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A Randomized Controlled Trial of Cognitive Remediation and Work Therapy in the Early Phase of Substance Use Disorder Recovery for Older Veterans: Neurocognitive and Substance Use Outcomes

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Objective: Cognitive remediation therapy (CRT) is reported to improve neurocognitive and substance use disorder (SUD) outcomes in residential treatments. This National Institute of Drug Abuse funded pilot study reports on CRT as an augmentation to outpatient treatment for SUD. ***Method:*** Recovering outpatient veterans were randomized into CRT + Work Therapy ($n = 24$) or work therapy ($n = 24$) with treatment-as-usual. Blind assessments of neurocognition and substance use were performed at baseline, 3 months (end of treatment), and 6-month follow-up. ***Results:*** Baseline assessments revealed high rates of cognitive impairment with 87.5% showing significant decline from premorbid IQ on at least 1 measure (median = 3/14 measures). Adherence to treatment was excellent. Follow-up rates were 95.7% at 3 months and 87.5% at 6 months. Mixed effects models of cognitive change over time revealed significant differences favoring CRT + Work Therapy on working memory (WM) and executive function indices. Global index of cognition showed a nonsignificant trend (effect size [ES] = .37) favoring CRT + Work Therapy. SUD outcomes were excellent for both conditions. CRT + Work Therapy had a mean of 97% days of abstinence at 3 months, 94% in the 30 days prior to 6-month follow-up, and 24/26 weeks of total abstinence; differences between conditions were not significant. ***Conclusions and Implications for Practice:*** CRT was well accepted by outpatient veterans with SUDs and led to significant improvements in WM and executive functions beyond that of normal cognitive recovery. No difference between conditions was found for SUD outcomes, perhaps because work therapy obscured the benefits of CRT.

Keywords: substance use disorders, alcohol use disorder, cognitive remediation, work therapy, neurocognition

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Substantial cognitive impairment is associated with substance use disorders (SUDs; Schrimsher, Parker, & Burke, 2007; Vocci, 2008) and becomes worse with years of use and the aging process. One possible avenue for improving SUD treatment outcomes may be to address neurocognitive impairments especially common in the early phase of recovery but often persisting over years (Bernardin, Maheut-Bosser, & Paille, 2014) that interfere with the acquisition of new learning (e.g., attention and memory) and with better decision making (executive functioning). Indeed, SUD related brain defects and associated cognitive impairments may contribute to the progression of SUDs by affecting the individual's ability to benefit from treatment (Blume, Schmaling, & Marlatt, 2005) and by impairing their daily community functioning, which, in turn, increases stress and subsequent relapse (Blume & Marlatt, 2009; Bowden, Crews, Bates, Fals-Stewart, & Ambrose, 2001). Recent research has suggested that Cognitive remediation therapy (CRT) may improve attention, memory, and executive function in schizophrenia and related disorders (Anaya et al., 2012; McGurk, Twamley, Sitzer, McHugo, & Mueser, 2007; Wykes, Huddy, Cellard, McGurk, & Czobor, 2011), and there is evidence that these improvements are, in turn, associated with better skill acquisition in structured groups (Silverstein et al., 2009). Many SUD treatments also require skill acquisition such as learning new ways of coping with craving, learning better methods for tolerating distress, being able to integrate feedback, and finding more constructive problem-solving strategies; therefore, improving attention, WM, and executive functioning could allow service recipients to get more out of these treatments.

There is a small amount of research to suggest that a CRT intervention could improve neurocognition for individuals with SUDs. In a landmark study, CRT was integrated into the context of a residential treatment, and service recipients receiving CRT had better SUD outcomes (Fals-Stewart & Lam, 2010; Grohman & Fals-Stewart, 2003). However, it is a major limitation of that research that the CRT was administered in the context of long-term

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residential treatment settings (Fals-Stewart & Schafer, 1992). The only other published study of CRT for any SUD, also found significant improvement in neurocognition, well-being, and compulsive craving, but it was limited to alcohol use disorder (AUD) service recipients and was within the context of an inpatient treatment unit (Rupp, Kemmler, Kurz, Hinterhuber, & Fleischhacker, 2012). These residential and inpatient studies provided CRT in a context that ensured that participation in the interventions could be tightly controlled and monitored. There were also other nonspecific but stimulating activities such as a work-focused daily routine in the residential treatment that may have combined synergistically with the cognitive treatment. Although promising, these findings provide only limited support for CRT as a possible augmentation to SUD treatment and may not generalize to outpatient treatments.

