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Serial mediators of memory support strategies used with Cognitive Therapy for depression: Improving outcomes through patient adherence and treatment skills

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Abstract

Patient memory for treatment is poor. Memory support strategies can be integrated within evidence-based psychological treatments to improve patient memory for treatment, and thereby enhance patient outcomes. The present study evaluated possible mechanisms of these memory support strategies. Specifically, we tested whether therapist use of memory support strategies indirectly predicts improved patient outcomes via serial improvements in (a) patient adherence throughout treatment and (b) patient utilization and competency of treatment skills. Adults with major depressive disorder (N=178, mean age=37.93, 63% female, 17% Hispanic or Latino) were randomized to Cognitive Therapy plus a Memory Support Intervention or Cognitive Therapy-as-usual. Because therapists from both treatment groups used memory support strategies, data from conditions were combined. Blind assessments of depression severity and overall impairment were conducted before treatment, immediately post-treatment (POST), at six-month follow-up (6FU), and at 12-month follow-up (12FU). Patient adherence to treatment was rated by therapists and averaged across treatment sessions. Patients completed measures of treatment mechanisms – namely, utilization and competency in cognitive therapy skills – at POST, 6FU, and 12FU. Results of serial mediation models indicated that more therapist use of memory support predicted lower depression severity at POST, 6FU, and 12FU indirectly and sequentially through (a) increased patient adherence during treatment and (b) more utilization and competency of Cognitive Therapy skills at POST, 6FU, and 12FU. The same patterns were found for serial mediation models predicting lower overall impairment at POST, 6FU, and 12FU. Together, boosting memory for

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treatment may represent a promising means to enhance pantreatment mechanisms (i.e., adherence and treatment skills) as well as patient outcomes.

Keywords

adherence; treatment skills; depression; cognitive therapy; memory support

Introduction

Evidence-based psychological treatments (EBPTs) reduce symptoms of mental illness, but there is room for improvement. When looking across treatment trials, many patients relapse or never fully recover, effect sizes are variable, and some patients derive little or no benefit (e.g., Cuijpers et al., 2020; Springer et al., 2018). One reason EBPT outcomes may not reach their full potential is that patient memory for treatment is poor. Across medical and psychosocial literatures, findings indicate that patients recall only about one third of treatment recommendations (Bober et al., 2007; Lee & Harvey, 2015; Lewkovich & Haneline, 2005). Intuitively, if patients cannot remember treatment strategies or recommendations, they will not be able to enact those recommendations, diminishing treatment effects. And indeed, poor memory for treatment is associated with worse treatment outcomes for patients (e.g., Lee & Harvey, 2015).

Poor memory for treatment persists despite efforts to build learning strategies into EBPTs. For example, by design, Cognitive Therapy (CT) helps patients build connections, think deeply about treatment content, and practice treatment skills, which may enhance memory for treatment (Beck, 1995). However, evidence suggests that therapists delivering CT-as-usual do not use enough memory enhancing strategies to optimize treatment outcomes (Lee et al., 2020). For example, in one study, therapists delivering CT-as-usual integrated memory support strategies approximately eight times per session (Harvey et al., 2016), whereas a recent study found that more than 12 instances per session are needed to maximize patient recall and outcomes (Lee et al., 2020). Thus, to help therapists integrate additional learning and cognitive strategies into treatment as usual, the Memory Support Intervention was developed as an adjunct to EBPTs (Harvey et al., 2014). Therapists using the Memory Support Intervention integrate eight memory support strategies. These memory support strategies were derived from the cognitive psychology and education literatures on learning and memory (Harvey et al., 2014). Specifically, as detailed in Harvey et al. (2014), the strategies are designed to promote the following: encoding as specified within multicomponent theory of memory (Baddeley, 2012; Baddeley & Hitch, 1974), deepening learning as described by the levels of processing theory (Craik & Lockhart, 1972), new skill acquisition (Fitts & Posner, 1967), and transfer of learning to new situations (Thorndike, 1932). Four of these memory support strategies are “constructive.” Specifically, they help the patient to (1) *apply* treatment principles to past or future situations, (2) *identify cues* as to when/where to apply to treatment principles, (3) *evaluate* the benefits and drawbacks of treatment principles, and (4) *categorize* treatment principles into superordinate themes or groups (Zieve et al., 2019). These strategies are considered constructive, because they go beyond information already presented by therapists in treatment-as-usual and ask patients

to do something *new* with the material (e.g., make connections between ideas, figure out how to apply skills in daily life). The other four memory support strategies are "nonconstructive"—specifically (1) *repeating* treatment principles for the patient, (2) asking the patient to *practice remembering* treatment principles, (3) *praising patients' memory* for treatment principles, and (4) boosting patients' *attention* to treatment principles (e.g., using of emphatic language, asking the patient to take notes). In contrast to constructive strategies, these nonconstructive strategies help patients grasp treatment principles by reinforcing only the materials that are already presented during treatment (i.e., without generating new content). See Table 1 for definitions and examples of each strategy. Together, the Memory Support Intervention is designed to help therapists integrate a wider range of memory support strategies, relative to treatment as usual, at a dose that will maximize patient recall and outcomes (Lee et al., 2020).

In a pilot trial for major depressive disorder, the Memory Support Intervention plus Cognitive Therapy (CT+Memory Support) was associated with improved recall for treatment and depression severity, relative to CT-as-usual (NCT01790919; Harvey et al., 2016). In a fully powered randomized controlled trial—the parent trial of the present study (NCT02938559; Dong et al., 2022)—there was also evidence to suggest that the memory support strategies were associated with better recall and clinical outcome, but the between-group differences were somewhat weaker than anticipated (Dong et al., 2022). Specifically, with respect to recall, CT+Memory Support was associated with higher past session recall —but not overall recall—at post-treatment, relative to CT-as-usual. With respect to clinical outcome, CT+Memory Support was associated with lower depression severity and greater reductions in overall impairment at six-month follow-up, but the treatment groups were associated with similar reductions in depression severity and overall impairment at post-treatment. Research is currently underway to investigate whether suboptimal dosage of specific memory support strategies may account for these smaller-than-anticipated effects (Sarfan et al., 2022). Of note, while the Memory Support Intervention has been applied to CT and major depressive disorder, the eight memory support strategies were designed to be "transdiagnostic" (relevant to a broad range of mental disorders) and "pantreatment" (relevant to a broad range of types of treatment).

