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Mechanistic pathways of change in twice weekly versus once weekly sessions of psychotherapy for depression

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ABSTRACT

Background: Recently, we showed that twice weekly sessions of cognitive-behavioral therapy (CBT) and interpersonal psychotherapy (IPT) for depression lead to better and faster treatment outcomes compared to once weekly sessions (Bruijniks et al., 2020). The present study investigated which pathways of change may account for the effects of different session frequencies.

Method: The sample consisted of 200 patients who were randomized to CBT weekly, CBT twice weekly, IPT weekly, or IPT twice weekly. Outcome and therapy processes were measured at baseline, two weeks and monthly up to month 6 after the start of treatment. Latent change score models investigated temporal relations between change in therapy processes and change in depression and tested whether change in the therapy processes mediated the effect of session frequency on change in depression.

Results: IPT skills mediated the relation between session frequency and change in depression. A decrease in depression was related to subsequent improvement in CBT skills and subsequent decrease in motivation for therapy.

Conclusion: The development of IPT skills may explain why a twice weekly higher session frequency is more effective in reducing depression compared to a once-weekly session frequency. Future studies should disentangle the causal effects of therapy process change throughout the course of therapy.

1. Introduction

Insight into the mechanisms of change of psychotherapy for depression is needed to improve outcomes for the treatment of major depressive disorder (MDD). Mechanisms of change can be seen as the combination of procedures delivered by the therapist and the therapy processes in the patient that are mobilized by those procedures to subsequently reduce symptoms (Bruijniks, DeRubeis, Hollon, & Huibers, 2019; Huibers, Lorenzo-Luaces, Cuijpers, & Kazantzis, 2021; Kazdin, 2009). Psychotherapy literature mostly focused on investigating different therapy processes as potential mechanisms of change and can be divided into common therapy processes that are present across therapies versus therapy processes hypothesized to be specific to a certain type of psychotherapy (Cuijpers, Reijnders, & Huibers, 2019; DeRubeis, Brotman, & Gibbons, 2005; Mulder, Murray, & Rucklidge, 2017). For example, an often investigated potential common therapy process is the therapeutic alliance, defined as the working relationship between the therapist and patient (Flückiger, Del, Wampold, & Horvath, 2018). On the other hand, change in dysfunctional thinking is a therapy process hypothesized to be specific to cognitive-behavioral therapy (CBT), one of the most investigated psychotherapies for depression (Beck, Rush, Shaw, & Emery, 1979; Lorenzo-luaces, Lemmens, Keefe, Cuijpers, & Bockting, 2021). Despite the many studies that focused on identifying the therapy processes that are responsible for improvement during psychotherapy for depression, it remains unclear which exact therapy processes are responsible for a reduction in depressive symptoms (Lemmens, Müller, Arntz, & Huibers, 2016).

Studying mechanisms of change in psychotherapy is challenging

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from a methodological perspective. Several statistical and methodological requirements need to be satisfied to show that change in a certain therapy process is causally related to change in depressive symptoms (Kazdin, 2007, 2009). Most studies on mechanisms of change in psychotherapy tested the assumption of statistical mediation, showing that the effect of treatment on outcome is at least partly explained by a variable that measures the therapy process (i.e., also referred to as the mediator). However, statistical mediation does not test whether the mediator changes before the outcome does (i.e., temporality), and to conclude that the mediator affects the outcome and not the other way around, tests should control for the presence of reverse relationships. Additionally, it has been argued that to demonstrate that a certain therapy process is a mechanism of change, the investigated relations should be plausible, consistent across studies and rule out the effects of other mediators or potential unknown confounding variables that may explain the relation between the therapy process and outcome. Moreover, showing that a mediator is related to outcome in one treatment, but not in another, would support the specificity of the potential mechanism in treatment (Kazdin, 2007, 2009). The best way to demonstrate a causal relationship between a potential change mechanism and the outcome would be to conduct an experiment that manipulates the hypothesized mechanism of change and tests its direct effect on the outcome. Experimentally manipulating a process of change is challenging and scarce in the field of CBT for depression (Bruijniks, Sijbrandij, Schlinkert, & Huibers, 2018). Most data that have investigated mechanisms of change used data from randomized controlled trials. In these datasets, statistical mediation of therapy processes has been often demonstrated, but experimental manipulation or controlling for temporality is rare (Lemmens et al., 2016).

Recent mechanism studies have used more sophisticated statistical methods to model changes during therapy over time in non-experimental data (Falkenström, Solomonov, & Rubel, 2020; Mund & Nestler, 2018; Usami, Murayama, & Hamaker, 2019). For example, in a study focusing on potential mechanisms of change in two treatments for panic disorder, Solomonov et al. (2019) separated between-patient from within-patient variation in the therapy processes and symptoms. In separate models they were able to investigate whether the therapeutic alliance or use of certain therapeutic techniques predicted subsequent improvement in therapy processes and outcome, while controlling for the stable differences between patients and prior levels of these variables and testing the reverse relationships. Results showed that different processes functioned differently in different treatments. Another example comes from the field of depression. In the study of Lemmens et al. (2017), change in therapy processes and symptoms during CBT and interpersonal psychotherapy (IPT) were modelled using latent change scores representing change between the measurement points. In this way, it was possible to model and test temporal relations between changes in therapy processes and changes in depressive symptoms over time and test for mediational effects at the same time. Results pointed to concurrent change of the processes and symptoms while nearly no temporal relations were found (i.e., only improvement in self-esteem was related to subsequent change in depression), possibly explained by the long time periods between the measurements (i.e., three months).