In a Proof of Concept study sponsored by Department of Veterans Affairs Mental Illness Research, Education and Clinical Center (MIRECC) at Department of Veterans Affairs Connecticut Healthcare System (principal investigator [PI]: Morris D. Bell), CRT was offered to an outpatient SUD sample participating in a Department of Veterans Affairs 21-day SUD day treatment program. However, results did not support the feasibility of CRT in that setting. While nearly two thirds of participants in the cognitive training condition participated to some extent and most said that they enjoyed it, the mean number of training sessions was only 9 and only two participants completed training. This poor adherence was despite the fact that participants were compensated $3.00 per hour of CRT. These individuals appeared to be too preoccupied with finding a job and stable housing to commit to CRT training. They scattered geographically and more than half never attended their first outpatient treatment appointment. Clearly, the CRT was not powerful enough to overcome the problems with treatment adherence. However, we did learn a great deal about the cognitive status of the participants in the early phase of substance abuse recovery. Neuropsychological assessment from this MIRECC Proof of Concept study with substance-abusing veterans in day treatment ($N = 74$; $M_{age} = 48.2$ (8.3), 60% non-White), indicated substantial cognitive impairment in multiple domains. We also found in that study, that when we compared current cognitive performance to a measure of premorbid IQ, 37% of participants had experienced a clinically meaningful decline (1 *SD*) from premorbid estimates. Moreover, they reported twice as many cognitive complaints on a self-report assessment as compared to a non-SUD control group (Richardson-Vejlgaard, Dawes, Heaton, & Bell, 2009). Thus, this sample of service recipients in the early phase of substance abuse recovery underwent a cognitive decline and experienced a felt need for improving their cognition if an intervention could be provided in a context that made sense for them.

In 2010, the National Institute on Drug Abuse was sufficiently encouraged by CRT findings as well as by the large neuroscience literature on the effects of SUD's on cognition to issue an Request for Applications (RFA) entitled "Cognitive Remediation Approaches to Improve Drug Abuse Treatment Outcomes." Our group (PI: Morris D. Bell) was awarded an R21 pilot grant under this mechanism with the specific aims of testing feasibility and acceptability of CRT for outpatients with SUDs and to determine ESs on neurocognitive and substance abuse outcomes.

Since our proof of concept study suggested that the outpatient SUD day program was not a good treatment context for this study, we chose instead to include an outpatient Department of Veterans Affairs work therapy program for both arms of the study. We did so because we had previous research demonstrating the effectiveness of this combination on cognitive and functional outcomes among individuals experiencing psychotic symptoms (Bell, Bryson, Greig, Fiszdon, & Wexler, 2005; Bell, Fiszdon, Bryson, & Wexler, 2004; Bell, Fiszdon, Greig, Wexler, & Bryson, 2007; Bell, Zito, Greig, & Wexler, 2008; Wexler & Bell, 2005) and because we had 35 years of clinical experience showing that substance abusing veterans show good adherence to work therapy. Work therapy would also serve as an active control condition lending equipoise to the study. CRT + Work Therapy was the active intervention compared with work therapy in the R21 (Cognitive Training and Work Therapy in the Initial Phase of Substance Abuse Treatment; PI: Morris D. Bell) that was funded through the National Institute on Drug Abuse program announcement mentioned above. The aims of the pilot study were to determine whether such a study was feasible in terms of participation in the intervention and follow-up assessments and to test the hypotheses that participants in the CRT + Work Therapy would show significantly greater improvements in neurocognitive functioning and SUD outcomes than those who received work therapy. Examination of possible differences between AUD participants and other SUD participants was a secondary aim. This report presents the results of that pilot study.

Method

Participants: United States veterans 18 years of age and older (Table 1) were recruited for a randomized clinical trial of cognitive training and work therapy (NCT 01410110) by referral from clinicians at a Department of Veterans Affairs substance abuse program, including a 21-day substance abuse day program. Recruitment began in January 2011 and was completed in March 2014. Eighty-seven participants were assessed for eligibility and consented. Eligibility for the study required that the individual have an SUD chart diagnosis confirmed by the Mini International Neuropsychiatric Interview and Addiction Severity Index (see below) and be within the first 30 days of sobriety or abstinence at time of recruitment. Baseline assessments occurred shortly afterward with an average length of abstinence of 40.15 (65.10) days. Neurocognitive baseline assessments were not performed until the participant had at least one week of sobriety or abstinence. Exclusion criteria included untreated psychotic disorder, benzodiazepines (which can interfere in cognitive training), a legal case that might lead to incarceration, a living arrangement that would interfere with participation, and the presence of a developmental disability or medical illness that might significantly compromise cognition or prevent work activity. Ten did not meet inclusion criteria, six declined to complete the intake, and 23 were excluded for other reasons such as moving away or participating in other vocational programs that were not part of the study. Forty-eight participants were included in the study. Twenty-nine participants primarily abused alcohol, 14 primarily abused either opiates or cocaine, and the remaining five participants were

Table 1
Background Characteristics[a]

