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Cognitive Outcomes Following Psychotherapeutic Interventions for Major Depression in Older Adults with Executive Dysfunction

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Abstract

Objective—The purpose of this study was to determine the impact of psychotherapy on cognitive functioning in older adults with late life depression (LLD) and executive dysfunction.

Method—221 adults aged 60 years and older participated in a randomized clinical trial comparing the efficacy of Problem Solving Therapy (PST) and Supportive Therapy (ST) for LLD. Cognitive performance on 7 tests of executive functioning, verbal learning, and memory was evaluated at baseline, after 12 weeks of treatment, and at 24 weeks following the completion of treatment.

Results—Performance on a measure of executive functioning with a significant information processing speed component (Stroop Color Word test; SCWT) improved following treatment, $F(1, 312) = 8.50$, $p = .002$ and improved performance was associated with a reduction in depressive symptoms but not treatment type. Performance on other measures of executive functioning, verbal learning, and memory did not change significantly following 12 weeks of psychotherapy treatment.

Conclusions—Our results suggest that improvements in cognitive functioning following psychotherapy treatment for depression in older adults with executive dysfunction are likely focal and not distributed across all cognitive domains. Although previous analyses reported that PST

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was superior to ST in the treatment of depression, this analysis indicated no difference between the two treatments with regard to improvements in cognitive functioning.

Keywords

cognitive functioning; psychotherapy; late life depression; mild cognitive impairment; memory; executive dysfunction; learning; information processing speed

INTRODUCTION

Late life depression (LLD) is a disabling illness associated with significant economic and societal costs (1) and cognitive dysfunction represents a concurrent and debilitating aspect of this disorder. Mild cognitive impairments have consistently been documented in up to 60% of individuals with LLD (2, 3, 4, 5) and these cognitive impairments contribute to increased mental healthcare costs (6), disability (7), and poor treatment outcomes (8). Executive dysfunction and information processing speed deficits are often considered to be hallmark cognitive features of LLD (2, 9); however impairments of memory and verbal learning are also frequently reported (2, 10, 11). Given the heterogeneity of cognitive impairments exhibited by individuals with LLD, differentiating the direct impact of LLD on cognition from the effects of other concurrent conditions, such as neurodegenerative disease, represents a significant challenge in older adults. One underutilized avenue to clarify this relationship is the evaluation of cognitive functioning following treatment for depression.

Both antidepressant medication treatments and psychotherapeutic interventions have been shown to be effective in treating LLD mood symptoms (12, 13) but their impact on cognition has not been evaluated sufficiently. Despite the efficacy of treatments, few studies have been conducted to evaluate cognitive outcomes following treatment using standardized neuropsychological measures and these studies have focused exclusively outcomes following antidepressant medication treatments (14–19). This existing literature largely suggests that positive antidepressant treatment response is associated with relatively focal improvements on measures of executive functioning with a significant information processing speed component (14, 17–19), while memory and verbal learning performance typically remain unchanged (14, 17). However, these findings are not always consistent and some previous studies have also found that antidepressant medication treatments are associated with improved verbal learning and memory performance (16), widely distributed improvements across several cognitive domains (11), or no significant changes in cognition across any cognitive domain (15). Further, non-response to antidepressant medication treatments has been linked to decreases in verbal learning performance (19) and short memory performance (18), with these decrements attributed in part to anti-cholinergic antidepressant effects.

The efficacy of psychotherapeutic interventions for the treatment of LLD are well recognized (20–25) and recently have been shown to be effective in reducing depressive symptoms (12) and disability (26) in older adults with executive dysfunction. However, to date, there have been no studies published that have investigated the impact of psychotherapy on cognitive outcomes in older adults as has been done with antidepressant

medication investigations. There are a number of advantages to studying the impact of psychotherapy on cognitive functions in this context. First, such an investigation may clarify if changes in cognitive functioning following treatment are similar across treatment modalities and are primarily a function of improvement in depressive symptoms. Second, psychotherapies, particularly those that provide cognitive skill building, may provide a compensatory framework for cognitive deficits associated with late-life depression and as a result, improve cognitive functioning. Third, there are no known anti-cholinergic effects of psychotherapy treatments which have been associated with worsening of cognitive functioning in previous medication studies.