Recently, we showed that a higher session frequency (twice weekly versus once weekly sessions) of CBT and IPT for depression leads to better and faster treatment outcomes (Bruijniks, van Grootheest, et al., 2020). While this study led to a clinical recommendation to improve treatment outcome for depression by enhancing its session frequency, a difference between treatment effects also indicates that the two treatments might work through different mechanisms. Identifying the mechanisms of change that are responsible for the better treatment effects of a higher session frequency will inform us on which mechanisms need to be targeted to make treatments more effective. For example, if an increased capacity to perform therapeutic skills mediates the treatment effect, interventions targeted at this specific change process can be refined. We hypothesized that a higher session frequency might lead to better treatment outcome (decreased depressive symptoms) through two potential pathways (also see Fig. 1; Bruijniks et al., 2015). First, we expected that a higher session frequency might lead to better recall of the session content, which leads to the better development of specific therapy skills and subsequent better outcomes (therapy-specific learning pathway). Second, a higher session frequency might improve the therapeutic alliance, which in turn might increase compliance and motivation and in this way lead to better outcomes (common therapy process pathway). To overcome methodological shortcomings of previous studies in which the limited number of measurement moments might have interfered with the ability to capture temporal relationships (Lemmens et al., 2016, 2017), we included 4–8 different measurements moments (baseline, two weeks and monthly up to 6 months after start of treatment) during the therapy phase of the study. Using a latent change score model, the present study investigated whether the two proposed mechanistic pathways of change explain differences between weekly versus twice weekly sessions of psychotherapy (CBT and IPT) for depression. In addition, based on our recent studies that indicate that individual differences in learning capacity may moderate the success of therapy procedures in bringing change in the therapy process and outcome (Bruijniks et al., 2019, 2020; Bruijniks, Sijbrandij, & Huibers, 2020), we explored whether a baseline measure of working memory would affect change in the therapy processes and outcome.

2. Methods

2.1. Design and participants

The study was conducted in context of a multicenter randomized trial that investigated the effects of session frequency and mechanisms of change in cognitive-behavioral therapy (CBT) and interpersonal psychotherapy (IPT) for depression (Bruijniks et al., 2015). A total of 200 patients with major depressive disorder were randomized to CBT weekly ($n = 49$), CBT twice weekly ($n = 49$), IPT weekly ($n = 55$), IPT twice weekly ($n = 47$). Participants who were randomized to the condition with twice weekly sessions received 16 sessions during the first 8 weeks of treatment, and 4 sessions during the last 8 weeks (up to 20 sessions over a period of 16 weeks). Patients who were randomized to the condition with once weekly sessions received 16 sessions during the first 16 weeks and 4 sessions during the last 8 weeks (up to 20 sessions over a period of 24 weeks). Patients were recruited from specialized out-patient mental healthcare centers located across the Netherlands and included if they received a primary diagnosis of a DSM-5 major depressive disorder (including chronic depression), were aged 18 to <65 years, had sufficient knowledge of the Dutch language, had a pre-treatment score ≥20 on the Beck Depression Inventory-II (BDI-II) and access to internet facilities. Patients were excluded if they had planned to start antidepressants or changed their dosage in the past 3 months, showed acute risk for suicide, had a diagnosis of drug or alcohol dependence, a diagnosis of a cluster A or B personality disorder was present or if participants had more than five sessions of adequate CBT or IPT in the previous year. In addition to primary outcome measures, the study included multiple measurements of common and specific therapy processes during the treatment phase (i.e., up to six months after start of treatment), the study included multiple measurements of common and specific therapy processes alongside the measurement of therapy outcome, which will be the focus in the present study. Measurements were completed during the session (i.e., recall of the previous session content, compliance) or on standardized time points (baseline and two weeks and monthly after start of treatment up to month 6) separately from the treatment sessions (i.e., therapeutic alliance, therapy skills, motivation). The study was approved by the Medical Ethical Committee of VU Medical Centre Amsterdam (registration number 2014.337). All patients signed informed consent. 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, 2020).

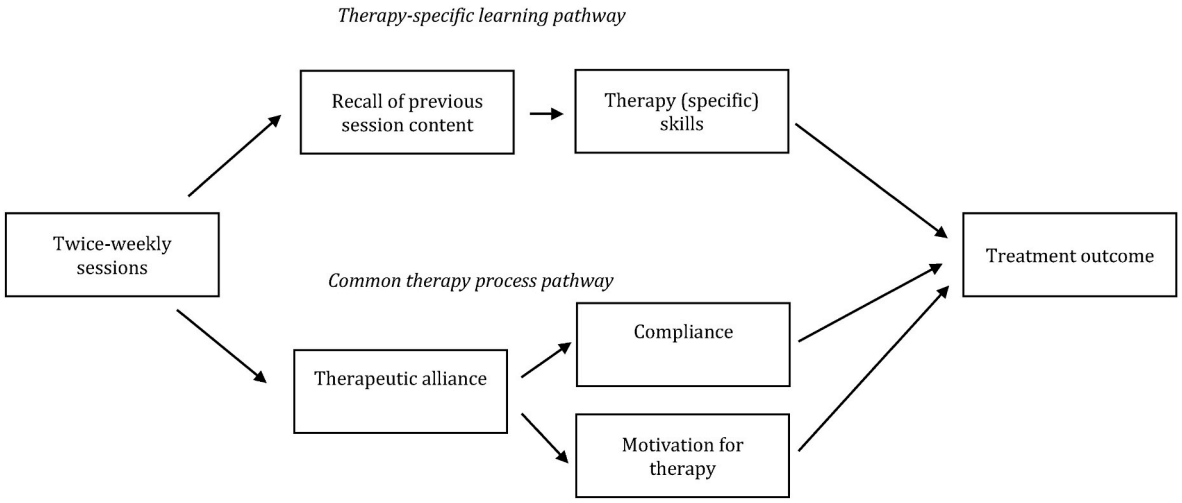

Fig. 1. Hypothesized pathways of change in psychotherapy. Derived from Bruijniks et al. (2015).

2.2. Measurement instruments

2.2.1. Outcome

2.2.1.1. Depression: Beck Depression Inventory II (BDI-II). The BDI-II is a 21-item patient 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 mechanisms

2.2.2.1. Therapy-specific learning pathway of change. Recall of the previous session content: Recall was rated after each session by the therapist. The following question was rated on an 11-point Likert Scale: 'If you had to rate how well the patient remembered the content of the previous session, what rating would you give?' (0 = patient cannot remember anything, 5 = the patient remembers some parts, but does not remember other parts, 10 = patient seems to remember everything). Because the recall ratings were completed during the session, ratings were matched to represent recall measured 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).