Arm/group title	Cognitive training + Work therapy (n = 24)	Work therapy only (n = 24)	Total (n = 48)
Age years mean (*SD*)	51.3 (9.7)	53.8 (7.4)	52.55 (8.55)
Gender, male/female			
Female	2	1	3
Male	22	23	45
Ethnicity			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	24	24	48
Race			
American Indian or Alaska Native	0	3	3
Black or African American	11	13	24
White	13	7	20
More than one race	0	1	1
Other		3	3
Marital status			
Married	3	6	9
Never married	5	8	13
Divorced/widowed	16	10	26
Axis 1 primary diagnosis			
Alcohol use disorder	13	15	28
Cocaine	3	7	10
Opioids	6	0	6
Other	2	2	4
Education years mean (*SD*)	13.2 (1.6)	12.21 (1.5)	12.71 (1.55)
Felony convictions			
Yes	11	12	23
No	13	12	25
Disability (SSDI or Veterans Administration Service connected)			
Yes	2	3	5
No	22	21	43
GAF mean (*SD*)	45.17 (3.6)	47.67 (5.9)	46.42 (4.75)

Note. SSDI = Social Security Disability Insurance; GAF = Global Assessment of Functioning.
[a] No significant differences between conditions.

polysubstance abusers that had more than one primary drug of abuse in addition to alcohol.

Measures

The Mini International Neuropsychiatric Interview is a short diagnostic structured interview used to diagnose different types of Axis I psychiatric disorders using the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.; American Psychiatric Association, 1994) criteria, as well as suicidality and antisocial personality disorder. The interviewer asks the participants a series of yes or no questions to determine the presence of a disorder (Sheehan et al., 1998).

The Addiction Severity Index is used to determine the extent to which alcohol and drug abuse has affected the participant's life. There are seven different aspects of everyday life: medical, employment, alcohol, drug, legal, family/social, and psychiatric problems. Frequency of use of alcohol and drugs of abuse are recorded for the prior 30 days and throughout the lifetime of the participants (McLellan, Luborsky, Woody, & O'Brien, 1980).

The Wechsler Test of Adult Reading is a neuropsychological assessment used as a baseline test of intelligence. In the test, the examiner asks the participant to pronounce 50 irregularly spelled words. Each of these words does not follow grammatical rules, and thus cannot be sounded out. The test is discontinued following 12 consecutive incorrect pronunciations of words or until all 50 words are sounded out. This is a standard test of verbal ability and commonly used as a premorbid IQ estimate because this ability is usually preserved despite cognitive decline and correlates highly with lengthier measures of IQ (Holdnack, 2001).

Neurocognitive assessment. Index scores for five domains of cognitive function used the following assessments: Attention was measured by Continuous Performance Test-Identical Pairs (d' T score; Cornblatt, Risch, Faris, Friedman, & Erlenmeyer-Kimling, 1988) and Trails A (time T score; Reitan & Wolfson, 1985). Processing speed was measured using Wechsler Adult Intelligence Scale (WAIS)-III Digit Symbol Coding and Symbol Search (T scores; Wechsler, 1997). WM was assessed with WAIS-III Digit Span (T score; Wechsler, 1997) and Wechsler Memory Scale-III Spatial Span (T score Wechsler, 1987). Visual and verbal learning and memory was assessed using Hopkins Verbal Learning Test (Total score T score; Brandt, 1991) and Brief Visual Motor Test (Total score T score; Benedict, 1997). And executive function was measured using Wisconsin Card Sorting Task (Perseverative Error and Conceptual Level T scores; Heaton, 1981) and Neuropsychological Assessment Battery Mazes (T score; Stern & White,

2005). Where available, different versions of tasks (e.g., Hopkins Verbal Learning Test, Neuropsychological Assessment Battery Mazes) were used at different observation points.

Substance use assessment. At baseline and at each of the 13 weeks of active intervention, participants were asked about how many substances they used and the frequency of use during the preceding week using standard Time Line Followback (TFLB; Robinson, Sobell, Sobell, & Leo, 2014) procedures. They were also administered Breathalyzer assessment and a urine toxicology screen each week. At 6-month follow-up, the Addiction Severity Index was used to determine substance use in the prior 30 days and a substance abuse calendar and TFLB was used to determine intensity and frequency of use for the preceding 3-month period. Medical record clinician notes and lab reports of toxicology screens were also reviewed for any evidence of substance use. There were no examples where medical record reports were denied by participants.

Procedures

Recruitment, informed consent, and randomization. Potential participants were referred by clinicians. After an initial phone screening, they were invited for informed consent procedures. Following a complete discussion of the study, written informed consent was obtained in accordance with the procedures of the Department of Veterans Affairs Connecticut Health Care System Institutional Review Board which approved and monitored this study. After informed consent, baseline assessments were obtained and those that met all inclusion and exclusion criteria were randomized according to a randomization scheme based on blocks of six that was performed by a statistician not otherwise associated with the study. Block randomization assured approximately equal distribution to the two arms of the study. No attempt was made to stratify by type of primary diagnosis or any other variable, but type of SUD was similarly distributed between the two conditions of the study, and there were no differences in baseline characteristics between conditions (see Table 1).