Although memory support strategies show potential for improving treatment outcomes (Dong et al., 2022; Harvey et al., 2016), there is still much to learn about their mechanisms of action. Identifying mechanisms of action is a critical component of the experimental therapeutics approach, a framework advocated by the National Institute of Mental Health (NIMH) and other federal agencies, intended to maximize efficacy of the next generation of psychosocial treatments (Insel, 2015). In the context of memory support strategies, studies of mechanisms promise to illuminate how memory support can be leveraged to improve patient outcomes across other existing EBPTs and diagnoses.

One possible mechanism whereby memory support strategies exert their effects may be through boosting patient adherence throughout treatment. In the present study, patient adherence is operationalized based on Lichstein et al.'s (1994) treatment implementation model. According to this model and prior research (e.g., Dong et al., 2017a, 2017b), patient adherence is conceptualized as (1) treatment receipt (i.e., treatment is understood

and accepted by the patient as intended), and (2) out-of-session enactment (i.e., treatment recommendations and homework are practiced between sessions as intended). This conceptualization of adherence maps onto the World Health Organization recommendations that definitions of adherence should emphasize both (1) agreement between provider and patient, and (2) compliance with providers' recommendations (World Health Organization, 2003).

Bridging this conceptualization of patient adherence to memory for treatment, if a patient can remember treatment recommendations, they may be more adherent to those recommendations than a patient who cannot remember treatment recommendations. This is illustrated by Ley's theoretical model of effective medical communication, wherein patient recall for treatment recommendations, along with patient understanding and satisfaction of those recommendations, are critical to adherence (Ley, 1979; see Figure 1 of Kessels et al., 2003). Consistent with this model, secondary findings from the Memory Support Intervention pilot trial indicated that higher patient recall was associated with better patient adherence to treatment (Dong et al., 2017a). Similarly, more recall for content specific to cognitive behavioral therapy predicted higher patient adherence (Dong et al., 2017b). In other words, emerging evidence supports the positive link between memory for treatment and patient adherence. However, it is unclear whether this boost in adherence via enhanced memory for treatment is associated with clinically relevant change for patients, such as improved outcomes.

Why might improving patient adherence mediate better outcomes? One proposed reason is that increased adherence leads to learning and integration of treatment skills (Glenn et al., 2013), which may sequentially lead to better patient outcomes. Indeed, a handful of findings support a relationship between greater adherence throughout treatment and more use and competency of treatment skills. For example, among individuals with cocaine-dependence who completed cognitive behavioral therapy, adherence was related to more learning and competency of coping skills (Carroll et al., 2005). In parent-child interaction therapy, mothers' adherence was associated with more utilization of evidence-based parenting skills (Ros et al., 2016). Similarly, parents' adherence during parent-child interaction therapy was associated with less time needed to develop competency in parenting skills (Stokes et al., 2016).

In turn, with respect to treatment skills and patient outcomes, the *frequency* with which patients use skills learned during a course of treatment (i.e., utilization) has been associated with better treatment outcomes (e.g., Gallagher-Thompson et al., 2008; Gumport et al., 2019). For example, following an intervention designed to increase caregivers' skills to cope with caregiving stressors, caregivers' utilization and perceived helpfulness of skills mediated the relation between intervention effects and improved outcomes (Gallagher-Thompson et al., 2008). Similarly, how *well* patients use skills that were acquired during treatment (i.e., competency) has been found to predict better treatment outcomes (Hundt et al., 2013; Strunk et al., 2014). For instance, in a study of CT for depression, improvements in CT skill competency predicted improvements in depression symptoms (Strunk et al., 2014). Consistent with these findings, a review of the literature found promising evidence for

frequency and competency of skill use as mediators of the relation between cognitive behavior therapy and patient outcomes (Hundt et al., 2013).

Examining this evidence together, a picture emerges: enhanced memory for treatment may boost patient adherence, leading to more utilization and competency of treatment skills, which sequentially may result in better outcomes. However, to the best of our knowledge, this series of links has not been tested. Thus, the present study sought to test this mechanistic chain. If supported, findings would suggest that approaches to enhance memory for treatment—such as the Memory Support Intervention—represent a route to improving (a) *pantreatment mechanisms* (i.e., patient adherence throughout treatment and utilization and competency of treatment skills), and (b) *patient outcomes* of existing EBPTs.

Using data from the aforementioned parent trial, the present study had two aims. Note that, for the present study, the CT+Memory Support and CT-as-usual groups were combined, as memory support strategies—not treatment condition—were of primary interest (see Data Analyses for more details). Aim 1 was to test the following serial models: whether use of memory support strategies by therapists predicted treatment outcomes—namely depression symptom severity and overall impairment—indirectly and serially through patient adherence throughout treatment and utilization of CT skills at post-treatment (POST), six-month follow-up (6FU), and 12-month follow-up (12FU). Hypothesis 1 was that more therapist use of memory support would predict higher patient adherence. Sequentially, higher adherence would predict more utilization of treatment skills, ultimately predicting lower depression severity and overall impairment at POST, 6FU, and 12FU. Aim 2 was to test a second set of serial mediation models as follows: whether use of memory support strategies by therapists predicted treatment outcomes—namely depression symptom severity and overall impairment—indirectly and sequentially through patient adherence throughout and *competency* of CT skills at POST, 6FU, and 12FU. Hypothesis 2 was that more therapist use of memory support would predict higher patient adherence. Sequentially, higher adherence would predict more competency of treatment skills, ultimately predicting lower depression severity and overall impairment at POST, 6FU, and 12FU.[1]