Therapy (specific) skills: Therapy skills were measured on the standardized time points using two different patient-rated questionnaires, one questionnaire measuring skills related to CBT, the other questionnaire measuring skills related to IPT. Both questionnaires were completed by all patients (i.e., regardless of whether patients received IPT or CBT, all patients completed both skill measures).

CBT skills: CBT skills are defined as the ability to reevaluate the accuracy of one's automatic thoughts and to engage proactively in pleasurable activities (Strunk, Hollars, Adler, Goldstein, & Braun, 2014), and were measured with the Competencies of 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, DeRubeis, Chiu, & Alvarez, 2007; Strunk et al., 2014).

IPT skills: IPT skills are defined as the patient's ability to link interpersonal events to depressive symptoms; to deal with grief, role dispute, and major life changes; and to practice social skills (Bruijniks, Peeters, et al., 2019) and were measured using the Interpersonal Psychotherapy Skills Scale–Self-Report (IPSS- SR). The IPSS-SR consists of 25 items measured on a 7-point Likert Scale. Initial psychometric properties have been supported (Bruijniks, Sijbrandij, & Huibers, 2019).

Therapy-specific skills: A specific therapy skills measure was computed by standardizing the CCTS-SR and IPSS-SR scores and including the standardized CCTS-SR scores in case the patient had received CBT, while the standardized IPSS-SR scores were included when the patient had received IPT. This resulted in one extra variable representing the skills that are specific to the therapy the patient actually received.

2.2.2.2. Common pathway of change. Therapeutic alliance: Therapeutic alliance was measured on the standardized time points with the 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: Motivation for therapy was measured on the standardized time points with the Autonomous and Controlled Motivation for Treatment Questionnaire (ACMTQ) that 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 by the patient on a 7-point rating scale and a total score was computed by combining the questionnaires. Initial reliability and validity have been supported (McBride et al., 2010; Zuroff, Koestner, Moskowitz, McBride, & Bagby, 2012).

Compliance: Patients rated their effort in treatment between sessions before each session 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 and their timing was matched to recall, 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).

2.2.3. Potential moderator

Working memory: Working memory (WM) was measured at baseline with the n-back task (Braver et al., 1997). The exact same version was

used in one of our previous studies (Bruijniks, Sijbrandij, & Huibers, 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. First, the participants were asked to run 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'). Second, 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). 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). WM load increased as the task progressed from 1-back to 3-back. The task took a maximum of 12.5 min. 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 analysed according to the intention-to-treat principle, meaning that all patients were analysed according to their randomized condition and available information from all patients was used in the analysis. First, descriptives (mean, standard deviations, within-group and between-group effect sizes) on the outcome and on all therapy processes at each time-point and concurrent and temporal correlations between change in depression and change in the therapy processes were described for the whole sample and per session frequency. 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 therapy process 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 therapy processes was related to change in the outcome, Latent Change Score (LCS) models were analysed using Mplus (Grimm, Ram, & Estabrook, 2017). In contrast to traditional mediation models, change is presented by a latent variable in LCS models. In addition, LCS models allow us to separate the model change in the therapy processes and outcome between and across the different time points separately (Castro-Schilo & Grimm, 2018; McArdle, 2009). Note that a positive latent difference score points to an increase in the variable score while a negative latent difference score means a decrease in the score of the variable. For our models, this means that positive latent difference scores indicate worsening of depression (i.e., as higher BDI-II scores indicate worse depression), but improvement in any of the therapy processes (i.e., as for these variables higher scores indicate more presence of the therapy process). Thus, a positive relationship between change in the therapy process and change in the outcome indicated that improvement in the mediator was associated with a worsening of depression. In contrast, a negative relationship indicated that improvement in the therapy process was associated with improvement of depression.

Before change in the therapy process was linked to change in the outcome, single change models were fit for each putative therapy process and the outcome separately to determine how change could be best modelled for this variable (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 therapy process was linked to the outcome in a LCS model to test temporal relations between change in the therapy process and change in the outcome. A temporal relation indicated that change in the therapy process would precede 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 therapy process), and the directions modelled in both ways and compared model fit. Raw and standardized betas of the significant pathways were reported. Standardized pathways indicated change in standard deviations of the therapy process when session frequency 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).

Third, mediation (session frequency → change in the therapy process → change in the outcome) was tested by adding session frequency 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 therapy process) showed similar or better fit compared to the initial model, mediation was also tested in the reversed direction. 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

Table 1
Measurement of outcome and potential mechanisms of change.

	Baseline	Week 2	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6
Outcome								
Depression: BDI-II	X	X	X	X	X	X	X	X
Therapy process								
Recall		X	X	X	X			
CBT skills: CCTS-SR	X	X			X			X
IPT skills: IPSS-SR	X	X			X			X
Therapeutic alliance: WAI		X	X	X	X	X	X	X
Motivation for therapy: ACMTQ	X	X	X	X	X	X	X	X
Compliance		X	X	X	X			
Potential moderator								
Working memory: n-back task	X							

Note: ACMTQ = Autonomous and Controlled Motivation for Treatment Questionnaire; BDI-II = Beck Depression Inventory II; CCTS-SR = Competencies of Cognitive Therapy Scale-Self Report; IPSS-SR = Interpersonal Psychotherapy Skills Scale–Self-Report; WAI = Working Alliance Inventory. Note that recall and compliance were measured before each session and the ratings that were used in this study were matched to the standard time points at which the other measurements were conducted. Also note that all patients completed both the IPSS-SR and CCTS-SR and change in IPT skills and CBT skills was investigated in the whole sample (regardless of who received IPT or CBT). The therapy-specific skill measure however investigates therapy-specific skills by including the standardized CCTS-SR scores in case the patient had received CBT, while the standardized IPSS-SR scores were included when the patient had received IPT.

standard deviations of the outcome (depression) resulting from changing from weekly to twice weekly sessions through change in the therapy process.

