Skill Improvement through Learning in Therapy (SKILT): a study protocol for a randomized trial testing the direct effects of cognitive behavioral therapy skill acquisition and role of learning capacity in major depressive disorder

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Abstract

Background To improve and innovate psychological treatments for major depressive disorder (MDD), a better understanding on how symptoms ameliorate during treatment is essential. In cognitive behavioral therapy (CBT), one of the most investigated treatments for MDD, a prominently hypothesized key therapy process to reduce depressive symptoms is the acquisition of CBT skills. However, it is unclear whether procedures focused on the acquisition of CBT skills play a causal role in the improvement of CBT skills. In addition, cognitive and neurobiological impairments inherent to MDD might interfere with efficient skill learning and patients may vary in these impairments and their capacity to learn. In this randomized trial, we isolate a single CBT Skill Acquisition Procedure (CBTSAP) and test its direct effects on CBT skills, change in related therapy processes and outcome. We hypothesize that the CBTSAP causes improvements in CBT skills, related therapy processes and outcome compared to an active control condition. In addition, we hypothesize that learning capacity moderates the effects of CBTSAP on change in CBT skills, related therapy processes and outcome. Last, we hypothesize that integrating mental imagery as cognitive support to strengthen the effects of the CBTSAP will be most beneficial for patients with low learning capacity.

Method 150 patients with a DSM-5-diagnosis of MDD (of mild to severe intensity) who are on a waiting list to receive psychotherapy for depression will be randomized to one of three conditions: 1. CBTSAP, 2. CBTSAP plus cognitive support (mental imagery) or, 3. an active control condition, all consisting of three sessions. Primary outcomes will be change in CBT skills and depressive symptoms. Measured relevant therapy processes are changes in idiosyncratic dysfunctional thoughts and behaviors, dysfunctional thinking, reward processing. Measures of learning capacity measuring cognitive control and emotional bias will be conducted at baseline and tested as a potential moderator. Secondary outcomes are general psychological distress and session recall. Follow-up measurements will take place directly and one week after the last session.

Discussion Knowing whether and for whom the acquisition of CBT skills leads to a reduction of depressive symptoms will inform on how to personalize and optimize psychotherapy outcomes for depression.

Trial registration The trial is registered at the German Clinical Trial Register (DKTR; registration number: DRKS00024116).

Background

Current psychological treatments for depression are only effective for half of the patients (1). Response to psychological treatments is limited and relapse rates high (2,3). To improve and innovate psychological treatments, a better understanding on how symptoms improve during treatment is essential.

Psychotherapies aim to reduce depressive symptoms by mobilizing therapy processes that seem central to the development and maintenance of depressive symptoms. Therapy processes can be defined as the mechanisms inside the mind of the patient that are activated by the therapeutic procedures delivered by the therapist with the intent of producing change. In cognitive behavioral therapy (CBT; Beck, Rush, Shaw, & Emery, 1979), one of the most investigated treatments for depression, therapeutic procedures focus on three major therapy processes: dysfunctional thinking, reward processing and the acquisition of CBT skills. First, cognitive change procedures aim to change the process of dysfunctional thinking (5). Dysfunctional thoughts can be organized into different levels, some negative thoughts seem to occur more on a superficial level (negative automatic thoughts), while other thoughts are derived from more deeply integrated dysfunctional mental representations, that can include rules, expectations, or assumptions (attitudes) and sometimes even originate from early experiences in the childhood (schemas) (6). Second, CBT includes procedures aimed at behavioral activation in order to improve deficits in reward processing, such as reduced responses to reward or oversensitive responses to negative feedback (7–9). The third therapy process, the acquisition of CBT skills, is related to both dysfunctional thinking and behavioral activation. CBT skills are defined as the ability to re-evaluate the accuracy of one's own dysfunctional beliefs (CT skills) and in this way change patterns of dysfunctional thinking and the ability to engage proactively in pleasurable activities as a way to target reward experience (BT skills) (10).