Assessment procedures. Forty-eight participants were assessed on a battery of neurocognitive tests at baseline, 3 months (end of active treatment), and 6-month follow-up. They were not administered baseline assessments if they used substances in the previous 7 days in order to insure that baseline assessments were not influenced by proximal substance use or intoxication. Assessments were postponed until this criterion was met. Substance use diagnosis at baseline was determined based upon chart review, Mini International Neuropsychiatric Interview structure interview, and the Addiction Severity Index. Assessments were scored using standard scoring procedures and *T* scores were based on age-corrected norms. Index scores were created by averaging *T* scores of testing measures included in the index.

Interventions. CRT was completed using auditory and visual Posit Science software. At that time, Posit Science offered two separate but complete suites of training software on CDs, one called Brain Fitness (auditory) and the other Insight (visual). Training games began with the most elementary sensory processing tasks (i.e., auditory or visual sweeps) and progressed through a preset curriculum of more and more complex and demanding games. For example, the most difficult auditory memory task involved recalling details from audio-presented stories that increased memory load by becoming progressively longer and more complicated as the person's performance improved. Participants in the CRT + Work Therapy condition were offered cognitive training for 5 hr/week for 13 weeks. In addition to the cognitive training, they also participated in work therapy for up to 15 hr/week doing entry-level duties at medical center job sites supervised by regular medical center staff. Work therapy is a transitional work program, which is distinct from Compensated Work Therapy in the Department of Veterans Affairs system because it is part-time and is paid at a rate that cannot exceed half minimum wage. It is unrelated to supported employment. They also participated in group sessions for 30 min/week to receive support and encouragement and discuss issues in the workplace.

Participants in the work therapy only condition could work up to 20 hr/week of work therapy as well as participate in the same weekly group sessions as those in CRT + Work Therapy. Participants in the work therapy condition did not participate in any cognitive training.

Participants received payment of half federal minimum wage (according to Department of Veterans Affairs regulations) for their hours of productivity whether in CRT + Work Therapy or work therapy. Offering 20 hr/week of work therapy in the work therapy only active control condition created equipoise between conditions in terms of the number of hours of compensated productive activity offered to participants. They also received a modest payment for the time and inconvenience of attending follow-up assessments.

All participants were allowed to continue with whatever Department of Veterans Affairs substance abuse treatment, medical care, or psychosocial programs were in their treatment plan prior to study inclusion. Services available included supported housing, community reintegration programs, primary care clinics, specialized medical care, and outpatient mental health and substance abuse counseling. None of these participants were engaged in intensive case management services or other programs that were time intensive because of their involvement in 20 hr/week of activity through their research interventions.

Analyses

Mixed effects, or multilevel analyses were conducted using the MIXED procedure in SPSS, which accounts for the interdependence in multiple repeated measures within the same individual. Models were estimated using restricted maximum likelihood estimation, which can appropriately model data even if subjects have some missing values. Thus we were able to retain the entire intent-to-treat sample in our analyses, even though some individuals were missing one or more follow-up assessments. Random effects were included for both the intercept and change over time, and were fixed to zero in reported analyses if significant variance was not found in initial analyses. Models tested whether there was a difference between the two groups at baseline (condition), whether there was significant change in each outcome in the six months after baseline (time), and whether there was an interaction between the two (Condition × Time). For each model, the treatment condition variable was effects coded 0 for the work therapy condition and

1 for the CRT + Work Therapy condition. Time was centered on the baseline visit and scaled so that one unit change represents the passage of 3 months. Thus, the intercept of these models represents the average value of the outcome at baseline for the work therapy condition group, the CRT + Work Therapy coefficient represents the difference between the CRT + Work Therapy and the work therapy group baseline scores, the time coefficient reflects the average rate of change per 3 months for the work therapy condition, and the Condition × Time coefficient tests whether the CRT + Work Therapy change slope is significantly different from the work therapy change slope. Analyses were run separately for each outcome: WM, executive function, visual/verbal learning, processing speed, attention, and the global index. The processing speed and attention measures were collected at three time points (baseline, 3 months, and 6-month follow-up), and other outcomes had an additional measurement at 1.5 months after baseline. A global score that average all measures was included to determine the overall effect-size change between conditions on neurocognitive function. Analyses related to SUD outcomes used *t*-tests for between-groups comparisons for continuous variables related to days and weeks of sobriety.