Fourth, the full therapy-specific learning and common pathways were explored, according to our initial hypotheses. The number of pathways per hypothesis depended on the number of available measurements. An overview of each tested pathway and the related time points of the change can be found in Fig. 2.

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 (i.e., the root-mean-square error of approximation (RMSEA), cut-off value $< .08$, and even better <0.05 and; 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.) (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 and therefore missing values were not imputed.

2.4.2. Explorative analyses

First, correlations between baseline working memory and change in therapy processes and outcome were computed. Second, in case of a significant mediation of change in a therapy process between session frequency and change in the outcome, moderation of working memory of the relation between change in the therapy process and change in depression was tested. In case mediation was found, moderated mediation was tested. Baseline depression, session frequency, baseline working memory, baseline therapy process, therapy process change (i.e., change in the therapy process during the specific measurement points where mediation was found) and the interaction between baseline working memory and session frequency (i.e., the moderator) were modelled as independent variables, and therapy process change and change in depression (during the specific measurement points where mediation was found) as dependent variables. The significance of the moderator on therapy process change was tested using bias-corrected 95% bootstrap confidence intervals (CI) with 10000 bootstrap samples.

3. Results

3.1. Descriptive statistics

Tables 2 and 3 show the descriptive statistics and within- and between group effect sizes on the therapy processes and outcome. Data Supplement 1 shows the concurrent and temporal correlations between change in the therapy processes and change in the outcome for the whole group and per session frequency.

3.2. Multivariate latent change score models

Change in all variables was best modelled using a constant change factor, except for therapeutic alliance and recall where a dual change model (i.e., modelling both a constant change and a proportional change between measurement moments) showed the best fit. Fit parameters of the original (change in the therapy process on subsequent change in the outcome), the reversed (change in the outcome on subsequent change in the therapy process) and all direction (change modelled in both directions) model can be found in Data Supplement 2. Fit parameters of the final models are given in Table 4. Model estimates of the final multivariate latent change score models can be found in Table 5.

3.2.1. Recall

Change in recall did not significantly affect subsequent change in depression on any of the time points. Running the reversed model (change in depression to change in recall) did slightly improve model fit (see Data Supplement 2 and Table 5) but did not point to significant relations between change in depression and subsequent change in recall. Higher recall at week 2 was related to improvement in depression during treatment. Running the model with both directions included did not improve model fit.

3.2.2. Cognitive-behavioral therapy skills

Change in CBT 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 CBT skills was related to a subsequent decrease in depression (raw estimate (95% CI): −0.29 (−0.53/-0.07), standardized estimate (95% CI): −0.53 (−0.79/-0.16)). Running the

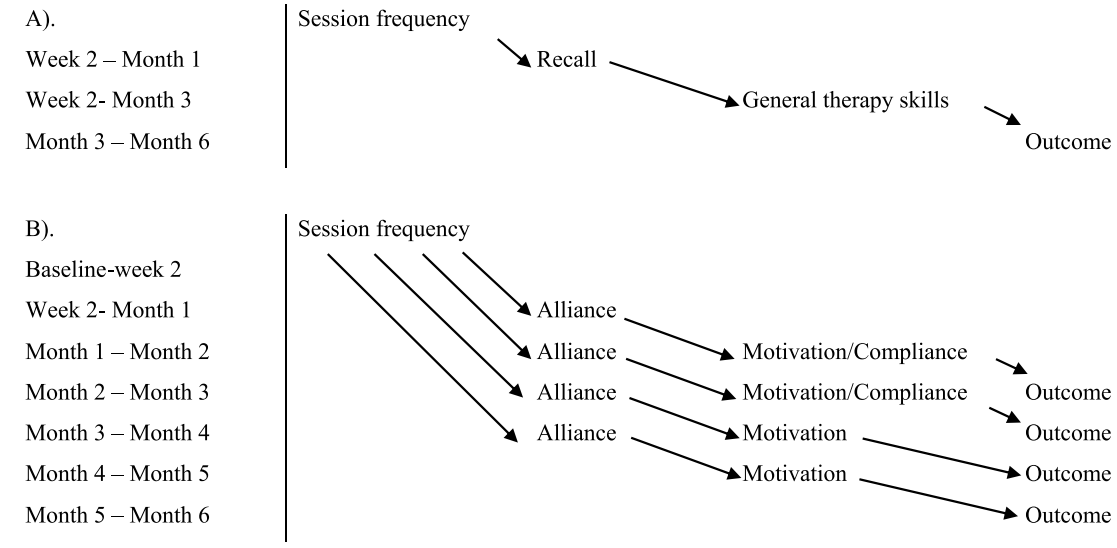

Fig. 2. Tested pathways of change. A). Therapy-specific learning pathway, B) Common pathways. Note that the number of pathways per hypothesis depended on the number of available measurements.