Method

Study Overview and Participants

Data for the current study were drawn from the parent randomized controlled trial (NCT02938559), which was funded by the NIMH (R01MH108657; Dong et al., 2022). Adults who met criteria for major depressive disorder were recruited in the greater San Francisco area of California by clinician referrals and advertisements. Eligibility was subsequently determined by phone and in-person interviews. Eligible participants ($N = 178$) were randomly assigned to CT+Memory Support ($n = 87$) or CT-as-usual ($n = 91$) (see Supplement Figure 1 for CONSORT Diagram). Randomization was stratified by age (≤ 49, 50+) and depression chronicity (< 2 yrs, ≥ 2 yrs; Fournier et al., 2009). Blind assessments

[1]It is worth considering the reverse ordering of mediation paths. Specifically, patients' utilization and competency of skills during treatment may influence therapist ratings of patient adherence. Unfortunately, this alternative could not be evaluated in the present study, because of the temporal ordering of assessments (i.e., adherence assessed throughout treatment; utilization and competency only assessed at POST, 6FU, and 12FU). However, this possibility merits future investigation.

of outcome, including depression severity and overall impairment, were conducted before treatment, immediately post-treatment (POST) as well as six months (6FU) and 12 months (12FU) after treatment. Patient adherence throughout treatment was rated by therapists and averaged across treatment sessions. Patients completed measures of treatment mechanisms – utilization and competency in CT skills – at POST, 6FU, and 12FU. Additional details about the eligibility and procedures for the trial are described elsewhere (Dong et al., 2022). All participants provided consent to participate, and the University of California, Berkeley, Committee for the Protection of Human Subjects approved the study.

The inclusion criteria were: age 18+ years; willing and able to give consent; consent to being video recorded (necessary for memory support scoring) and NIMH data sharing[2]; English language fluency; diagnosis of major depressive disorder, first episode, recurrent or chronic according to the DSM-5; minimum score 26 or above on the Inventory of Depressive Symptomatology, Self-Report (IDS-SR) which denotes at least ‘moderate’ depression (Rush et al., 1996); if taking medications for mood, medications must have been stable for the past four weeks. The exclusion criteria were: history of bipolar disorder, history of psychosis or psychotic features, lifetime history of failure to respond to 4 or more sessions of CBT/CT for depression (McGrath et al., 2014); current non-psychotic disorder if constitutes the principal diagnosis and if requires treatment other than that offered in the project; moderate or severe substance use in the past 6 months where ‘moderate’ is defined as 4–5 symptoms and ‘severe’ is defined as 6+ symptoms of those listed in DSM-5 for each of the substance-related disorders; evidence of any medical disorder or condition that could cause depression, preclude participation in CT, or is associated with memory problems, that is not currently stabilized and/or managed under the care of a physician; the presence of an active and progressive physical illness or neurological degenerative disease; current suicide risk sufficient to preclude treatment on an outpatient basis (assessed by the Columbia-Suicide Severity Rating Scale; Posner et al., 2011) or current homicide risk (assessed by our staff or referring treatment provider); pregnancy or breastfeeding; not able or willing to participate in and/or complete the pre-treatment assessments; and medication dose had to be stable for 4 weeks prior to randomization. Medication use and changes, along with participation in other treatments/therapy, were recorded.

Treatments

Treatment was administered by a licensed therapist or graduate students in social work or clinical psychology. Both treatments were comprised of 20 to 26, 50-minute sessions conducted over 16 weeks. To help ensure purity of delivery (Manber et al., 2008), each treatment provider was randomly allocated to deliver only one of the two treatment approaches. For both conditions, clinicians used a treatment manual and received weekly supervision to standardize treatment administration. Weekly supervision was conducted separately for therapists in each condition, except that all therapists attended a monthly master class—specifically focused on delivery of CT (not memory support)—with Dr.

[2]This was added in July 2017. NIH/NIMH data sharing requirements necessitated reconsent of participants already randomized. If a patient does not agree to data sharing we have been instructed to exclude them from the analysis.

Steven Hollon, a licensed psychologist and expert in the etiology and treatment of depression.

CT-as-usual—CT was developed by Beck et al. (1979) and has incorporated a number of innovations (Beck et al., 2011; Bennett-Levy et al., 2004). Treatment strategies are designed to identify, reality test, and correct distorted beliefs and information processing (Beck, 1979). CT for major depressive disorder was conducted according to the standard manuals (Beck, 1979; Beck, 2011; Greenberger & Padesky, 2015). Patients were also given a copy of a CT self-help book (Greenberger & Padesky, 2015).

CT+Memory Support—The Memory Support Intervention is a manualized adjunctive treatment that was delivered alongside CT-as-usual. As mentioned above, the Memory Support Intervention is comprised of eight memory promoting strategies, with four constructive and four nonconstructive strategies. See Table 1 for examples of each memory support strategy. These strategies are proactively, strategically, and intensively integrated into treatment-as-usual to support encoding. Memory support strategies are always delivered in the context of a 'treatment point,' defined as a main idea, principle, or experience that the treatment provider wants the patient to remember or implement as part of the treatment (Lee & Harvey, 2015). Treatment points can range from specific skills to broader theoretical principles; however, the key idea is that a treatment point is something that would be useful for the patient to remember many years after treatment. To help patients remember treatment points, memory support strategies can be utilized when a provider first explains a treatment point (e.g., using 'attention recruitment' by encouraging the patient to take notes), directly after a provider explains a treatment point (e.g., using 'evaluation' by helping the patient identify the pros and cons of a new skill), or later on in treatment (e.g., using 'practice recall' by asking the patient to list cognitive skills learned from the prior session).

Measures

Blind assessors were research assistants and graduate students in clinical psychology. Demographics were assessed, as well as predictors, mediators, and outcomes described below.

Memory Support—The Memory Support Rating Scale (MSRS) is a reliable and valid, observer-rated measure of memory support use by treatment providers (Lee et al., 2016). Selected session video recordings were coded using the MSRS to establish the frequency and type of memory support delivered. The MSRS coders (except for the expert coder) were blind to therapists' assignment to treatment conditions. MSRS coders were required to individually establish 80% or higher inter-coder agreement with an expert coder across five consecutive 30-minute treatment session recordings from the study. Cohen's kappa between each coder and the expert coder ranged from 0.71 to 0.84, indicating that all coders had at least "substantial" agreement with the expert coder (Landis & Koch, 1977). The schedule for coding tapes was as follows: session 2, sessions that occurred in weeks 4, 8, and 12 of treatment as well as the final session. For the present study, the average total amount of memory support delivered by therapists was derived for each participant. See Table 2 for the average amount of memory support delivered by therapists in each treatment condition.