The acquisition of CBT skills is maybe one of the most promising therapy processes of CBT for depression. In contrast to the procedures focused on cognitive change and behavioral activation, CBT skill acquisition is a therapy process that emphasizes the patients' ability to use these cognitive change and behavioral activation procedures themselves, outside the therapy sessions. In addition, successful use of CBT skills may protect the patient from developing new

future episodes after successful treatments. Research shows that even after successful treatment impairments such as dysfunctional mental representations (11,12), negative processing of information (13–15) or blunted reward processing (16,17) may remain, thereby increasing risk of new depressive episodes. The acquisition of CBT skills might be essential to transfer learned content from the therapy session to daily life and to cope with dysfunctional therapy processes or symptoms in future scenarios outside the therapeutic context.

However, although multiple studies have pointed to an association between the acquisition of CBT skills and depression (Adler, Strunk, & Fazio, 2015; Forand et al., 2018; Strunk, Hollars, Adler, Goldstein, & Braun, 2014; Webb, Beard, Forgeard, & Björgvinsson, 2018), it is still unknown whether CBT skill acquisition directly causes a reduction of symptoms of depression. In order to test the causal effects of a certain therapeutic procedure, it is necessary to isolate the procedure and investigate its direct effects on the hypothesized changes in therapy processes and outcome (Bruijniks, Sijbrandij, Schlinkert, & Huibers, 2018). Two preliminary experiments that focused on the acquisition of CT skills already evaluated how a procedure focused on the acquisition of CT skills could be isolated (Bruijniks et al., 2018) and showed that a short cognitive skill acquisition procedure in the form of a group masterclass led to better CT skill acquisition compared to an active control procedure in a sample of distressed students (Bruijniks, Los, & Huibers, 2019). A next step towards the clinical application of this finding would be to evaluate how a procedure focused on CBT skill acquisition causally affects the acquisition of CBT skills and subsequent symptom reduction in a clinical sample.

In addition, depressed patients suffer from cognitive and neurobiological impairments that may interfere with the success of CBT skill acquisition procedures in improving CBT skills and leading to subsequent change in other relevant therapy processes and depressive symptoms (Bruijniks, DeRubeis, Hollon, & Huibers, 2019). Compared to healthy individuals, depressed individuals have the tendency to direct their attention to negative rather than positive information (25–28) and suffer from a variety of deficits related to executive functioning, such as inhibition, planning and working memory (29). One hypothesis on how emotional biases persist is that deficits in cognitive control interfere with the ability to regulate or change emotional biases or dysfunctional thinking, while on the other hand cognitive biases are facilitated by increased influence from subcortical emotion processing regions, in this way maintaining the depression (Beevers, 2005; Disner, Beevers, Haigh, & Beck, 2011). Recent studies supported the hypothesis

that individual differences in cognitive or neurobiological impairments may interfere with the success of treatment. In a systematic review, cognitive and neurobiological impairments showed to be associated with impairments in dysfunctional thinking and reward processing while depressed patients with better cognitive control but more emotional bias before start of CBT seemed to benefit more from CBT's procedures (Brujiniks et al., 2019). A recent experiment indicated that in healthy participants who received a stress induction, executive control under stress, but not under non-stressful circumstances, predicted the ability to reappraise negative material to become less negative (32). It is possible that individual differences in cognitive or neurobiological impairments also affect the success of CBT skill acquisition, especially because skill acquisition seems to be a multifaceted process (33–36), that may require sufficient cognitive and neurobiological resources to be successful.

The success of CBT skill acquisition might be improved by increasing the patients' capacity to learn from procedures focused on CBT skill acquisition to improve CBT skills. One way to address and improve cognitive and neurobiological processes during treatment is by providing cognitive support. Examples are to provide memory strategies within sessions of CBT (37,38) or short retrieval tests between the sessions (Brujiniks, Sijbrandij, & Huibers, 2019). The major hypothesis is that by enhancing recall for the session content, the success of psychotherapy outcomes for depression can be improved and some studies provided preliminary evidence for this hypothesis (40). However, to improve psychotherapy it might not only be important to improve recall of the session content but also improve and develop the therapy process. Yet, while current cognitive support strategies such as retrieval of newly learned information may improve recall of the session content, it might not be enough to improve CBT skill acquisition. According to theories on skill acquisition, the process of skill acquisition starts with learning new information (this can also be seen as the 'declarative' part of skill acquisition), but then repeated practice is necessary to turn it into a more procedural form in which the newly learned skill becomes more and more automatized over time (Anderson, Betts, Bothell, & Hope, 2018; Tenison & Anderson, 2016; VanLehn, 1996). To increase skill acquisition, it might be necessary to use a cognitive support strategy that affects both the declarative and procedural parts of memory.