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)
Weekly	34.62 (9.48)	30.71 (10.70)	31.22 (11.22)	28.68 (12.74)	26.75 (12.46)	23.96 (13.02)	23.79 (14.42)	23.56 (14.85)
Twice weekly	34.80 (10.50)	32.73 (10.39)	30.39 (12.72)	26.59 (13.56)	24.67 (13.19)	24.13 (14.83)	21.52 (15.09)	20.75 (14.51)
Therapy process								
Recall		7.63 (2.10)	7.92 (1.78)	7.93 (1.81)	8.35 (1.81)			
Weekly		7.47 (1.93)	7.65 (1.91)	7.70 (1.83)	8.09 (1.78)			
Twice weekly		7.80 (2.26)	8.22 (1.58)	8.20 (1.76)	8.17 (1.85)			
CBT skills	80.79 (22.35)	87.68 (22.76)			105.03 (27.06)			107.31 (30.06)
Weekly	81.04 (23.75)	87.64 (21.43)			103.32 (28.91)			104.11 (29.55)
Twice weekly	80.52 (20.87)	87.73 (24.11)			106.64 (25.31)			110.38 (30.43)
IPT skills	91.03 (20.29)	93.95 (19.28)			99.31 (20.53)			102.61 (22.69)
Weekly	90.99 (20.05)	91.54 (15.59)			96.35 (17.43)			100.91 (21.46)
Twice weekly	91.07 (20.65)	96.25 (22.11)			102.11 (22.85)			104.18 (23.82)
Therapy-specific skills	-.05 (.89)	-.01 (1.00)			.01 (1.02)			.01 (.97)
Weekly	-.06 (.90)	-.02 (.83)			-.06 (.83)			-.05 (.96)
Twice weekly	-.03 (.89)	-.002 (1.14)			.08 (1.07)			.07 (.98)
Therapeutic alliance		40.67 (10.41)	41.21 (9.39)	41.79 (10.31)	43.48 (10.01)	44.44 (9.52)	44.20 (9.84)	42.53 (10.16)
Weekly		39.25 (9.41)	40.86 (8.37)	40.52 (9.80)	42.98 (9.98)	44.56 (9.01)	43.92 (10.08)	42.82 (9.90)
Twice weekly		42.03 (11.19)	41.60 (10.42)	43.05 (10.70)	43.94 (10.09)	43.33 (10.04)	44.50 (9.66)	42.25 (10.46)
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)
Weekly	50.98 (10.47)	55.46 (11.45)	53.40 (9.79)	52.48 (10.15)	54.81 (9.83)	54.10 (9.77)	53.08 (9.78)	52.47 (9.75)
Twice weekly	52.29 (9.84)	53.16 (9.30)	53.04 (10.56)	53.06 (11.84)	53.25 (11.19)	52.56 (12.00)	52.09 (11.30)	50.94 (12.06)
Compliance		5.16 (2.35)	5.71 (2.25)	6.21 (2.43)	6.39 (2.41)			
Weekly		5.15 (2.33)	5.64 (2.15)	6.29 (2.38)	6.63 (2.35)			
Twice weekly		5.17 (2.38)	5.79 (2.36)	6.11 (2.50)	6 (2.49)			

Note that the following data was missing: 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: $n = 54$; Recall, week 2: $n = 23$, month 1: $n = 24$, month 2: $n = 57$, month 3: $n = 62$; General skills, baseline: $n = 1$, month 3: $n = 57$, month 6: $n = 59$; 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: $n = 54$; IPT skills (IPSS-SR), baseline: $n = 1$, week 2: $n = 89$, month 3: $n = 58$, month 6: $n = 63$; 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: $n = 53$; Compliance, week 2: $n = 18$, month 1: $n = 25$, month 2: $n = 46$, month 3: $n = 77$. ACMTQ = Autonomous and Controlled Motivation for Treatment Questionnaire (ACMTQ), BDI-II = Beck Depression Inventory II, CCTS-SR = Cognitive Competencies of Cognitive Therapy Scale-Self Report, IPSS-SR = IPT Skill Scale-Self Report, WAI = Working Alliance Inventory.

reversed model (change in depression to change in CBT skills, see Data Supplement 2) improved model fit 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; raw estimate (95% CI): −1.87 (−2.98/-1.05), standardized estimate (95% CI): −0.59 (−0.79/-0.31)). Running the model with both directions included did not improve model fit.

3.2.3. 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 (raw estimate (95% CI): −0.83 (−1.59/-0.27), standardized estimate (95% CI): −0.69 (−0.94/-0.25)). 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.

3.2.4. Therapy-specific skills

Change in specific therapy skills between baseline and week 2 had a significant effect on subsequent change in depression between week 2 and month 3 (raw estimate (95% CI): −22.14 (−66.60/-6.39), standardized estimate (95% CI): −0.82 (−1.09/-0.35)), indicating that improvement in specific skills preceded a decrease in depression. Running the reversed model (change in depression to subsequent change in specific 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 a similar model fit (see Data Supplement 2). Patients with higher initial alliance (i.e., at week 2) showed more improvement in depression and change in depression from month 1 to month 2 led to 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 (raw estimate (95% CI): −0.58 (−1.12/-0.02), standardized estimate (95% CI): −0.57 (−0.96/-0.02)). 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.

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 than the model testing the relation between change in motivation for therapy and subsequent change in depression (see Data Supplement 2), and pointed to significant relations between change in depression between month 2–3 on change in motivation for therapy between month 3–4 (raw estimate (95% CI): 0.85 (0.07/1.62), standardized estimate (95% CI): 1.43 (0.12/2.48)) and change in depression between month 3–4 on change in motivation for therapy between month 4–5 (raw estimate (95% CI): 0.96 (0.17/1.75), standardized estimate (95% CI): 1.52 (0.28/2.52)), all indicating that a decrease in depression is related to a decrease in motivation for therapy. A model including effects in both directions did not converge.

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

	Within-group	Between-group
Depression		
Total	1.26	.17
Weekly	1.16	
Twice weekly	1.33	
Recall		
Total	.34	.15
Weekly	.32	
Twice weekly	.16	
CBT skills		
Total	1.18	.45
Weekly	.97	
Twice weekly	1.43	
IPT skills		
Total	.57	.14
Weekly	.49	
Twice weekly	.63	
General skills		
Total	.06	.10
Weekly	.01	
Twice weekly	.11	
Therapeutic alliance		
Total	.17	.35
Weekly	.37	
Twice weekly	.01	
Motivation for therapy		
Total	.01	.00
Weekly	.14	
Twice weekly	.13	
Compliance		
Total	.52	.28
Weekly	.63	
Twice weekly	.34	

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 session frequency conditions.

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, that higher baseline levels of compliance were related to improvement in depression during treatment but no significant relations between change in depression and subsequent change in compliance (see Data Supplement 2). Running the model with both directions included did not improve model fit.

3.3. Mediation

Change in IPT skills between baseline and week 2 significantly mediated the relation between session frequency and change in depression between week 2 and month 3 (significant indirect effect = −1.26 (−2.67/−0.02). Interpretation of the individual coefficients showed that a higher session frequency was non-significantly related to an improvement in IPT skills (raw estimate = 1.48 (−0.03/2.69), standardized estimate: 0.31 (−0.007/.57)), which was related to subsequent significant decrease in depression (estimate = −0.84 (−1.50/−0.30), standardized estimate: −0.72 (−0.94/-0.36)). The partially standardized indirect effect was: −0.14 (95% CI: −0.30/-0.003), indicating that when the session frequency changes from weekly to twice weekly sessions, BDI-II decreases by 0.14 standard deviations or 1.26 points between week 2 and month 3 after start of treatment as a consequence of prior change in IPT skills between baseline and week 2 of treatment.

