way around. Regarding autonomous motivation, results indicated that a decrease in depression was related to a subsequent decrease in autonomous motivation on each of the temporal paths that were tested. Autonomous motivation did not lead to subsequent changes in depression. Running the model with both directions included did improve model fit for both autonomous and controlled motivation but pointed to zero significant paths.

3.2.7. Compliance

Change in compliance was not related to subsequent change in depression, but higher baseline levels of compliance were related to improvement in depression during treatment (see Table 5). Running the reversed model (change in depression to change in compliance) showed a similar model fit (see data supplement 1) and no significant relations between change in depression and subsequent change in compliance. Running the model with both directions included did not improve model fit.

3.3. Mediation analyses

In the mediation analyses, treatment modality was added to the multivariate LCS models to investigate where change in the therapy process mediated the relationship between treatment modality and depression. Mediation was also tested in the reversed direction, in case the model with reversed causality (i.e., change in the outcome linked to subsequent change in the putative mechanism) showed similar or better fit compared to the initial model (see Table 6 and Fig. 1).

3.3.1. Cognitive change

Treatment was related to change in dysfunctional thinking between month 3 and 4 (raw estimate = −0.58 (−2.41/-0.11), standardized estimate = −0.25 (−0.77/-0.05)) and between month 4 and 5 (raw estimate = −0.43 (−0.90/-0.08), standardized estimate = −0.19 (−0.36/-0.04)), with IPT leading to stronger decrease than CBT. Decrease in dysfunctional thinking between month 3 and 4 and month 4 and 5 was related to subsequent increase in depression between month 4 and 5 (raw estimate = −0.97 (−1.81/-0.15), standardized estimate = −1.97 (−4.25/-0.25)) and month 5 and 6 (raw estimate = −1.32 (−2.12/-0.67), standardized estimate = −3.15 (−4.69/-1.82)). Mediation of change in dysfunctional thinking between month 4 and month 5 between treatment and change in depression between month 5 and 6 was significant (raw estimate = 0.56 (0.10/1.06), standardized estimate = 0.06 (0.01/.11)). This indicates that when the treatment modality changes from CBT to IPT, BDI-II increases by 0.06 standard deviations or 0.56 points between month 5 and month 6 after start of treatment as a consequence of prior change in dysfunctional thinking between month 4 and month 5 after start of treatment. Decrease in depression between week 2 and month 1, month 1 and 2, month 3 and 4 and month 4 and 5 was related to subsequent decrease in dysfunctional thinking between month 1 and 2 (raw estimate = 1.55 (0.39/2.48), standardized estimate = 1.06 (0.37/1.61)), month 2 and 3 (raw estimate = 1.61 (0.32/2.88), standardized estimate = 1.06 (0.29/1.58)), month 4 and 5 (raw estimate = 2.09 (0.84/3.11), standardized estimate = 1.06 (0.54/1.53)) and month 5 and 6 (raw estimate = 2.14 (0.52/3.11), standardized estimate = 1.06 (0.41/1.47)), but no mediation in the reversed direction was found.

3.3.2. Behavioral activation

No significant paths or mediation were found when behavioral activation was tested as a mediator.

3.3.3. Cognitive behavioral therapy skills

Treatment was related to change in skills between week 2 and month 3 (raw estimate = −3.91 (−6.89/-0.56), standardized estimate = −0.42 (−0.65/-0.06)), with larger increase in skills for CBT. An improvement in CBT skills between baseline and week 2 and week 2 and month 3 was related to subsequent decrease in depression between week 2 and month 3 (raw estimate = −0.31 (−0.54/-0.09), standardized estimate = −0.55 (−0.79/-0.19)) and between month 3 and month 6 (raw estimate = −0.18 (−0.35/-0.02), standardized estimate = −0.43 (−0.69/-0.05)). Mediation of change in CBT skills between week 2 and month 3 between treatment and change in depression between month 3 and 6 was significant (raw estimate =.72 (0.01/1.71), standardized estimate = 0.08 (0.001/0.19)). This indicates that when the treatment modality changes from CBT to IPT, BDI-II increases by 0.08 standard deviations or 0.72 points between month 3 and month 6 after start of treatment as a consequence of prior change in CBT skills between week 2 and month 3 after start of treatment. Decreases in depression between baseline and week 2 were related to improvements in CBT skills between week 2 and month 3 (raw estimate = −2.05 (−23.07/-0.98), standardized estimate = −0.64 (−0.85/-0.35)), but no mediation in the reversed direction was found.