One strategy that seems promising in affecting both declarative and procedural memory is mental imagery. Mental imagery refers to perceptual experiences in the absence of sensory input and constitutes a non-verbal way of information processing, closely related to the experience of

emotions (Holmes & Mathews, 2010). Mental imagery allows us to simulate past and future experiences and because of this allows us to “try-out” different courses of actions and their emotional consequences (42,43). Given these properties of mental imagery, when applied to CBT skills, imagery could be used to simulate skill application (44). Mental imagery has been linked to improved acquisition of skills in non-clinical settings, such as tennis performance or the development of surgical skills (45–49), but also to increased BT skills in a clinically depressed population (50). Additionally, mental imagery has been related to the improvement of cognitive functioning, such as recall of memories (Dalglish et al., 2013) and prospective memory (i.e., memorizing to execute a previously formed intention at some point in the future; McFarland & Glisky, 2012; McFarland & Vasterling, 2018). One recent study showed that the effect of cognitive change procedures on reducing hostile beliefs and aggressive tendencies could be increased by integrating mental imagery techniques into the session (51). We suggest that simulating applying CBT skills using mental imagery might be a potential efficient way to increase skill acquisition during psychotherapy (44).

The aims of this randomized trial are three-fold. The first aim is to investigate the direct effects of a procedure focused on CBT skill acquisition (CBTSAP) on the acquisition of CBT skills, related therapy processes (changes in idiosyncratic dysfunctional thoughts and behaviors, change in dysfunctional thinking and reward processing) and depressive symptoms compared to an active control procedure. Second, we will investigate whether the effect of CBTSAP is moderated by individual differences in learning capacity. Third, we investigate whether mental imagery is an effective cognitive support strategy for CBTSAP by testing whether the effect of cognitive support is larger for patients with lower learning capacity compared to the CBTSAP without cognitive support. A conceptual model for the proposed study can be found in Figure 1.

Insert Figure 1

Method

Design Between-subject experimental design with three parallel conditions, each having an equal length of 3 x 45-minute sessions: 1) Active control procedure ($n = 50$), 2) CBT skill acquisition procedure (CBTSAP) ($n = 50$), 3) CBTSAP with cognitive support (mental imagery) ($n = 50$). The Ethic Committee of Freiburg University approved the study (registration number: 20-1022) and the trial is registered at the German Clinical Trial Register (DKTR; registration number: DRKS00024116).

Participants We aim to include 150 patients with a primary diagnosis of a major depressive disorder (MDD) (excluding non-dysthymic persistent major depressive disorder) as indicated by Structural Clinical Interview for DSM-5 Axis I Disorders (SCID-5-CV) and a score on Beck's Depression Inventory II (BDI-II) ≥ 14 . Patients should currently not be taking antidepressants or be stable on antidepressant dose for at least three months before start of treatment while no change in the use of antidepressants is planned. In addition, patients should be aged between 18-65 and have sufficient knowledge of the German language. Excluded are patients with the presence of a previously stated diagnosis of attention-deficit/hyperactivity disorder or attention-deficit disorder, current drug or alcohol dependence according to the Structural Clinical Interview for DSM-5 Axis I (SCID-5-CV), patients who have received CBT focusing on a major depressive disorder in the previous year or show a high risk of suicide according to the intake staff. Patients will be excluded when there is a previously diagnosed cluster A or B personality disorder or indication for a cluster A or B personality disorder according to the intake staff.

Sample size Based on a medium effect size, $\alpha = .05$, power = .80, number of experimental conditions = 3, number of repeated measurements = 2 to 4 (G*power (52)), we need a total sample size of 102 to 120 participants is needed. Taking into account 20% drop-out and the fact that we aim to conduct multilevel analyses, we aim to include a total of 150 participants.