Patient Adherence Throughout Treatment—Patient adherence throughout treatment was assessed by Therapist Adherence Rating Scale (TARS), developed by our team and used in prior research to assess the two components of adherence described above: (1) treatment receipt, and (2) treatment enactment (TARS; Dong et al. 2017a; Gumport et al., 2021; Lichstein et al., 1994; World Health Organization, 2003). At the end of each weekly treatment session, the TARS was completed by the patient's therapist. Specifically, the therapist rated the patient's treatment receipt on three items (e.g., "To what extent did your patient understand the content of this session?") and treatment enactment on three items (e.g., "To what extent did your patient complete the practice exercises outside of session this past week?"). Each item was rated on a scale from 0% to 100% with 10% increments. A total score for each patient at each session was created by averaging all six items. Then, for each participant, scores were averaged across sessions to assess average adherence throughout treatment. Higher scores indicate higher average adherence. The TARS has demonstrated adequate convergent validity, and the scales have been supported by factor analysis (Dong et al., 2017a). In the present study, internal consistency of this measure was good (Cronbach's alpha = 0.81).

Utilization and Competency—Participant ratings of utilization were assessed with a Utilization Scale, adapted for the present study based on Gumport et al. (2019). This scale lists 14 treatment skills from CT. Each treatment skill is rated on a 5-point Likert scale, with higher scores indicating more utilization. The anchors are 0 = *I never use it* to 4 = *I always use it*. This scale was delivered to participants at POST, 6FU, and 12FU to assess continued utilization of treatment skills after the course of treatment had ended. A total Utilization score was created at each timepoint by summing and averaging the 14 items. In the present study, internal consistency was good to excellent at each timepoint (Cronbach's alpha: POST = 0.88, 6FU = 0.89, 12FU = 0.91).

Competency in treatment skills was assessed with the Competencies in Cognitive Therapy Scale – Self Report (CCTS-SR; Strunk et al., 2014). This measure asks patients to rate "how well" 29 statements about specific CT skills describe their thoughts, beliefs, and behaviors over the past two weeks. Statements are rated on a Likert scale from 1 = *not at all* to 7 = *completely*. Scores were created for each timepoint by summing and averaging the 29 items on this scale with higher scores indicating greater competency of skill use. This measure was delivered at POST, 6FU, and 12FU to assess competency of treatment skills after the course of treatment had ended. The CCTS-SR has demonstrated adequate construct validity (Strunk et al., 2014). In the present study, internal consistency was excellent at each timepoint (Cronbach's alpha: POST = 0.95, 6FU = 0.96, 12FU = 0.95).

Outcomes—Depression severity was indexed by the IDS-SR (Rush et al., 1996), a widely-used self-report measure of depression severity, at pre-treatment assessment as well as POST, 6FU, and 12FU. IDS-SR consists of 30 items rated on a 4-point scale. Items were summed, with higher scores indicating more severe symptoms (Rush et al., 1996). This measure has demonstrated satisfactory reliability and validity (Trivedi et al., 2004). In the present study, internal consistency was good to excellent (Cronbach's alpha: POST = 0.92, 6FU = 0.89, 12FU = 0.91).

Overall impairment was assessed with the World Health Organization Disability Assessment Schedule (WHODAS) 2.0 at pre-treatment assessment as well as POST, 6FU, and 12FU. The WHODAS is a 36-item measure that assesses disability on a scale from 1 to 5 ("*none*" to "*extreme or cannot do*"). For each item, participants are asked to rate how much difficulty they had in specific areas of functioning during the past 30 days. Items were summed, with higher scores indicating greater disability (Usten et al., 2010). The WHODAS 2.0 has strong psychometric properties (Konecky et al., 2014). In the present study, internal consistency was excellent (Cronbach's alpha: POST = 0.98, 6FU = 0.96, 12FU = 0.97).

Data Analyses

Note that the following analyses combined treatment groups. This decision was made because (a) mechanisms of memory support strategies (not treatment condition) were of primary interest in the present study, and (b) therapists in both treatment conditions delivered an average of at least eight memory support strategies per session (see Table 2). Therapists in CT+Memory Support used memory support strategies significantly more times per session on average, relative to therapists in CT-as-usual ($t(177) = -12.73$, $p < 0.001$, $d = 1.91$) (Dong et al., 2022), and exceeded the dose recommended by prior research to maximize patient recall and outcomes (Lee et al., 2020). See Supplement Table 1 for the mean number of strategies delivered per session by condition, and independent samples *t*-tests comparing these means by condition. Note that all *t*-tests were significant, indicating significantly higher use of all memory support strategies in the CT+Memory Support condition relative to CT-as-usual. Otherwise however, the two treatment groups were very similar. Thus, combining treatment groups allowed us maximize available data.

Serial mediation models were evaluated with the PROCESS macro v3.5.3 in IBM SPSS v27. Specifically, Model 6 of the PROCESS macro was used, which is able to determine the indirect effect of two mediators in sequence. Following recommendations (Hayes, 2018), the indirect effects were estimated with 95% percentile-based bootstrapped confidence intervals based on 10,000 bootstrap samples. For Aim 1, Models 1, 2, and 3 tested whether use of memory support predicted *depression severity* indirectly and sequentially through patient adherence and *utilization* at POST, 6FU, and 12FU, respectively. Models 4, 5, and 6 of Aim 1 tested whether use of memory support predicted *overall impairment* indirectly and sequentially through patient adherence and *utilization* at POST, 6FU, and 12FU, respectively. For Aim 2, Models 1, 2, and 3 tested whether use of memory support predicted *depression severity* indirectly and sequentially through patient adherence and *competency* at POST, 6FU, and 12FU, respectively. Models 4, 5, and 6 of Aim 2 tested whether use of memory support predicted *overall impairment* indirectly and sequentially through patient adherence and *competency* at POST, 6FU, and 12FU, respectively. See Supplement Figures 2–5 for conceptual diagrams of each hypothesized model. Confidence intervals that do not contain zero indicate a significant effect. As a measure of effect size for the indirect effect, the mediation proportion was used, which is interpreted as the proportion of the total effect that is explained by the indirect effect (Beydoun & Wang, 2010; Ditlevsen et al., 2005). All models controlled for baseline levels of the outcome (either depression severity or overall impairment). Missing data of the variables in the present study ranged from 0.60%

to 12.90%. Listwise deletion was used for these missing data. Note that path labels were chosen to be consistent with norms in the field (e.g., Collier, 2020; Hayes, 2018).