3.4. Exploring the pathways of change

Testing the entire therapy-specific learning pathway (change in recall on change in therapy skills on change in depression) was not possible due to negative variance of the constant change variable of the BDI-II. Mediation and paths estimated in the common pathways (i.e., from change in therapeutic alliance to change in motivation or compliance to change in depression) were not significant.

Significant paths in the final multivariate LCS models are presented in Fig. 3.

Table 4
Estimates of the final models.

	X^2	df	RMSEA	SRMR	TLI	CFI	AIC
Recall *Depression - > recall*	40.49	24	.06	.04	.97	.97	6457.23
CBT skills *Depression - > CBT skills*	73.44	25	.09	.08	.91	.92	9754.14
IPT skills *IPT skills - > depression*	54.94	25	.07	.06	.95	.96	9247.67
Session frequency - > IPT skills - > depression	59.51	31	.07	.06	.95	.96	9246.34
General skills *Skills - > depression*	54.59	25	.07	.06	.95	.95	5726.44
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
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. The Akaike Information Criterion (AIC) was used for model comparison, with a lower AIC reflecting better model fit. Lower AIC by > 2 was considered reflecting a better model.

3.5. Explorative analyses

Explorative analyses investigated whether individual differences in working memory moderated the success of therapy in facilitating change in the therapy processes and outcome. Correlations between baseline working memory and therapy process change can be found in Table 6 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 improvement in CBT skills and IPT skills during treatment. Working memory did not moderate the relation between session frequency and change in IPT skills, or the relation between session frequency and change in depression.

4. Discussion

Change in IPT skills in the first two weeks of treatment significantly

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

	Recall	Therapy-specific skills	IPT skills	CBT skills	Therapeutic alliance[a]	Therapeutic alliance[b]	Motivation for therapy	Compliance
Correlations								
Baseline depression and change in the therapy process	−0.26	−0.42	−3.95	2.80	.008		−1.90	.09
Baseline therapy process and change in depression	−1.68[a]	0.02	.04	−1.83	−9.40		−1.63	-1.84[a]
Change parameters								
Constant change depression	−2.02[a]	−3.94[a]	−2.75[a]	−4.31[a]	−1.30[a]		−1.81[a]	-2.07[a]
Constant change therapy process	5.38[a]	0.03	3.56[a]	6.33[a]	−1.10		1.14	.59
Proportional change depression	NA	NA	NA	NA	NA		NA	NA
Proportional change therapy process	−0.67[a]	NA	NA	NA	.06		NA	NA
Coupling parameters								
Δ baseline – week 2-> Δ week 2 – month 3		−22.14[a]	-.83[a]	−1.87[a]				
Δ week 2 – month 3 -> Δ month 3 – month 6		−11.06	-.39	-.03				
Δ baseline – week 2 -> Δ week 2 – month 1							.64	
Δ week 2 – month 1 -> Δ month 1 – month 2	.06				−1.32	.30	.63	.07
Δ month 1 – month 2 -> Δ month 2 – month 3	-.09				−1.09	-.16	.68	.17
Δ month 2– month 3 -> Δ month 3 – month 4					-.46	.60	.85[a]	
Δ month 3 – month 4 -> Δ month 4 – month 5					−2.47	.25	.97[a]	
Δ month 4 – month 5 -> Δ month 5 – month 6					.29	1.33	.73	

[a] Significant estimates using bias corrected 95% bootstrap confidence intervals (CI) with 1000 bootstrap samples. The present table shows the uncorrected estimates. Note that coefficients for the model with the best fit were reported: 1. Change in depression - > change in recall; 2. Change in skills - > change in depression, 3. Change in IPT skills - > change in depression, 4. Change in depression - > change in CBT skills, 5a. Change in alliance - > change in depression, 5b. Change in depression - > change in 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.

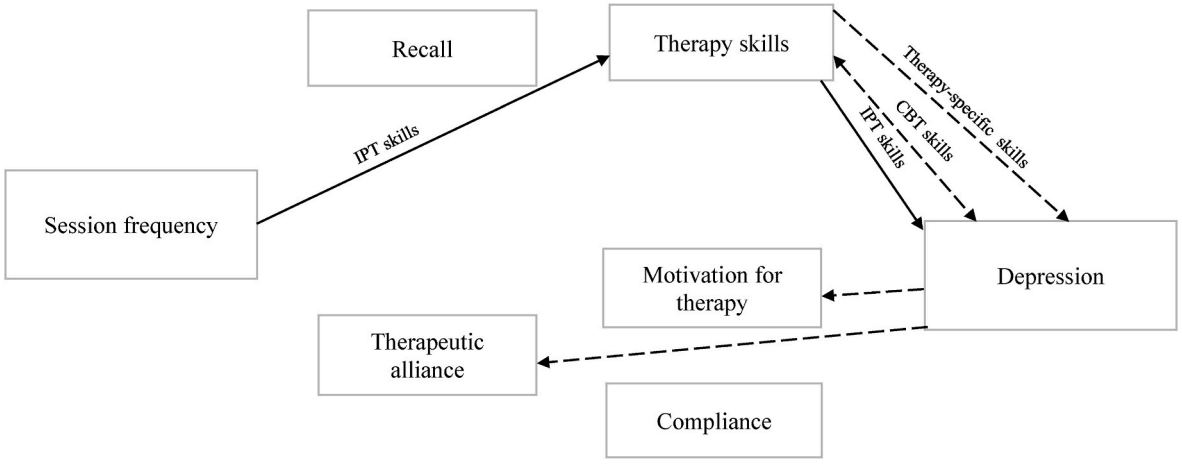

Fig. 3. Significant mediation (solid lines), paths (dashed lines) and directions (arrows) resulting from the final multivariate latent change score models. Note that for therapeutic alliance, because the two models (i.e., change in therapeutic alliance on change in depressive symptoms versus change in depressive symptoms on change in therapeutic alliance) did not differ in model fit, the model with both directions included was considered as the best model. The relation between change in depressive symptoms and change in therapeutic alliance did not remain significant in this final model. Note that although CBT skills and depressive symptoms influenced each other reciprocally, the model where change in depressive symptoms was related to subsequent change in CBT skills showed better fit, but model fit remained suboptimal.