The present study was a secondary data analysis of archived data from a randomized clinical trial of evidence-based psychotherapy for LLD (12) which utilized Problem Solving Therapy (PST)(27) in comparison to a psychotherapy control condition, Supportive Therapy (ST)(28). The present study was conducted in order to evaluate the impact of psychotherapeutic treatment for depression on memory, learning, and executive functioning for older adults. Based on the existing literature evaluating cognitive functioning following antidepressant treatment (14, 17–19), we hypothesized that : 1) measures of executive functioning with a significant information processing speed component would show improvement following treatment of depression, 2) these cognitive improvements would be associated with improvements in depression severity over time, 3) performance on measures of memory, verbal learning, and tests of executive functioning without an information processing speed component would not show significant improvement, and 4) there would not be significant worsening of cognitive performance across any cognitive domain following 12 weeks of treatment which has been previously shown in antidepressant studies due to a lack of anticholinergic effect in psychotherapy interventions. Additionally, in our original study, we found that PST was superior to ST in improving depression and disability outcomes. Therefore, we also explored if PST treatment was associated with greater cognitive improvement following treatment.

METHOD

Participants

Data for this study were obtained from a two-site, randomized controlled trial comparing a modified version of Problem Solving Therapy (PST) to Supportive Therapy (ST) in 221 patients ages 60 and over with major depression and executive dysfunction (12). Participants were recruited for participation in this study by community advertisements and referrals from psychiatry clinics at each study site. All participants provided informed consent to participate in the study and all study procedures were approved by a committee for human research institutional review board at each site.

Psychiatric diagnoses were made by licensed psychologists utilizing DSM-IV criteria and the Structured Clinical Interview for the Diagnosis of DSM-IV Disorders and were reviewed at a consensus conference comprised of psychologists, psychiatrists, and social workers. Depression severity at intake was evaluated with the Hamilton Depression Rating Scale (HDRS) (29) and participants with moderate to severe depression severity (HDRS score of ≥20) were included in the study. Inclusion criteria with regard to cognitive functioning were

based on screening performance on the Initiation/Perseveration index of the Mattis Dementia Rating Scale (DRS-IP; score ≤25) and the Stroop Word Color Test (SCWT; score ≤ 33) (12). Exclusion criteria consisted of current psychotherapy or antidepressant treatments, presence of psychotic depression (SCID-R), high suicide risk (i.e., intent or plan to attempt suicide in near future), any Axis I psychiatric disorder other than unipolar major depression (DSM-IV), history of head trauma, dementia (MMSE<24 or diagnosis of dementia by DSM-IV), acute or severe medical illness, drugs known to cause depression (e.g., reserpine, alpha-methyl-dopa, steroids), and inability to perform any activities of daily living even with assistance.

Of the 653 participants referred to the study, 183 were determined to be ineligible through an initial telephone screen because they were not depressed (n=136) or they declined to participate (n=47). The remaining 470 underwent a structured interview, which led to exclusion of 191 individuals: 40 did not meet criteria for MDD; 96 did not exhibit evidence of executive dysfunction, 42 had another psychiatric diagnosis, and 13 declined to participate. Of the 279 who were eligible for the study, 58 (21%) were not randomized because they failed to complete baseline evaluation and did not return for further assessment or treatment. Of the 221 randomized, antidepressant-free participants, 110 were assigned to the PST arm and 111 to the ST arm.

Measures

All measures of depression severity and cognitive functioning were obtained for each participant during a single assessment at each evaluation time point (baseline, week 12, week 36) by trained research staff and research staff were blinded to treatment type. The specific measures utilized and outcome variables for each of these measures are described below. Additionally, demographic information (age, years of education, ethnicity, gender) was obtained for each participant.

VERBAL LEARNING AND MEMORY

Hopkins Verbal Learning Test - Revised (HVLT-R) (30)

The HVLT-R is a measure of verbal learning and memory for lists of verbally presented information. The outcome variable utilized for verbal learning performance was the total number of correct responses on the three learning trials of this test (HVLT-L). The outcome variable utilized to evaluate memory (HVLT-M) was the total number of correct responses on the delayed free recall trial of this test.

EXECUTIVE FUNCTIONING

Mattis Dementia Rating Scale-2 Initiation/Perseveration Scale (DRS IP) (31)

The DRS-IP is a measure of executive functioning for older adults with an information processing speed component; the total number of correct responses was utilized as the primary outcome variable.

Wisconsin Card Sorting Test-64 Computer Version 2 (WCST-64) (32)

The WCST is a non-speeded measure of problem solving ability, cognitive flexibility, and ability to maintain a cognitive set; the outcome variable was the total number of correct responses.