3.3.4. Interpersonal psychotherapy skills

Increase in IPT skills between baseline and week 2 was related to decrease in depression between week 2 and month 3 (raw estimate = −0.81 (−1.61/-0.16), standardized estimate = −0.70 (−0.95/-0.22)), but no mediation was found.

3.3.5. Therapeutic alliance

Treatment was related to change in therapeutic alliance between month 4 and 5 (raw estimate = 0.92 (0.05/1.97), standardized estimate = 0.59 (0.04/0.89)) with a larger increase in alliance for IPT. Mediation was not significant. No significant paths or mediation were found when depression was tested as the mediator between treatment and therapeutic alliance.

3.3.6. Motivation for therapy

No significant paths or mediation were found when motivation or depression was tested as the mediator. When motivation was split into autonomous motivation and controlled motivation, no mediation was found for either form of motivation. In regard to autonomous motivation, decrease in depression between week 2 and month 1, month 2 and month 3, month 3 and month 4 and month 4 and month 5 was related to decrease in autonomous motivation between month 1 and 2, month 3 and 4, month 4 and 5 and month 5 and 6 respectively (raw estimate = 0.47 (0.04/.89), standardized estimate = 1.26 (0.10/2.69); raw estimate = 0.65 (0.18/1.09), standardized estimate = 1.81 (0.47/2.94); raw estimate = 0.60 (0.004/1.11), standardized estimate = 1.69 (0.01/2.82); raw estimate = 0.55 (0.08/.98), standardized estimate = 1.40 (0.19/2.45)). No paths in the other direction were found. In regard to controlled motivation, higher controlled motivation at baseline was related to a decrease in depression during treatment (−2.99 (−5.76/-0.19) and treatment was related to a decrease in controlled motivation between month 1 and 2 (raw estimate = −0.96 (−1.72/-0.01), standardized estimate = −0.83 (−0.99/-0.05)), with a larger decrease for IPT. No other paths were significant.

3.3.7. Compliance

Mediation was not tested because no relations were found between change in compliance and change in depression.

3.4. The relation between baseline working memory and change in the therapy processes

Explorative analyses investigated whether individual differences in working memory moderated the success of therapy in facilitating change in the putative mechanisms and outcome. Correlations between baseline working memory and change in the putative mechanism can be found in Table 7 and point to a positive correlation between baseline working memory and change in CBT and IPT skills. In other words, higher baseline working memory scores were positively related to

Table 6
Main findings (as summarized in Fig. 1)

Treatment specific temporal effects
- A decrease in dysfunctional thinking between 4 and 5 months after start of treatment mediated an increase in depressive symptoms in IPT between month 5–6 after start of treatment
- Improvement in CBT skills in the first half of treatment mediated decrease in depressive symptoms in CBT till the end of treatment
- Increases in therapeutic alliance 4–5 months after start of treatment and decreases in controlled motivation 1–2 months after start of treatment were higher in IPT compared to CBT

Treatment non-specific temporal effects
- Decrease in depressive symptoms was related to decrease in dysfunctional thinking along treatment
- Decrease in dysfunctional thinking between month 3 and 4 was related to increase in depressive symptoms between month 4 and 5
- An increase in behavioral activation at the end of treatment was related to an increase in depressive symptoms
- A decrease in depressive symptoms during the first two weeks of treatment was related to an increase in CBT skills in the first half of treatment
- Improvement in CBT skills during the first two weeks of treatment was related to a decrease of depressive symptoms in the first half of treatment
- An increase in IPT skills at the first two weeks of treatment was related to subsequent decrease of depressive symptoms in the first half of treatment
- A decrease in depressive symptoms was related to decreases in autonomous motivation along the course of treatment
- A decrease in depressive symptoms was related to an increase in therapeutic alliance in the first half of treatment

improvement in CBT skills and IPT skills during treatment. Working memory did not moderate the relation between treatment modality and change in CBT skills and cognitive change, or the relation between treatment modality and change in depression.