Recruitment Patients will be recruited from the academic outpatient treatment center at the Department of Psychology, Unit for Clinical Psychology and Psychotherapy at the Albert-Ludwigs University of Freiburg. During the intake patients will be checked on in- and exclusion criteria and

receive the patient information letter if they are potentially eligible for study participation. After one week, patients will be called to check whether they are interested in participating in the study. If interested, the remaining in- and exclusion criteria will be checked, and a SCID-5-CV interview will be conducted by phone.

Randomization and procedure Patient who are eligible to participate in the study will complete a baseline measurement and an introduction session on different days. The baseline measurement will take place in the lab and includes a measurement of learning capacity. Informed consent will be signed before the baseline measurement. The introduction session is conducted by the therapist and focuses on introducing the principles of CBT and completing the Core Belief Interview (CBI; McBride, Farvolden, & Swallow, 2007). After the introduction session, patients will be randomized into one of the three conditions using a computer script performing block randomization (1:1:1, block size = 15). Randomization will be pre-stratified on severity of depression (mild [Beck Depression Inventory-II (BDI-II) = 14-19] vs. moderate [BDI-II = 20-28]). Therapy sessions will be completed weekly and the total procedure from baseline measurement to the post-procedure measurement will take a maximum of 5 weeks. The procedures will take place while the patient is on a waiting list for regular treatment at the outpatient clinic. The full procedure is also presented in Figure 2.

Insert Figure 2

Introduction session

The introduction session will focus on introducing the principles of CBT (central focus will be on the relation between thoughts, behaviors and mood) and completing the CBI. During the CBI, the therapist and patient try to gain insight in the current three most relevant dysfunctional beliefs and current three most relevant dysfunctional behaviors for the patient. These beliefs and behaviors will be used in the subsequent sessions to discuss in relation with depressive symptoms (control procedure) or to practice CBT skills (CBTSAP and CBTSAP+MI condition).

Therapeutic procedures All therapeutic procedures use techniques from the protocol for cognitive behavioral therapy (CBT; Beck et al., 1979) for depression and use agenda setting to

structure the sessions. In addition, each procedure will focus on targeting the idiosyncratic beliefs and behaviors that were established during the Core Belief Interview (CBI). However, the procedures differ in the number of active ingredients (see Figure 3). During the CBT skill acquisition procedure (CBTSAP), the therapist and patient will choose one of the cognitive or behavioral skills from a predefined list of CBT skills (i.e., consisting of behavioral activation (behavioral therapy skill) and questions used for evaluating dysfunctional thoughts (cognitive therapy skill) and subsequently discuss application of the skill to the idiosyncratic beliefs and behaviors that have been discussed during the introduction session. During the CBTSAP plus mental imagery, the therapist and patient will follow a similar agenda, but in addition, as a third step, patients will be instructed to engage in a mental imagery exercise of skill application. The mental imagery exercise is based on a guided mental imagery procedure and has been shown to increase motivation for goal directed behaviors (54). During the mental imagery procedure, participants are instructed to imagine as vividly as possible and focusing on the positive aspects of the image. The procedure consists of the following steps: 1) imagine the contextual cues (e.g., place, date) of a future situation with depressive symptom(s), 2) engaging in multi-sensory imagery of applying the CBT skill in this situation, 3) imaging and experiencing the positive aspects related to successfully applying the CBT skill. During the active control procedure, the therapist and patient will focus on discussion of dysfunctional thoughts and behaviors only. All sessions will be videotaped for treatment fidelity checks. Before the start of the study, therapists will be trained in each procedure by experts in CBT and mental imagery for depression. Research intervention will take place regularly.

Insert Figure 3

Instruments

An overview of all patient measurements is given in Table 1. An overview of all measurements completed by the therapists or third observers can be found in Table 2.