The Stroop Color and Word Test (SCWT) (33)

The SCWT is a timed measure of response inhibition, ability to maintain cognitive set, and information processing speed; the total number of correct responses on the 45-second color word trial was utilized as the outcome variable.

Trail Making Test Part A & B (TMT) (34)

Part A of the TMT is a timed measure of sequencing ability and visuomotor speed. Part B of the TMT is a timed measure of sequencing ability, visuomotor speed, and response inhibition. The time required to complete both trials was utilized as the outcome variables for this test.

SEVERITY OF SYMPTOMS OF DEPRESSION

Hamilton Depression Rating Scale (29)

The HDRS is a 24-item instrument utilized to assess severity of depressive symptoms; high scores indicate greater severity of depression.

Procedures

Two psychotherapeutic interventions were utilized in this study, Problem Solving Therapy (PST) and Supportive Psychotherapy (ST). PST consisted of 12 weekly sessions to teach participants a five-step problem-solving model taught over the first five weeks of treatment (12, 35). Subsequent sessions are utilized to refining participants' PST skills. Using PST, participants set treatment goals, discuss and evaluate different ways to reach goals, create action plans, and evaluate the plans' effectiveness in reaching goals. Participants are expected to implement plans and apply the problem-solving model to additional problems between sessions. In the last two PST sessions, participants create a relapse prevention plan using the PST model.

ST is a manualized therapy (Sachs, unpublished manuscript, 2000) consisting of 12 weekly individual sessions. ST focuses on the non-specific elements of psychotherapy (warmth, empathy, support) without any active ingredients found in evidence based therapies such as PST(36, 37). ST therapists create a comfortable, non-judgmental environment by demonstrating genuineness, empathy, and acceptance of patients without imposing any judgments on their decisions. Participants receiving ST meet once a week with a study therapist and are encouraged to discuss their depression and any contributing life events. Therapists do not engage in any therapeutic strategy other than active listening and offering support focusing on participants' problems and concerns.

Four PhD-level clinical psychologists and four licensed social workers served as therapists across the two sites for this study. To evaluate treatment adherence and quality all sessions

were audiotaped and 20% of audiotapes were randomly rated by independent experts in both treatments to ensure treatment fidelity (12). Average therapist ratings for both treatments were excellent and ranged between excellent and exceptional. No differences in quality ratings were observed for any therapist for either treatment

Data Analysis

To study the course of cognitive functioning following psychotherapy treatment a series of repeated-measures mixed-effects models with random intercept terms of the cognitive function measures were estimated and tested. Covariates in the models included depression severity (time-dependent HDRS scores), treatment condition (PST vs. ST), treatment site (Cornell vs. UCSF), time (12 and 36 weeks), and demographic variables (age, years of education, ethnicity, gender). Interactions of depression severity with treatment group and treatment group with time were also tested. Linear regression models were used to model factors associated with cognitive outcomes for cognitive tests that changed significantly over the evaluation period and colinearity thresholds were also considered. Analyses were conducted using SAS (version 9.2, SAS Institute, Cary NC).

RESULTS

The mean age for the sample was 73.1 years (SD=7.8), the mean years of education was 15.4 (SD=2.8), the mean MMSE score was 27.8 (SD=1.7), and 65% of the sample was female. There were no significant differences in demographic or baseline clinical variables among participants assigned to the PST and ST arms. Of the 221 randomized participants, 91% remained in the treatment trial. Five percent dropped out prior to week four of treatment; 4% dropped out after week four. Six percent completed the treatment trial but did not complete the 12-week assessment and 24% did not complete the week 36 assessment. Not all participants completed all measures at each assessment. There were no differences in attrition between the two interventions and the psychotherapeutic interventions were effective in reducing depressive symptom severity across both treatment types ($F=47.7$, $df=1, 204$, $p <.000$). Further, there were no differences in baseline cognitive function for individuals who discontinued study participation prior to the 36 week evaluation and those who participated in all three cognitive evaluations. At baseline cognitive tests were modestly correlated with correlation coefficients ranging from 0.11 to 0.38. Colinearity diagnostics suggested no evidence of shared variance that would preclude including all variables in the regression model.

Prior to treatment the mean HDRS score for the sample was 24.0 (SD=4.4), following 12 weeks of psychotherapy the mean HDRS score for the sample was 14.4 (SD=8.0) and 24 weeks after psychotherapy interventions were completed the mean HDRS score for the sample was 13.2 (SD=7.2). Cognitive performance for the sample at baseline, week 12, and week 36 is shown in Table 1. In a mixed effects model only the SCWT outcome (Table 2) showed significant change (improvement) relative to baseline performance ($F=8.50$, $df=1, 312$, $p = 0.002$; $d = 0.49$). This improvement in SCWT performance was associated with reductions in depressive symptom severity (HDRS; $F=8.51$, $df = 1, 312$, $p = 0.004$). Gender effects were not significant in this model.