4. Discussion

The present study investigated the temporal and specific role of potential common (therapeutic alliance, motivation for therapy, compliance) and specific (cognitive change, behavioral activation, CBT skills, IPT skills) mechanisms of change in CBT and IPT for depression. Results pointed to mediational effects for CBT skills and dysfunctional thinking, while specific directions of change were found for change in IPT skills and behavioral activation on change in depression and of change in depression on change in therapeutic alliance and autonomous motivation. Change in compliance was not related to any of the treatments or change in depression.

Both change in CBT skills and dysfunctional thinking mediated the relation between treatment and change in depression. More specifically, CBT was related to increased CBT skills between week 2 and month 3 after start of treatment, which led to a subsequent decrease of 0.72 points on the BDI-II (depressive symptoms) from month 3 till the end of treatment. IPT was related to a larger decrease in dysfunctional thinking late in the therapy (month 4–5 after start of treatment), which was, paradoxically related to a subsequent 0.56 points on the BDI-II increase in depression at the end of treatment (month 5–6 after the start of treatment). Change in CBT skills and dysfunctional thinking did not only subsequently affect change in depression, but also the other way around, improvement in depression at the start of treatment was related to the subsequent development of CBT skills later in treatment and to subsequent decreases in dysfunctional thinking during the course of treatment. Our results support the hypothesis that change in CBT skills plays a specific role in CBT for depression while, on the other hand, results indicate that cognitive change might be a mechanism not specific to CBT. Previous studies defined a proposed mechanism to be specific if the change in the proposed mechanism is larger in the relevant therapy compared to comparison treatments (Garratt et al., 2007). This is the case with the change in CBT skills in our study. In contrast, against our expectations, although dysfunctional thinking decreased over time in both treatments, IPT was related to larger decreases of dysfunctional

Table 7
Correlations between baseline working memory and outcome and change in the putative mechanism.

	Baseline working memory
Outcome change	
Δ Depression	.06
Change in the putative mechanism	
Δ IPT skills	.22*
Δ CBT skills	.22*
Δ Behavioral activation	.18
Δ Cognitive change	.08
Δ Therapeutic alliance	.05
Δ Motivation	.09
Δ Compliance	.03

Note. Note that variables were coded in a way that a positive correlation indicates that a higher baseline working memory score is related to improvement in depression or the putative mechanism.