Results

See Table 2 for participant characteristics and memory support. See Tables 3 and 4 for indirect effects, specific paths generated by each model, confidence intervals, and effect sizes for Aims 1 and 2, respectively. See Supplement Figures 2–5 for conceptual diagrams of each model.[3]

Aim 1: Memory Support → Adherence → Utilization → Outcomes

In Aim 1 Models 1–3, the indirect effects of patient adherence and utilization on the relations between memory support and depression severity were significant at POST (indirect effect: −0.04, 95% CI: −0.08, −0.01), 6FU (indirect effect: −0.03, 95% CI: −0.07, −0.01), and 12FU (indirect effect: −0.05, 95% CI: −0.11, −0.01). Looking at the specific paths generated by each of these models (see Table 3), more memory support predicted higher adherence. Higher adherence predicted greater utilization, which in turn, predicted lower depression severity at each timepoint.

In Aim 1 Models 4–6, the indirect effects of patient adherence and utilization on the relations between memory support and overall impairment were significant at POST (indirect effect: −0.07, 95% CI: −0.14, −0.02), 6FU (indirect effect: −0.04, 95% CI: −0.09, −0.004), and 12FU (indirect effect: −0.07, 95% CI: −0.15, −0.01). Looking at the specific paths generated by each of these models (see Table 3), more memory support predicted higher adherence. Higher adherence predicted greater utilization, which in turn, predicted lower overall impairment at each timepoint.

Aim 2: Memory Support → Adherence → Competency → Outcomes

In Aim 2 Models 1–3, the indirect effects of patient adherence and competency on the relations between memory support and depression severity were significant at POST (indirect effect: −0.05, 95% CI: −0.09, −0.01), 6FU (indirect effect: −0.04, 95% CI: −0.09, −0.01), and 12FU (indirect effect: −0.07, 95% CI: −0.15, −0.02). Looking at the specific paths generated by each of these models (see Table 4), more memory support predicted higher adherence. Higher adherence predicted greater competency, which in turn, predicted lower depression severity at each timepoint.

In Aim 2 Models 4–6, the indirect effects of patient adherence and competency on the relations between memory support and overall impairment were significant at POST (indirect effect: −0.07, 95% CI: −0.15, −0.02), 6FU (indirect effect: −0.05, 95% CI: −0.11,

[3]The pattern of results was the same for each model when using “constructive memory support strategies” as the predictor and “nonconstructive memory support strategies” as the predictor, mirroring the main models with average total memory support as a continuous predictor (see Supplement Table 2 for indirect effects). The pattern was also the same when using treatment condition as the predictor, such that CT+Memory Support was associated with higher adherence, which in turn was associated with higher utilization/competency, and sequentially, with lower depression/impairment (see Supplement Table 3 for indirect effects) Further, although indirect effects did not reach significance likely due to the reduction in power, the pattern of results held when serial mediation models were analyzed in just the CT+Memory Support condition (see Supplement Table 4 for paths and indirect effects). Together, these results corroborate findings from the present study.

−0.01), and 12FU (indirect effect: −0.10, 95% CI: −0.21, −0.02). Looking at the specific paths generated by each of these models (see Table 4), more memory support predicted higher adherence. Higher adherence predicted greater competency, which in turn, predicted lower impairment at each timepoint.

Discussion

The present study evaluated whether memory support strategies predict improved patient outcomes—namely, depression severity and overall impairment—via serially predicting higher (a) patient adherence throughout treatment and (b) utilization and competency of treatment skills. Findings offered support for these hypothesized, serial mediators at post-treatment, six-months follow-up, and 12-month follow-up. Together, the results suggest that enhancing existing evidence-based psychological treatments to systematically include more memory support (e.g., through the Memory Support Intervention) may represent a route to improve pantreatment mechanisms (i.e., adherence and utilization/competency of treatment skills) and patient outcomes.

These findings build on prior research that has found support for relationships between memory for treatment, patient adherence, utilization and competency of treatment skills, and patient outcomes. Although this prior research had established support for each individual link of the serial mediation models evaluated in the present study (e.g., Dong et al., 2017a, 2017b; Gallagher-Thompson et al., 2008; Gumport et al., 2019; Hundt et al., 2013; Strunk et al., 2014), the present study is the first, to our knowledge, to test the serial mechanistic chains linking these variables. This contribution is important, as identifying mechanisms has been highlighted as a critical step to improve treatments (Insel, 2015). Indeed, as articulated by Kazdin (2009, p. 418): “If we know how changes come about, perhaps we can identify better, different, or more strategies that trigger critical change processes… Arming practitioners with evidence-based treatments is a valuable advance, but it would be even better if we could convey what facets are critical to include.” Applying this to the present study, the critical strategies and change processes to convey to practitioners may include memory support strategies, patient adherence to treatment, and utilization and competency of treatment skills, which collectively and sequentially appear to predict better patient outcomes.

Additionally, these findings are relevant to two major goals that are commonly articulated in the field of clinical science. First, many evidence-based psychological treatments seek to empower patients by imparting a personalized ‘toolbox’ of skills that patients can continue using long after treatment ends (e.g., Linehan et al., 2015; Manber et al., 2014; Resick et al., 2014). The hope is that, with this toolbox of skills, patients can “tak[e] over as therapist” by recognizing and managing symptoms, thereby preventing relapse and promoting long-term recovery (Resick et al., 2014, p. 190). Second, adherence has been pinpointed as a key obstacle to patient recovery and is robustly associated with patient outcomes (e.g., Glenn et al., 2013; Leeuwerik et al., 2019). Due to this robust link between adherence and outcomes, the World Health Organization and NIMH have called for interventions to promote adherence (National Institute of Health, 2021; World Health Organization, 2003). Encouragingly, memory support strategies appear to be effective vehicles to help health care

providers simultaneously achieve these two goals, which may ultimately improve long-term patient outcomes.