Insert Table 1 and 2

Primary outcomes

CBT skills: CBT skill acquisition will be measured in two different ways. Before and one

week after the procedure patients will complete the Ways of Responding (Barber & DeRubeis, 1992). During the WOR, CBT skills of the participants are tested by asking them to think about themselves in various situations and to tell what they would think and do in such situations. Patients will receive three scenarios before treatment and three different scenarios after treatment. The scores derived from the WOR reflect the level of CBT skills demonstrated by the patient. Interrater reliability and validity have been supported (Barber & DeRubeis, 2001; Strunk et al., 2014). Change in CBT skills during the procedures will be measured using the Behavioral Activation for Depression Scale – short form (BADS-SF) (BA skills) and Cognitive Change Sustained Change (CCSC) (CT skills). The BADS-SF consists of nine items, each rated on a 7-point Likert Scale and internal consistency and construct and predictive validity were supported (57). The CCSC consists of 9 items rated on a 7-point Likert scale and internal consistency was supported (58). Both the CCSC and BADS-SF will be completed before, during and after the procedure.

Depression: Depression will be measured with the Beck Depression Inventory-II (BDI-II; Beck, Steer, & Brown, 1996). The BDI-II is a 21-item self-report instrument assessing depressive symptoms during the last two weeks. The items are rated from 0 to 3, higher scores representing more symptom severity. 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 (60,61). For the purpose of this study, the BDI-II will be adjusted to assess depressive symptoms during the past week.

Therapy processes

Idiosyncratic thoughts and behaviors: Idiosyncratic thoughts and behaviors will be measured with the Core Belief Interview (CBI; McBride, Farvolden, & Swallow, 2007). This interview will be completed by the therapist during the introduction session. Together the therapist and patient will form an idiosyncratic top three of dysfunctional thoughts and top three of dysfunctional behaviors. Note that the behaviors can both exist of the presence of unhelpful behaviors or the absence of rewarding behaviors. Based on the identified beliefs and behaviors, six idiosyncratic visual analogue scales (VAS) (0-100) will be constructed for each patient (i.e., three dysfunctional beliefs, three dysfunctional behaviors). Patients asked to indicate the degree to which they agree with each statement. For the dysfunctional beliefs, credibility of the beliefs and

strength of related emotions will be rated. Presence, reward and pleasure related to the behaviors will be measured.

Dysfunctional thinking: General dysfunctional thinking will be measured using the Cognition Checklist (CCL; Taylor, Koch, Woody, & McLean, 1997). The CCL consists of 26 items rated on a 5-point Likert Scale and can be divided into two subscale measuring dysfunctional thoughts related to depression versus anxiety. Internal consistency and validity was supported (63).

Reward processing: Reward processing will be measured using the Reward Probability Index (RPI; Carvalho et al., 2011) and the Temporal Experience of Pleasure Scale (TEPS; Gard, Gard, Kring, & John, 2006). The RPI is a 20-item self-report instrument that measures the presence of environmental reward, while the TEPS is an 18-item self-report instrument that measures the ability to experience pleasure. Reliability and validity have been supported for both instruments (64–66).

Secondary outcomes

General psychological distress: Additional psychological symptoms will be measured using the Brief Symptom Inventory (BSI; Derogatis & Melisaratos, 1983). The BSI consist of 53 items rated on a 0 (not at all) to 4 (extremely) scale and includes the following subscales: somatization, obsessives-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism. Reliability and validity of the scale have been supported (68,69).

Recall: Recall will be measured using the Patient Recall Test (PRT; Lee & Harvey, 2015). The PRT measures recall of the previous session content. Following procedures of Lee & Harvey, the patient will be given 10 minutes to remember as much treatment points from the previous session as possible. Treatment points will be defined as remembering skills and skill applications (1 point per skill and/or skill application; note that these will be noted by the therapist after each session). Scores will be rated by two independent raters, inconsistencies in scoring will be resolved by discussion. Interrater reliability between raters will be computed.

Potential moderators: learning capacity

Cognitive control

Verbal working memory: Verbal working memory will be measured using the N-back task

(71). The n-back task measures verbal working memory. During the n-back task participants will be asked if a letter on the screen matches a letter previously (1-back, 2-back, 3-back) presented for 500 ms with an interval of 2000 ms. WM load increases as the task progresses from 1-back to 3-back. Accuracy of responses (total of correct hits (% correctly identified n-backs) and correct no hits (% correctly identified no presence of a n-back)) are measured and will be used as an outcome measure. The n-back task has been considered as a valid measure of working memory (72,73).