Results

Study Feasibility and Adherence to Treatment

Participation in both conditions was excellent. CRT + Work Therapy participants averaged 41.2 (*SD* = 20.8) hr of cognitive training and 190.9 (*SD* = 173.7) hr of work therapy for a total of 232.2 (*SD* = 179.7) hr of productive activity. They also attended an average of 10.5 (*SD* = 3.0) out of 13 possible group sessions. Work therapy only participants averaged 252.9 (*SD* = 112.4) hr of work therapy and 10.7 (*SD* = 3.0) group sessions. There were no statistically significant differences between conditions on total hours of productive activity or number of groups attended. Follow-up rates were also very good, with 44 out of 48 (95.7%) completing 3-month follow-up and 42 out of 48 (87.5%) completing 6-month follow-up (see Consort flow chart, Figure 1).

Baseline Cognitive Impairment

Our analysis of baseline neurocognitive assessments revealed much higher baseline rates of cognitive impairment than in our MIRECC proof of concept study, with 87.5% showing a clinically

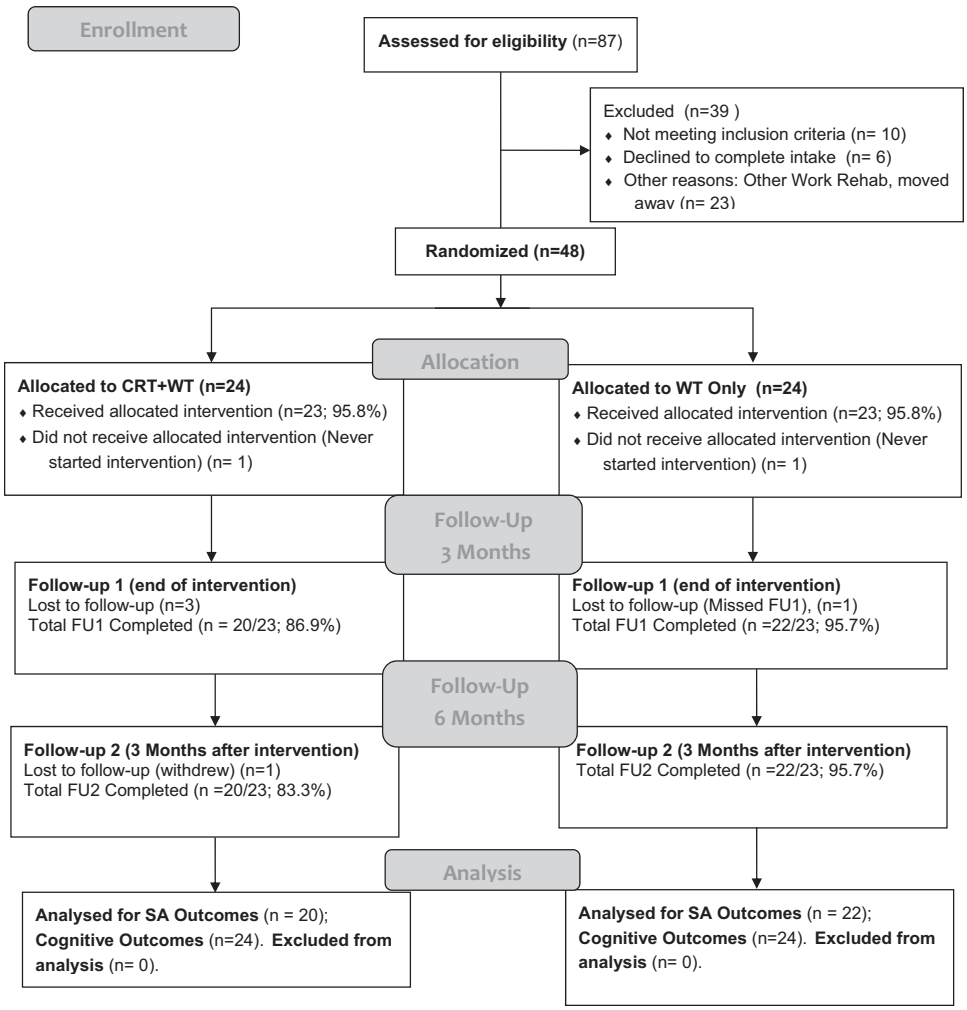

Figure 1. Consort flow chart. CRT = cognitive remediation therapy; WT= work therapy.

meaningful decline (1 *SD*) from a measure of their premorbid IQ on at least one cognitive measure. Moreover, 77.1% showed decline on two measures or more and the median was three measures out of 14 possible measures showing such a decline. The highest rates of significant cognitive decline and impairment were on measures of verbal (50%) and nonverbal (45.8%) learning and memory with measures of executive function (41.7%) and WM (37.5%) commonly deteriorated.