With regard to our exploratory hypothesis regarding PST and ST differences, we did not find a statistically significant time by treatment difference between the groups. Finally treatment site, depression and time by treatment (PST vs. ST) interactions, and other demographic variables did not significantly contribute to SCWT variance over time.

DISCUSSION

To our knowledge, this is the first study to evaluate cognitive functioning after psychotherapy for depression in older adults. There are three primary results for this study: 1) We found improvements on a measure of executive function with a significant information processing speed component following treatment and improvement on this measure was associated with decreased depressive symptom severity, 2) Performance on other cognitive tests, including measures of verbal learning, memory, and other tests executive functioning did not change significantly following psychotherapeutic intervention for LLD, and 3) We did not observe declines in cognitive functioning following psychotherapy intervention on any cognitive tests. Additionally, our results did not suggest that specific treatment type (PST, ST) significantly influenced cognitive outcomes at follow up.

Our finding that performance on the SCWT improved following psychotherapy is consistent with previous studies suggesting that this measure is particularly sensitive to changes in cognition associated with LLD (38, 39). As such, it is not surprising that performance on the SCWT improved following treatment. Of note, SCWT performance improved 23% following treatment relative to baseline performance and that these improvements were significantly associated with reduced depression severity in our sample. These findings are also consistent with previous studies documenting improvement in this cognitive domain with antidepressant treatments for LLD (14, 17–19). However, unlike our previous findings that demonstrated a significant advantage to PST over ST with regard to depression and disability outcomes (12, 26), we did not see any effect of treatment type on SCWT improvement. As such, our results suggest that reduction in depressive symptoms may represent a more salient contributor to improvements in cognitive function than the type of treatment utilized, however further research in this area is necessary.

A lack of improvement in our sample on other measures of executive functioning with an information processing speed component, the TMT B, and to a lesser extent the DRS-IP, following treatment was also unexpected. Like the SCWT, poor performance on the TMT B and DRS-IP is often reported in LLD (2), yet information processing speed is only relevant on some portions of the DRS-IP and as a result this measure may have been less sensitive to change in our sample. Similarly, the TMT B also has a significant psychomotor component, in addition to information processing speed, which could impact the sensitivity of this measure as an index of information processing speed and explain a lack of significant improvement on these measures following treatment in our sample. As has been demonstrated in antidepressant trials (14, 17), our results also demonstrated that performance on other measures of executive functioning without information processing speed requirements (WCST), and measures of verbal learning (HVLT-L) and memory (HVLT-M) did not improve significantly following psychotherapy for late life depression.

Given findings of impaired performance on these tests in other LLD sampless (2, 10, 11), our results would suggest that cognitive dysfunction in these domains may be more strongly related to other etiologies in older adults, such as neurodegenerative disease (40, 41), which would not be expected to change following depression treatment.

As expected, we also did not see any significant worsening in cognitive performance in any of the cognitive domains that we assessed. In conjunction with previous studies that have reported worsening of memory and verbal learning performance for participants taking antidepressant medications who do not respond to treatment (18, 19), our findings suggest that psychotherapy may be a good alternative for patients who are at particular risk for anticholinergic side effects. Also of interest, we did not see any practice effects, i.e., improvements on cognitive tests associated with prior test experience, on any of the cognitive measures that we administered. This lack of practice effect in our sample is noteworthy and could also potentially reflect a generalized detrimental effect of depression on cognition, specifically learning associated with test demands. However our study was not designed specifically to evaluate the impact of LLD on practice effects and did not include a non-depressed comparison group.

Overall, our findings indicate that cognitive dysfunction in LLD is likely multi-factorial, with acute and potentially reversible cognitive symptoms being most apparent with respect to tasks requiring rapid processing of information. In contrast, cognitive dysfunction in other domains, such as memory or verbal learning, may be the result of brain abnormalities that predispose some older adults to experience depression (41), and are therefore less likely to remit following treatment despite reductions in depression severity. Therefore, the efficacy of interventions for LLD, and in particular psychotherapeutic interventions, may be improved if accommodations in treatment are made for both remitting and non-remitting forms of cognitive dysfunction during treatment (42). Further, the addition of psychoeducational components of treatment designed to educate patients and their families regarding the potential for experiencing cognitive symptoms (either improvement or persistent impairment) following successful treatment of LLD could result in more accurate expectations for post-treatment functioning.