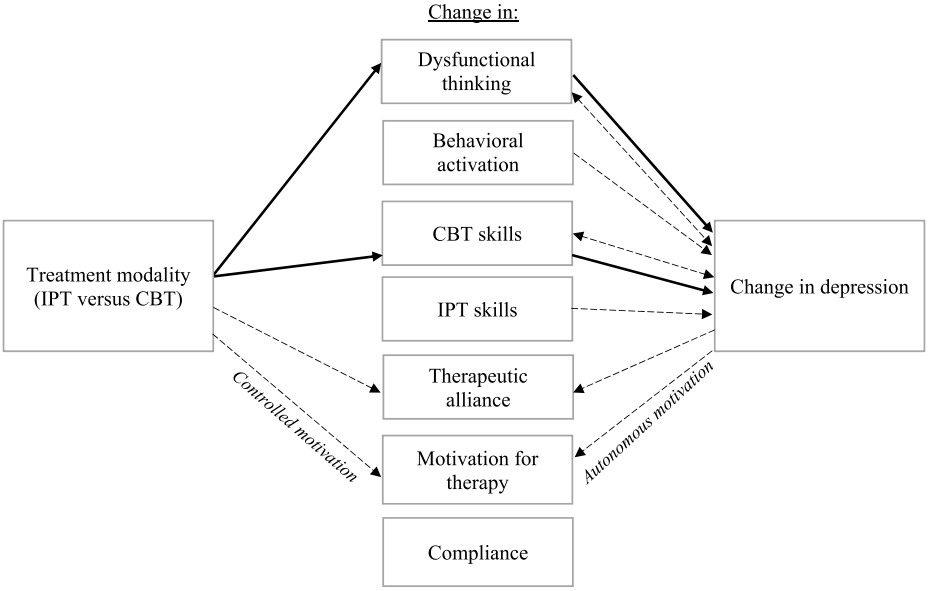

Fig. 1. Significant mediation (solid lines) and the paths (dashed lines) and directions (arrows) resulting from the multivariate latent change score/mediation models.

thinking compared to CBT. This result complements to findings showing that comparison treatments also relate to or are mediated through cognitive change (Garratt et al., 2007; Hofheinz et al., 2020; Lorenzo-Luaces, German, & DeRubeis, 2015; Quigley et al., 2019) and that dysfunctional thinking improves during IPT (Bernecker, Constantino, Pazzaglia, Ravitz, & Mcbride, 2014). We may conclude that change in dysfunctional thinking is a mechanism of change that seems not specific to CBT, and also related to subsequent changes in depression during IPT. It remains however unclear why patients who received IPT showed a larger decrease in dysfunctional thinking and why a decrease in dysfunctional thinking later in treatment was related to a subsequent increase of depression. One potential explanation for the difference between treatment modalities is that compared to patients who received IPT, the patients who received CBT might have gained insights into their dysfunctional thinking patterns at the end of treatment and therefore tend to have higher scores on dysfunctional thinking (explaining why patients who received IPT showed a larger decrease in dysfunctional thinking). It remains unclear why a decrease in dysfunctional thinking is related to increases in depression. An additional possible interpretation is that although IPT does seem to reduce dysfunctional thinking, it is not the mechanism through which IPT achieves a reduction in depression.

Besides the mediational effects, some specific directions of change were found: improvement in IPT skills was related to subsequent decrease of depression and a decrease in depression led to subsequent improvement in the therapeutic alliance and a decrease of autonomous motivation for therapy. Improvement in behavioral activation at the end of treatment was related to subsequent increase of depression. Changes in these variables were not related to each other when tested in the other direction. That therapeutic alliance was not related to subsequent change in depression is in line with some previous studies that investigated the role of therapeutic alliance in CBT and IPT for depression (Lemmens et al., 2017; Strunk, Brotman, & DeRubeis, 2010; Webb, DeRubeis, & Shelton, 2011). The studies that, in contrast to our finding, did find that therapeutic alliance played a role in CBT or IPT for depression focused on the role of personality characteristics at baseline and found that therapeutic alliance mediated the relationships between these personality characteristics at baseline and outcome (Kushner, Quilty, Uliaszek, McBride, & Bagby, 2016; Penedo et al., 2020; Zuroff et al., 2000). Other studies that found an effect of therapeutic alliance on subsequent outcome differ from our study in that they had a smaller sample size (Falkenström, Ekeblad, & Holmqvist, 2016) or that change in alliance was tested on session level (Falkenström et al., 2016; Penedo et al., 2020; Webb et al., 2011). However, reversed causality could also not be excluded in these studies. Based on our and previous findings on the role of therapeutic alliance in CBT and IPT for depression, several hypotheses on the role of the therapeutic alliance in psychotherapy can be made. First, it is possible that compared to alliance-based therapies, therapeutic alliance plays no causal role in decreasing symptoms in CBT or IPT for depression (Huibers & Cuijpers, 2015). Change in depression may affect changes in therapeutic alliance, and IPT might lead to larger increase in therapeutic alliance compared to CBT (as was also supported by the difference in effect size), but changes in therapeutic alliance do not causally relate to changes in depression. This hypothesis is in line with our and previous findings that find no effect of effects in both directions, but also with studies that pointed out that therapeutic alliance played a larger, role in alliance-focused therapies compared to CBT (Zilcha-Mano et al., 2016; Zilcha-mano, Eubanks, & Muran, 2019). Second, it is also possible that alliance plays a causal role across psychotherapies but that it is not the treatment, but individual patient characteristics are most important in determining the relevance of the relation between therapeutic alliance and outcome for a particular patient. An example can be found in Zilcha-Mano, Muran, Eubanks, Safran, and Winston (2017) who showed that in clients described as overly cold and low on intrusiveness, state-like strengthening of alliance predicted better outcome, while for clients described as overly exploitable, the general tendency of the client to report stronger alliance was associated with better outcome (Zilcha-Mano et al., 2017). Not only the therapeutic alliance, but also change in autonomous motivation was affected by change in depression. Change in depression related to change in autonomous motivation during the full course of treatment. In line with previous studies that indicated that autonomous, compared to controlled motivation, is related to treatment outcome (McBride et al., 2010; Zuroff et al., 2017), changes in controlled motivation were not related to changes in depression. Our results however suggested that a decrease in depression was related to a subsequent decrease in autonomous motivation (instead of the other way around) and suggested a specific effect of IPT on reducing controlled motivation during treatment.