mediated the relation between session frequency and change in depressive symptoms, where a higher session frequency led to improvement in IPT skills which was related to subsequent improvement in depression. There was a bidirectional relation between change in CBT skills and change in depression. 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. 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. A decrease in depressive symptoms was related to a subsequent decrease in motivation for therapy. Changes in recall and compliance were not related to change in depression. Higher baseline working memory scores were

Table 6
Correlations between baseline working memory and outcome and therapy process changes.

	Baseline working memory
Outcome change	
Δ Depression	.06
Therapy process change	
Δ Recall	-.05
Δ Specific therapy skills	.19
Δ IPT skills	.22*
Δ CBT skills	.22*
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 therapy process.

positively related to improvement in CBT skills and IPT skills during treatment but did not moderate the mediation of IPT skills between session frequency and change in depression.

Our findings suggest that the development of IPT skills at the start of treatment might explain why a twice weekly higher session frequency is more effective in reducing depression compared to a once weekly session frequency. IPT skills are a relatively new construct that was recently developed to investigate whether IPT may enable patients to develop a set of therapy-specific skills that are primarily responsible for the effects of treatment (Bruijniks, Sijbrandij, & Huibers, 2019). The Interpersonal Psychotherapy Skills Scale – Self Report (IPSS-SR) consists of four subscales focusing on communication skills and social support, understanding of own feelings, coping with grief and major life change, and understanding feelings of others, all skills that are hypothesized to be specifically developed in IPT. Our findings suggest that in a sample that received CBT or IPT, IPT skills at least partly explain why a higher session frequency is more effective compared to a lower session frequency.

The relation of change in CBT skills with change in depressive symptoms was less clear: although improvement in CBT skills was also related to subsequent improvement in depression, better model fit was reached when improvement in depression was related to subsequent improvement in CBT skills. Previous studies have linked change in CBT skills to subsequent change in depression, but did not always investigate the effect in the reverse direction (Forand et al., 2018; Hundt, Mignogna, Underhill, & Cully, 2013). In contrast to our results, a previous study pointed out that CBT skills were related to subsequent depressive symptoms and not the other way around (Jarrett, Vittengl, Clark, & Thase, 2018). However, a different measure of CBT skills and different measurement points (baseline to mid-treatment versus baseline to week 2) were included in this study, potentially explaining the discrepancy with our findings. Another reason why CBT skills might have played a less prominent role in the present sample is that the patients in our sample received CBT or IPT. If CBT skills is a therapy process that is specific to CBT, the presence of IPT in the present sample may have clouded the effect. It should be noted that the difference in effect size in CBT skills between session frequencies was 0.45 larger for the higher session frequency. It is possible that a higher session frequency increases the development of CBT skills, but this effect might be specific to CBT.

In contrast to our hypotheses and some earlier literature (Arnow et al., 2013; Knittle, Gellert, Moore, Bourke, & Hull, 2019), therapeutic alliance and motivation were not related to subsequent a reduction in depressive symptoms. In contrast, evidence for a relation in the opposite direction was found: a decrease in depressive symptoms was related to subsequent improvement in the therapeutic alliance, and to a decrease in motivation for therapy. Other studies on the role of the therapeutic alliance suggested that the therapeutic alliance and depression are concurrently related (Renner et al., 2018) and reciprocally influence each other (Flückiger et al., 2020; Webb et al., 2011), but also that therapeutic alliance can be an unreliable predictor of outcome (Zlotnick et al., 2020) or cannot be well investigated if not disentangled into its trait and state component (Zilcha-Mano, 2017). Our study suggested that change in depression may be related to an improvement in therapeutic alliance, but as no clear differences in model fit between the different models were found, the exact relation between change in therapeutic alliance and change in depression remains unclear. In regard to motivation, although motivation has been related to treatment outcome (McBride et al., 2010; Zuroff et al., 2017), studies that also included an investigation of the reversed relationships have been scarce (for one exception see: Knittle et al., 2019). Our study suggests that an improvement in symptoms may also lead to a decrease in motivation for therapy.

Our hypotheses in regard to recall and compliance could not be confirmed. Recall and compliance were not related to change in depression symptoms, in contrast to studies supporting these relations (Dong, Zhao, & Harvey, 2017; Kazantzis et al., 2016). While one explanation is that these constructs do not play a role in reducing depression, an alternative explanation is that both constructs were poorly measured. Both constructs were measured using 0–100 VASs. It is possible that these measurements were not reliable and that this influenced the results. Also, recall was rated by the therapist and the quality of the rating therefore dependent on the therapists' ability to make this estimation.

Results were mixed in regard to our earlier hypothesis that individual differences in learning capacity may moderate the success of therapy procedures in bringing about change in the therapy process and outcome (Bruijniks, Sijbrandij, & Huibers, 2019). While working memory did not moderate the relation between session frequency and change in the therapy processes, working memory was correlated with change in CBT and IPT skills. This latter finding is in line with earlier results showing that working memory plays a role in predicting the success of psychotherapy (Bruijniks, Sijbrandij, & Huibers, 2019, 2020), but also with recent studies that emphasize that interventions work differently for subgroups of patients (Huibers et al., 2021; Kaiser, Volkmann, Volkmann, Karyotaki, & Cuijpers, 2020). In addition, this finding may suggest that the role of baseline working memory might be specific for the therapy processes that seem to rely mostly on cognitive functioning since the acquisition of skills is a highly cognitive process (Tenison & Anderson, 2017; VanLehn, 1996) that not only needs to be activated during treatment, but also involves practice within sessions. A certain baseline degree of working memory might be crucial for the adequate acquisition of therapy skills, while baseline working memory seems not to be associated with change in the common mechanism pathway. Nevertheless, our finding was only correlational, and conclusions remain limited.