Neurocognitive Outcomes

WM results indicated that there was no random variance in the time slope for WM, so this parameter was fixed in order to draw correct inferences from a more parsimonious and properly specified model. Results indicated that there was no difference between the two groups in terms of baseline WM. The work therapy group showed no significant change in WM. Results showed a significantly higher rate of change in WM for the CRT + Work Therapy group as compared with the work therapy group ($p < .01$; Table 2). ES for the Condition × Time effect was calculated using recommendations made by Rosnow and Rosenthal (1988). The ES for the Working Memory Condition × Time interaction was in the moderate range, Cohen's $d = .66$. Follow-up simple slopes analyses confirmed that WM scores significantly increased for the CRT + Work Therapy group compared with the work therapy group (1.65, $t_{68} = 2.70$, $p < .01$). WM changes during the 6-month treatment and follow-up period for each condition are presented in Figure 1.

Executive function results showed a trend-level difference between groups on executive functioning at baseline, with the CRT + Work Therapy group having slightly higher baseline executive functioning than the work therapy group alone. The work therapy group showed no significant increase in executive function as the study progressed. The CRT + Work Therapy group, by contrast, had a significantly higher rate of change than the work therapy group ($p < .05$; Table 2). Follow-up simple slopes analyses confirmed that the rate of increase in executive function for the CRT + Work Therapy was statistically significant, 2.47, $t_{40} = 4.37$, $p < .001$. The ES for the Time × Group effect for the executive function index was of moderate strength, Cohen's $d = .68$. Executive function change during the 3-month treatment and follow-up period for each condition are presented in Figure 2.

Visual/verbal learning results showed a difference between groups on the visual/verbal learning index at baseline, with the CRT + Work Therapy group having significantly higher baseline scores than the work therapy group alone. The work therapy group showed no significant increase in visual/verbal learning as the study progressed. The CRT + Work Therapy group's rate of change was not statistically different from the work therapy group's rate of change in visual/verbal learning (see Table 2).

Attention results showed a difference between groups on the attention index at baseline, with the CRT + Work Therapy group having significantly higher baseline scores than the work therapy group alone. The Work Therapy group showed no significant increase in attention as the study progressed. The CRT + Work Therapy group's rate of change was not statistically different from the work therapy group's rate of change in attention (see Table 2).

Processing speed results showed a trend-level difference between groups in processing speed at baseline, with the CRT + Work Therapy group having slightly higher baseline scores than the work therapy group alone. The work therapy group showed no significant increase in processing speed as the study progressed. The CRT + Work Therapy group's rate of change was not statistically different from the work therapy group's rate of change in processing speed (see Table 2).

The global neurocognitive index results showed a trend-level difference between groups at baseline with the CRT + Work Therapy group having slightly higher baseline scores than the work therapy group. The global index improved significantly (time, $p = .002$; Table 2) regardless of groups as the study progressed. The CRT + Work Therapy group's rate of change showed a trend-level difference that did not achieve statistical significance from the work therapy group's rate of change (Condition × Time, $p = .16$; Table 2), although the ES was within the medium range, Cohen's $d = .36$. A postpriori subanalysis of Condition × Time effect using participants with AUD ($n = 28$) revealed a larger ES of Cohen's $d = .71$.[1]

Substance use outcomes. Using all sources of information including the TLFB procedure, breathalyzer and toxicology screens, and chart note review, CRT + Work Therapy had a mean of 87.3 (7.8) days of abstinence (percent days of abstinence = 97%) in the first 90 days, and 28.2 (9.4) days of abstinence in the 30 days (percent days of abstinence = 94%) prior to 6-month follow-up. They also averaged 23.8 (2.8) weeks of abstinence out of 26 weeks (91.5%). Work therapy had very similar SUD outcomes with a mean of 84.6 (18.2) days of abstinence (percent days of abstinence = 87%) in the first 90 days, and 28.6 (6.0) days of abstinence in the 30 days (percent days of abstinence = 94%) prior to 6 month follow-up. They also averaged 24.0 (3.3) weeks of abstinence out of 26 weeks (92.3%). There were no significant differences between condition, $t(40) = .61$, $p = .72$; $t(40 = -1.03$, $p = .16$; $t(39) = .87$, $p = .81$, respectively).

Discussion

The first aim of this study was to determine the feasibility of an outpatient study of cognitive remediation for an SUD sample in terms of treatment adherence and follow-up rates. This study proved to be highly feasible with remarkable adherence to treatment in both arms of the study and follow-up rates seldom seen in this population. The best explanation for this outcome is most likely because of the special context of providing CRT within an outpatient work therapy program along with the Department of Veterans Affairs usual outpatient SUD and rehabilitation services. Work therapy was highly valued by the participants and almost all completed the 13 weeks of work therapy. But even after work therapy was over, most (87.5%) still agreed to come in 3 months later for the 6-month follow-up assessment, suggesting that their commitment to the study went beyond the value of work therapy. It may be that these participants were a self-selected sample because they were willing to engage in work therapy rather than seek other employment and that their involvement in work therapy increased their engagement in Department of Veterans Affairs services more generally, which then had a favorable effect upon their study participation. They were also incentivized to participate

[1] Supplementary figures showing additional neurocognitive results are available on-line.