While change in depressive symptoms affected subsequent therapeutic alliance and autonomous motivation, the specific direction for the IPT skills and behavioral activation was the other way around: an improvement in IPT skills and behavioral activation led to a subsequent change in depression. IPT skills is a newly developed construct that aims to measures skills that are specifically developed in IPT, divided into communication skills and social support, understanding of the patient's own feelings, coping with grief and major life change, and understanding feelings of others. In a recent paper we found that IPT skills during the first two weeks of treatment mediated the relation between session frequency and outcomes after CBT and IPT for depression (Bruijniks et al., 2021), and (partly) explained why a higher session frequency led to better outcomes compared to a lower session frequency. Our present findings suggest that the role of IPT skills is not specific to IPT and suggest that the development of IPT skills during the first treatment sessions might be skills important for the reduction of depressive symptoms across different psychotherapies. In regard to behavioral activation, change in behavioral activation negatively affected change in depression at the end of treatment and did not differ between treatment modalities. As behavioral activation procedures mostly conducted at the beginning of therapy it was unexpected that behavioral activation did not lead to decrease in depression the at start of treatment and is unclear why an increase in behavioral activation was related to increases in depression towards the end of treatment. The absence of a difference between treatment modalities suggests that behavioral activation might not be a specific mechanism of change in CBT for depression but that also during IPT, change in behavioral activation and change in depression are related.

Strengths of the present study are that it fulfilled to multiple criteria (RCT data with two treatment conditions, sample size $\geq$40 and multiple measurements of common and specific factors to measure temporal and reversed relationships) for successful mechanism research (Lemmens et al., 2016). The present study was one of the few studies so far that included multiple measurements of both hypothesized common and specific mechanisms of change and investigated its temporal and reverse relation with depressive symptoms in CBT and IPT for depression. By using these advanced analyses, the present study contributed to clearing up the 'black box' that explains how CBT and IPT work. However, the sixth criteria, experimental manipulation of the proposed mechanism is unfortunately almost (if not totally) within the context of a RCT. A second limitation of the study is that the sample size was small to detect mediation effects of medium to large size (Koopman, Howe, Hollenbeck, & Sin, 2015) and to investigate how the relevant therapy processes relate to each other by including multiple concurrent therapy processes and relate them to subsequent change in depression into one model. Third, it should be noted that some of the models showed suboptimal model fit (i.e., the models including CBT skills and motivation, also see Table 4). Fourth, the sizes of the mediation effects were only of limited clinical significance (explaining up to only one point change on the BDI-II). Fifth, the power to test working memory as a moderated of mediation was limited. Sixth, the quality of therapy was variable across therapies (Bruijniks et al., 2021) and it might be possible that with less quality of the conducted therapeutic procedures, there has been less power to change the mechanisms that are hypothesized to be activated

by these procedures. Seventh, the current study included more measurements of potential mechanisms specific to CBT than to IPT.