Several strengths and limitations can be mentioned. A major strength was that by using latent change score models the present study was able to model temporal relations between process change and change in depression while at the same time testing the direction of the effects. Our analyses allowed us to test temporal mediation effects at different time points during treatment and test these relations for multiple hypothesized mechanisms of change in CBT and IPT for depression. That our results pointed to the causal effect of session frequency on depression through change in IPT skills but none of the other therapy processes, points to a potential important role of IPT skills in the effects of a higher session frequency. However, while this study was powered to test differences between session frequency conditions in the main outcome, the sample size was limited to find medium to large mediation effects (Koopman, Howe, Hollenbeck, & Sin, 2015). In addition, the sample size was too small to link change in multiple concurrent therapy processes to subsequent change in depression in one model, to test the full pathways of change we hypothesized and not sufficient large to explore pathways of change of a higher session frequency in CBT versus IPT. Second, it should be noticed that while motivation and therapeutic alliance were

measured at week 2 and monthly after start of treatment, therapy skills (both IPT and CBT skills) were only measured at week 2, month 3 and 6, and compliance and recall only up to month 3, limiting the number of potential pathways of change that could be tested accordingly. It is yet unclear how change in CBT and IPT skills exactly is related to change in depression when it would have been measured more frequently (which might have been more appropriate to capture the effects) or which role recall and compliance could play later in treatment. Third, it should be noted that the model fit of the relation between change in depressive symptoms and change in CBT skills was suboptimal (also see Table 4). Fourth, because of the non-experimental nature of the study we cannot exclude the possibility that our findings cannot be explained by potential unknown confounding variables. Fifth, although change in IPT skills was a significant mediator of session frequency on change in depression, change in IPT skills in the first two weeks of treatment only explained 1.26 points decrease on the BDI-II between week 2 and month 3 after start of treatment, a decrease that can be considered only of small clinical significance. Although this is a step forward towards explaining why a higher session frequency leads to more improvement in depression compared to weekly sessions, future studies are necessary.

The present study leads to the following recommendations for future studies. First, future studies should further investigate the potential of increasing the treatment focus on the development of CBT and IPT skills to increase treatment outcomes. Our results that show that CBT and IPT skills predict subsequent change in depression suggest that these skills might drive subsequent change in depression, at least at some timepoints during 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. Second, future mechanistic studies should further investigate the causal relation between putative therapy processes and symptom change by disentangling these effects along the timeline from start to the end of treatment. Finding that change in the process predicts subsequent change in the outcome while controlling for earlier change in the outcome, does not exclude the possibility that reversed relationships are also present. Therefore, studies should not only test whether a certain therapy process change predicts subsequent change in depressive symptoms while controlling for earlier change in the depressive symptoms, but also include a test of the reversed relationship (i.e., change in depression to change in the process) to investigate and potentially exclude reversed causality. Future studies should recognize that these effects may differ within different stages of treatment. One way to do this might be by using ecological momentary assessment, a method that seems well-suited to assess individual temporal processes over time (Lane, Pike, & Wright, 2019). Another way to strengthen the evidence for potential causal relationships where change in a process has shown to be related to subsequent change in symptoms (and not the other way around) would be by conducting an experiment that manipulates the hypothesized mechanism of change and tests its direct effect on the outcome. Our findings suggest that therapy skills, motivation and therapeutic alliance might be great candidates for such experiments. Third, treatments might not work the same for each individual and future mechanistic studies should include individual patient characteristics that have shown to be promising candidates for moderating pathways of change. One reason we only found one mediation effect, that also was 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. Although underpowered, our study suggests that it might be interesting to further investigate the relation between baseline working memory, therapy skill acquisition and therapy outcomes. Potentially, individuals with low or high levels of baseline working memory improve through different pathways of change (i.e., while individuals with high levels of baseline working memory may improve through both the therapy-specific learning- and common pathway, the therapy-specific learning pathway may not be relevant for individuals with low levels of baseline working memory). Insight into how these pathways differ could inform clinical practice on what therapy process is important for whom. Fourth, future studies need larger sample sizes (Kyriazos, 2018; Wolf, Harrington, Clark, & Miller, 2013), especially when investigating larger models including many latent variables relative to the observed variables. Instead of conducting (underpowered) secondary analyses on RCT data, studies should be powered to investigate mechanistic models. In larger sample sizes, it would be interesting 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. Fifth, the construct of IPT skills should be further investigated. So far, the IPSS-SR has only been subject to initial psychometric validation, and another possible interpretation of our findings is that the IPSS-SR taps into common factor processes that explain why a higher session frequency led to better outcomes compared to a lower session frequency. This might also explain why IPT skills seem relevant in a sample including both CBT and IPT. However, our exploratory analyses suggest that the concept of IPT skills, like CBT skills, also distinguishes itself from the common processes because it is related to baseline working memory. Future studies should investigate its discriminant validity and test whether the acquisition of CBT and IPT skills are specific to their hypothesized related therapy modalities, as we plan to do. Sixth, future studies that measure recall should use a more elaborate recall test that is completed by the patient instead of the therapist, also see Gumport, Dong, Lee, and Harvey (2018) for an example.

In sum, in a sample receiving CBT or IPT for depression, the development of IPT skills may explain why a twice weekly higher session frequency is more effective in reducing depression compared to a once weekly session frequency. In addition, findings suggested that improvement in depressive symptoms preceded increases in CBT skills and decreases in motivation for therapy, while the relation between therapeutic alliance and depressive symptoms remained less clear. A focus on improving therapy skills may be a promising therapy process for improving future treatment outcomes. Future studies should focus on the causal relationships and timeline of change in therapy processes and outcome and further specify whether individual patient characteristics play a role in the mechanistic pathway as well.

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.2022.104038.

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