Notably, in the present study, the Memory Support Intervention was applied to CT. However, as seen in Table 1, the memory support strategies themselves are not directly tied to CT. Instead, they are based on approaches from the cognitive psychology and education literature on learning and memory (Harvey et al., 2014). Thus, theoretically, the Memory Support Intervention could be added to support a range of evidence-based psychological treatments. Testing whether the Memory Support Intervention sequentially predicts improved patient adherence, utilization and competency of treatment skills, and outcomes when added to other psychosocial approaches is an exciting direction for future research.

The present study should be considered in light of several limitations. First, as noted above, the Memory Support Intervention was derived to be “transdiagnostic” (relevant to a broad range of mental disorders) and “pantreatment” (relevant to a broad range of types of treatment). However, the present study was limited to CT for major depressive disorder. Whether these findings generalize to other patient groups and treatments remains to be tested. Second, the sample was predominantly White and not Hispanic or Latino. The extent to which the findings generalize to other racial and ethnic groups represents an important direction for future research. Third, assessments in the present study included measures that were observer-rated, therapist-rated, and patient-rated. This may have introduced rater effects, particularly as some evidence suggests that health care providers may overestimate patient adherence (Gearing et al., 2014; World Health Organization, 2003). Thus, it is possible that variance across raters may have partially accounted for the findings. Replicating and extending the present results with objective and behavioral measures—ideally coded by the same group of assessors—may be important. Fourth, although PROCESS has many advantages, including published syntax for serial mediation models with covariates (Hayes, 2018), a limitation is that it uses listwise deletion to handle missing data, which can lead to underpowered or biased estimates. Fifth, although the Utilization Scale demonstrated good to excellent internal consistency in the present study, the factor structure of this measure has not been evaluated. The extent to which items on this scale share variance and predict outcomes reflect exciting directions for future research. Sixth, individuals who were pregnant or breastfeeding were not included in the parent trial (Dong et al., 2022), and thus were not included in the present analyses, despite the need to establish effective, acceptable, and evidence-based treatments for these individuals (e.g., O’Mahen et al., 2012). Accordingly, future trials of CT+Memory Support should strongly consider including this important subpopulation. Seventh, although several steps were taken to prevent contamination between therapists across conditions (e.g., randomizing therapists to only one condition, conducting separate supervision sessions), it is possible that some contamination may have occurred during the shared monthly master class. The master class focused on delivery of CT, not memory support. However, therapists may have unwittingly discussed or asked questions related to memory support, thus exposing therapists in the CT-as-usual condition to these strategies. Eighth, the present study focused on average memory support per session as the predictor, and these findings were similar using (a) constructive and nonconstructive strategies as the predictor, (b) treatment condition as the

predictor, and (c) just participants in the CT+Memory Support (see Supplement Tables 2, 3, and 4). Although the findings reflect important first steps toward evaluating serial mechanisms of the relation between memory support and improved outcomes, we recognize that focusing on average memory support may oversimplify the story. Exciting next steps include evaluating which combinations of strategies most effectively trigger this cascade of serial mediators. Ninth, the effect size ranged from 8.57% to 50.00%, suggesting that the serial mediators explained a substantial amount of the total effects. However, other factors not directly tested in the present study (e.g., treatment recall) likely played an important role as well. Finally, prior evidence suggests that patient adherence predicts utilization and competency of treatment skills (e.g., Carroll et al., 2005; Ros et al., 2015; Stokes et al., 2015). That said, it is possible that more utilization and competency in treatment skills may also predict higher therapist ratings of patient adherence. Unfortunately, this alternative could not be investigated in the present study, due to the temporal ordering of assessments, but it reflects an interesting possibility for future research.

In conclusion, we have presented evidence that use of memory support strategies predicts improved patient outcomes indirectly through sequentially predicting higher patient adherence as well as utilization and competency of treatment skills. These effects were observed at post-treatment, six months after treatment, and 12 months after treatment, suggesting that memory support strategies may boost important mediators to improve patient outcomes over the long-term. Testing whether these findings transfer to other evidence-based psychological treatments and mental health diagnoses represents a promising next step for future research.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Memory Support Strategies

Type of Memory Support	Description	Examples: Therapist Use of Memory Support
Constructive	Go beyond information already presented by therapists; ask patients to do something *new* with the treatment materials.	*See below for examples of specific constructive strategies*
Application	Apply skills, concepts, or strategies to past, present, or future situations.	*"Can you think of a time when you could have used this skill last week?"* *"When could you envision using this skill during the upcoming week?"*
Evaluation	Identify pros and cons of skills, concepts, or strategies OR compare new perspectives/skills to old perspectives/skills.	*"What are 2 pros and 2 cons of challenging negative thoughts?"* *"How does your current perspective on negative thoughts compare to your perspective when you started treatment?"*
Categorization	Group skills, concepts, or strategies into similar themes. Must include at least 2 items.	*"What are 3 examples of negative automatic thoughts, and 3 examples of core beliefs?"* *"Consider the skills you've learned: which would you say are related to 'behaviors' and which would you say are related to 'thoughts'?"*
Cue-Based Reminder	Develop a cue to prompt the patient to use any skills, concepts, or strategies. Cue can be external (e.g., alarm) or internal (e.g., physiological sensation).	*"I'll help you set an alarm to remind you when you practice this skill."* *"What feeling might trigger you to remember to use this skill?"*
Hypothetical example of constructive memory support (i.e., cue-based reminder) in proposed mediation model: In session, a therapist helps their patient set up an alarm to conduct a behavioral experiment. When the alarm goes off, the patient conducts the behavioral experiment, thereby adhering to the treatment recommendations. This adherence equips the patient to continue utilizing behavioral experiments in the future, even after treatment has ended, contributing to less depression and overall impairment that is sustained over time.		
Nonconstructive	Focus only on reinforcing information that is already presented during treatment, without generating new content	*See below for examples of specific nonconstructive strategies*
Attention Recruitment	Draw attention to treatment skills, concepts, or strategies. Can include: expressive language, multimedia, humor, analogies, catch phrases, in-session exercises, note taking.	*"Let's take 10 deep breaths to get present in this session."* *"Here's a pen and paper for you to take notes."*
Repetition	Therapist repeats or restates skills, concepts, or strategies.	*"Let me say that again…"* *"I'll define core beliefs in a different way now…"*
Practice Remembering	Ask the patient to recall, restate, or summarize skills, concepts, or strategies.	*"What are the main ideas you've taken from today's session?"* *"Without looking, can you define negative automatic thoughts and core beliefs, in your own words?"*
Praise Recall	Verbally praising the patient for correctly remembering or implementing skills, concepts, or strategies.	*"Great job remembering that point from last session!"* *"Wow, wonderful work challenging that negative automatic thought!"*
Example of nonconstructive memory support (i.e., practice remembering) in proposed mediation model: After teaching each treatment skill, a therapist asks their patient to describe it in their own words, without looking at the treatment materials. Because of these "pop quizzes" (i.e., practice remembering), the patient remembers the skills between sessions. As a result, they are better able to follow treatment recommendations (i.e., more adherent) and to use the skills even after treatment ends, leading to less depression and overall impairment.		