Table 2
Model Coefficients and Associated Standard Errors Testing the Impact of CRT + Work Therapy Versus Work Therapy Cognitive Outcomes

	Working memory		Executive function		Visual verbal learning		Attention		Processing speed		Global cognitive index	
Variable	Estimate *(SE)*	*p*	Estimate *(SE)*	*p*	Estimate *(SE)*	*p*	Estimate *(SE)*	*p*	Estimate *(SE)*	*p*	Estimate *(SE)*	*p*
Intercept	42.80 (1.67)	<.001	46.09 (1.47)	<.001	35.06 (1.91)	<.001	42.55 (1.62)	<.001	45.49 (1.74)	<.001	42.93 (1.38)	<.001
Condition	2.75 (2.35)	.247	3.65 (2.07)	.085	5.61 (2.69)	.042	5.18 (2.29)	.028	4.28 (2.46)	.088	4.25 (2.00)	.040
Time	−.67 (.58)	.253	.52 (.63)	.412	1.33 (.86)	.131	.89 (.64)	.172	.82 (.58)	.164	1.15 (.36)	.002
Condition × Time	2.33 (.85)	.008	1.96 (.92)	.039	−.84 (1.24)	.503	.16 (.94)	.864	−.37 (.84)	.665	.09 (.52)	.164

Note. CRT = cognitive remediation therapy. Condition had a value of 1 for CRT + Work Therapy and a value of 0 for Work Therapy. A 1-unit change in time reflected the passage of 3 months.

in both CRT and work therapy with hourly compensation, but similar compensation had been offered in the proof of concept study, which did not have good adherence. We therefore believe that future studies of this kind might also be feasible in a Department of Veterans Affairs sample.

Rates of clinically meaningful cognitive decline from premorbid assessment at baseline for this sample were much greater than what had been found in our MIRECC proof of concept study described in the introduction, perhaps because participants were a little older and willing to be in work therapy. Almost all had at least one deficit of 1 *SD* or greater from their premorbid IQ estimate, and the median number of deficits was 3. These findings add to the significance of addressing cognitive impairment in a sample of older veterans with SUDs. Moreover, the most common areas of impairment were in verbal and visual learning and memory, verbal and visual WM, and executive function. These findings add justification to focusing our cognitive training on learning, memory, and executive function, cognitive functions necessary to benefit from recovery-oriented treatment and to remain abstinent (Teichner, Horner, Roitzsch, Herron, & Thevos, 2002; Wölwer, Burtscheidt, Redner, Schwarz, & Gaebel, 2001).

Neurocognitive outcomes were analyzed by creating five composite indices: visual and verbal working memory, visual and verbal learning, processing speed, attention, and executive function. Mixed effects model for three points in time (baseline, 3-month, and 6-month follow-up) revealed significant time effects on all indices and significant differences (Condition × Time) favoring CRT + Work Therapy on the executive function index and on the visual and verbal working memory index. All index trends favored the CRT + Work Therapy condition, and a global index composite score showed a nonsignificant trend with a moderate ES of Cohen's $d = .36$. Moreover, a post hoc analysis found a greater global composite score ES of .76 for those with AUD, in part because they had a much better response on verbal learning, which was a significant finding within the AUD subsample (Bell, Vissichio, & Weinstein, 2016), suggesting that older veterans with AUD may benefit more from CRT. These cognitive outcomes are made all the more compelling because of the similarity between groups in overall participation and in SUD outcomes, so that improved cognitive outcomes were not mediated by greater abstinence or the nonspecific benefits of treatment engagement.

Regarding SUD outcomes, CRT + Work Therapy had a mean percent days of abstinence of 97% in the first 90 days, and a mean percent days of abstinence of 94% in the 30 days prior to 6-month follow-up. They also averaged 91.5% weeks of abstinence during the 26 weeks on the study. However, the work therapy only condition produced similarly impressive SUD outcomes, so there were no differences by condition at either 3-month or 6-month follow-up. These abstinence rates are higher than what is usually found in the literature. For example, the landmark naltrexone multisite study (Krystal et al., 2001) showed a 90-day percent days of abstinence of 72.3% for the naltrexone treatment group and 62.4% for the placebo group. The COMBINE study, the largest thus far conducted on pharmacological and behavioral treatments for AUD, reported 16-week percent days of abstinence between 81% and 75% across all conditions (Anton et al., 2003). A recent study of mindfulness based relapse prevention (MBRP; Bowen et al., 2014) for SUD participants reported a 90-day percent days of abstinence of 78% in their treatment-as-usual condition (TAU) and 84% in the MBRP condition. Their rate of abstinence for the 30 days prior to 6-months follow-up was percent days of abstinence of 33% for TAU and 67% for MBRP.