Our study has several strengths, including a thorough diagnostic evaluation of depression and evaluation of cognitive functioning over 36 weeks for individuals participating in a controlled psychotherapy treatment study. Yet our results should also be interpreted in recognition of some limitations. First, and perhaps most importantly, to be eligible for this study participants were required to show evidence of executive dysfunction on the SCWT or DRS IP prior to initiating treatment. As such, our ability to generalize our results to the larger population is limited. Similarly, by design, we did not compare the cognitive performance of our sample to normative data and as such we cannot conclude that our sample demonstrated clinically significant cognitive deficits in any of the cognitive domains we assessed. Further we did not collect cognitive assessment data from a non-depressed comparison group, so we cannot determine if the cognitive improvements we reported represented clinically significant improvements. Also, as most participants showed improvement in depression severity, our ability to detect an association between worsening depression and cognitive function was limited. Additionally, the mean level of education of

our sample was higher than in most community based samples and some participants dropped out of the study prior to treatment which further limits our ability to generalize our results to the larger population.

Conclusions

Our results suggest that improvements in cognitive functioning following psychotherapy treatment for depression in older adults is limited to performance on measures of executive functioning with a significant information processing speed component. These findings support conceptualizations of cognitive dysfunction in LLD as being multi-factorial and have implications for both the treatment of LLD and the cognitive symptoms that are frequently concurrent with this disorder.

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Table 1

Depression Severity and Cognitive Performance for Individuals with Late Life Depression Over 36 weeks (n=221)

	Baseline		**Week 12**		**Week 36**		**Test**	***p***
	n	**M (SD)**	**n**	**M (SD)**	**n**	**M (SD)**		
HDRS	221	24.0 (4.4)	192	14.4 (8.0)	160	13.2 (7.2)	F(2,571) = 47.7	**<0.001**
MMSE	218	27.8 (1.7)	19	27.9 (2.0)	158	27.0 (4.9)	F(2,355) = 1.8	0.140
SCWT	217	22.0 (8.2)	181	26.8 (11.3)	150	27.4 (10.9)	F(2,546) = 16.7	**<0.001**
DRS IP	218	32.2 (3.7)	189	32.7 (6.1)	159	32.6 (7.2)	F(2,565) = 0.4	0.707
WCST	163	36.0 (11.4)	131	38.1 (11.2)	117	37.1 (11.9)	F(2, 411) = 0.8	0.482
TMT A	213	55.8 (31.4)	179	54.0 (30.6)	136	56.6 (35.6)	F(2,542) = 0.3	0.742
TMT B	190	137.6 (63.5)	158	130.3 (66.7)	136	127.7 (63.0)	F(2,483) = 1.1	0.347
HVLT L	210	21.2 (5.6)	186	21.4 (5.8)	155	22.3 (5.9)	F(2,550) = 2.0	0.135
HVLT M	209	7.0 (3.4)	186	7.2 (2.9)	155	7.9 (8.1)	F(2,549) = 1.5	0.235

HDRS=Hamilton Depression Rating Scale, MMSE=Mini Mental State Exam, SCWT=Stroop Color Word Test, DRS-IP=Dementia Rating Scale –Initiation/Perseveration, WCST=Wisconsin Card Sort Test, TMT =Trail Making Test, HVLT-L =Hopkins Verbal Learning Test-Learning, HVLT-M=Hopkins Verbal Learning Test Memory

Note: F statistics and p values correspond to the main effect of time on measures of cognitive function

Table 2

Mixed Effects Regression Model for Stroop Color Word Test Performance (n=221)

Effect	Num DF	Den DF	F Value	P-value
HDRS	1	312	8.51	**0.004**
Treatment type	1	203	0.00	1.00
HDRS * Treatment type	1	312	1.70	0.193
Site	1	203	0.85	0.359
Week	1	312	8.50	**0.002**
Week * Treatment type	1	312	3.25	0.072
Age	1	202	2.12	0.147
Gender	1	202	3.81	**0.052**
Education	1	202	0.96	0.329
Ethnicity	1	202	0.05	0.829

HDRS=Hamilton Depression Rating Scale total score; Treatment type=Problem Solving Therapy or Supportive Psychotherapy; Week = Weeks from baseline evaluation; Age = Age in years; Education = years of education