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Table 2.

Participant Characteristics and Average Memory Support by Condition

Patient Characteristic and Memory Support	CT-as-usual (*n* = 91)		CT + Memory Support (*n* = 87)	
	M* or *n	**% or *SD***	***M* or *n***	**% or *SD***
Sex Assigned at Birth				
Female	50	55.56	62	71.26
Male	39	43.33	25	28.74
Prefer not to answer	1	1.11	0	0.00
Ethnicity				
Hispanic or Latino	14	15.38	16	18.39
Not Hispanic or Latino	74	81.32	70	80.46
Race				
American Indian/Alaska Native	0	0.00	1	1.15
Native Hawaiian/Pacific Islander	1	1.10	0	0.00
Asian	12	13.19	15	17.24
African American	1	1.10	5	5.74
White	53	58.24	54	62.07
Bi-racial/Multi-racial	23	25.27	11	12.64
Decline to answer/other	1	1.10	1	1.15
Employed				
Full-time	36	39.56	29	33.33
Part-time	27	29.67	16	18.39
Unemployed	19	20.88	24	27.59
Retired	5	5.49	8	9.20
Declined to state/ other	4	4.40	10	11.49
Age (years)	38.57	15.14	37.26	16.35
Education (years)	16.01	4.27	15.72	5.82
Average Memory Support				
Total Memory Support Amount	8.13	2.98	16.54	5.48
Memory Support Number of Types	3.85	0.83	5.44	0.71

Note. CT = cognitive therapy. M = mean. SD = standard deviation.

Table 3.

Aim 2: Indirect Effects of Adherence and Utilization on Relationships between Memory Support and Outcome at POST, 6FU, and 12FU

	coefficient	SE	*t*	*p*	95% Confidence Interval of effect	%MP
Aim 1 Model 1: MS → Average TARS → Utilization POST → IDS-SR POST						
Path a	0.42	0.12	3.38	**< 0.001**	**0.17, 0.67**	-
Path d	0.22	0.07	3.09	**0.002**	**0.08, 0.36**	-
Path b	−0.43	0.10	−4.35	**< 0.001**	**−0.63, −0.24**	-
Total effect	−0.25	0.14	−1.75	0.08	−0.53, 0.03	-
Indirect effect	−0.04	0.02	-	-	**−0.08, −0.01**	16.00%
Aim 1 Model 2: MS → Average TARS → Utilization 6FU → IDS-SR 6FU						
Path a	0.53	0.13	4.10	**< 0.001**	**0.27, 0.78**	-
Path d	0.18	0.08	2.38	**0.02**	**0.03, 0.34**	-
Path b	−0.33	0.08	−4.04	**< 0.001**	**−0.50, −0.17**	-
Total effect	−0.35	0.13	−2.61	**0.01**	**−0.62, −0.09**	-
Indirect effect	−0.03	0.02	-	-	**−0.07, −0.01**	8.57%
Aim 1 Model 3: MS → Average TARS → Utilization 12FU → IDS-SR 12FU						
Path a	0.48	0.14	3.40	**< 0.001**	**0.20, 0.76**	-
Path d	0.20	0.08	2.55	**0.01**	**0.05, 0.35**	-
Path b	−0.54	0.08	−6.45	**< 0.001**	**−0.71, −0.38**	-
Total effect	−0.14	0.16	−0.89	0.38	−0.45, 0.17	
Indirect effect	−0.05	0.03	-	-	**−0.11, −0.01**	35.71%
Aim 1 Model 4: MS → Average TARS → Utilization POST → WHODAS POST						
Path a	0.42	0.12	3.39	**< 0.001**	**0.18, 0.67**	-
Path d	0.24	0.07	3.32	**0.001**	**0.10, 0.38**	-
Path b	−0.71	0.14	−5.16	**< 0.001**	**−0.99, −0.44**	-
Total effect	−0.16	0.20	−0.77	0.44	−0.55, 0.24	-
Indirect effect	−0.07	0.03	-	-	**−0.14, −0.02**	43.75%
Aim 1 Model 5: MS → Average TARS → Utilization 6FU → WHODAS 6FU						
Path a	0.52	0.13	4.05	**< 0.001**	**0.27, 0.78**	-
Path d	0.19	0.08	2.50	**0.01**	**0.04, 0.35**	-
Path b	−0.37	0.12	−3.01	**0.003**	**−0.61, −0.13**	-

	coefficient	SE	*t*	*p*	95% Confidence Interval of effect	%MP
Total effect	−0.22	0.21	−1.05	0.30	−0.63, 0.19	-
Indirect effect	−0.04	0.02	-	-	**−0.09, −0.004**	18.18%
Aim 1 Model 6: MS → Average TARS → Utilization 12FU → WHODAS 12FU						
Path a	0.49	0.14	3.55	< **0.001**	**0.22, 0.77**	-
Path d	0.20	0.08	2.53	**0.01**	**0.04, 0.35**	-
Path b	−0.74	0.12	−6.07	< **0.001**	**−0.98, −0.50**	-
Total effect	−0.15	0.22	−0.66	0.51	−0.59, 0.29	-
Indirect effect	−0.07	0.03	-	-	**−0.15, −0.01**	46.67%