The present study leads to several recommendations for future research. First, our findings pointed to two therapy processes that seemed to affect subsequent changes in depression at the beginning of treatment: CBT skills and IPT skills. This suggests that, from a clinical perspective, focusing on the development of the therapy skill processes at the beginning of treatment might provide an opportunity to optimize subsequent reduction in depression later in treatment. Future studies should additionally investigate if the relation between depressive symptoms and CBT skills shows better model fit when tested in a sample that received CBT only. Although change in dysfunctional thinking and behavioral activation where also related to subsequent change in depression, the direction of the relation between dysfunctional thinking and depression was unexpected and change in behavioral activation affected subsequent change in depressive symptoms negatively at the end of treatment. In contrast to CBT treatment manuals that suggest starting with the behavioral part of CBT and then continue with the cognitive part of CBT, our results might suggest that changes in behavioral activation somewhat later in treatment might affect subsequent changes in depression. Second, future studies should consider measuring cognitive change and behavioral activation at each session to further disentangle their changes and relation with change in depression at more detailed level. Our findings suggest that these mechanisms might not be specific to CBT and that dysfunctional thinking seems to be more often affected by depressive symptoms than the other way around. It would be interesting to see whether these findings can be replicated in future studies by investigating how change in these variables relate to each other and to change in depression on a session-to-session level. Third, future studies on cognitive change should explicitly measure different levels of cognitive change. When we compare our findings on dysfunctional thinking with recent other studies that investigated potential mediation of cognitive change in CBT for depression, the other study that found significant mediation of cognitive change specific to CBT (compared to light therapy) also used a measure of automatic negative thoughts (Rohan, Burt, Camuso, Perez, & Meyerhoff, 2020), while two other studies that did not find mediation or any temporal effects, but did show that dysfunctional attitudes decreased in all treatment conditions, did measure cognitive change with a measure of dysfunctional attitudes (Lemmens et al., 2017; Quigley et al., 2019). Future studies should take into account that different levels of cognitive change (automatic thoughts, dysfunctional attitudes, core beliefs or schemas) may play different roles within psychotherapy for depression. Fourth, it is also possible that for some of the mechanisms (for example for the therapeutic alliance, motivation and compliance) it is not the change in these mechanisms but the baseline level that plays an important role in predicting changes in other therapy processes and outcome. Future studies should address this possibility. Fifth, future studies should take into account individual differences in pathways of change. Examples are the studies on therapeutic alliance described above, but these hypotheses may also hold for other potential mechanisms of change (for example see the study of Fitzpatrick and colleagues that indicated that cognitive change predicted symptoms change more for patients with fewer perceived social skills and with greater interpersonal problems; Fitzpatrick, Whelen, Falkenström, & Strunk, 2019). One potential reason why we only found mediation effects of small clinical significance, is that the mediation effects were investigated on group level, ignoring the hypothesis that different mechanisms of change might be relevant for different subgroups of patients.

In sum, improvements in CBT skills seems to be a mechanism of change leading to subsequent decreases in depression and that is specific to CBT. Across two types of psychotherapy, improvement in IPT skills might be a non-specific mechanism of change leading to subsequent decrease in depression in the beginning of treatment. The mediational effects of cognitive change and behavioral activation were unexpected, and the specificity and directions of both putative mechanisms should be further tested. As a decrease in depression led to subsequent improvement in the therapeutic alliance and a decrease in autonomous motivation (and not in the reverse direction), our findings suggest that, at least in CBT and IPT for depression, these processes do not act as mechanisms of change. Changes in CBT skills and IPT skills at the beginning of treatment affected subsequent change in depression and focusing on these processes at the beginning of treatment might provide an opportunity to optimize subsequent reduction in depression later in treatment. Future studies should further focus on testing the specificity and direction of the potential mechanisms of change throughout the course of treatment and investigate whether these pathways differ between different individuals.

Author contributions

SB, MM, MH made the design and analysis plan for the study. MH, FP and PC received the funding for this study. SB conducted the analyses and wrote the manuscript. All authors read, contributed to, and approved the final manuscript.

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Disclosure of interest

The authors report no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.brat.2021.104010.

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