Visual working memory: Visual working memory will be measured using the probe change detection task (PCDT; Dai, Li, Gan, & Du, 2019). The PCDT consists of the following steps: 1. Participants are instructed by an arrow on their screen to focus on the left or right side of the screen (200 ms), 2. After a short break (300 ms) the screen is filled with colored squares on a gray background (100 ms). The squares are equally distributed between the left and right side of the screen. Participants are instructed to remember only the squares on the side that was instructed under step 1, 3. After a second blank screen (900 ms), participants see again a field with colored squares (750 ms) and have to indicate whether the squares on the side of the screen are the same as under step 2. Set sizes of the trial different between 8 to 12 colored squares in total. Participants will receive a total of 300 trials. Reliability and validity has been supported (74).

Long-term memory: Long-term memory will be measured using the paired associates task (PAT; Unsworth, Brewer, & Spillers, 2009). Long-term memory can also be considered as 'secondary memory', i.e., the part of memory where information is stored when the primary memory, where new information is temporary maintained is full. During the PAT, participants will be given three lists of 10 non-semantically related word pairs. All words are common nouns, and the word pairs will be presented vertically for 2 sec each. Participants will be told that the cue would always be the word on top and that the target would be on bottom. After the presentation of the last word, participants will see the cue word and "???" in place of the target word. Participants will be instructed to type in the target word from the current list that matches the cue. Cues will be randomly mixed so that the corresponding target words are not recalled in the same order as that in which they had been presented. Participants will have 5 sec to type in the corresponding word. A participant's score is the proportion of items recalled correctly. Words will be taken from the Toronto Word Pool (76). The paired associates task has been considered a valid task of long-term memory (72,75).

Emotional bias

Sustained selective attention to emotional stimuli: Selective attention will be measured using a free-viewing eye-tracking task (77). Participants will view two blocks of neutral and happy and neutral and sad faces in counterbalanced order while their gaze patterns are concurrently recorded as index of selective spatial attention. Each block will take 30 trials that last 6 seconds. Each trial will show 16 different faces and participants will be asked to freely view the trials. Participants' gaze location and duration will be assessed using Eyelink eye-tracker software (<https://www.sr-research.com/>). The present study will use the exact same task as was recently used and validated by Klawohn and colleagues (2020). To maximize reliability of the task (78), it will be completed twice at baseline and once posttreatment.

Other measures

Manipulation check: To check if patients in the CBT skill acquisition + mental imagery condition engaged in vivid mental imagery, they will be asked to note how vivid the imagery of the skills practiced in this session was on a scale from 1 (not vivid at all) to 10 (extremely vivid). Participants in all conditions will complete questions on a 0-10 scale and asked to rate based on today's session how capable they feel in coping with their dysfunctional beliefs and behaviors, their motivation to use the content of today's session to do something different in the upcoming week and their anticipated reward of doing something different in the upcoming week based on today's session. In addition, expected success of the SKILT study sessions in reducing depressive symptoms will be asked at baseline and after the first session. At the end of the experiment, patients will be asked to rate on a 0-10 scale to what degree the received sessions contributed to an improvement in depressive symptoms.

Protocol deviations: After each session, the therapist will complete a short questionnaire to check 1. how many skills and application of these skills were discussed, 2. How many mental imagery exercises were conducted, and 3. ask for the presence of deviations to the protocol in that session.

Procedure integrity: To ensure the procedures differ in the presence of active components (i.e., CBT skill application and use of mental imagery) all sessions will be video-taped and judged by two independent raters on the presence of these components.

Diagnosis: The SCID-5-CV will be completed by phone during the recruitment phase.

Data analyses All statistical tests will be two-tailed (significance level alpha .05) and conducted in Stata and Mplus. First, descriptives (means, standard deviations) for all outcome, moderator and therapy process measures will be provided for each condition. All analyses will be intention-to-treat.