Note. Significant effects are highlighted in bold. Confidence intervals that do not contain zero indicate a significant effect. "-" = value is not generated by model. %MP = mediation proportion (i.e., the proportion of the total effect that is explained by the indirect effect expressed as a percentage). MS = average total memory support. TARS = Therapist Adherence Rating Scale. IDS-SR = Inventory of Depressive Symptomatology, Self-Report. POST = post-treatment assessment. 6FU = six-month follow-up assessment. 12FU = 12-month follow-up assessment. WHODAS = World Health Organization Disability Assessment Schedule 2.0. Path a = path from the independent variable to Mediator 1 (i.e., average memory support --> adherence). Path d = path from the Mediator 1 to Mediator 2 (i.e., adherence --> utilization or competency). Path b = path from the Mediator 2 to the outcome (utilization or competency --> depression severity or overall impairment). All models controlled for pre-treatment levels of the relevant outcome (i.e., depression severity or overall impairment).

Table 4.

Aim 2: Indirect Effects of Adherence and Competency on Relationships between Memory Support and Outcome at POST, 6FU, and 12FU

	coefficient	SE	*t*	*p*	95% Confidence Interval of effect	%MP
Aim 2 Model 1: MS → Average TARS → Competency POST → IDS-SR POST						
Path a	0.43	0.13	3.37	**< 0.001**	**0.18, 0.68**	-
Path d	0.64	0.23	2.80	**0.01**	**0.19, 1.09**	-
Path b	−0.17	0.03	−6.26	**< 0.001**	**−0.23, −0.12**	-
Total effect	−0.25	0.14	−1.78	0.08	−5.65, 13.16	-
Indirect effect	−0.05	0.02	-	-	**−0.09, −0.01**	20.00%
Aim 2 Model 2: MS → Average TARS → Competency 6FU → IDS-SR 6FU						
Path a	0.53	0.13	4.05	**< 0.001**	**0.27, 0.79**	-
Path d	0.67	0.24	2.76	**0.01**	**0.19, 1.15**	-
Path b	−0.12	0.02	−5.19	**< 0.001**	**−0.17, −0.08**	-
Total effect	−0.38	0.13	−2.87	**0.005**	**−0.65, −0.12**	-
Indirect effect	−0.04	0.02	-	-	**−0.09, −0.01**	10.53%
Aim 2 Model 3: MS → Average TARS 12FU → Competency 12FU → IDS-SR 12FU						
Path a	0.53	0.15	3.63	**< 0.001**	**0.24, 0.83**	-
Path d	0.70	0.24	2.95	**0.004**	**0.23, 1.17**	-
Path b	−0.19	0.03	−7.11	**< 0.001**	**−0.24, −0.13**	-
Total effect	−0.17	0.13	−1.09	0.28	−0.49, 0.14	-
Indirect effect	−0.07	0.03	-	-	**−0.15, −0.02**	41.18%
Aim 2 Model 4: MS → Average TARS → Competency POST → WHODAS POST						
Path a	0.42	0.12	4.41	**< 0.001**	**0.18, 0.66**	-
Path d	0.65	0.24	2.73	**0.01**	**0.18, 1.12**	-
Path b	−0.27	0.04	−7.11	**< 0.001**	**−0.35, −0.20**	-
Total effect	−0.14	0.20	−0.73	0.47	−0.54, 0.25	-
Indirect effect	−0.07	0.03	-	-	**−0.15, −0.02**	50.00%
Aim 2 Model 5: MS → Average TARS → Competency 6FU → WHODAS 6FU						
Path a	0.52	0.13	3.88	**< 0.001**	**0.26, 0.78**	-
Path d	0.68	0.24	2.86	**0.005**	**0.21, 1.15**	-
Path b	−0.13	0.04	−3.64	**< 0.001**	**−0.20, −0.06**	-

	coefficient	SE	*t*	*p*	95% Confidence Interval of effect	%MP
Total effect	−0.23	0.20	−1.15	0.25	−0.62, 0.16	-
Indirect effect	−0.05	0.03	-	-	**−0.11, −0.01**	21.74%
Aim 2 Model 6: MS → Average TARS → Competency 12FU → WHODAS 12FU						
Path a	0.53	0.14	3.72	**< 0.001**	**0.25, 0.82**	-
Path d	0.71	0.24	2.99	**0.003**	**0.24, 1.18**	-
Path b	−0.25	0.04	−6.69	**< 0.001**	**−0.33, −0.18**	-
Total effect	−0.23	0.23	−1.00	0.32	−0.69, 0.23	-
Indirect effect	−0.10	0.05	-	-	**−0.21, −0.02**	43.48%

Note. Significant effects are highlighted in bold. Confidence intervals that do not contain zero indicate a significant effect. "-" = value is not generated by model. %MP = mediation proportion (i.e., the proportion of the total effect that is explained by the indirect effect expressed as a percentage). MS = average total memory support. TARS = Therapist Adherence Rating Scale. IDS-SR = Inventory of Depressive Symptomatology, Self-Report. POST = post-treatment assessment. 6FU = six-month follow-up assessment. 12FU = 12-month follow-up assessment. WHODAS = World Health Organization Disability Assessment Schedule 2.0. Path a = path from the independent variable to Mediator 1 (i.e., average memory support --> adherence). Path d = path from the Mediator 1 to Mediator 2 (i.e., adherence --> utilization or competency). Path b = path from the Mediator 2 to the outcome (utilization or competency --> depression severity or overall impairment). All models controlled for pre-treatment levels of the relevant outcome (i.e., depression severity or overall impairment).