One possible explanation for the lack of group differences between CRT + Work Therapy and work therapy on SUD outcomes may be that Fals-Stewart and Lam (2010) had found that their better SUD outcomes for CRT was mediated by longer treatment participation in their residential program. They suggested that improved cognition may have made it possible for participants to get more out of their treatment and that they therefore stayed in treatment longer. In our study, our adherence was so good for both conditions that this mechanism of action was not a factor.

Results of this study suggest that cognitive training may be acceptable to older veterans with SUD in outpatient treatment and may lead to significant improvements in cognitive functioning beyond that of normal cognitive recovery, particularly for executive functioning and working memory. It may also be that participants with AUD are more responsive, possibly because of greater deficits. There are, however, a number of limitations to this pilot study. While the work therapy requirement certainly increased equipoise between conditions, it may have led to a selective sample of veterans who were willing to make such a commitment and were not planning to return to competitive employment right away. The work therapy control condition may also have been so powerful that it obscured the benefits of CRT. Working 20 hr/week may have nonspecific cognitive benefits because it

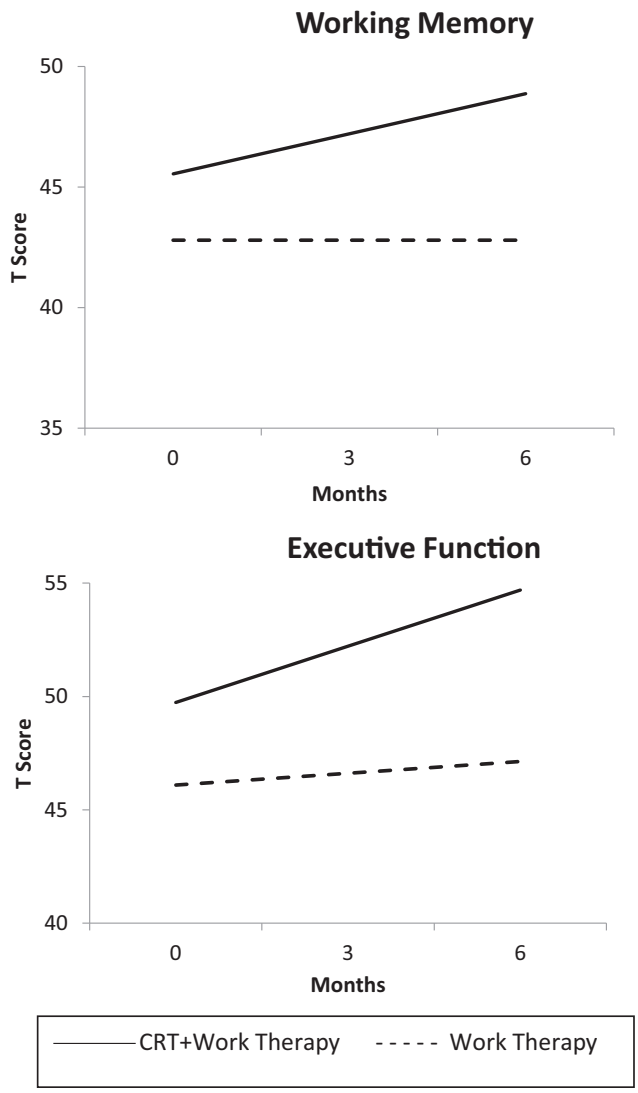

Figure 2. Executive functioning (EF) and Working memory (WM) improved significantly in the Cognitive Remediation Therapy (CRT) + Work therapy condition (solid lines) compared with the condition with work therapy (dashed lines). Follow-up simple slopes analyses showed that both inclines were statistically significant for the CRT + Work Therapy Condition, EF$\gamma = 2.47$, $SE = .67$, $p = .001$; WM$\gamma = 1.65$, $SE = 61$, $p = .008$. Neither slope was significant in the work therapy condition, however, EF$\gamma = .52$, $SE = .63$, $p = .412$; WM$\gamma = -.67$, $SE = .58$, $p = .253$.

increased physical activity, social engagement, and opportunities for problem solving. Thus, work therapy may have been a factor in improvement for both conditions. We therefore cannot know whether CRT without the benefits of work therapy will be as effective in this population in improving cognition. It may be that CRT works synergistically with activating interventions that provide nonspecific stimulation and opportunities to reinforce and generalize cognitive gains. While this pilot study provides some encouragement for including CRT in the treatment of SUDs, it must be recognized that generalization may be limited because this was an older sample, mostly of men with AUDs who were willing to engage in work therapy and other Department of Veterans Affairs services, and compensation was provided for participation. Further research is needed regarding its efficacy for individuals of younger age and women and whether it may have differential effects on participants with specific drugs of abuse.

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