Test effects of CBTSAP versus an active control procedure on CBT skills, related therapy processes and depressive symptoms (hypothesis 1)

Differences between conditions (CBTSAP versus active control; presented by a dummy variable) in changes in CBT skills (CCSC and BADS-SF) and depression (BDI-II) (primary outcomes) and changes in idiosyncratic dysfunctional thoughts and behaviors (CBI), dysfunctional thinking (CCL) and reward processing (PSI/RPI) (therapy processes), and general psychological distress (BSI) and recall (PRT) (secondary outcomes) will be tested using multilevel analysis (patients (level 1) nested within therapists (level 2)). The difference between CBTSAP and active control on the CBT skill test (WOR) will be tested using repeated measures ANOVA.

Test whether the effect of CBTSAP is moderated by individual differences in learning capacity (hypothesis 2)

Moderation will be tested by adding the interaction between learning capacity and condition to the multilevel regression model and repeated measures ANOVA that were conducted for the first hypothesis. The interaction between learning capacity will be tested separately for cognitive control and emotional bias while controlling for type I error, using $p < .016$ (cognitive control) and $p < .05$ (emotional bias).

Test whether the effect of cognitive support is larger for patients with lower learning capacity (hypothesis 3)

First, differences between conditions (CBTSAP versus CBTSAP + MI; presented by a dummy variable) in changes in CBT skills (CCSC and BADS-SF) and depression (BDI-II) (primary outcomes) will be tested using multilevel analysis (patients (level 1) nested within therapists (level 2)). The difference between CBTSAP and CBTSAP + MI on the CBT skill test (WOR) will be tested using repeated measures ANOVA. Subsequently, moderation will be tested by adding the interaction between learning capacity and condition to the multilevel regression model or repeated

measures ANOVA. The interaction between learning capacity will be tested separately for cognitive control and emotional bias while controlling for type I error, using $p < .016$ (cognitive control) and $p < .05$ (emotional bias).

Mediation analyses

The potential role of therapy processes as mechanisms of change will be tested by testing mediation within latent difference score (LDS) models. LDS models will relate the procedure (CBTSAP versus active control) to change in CBT skills to subsequent change in the outcome (depressive symptoms). LDS models allow tests of mediation, include the temporality of the effects and are therefore capable of testing potential reverse causality (79,80). Other relevant therapy processes and recall will be explored as potential mediators between the procedures and outcome in additional models.

Discussion

We presented a protocol for a randomized controlled study that isolates an often-used therapeutic procedure focused on the acquisition of cognitive behavioral therapy skills (CBTSAP) to test its causal effects on psychotherapy outcomes compared to an active control condition. We hypothesized that, compared to an active control condition, the CBTSAP would lead to direct improvement in CBT skills, changes in other relevant therapy processes and reduce depressive symptoms. In addition, we suggested that individual differences in cognitive and neurological impairments (learning capacity) in depressed patients may interfere with the successful acquisition of CBT skills and hypothesized that individual differences in learning capacity might moderate the effects of the CBTSAP. Last, we hypothesized that especially the patients with low learning capacity might benefit from a cognitive support strategy added to the CBTSAP compared to the CBTSAP without cognitive support.

This study will be the first to investigate the direct effects of an isolated procedure focused on the acquisition of CBT skills. Knowing whether and how therapeutic procedures have a direct effect on psychotherapeutic outcomes will be an important step in optimizing psychotherapy for depression. Although their potential has been recognized (81–83), experimental studies that isolate therapeutic procedures in the field of depression have been scarce so far (Bruijniks et al., 2018). In addition, by performing an experiment that informs us about which therapeutic procedure works best for whom, the proposed study taps into the field of personalized medicine (i.e., optimizing the effects of treatment by matching the treatment to the patient (84)). Insight in the direct effects of therapeutic procedures on how and for whom they reduce depression can inform and have the potential to improve clinical practice (85).

One strength of the study will be the elaborate assessment of learning capacity at baseline. Studies have indicated that depressed patients with more emotional bias and more cognitive control might show better improvement during CBT (Bruijniks et al., 2019), but investigated the role of learning capacity on complete treatment packages and used neurobiological measures or where conducted in an elderly depressed population. The proposed study will investigate the moderating role of cognitive control and emotional bias in patients with major depressive disorder who receive a specific isolated procedure focused on the acquisition of CBT skills. In this way, the present study will be able to inform on the specific role of learning capacity in a key therapeutic procedure in the CBT for depression. Moreover, a better understanding of the role of learning capacity and a

CBT skill acquisition procedure on CBT outcomes might open up new avenues for future research on the role of skill acquisition and learning capacity in psychotherapy for depression in general. In addition, by repeated measurement of therapy processes we will be also able to investigate how learning capacity affects the hypothesized mechanisms underlying the success of a CBT skill acquisition procedure. Last, a strength of the present study is that it includes a multimodal assessment, using not only self-report instruments but also a CBT skill test, idiosyncratic measures of therapy process change, behavioral tasks and eye tracking.

List of abbreviations

BADS-SF - Behavioral Activation for Depression Scale – short form

BSI - Brief Symptom Inventory

CBI - Core Belief Interview

CBT – cognitive behavioral therapy

CBTSAP – cognitive behavioral therapy skill acquisition procedure

CCSC - Cognitive Change Sustained Change

CCL - Cognition Checklist

IPT – interpersonal psychotherapy

MI – Mental imagery

PAT - Paired associates task

PCDT - Probe change detection task

PRT - Patient Recall Test

RPI - Reward Probability Index

LDS – Latent difference scores

SCID-5-CV - Structural Clinical Interview for DSM-V Axis I

SCID-5-PD - Structural Clinical Interview for DSM-V Axis II Disorders

TEPS - Temporal Experience of Pleasure Scale

VAS - Visual analogue scale

Declarations

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Author contributions

SB designed the study and wrote the manuscript. UF, BTC, FR and SB are involved in the coordination of the recruitment of patients and data collection. JW is involved as an eye-tracking expert. All authors read, contributed to, and approved the final manuscript.

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Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

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Figure legends

Figure 1. Conceptual model for the proposed study

Figure 2. Recruitment and study procedure

Figure 3. Therapeutic elements per procedure

preprint

Table 1. *Overview of patient instruments per time point*

	Baseline	Introduction session	Session 1	Session 2	Session 3	One day after session 3	Follow-up
Primary outcomes							
<i>Depression</i>							
Beck Depression Inventory II (BDI-II)	X	X	X	X	X		X
<i>CBT skills</i>							
Ways of Responding (WOR)	X						X
Behavioral Activation for Depression Scale – short form (BADS-SF)	X	X	X	X	X		X
Cognitive Change Sustained Change (CCSC)	X	X	X	X	X		X
Secondary outcomes							
<i>Symptoms other than depression</i>							
Brief Symptom Inventory (BSI)	X						X
Therapy processes							
<i>Idiosyncratic thoughts and behaviors</i>							
Core Belief Interview (CBI)		X	X	X	X	X	X
<i>Dysfunctional thinking</i>							
Cognition Checklist (CCL)	X					X	X
<i>Reward processing</i>							
Reward Probability Index (RPI)	X					X	X

Temporal Experience of Pleasure (TEPS)	X					X	X
<i>Recall</i>							
Patient Recall Test (PRT)			X	X	X	X	X
Potential moderators							
<i>Learning capacity</i>							
<i>Cognitive control</i>							
Verbal working memory: n-back task	X						
Visual working memory: Single probe detection task	X						
Long-term memory Paired-associates task	X						
<i>Emotional bias</i>							
Free viewing eye-tracking task	X	X				X	
Other measures							
<i>Diagnostics</i>							
SCID-5-CV	X						
<i>Demographics</i>	X						
<i>Treatment evaluation</i>							X
<i>Manipulation check</i>			X	X	X		
<i>Procedure check</i>							X
<i>Expected success</i>	X		X				

Note. CBTSAP = CBT Skill Acquisition Procedure; MI= Mental Imagery; Structural Clinical Interview for DSM-V Axis I (SCID-5-CV); Structural Clinical Interview for DSM-V Axis II Disorders (SCID-5-PD).

Table 2. *Overview of therapist/observer instruments per time point*

	Baseline	Introduction session	Session 1	Session 2	Session 3	Post- procedure	Follow-up
Therapy processes							
Therapist-rated recall			X	X	X		
Manipulation check							
Therapy integrity							X
Protocol deviations			X	X	X

Figure 1. Conceptual model for the proposed study

Figure 2. Recruitment and study procedure

Figure 3. Therapeutic elements per procedure